PUBMED ID: 32982596
DOI: doi.org/10.1016/j.rpor.2020.08.010
Titolo: Hypofractionated radiation therapy with temozolomide versus standard chemoradiation in patients with glioblastoma multiforme (GBM): A prospective , single institution experience.
Autori: Rayan A., Abdel-Kareem S., Hasan H., Zahran AM., Gamal DA.
Data di Pubblicazione: 2020-09-28
Abstract: Our results showed that HFRT with concurrent TMZ is a feasible therapeutic approach in patients with GBM, especially those with poor prognostic factors, assuring high treatment compliance and low toxicity rates. Dose escalation and reduction in overall treatment time are clear advantages of HFRT, while at least the same survival rates as conventional fractionated RT are maintained.
Journal Title: Reports of practical oncology and radiotherapy : journal of Greatpoland Cancer Center in Poznan and Polish Society of Radiation Oncology

PUBMED ID: 32935821
DOI: doi.org/10.6061/clinics/2020/e1553
Titolo: Patterns of recurrence and outcomes of glioblastoma multiforme treated with chemoradiation and adjuvant temozolomide.
Autori: Faustino AC., Viani GA., Hamamura AC.
Data di Pubblicazione: 2020-09-16
Abstract: The median OS of Brazilian patients with GBM treated with RT and TMZ was satisfactory. Although TMZ therapy has become the standard of care for patients with newly diagnosed GBM, the recurrence rate is extremely high. Metronomic TMZ as salvage treatment improved survival in these patients.
Journal Title: Clinics (Sao Paulo, Brazil)

PUBMED ID: 32917486
DOI: doi.org/10.1016/j.clon.2020.08.011
Titolo: Prospective Longitudinal Assessment of Quality of Life and Activities of Daily Living as Patient-Reported Outcome Measures in Recurrent/Progressive Glioma Treated with High-dose Salvage Re-irradiation.
Autori: Maitre P., Gupta T., Maitre M., Goda J., Krishnatry R., Chatterjee A., Sridhar E., Sahay A., Mokal S., Moiyadi A., Shetty P., Patil V., Jalali R.
Data di Pubblicazione: 2020-09-12
Abstract: High-dose salvage re-irradiation in carefully selected patients with recurrent/progressive glioma is associated with stable QOL (preserved functional domains and reduced symptom burden) and improvement in ADL (greater functional independence) over time with encouraging survival outcomes.
Journal Title: Clinical oncology (Royal College of Radiologists (Great Britain))

PUBMED ID: 32913543
DOI: Mancante
Titolo: IL13RA2 is overexpressed in malignant gliomas and related to clinical outcome of patients.
Autori: Zeng J., Zhang J., Yang YZ., Wang F., Jiang H., Chen HD., Wu HY., Sai K., Hu WM.
Data di Pubblicazione: 2020-09-11
Abstract: IL13RA2 was high expression in some glioma subtypes, and significantly correlated with poor prognosis. Based on its role in CAR-T therapy, it might act as an extremely important and specific therapeutic target for human malignant gliomas, especially in IDH wild-type LGG, "IDH wild-type and TERT promoter mutated" GBM and H3K27M-mutated diffuse midline glioma, and improve the clinical outcomes of these patients.

Journal Title: American journal of translational research

PUBMED ID: 32883128
DOI: doi.org/10.1177/0300060520951395
Titolo: Anti-PD-1, anti-VEGF, and temozolomide therapy in a patient with rec urrent glioblastoma: a case report.
Autori: Chen C., Zuo W., Yang P., Zhang Y.
Data di Pubblicazione: 2020-09-05
Abstract: The experience of this complicated case indicates the possible app lication of immune checkpoint inhibitors, anti-angiogenesis agents, and cyto toxic reagents for recurrent glioblastoma. The administration of this three- agent regimen appears safe and effective. However, further clinical trials a re warranted.
Journal Title: The Journal of international medical research

PUBMED ID: 32859817
DOI: doi.org/10.4103/0028-3886.293441
Titolo: Risk Stratification in Low Grade Glioma: A Single Institutional Expe rience.
Autori: Keshri V., Deshpande RP., Chandrasekhar YBVK., Panigrahi M., Rao IS. , Babu PP.
Data di Pubblicazione: 2020-08-30
Abstract: Taken together, the clinical symptoms, expression of molecular mar kers and the prognosis details provided by our results can help for better m anagement of LGG cases. We further propose to use following five factors to accurately describe the prognosis and tumor recurrence: 1) Age >50 years, 2) tumor size >5 cm, 3) MIB index >5%, 4) KPS score < 70 and 5) gemistocytic pa thology.
Journal Title: Neurology India

PUBMED ID: 32847475
DOI: doi.org/10.1080/0284186X.2020.1778181
Titolo: Longitudinal study of cognitive function in glioma patients treated with modern radiotherapy techniques and standard chemotherapy.
Autori: Rydelius A., Lätt J., Kinhult S., Engelholm S., Van Westen D., Pihls gård M., Bengzon J., Sundgren PC., Lilja Å.
Data di Pubblicazione: 2020-08-28
Abstract: Taken together, the clinical symptoms, expression of molecular mar kers and the prognosis details provided by our results can help for better m anagement of LGG cases. We further propose to use following five factors to accurately describe the prognosis and tumor recurrence: 1) Age >50 years, 2) tumor size >5 cm, 3) MIB index >5%, 4) KPS score < 70 and 5) gemistocytic pa thology.
Journal Title: Acta oncologica (Stockholm, Sweden)

PUBMED ID: 32823939
DOI: doi.org/10.3390/cancers12082284
Titolo: Multi-Parametric Deep Learning Model for Prediction of Overall Survi val after Postoperative Concurrent Chemoradiotherapy in Glioblastoma Patient s.
Autori: Yoon HG., Cheon W., Jeong SW., Kim HS., Kim K., Nam H., Han Y., Lim DH.
Data di Pubblicazione: 2020-08-23
Abstract: This study aimed to investigate the performance of a deep learning -based survival-prediction model, which predicts the overall survival (OS) t ime of glioblastoma patients who have received surgery followed by concurren

t chemoradiotherapy (CCRT). The medical records of glioblastoma patients who had received surgery and CCRT between January 2011 and December 2017 were re trospectively reviewed. Based on our inclusion criteria, 118 patients were s elected and semi-randomly allocated to training and test datasets (3:1 ratio , respectively). A convolutional neural network-based deep learning model wa s trained with magnetic resonance imaging (MRI) data and clinical profiles t o predict OS. The MRI was reconstructed by using four pulse sequences (22 sl ices) and nine images were selected based on the longest slice of glioblasto ma by a physician for each pulse sequence. The clinical profiles consist of personal, genetic, and treatment factors. The concordance index (C-index) an d integrated area under the curve (iAUC) of the time-dependent area-under-th e-curve curves of each model were calculated to evaluate the performance of the survival-prediction models. The model that incorporated clinical and rad iomic features showed a higher C-index (0.768 (95% confidence interval (CI): 0.759, 0.776)) and iAUC (0.790 (95% CI: 0.783, 0.797)) than the model using clinical features alone (C-index = 0.693 (95% CI: 0.685, 0.701); iAUC = 0.72 3 (95% CI: 0.716, 0.731)) and the model using radiomic features alone (C-ind ex = 0.590 (95% CI: 0.579, 0.600); iAUC = 0.614 (95% CI: 0.607, 0.621)). The se improvements to the C-indexes and iAUCs were validated using the 1000-tim es bootstrapping method; all were statistically significant (
Journal Title: Cancers

PUBMED ID: 32817593
DOI: doi.org/10.1172/JCI140378
Titolo: Mass cytometry detects H3.3K27M-specific vaccine responses in diffus e midline glioma.
Autori: Mueller S., Taitt JM., Villanueva-Meyer JE., Bonner ER., Nejo T., Lu lla RR., Goldman S., Banerjee A., Chi SN., Whipple NS., Crawford JR., Gauvai n K., Nazemi KJ., Watchmaker PB., Almeida ND., Okada K., Salazar AM., Gilber t RD., Nazarian J., Molinaro AM., Butterfield LH., Prados MD., Okada H.
Data di Pubblicazione: 2020-08-21
Abstract: Administration of the H3.3K27M-specific vaccine is well tolerated. Patients with H3.3K27M-specific CD8+ immunological responses demonstrated pr olonged OS compared to non-responders.
Journal Title: The Journal of clinical investigation

PUBMED ID: 32811600
DOI: doi.org/10.29271/jcpsp.2020.07.713
Titolo: Prognostic Value of ABO Blood Groups in Patients with Glioblastoma M ultiforme.
Autori: Sokmen FC., Karacin C.
Data di Pubblicazione: 2020-08-20
Abstract: An association was detected among ABO blood groups and prognosis i n patients with GBM. It was observed that blood groups significantly affecte d survival and that median survival was significantly shorter in Non-O blood groups when compared blood group O. Key Words: Glioblastoma multiforme, ABO blood group, Prognosis, Survival.
Journal Title: Journal of the College of Physicians and Surgeons--Pakistan : JCPSP

PUBMED ID: 32793502
DOI: doi.org/10.3389/fonc.2020.01257
Titolo: Development of a Nomogram With Alternative Splicing Signatures for P redicting the Prognosis of Glioblastoma: A Study Based on Large-Scale Sequen cing Data.
Autori: Wang Z., Gao L., Guo X., Feng C., Lian W., Deng K., Xing B.
Data di Pubblicazione: 2020-08-15

Abstract: An association was detected among ABO blood groups and prognosis i
n patients with GBM. It was observed that blood groups significantly affecte
d survival and that median survival was significantly shorter in Non-O blood
groups when compared blood group O. Key Words: Glioblastoma multiforme, ABO
blood group, Prognosis, Survival.
Journal Title: Frontiers in oncology

PUBMED ID: 32793467
DOI: doi.org/10.3389/fonc.2020.01057
Titolo: Prognostic and Predictive Value of a Long Non-coding RNA Signature i
n Glioma: A lncRNA Expression Analysis.
Autori: Pan YB., Zhu Y., Zhang QW., Zhang CH., Shao A., Zhang J.
Data di Pubblicazione: 2020-08-15
Abstract: The current histologically based grading system for glioma does no
t accurately predict which patients will have better outcomes or benefit fro
m adjuvant chemotherapy. We proposed that combining the expression profiles
of multiple long non-coding RNAs (lncRNAs) into a single model could improve
prediction accuracy. We included 1,094 glioma patients from three different
datasets. Using the least absolute shrinkage and selection operator (LASSO)
Cox regression model, we built a multiple-lncRNA-based classifier on the bas
is of a training set. The predictive and prognostic accuracy of the classifi
er was validated using an internal test set and two external independent set
s. Using this classifier, we classified patients in the training set into hi
gh- or low-risk groups with significantly different overall survival (OS, HR
= 8.42, 95% CI = 4.99-14.2,
Journal Title: Frontiers in oncology

PUBMED ID: 32776277
DOI: doi.org/10.1007/s00401-020-02194-y
Titolo: Infratentorial IDH-mutant astrocytoma is a distinct subtype.
Autori: Banan R., Stichel D., Bleck A., Hong B., Lehmann U., Suwala A., Rein
hardt A., Schrimpf D., Buslei R., Stadelmann C., Ehlert K., Prinz M., Acker
T., Schittenhelm J., Kaul D., Schweizer L., Capper D., Harter PN., Etminan N
., Jones DTW., Pfister SM., Herold-Mende C., Wick W., Sahm F., von Deimling
A., Hartmann C., Reuss DE.
Data di Pubblicazione: 2020-08-11
Abstract: Diffuse IDH-mutant astrocytic tumors are rarely diagnosed in the c
erebellum or brainstem. In this multi-institutional study, we characterized
a series of primary infratentorial IDH-mutant astrocytic tumors with respect
to clinical and molecular parameters. We report that about 80% of IDH mutati
ons in these tumors are of non-IDH1-R132H variants which are rare in suprate
ntorial astrocytomas. Most frequently, IDH1-R132C/G and IDH2-R172S/G mutatio
ns were present. Moreover, the frequencies of ATRX-loss and MGMT promoter me
thylation, which are typically associated with IDH mutations in supratentori
al astrocytic tumors, were significantly lower in the infratentorial compart
ment. Gene panel sequencing revealed two samples with IDH1-R132C/H3F3A-K27M
co-mutations. Genome-wide DNA methylation as well as chromosomal copy number
profiling provided further evidence for a molecular distinctiveness of infra
tentorial IDH-mutant astrocytomas. Clinical outcome of patients with infrate
ntorial IDH-mutant astrocytomas is significantly better than that of patient
s with diffuse midline gliomas, H3K27M-mutant ($p < 0.005$) and significantly w
orse than that of patients with supratentorial IDH-mutant astrocytomas ($p = 0$
.028). The presented data highlight the very existence and distinctiveness o
f infratentorial IDH-mutant astrocytomas that have important implications fo
r diagnostics and prognostication. They imply that molecular testing is crit
ical for detection of these tumors, since many of these tumors cannot be ide

ntified by immunohistochemistry applied for the mutated IDH1-R132H protein o r loss of ATRX.
Journal Title: Acta neuropathologica

PUBMED ID: 32727404
DOI: doi.org/10.1186/s12885-020-07211-7
Titolo: Multiple formin proteins participate in glioblastoma migration.
Autori: Heuser VD., Kiviniemi A., Lehtinen L., Munthe S., Kristensen BW., Po sti JP., Sipilä JOT., Vuorinen V., Carpén O., Gardberg M.
Data di Pubblicazione: 2020-07-31
Abstract: Formins FHOD1 and INF2 participate in glioblastoma cell migration. Moderate/high expression of INF2 in glioblastoma tissue is associated with w orse outcome. Taken together, our in vitro and tissue studies suggest a pivo tal role for INF2 in glioblastoma. When specific inhibiting compounds become available, INF2 could be a target in the search for novel glioblastoma thera pies.
Journal Title: BMC cancer

PUBMED ID: 32721125
DOI: doi.org/10.1002/cnr2.1216
Titolo: Current clinical management of patients with glioblastoma.
Autori: Lowe S., Bhat KP., Olar A.
Data di Pubblicazione: 2020-07-29
Abstract: GB is an extremely complex disease, and despite recent progress an d advanced therapeutic strategies, the overall patient's prognosis remains d ismal. Innovative strategies and integrative ways of approach to disease are urgently needed.
Journal Title: Cancer reports (Hoboken, N.J.)

PUBMED ID: 32680476
DOI: doi.org/10.1186/s12885-020-07153-0
Titolo: The predominant expression of cancer stem cell marker ALDH1A3 in tum or infiltrative area is associated with shorter overall survival of human gl ioblastoma.
Autori: Gan C., Pierscianek D., El Hindy N., Ahmadipour Y., Keyvani K., Sure U., Zhu Y.
Data di Pubblicazione: 2020-07-19
Abstract: Inter- and intra-tumoral heterogeneous expression of ALDH1A3 was e xhibited in GBMs. A high immunoreactivity of ALDH1A3 in tumor infiltrative a rea was associated with shorter OS, especially in patients with MGMT promote r methylation. Our findings propose ALDH1A3 not only as a predictive biomark er but also as a potential target for personalized therapy of GBM.
Journal Title: BMC cancer

PUBMED ID: 32674977
DOI: doi.org/10.1016/j.jgo.2020.07.001
Titolo: Chemotherapy toxicities and geriatric syndromes in older patients wi th malignant gliomas.
Autori: Wasilewski A., Alam A., Mohile N.
Data di Pubblicazione: 2020-07-18
Abstract: Older patients with MG experience significant polypharmacy, treatm ent toxicities and falls. Studies incorporating geriatric assessment tools m ay better determine associations between geriatric syndromes and survival. C linical trials in older patients should also include non-survival outcomes.
Journal Title: Journal of geriatric oncology

PUBMED ID: 32664146
DOI: doi.org/10.1097/MD.0000000000021147
Titolo: Effect of valproic acid on overall survival in patients with high-grade gliomas undergoing temozolomide: A nationwide population-based cohort study in Taiwan.
Autori: Kuo YJ., Yang YH., Lee IY., Chen PC., Yang JT., Wang TC., Lin MH., Yang WH., Cheng CY., Chen KT., Huang WC., Lee MH.
Data di Pubblicazione: 2020-07-16
Abstract: High-grade gliomas (HGGs) are a rapidly progressive and highly recurrent group of primary brain tumors. Despite aggressive surgical resection with chemoradiotherapy, prognoses remained poor. Valproic acid (VPA), a histone deacetylase inhibitor has shown the potential to inhibit glioma cell growth in vitro through several diverse mechanisms. However clinical studies regarding the effect of VPA on HGGs are limited. This study aimed to investigate whether using VPA in patients with HGGs under temozolomide (TMZ) would lead to a better overall survival (OS).We used the Taiwan National Health Insurance Research database to conduct this population-based cohort study. A total of 2379 patients with HGGs under TMZ treatment were included and were further classified into VPA (n=1212, VPA ≥ 84 defined daily dose [DDD]) and non-VPA (n=1167, VPA < 84 DDD) groups. Each patient was followed from 1998 to 2013 or until death. A Cox proportional hazard regression was performed to evaluate the effect of VPA and OS.The VPA group had a longer mean OS time compared with the non-VPA group (OS: 50.3±41.0 vs 42.0±37.2 months, P<.001). In patients between 18 and 40 years old, the difference is most significant (OS: 70.5±48.7 vs 55.1±46.0, P=.001). The adjusted hazard ratio is 0.81 (95% confidence interval, 0.72-0.91) for the VPA group relative to the non-VPA group.VPA at over 84 DDD improved OS in HGGs TMZ treatment.
Journal Title: Medicine

PUBMED ID: 32648211
DOI: doi.org/10.1007/s12253-020-00868-2
Titolo: Low Fraction Size Re-irradiation for Large Volume Recurrence of Glial Tumours.
Autori: Dobi Á., Darázs B., Fodor E., Cserháti A., Együd Z., Maráz A., László S., Dodd L., Reisz Z., Barzó P., Oláh J., Hideghéty K.
Data di Pubblicazione: 2020-07-11
Abstract: The aim of the present study was to evaluate the efficacy of re-irradiation (re-RT) in patients with advanced local relapses of glial tumours and to define the factors influencing the result of the hyper-fractionated external beam therapy on progression after primary management. We have analysed the data of 55 patients with brain tumours (GBM: 28) on progression, who were re-irradiated between January 2007 and December 2018. The mean volume of the recurrent tumour was 118 cm
Journal Title: Pathology oncology research : POR

PUBMED ID: 32642720
DOI: doi.org/10.1093/noajnl/vdz052
Titolo: Phase I trial of dimethyl fumarate, temozolomide, and radiation therapy in glioblastoma.
Autori: Shafer D., Tombes MB., Shrader E., Ryan A., Bandyopadhyay D., Dent P., Malkin M.
Data di Pubblicazione: 2020-07-10
Abstract: DMF may be safely combined with RT and TMZ in patients with newly diagnosed GBM. The RP2D for DMF is 240 mg three times daily.
Journal Title: Neuro-oncology advances

PUBMED ID: 32642703
DOI: doi.org/10.1093/noajnl/vdaa050
Titolo: Value of [
Autori: Graham MS., Krebs S., Bale T., Domfe K., Lobaugh SM., Zhang Z., Dunp hy MP., Kaley T., Young RJ.
Data di Pubblicazione: 2020-07-10
Abstract: FDG PET is a promising imaging tool to further stratify prognosis in recurrent GBM patients on antiangiogenic therapy.
Journal Title: Neuro-oncology advances

PUBMED ID: 32642664
DOI: doi.org/10.1093/noajnl/vdz033
Titolo: Constitutional mismatch repair deficiency-associated brain tumors: r eport from the European C4CMMRD consortium.
Autori: Guerrini-Rousseau L., Varlet P., Colas C., Andreiuolo F., Bourdeaut F., Dahan K., Devalck C., Faure-Conter C., Genuardi M., Goldberg Y., Kuhlen M., Moalla S., Opocher E., Perez-Alonso V., Sehested A., Slavc I., Unger S., Wimmer K., Grill J., Brugières L.
Data di Pubblicazione: 2020-07-10
Abstract: Several characteristics could help suspecting CMMRD in pediatric m alignant BTs: giant cells on histology, previous malignancies, parental cons anguinity, café-au-lait macules, multiple BTs, and developmental brain anoma lies. The prognosis of CMMRD-associated BT treated with standard therapies i s poor requiring new therapeutic up-front approaches.
Journal Title: Neuro-oncology advances

PUBMED ID: 32582531
DOI: doi.org/10.3389/fonc.2020.00747
Titolo: Constitutional mismatch repair deficiency-associated brain tumors: r eport from the European C4CMMRD consortium.
Autori: Berberich A., Bartels F., Tang Z., Knoll M., Pusch S., Hucke N., Kes sler T., Dong Z., Wiestler B., Winkler F., Platten M., Wick W., Abdollahi A. , Lemke D.
Data di Pubblicazione: 2020-06-26
Abstract: Several characteristics could help suspecting CMMRD in pediatric m alignant BTs: giant cells on histology, previous malignancies, parental cons anguinity, café-au-lait macules, multiple BTs, and developmental brain anoma lies. The prognosis of CMMRD-associated BT treated with standard therapies i s poor requiring new therapeutic up-front approaches.
Journal Title: Frontiers in oncology

PUBMED ID: 32557428
DOI: doi.org/10.4414/smw.2020.20256
Titolo: A contemporary perspective on the diagnosis and treatment of diffuse gliomas in adults.
Autori: Roth P., Hottinger AF., Hundsberger T., Läubli H., Schucht P., Reine rt M., Mamot C., Roelcke U., Pesce G., Hofer S., Weller M.
Data di Pubblicazione: 2020-06-20
Abstract: Gliomas are intrinsic brain tumours, which are classified by the W orld Health Organization (WHO) into different grades of malignancy, with gli oblastoma being the most frequent and most malignant subtype (WHO grade IV). Mutations in the isocitrate dehydrogenase (IDH) 1 or 2 genes are frequent in lower (WHO II/III) grade tumours but typically absent in classical glioblast oma. IDH mutations are associated with a better prognosis compared with IDH wild-type tumours of the same WHO grade. Following detection of a tumour mas s by imaging, maximum safe surgery as feasible is commonly performed to redu

ce mass effect and to obtain tissue allowing histopathological diagnosis and molecular assessment. Radiotherapy has been the mainstay in the treatment of diffuse gliomas for several decades. It provides improved local control, but is not curative. Furthermore, several randomised trials have shown that the addition of alkylating chemotherapy, either temozolomide or nitrosourea-base d regimens, to radiotherapy results in prolonged survival. Tumour-treating f ields (TTFields) have emerged as an additional treatment option in combinati on with maintenance temozolomide treatment for patients with newly diagnosed glioblastoma. Treatment at recurrence is less standardised and depends on th e patient’s performance status, symptom burden and prior treatments. B evacizumab prolongs progression-free survival in newly diagnosed and recurre nt glioblastoma, but does not impact overall survival. However, in Switzerla nd and some other countries, it is still considered a valuable treatment opt ion to reduce clinical symptom burden. Given the generally poor outcome for these patients, various novel treatment approaches are currently being explo red within clinical trials including immunotherapeutic strategies such as im mune checkpoint inhibition and the brain-penetrant proteasome inhibitor mari zomib.
Journal Title: Swiss medical weekly

PUBMED ID: 32546647
DOI: doi.org/10.1158/1078-0432.CCR-19-3874
Titolo: Advanced Age Increases Immunosuppression in the Brain and Decreases Immunotherapeutic Efficacy in Subjects with Glioblastoma.
Autori: Ladomersky E., Zhai L., Lauing KL., Bell A., Xu J., Kocherginsky M., Zhang B., Wu JD., Podojil JR., Platanias LC., Mochizuki AY., Prins RM., Kumt hekar P., Raizer JJ., Dixit K., Lukas RV., Horbinski C., Wei M., Zhou C., Pa welec G., Campisi J., Grohmann U., Prendergast GC., Munn DH., Wainwright DA.
Data di Pubblicazione: 2020-06-18
Abstract: Immunosuppression increases in the brain during advanced age and i nhibits antiglioma immunity in older adults. Going forward, it will be impor tant to fully understand the factors and mechanisms in the elderly brain tha t contribute to the decreased survival of older patients with GBM during tre atment with ICB.
Journal Title: Clinical cancer research : an official journal of the America n Association for Cancer Research

PUBMED ID: 32543245
DOI: doi.org/10.1080/14737175.2020.1775584
Titolo: Improving long-term survival in diffuse intrinsic pontine glioma.
Autori: Felker J., Broniscer A.
Data di Pubblicazione: 2020-06-17
Abstract: The authors propose four main opportunities to improve long-term s urvival. First, patients should be enrolled in scientifically sound clinical trials that include molecularly profiling either via stereotactic biopsy or liquid biopsy. Second, clinical trials should include more innovative endpoi nts other than traditional EFS and OS such as MRI/PET imaging findings combi ned with surrogates of activity (e.g. serial liquid biopsies) to better asce rtain biologically active treatments. Third, innovative clinical trial appro aches are needed to help allow for the rapid development of combination ther apies to be tested. Finally, effort should be concentrated on reversing the effects of the histone mutation, as this malfunctioning development program seems to be key to DIPG relentlessness.
Journal Title: Expert review of neurotherapeutics

PUBMED ID: 32518098
DOI: doi.org/10.1158/1078-0432.CCR-19-4055

Titolo: Phosphorylated Acetyl-CoA Carboxylase Is Associated with Clinical Be
nefit with Regorafenib in Relapsed Glioblastoma: REGOMA Trial Biomarker Anal
ysis.
Autori: Indraccolo S., De Salvo GL., Verza M., Caccese M., Esposito G., Piga
I., Del Bianco P., Pizzi M., Gardiman MP., Eoli M., Rudà R., Brandes AA., Ib
rahim T., Rizzato S., Lolli I., Zagonel V., Lombardi G.
Data di Pubblicazione: 2020-06-11
Abstract: We found that AMPK pathway activation is associated with clinical
benefit from treatment with regorafenib in relapsed GBM.
Journal Title: Clinical cancer research : an official journal of the America
n Association for Cancer Research

PUBMED ID: 32506137
DOI: doi.org/10.1093/neuonc/noaa140
Titolo: MR Imaging features of Diffuse Intrinsic Pontine Glioma (DIPG) and R
elationship to Overall Survival: Report from the International DIPG Registry
.
Autori: Leach JL., Roebker J., Schafer A., Baugh J., Chaney B., Fuller C., F
ouladi M., Lane A., Doughman R., Drissi R., DeWire-Schottmiller M., Ziegler
DS., Minturn JE., Hansford JR., Wang SS., Monje-Deisseroth M., Fisher PG., G
ottardo NG., Dholaria H., Packer R., Warren K., Leary SES., Goldman S., Bart
els U., Hawkins C., Jones BV.
Data di Pubblicazione: 2020-06-08
Abstract: Baseline imaging features are assessed in the IDIPGR. There was a
9.5% discordance in DIPG diagnosis between local and central review demonstr
ating need for central imaging confirmation for prospective trials. Although
several imaging features were significantly associated with OS (univariable)
only age and distant disease were significant on multivariable analyses. The
re was limited association of imaging features with histone mutation status
although numbers are small and evaluation exploratory.
Journal Title: Neuro-oncology

PUBMED ID: 32452588
DOI: doi.org/10.1634/theoncologist.2020-0440
Titolo: A Phase II, Single-Arm, Open-Label, Bayesian Adaptive Efficacy and S
afety Study of PBI-05204 in Patients with Stage IV Metastatic Pancreatic Ade
nocarcinoma.
Autori: Roth MT., Cardin DB., Borazanci EH., Steinbach M., Picozzi VJ., Rose
mury A., Wadlow RC., Newman RA., Berlin J.
Data di Pubblicazione: 2020-05-27
Abstract: PBI-05204 did not meet its primary endpoint for OS in this study.
Recent preclinical data indicate a role for PBI-05204 against glioblastoma m
ultiforme when combined with chemotherapy and radiotherapy. A randomized pha
se II trial is currently being designed.
Journal Title: The oncologist

PUBMED ID: 32450499
DOI: doi.org/10.1016/j.clineuro.2020.105888
Titolo: Long term follow-up and outcomes in adult patients with thalamic gli
omas.
Autori: Li Z., Wu H., Wu B., Lyu J., Liu Y., Tang C., Hua W., Hu S., Wang Y.
, Zhang Y.
Data di Pubblicazione: 2020-05-26
Abstract: The OS and PFS of adult patients with thalamic glioma were not sig
nificantly different between patients in the surgical group and in the IMRT
group. IMRT might be an acceptable alternative to surgery for adult patients
with unresectable thalamic glioma.

Journal Title: Clinical neurology and neurosurgery

PUBMED ID: 32392361
DOI: doi.org/10.1002/1878-0261.12707
Titolo: Classification of diffuse lower-grade glioma based on immunological profiling.
Autori: Wu F., Wang ZL., Wang KY., Li GZ., Chai RC., Liu YQ., Jiang HY., Zhai Y., Feng YM., Zhao Z., Zhang W.
Data di Pubblicazione: 2020-05-12
Abstract: Transcriptomic data derived from bulk sequencing have been applied to delineate the tumor microenvironment (TME) and define immune subtypes in various cancers, which may facilitate the design of immunotherapy treatment strategies. We herein gathered published gene expression data from diffuse lower-grade glioma (LGG) patients to identify immune subtypes. Based on the immune gene profiles of 402 LGG patients from The Cancer Genome Atlas, we performed consensus clustering to determine robust clusters of patients, and evaluated their reproducibility in three Chinese Glioma Genome Atlas cohorts. We further integrated immunogenomics methods to characterize the immune environment of each subtype. Our analysis identified and validated three immune subtypes-Im1, Im2, and Im3-characterized by differences in lymphocyte signatures, somatic DNA alterations, and clinical outcomes. Im1 had a higher infiltration of CD8+ T cells, Th17, and mast cells. Im2 was defined by elevated cytolytic activity, exhausted CD8+ T cells, macrophages, higher levels of aneuploidy, and tumor mutation burden, and these patients had worst outcome. Im3 displayed more prominent T helper cell and APC coinhibition signatures, with elevated pDCs and macrophages. Each subtype was associated with distinct somatic alterations. Moreover, we applied graph structure learning-based dimensionality reduction to the immune landscape and revealed significant intracluster heterogeneity with Im2 subtype. Finally, we developed and validated an immune signature with better performance of prognosis prediction. Our results demonstrated the immunological heterogeneity within diffuse LGG and provided valuable stratification for the design of future immunotherapy.
Journal Title: Molecular oncology

PUBMED ID: 32384274
DOI: doi.org/10.3171/2020.2.JNS192767
Titolo: Extent of resection, molecular signature, and survival in 1p19q-codeleted gliomas.
Autori: Garton ALA., Kinslow CJ., Rae AI., Mehta A., Pannullo SC., Magge RS., Ramakrishna R., McKhann GM., Sisti MB., Bruce JN., Canoll P., Cheng SK., Sonabend AM., Wang TJC.
Data di Pubblicazione: 2020-05-09
Abstract: By using the NCDB, the authors have demonstrated a side-by-side comparison of the survival benefits of greater EOR in 1p/19q-codeleted gliomas.
Journal Title: Journal of neurosurgery

PUBMED ID: 32340318
DOI: doi.org/10.3390/diagnostics10040247
Titolo: Magnetic Resonance Imaging Derived Biomarkers of IDH Mutation Status and Overall Survival in Grade III Astrocytomas.
Autori: Feraco P., Bacci A., Ferrazza P., van den Hauwe L., Pertile R., Girlando S., Barbareschi M., Gagliardo C., Morganti AG., Petralia B.
Data di Pubblicazione: 2020-04-29
Abstract: The evaluation of the isocitrate dehydrogenase (IDH) mutation status in the glioma decision-making process has diagnostic, prognostic and therapeutic implications. The aim of this study was to evaluate whether conventi

onal magnetic resonance imaging (MRI) and apparent diffusion coefficient (AD C) can noninvasively predict the most common IDH mutational status (R132H) i n GIII-astrocytomas and the overall survival (OS). Hence, twenty-two patient s (9-F, 13-M) with a histological diagnosis of GIII-astrocytoma and evaluati on of IDH-mutation status (12-wild type, 10-mutant) were retrospectively eva luated. Imaging studies were reviewed for the morphological feature and mean ADC values (ADCm). Statistics included a Fisher's exact test, Student's
Journal Title: Diagnostics (Basel, Switzerland)

PUBMED ID: 32249134
DOI: doi.org/10.1016/j.jmir.2020.01.007
Titolo: Cannabis and Radiation Therapy: A Scoping Review of Human Clinical T rials.
Autori: Rosewall T., Feuz C., Bayley A.
Data di Pubblicazione: 2020-04-07
Abstract: The existing body of literature evaluating the use of cannabinoids by patients undergoing RT is very limited. Well-designed randomized controll ed trials are urgently needed, which address the significant design flaws of previous studies and evaluate the impact of phytocannabinoids in patients un dergoing RT.
Journal Title: Journal of medical imaging and radiation sciences

PUBMED ID: 32245342
DOI: doi.org/10.1080/01616412.2020.1748323
Titolo: Low expression of
Autori: Zhu J., Zhao YP., Zhang YQ.
Data di Pubblicazione: 2020-04-05
Abstract: The existing body of literature evaluating the use of cannabinoids by patients undergoing RT is very limited. Well-designed randomized controll ed trials are urgently needed, which address the significant design flaws of previous studies and evaluate the impact of phytocannabinoids in patients un dergoing RT.
Journal Title: Neurological research

PUBMED ID: 32199197
DOI: doi.org/10.1016/j.ctrv.2020.101993
Titolo: Evolving role of regorafenib for the treatment of advanced cancers.
Autori: Grothey A., Blay JY., Pavlakis N., Yoshino T., Bruix J.
Data di Pubblicazione: 2020-03-22
Abstract: Regorafenib is an oral tyrosine kinase inhibitor (TKI) approved fo r the treatment of refractory metastatic colorectal cancer (mCRC), advanced gastrointestinal stromal tumors (GIST) previously treated with imatinib and sunitinib, and unresectable hepatocellular carcinoma (HCC) following progres sion on sorafenib. Regorafenib was initially approved for mCRC based on impr oved overall survival (OS) in the randomized, placebo-controlled, phase 3 CO RRECT trial, which was confirmed in an expanded population of Asian patients in the randomized, placebo-controlled phase 3 CONCUR trial. Approvals in GIS T, and more recently in HCC, were based on the results from the randomized, placebo-controlled, phase 3 GRID and RESORCE trials, respectively. In this r eview, we provide a comprehensive summary of the clinical evidence for appro val of regorafenib in mCRC, GIST, and HCC, present emerging evidence of rego rafenib activity in other tumor types (namely, gastroesophageal cancer, sarc omas, biliary tract cancer, and glioblastoma), and discuss trials in progres s within the context of regorafenib's mechanism of action. We describe recen t advances and key lessons learned with regorafenib, including the importanc e of managing common drug-related toxicities using dose-optimization strateg ies, the search for biomarkers to predict response to treatment, and highlig

ht some of the unaddressed questions and future directions for regorafenib a cross tumors.
Journal Title: Cancer treatment reviews

PUBMED ID: 32197147
DOI: doi.org/10.1016/j.tranon.2020.100755
Titolo: Cancer Stem Cell Chemotherapeutics Assay for Prospective Treatment o f Recurrent Glioblastoma and Progressive Anaplastic Glioma: A Single-Institu tion Case Series.
Autori: Ranjan T., Howard CM., Yu A., Xu L., Aziz K., Jho D., Leonardo J., H ameed MA., Karlovits SM., Wegner RE., Fuhrer R., Lirette ST., Denning KL., V alluri J., Claudio PP.
Data di Pubblicazione: 2020-03-21
Abstract: Glioblastoma (GBM) and progressive anaplastic glioma are the most aggressive brain tumor in adults and their prognosis is very poor even if tr eated with the standard of care chemoradiation Stupp's protocol. Recent know ledge pointed out that current treatments often fail to successfully target cancer stem cells (CSCs) that are responsible for therapy resistance and rec urrence of these malignant tumors. ChemoID is the first and only CLIA (clini cal laboratory improvements amendment) -certified and CAP (College of Americ an Pathologists) -accredited chemotherapeutic assay currently available in o ncology clinics that examines patient's derived CSCs susceptibility to conve ntional FDA (Food and Drugs Administration) -approved drugs. In this study w e observed that although the majority of our patients (71.5%) presented with unfavorable prognostic predictors (wild type IDH-1/2 and unmethylated MGMT p romoter), patients treated with ChemoID assay-directed therapy had an overal l response rate of 86% and increased median OS of 13.3 months compared to th e historical median OS of 9.1 months (8.1-10.1 months) previously reported [1] suggesting that the ChemoID assay may be beneficial in personalizing trea tment strategies.
Journal Title: Translational oncology

PUBMED ID: 32191542
DOI: doi.org/10.1200/CCI.19.00121
Titolo: Cancer Imaging Phenomics via CaPTk: Multi-Institutional Prediction o f Progression-Free Survival and Pattern of Recurrence in Glioblastoma.
Autori: Fathi Kazerooni A., Akbari H., Shukla G., Badve C., Rudie JD., Sako C., Rathore S., Bakas S., Pati S., Singh A., Bergman M., Ha SM., Kontos D., Nasrallah M., Bagley SJ., Lustig RA., O'Rourke DM., Sloan AE., Barnholtz-Slo an JS., Mohan S., Bilello M., Davatzikos C.
Data di Pubblicazione: 2020-03-20
Abstract: Imaging signatures of presurgical MP-MRI scans reveal relatively h igh predictability of time and location of GBM recurrence, subject to the pa tients receiving standard first-line chemoradiation therapy. Through its gra phical user interface, CaPTk offers easy accessibility to advanced computati onal algorithms for deriving imaging signatures predictive of clinical outco me and could similarly be used for a variety of radiomic and radiogenomic an alyses.
Journal Title: JCO clinical cancer informatics

PUBMED ID: 32154775
DOI: doi.org/10.1148/radiol.2020191376
Titolo: Identification of Early Response to Anti-Angiogenic Therapy in Recur rent Glioblastoma: Amide Proton Transfer-weighted and Perfusion-weighted MRI compared with Diffusion-weighted MRI.
Autori: Park JE., Kim HS., Park SY., Jung SC., Kim JH., Heo HY.
Data di Pubblicazione: 2020-03-11

Abstract: Background Amide proton transfer (APT) MRI has the potential to de monstrate antitumor effects by reflecting biologically active tumor portion, providing different information from diffusion-weighted imaging (DWI) or dyn amic susceptibility contrast (DSC) imaging. Purpose To evaluate whether a ch ange in APT signal intensity after antiangiogenic treatment is predictive of early treatment response in recurrent glioblastoma. Materials and Methods In this retrospective study, APT MRI, DWI, and DSC imaging were performed in pa tients with recurrent glioblastoma from July 2015 to April 2019, both before treatment and 4-6 weeks after initiation of bevacizumab (follow-up). Progres sion was based on pathologic confirmation or clinical-radiologic assessment, and progression patterns were defined as local enhancing or diffuse nonenhan cing. Changes in mean and histogram parameters (fifth and 95th percentiles) of APT signal intensity, apparent diffusion coefficient, and normalized cere bral blood volume (CBV) between imaging time points were calculated. Predict ors of 12-month progression and progression-free survival (PFS) were determi ned by using logistic regression and Cox proportional hazard modeling and ac cording to progression type. Results A total of 54 patients were included (m edian age, 56 years [interquartile range, 49-64 years]; 24 men). Mean APT si gnal intensity change after bevacizumab treatment indicated a low 12-month p rogression rate (odds ratio [OR], 0.36; 95% confidence interval [CI]: 0.13, 0.90;
Journal Title: Radiology

PUBMED ID: 32089384
DOI: doi.org/10.1016/j.jocn.2020.01.086
Titolo: Patterns of management and outcomes of unifocal versus multifocal gl ioblastoma.
Autori: Haque W., Thong Y., Verma V., Rostomily R., Brian Butler E., Teh BS.
Data di Pubblicazione: 2020-02-25
Abstract: This is the largest study to date describing outcomes for patients with multifocal GBM, and it shows that multifocal GBM is associated with a d ecreased use both of GTR and conventionally fractionated RT, as well as wors e median OS. Further research is needed to improve clinical outcomes for pat ients with multifocal GBM.
Journal Title: Journal of clinical neuroscience : official journal of the Ne urosurgical Society of Australasia

PUBMED ID: 32074098
DOI: doi.org/10.3855/jidc.11582
Titolo: Nocardia farcinica meningitis in a patient with high-grade astrocyto ma.
Autori: Nasri E., Fakhim H., Barac A., Yousefi S., Aghazade K., Boljevic D., Mardani M.
Data di Pubblicazione: 2020-02-20
Abstract: We describe a case of 91-year-old male with astrocytoma who develo ped meningitis caused by Nocardia farcinica. He had a past medical history o f anaplastic astrocytoma grade III. Endocranial computed tomography (CT) sca n revealed mass lesion in the left occipital region associated with perilesi onal edema, without evidence of midline shift issue. The analyses of cerebro spinal fluid (CSF) revealed neutrophilic pleocytosis, hyperproteinorrachia a nd hypoglycorrhachia. Combined antimicrobial therapy was initiated (vancomyc in, meropenem, acyclovir). CSF culture revealed Nocardia farcinica. Suscepti bility testing revealed intermediate sensitivity to meropenem and antibiotic treatment was switched to trimethoprim-sulfamethoxazole and imipenem. After 7 days of treatment the patient developed progressive dyspnea. The chest CT scan revealed bilateral pleural effusion and alveolar infiltrate mostly in t he right lobe. Ceftriaxone was added to the therapy, but the outcome was let hal. Nocardia spp. should be considered as differential diagnosis in the pat

ients with brain tumor or meningitis in the setting of immune suppression an d corticosteroid use. CSF cultures should be incubated longer with aim to al low fastidious organisms to grow, such as Nocardia spp.
Journal Title: Journal of infection in developing countries

PUBMED ID: 32055850
DOI: doi.org/10.1093/neuonc/noaa034
Titolo: Glycine by MR spectroscopy is an imaging biomarker of glioma aggress iveness.
Autori: Tiwari V., Daoud EV., Hatanpaa KJ., Gao A., Zhang S., An Z., Ganji S K., Raisanen JM., Lewis CM., Askari P., Baxter J., Levy M., Dimitrov I., Tho mas BP., Pinho MC., Madden CJ., Pan E., Patel TR., DeBerardinis RJ., Sherry AD., Mickey BE., Malloy CR., Maher EA., Choi C.
Data di Pubblicazione: 2020-02-15
Abstract: 1. Glycine and 2-hydroxyglutarate in glioma patients are precisely co-detected using MRS at 3T.2. Tumors with elevated glycine proliferate and progress rapidly.3. A high glycine/2HG ratio is predictive of shortened pati ent survival.
Journal Title: Neuro-oncology

PUBMED ID: 32034261
DOI: doi.org/10.1038/s41598-020-59152-7
Titolo: The application of point source electroporation and chemotherapy for the treatment of glioma: a randomized controlled rat study.
Autori: Sharabi S., Guez D., Daniels D., Cooper I., Atrakchi D., Liraz-Zalts man S., Last D., Mardor Y.
Data di Pubblicazione: 2020-02-09
Abstract: The prognosis of Glioblastoma Multiforme patients is poor despite aggressive therapy. Reasons include poor chemotherapy penetration across the blood-brain barrier and tumor infiltration into surrounding tissues. Here we studied the effects of combined point-source electroporation (EP) and system ic chemotherapy in glioma-bearing rats. 128 rats were studied. Treatment gro ups were administered systemic Cisplatin/Methotrexate before EP (either 90 o r 180 pulses). Control groups were treated by EP, chemotherapy, or no treatm ent. Tumor volumes were determined by MRI. Tumors growth rates of the EP+Me thotrexate group (1.02±0.77) were significantly lower ($p<0.01$) than the con trol (5.2±1.0) 1-week post treatment. No significant difference was found c ompared to Methotrexate (1.7±0.5). Objective response rates (ORR) were 40% and 57% for the Methotrexate and EP+Methotrexate groups respectively. Tumor growth rates and ORR of the EP+Cisplatin groups (90 pulses 0.98±0.2, 57%, 1 80 pulses 1.2±0.1, 33%) were significantly smaller than the control (6.4±1. 0, $p<0.01$, $p<0.02$, 0%) and Cisplatin (3.9±1.0, $p<0.04$, $p<0.05$, 13%) group s. No significant differences were found between the control groups. Increas ed survival was found in the EP+Cisplatin group, X
Journal Title: Scientific reports

PUBMED ID: 32034238
DOI: doi.org/10.1038/s41598-020-59089-x
Titolo: Extent of resection and molecular pathologic subtype are potent prog nostic factors of adult WHO grade II glioma.
Autori: Choi J., Kim SH., Ahn SS., Choi HJ., Yoon HI., Cho JH., Roh TH., Kan g SG., Chang JH., Suh CO.
Data di Pubblicazione: 2020-02-09
Abstract: We evaluated prognostic factors of adult low-grade glioma (LGG) ac cording to the new 2016 WHO classification. Records of 153 patients diagnose d with WHO grade II LGG between 2003 and 2015 were retrospectively reviewed.

Based on the 2016 WHO classification, 80 patients (52.3%) had diffuse astrocytoma, IDH-mutant; 45 (29.4%) had oligodendroglioma, IDH-mutant and 1p/19q-codeleted (ODG); and 28 (18.3%) had diffuse astrocytoma, IDH-wildtype. Gross total resection (GTR) was performed in 71 patients (46.4%), subtotal resection in 31 (20.3%), partial resection in 43 (28.1%), and biopsy in 8 (5.2%). One hundred two patients (66.7%) received postoperative radiotherapy. The 5- and 10-year progression-free survival (PFS) rates were 72.7% and 51.5%, respectively, and the 5- and 10-year overall survival (OS) rates were 82.5% and 63.5%, respectively. GTR and IDH-mutant and/or 1p/19q codeletion were favorable prognostic factors for PFS and OS. Patients with IDH-wildtype had significantly decreased OS. Among patients with ODG who underwent GTR, no recurrence was observed after radiotherapy. Patients who underwent non-GTR frequently experienced recurrence after radiotherapy (IDH-mutant: 47.6%, IDH-wildtype: 57.9%). In conclusion, molecular classification of LGG was of prognostic relevance, with IDH-wildtype patients having a particularly poor outcome, regardless of the treatment. Favorable results were observed in patients who underwent GTR.
Journal Title: Scientific reports

PUBMED ID: 32034072
DOI: doi.org/10.1158/1078-0432.CCR-18-1140
Titolo: Rindopepimut with Bevacizumab for Patients with Relapsed EGFRvIII-Expressing Glioblastoma (ReACT): Results of a Double-Blind Randomized Phase II Trial.
Autori: Reardon DA., Desjardins A., Vredenburgh JJ., O'Rourke DM., Tran DD., Fink KL., Nabors LB., Li G., Bota DA., Lukas RV., Ashby LS., Duic JP., Mrugala MM., Cruickshank S., Vitale L., He Y., Green JA., Yellin MJ., Turner CD., Keler T., Davis TA., Sampson JH., Sampson JH.
Data di Pubblicazione: 2020-02-09
Abstract: Our randomized trial supports the potential for targeted immunotherapy among patients with GBM, but the therapeutic benefit requires validation due to the small sample size and potential heterogeneity of bevacizumab response among recurrent patients with GBM.
Journal Title: Clinical cancer research : an official journal of the American Association for Cancer Research

PUBMED ID: 32016716
DOI: doi.org/10.1007/s11060-020-03415-w
Titolo: Radiation dose response of neurologic symptoms during conformal radiotherapy for diffuse intrinsic pontine glioma.
Autori: Tinkle CL., Campbell K., Han Y., Li Y., Bianski B., Broniscer A., Khan RB., Merchant TE.
Data di Pubblicazione: 2020-02-05
Abstract: Low cumulative RT doses resulted in neurologic improvement in most patients with DIPG. The volume of brainstem spared by tumor influenced time to symptomatic improvement. Neurologic improvement during RT was associated with superior survival.
Journal Title: Journal of neuro-oncology

PUBMED ID: 31973881
DOI: doi.org/10.1016/j.tips.2019.12.003
Titolo: Immunotherapy for Malignant Glioma: Current Status and Future Directions.
Autori: Wang H., Xu T., Huang Q., Jin W., Chen J.
Data di Pubblicazione: 2020-01-25
Abstract: Glioma is the most common intracranial primary malignancy, with limited treatment options and a poor overall survival (OS). Immunotherapy has

been used successfully in various cancers, leading to the development of sim ilar therapies that activate the patient's immune system to eliminate glioma . In this review, we introduce the diverse immunotherapeutic approaches avai lable for treating glioma, highlighting the successes and challenges resulti ng from current clinical trials. Additionally, we emphasize the effect of mu ltiple clinical factors on immunotherapy to help optimize individualized tre atment regimens. Finally, we also highlight several novel concepts and techn ologies that could be used to design new and/or improve existing immunothera pies. Such approaches will delineate a new blueprint for glioma treatment.
Journal Title: Trends in pharmacological sciences

PUBMED ID: 20541421
DOI: doi.org/10.1016/j.jocn.2009.12.009
Titolo: Carboplatin and etoposide combined with bevacizumab for the treatmen t of recurrent glioblastoma multiforme.
Autori: Francesconi AB., Dupre S., Matos M., Martin D., Hughes BG., Wyld DK. , Lickliter JD.
Data di Pubblicazione: 2010-06-15
Abstract: Relapsed glioblastoma multiforme (GBM) responds poorly to standard therapies. Vascular endothelial growth factor (VEGF) is implicated in the de velopment of GBM and the anti-VEGF monoclonal antibody bevacizumab has shown early clinical promise against malignant glioma. We treated six patients wit h recurrent GBM using bevacizumab combined with carboplatin and etoposide ch emotherapy (ACE regimen). Toxicity was that expected for carboplatin and eto poside alone, except for an ischemic stroke in one patient. We observed part ial responses in five patients and one responding patient developed extensiv e tumour necrosis after 2 cycles of treatment. Median progression-free and o verall survival was 19 and 29.9weeks, respectively. Four responding patients developed recurrence, which was characterized by markedly less peri-tumoral edema, mass effect and necrosis compared with tumours at baseline. Two patie nts developed local extracranial extension. In conclusion, ACE was active in recurrent GBM and was mostly well tolerated.
Journal Title: Journal of clinical neuroscience : official journal of the Ne urosurgical Society of Australasia

PUBMED ID: 31936544
DOI: doi.org/10.3390/ijms21020423
Titolo: Crocetin Extracted from Saffron Shows Antitumor Effects in Models of Human Glioblastoma.
Autori: Colapietro A., Mancini A., Vitale F., Martellucci S., Angelucci A., Llorens S., Mattei V., Gravina GL., Alonso GL., Festuccia C.
Data di Pubblicazione: 2020-01-16
Abstract: Over recent years, many authors discussed the effects of different natural compounds on glioblastoma (GBM). Due to its capacity to impair survi val and progression of different cancer types, saffron extract (SE), named c rocetin (CCT), is particularly noteworthy. In this work, we elucidated the a ntitumor properties of crocetin in glioma in vivo and in vitro models for th e first time. The in vitro results showed that the four tumor cell lines obs erved in this study (U251, U87, U138, and U373), which were treated with inc reasing doses of crocetin, showed antiproliferative and pro-differentiative effects as demonstrated by a significant reduction in the number of viable c ells, deep changes in cell morphology, and the modulation of mesenchymal and neuronal markers. Indeed, crocetin decreased the expression of Cluster of Di fferentiation CD44, CD90, CXCR4, and OCT3/4 mesenchymal markers, but increas ed the expression of βIII-Tubulin and neurofilaments (NFH) neuronal linage-r elated markers. Epigenetic mechanisms may modulate these changes, since Hist one Deacetylase, HDAC1 and HDAC3 were downmodulated in U251 and U87 cells, w hereas HDAC1 expression was downmodulated in U138 and U373 cells. Western bl

otting analyses of Fatty Acid Synthase, FASN, and CD44 resulted in effective inhibition of these markers after CCT treatment, which was associated with i mportant activation of the apoptosis program and reduced glioma cell movemen t and wound repair. The in vivo studies aligned with the results obtained in vitro. Indeed, crocetin was demonstrated to inhibit the growth of U251 and U 87 cells that were subcutaneously injected into animal models. In particular , the Tumor To Progression or TTP values and Kaplan-Meier curves indicated t hat crocetin had more major effects than radiotherapy alone, but similar eff ects to temozolomide (TMZ). An intra-brain cell inoculation of a small numbe r of luciferase-transfected U251 cells provided a model that was able to rec apitulate recurrence after surgical tumor removal. The results obtained from the orthotopic intra-brain model indicated that CCT treatment increased the disease-free survival (DFS) and overall survival (OS) rates, inducing a dela y in appearance of a detectable bioluminescent lesion. CCT showed greater ef ficacy than Radio Therapy (RT) but comparable efficacy to temozolomide in xe nograft models. Therefore, we aimed to continue the study of crocetin's effe cts in glioma disease, focusing our attention on the radiosensitizing proper ties of the natural compound and highlighting the ways in which this was rea lized.
Journal Title: International journal of molecular sciences

PUBMED ID: 31914946
DOI: doi.org/10.1186/s12885-019-6467-6
Titolo: Combining therapy with recombinant human endostatin and cytotoxic ag ents for recurrent disseminated glioblastoma: a retrospective study.
Autori: Ge JJ., Li C., Qi SP., Xue FJ., Gao ZM., Yu CJ., Zhang JP.
Data di Pubblicazione: 2020-01-10
Abstract: Rh-ES, in combination with cytotoxic drugs, was an alternative eff ective regimen with manageable toxicities in treatment of recurrent dissemin ated glioblastoma.
Journal Title: BMC cancer

PUBMED ID: 31908598
DOI: doi.org/10.1186/s12935-019-1086-5
Titolo: Patient-derived xenografts of different grade gliomas retain the het erogeneous histological and genetic features of human gliomas.
Autori: Zeng W., Tang Z., Li Y., Yin G., Liu Z., Gao J., Chen Y., Chen F.
Data di Pubblicazione: 2020-01-08
Abstract: The panel of patient-derived glioma xenografts in this study repro duced the diverse heterogeneity of different grade gliomas, thereby allowing the study of the growth characteristics of various glioma types and the iden tification of tumor-specific molecular markers, which has applications in dr ug discovery and patient-tailored therapy.
Journal Title: Cancer cell international

PUBMED ID: 31842801
DOI: doi.org/10.1186/s12885-019-6414-6
Titolo: A systematic analysis of immune genes and overall survival in cancer patients.
Autori: Wang Q., Li P., Wu W.
Data di Pubblicazione: 2019-12-18
Abstract: The TCR signaling pathway played a distinct role in the OS of thes e 6 cancer types.
Journal Title: BMC cancer

PUBMED ID: 31819537

DOI: doi.org/10.2147/OTT.S226804
Titolo: Apatinib Plus Temozolomide for Recurrent Glioblastoma: An Uncontroll ed, Open-Label Study.
Autori: Wang Y., Meng X., Zhou S., Zhu Y., Xu J., Tao R.
Data di Pubblicazione: 2019-12-11
Abstract: Apatinib combined with dose-dense TMZ was effective in terms of PF S, ORR, and DCR and was well tolerated after appropriate dose reduction in t he Chinese population tested. Further randomized controlled clinical studies are needed to confirm the efficacy of apatinib combined with TMZ for treatme nt of rGBM.
Journal Title: OncoTargets and therapy

PUBMED ID: 31785339
DOI: doi.org/10.1016/j.ijrobp.2019.11.020
Titolo: Defining Optimal Target Volumes of Conformal Radiation Therapy for D iffuse Intrinsic Pontine Glioma.
Autori: Tinkle CL., Simone B., Chiang J., Li X., Campbell K., Han Y., Li Y., Hover LD., Molitoris JK., Becksfort J., Lucas JT., Patay Z., Baker SJ., Bron iscer A., Merchant TE.
Data di Pubblicazione: 2019-12-01
Abstract: All patients who experienced local failure showed progression with in the high-dose volume, and there was no apparent survival or tumor-control benefit to extending the CTV margins beyond 1 cm. Given the increasing use o f reirradiation, standardizing the CTV margin to 1 cm may improve retreatmen t tolerance.
Journal Title: International journal of radiation oncology, biology, physics

PUBMED ID: 31782181
DOI: doi.org/10.1002/ana.25655
Titolo: Randomized Placebo-Controlled Trial of Intravenous Immunoglobulin in Autoimmune LGI1/CASPR2 Epilepsy.
Autori: Dubey D., Britton J., McKeon A., Gadoth A., Zekeridou A., Lopez Chir iboga SA., Devine M., Cerhan JH., Dunlay K., Sagen J., Ramberger M., Waters P., Irani SR., Pittock SJ.
Data di Pubblicazione: 2019-11-30
Abstract: Superiority of IVIG to placebo reached statistical significance fo r the primary endpoint for all patients and the subset with LGI1-IgG. These results have to be interpreted with the caveat that the study did not reach its originally selected sample size. ANN NEUROL 2020;87:313-323.
Journal Title: Annals of neurology

PUBMED ID: 31779130
DOI: doi.org/10.3390/ijms20235942
Titolo: CSPG4 as Target for CAR-T-Cell Therapy of Various Tumor Entities-Mer its and Challenges.
Autori: Harrer DC., Dörrie J., Schaft N.
Data di Pubblicazione: 2019-11-30
Abstract: Targeting cancer cells using chimeric-antigen-receptor (CAR-)T cel ls has propelled adoptive T-cell therapy (ATT) to the next level. A plentitu de of durable complete responses using CD19-specific CAR-T cells in patients suffering from various lymphoid malignancies resulted in the approval by the food and drug administration (FDA) of CD19-directed CAR-T cells for the trea tment of acute lymphoblastic leukemia (ALL) and diffuse large B-cell lymphom a (DLBCL). A substantial portion of this success in hematological malignanci es can be traced back to the beneficial properties of the target antigen CD1 9, which combines a universal presence on target cells with no detectable ex pression on indispensable host cells. Hence, to replicate response rates ach

ieved in ALL and DLBCL in the realm of solid tumors, where ideal target anti gens are scant and CAR-T cells are still lagging behind expectations, the qu est for appropriate target antigens represents a crucial task to expedite th e next steps in the evolution of CAR-T-cell therapy. In this review, we want to highlight the potential of chondroitin sulfate proteoglycan 4 (CSPG4) as a CAR-target antigen for a variety of different cancer entities. In particul ar, we discuss merits and challenges associated with CSPG4-CAR-T cells for t he ATT of melanoma, leukemia, glioblastoma, and triple-negative breast cance r.
Journal Title: International journal of molecular sciences

PUBMED ID: 31766326
DOI: doi.org/10.3390/jcm8122031
Titolo: Regorafenib CSF Penetration, Efficacy, and MRI Patterns in Recurrent Malignant Glioma Patients.
Autori: Zeiner PS., Kinzig M., Divé I., Maurer GD., Filipski K., Harter PN., Senft C., Bähr O., Hattingen E., Steinbach JP., Sörgel F., Voss M., Steidl E ., Ronellenfitsch MW.
Data di Pubblicazione: 2019-11-27
Abstract: (1) Background: The phase 2 Regorafenib in Relapsed Glioblastoma (REGOMA) trial indicated a survival benefit for patients with first recurrenc e of a glioblastoma when treated with the multikinase inhibitor regorafenib (REG) instead of lomustine. The aim of this retrospective study was to inves tigate REG penetration to cerebrospinal fluid (CSF), treatment efficacy, and effects on magnetic resonance imaging (MRI) in patients with recurrent high-grade gliomas. (2) Methods: Patients were characterized by histology, advers e events, steroid treatment, overall survival (OS), and MRI growth pattern. REG and its two active metabolites were quantified by liquid chromatography/ tandem mass spectrometry in patients' serum and CSF. (3) Results: 21 patient s mainly with IDH-wildtype glioblastomas who had been treated with REG were retrospectively identified. Thirteen CFS samples collected from 3 patients o f the cohort were available for pharmacokinetic testing. CSF levels of REG a nd its metabolites were significantly lower than in serum. Follow-up MRI was available in 19 patients and showed progressive disease (PD) in all but 2 pa tients. Two distinct MRI patterns were identified: 7 patients showed classic PD with progression of contrast enhancing lesions, whereas 11 patients showe d a T2-dominant MRI pattern characterized by a marked reduction of contrast enhancement. Median OS was significantly better in patients with a T2-domina nt growth pattern (10 vs. 27 weeks respectively,
Journal Title: Journal of clinical medicine

PUBMED ID: 31760930
DOI: doi.org/10.2174/1389557519666191018155426
Titolo: Will Arsenic Trioxide Benefit Treatment of Solid Tumor by Nano- Enca psulation?
Autori: Fu X., Li YS., Zhao J., Yu LL., Luo RG., Liang QR., Tang Q.
Data di Pubblicazione: 2019-11-26
Abstract: Arsenic trioxide (ATO) has remarkably enhanced therapeutic efficac y in treating both newly diagnosed and relapsed patients suffering from Acut e Promyelocytic Leukemia (APL). Unfortunately, whether as a single agent, co mponent of combined chemotherapy, or as a chemosensitizer or radiosensitizer combined with interventional therapy/radiotherapy, it did not benefit treatm ent of solid tumor (liver cancer, bladder cancer, glioma, breast cancer, cer vical cancer, colorectal cancer, lung cancer, and melanoma) as seen from the clinical trials reported from the published journals or FDA-approved trials in the past decades. The clinical outcome failed to live up to our expectati ons, which was attributed to severe systemic toxicity and inappropriate phar macokinetic such as low delivery efficiency and rapid renal elimination. Nan

omedicine is designed to fuel up pharmaceuticals and polish off adverse effe cts by the moderation of their absorption, distribution, metabolism, and exc retion. Nevertheless, quite a few nanodrugs (such as Doxil, Abraxane) were a pproved to be used clinically, and "from bench to bedside" it seems to be no easy way for most of them, such as nano-ATO. Encapsulating ATO into several types of nano-vehicles (liposome, polymer micelle, porous silicon, etc.), na no-TO can improve pharmacokinetic and become a prominent candidate to penetr ate into tumor tissue, but so far no nano- ATO clinical trials have been app roved around the world. On summarizing the clinical trials of ATO on solid t umor and preclinical study of nano-ATO, it is believed there is still a chan ce for ATO to play a critical co-helper in a comprehensive therapy to fight with solid tumor.
Journal Title: Mini reviews in medicinal chemistry

PUBMED ID: 31756059
DOI: doi.org/10.1002/cam4.2616
Titolo: Similar overall survival with reduced vs. standard dose bevacizumab monotherapy in progressive glioblastoma.
Autori: Gleeson JP., Keane F., Keegan NM., Mammadov E., Harrold E., Alhusain i A., Harte J., Eakin-Love A., O'Halloran PJ., MacNally S., Hennessy BT., Br eathnach OS., Grogan L., Morris PG.
Data di Pubblicazione: 2019-11-23
Abstract: In this retrospective study, reduced-dose bevacizumab schedule res ulted in similar OS to standard-dose bevacizumab monotherapy with substantia l cost savings. MGMT methylation appears to convey a survival benefit in the setting of bevacizumab treatment for progressive GBM.
Journal Title: Cancer medicine

PUBMED ID: 31755915
DOI: doi.org/10.1093/neuonc/noz185
Titolo: Window-of-opportunity clinical trial of pembrolizumab in patients wi th recurrent glioblastoma reveals predominance of immune-suppressive macroph ages.
Autori: de Groot J., Penas-Prado M., Alfaro-Munoz K., Hunter K., Pei BL., O' Brien B., Weathers SP., Loghin M., Kamiya Matsouka C., Yung WKA., Mandel J., Wu J., Yuan Y., Zhou S., Fuller GN., Huse J., Rao G., Weinberg JS., Prabhu S S., McCutcheon IE., Lang FF., Ferguson SD., Sawaya R., Colen R., Yadav SS., Blando J., Vence L., Allison J., Sharma P., Heimberger AB.
Data di Pubblicazione: 2019-11-23
Abstract: Immune analyses indicated that pembrolizumab anti-programmed cell death 1 (PD-1) monotherapy alone can't induce effector immunologic response in most GBM patients, probably owing to a scarcity of T cells within the tum or microenvironment and a CD68+ macrophage preponderance.
Journal Title: Neuro-oncology

PUBMED ID: 31741234
DOI: doi.org/10.1007/s11060-019-03344-3
Titolo: A multi-institutional analysis of clinical outcomes and patterns of care of 1p/19q codeleted oligodendrogliomas treated with adjuvant or salvage radiation therapy.
Autori: Lin AJ., Kane LT., Molitoris JK., Smith DR., Dahiya S., Badiyan SN., Wang TJC., Kruser TJ., Huang J.
Data di Pubblicazione: 2019-11-20
Abstract: Delaying RT for selected oligodendroglioma patients appears safe. Adjuvant chemotherapy does not delay sRT longer than observation and may be associated with worse PFS after RT.
Journal Title: Journal of neuro-oncology

PUBMED ID: 31728883
DOI: doi.org/10.1007/s11060-019-03340-7
Titolo: Hypofractionated radiotherapy with temozolomide in diffuse intrinsic pontine gliomas: a randomized controlled trial.
Autori: Izzuddeen Y., Gupta S., Haresh KP., Sharma D., Giridhar P., Rath GK.
Data di Pubblicazione: 2019-11-16
Abstract: The above study shows that hypofractionated radiotherapy with conc urrent and adjuvant temozolomide does not improve OS and has higher hematolo gical toxicity. Conventional radiotherapy remains the standard of care.
Journal Title: Journal of neuro-oncology

PUBMED ID: 31672491
DOI: doi.org/10.1016/j.canlet.2019.10.034
Titolo: Imatinib revives the therapeutic potential of metformin on ewing sar coma by attenuating tumor hypoxic response and inhibiting convergent signali ng pathways.
Autori: Nan X., Wang J., Cheng H., Yin Z., Sheng J., Qiu B., Lau CC., Yustei n JT., Zhao H., Wong STC.
Data di Pubblicazione: 2019-11-02
Abstract: Ewing sarcoma (EwS) is an aggressive pediatric tumor treated with intensive cytotoxic chemotherapies. Overall survival for metastatic or relap sed disease is only 20-30%. Metformin has long been an attractive therapeuti c option for EwS, but hypoxia limits its efficacy. Through a systematic inte gration of drug combination screening, bioinformatics analyses, functional a nd in vivo studies, and correlation with clinical outcome, we identified ano ther known drug, imatinib that could augment the in vivo anti-tumor capacity of metformin by attenuating tumor hypoxic response. This drug combination re gimen widely suppressed multiple dominant mechanisms in EwS genesis, growth, and metastasis, including key EWS-FLI1 downstream targets that converge into the PI3K/AKT/mTOR signaling pathway. In addition, the combination significan tly enhanced inhibition on tumor cell proliferation by standard EwS chemothe rapy drugs, including cyclophosphamide and ifosfamide. This suggests a poten tial clinical benefit of the metformin/imatinib combination by allowing the reduction in dose intensity of standard chemotherapy without compromising su rvival outcome and represents a potential faster track application for EwS p atients.
Journal Title: Cancer letters

PUBMED ID: 31643011
DOI: doi.org/10.1007/s11060-019-03304-x
Titolo: Treatment strategies for glioblastoma in older patients: age is just a number.
Autori: Youssef M., Ludmir EB., Mandel JJ., Patel AJ., Jalali A., Treiber J. , Wu J., McAleer MF., de Groot JF.
Data di Pubblicazione: 2019-10-24
Abstract: Our cohort of elderly GBM patients was predominantly treated with standard of care therapy based on EORTC 22,981. Despite their age, these pat ients generally tolerated treatment well and had favorable outcomes compared to those reported for patients treated on EORTC 22,981. Based on these findi ngs, using advanced age as the basis for treatment de-escalation or as an ex clusionary criterion in clinical trials should be discouraged.
Journal Title: Journal of neuro-oncology

PUBMED ID: 31625205
DOI: doi.org/10.1111/neup.12594

Titolo: Analysis of PD-L1 expression and T cell infiltration in different molecular subgroups of diffuse midline gliomas.
Autori: Jha P., Manjunath N., Singh J., Mani K., Garg A., Kaur K., Sharma MC., Raheja A., Suri A., Sarkar C., Suri V.
Data di Pubblicazione: 2019-10-19
Abstract: Diffuse midline gliomas (DMGs) are rare and devastating tumors with limited therapeutic options. Programmed death-ligand 1 (PD-L1) expression represents a potential predictive biomarker for immunotherapy. One hundred and twenty-six DMGs (89 adult and 37 pediatric) were assessed for immune profile (PD-L1, cluster of differentiation (CD3, CD8) and genetic markers (mutation in 27th amino acid of histone H3 (H3K27M), alpha thalassemia/mental retardation syndrome X-linked (ATRX), isocitrate dehydrogenase 1 (IDH1), p53) by immunohistochemistry. Sanger sequencing was done for IDH1 and H3K27M. The thalamus was the commonest site. Four molecular subgroups of DMGs were identified. H3K27M mutation was more frequent in children (P = 0.0001). The difference in median overall survival (OS) was not significant in any of the four molecular subgroups (P >0.05). PD-L1 expression was significantly higher in H3K27M/IDH1 double-negative adult glioblastomas (GBMs) (P =0.002). Strong PD-L1 expression was more frequent in grade IV tumors and thalamic location, although the difference was not significant (P = 0.14 and P = 0.19 respectively). Positive PD-L1 expression was significantly associated with high tumor-infiltrating lymphocytes count (P<0.05). There was no significant difference in median OS in PD-L1-positive versus negative cases among four genetic subgroups (P >0.05). On univariate analysis, there was no direct correlation of PD-L1 with any genetic alteration, except H3K27M mutation (P = 0.01). CD3 infiltration was similar in both adults and pediatric ages (84.3% and 78.4%, respectively) while CD8 expression was significantly greater in adults compared to children (74.1% vs 37.8%, P = 0.0001). This is the first comprehensive analysis highlighting molecular and immune profiles of DMGs. Despite molecular and clinicopathological diversity, overall survival in DMGs remains dismal. Multicentric studies with larger numbers of cases should be undertaken for stratifying DMGs according to their age, immune and molecular profiles, to develop effective immunotherapies.
Journal Title: Neuropathology : official journal of the Japanese Society of Neuropathology

PUBMED ID: 31624332
DOI: doi.org/10.1038/s41397-019-0107-z
Titolo: ABCB1 single-nucleotide variants and survival in patients with glioblastoma treated with radiotherapy concomitant with temozolomide.
Autori: Malmström A., Łysiak M., Åkesson L., Jakobsen I., Mudaisi M., Milos P., Hallbeck M., Fomichov V., Broholm H., Grunnet K., Poulsen HS., Bratthäll C., Strandeus M., Papagiannopoulou A., Stenmark-Askmalm M., Green H., Söderkvist P.
Data di Pubblicazione: 2019-10-19
Abstract: Standard treatment for glioblastoma (GBM) patients is surgery and radiochemotherapy (RCT) with temozolomide (TMZ). TMZ is a substrate for ABCB1, a transmembrane drug transporter. It has been suggested that survival for GBM patients receiving TMZ is influenced by different single-nucleotide variants (SNV) of ABCB1. We therefore examined SNV:s of ABCB1, namely 1199G>A, 1236C>T, 2677G>T/A, and 3435C>T and correlated to survival for GBM patients receiving RCT. In a pilot cohort (97 patients) a significant correlation to survival was found for SNV 1199G>A, with median OS for variant G/G patients being 18.2 months versus 11.5 months for A/G (p=0.012). We found no correlation to survival for the other SNV:s. We then expanded the cohort to 179 patients (expanded cohort) and also included a confirmatory cohort (49 patients) focusing on SNV 1199G>A. Median OS for G/G versus A/G plus A/A was 15.7 and 11.5 months, respectively (p=0.085) for the expanded cohort and 13.8 versus

16.8 months (p=0.19) for the confirmatory. In conclusion, in patients with GBM receiving RCT with TMZ, no correlation with survival was found for the SNV:s 1236C>T, 2677G>T/A, and 3435C>T of ABCB1. Although the SNV 1199G>A might have some impact, a clinically significant role could not be confirmed.
Journal Title: The pharmacogenomics journal

PUBMED ID: 31568700
DOI: doi.org/10.1002/cam4.2583
Titolo: MIR155HG is a prognostic biomarker and associated with immune infiltration and immune checkpoint molecules expression in multiple cancers.
Autori: Peng L., Chen Z., Chen Y., Wang X., Tang N.
Data di Pubblicazione: 2019-10-01
Abstract: In recent years, immune checkpoint inhibitor has achieved remarkable success in multiple cancer treatment. However, how to pre-judge which patients are suitable for immune checkpoint inhibitor is a difficult problem. We use the existing public bioinformatics database to comprehensively analyze the relationship between clinical data of various cancers with immune checkpoint blocking molecules and long non-coding RNAs (lncRNAs), and try to find the potential predictive value of lncRNA for immunotherapy with checkpoint inhibitors. In this study, we found that: (a) high expression of lncRNA MIR155 host gene (MIR155HG) was closely related to better overall survival (OS) in cholangiocarcinoma (CHOL), lung adenocarcinoma (LUAD), and skin cutaneous melanoma (SKCM), and have better disease-free survival (DFS) in CHOL. Meanwhile, the high level of MIR155HG was associated with poorer OS in glioblastoma multiforme (GBM), kidney renal clear cell carcinoma (KIRC), brain lower grade glioma (LGG), and uveal melanoma (UVM). (b) The expression of MIR155HG was significantly correlated with infiltrating levels of immune cells and immune molecules, especially with immune checkpoint molecules such as programmed cell death protein 1 (PD-1), PD-1 ligand 1 (PD-L1), and cytotoxic T lymphocyte-associated antigen 4 (CTLA4) in most kinds of cancers. (c) Detection of clinical CHOL and liver hepatocellular carcinoma tissues confirmed that there was a strong positive correlation between MIR155HG expression and the levels of CTLA4 and PD-L1. MIR155 host gene can be used as a prognostic marker in multiple cancers, and of great value in predicting the curative effect of immune checkpoint inhibitor therapy owing to it is closely related with immune cells infiltration and immune checkpoint molecules expression.
Journal Title: Cancer medicine

PUBMED ID: 31561219
DOI: doi.org/10.3171/2019.6.JNS19409
Titolo: Impact of facility type and volume in low-grade glioma outcomes.
Autori: Zhu P., Du XL., Blanco AI., Ballester LY., Tandon N., Berger MS., Zhu JJ., Esquenazi Y.
Data di Pubblicazione: 2019-09-28
Abstract: This study provides evidence of survival benefits among LGG patients treated at HVFs and ACs. An increased likelihood of undergoing resections, receiving adjuvant therapies, having shorter LOSs, and the multidisciplinary environment typically found at ACs and HVFs are important contributors to the authors' finding.
Journal Title: Journal of neurosurgery

PUBMED ID: 31556015
DOI: doi.org/10.1007/s11060-019-03277-x
Titolo: Efficacy of initial temozolomide for high-risk low grade gliomas in a phase II AINO (Italian Association for Neuro-Oncology) study: a post-hoc analysis within molecular subgroups of WHO 2016.

Autori: Rudà R., Pellerino A., Pace A., Carapella CM., Dealis C., Caroli M., Faedi M., Bello L., Migliore E., Marchese G., Bertero L., Cassoni P., Soffietti R.
Data di Pubblicazione: 2019-09-27
Abstract: The beneficial effects of initial temozolomide prevail in oligodendrogliomas IDH-mutant and 1p/19q codeleted: thus, these tumors, when incompletely resected or progressive after surgery alone, or with intractable seizures, should receive temozolomide as initial treatment with salvage radiotherapy and/o reoperation and/or second-line chemotherapy at recurrence.
Journal Title: Journal of neuro-oncology

PUBMED ID: 31527881
DOI: doi.org/10.1371/journal.pcbi.1006789
Titolo: 3D spatial organization and network-guided comparison of mutation profiles in Glioblastoma reveals similarities across patients.
Autori: Dincer C., Kaya T., Keskin O., Gursoy A., Tuncbag N.
Data di Pubblicazione: 2019-09-19
Abstract: Glioblastoma multiforme (GBM) is the most aggressive type of brain tumor. Molecular heterogeneity is a hallmark of GBM tumors that is a barrier in developing treatment strategies. In this study, we used the nonsynonymous mutations of GBM tumors deposited in The Cancer Genome Atlas (TCGA) and applied a systems level approach based on biophysical characteristics of mutations and their organization in patient-specific subnetworks to reduce inter-patient heterogeneity and to gain potential clinically relevant insights. Approximately 10% of the mutations are located in "patches" which are defined as the set of residues spatially in close proximity that are mutated across multiple patients. Grouping mutations as 3D patches reduces the heterogeneity across patients. There are multiple patches that are relatively small in oncogenes, whereas there are a small number of very large patches in tumor suppressors. Additionally, different patches in the same protein are often located at different domains that can mediate different functions. We stratified the patients into five groups based on their potentially affected pathways that are revealed from the patient-specific subnetworks. These subnetworks were constructed by integrating mutation profiles of the patients with the interactome data. Network-guided clustering showed significant association between the groups and patient survival (P-value = 0.0408). Also, each group carries a set of signature 3D mutation patches that affect predominant pathways. We integrated drug sensitivity data of GBM cell lines with the mutation patches and the patient groups to analyze the possible therapeutic outcome of these patches. We found that Pazopanib might be effective in Group 3 by targeting CSF1R. Additionally, inhibiting ATM that is a mediator of PTEN phosphorylation may be ineffective in Group 2. We believe that from mutations to networks and eventually to clinical and therapeutic data, this study provides a novel perspective in the network-guided precision medicine.
Journal Title: PLoS computational biology

PUBMED ID: 31521589
DOI: doi.org/10.1016/j.jgo.2019.08.014
Titolo: Failure to complete standard radiation therapy in glioblastoma patients: Patterns from a national database with implications for survival and therapeutic decision making in older glioblastoma patients.
Autori: Burton E., Yusuf M., Gilbert MR., Gaskins J., Woo S.
Data di Pubblicazione: 2019-09-16
Abstract: Failure to complete standard chemoradiation was associated with decreased survival in our cohort. Patients with risk factors for failure (like advanced age) should be considered for alternative treatments such as hypofractionated radiotherapy.
Journal Title: Journal of geriatric oncology

PUBMED ID: 31515159
DOI: doi.org/10.1016/j.jfma.2019.08.024
Titolo: Clinical implications of multiple glioblastomas: An analysis of prog nostic factors and survival to distinguish from their single counterparts.
Autori: Shieh LT., Guo HR., Chang YK., Lu NM., Ho SY.
Data di Pubblicazione: 2019-09-14
Abstract: Patients with multiple GBMs had worse survival compared to those w ith single GBM. GBM patients without post-operative radiotherapy were also a predictor of worse survival.
Journal Title: Journal of the Formosan Medical Association = Taiwan yi zhi

PUBMED ID: 31514200
DOI: doi.org/10.1159/000502483
Titolo: Open-Label Phase II Evaluation of Imatinib in Primary Inoperable or Incompletely Resected and Recurrent Glioblastoma.
Autori: Sautter L., Hofheinz R., Tuettenberg J., Grimm M., Vajkoczy P., Grod en C., Schmieder K., Hochhaus A., Wenz F., Giordano FA.
Data di Pubblicazione: 2019-09-13
Abstract: Imatinib showed no measurable activity in patients with newly diag nosed or recurrent glioblastoma.
Journal Title: Oncology

PUBMED ID: 31502042
DOI: doi.org/10.1007/s11060-019-03286-w
Titolo: CBX3 promotes glioma U87 cell proliferation and predicts an unfavora ble prognosis.
Autori: Zhao SP., Wang F., Yang M., Wang XY., Jin CL., Ji QK., Li S., Zhao X L.
Data di Pubblicazione: 2019-09-11
Abstract: In the present study, CBX3 was demonstrated to be highly expressed in human glioma tissues, and high CBX3 expression predicted the dismal recur rence-free survival (RFS) and poor overall survival (OS) for glioma patients . High CBX3 expression was dependent on the tumor size, Karnofsky performanc e scale (KPS) score, WHO grade, recurrence and survival status. Moreover, CB X3 expression knockdown could remarkably suppress the proliferation and colo ny formation ability of U87 cells, which was achieved through blocking cell arrest at G0/G1 phase and inducing apoptosis. Additionally, our findings als o suggested that, compared with shRNA-Ctrl transfection, the mRNA and protei n expression levels of CDKN1A have been dramatically up-regulated in vitro a fter transfection with shRNA-CBX3. Consistent with the results of in vitro a ssays, the outcomes of xenograft assay and immunohistochemistry (IHC) also i ndicated that, the tumor growth and Ki-67 expression level were restrained i n response to CBX3 inhibition, while the CDKN1A expression level in vivo was up-regulated. Down-regulation of CDKN1A expression partially restored the ab ility of cell proliferation in the U87 cells, which was inhibited by shRNA-C BX3 CONCLUSIONS: In conclusion, results of the current research suggest that a high CBX3 expression level predicts the poor prognosis for glioma patients . CBX3 can stimulate the growth of glioma U87 cells through targeting CDKN1A and CBX3 may become a novel target in the clinical treatment for glioma.
Journal Title: Journal of neuro-oncology

PUBMED ID: 31480064
DOI: doi.org/10.1159/000501913
Titolo: Medulloblastoma: Distinctive Histo-Molecular Correlation with Clinic al Profile, Radiologic Characteristics, and Surgical Outcome.

Autori: Narayan V., Sugur H., Jaiswal J., Arvinda HR., Arivazhagan A., Soman na S., Santosh V.
Data di Pubblicazione: 2019-09-04
Abstract: Majority of the patients were pediatric in the study. Age, hemisph eric location of tumor, extent of resection, and adjuvant treatment status w ere the important clinical prognostic factors for survival. Surgery for MB i s formidable, and VPS can be considered in persistent symptomatic and progre ssive HCP. Our study on pediatric and adult MB validates the prognostic sign ificance of various clinical, radiologic, and histo-molecular parameters of MB.
Journal Title: Pediatric neurosurgery

PUBMED ID: 31435963
DOI: doi.org/10.1111/bpa.12782
Titolo: Clinical relevance of molecular subgrouping of gliomatosis cerebri p er 2016 WHO classification: a clinicopathological study of 89 cases.
Autori: Kwon MJ., Kang SY., Cho H., Lee JI., Kim ST., Suh YL.
Data di Pubblicazione: 2019-08-23
Abstract: The extremely invasive phenotypes and genotypes related to progres sion of gliomatosis cerebri (GC) remain unclear although GC has been removed as an independent entity from the 2016 WHO classification. Hence, categoriza tion of GC under the current WHO molecular classification is essential, and the molecular subgroups that might contribute to GC progression should be co mpared with the histopathological differences between initial and new lesion s identified during follow-up. Analyses of IDH1/2 and TERTp mutations and 1p /19q co-deletion, and immunohistochemistry of IDH1-R132H, ATRX, p53 and gale ctin-3 were performed. Anaplastic astrocytoma, IDH-wildtype (AA-IDHwt) was t he common molecular subgroup (52.8%), followed by diffuse astrocytoma, IDH-w ildtype (DA-IDHwt) and AA, IDH-mutant (AA-IDHmt) (each 16.9%), DA-IDHmt (7.9 %), glioblastoma (GBM)-IDHwt (3.3%) and GBM-IDHmt (2.2%). Approximately 92% of the AA-IDHwt lesions progressed to histologically confirmed GBM in the ne wly enhanced lesions harboring the TERTp mutation and expressing galectin-3. Similar to primary GBMs, GC-related GBMs that progressed from the IDHwt subg roups showed microvascular proliferation, palisading necrosis or thrombotic occlusion, implying that a subset of IDHwt subgroups may evolve to overt GBM . Molecular subgrouping did not provide the perfect prediction for the survi val of GC patients. The AA-IDHwt group showed worse overall and progression- free survival (PFS) than the AA-IDHmt group. Biopsy plus radiotherapy, chemo therapy and temozolomide treatment for DA-IDHwt, and resection plus radiothe rapy and temozolomide treatment for AA-IDHwt prolonged PFS. In conclusions, majority of GC was of the AA-IDHwt subgroup, which progressed to GBM. Molecu lar subgroups may assist in the selection of treatment modalities, because " GC pattern" still remains as a special growth of gliomas in WHO 2016 classif ication without established treatment guideline.
Journal Title: Brain pathology (Zurich, Switzerland)

PUBMED ID: 31427235
DOI: doi.org/10.1016/j.jocn.2019.08.039
Titolo: Pretreatment intratumoral susceptibility signals correlate with resp onse to high-dose methotrexate and progression-free survival in primary cent ral nervous system lymphoma.
Autori: Deguchi S., Nakashima K., Muramatsu K., Mitsuya K., Oishi T., Shirat a K., Hayashi N., Sugino T., Endo M., Nakasu Y.
Data di Pubblicazione: 2019-08-21
Abstract: We aimed to estimate the frequency of intratumoral susceptibility signals (ITSS) in susceptibility-weighted imaging (SWI) in consecutive patie nts with primary central nervous system lymphoma (PCNSL), and to determine i f pretreatment heterogeneity of PCNSL is predictive of response to chemother

apy by using ITSS on SWI. We retrospectively examined 29 immunocompetent pat ients with PCNSL who underwent SWI-MRI before treatment. A univariate analys is was conducted with Fisher's exact test. Progression free survival (PFS) w as calculated by the Kaplan-Meier method and compared by the log rank test. The patients, including 16 males, were initially treated at a median age of 69 years. All tissue types were diffuse large B-cell lymphoma. Nineteen patie nts (66%) presented lesions with ITSS. Sixteen patients (55%) received initi al treatment with R-MTX (rituximab plus high-dose methotrexate). Seven out o f nine patients with ITSS exhibited a poor response, whereas all seven witho ut ITSS exhibited a good response to R-MTX. Regarding the absence of ITSS, t he sensitivity, specificity, and diagnostic accuracy for a good response to R-MTX were 0.78, 1.00, and 0.88, respectively. Patients without ITSS showed significantly longer PFS compared to patients with ITSS (median PFS: 28.9 vs 2.1 months, $P < 0.01$). In conclusion, ITSS in PCNSL patients were more common than previously reported. We have to be careful to use ITSS for differentiat ing PCNSL and glioblastoma. Presence of ITSS correlated significantly with t herapeutic response to R-MTX. ITSS may be a new marker for the response to c hemotherapy in patients with PCNSL. A prospective multi-institutional analys is is needed.
Journal Title: Journal of clinical neuroscience : official journal of the Ne urosurgical Society of Australasia

PUBMED ID: 31400262
DOI: doi.org/10.2174/0929867326666190809221332
Titolo: Phytochemical-Mediated Glioma Targeted Treatment: Drug Resistance an d Novel Delivery Systems.
Autori: Cao H., Li X., Wang F., Zhang Y., Xiong Y., Yang Q.
Data di Pubblicazione: 2019-08-11
Abstract: Glioma, especially its most malignant type, Glioblastoma (GBM), is the most common and the most aggressive malignant tumour in the central nerv ous system. Currently, we have no specific therapies that can significantly improve its dismal prognosis. Recent studies have reported promising in vitr o experimental results of several novel glioma-targeting drugs; these studie s are encouraging to both researchers and patients. However, clinical trials have revealed that novel compounds that focus on a single, clear glioma gene tic alteration may not achieve a satisfactory outcome or have side effects t hat are unbearable. Based on this consensus, phytochemicals that exhibit mul tiple bioactivities have recently attracted much attention. Traditional Chin ese medicine and traditional Indian medicine (Ayurveda) have shown that phyt ocompounds inhibit glioma angiogenesis, cancer stem cells and tumour prolife ration; these results suggest a novel drug therapeutic strategy. However, si ngle phytocompounds or their direct usage may not reverse comprehensive mali gnancy due to poor histological penetrability or relatively unsatisfactory i n vivo efficiency. Recent research that has employed temozolomide combinatio n treatment and Nanoparticles (NPs) with phytocompounds has revealed a power ful dual-target therapy and a high blood-brain barrier penetrability, which is accompanied by low side effects and strong specific targeting. This revie w is focused on major phytocompounds that have contributed to glioma-targeti ng treatment in recent years and their role in drug resistance inhibition, a s well as novel drug delivery systems for clinical strategies. Lastly, we su mmarize a possible research strategy for the future.
Journal Title: Current medicinal chemistry

PUBMED ID: 31397594
DOI: doi.org/10.1080/09537104.2019.1652263

Titolo: Fondaparinux cross-reactivity in heparin-induced thrombocytopenia successfully treated with high-dose intravenous immunoglobulin and rivaroxaban.
Autori: Manji F., Warkentin TE., Sheppard JI., Lee A.
Data di Pubblicazione: 2019-08-10
Abstract: HIT, a prothrombotic disorder caused by heparin-dependent antibodies, is often treated with fondaparinux, usually with good outcomes. A 70-year-old female developed severe HIT (platelet count, 25 × 10
Journal Title: Platelets

PUBMED ID: 31392595
DOI: doi.org/10.1007/s11060-019-03227-7
Titolo: Phase I/II study of bevacizumab with BKM120, an oral PI3K inhibitor, in patients with refractory solid tumors (phase I) and relapsed/refractory glioblastoma (phase II).
Autori: Hainsworth JD., Becker KP., Mekhail T., Chowdhary SA., Eakle JF., Wright D., Langdon RM., Yost KJ., Padula GDA., West-Osterfield K., Scarberry M., Shaifer CA., Shastry M., Burris HA., Shih K.
Data di Pubblicazione: 2019-08-09
Abstract: The efficacy seen in this study is similar to the efficacy previously reported with single-agent bevacizumab. This regimen was poorly tolerated, despite the low daily dose of BKM120. Further development of this combination for the treatment of glioblastoma is not recommended.
Journal Title: Journal of neuro-oncology

PUBMED ID: 31386038
DOI: doi.org/10.1093/nop/npy019
Titolo: Re-irradiation for recurrent high-grade gliomas: a systematic review and analysis of treatment technique with respect to survival and risk of radionecrosis.
Autori: Shanker M., Chua B., Bettington C., Foote MC., Pinkham MB.
Data di Pubblicazione: 2019-08-07
Abstract: The published literature suggests that OS is highest after re-irradiation using SRS, followed by FSRT and conventionally fractionated radiotherapy. Whether this represents superiority of the treatment technique or an uncontrolled selection bias is uncertain. The risk of radionecrosis was low for all modalities overall. Re-irradiation is a feasible option in appropriately selected patients.
Journal Title: Neuro-oncology practice

PUBMED ID: 31369680
DOI: doi.org/10.1093/neuonc/noz131
Titolo: Temporal muscle thickness is an independent prognostic marker in patients with progressive glioblastoma: translational imaging analysis of the EORTC 26101 trial.
Autori: Furtner J., Genbrugge E., Gorlia T., Bendszus M., Nowosielski M., Golfinopoulos V., Weller M., van den Bent MJ., Wick W., Preusser M.
Data di Pubblicazione: 2019-08-02
Abstract: Reduced TMT is an independent negative prognostic parameter in patients with progressive glioblastoma and may help to facilitate patient management by supporting patient stratification for therapeutic interventions or clinical trials.
Journal Title: Neuro-oncology

PUBMED ID: 31363920
DOI: doi.org/10.1007/s00701-019-04007-y

Titolo: Intraoperative fluorescence diagnosis in the brain: a systematic rev iew and suggestions for future standards on reporting diagnostic accuracy an d clinical utility.
Autori: Stummer W., Koch R., Valle RD., Roberts DW., Sanai N., Kalkanis S., Hadjipanayis CG., Suero Molina E.
Data di Pubblicazione: 2019-08-01
Abstract: Detailed, transparent, and uniform reporting on diagnostic accurac y of intraoperative imaging methods is necessary. In the absence of such rep orting, studies will not be comparable or reproducible. Future studies shoul d consider some of the recommendations given here.
Journal Title: Acta neurochirurgica

PUBMED ID: 31360809
DOI: doi.org/10.1016/j.adro.2019.03.009
Titolo: Role of Radiation Therapy in the Management of Diffuse Intrinsic Pon tine Glioma: A Systematic Review.
Autori: Gallitto M., Lazarev S., Wasserman I., Stafford JM., Wolden SL., Ter ezakis SA., Bindra RS., Bakst RL.
Data di Pubblicazione: 2019-07-31
Abstract: As one of the largest systematic reviews examining RT for DIPG, th is report may serve as a useful tool to help clinicians choose the most appr opriate treatment approach, while also providing a platform for future inves tigations into the utility of RT and systemic therapy.
Journal Title: Advances in radiation oncology

PUBMED ID: 31345255
DOI: doi.org/10.1186/s40478-019-0774-7
Titolo: Dramatic response of BRAF V600E-mutant epithelioid glioblastoma to c ombination therapy with BRAF and MEK inhibitor: establishment and xenograft of a cell line to predict clinical efficacy.
Autori: Kanemaru Y., Natsumeda M., Okada M., Saito R., Kobayashi D., Eda T., Watanabe J., Saito S., Tsukamoto Y., Oishi M., Saito H., Nagahashi M., Sasak i T., Hashizume R., Aoyama H., Wakai T., Kakita A., Fujii Y.
Data di Pubblicazione: 2019-07-27
Abstract: Epithelioid glioblastoma is a rare aggressive variant of glioblast oma (GBM) characterized by a dismal prognosis of about 6 months and frequent leptomeningeal dissemination. A recent study has revealed that 50% of epithe lioid GBMs harbor three genetic alterations - BRAF V600E mutation, TERT prom oter mutations, and homozygous deletions of CDKN2A/2B. Emerging evidence sup port the effectiveness of targeted therapies for brain tumors with BRAF V600 E mutation. Here we describe a dramatic radiographical response to combined therapy with BRAF and MEK inhibitors in a patient with epithelioid GBM harbo ring BRAF V600E mutation, characterized by thick spinal dissemination. From relapsed tumor procured at autopsy, we established a cell line retaining the BRAF V600E mutation, TERT promoter mutation and CDKN2A/2B loss. Intracranial implantation of these cells into mice resulted in tumors closely resembling the original, characterized by epithelioid tumor cells and dissemination, an d invasion into the perivascular spaces. We then confirmed the efficacy of t reatment with BRAF and MEK inhibitor both in vitro and in vivo. Epithelioid GBM with BRAF V600E mutation can be considered a good treatment indication f or precision medicine, and this patient-derived cell line should be useful f or prediction of the tumor response and clarification of its biological char acteristics.
Journal Title: Acta neuropathologica communications

PUBMED ID: 31343422

DOI: doi.org/10.1097/COC.0000000000000564
Titolo: ENvironmental Dynamics Underlying Responsive Extreme Survivors (ENDURES) of Glioblastoma: A Multidisciplinary Team-based, Multifactorial Analytical Approach.
Autori: Johnston SK., Whitmire P., Massey SC., Kumthekar P., Porter AB., Raghunand N., Gonzalez-Cuyar LF., Mrugala MM., Hawkins-Daarud A., Jackson PR., Hu LS., Sarkaria JN., Wang L., Gatenby RA., Egan KM., Canoll P., Swanson KR., Swanson KR.
Data di Pubblicazione: 2019-07-26
Abstract: Although glioblastoma (GBM) is a fatal primary brain cancer with short median survival of 15 months, a small number of patients survive >5 years after diagnosis; they are known as extreme survivors (ES). Because of their rarity, very little is known about what differentiates these outliers from other patients with GBM. For the purpose of identifying unknown drivers of extreme survivorship in GBM, the ENDURES consortium (ENvironmental Dynamics Underlying Responsive Extreme Survivors of GBM) was developed. This consortium is a multicenter collaborative network of investigators focused on the integration of multiple types of clinical data and the creation of patient-specific models of tumor growth informed by radiographic and histologic parameters. Leveraging our combined resources, the goals of the ENDURES consortium are 2-fold: (1) to build a curated, searchable, multilayered repository housing clinical and outcome data on a large cohort of ES patients with GBM; and (2) to leverage the ENDURES repository for new insights into tumor behavior and novel targets for prolonging survival for all patients with GBM. In this article, the authors review the available literature and discuss what is already known about ES. The authors then describe the creation of their consortium and some preliminary results.
Journal Title: American journal of clinical oncology

PUBMED ID: 31324990
DOI: doi.org/10.1007/s11864-019-0673-y
Titolo: A Second Course of Radiotherapy in Patients with Recurrent Malignant Gliomas: Clinical Data on Re-irradiation, Prognostic Factors, and Usefulness of Digital Biomarkers.
Autori: Straube C., Kessel KA., Zimmer C., Schmidt-Graf F., Schlegel J., Gempt J., Meyer B., Combs SE.
Data di Pubblicazione: 2019-07-21
Abstract: The treatment of malignant gliomas has undergone a significant intensification during the past decade, and the interdisciplinary treatment team has learned that all treatment opportunities, including surgery and radiotherapy (RT), also have a central role in recurrent gliomas. Throughout the decades, re-irradiation (re-RT) has achieved a prominent place in the treatment of recurrent gliomas. A solid body of evidence supports the safety and efficacy of re-RT, especially when modern techniques are used, and justifies the early use of this regimen, especially in the case when macroscopic disease is present. Additionally, a second adjuvant re-RT to the resection cavity is currently being investigated by several investigators and seems to offer promising results. Although advanced RT technologies, such as stereotactic radiosurgery (SRS), fractionated stereotactic radiotherapy (FSRT), intensity-modulated radiotherapy (IMRT), and image-guided radiotherapy (IGRT) have become available in many centers, re-RT should continue to be kept in experienced hands so that they can select the optimal regimen, the ideal treatment volume, and the appropriate techniques from their tool-boxes. Concomitant or adjuvant use of systemic treatment options should also strongly be taken into consideration, especially because temozolomide (TMZ), cyclohexyl-nitroso-urea (CCNU), and bevacizumab have shown a good safety profile; they should be considered, if available. Nonetheless, the selection of patients for re-RT remains crucial. Single factors, such as patient age or the progression-free interval (PFI), fall too short. Therefore, powerful prognostic scores have be

en generated and validated, and these scores should be used for patient sele ction and counseling.
Journal Title: Current treatment options in oncology

PUBMED ID: 31323633
DOI: doi.org/10.3171/2019.4.JNS183395
Titolo: To treat or not to treat? A retrospective multicenter assessment of survival in patients with IDH-mutant low-grade glioma based on adjuvant trea tment.
Autori: Paľa A., Coburger J., Scherer M., Ahmeti H., Roder C., Gessler F., J ungk C., Scheuerle A., Senft C., Tatagiba M., Synowitz M., Wirtz CR., Schmit z B., Unterberg AW.
Data di Pubblicazione: 2019-07-20
Abstract: In this series of IDH-mutated LGGs, adjuvant treatment with RT, CT with temozolomide (TMZ), or the combination of both showed no significant ad vantage in terms of PFS and OS. Even in high-risk patients, the authors obse rved a similar significantly negative impact of adjuvant treatment on PFS an d OS. These results underscore the importance of a CTR in LGG. Whether patie nts ≥ 40 years old should receive adjuvant treatment despite a CTR should be a matter of debate. A potential tumor dedifferentiation by administration of early TMZ, RT, or RT+CT in IDH-mutated LGG should be considered. However, th ese data are limited by the retrospective study design and the potentially h eterogeneous indication for adjuvant treatment.
Journal Title: Journal of neurosurgery

PUBMED ID: 31315671
DOI: doi.org/10.1186/s40425-019-0673-2
Titolo: Diverse immunotherapies can effectively treat syngeneic brainstem tu mors in the absence of overt toxicity.
Autori: Schuelke MR., Wongthida P., Thompson J., Kottke T., Driscoll CB., Hu ff AL., Shim KG., Coffey M., Pulido J., Evgin L., Vile RG.
Data di Pubblicazione: 2019-07-19
Abstract: It remains imperative to regard the brainstem with caution for imm unotherapeutic intervention. Nonetheless, we show that further careful devel opment of immunotherapies for pediatric brainstem tumors is warranted to har ness the potential potency of anti-tumor immune responses, despite their pos sible toxicity within this anatomically sensitive location.
Journal Title: Journal for immunotherapy of cancer

PUBMED ID: 31297242
DOI: doi.org/10.1136/esmoopen-2019-000520
Titolo: How we treat glioblastoma.
Autori: Weller M., Le Rhun E., Preusser M., Tonn JC., Roth P.
Data di Pubblicazione: 2019-07-13
Abstract: Glioblastoma is an intrinsic brain tumour thought to arise from ne uroglial progenitor cells. Its incidence increases steadily with age. Males are moderately more often affected. Genetic predisposition and exposure to i rradiation in childhood are the only established risk factors which, however , account only for a very small proportion of glioblastomas. Surgery as safe ly feasible not only to allow for tissue diagnosis but also to reduce tumour volume is usually the first therapeutic measure. Radiotherapy delivered to t he tumour region with a safety margin has been demonstrated to roughly doubl e survival four decades ago. Temozolomide given during radiotherapy followed by six cycles of maintenance chemotherapy was the first and so far only phar macological treatment shown to prolong survival. Adding tumour-treating fiel ds during maintenance, temozolomide chemotherapy has been reported to prolon g survival. There is little evidence that any intervention at relapse improv

es outcome, but nitrosourea-based chemotherapy, commonly lomustine, is proba bly the most agreed on standard of care. Bevacizumab prolongs progression-fr ee survival and probably quality of life in the first line or recurrent sett ing, but not overall survival, and is therefore not approved in the European Union. Immunotherapy remains experimental. Drugs in advanced clinical develo pment include the programmed death 1 antibody, nivolumab, the antibody drug conjugate depatuxizumab directed to the epidermal growth factor receptor and the proteasome inhibitor marizomib.
Journal Title: ESMO open

PUBMED ID: 31292802
DOI: doi.org/10.1007/s11060-019-03236-6
Titolo: Phase II study of Dovitinib in recurrent glioblastoma.
Autori: Sharma M., Schilero C., Peereboom DM., Hobbs BP., Elson P., Stevens GHJ., McCrae K., Nixon AB., Ahluwalia MS.
Data di Pubblicazione: 2019-07-12
Abstract: Dovitinib was not efficacious in prolonging the PFS in patients wi th recurrent GBM irrespective of prior treatment with anti-angiogenic therap y (including bevacizumab).
Journal Title: Journal of neuro-oncology

PUBMED ID: 31273578
DOI: doi.org/10.1007/s11060-019-03223-x
Titolo: Phase II study of weekly carboplatin in pretreated adult malignant g liomas.
Autori: Villani V., Pace A., Vidiri A., Tanzilli A., Sperati F., Terrenato I ., Mariantonia C., Casini B., Metro G., Maschio M., Tatiana K., Cognetti F., Fabi A.
Data di Pubblicazione: 2019-07-06
Abstract: Our findings show that single agent, weekly, intravenous administr ation of carboplatin may have a role in patients with recurrent glioma and s uggest that pre-treatment with corticosteroids may confer survival benefit.
Journal Title: Journal of neuro-oncology

PUBMED ID: 31236820
DOI: doi.org/10.1007/s11060-019-03225-9
Titolo: Outcomes of salvage re-irradiation in recurrent medulloblastoma corr elate with age at initial diagnosis, primary risk-stratification, and molecu lar subgrouping.
Autori: Gupta T., Maitre M., Sastri GJ., Krishnatry R., Shirsat N., Epari S. , Sahay A., Chinnaswamy G., Patil V., Shetty P., Moiyadi A.
Data di Pubblicazione: 2019-06-26
Abstract: Salvage re-RT provides good local control and encouraging survival outcomes with acceptable toxicity in selected patients with recurrent/progre ssive MB.
Journal Title: Journal of neuro-oncology

PUBMED ID: 31225627
DOI: doi.org/10.1093/neuros/nyz212
Titolo: ABC Transporter Inhibition Plus Dexamethasone Enhances the Efficacy of Convection Enhanced Delivery in H3.3K27M Mutant Diffuse Intrinsic Pontine Glioma.
Autori: Tsvankin V., Hashizume R., Katagi H., Herndon JE., Lascola C., Venka traman TN., Picard D., Burrus B., Becher OJ., Thompson EM.
Data di Pubblicazione: 2019-06-22

Abstract: ABC transporter inhibition plus dexamethasone enhances the efficac y of CED dasatinib, resulting in enhanced tumor cellular apoptosis and impro ved survival in H3.3K27M mutant DIPG.
Journal Title: Neurosurgery

PUBMED ID: 31203194
DOI: doi.org/10.1016/j.ejca.2019.05.012
Titolo: The added value of health-related quality of life as a prognostic in dicator of overall survival and progression-free survival in glioma patients : a meta-analysis based on individual patient data from randomised controlle d trials.
Autori: Coomans M., Dirven L., K Aaronson N., Baumert BG., van den Bent M., Bottomley A., Brandes AA., Chinot O., Coens C., Gorlia T., Herrlinger U., Ke ime-Guibert F., Malmström A., Martinelli F., Stupp R., Talacchi A., Weller M ., Wick W., Reijneveld JC., Taphoorn MJB., Taphoorn MJB.
Data di Pubblicazione: 2019-06-17
Abstract: Our findings demonstrate that several baseline HRQoL variables are independently prognostic for OS and PFS, yet the added value of HRQoL to the known clinical prognostic variables was small.
Journal Title: European journal of cancer (Oxford, England : 1990)

PUBMED ID: 31170245
DOI: doi.org/10.1371/journal.pone.0217881
Titolo: Hypofractionated radiation therapy and temozolomide in patients with glioblastoma and poor prognostic factors. A prospective, single-institution experience.
Autori: Jablonska PA., Diez-Valle R., Pérez-Larraya JG., Moreno-Jiménez M., Idoate MÁ., Arbea L., Tejada S., Garcia de Eulate MR., Ramos L., Arbizu J., Domínguez P., Aristu JJ.
Data di Pubblicazione: 2019-06-07
Abstract: Patients with poor clinical factors other than advanced age can be selected for hypofractionated radiotherapy. The OS and PFS rates obtained in our series are similar to those in patients treated with standard fractionat ion, assuring good treatment adherence, low rates of toxicity and probable i mproved cost-effectiveness.
Journal Title: PloS one

PUBMED ID: 31154523
DOI: doi.org/10.1007/s00280-019-03879-2
Titolo: Safety, tolerability, and pharmacokinetics of anti-EGFRvIII antibody -drug conjugate AMG 595 in patients with recurrent malignant glioma expressi ng EGFRvIII.
Autori: Rosenthal M., Curry R., Reardon DA., Rasmussen E., Upreti VV., Damor e MA., Henary HA., Hill JS., Cloughesy T.
Data di Pubblicazione: 2019-06-03
Abstract: AMG 595 exhibited favorable pharmacokinetics and is a unique thera py with possible benefit for some patients with EGFRvIII-mutated GBM with li mited therapeutic options.
Journal Title: Cancer chemotherapy and pharmacology

PUBMED ID: 31124566
DOI: doi.org/10.1093/annonc/mdz164
Titolo: Molecular pathology of tumors of the central nervous system.
Autori: Kristensen BW., Priesterbach-Ackley LP., Petersen JK., Wesseling P.
Data di Pubblicazione: 2019-05-25

Abstract: Since the update of the 4th edition of the WHO Classification of C
entral Nervous System (CNS) Tumors published in 2016, particular molecular c
haracteristics are part of the definition of a subset of these neoplasms. Th
is combined 'histo-molecular' approach allows for a much more precise diagno
sis of especially diffuse gliomas and embryonal CNS tumors. This review prov
ides an update of the most important diagnostic and prognostic markers for s
tate-of-the-art diagnosis of primary CNS tumors. Defining molecular markers
for diffuse gliomas are IDH1/IDH2 mutations, 1p/19q codeletion and mutations
in histone H3 genes. Medulloblastomas, the most frequent embryonal CNS tumor
s, are divided into four molecularly defined groups according to the WHO 201
6 Classification: wingless/integrated (WNT) signaling pathway activated, son
ic hedgehog (SHH) signaling pathway activated and tumor protein p53 gene (TP
53)-mutant, SHH-activated and TP53-wildtype, and non-WNT/non-SHH-activated.
Molecular characteristics are also important for the diagnosis of several ot
her CNS tumors, such as RELA fusion-positive subtype of ependymoma, atypical
teratoid rhabdoid tumor (AT/RT), embryonal tumor with multilayered rosettes,
and solitary fibrous tumor/hemangiopericytoma. Immunohistochemistry is a hel
pful alternative for further molecular characterization of several of these
tumors. Additionally, genome-wide methylation profiling is a very promising
new tool in CNS tumor diagnostics. Much progress has thus been made by trans
lating the most relevant molecular knowledge into a more precise clinical di
agnosis of CNS tumors. Hopefully, this will enable more specific and more ef
fective therapeutic approaches for the patients suffering from these tumors.
Journal Title: Annals of oncology : official journal of the European Society
for Medical Oncology

PUBMED ID: 31119479
DOI: doi.org/10.1007/s11060-019-03194-z
Titolo: Phase I-II trial of imatinib mesylate (Gleevec; STI571) in treatment
of recurrent oligodendroglioma and mixed oligoastrocytoma. North central can
cer treatment group study N0272 (ALLIANCE/NCCTG).
Autori: Jaeckle KA., Anderson SK., Twohy EL., Dixon JG., Giannini C., Jenkin
s R., Egorin MJ., Sarkaria JN., Brown PD., Flynn PJ., Schwerkoske J., Buckne
r JC., Galanis E.
Data di Pubblicazione: 2019-05-24
Abstract: Although adequate plasma levels were achieved, the observed PFS6 o
f 33% did not reach our pre-defined threshold for success. Although OS was l
onger in imatinib-treated patients than controls, this finding would require
forward validation in a larger cohort. Imatinib might show greater activity
in a population enriched for PDGF-dependent pathway activation in tumor tiss
ue.
Journal Title: Journal of neuro-oncology

PUBMED ID: 31113843
DOI: doi.org/10.1158/1078-0432.CCR-18-3850
Titolo: Overall Survival in Malignant Glioma Is Significantly Prolonged by N
eurosurgical Delivery of Etoposide and Temozolomide from a Thermo-Responsive
Biodegradable Paste.
Autori: Smith SJ., Tyler BM., Gould T., Veal GJ., Gorelick N., Rowlinson J.,
Serra R., Ritchie A., Berry P., Otto A., Choi J., Skuli N., Estevez-Cebrero
M., Shakesheff KM., Brem H., Grundy RG., Rahman R.
Data di Pubblicazione: 2019-05-23
Abstract: The significant survival benefit of intracavity chemotherapy demon
strates clinical applicability of PLGA/PEG paste-mediated delivery of temozo
lomide and etoposide adjuvant to radiotherapy. PLGA/PEG paste offers a futur
e platform for combination delivery of molecular targeted compounds.
Journal Title: Clinical cancer research : an official journal of the America
n Association for Cancer Research

PUBMED ID: 31089718
DOI: doi.org/10.1093/neuonc/noz071
Titolo: Regorafenib in advanced high-grade glioma: a retrospective bicentric analysis.
Autori: Tzaridis T., Gepfner-Tuma I., Hirsch S., Skardelly M., Bender B., Paulsen F., Schaub C., Weller J., Schäfer N., Herrlinger U., Tabatabai G.
Data di Pubblicazione: 2019-05-16
Abstract:
Journal Title: Neuro-oncology

PUBMED ID: 31076534
DOI: doi.org/10.1212/WNL.0000000000007643
Titolo: Imaging necrosis during treatment is associated with worse survival in EORTC 26101 study.
Autori: Nowosielski M., Gorlia T., Bromberg JEC., Sahm F., Harting I., Kickingereder P., Brandes AA., Taphoorn MJB., Taal W., Domont J., Idbaih A., Campone M., Clement PM., Weller M., Fabbro M., Le Rhun E., Platten M., Golfinopoulos V., van den Bent MJ., Bendszus M., Wick W.
Data di Pubblicazione: 2019-05-12
Abstract: Increase of and new development of imaging necrosis during treatment is a negative prognostic factor for patients with progressive glioblastoma. These data call for consideration of integrating the assessment of imaging necrosis as a separate item into the MRI response assessment criteria.
Journal Title: Neurology

PUBMED ID: 31060906
DOI: doi.org/10.1016/j.ebiom.2019.04.043
Titolo: Potent anti-tumor efficacy of palbociclib in treatment-naïve H3.3K27M-mutant diffuse intrinsic pontine glioma.
Autori: Sun Y., Sun Y., Yan K., Li Z., Xu C., Geng Y., Pan C., Chen X., Zhang L., Xi Q.
Data di Pubblicazione: 2019-05-08
Abstract: Our findings thus revealed that palbociclib could be the therapeutic strategy for treatment-naïve DIPG with H3.3K27M mutation. FUND: Beijing Municipal Administration of Hospitals Clinical Medicine Development of Special Funding Support, Beijing Municipal Natural Science Foundation, Ministry of Science and Technology of China, and National Natural Science Foundation of China.
Journal Title: EBioMedicine

PUBMED ID: 31050315
DOI: doi.org/10.1080/13696998.2019.1614933
Titolo: Tumor treating fields and maintenance temozolomide for newly-diagnosed glioblastoma: a cost-effectiveness study.
Autori: Guzauskas GF., Pollom EL., Stieber VW., Wang BCM., Garrison LP.
Data di Pubblicazione: 2019-05-04
Abstract: Our findings thus revealed that palbociclib could be the therapeutic strategy for treatment-naïve DIPG with H3.3K27M mutation. FUND: Beijing Municipal Administration of Hospitals Clinical Medicine Development of Special Funding Support, Beijing Municipal Natural Science Foundation, Ministry of Science and Technology of China, and National Natural Science Foundation of China.
Journal Title: Journal of medical economics

PUBMED ID: 31038851
DOI: doi.org/10.1002/cam4.2192
Titolo: Immune microenvironments differ in immune characteristics and outcom
e of glioblastoma multiforme.
Autori: Zhang B., Shen R., Cheng S., Feng L.
Data di Pubblicazione: 2019-05-01
Abstract: Understanding the interactions between tumors and the host immune
system holds great promise to uncover biomarkers for targeted therapies, pre
dict the prognosis of patients and guide clinical treatment. However, the im
mune signatures of glioblastoma multiforme (GBM) remain largely unstudied in
terms of systematic analyses. We aimed to classify GBM samples according to
immune-related genes and complement the existing immunotherapy system knowle
dge. In this study, we designed a strategy to identify 3 immune subtypes rep
resenting 3 different immune microenvironments (M1-M3) and associated with p
rognosis. The 3 subtypes were significantly different in terms of specific i
mmune characteristics (immune cell subpopulations, immune responses, immune
cells, and checkpoint gene interactions). In additional, copy number variati
ons and methylation changes were identified that correlated with genes relat
ed to a worse prognosis subtype in the microenvironment. More importantly, i
n M3 (worst prognosis subtype) and M2 (best prognosis subtype), the interact
ion between immune cells and checkpoint genes was different, which had an im
portant effect on the prognosis. Finally, we used risk scores of immune cell
s and checkpoint genes to evaluate the prognosis of GBM patients and validat
ed the results with 3 independent datasets. Disordered interactions between
immune cells and checkpoint genes result in a change in the immune microenvi
ronment and affects the prognosis of patients. We propose that a better unde
rstanding of the immune microenvironment of advanced cancers may provide new
insights into immunotherapy.
Journal Title: Cancer medicine

PUBMED ID: 31005212
DOI: doi.org/10.1016/j.radonc.2019.01.008
Titolo: Low perfusion compartments in glioblastoma quantified by advanced ma
gnetic resonance imaging and correlated with patient survival.
Autori: Li C., Yan JL., Torheim T., McLean MA., Boonzaier NR., Zou J., Huang
Y., Yuan J., van Dijken BRJ., Matys T., Markowetz F., Price SJ.
Data di Pubblicazione: 2019-04-22
Abstract: Our results suggest that the ADC
Journal Title: Radiotherapy and oncology : journal of the European Society f
or Therapeutic Radiology and Oncology

PUBMED ID: 30977058
DOI: doi.org/10.1007/s11060-019-03166-3
Titolo: Dose-intensified chemoradiation is associated with altered patterns
of failure and favorable survival in patients with newly diagnosed glioblast
oma.
Autori: Kim MM., Speers C., Li P., Schipper M., Junck L., Leung D., Orringer
D., Heth J., Umemura Y., Spratt DE., Wahl DR., Cao Y., Lawrence TS., Tsien C
I.
Data di Pubblicazione: 2019-04-13
Abstract: Dose-escalated chemoRT resulted in lower rates of central recurren
ce and prolonged time to progression compared to historical controls, althou
gh a significant number of central recurrences were still observed. Advanced
imaging and correlative molecular studies may enable targeted treatment adva
nces that reduce rates of in- and out-of-field progression.
Journal Title: Journal of neuro-oncology

PUBMED ID: 30974347
DOI: doi.org/10.1016/j.yebeh.2018.10.038
Titolo: Seizure characteristics, treatment, and outcome in autoimmune synaptic encephalitis: A long-term study.
Autori: Zhang W., Wang X., Shao N., Ma R., Meng H.
Data di Pubblicazione: 2019-04-12
Abstract: A complex of clinical and subclinical seizures, and nonepileptic events characterize ASE. Patients with anti-LGI1 or anti-GABA
Journal Title: Epilepsy & behavior : E&B

PUBMED ID: 30949360
DOI: doi.org/10.1093/nop/npy023
Titolo: Neurosurgical patterns of care for diffuse low-grade gliomas in Sweden between 2005 and 2015.
Autori: Carstam L., Smits A., Milos P., Corell A., Henriksson R., Bartek J., Jakola AS.
Data di Pubblicazione: 2019-04-06
Abstract: In this nationwide, population-based study we observed a shift over time in favor of LGG resection. Further, a positive correlation between the more active surgical strategy and longer survival is shown, although no causality can be claimed because of possible confounding factors.
Journal Title: Neuro-oncology practice

PUBMED ID: 30937703
DOI: doi.org/10.1007/s10014-019-00339-w
Titolo: Overview of DNA methylation in adult diffuse gliomas.
Autori: Aoki K., Natsume A.
Data di Pubblicazione: 2019-04-03
Abstract: Adult diffuse gliomas form a heterogeneous group of tumors of the central nervous system that vary greatly in histology and prognosis. A significant advance during the last decade has been the identification of a set of genetic lesions that correlate well with histology and clinical outcome in diffuse gliomas. Most characteristic driver mutations consist of isocitrate dehydrogenase 1 (IDH1) and IDH2, and H3 histone family member 3A, which are strongly associated with DNA and histone methylation patterns. A well-characterized DNA methylation aberration is on the O6-methylguanine-DNA methyltransferase promoter. This aberration is associated with an improved response to the DNA alkylating agent, temozolomide. Methylation alterations are used for classification or treatment decisions of diffuse gliomas. This supports the importance of considering epigenomic aberrations in the pathogenesis of gliomas. Recent DNA methylation analyses revealed a small group of IDH mutant diffuse gliomas exhibiting decreased DNA hypermethylation resulting in substantial unfavorable prognosis comparable to glioblastoma. Thus, DNA methylation patterns may become a new standard that replaces the conventional grading system based on histological diagnosis. In this review, we summarize recent developments regarding the contributions of methylation patterns to the pathogenesis of adult diffuse glioma, the interactions between methylation patterns and driver mutations, and potential epigenomic targeted therapies.
Journal Title: Brain tumor pathology

PUBMED ID: 30912721
DOI: doi.org/10.1148/radiol.2019182095
Titolo: Cost-effectiveness of Intraoperative MRI for Treatment of High-Grade Gliomas.

Autori: Abraham P., Sarkar R., Brandel MG., Wali AR., Rennert RC., Lopez Ramos C., Padwal J., Steinberg JA., Santiago-Dieppa DR., Cheung V., Pannell JS., Murphy JD., Khalessi AA.
Data di Pubblicazione: 2019-03-27
Abstract: Background Intraoperative MRI has been shown to improve gross-total resection of high-grade glioma. However, to the knowledge of the authors, the cost-effectiveness of intraoperative MRI has not been established. Purpose To construct a clinical decision analysis model for assessing intraoperative MRI in the treatment of high-grade glioma. Materials and Methods An integrated five-state microsimulation model was constructed to follow patients with high-grade glioma. One-hundred-thousand patients treated with intraoperative MRI were compared with 100 000 patients who were treated without intraoperative MRI from initial resection and debulking until death (median age at initial resection, 55 years). After the operation and treatment of complications, patients existed in one of three health states: progression-free survival (PFS), progressive disease, or dead. Patients with recurrence were offered up to two repeated resections. PFS, valuation of health states (utility values), probabilities, and costs were obtained from randomized controlled trials whenever possible. Otherwise, national databases, registries, and nonrandomized trials were used. Uncertainty in model inputs was assessed by using deterministic and probabilistic sensitivity analyses. A health care perspective was used for this analysis. A willingness-to-pay threshold of $100 000 per quality-adjusted life year (QALY) gained was used to determine cost efficacy. Results Intraoperative MRI yielded an incremental benefit of 0.18 QALYs (1.34 QALYs with intraoperative MRI vs 1.16 QALYs without) at an incremental cost of $13 447 ($176 460 with intraoperative MRI vs $163 013 without) in microsimulation modeling, resulting in an incremental cost-effectiveness ratio of $76 442 per QALY. Because of parameter distributions, probabilistic sensitivity analysis demonstrated that intraoperative MRI had a 99.5% chance of cost-effectiveness at a willingness-to-pay threshold of $100 000 per QALY. Conclusion Intraoperative MRI is likely to be a cost-effective modality in the treatment of high-grade glioma. © RSNA, 2019
Journal Title: Radiology

PUBMED ID: 30899304
DOI: doi.org/10.5114/aoms.2017.69374
Titolo: MiR-21, miR-34a, miR-125b, miR-181d and miR-648 levels inversely correlate with MGMT and TP53 expression in primary glioblastoma patients.
Autori: Jesionek-Kupnicka D., Braun M., Trąbska-Kluch B., Czech J., Szybka M., Szymańska B., Kulczycka-Wojdala D., Bieńkowski M., Kordek R., Zawlik I.
Data di Pubblicazione: 2019-03-23
Abstract: Our findings demonstrate that selected miRNAs are significantly correlated with
Journal Title: Archives of medical science : AMS

PUBMED ID: 30867563
DOI: doi.org/10.1038/s41416-019-0413-x
Titolo: High filamin-C expression predicts enhanced invasiveness and poor outcome in glioblastoma multiforme.
Autori: Kamil M., Shinsato Y., Higa N., Hirano T., Idogawa M., Takajo T., Minami K., Shimokawa M., Yamamoto M., Kawahara K., Yonezawa H., Hirano H., Furukawa T., Yoshimoto K., Arita K.
Data di Pubblicazione: 2019-03-15
Abstract: FLNC is a potential therapeutic target and biomarker for GBM progression.
Journal Title: British journal of cancer

PUBMED ID: 30857221
DOI: doi.org/10.3390/cancers11030336
Titolo: Glioblastoma in Elderly Patients: Current Management and Future Perspectives.
Autori: Minniti G., Lombardi G., Paolini S.
Data di Pubblicazione: 2019-03-13
Abstract: The incidence of glioblastoma (GBM) in the elderly population is slowly increasing in Western countries. Current management includes surgery, radiation therapy (RT) and chemotherapy; however, survival is significantly worse than that observed in younger patients and the optimal treatment in terms of efficacy and safety remains a matter of debate. Surgical resection is often employed as initial treatment for elderly patients with GBM, although the survival benefit is modest. Better survival has been reported in elderly patients treated with RT compared with those receiving supportive care alone, with similar survival outcome for patients undergoing standard RT (60 Gy over 6 weeks) and hypofractionated RT (25⁻40 Gy in 5⁻15 daily fractions). Temozolomide, an alkylating agent, may represent an effective and safe therapy in patients with promoter methylation of O^6-methylguanine-DNA-methyltransfera se (
Journal Title: Cancers

PUBMED ID: 30854437
DOI: doi.org/10.18383/j.tom.2018.00049
Titolo: Comparison of Voxel-Wise and Histogram Analyses of Glioma ADC Maps for Prediction of Early Therapeutic Change.
Autori: Chenevert TL., Malyarenko DI., Galbán CJ., Gomez-Hassan DM., Sundgren PC., Tsien CI., Ross BD.
Data di Pubblicazione: 2019-03-12
Abstract: Noninvasive imaging methods are sought to objectively predict early response to therapy for high-grade glioma tumors. Quantitative metrics derived from diffusion-weighted imaging, such as apparent diffusion coefficient (ADC), have previously shown promise when used in combination with voxel-based analysis reflecting regional changes. The functional diffusion mapping (fDM) metric is hypothesized to be associated with volume of tumor exhibiting an increasing ADC owing to effective therapeutic action. In this work, the reference fDM-predicted survival (from previous study) for 3 weeks from treatment initiation (midtreatment) is compared to multiple histogram-based metrics using Kaplan-Meier estimator for 80 glioma patients stratified to responders and nonresponders based on the population median value for the given metric. The ADC histogram metric reflecting reduction in midtreatment volume of solid tumor (ADC < 1.25 × 10
Journal Title: Tomography (Ann Arbor, Mich.)

PUBMED ID: 30832617
DOI: doi.org/10.1186/s12885-019-5413-y
Titolo: Phase I/IIa study of concomitant radiotherapy with olaparib and temozolomide in unresectable or partially resectable glioblastoma: OLA-TMZ-RTE-01 trial protocol.
Autori: Lesueur P., Lequesne J., Grellard JM., Dugué A., Coquan E., Brachet PE., Geffrelot J., Kao W., Emery E., Berro DH., Castera L., Goardon N., Lacroix J., Lange M., Capel A., Leconte A., Andre B., Léger A., Lelaidier A., Clarisse B., Stefan D.
Data di Pubblicazione: 2019-03-06
Abstract: NCT03212742 , registered June, 7, 2017. Protocol version: Version 2.2 dated from 2017/08/18.
Journal Title: BMC cancer

PUBMED ID: 30830679
DOI: doi.org/10.1007/s11060-019-03140-z
Titolo: Nimotuzumab and radiotherapy for treatment of newly diagnosed diffus e intrinsic pontine glioma (DIPG): a phase III clinical study.
Autori: Fleischhack G., Massimino M., Warmuth-Metz M., Khuhlaeva E., Janssen G., Graf N., Rutkowski S., Beilken A., Schmid I., Biassoni V., Gorelishev SK ., Kramm C., Reinhard H., Schlegel PG., Kortmann RD., Reuter D., Bach F., Iz naga-Escobar NE., Bode U.
Data di Pubblicazione: 2019-03-05
Abstract: Concomitant treatment with RT and nimotuzumab was feasible in an o utpatient setting. The PFS and OS were comparable to results achieved with R T and intensive chemotherapy in hospitalized setting.
Journal Title: Journal of neuro-oncology

PUBMED ID: 30820715
DOI: doi.org/10.1007/s00432-019-02868-5
Titolo: Regorafenib in patients with recurrent high-grade astrocytoma.
Autori: Kebir S., Rauschenbach L., Radbruch A., Lazaridis L., Schmidt T., St oppek AK., Pierscianek D., Stuschke M., Forsting M., Sure U., Keyvani K., Kl einschnitz C., Scheffler B., Glas M.
Data di Pubblicazione: 2019-03-02
Abstract: This retrospective study indicates a very poor performance of rego rafenib in recurrent high-grade astrocytoma with a fairly high number of CTC °3 adverse events. In addition, regorafenib does not seem to bear a potentia l for infiltrative tumor growth promotion.
Journal Title: Journal of cancer research and clinical oncology

PUBMED ID: 30810873
DOI: doi.org/10.1007/s11060-019-03133-y
Titolo: Quantifying radiation therapy response using apparent diffusion coef ficient (ADC) parametric mapping of pediatric diffuse intrinsic pontine glio ma: a report from the pediatric brain tumor consortium.
Autori: Ceschin R., Kocak M., Vajapeyam S., Pollack IF., Onar-Thomas A., Dun kel IJ., Poussaint TY., Panigrahy A.
Data di Pubblicazione: 2019-02-28
Abstract: Baseline ADC values are a stronger predictor of outcome compared t o radiation related ADC changes in pediatric DIPG. We show the feasibility o f employing parametric mapping techniques in multi-center studies to quantit ate spatially heterogeneous treatment response in pediatric tumors, includin g DIPG.
Journal Title: Journal of neuro-oncology

PUBMED ID: 30806888
DOI: doi.org/10.1007/s11060-019-03132-z
Titolo: pH-weighted amine chemical exchange saturation transfer echoplanar i maging (CEST-EPI) as a potential early biomarker for bevacizumab failure in recurrent glioblastoma.
Autori: Yao J., Tan CHP., Schlossman J., Chakhoyan A., Raymond C., Pope WB., Salamon N., Lai A., Ji M., Nghiemphu PL., Liau LM., Cloughesy TF., Ellingson BM.
Data di Pubblicazione: 2019-02-27
Abstract: This pilot study suggests pH-weighted amine CEST MRI may have valu e as a non-invasive, early imaging biomarker for bevacizumab treatment respo nse and failure. Early decreases MTR
Journal Title: Journal of neuro-oncology

PUBMED ID: 30771200
DOI: doi.org/10.1007/s11060-019-03125-y
Titolo: A multicenter phase II study of temozolomide plus disulfiram and cop per for recurrent temozolomide-resistant glioblastoma.
Autori: Huang J., Chaudhary R., Cohen AL., Fink K., Goldlust S., Boockvar J. , Chinnaiyan P., Wan L., Marcus S., Campian JL.
Data di Pubblicazione: 2019-02-17
Abstract: Addition of DSF/Cu to TMZ for TMZ-resistant IDH-wild type GBM appe ars well tolerated but has limited activity for unselected population.
Journal Title: Journal of neuro-oncology

PUBMED ID: 30768441
DOI: doi.org/10.1097/COC.0000000000000519
Titolo: Concurrent Versus Sequential Chemoradiation for Low-grade Gliomas Me eting RTOG 9802 Criteria.
Autori: Ryckman JM., Appiah AK., Lyden E., Verma V., Zhang C.
Data di Pubblicazione: 2019-02-16
Abstract: This is the only analysis of which we are aware of cCRT versus sCR T for LGG. There is no evidence that cCRT improves outcomes over sCRT.
Journal Title: American journal of clinical oncology

PUBMED ID: 30740109
DOI: doi.org/10.3389/fimmu.2018.03062
Titolo: Genetically Engineered T-Cells for Malignant Glioma: Overcoming the Barriers to Effective Immunotherapy.
Autori: Chuntova P., Downey KM., Hegde B., Almeida ND., Okada H.
Data di Pubblicazione: 2019-02-12
Abstract: Malignant gliomas carry a dismal prognosis. Conventional treatment using chemo- and radiotherapy has limited efficacy with adverse events. Ther apy with genetically engineered T-cells, such as chimeric antigen receptor (CAR) T-cells, may represent a promising approach to improve patient outcomes owing to their potential ability to attack highly infiltrative tumors in a t umor-specific manner and possible persistence of the adaptive immune respons e. However, the unique anatomical features of the brain and susceptibility o f this organ to irreversible tissue damage have made immunotherapy especiall y challenging in the setting of glioma. With safety concerns in mind, multip le teams have initiated clinical trials using CAR T-cells in glioma patients . The valuable lessons learnt from those trials highlight critical areas for further improvement: tackling the issues of the antigen presentation and T-c ell homing in the brain, immunosuppression in the glioma microenvironment, a ntigen heterogeneity and off-tumor toxicity, and the adaptation of existing clinical therapies to reflect the intricacies of immune response in the brai n. This review summarizes the up-to-date clinical outcomes of CAR T-cell cli nical trials in glioma patients and examines the most pressing hurdles limit ing the efficacy of these therapies. Furthermore, this review uses these hur dles as a framework upon which to evaluate cutting-edge pre-clinical strateg ies aiming to overcome those barriers.
Journal Title: Frontiers in immunology

PUBMED ID: 30737615
DOI: doi.org/10.1208/s12248-019-0302-5
Titolo: Estimation of Solid Tumor Doubling Times from Progression-Free Survi val Plots Using a Novel Statistical Approach.
Autori: Kay K., Dolcy K., Bies R., Shah DK.
Data di Pubblicazione: 2019-02-10

Abstract: Tumor doubling time can significantly affect the outcome of antica
ncer therapy, but it is very challenging to determine. Here, we present a st
atistical approach that extracts doubling times from progression-free surviv
al (PFS) plots, which inherently contains information regarding the growth o
f solid tumors. Twelve cancers were investigated and multiple PFS plots were
evaluated for each type. The PFS plot showing fastest tumor growth was deeme
d to best represent the inherent growth kinetics of the solid tumor, and sel
ected for further analysis. The exponential tumor growth rates were extracte
d from each PFS plot, along with associated variabilities, which ultimately
allowed for the estimation of solid tumor doubling times. The mean simulated
doubling times for pancreatic cancer, melanoma, hepatocellular carcinoma (HC
C), renal cell carcinoma, triple negative breast cancer, non-small cell lung
cancer, hormone receptor positive (HR+) breast cancer, human epidermal growt
h factor receptor-2 positive (HER-2+) breast cancer, gastric cancer, gliobla
stoma multiforme, colorectal cancer, and prostate cancer were 5.06, 3.78, 3.
06, 2.67, 2.38, 2.40, 4.31, 4.12, and 3.84 months, respectively. For all can
cers, clinically reported doubling times were within the estimated ranges. F
or all cancers, except HCC, the growth rates were best characterized by a lo
g-normal distribution. For HCC, the gamma distribution best described the da
ta. The statistical approach presented here provides a qualified method for
extracting tumor growth rates and doubling times from PFS plots. It also all
ows estimation of the distributional characteristics for tumor growth rates
and doubling times in a given patient population.
Journal Title: The AAPS journal

PUBMED ID: 30737018
DOI: doi.org/10.1016/j.bulcan.2019.01.008
Titolo: [MSI Metastatic solid tumors treatment and immunotherapies].
Autori: Bouchez C., Kempf E., Tournigand C.
Data di Pubblicazione: 2019-02-10
Abstract: Checkpoints inhibitors are known to induce striking tumor response
s in advanced MSI colorectal cancers, which used to be related to a poor cli
nical outcome. The incidence of the MSI phenotype is highly heterogeneous ac
ross non-colorectal cancers. The highest incidence rates are found in endome
trioid forms of uterine cancers and in gastric tumors (20 to 40 % and 10 to
33 %, respectively). The association between a "MSI" tumor phenotype and oth
er clinical or biological tumor characteristics is still under debate. Its p
rognostic value has not been determined yet. The deficiency of the DNA misma
tch repair (dMMR) system of such tumor cells increases their mutational load
and induces the production of so-called neo-antigens. Therefore, checkpoint
inhibitors are a target therapeutic class for this molecular group of tumors
. For example, response rates reach more than 50 % in pre-treated advanced e
ndometrial cancers and in metastatic gastric tumors in association with a fi
rst line of chemotherapy. Those promising results imply the development of r
eliable biomarkers predictive of tumor response to immunotherapy. The presen
t article summarizes the clinical outcomes related to the administration of
checkpoint inhibitors in non-colorectal cancers. The ongoing clinical trials
of such therapeutic class in this patient population are displayed.
Journal Title: Bulletin du cancer

PUBMED ID: 30713832
DOI: doi.org/10.3389/fonc.2018.00643
Titolo: Case Report: Clinical Outcome and Image Response of Two Patients Wit
h Secondary High-Grade Glioma Treated With Chemoradiation, PCV, and Cannabid
iol.
Autori: Dall'Stella PB., Docema MFL., Maldaun MVC., Feher O., Lancellotti CL
P.
Data di Pubblicazione: 2019-02-05

Abstract: We describe two patients with a confirmed diagnosis of high-grade gliomas (grades III/IV), both presenting with O6-methylguanine-DNA methyltransferase (MGMT) methylated and isocitrate dehydrogenase (IDH-1) mutated who, after subtotal resection, were submitted to chemoradiation and followed by PCV, a multiple drug regimen (procarbazine, lomustine, and vincristine) associated with cannabidiol (CBD). Both patients presented with satisfactory clinical and imaging responses at periodic evaluations. Immediately after chemoradiation therapy, one of the patients presented with an exacerbated and precocious pseudoprogression (PSD) assessed by magnetic resonance imaging (MRI), which was resolved in a short period. The other patient presented with a marked remission of altered areas compared with the post-operative scans as assessed by MRI. Such aspects are not commonly observed in patients only treated with conventional modalities. This observation might highlight the potential effect of CBD to increase PSD or improve chemoradiation responses that impact survival. Further investigation with more patients and critical molecular analyses should be performed.
Journal Title: Frontiers in oncology

PUBMED ID: 30705664
DOI: doi.org/10.3389/fneur.2018.01199
Titolo: ZEB1 Is a Transcription Factor That Is Prognostic and Predictive in Diffuse Gliomas.
Autori: Edwards LA., Kim S., Madany M., Nuno M., Thomas T., Li A., Berel D., Lee BS., Liu M., Black KL., Fan X., Zhang W., Yu JS.
Data di Pubblicazione: 2019-02-02
Abstract: We describe two patients with a confirmed diagnosis of high-grade gliomas (grades III/IV), both presenting with O6-methylguanine-DNA methyltransferase (MGMT) methylated and isocitrate dehydrogenase (IDH-1) mutated who, after subtotal resection, were submitted to chemoradiation and followed by PCV, a multiple drug regimen (procarbazine, lomustine, and vincristine) associated with cannabidiol (CBD). Both patients presented with satisfactory clinical and imaging responses at periodic evaluations. Immediately after chemoradiation therapy, one of the patients presented with an exacerbated and precocious pseudoprogression (PSD) assessed by magnetic resonance imaging (MRI), which was resolved in a short period. The other patient presented with a marked remission of altered areas compared with the post-operative scans as assessed by MRI. Such aspects are not commonly observed in patients only treated with conventional modalities. This observation might highlight the potential effect of CBD to increase PSD or improve chemoradiation responses that impact survival. Further investigation with more patients and critical molecular analyses should be performed.
Journal Title: Frontiers in neurology

PUBMED ID: 30668823
DOI: doi.org/10.1093/neuonc/noz016
Titolo: Accelerated progression of IDH mutant glioma after first recurrence.
Autori: Miller JJ., Loebel F., Juratli TA., Tummala SS., Williams EA., Batchelor TT., Arrillaga-Romany I., Cahill DP.
Data di Pubblicazione: 2019-01-23
Abstract: We report outcomes in a large cohort of IDH mutant glioma, providing a well-characterized historical control population for future clinical trial design. Notably, the interval between first and second recurrence (PFS2, 3.0 y) is shorter than time from diagnosis to first recurrence (PFS1, 5.7 y), evidence that these tumors clinically degenerate from an indolent course to an accelerated malignant phase. Thus, PFS2 represents a relevant outcome for trials investigating drug efficacy at recurrence.
Journal Title: Neuro-oncology

PUBMED ID: 30659522
DOI: doi.org/10.1007/s11060-019-03103-4
Titolo: 5-aminolevulinic acid photodynamic therapy for the treatment of high-grade gliomas.
Autori: Mahmoudi K., Garvey KL., Bouras A., Cramer G., Stepp H., Jesu Raj JG., Bozec D., Busch TM., Hadjipanayis CG.
Data di Pubblicazione: 2019-01-20
Abstract: PDT remains a promising therapeutic approach that requires further study in HGGs. Use of 5-ALA PDT permits selective tumor targeting due to the intracellular metabolism of 5-ALA. The immunomodulatory effects of PDT further strengthen its use for treatment of HGGs and requires a better understanding. The combination of PDT with adjuvant therapies for HGGs will need to be studied in randomized, controlled studies.
Journal Title: Journal of neuro-oncology

PUBMED ID: 30639498
DOI: doi.org/10.1016/j.wneu.2018.12.147
Titolo: H3 K27M Mutations in Thalamic Pilocytic Astrocytomas with Anaplasia.
Autori: El Ahmadieh TY., Plitt A., Kafka B., Aoun SG., Raisanen JM., Orr B., Pan E., Wardak Z., Nedzi LA., Patel TR.
Data di Pubblicazione: 2019-01-15
Abstract: Stereotactic biopsies may undergrade some adult thalamic pilocytic astrocytomas. Thus, we recommend that all of these tumors be evaluated for the H3 K27M mutation. Further, we believe that H3 K27M-mutant thalamic pilocytic astrocytomas require aggressive multi-modality treatment and that these treatments should be guided by the molecular findings, as opposed to the histologic ones.
Journal Title: World neurosurgery

PUBMED ID: 30635340
DOI: doi.org/10.1158/1078-0432.CCR-18-3101
Titolo: The Misclassification of Diffuse Gliomas: Rates and Outcomes.
Autori: Iorgulescu JB., Torre M., Harary M., Smith TR., Aizer AA., Reardon DA., Barnholtz-Sloan JS., Perry A.
Data di Pubblicazione: 2019-01-13
Abstract: On the basis of 1p/19q, IDH, ATRX, and p53, the misclassification rates of histologically encoded oligodendrogliomas, astrocytomas, and gliobl astomas are approximately 21%-35%, 6%-9%, and 9%, respectively; with significant clinical implications. Our findings suggest that when compared with historical histology-only classified data, in national registry, as well as, institutional databases, there is the potential for false-positive results in contemporary trials of molecularly classified diffuse gliomas, which could contribute to a seemingly positive phase II trial (based on historical comparison) failing at the phase III stage. Critically, findings from diffuse glioma clinical trials and historical cohorts using prior histology-only WHO schemes must be cautiously reinterpreted.
Journal Title: Clinical cancer research : an official journal of the American Association for Cancer Research

PUBMED ID: 30610982
DOI: doi.org/10.1016/j.wneu.2018.12.118
Titolo: The Role and Real Effect of an Iterative Surgical Approach for the Management of Recurrent High-Grade Glioma: An Observational Analytic Cohort Study.
Autori: Salvati M., Pesce A., Palmieri M., Floriana Brunetto GM., Santoro A., Frati A.

Data di Pubblicazione: 2019-01-06
Abstract: These data showed excellent outcomes in terms of OS and PFS and cl inical conditions after multiple surgical procedures. Therefore, reintervent ion appears to be a feasible and safe solution for selected patients.
Journal Title: World neurosurgery

PUBMED ID: 30610915
DOI: doi.org/10.1016/j.ijrobp.2018.12.043
Titolo: A Phase 1/2 Trial of Reirradiation for Diffuse Intrinsic Pontine Gli oma.
Autori: Amsbaugh MJ., Mahajan A., Thall PF., McAleer MF., Paulino AC., Gross hans D., Khatua S., Ketonen L., Fontanilla H., McGovern SL.
Data di Pubblicazione: 2019-01-06
Abstract: ReRT can safely be delivered for progressive diffuse intrinsic pon tine glioma. Clinical improvement was seen in almost all patients. Utility a nalysis suggests that a regimen of 24 Gy in 12 fractions is preferred.
Journal Title: International journal of radiation oncology, biology, physics

PUBMED ID: 30602457
DOI: doi.org/10.1073/pnas.1721434116
Titolo: Microglia are effector cells of CD47-SIRPα antiphagocytic axis disru ption against glioblastoma.
Autori: Hutter G., Theruvath J., Graef CM., Zhang M., Schoen MK., Manz EM., Bennett ML., Olson A., Azad TD., Sinha R., Chan C., Assad Kahn S., Gholamin S., Wilson C., Grant G., He J., Weissman IL., Mitra SS., Cheshier SH.
Data di Pubblicazione: 2019-01-04
Abstract: Glioblastoma multiforme (GBM) is a highly aggressive malignant bra in tumor with fatal outcome. Tumor-associated macrophages and microglia (TAM s) have been found to be major tumor-promoting immune cells in the tumor mic roenvironment. Hence, modulation and reeducation of tumor-associated macroph ages and microglia in GBM is considered a promising antitumor strategy. Resi dent microglia and invading macrophages have been shown to have distinct ori gin and function. Whereas yolk sac-derived microglia reside in the brain, bl ood-derived monocytes invade the central nervous system only under pathologi cal conditions like tumor formation. We recently showed that disruption of t he SIRPα-CD47 signaling axis is efficacious against various brain tumors inc luding GBM primarily by inducing tumor phagocytosis. However, most effects a re attributed to macrophages recruited from the periphery but the role of th e brain resident microglia is unknown. Here, we sought to utilize a model to distinguish resident microglia and peripheral macrophages within the GBM-TAM pool, using orthotopically xenografted, immunodeficient, and syngeneic mouse models with genetically color-coded macrophages (
Journal Title: Proceedings of the National Academy of Sciences of the United States of America

PUBMED ID: 30563210
DOI: doi.org/10.3390/ijms19123905
Titolo: Intranasal Perillyl Alcohol for Glioma Therapy: Molecular Mechanisms and Clinical Development.
Autori: Chen TC., da Fonseca CO., Schönthal AH.
Data di Pubblicazione: 2018-12-20
Abstract: Intracranial malignancies, such as primary brain cancers and brain -localized metastases derived from peripheral cancers, are particularly diff icult to treat with therapeutic agents, because the blood-brain barrier (BBB) effectively minimizes brain entry of the vast majority of agents arriving from the systemic circulation. Intranasal administration of cancer drugs has the potential to reach the brain via direct nose-to-brain transport, thereby

circumventing the obstacle posed by the BBB. However, in the field of cancer therapy, there is a paucity of studies reporting positive results with this type of approach. A remarkable exception is the natural compound perillyl alcohol (POH). Its potent anticancer activity was convincingly established in preclinical studies, but it nonetheless failed in subsequent clinical trials, where it was given orally and displayed hard-to-tolerate gastrointestinal side effects. Intriguingly, when switched to intranasal delivery, POH yielded highly promising activity in recurrent glioma patients and was well tolerated. As of 2018, POH is the only intranasally delivered compound in the field of cancer therapy (outside of cancer pain) that has advanced to active clinical trials. In the following, we will introduce this compound, summarize its molecular mechanisms of action, and present the latest data on its clinical evaluation as an intranasally administered agent for glioma.
Journal Title: International journal of molecular sciences

PUBMED ID: 30561851
DOI: doi.org/10.1002/cam4.1908
Titolo: Combining multimodal imaging and treatment features improves machine learning-based prognostic assessment in patients with glioblastoma multiforme.
Autori: Peeken JC., Goldberg T., Pyka T., Bernhofer M., Wiestler B., Kessel KA., Tafti PD., Nüsslin F., Braun AE., Zimmer C., Rost B., Combs SE.
Data di Pubblicazione: 2018-12-19
Abstract: MRI-based features were the most relevant feature class for prognostic assessment. Combining clinical, pathological, and imaging information increased predictive power for OS and PFS. A further increase was achieved by adding treatment features.
Journal Title: Cancer medicine

PUBMED ID: 30544336
DOI: doi.org/10.3171/2018.7.JNS18422
Titolo: Role of photodynamic therapy using talaporfin sodium and a semiconductor laser in patients with newly diagnosed glioblastoma.
Autori: Nitta M., Muragaki Y., Maruyama T., Iseki H., Komori T., Ikuta S., Saito T., Yasuda T., Hosono J., Okamoto S., Koriyama S., Kawamata T.
Data di Pubblicazione: 2018-12-15
Abstract: The results of the present study suggest that PDT with talaporfin sodium and a semiconductor laser provides excellent local control, with few adverse effects even in cases of multiple laser irradiations, as well as potential survival benefits for patients with newly diagnosed glioblastoma.
Journal Title: Journal of neurosurgery

PUBMED ID: 30523606
DOI: doi.org/10.1007/s11060-018-03065-z
Titolo: Association of patterns of care, prognostic factors, and use of radiotherapy-temozolomide therapy with survival in patients with newly diagnosed glioblastoma: a French national population-based study.
Autori: Fabbro-Peray P., Zouaoui S., Darlix A., Fabbro M., Pallud J., Rigau V., Mathieu-Daude H., Bessaoud F., Bauchet F., Riondel A., Sorbets E., Charissoux M., Amelot A., Mandonnet E., Figarella-Branger D., Duffau H., Tretarre B., Taillandier L., Bauchet L.
Data di Pubblicazione: 2018-12-08
Abstract: In non-progressive patients, prolonging the adjuvant temozolomide beyond 6 cycles may improve OS.
Journal Title: Journal of neuro-oncology

PUBMED ID: 30522967
DOI: doi.org/10.1016/S1470-2045(18)30675-2
Titolo: Regorafenib compared with lomustine in patients with relapsed glioblastoma (REGOMA): a multicentre, open-label, randomised, controlled, phase 2 trial.
Autori: Lombardi G., De Salvo GL., Brandes AA., Eoli M., Rudà R., Faedi M., Lolli I., Pace A., Daniele B., Pasqualetti F., Rizzato S., Bellu L., Pambuku A., Farina M., Magni G., Indraccolo S., Gardiman MP., Soffietti R., Zagonel V.
Data di Pubblicazione: 2018-12-08
Abstract: Veneto Institute of Oncology and Bayer Italy.
Journal Title: The Lancet. Oncology

PUBMED ID: 30535596
DOI: doi.org/10.1007/s11060-018-03075-x
Titolo: Baseline multicentric tumors, distant recurrences and leptomeningeal dissemination predict poor survival in patients with recurrent glioblastomas receiving bevacizumab.
Autori: Toh CH., Liau CT., Wei KC., Castillo M.
Data di Pubblicazione: 2018-12-12
Abstract: Baseline multicentric tumors, distant recurrence and leptomeningeal dissemination predicted poor survival among patients receiving bevacizumab for recurrent GB. Conventional MRI may help selecting patients with recurrent GB for bevacizumab treatment.
Journal Title: Journal of neuro-oncology

PUBMED ID: 30515706
DOI: doi.org/10.1007/s11060-018-03059-x
Titolo: Re-irradiation for recurrent glioma: outcome evaluation, toxicity and prognostic factors assessment. A multicenter study of the Radiation Oncology Italian Association (AIRO).
Autori: Navarria P., Minniti G., Clerici E., Tomatis S., Pinzi V., Ciammella P., Galaverni M., Amelio D., Scartoni D., Scoccianti S., Krengli M., Masini L., Draghini L., Maranzano E., Borzillo V., Muto P., Ferrarese F., Fariselli L., Livi L., Pasqualetti F., Fiorentino A., Alongi F., di Monale MB., Magrini S., Scorsetti M.
Data di Pubblicazione: 2018-12-06
Abstract: our data underline re-RT as a safe and feasible treatment with limited rate of toxicity, and a combined ones as a better option for selected patients. The identification of a BED threshold able to obtain a greater benefit on OS, can help in designing future prospective studies.
Journal Title: Journal of neuro-oncology

PUBMED ID: 30488830
DOI: doi.org/10.4103/jcrt.JCRT_295_17
Titolo: Impact of subventricular zone irradiation on outcome of patients with glioblastoma.
Autori: Mathew BS., Kaliyath SB., Krishnan J., Bhasi S.
Data di Pubblicazione: 2018-11-30
Abstract: This retrospective study indicated a trend toward improved-albeit nonsignificant-survival with higher dose to the ipsilateral and contralateral SVZs. A well-designed prospective randomized study is required to identify patients who would benefit from intentional SVZ targeting.
Journal Title: Journal of cancer research and therapeutics

PUBMED ID: 30488294

DOI: doi.org/10.1007/s11060-018-03063-1
Titolo: Increase of pseudoprogression and other treatment related effects in low-grade glioma patients treated with proton radiation and temozolomide.
Autori: Dworkin M., Mehan W., Niemierko A., Kamran SC., Lamba N., Dietrich J ., Martinez-Lage M., Oh KS., Batchelor TT., Wen PY., Loeffler JS., Shih HA.
Data di Pubblicazione: 2018-11-30
Abstract: TMZ use, when added to PRT, was associated with increased PsP in p atients with LGG; however, patients with PsP tended to achieve longer surviv al.
Journal Title: Journal of neuro-oncology

PUBMED ID: 30485241
DOI: doi.org/10.3171/2018.7.SPINE18230
Titolo: Intramedullary spinal cord ependymoma and astrocytoma: intraoperativ e frozen-section diagnosis, extent of resection, and outcomes.
Autori: Hongo H., Takai K., Komori T., Taniguchi M.
Data di Pubblicazione: 2018-11-29
Abstract: OBJECTIVEThe intraoperative differentiation of ependymomas from as trocytomas is important because neurosurgical strategies differ between thes e two tumor groups. Previous studies have reported that the diagnostic accur acy of intraoperative frozen sections of intracranial central nervous system (CNS) tumors is higher than 83%-97%, whereas that for spinal intramedullary tumors remains unknown. Herein, authors tested the hypothesis that intraoper ative frozen-section diagnosis is the gold standard for a differential diagn osis of intramedullary spinal cord tumors.METHODSThe clinical characteristic s, intraoperative histological diagnosis from frozen sections, extent of tum or resection, progression-free survival (PFS), and overall survival (OS) of 49 cases of intramedullary spinal cord ependymomas (n = 32) and astrocytomas (n = 17) were retrospectively evaluated.RESULTSThe frozen-section diagnosis and final diagnosis with permanent sections agreed in 23 (72%) of 32 cases o f ependymoma. Of the 9 cases of ependymoma in which the frozen-section diagn osis disagreed with the final diagnosis, 4 were incorrectly diagnosed as ast rocytoma and the other 5 cases had a nonspecific diagnosis, such as glioma. Nonetheless, gross-total resection was achieved in 6 of these 9 cases given the presence of a dissection plane. The frozen-section diagnosis and final d iagnosis agreed in 12 (71%) of 17 cases of astrocytoma. Of the 5 cases of as trocytoma in which the frozen-section diagnosis disagreed with the final dia gnosis, 1 was incorrectly diagnosed as ependymoma and the other 4 had a nons pecific diagnosis. Gross-total resection was achieved in only 1 of these 5 c ases.A relationship between the size of tumor specimens and the diagnostic a ccuracy of frozen sections was not observed. Ependymal rosettes and perivasc ular pseudorosettes were observed in 30% and 57% of ependymomas, respectivel y, but were absent in astrocytomas.Progression-free survival and OS were bot h significantly longer in cases of ependymoma than in cases of astrocytoma ($p < 0.001$). Gross-total resection was achieved in 69% of ependymomas and was associated with longer PFS ($p = 0.041$). In the astrocytoma group, gross-tota l resection was achieved in only 12% and there was no relationship between e xtent of resection and OS. Tumor grades tended to correlate with OS in astro cytomas ($p = 0.079$).CONCLUSIONSThe diagnostic accuracy of intraoperative fro zen sections was lower for intramedullary spinal cord ependymomas and astroc ytomas in the present study than that for intracranial CNS tumors reported o n in the literature. Surgical strategies need to be selected based on multip le factors, such as clinical characteristics, preoperative imaging, frozen-s ection diagnosis, and intraoperative findings of the tumor plane.
Journal Title: Journal of neurosurgery. Spine

PUBMED ID: 30467813
DOI: doi.org/10.1007/s11060-018-03030-w

Titolo: Surgical management of lower-grade glioma in the spotlight of the 20 16 WHO classification system.
Autori: Delev D., Heiland DH., Franco P., Reinacher P., Mader I., Staszewski O., Lassmann S., Grau S., Schnell O.
Data di Pubblicazione: 2018-11-24
Abstract: The impact of surgical treatment on the outcome of lower-grade gli omas depends to a great extent on the molecular subtype of the tumors. Patie nts with more aggressive tumors (IDH-wildtype) seem to profit from more inte nsive treatment like GTR, multiple resections and combined radio-/chemothera py.
Journal Title: Journal of neuro-oncology

PUBMED ID: 30464150
DOI: doi.org/10.2176/nmc.oa.2018-0111
Titolo: Boron Neutron Capture Therapy Combined with Early Successive Bevaciz umab Treatments for Recurrent Malignant Gliomas - A Pilot Study.
Autori: Shiba H., Takeuchi K., Hiramatsu R., Furuse M., Nonoguchi N., Kawaba ta S., Kuroiwa T., Kondo N., Sakurai Y., Suzuki M., Ono K., Oue S., Ishikawa E., Michiue H., Miyatake SI.
Data di Pubblicazione: 2018-11-23
Abstract: Recurrent malignant gliomas (RMGs) are difficult to control, and n o standard protocol has been established for their treatment. At our institu te, we have often treated RMGs by tumor-selective particle radiation called boron neutron capture therapy (BNCT). However, despite the cell-selectivity of BNCT, brain radiation necrosis (BRN) may develop and cause severe neurolo gical complications and sometimes death. This is partly due to the full-dose X-ray treatments usually given earlier in the treatment course. To overcome BRN following BNCT, recent studies have used bevacizumab (BV). We herein use d extended BV treatment beginning just after BNCT to confer protection again st or ameliorate BRN, and evaluated; the feasibility, efficacy, and BRN cont rol of this combination treatment. Seven patients with RMGs (grade 3 and 4 c ases) were treated with BNCT between June 2013 and May 2014, followed by suc cessive BV treatments. They were followed-up to December 2017. Median overal l survival (OS) and progression-free survival (PFS) after combination treatm ent were 15.1 and 5.4 months, respectively. In one case, uncontrollable brai n edema occurred and ultimately led to death after BV was interrupted due to meningitis. In two other cases, symptomatic aggravation of BRN occurred afte r interruption of BV treatment. No BRN was observed during the observation p eriod in the other cases. Common terminology criteria for adverse events gra de 2 and 3 proteinuria occurred in two cases and necessitated the interrupti on of BV treatments. Boron neutron capture therapy followed by BV treatments well-prevented or well-controlled BRN with prolonged OS and acceptable incid ence of adverse events in our patients with RMG.
Journal Title: Neurologia medico-chirurgica

PUBMED ID: 30446361
DOI: doi.org/10.1016/j.jocn.2018.11.005
Titolo: Tumour volume reduction following PET guided intensity modulated rad iation therapy and temozolomide in IDH mutated anaplastic glioma.
Autori: Back M., Jayamanne D., Brazier D., Bailey D., Hsiao E., Guo L., Whee ler H.
Data di Pubblicazione: 2018-11-18
Abstract: The role of maximal surgical debulking in isocitrate dehydrogenase (IDH) mutated anaplastic glioma prior to adjuvant radiation therapy remains uncertain. This study assessed the reduction in tumour volume following inte nsity modulated radiation therapy (IMRT) and temozolomide in this favourable and more responsive tumour pathology. 56 patients were managed from 2011 to 2014 and 53 had residual disease. To assess radiological response, tumour vo

lumes were created on representative T1/T2Flair MRI sequences using identica l slice-levels in three planes for pre-IMRT, month + 3 and month + 12 post-IMRT scans. Change in volumes was assessed between time periods. Progression-free survival (PFS) was calculated from start of radiotherapy. Median follow-up f or survivors is 48.2 months. Pathology was anaplastic oligodendroglioma (AOD) and anaplastic astrocytoma IDH-mutated (AAmut) in 32 and 21 patients respect ively. 93% received sequential chemotherapy. The median residual disease on T1 and T2Flair imaging was 9.7 cm
Journal Title: Journal of clinical neuroscience : official journal of the Ne urosurgical Society of Australasia

PUBMED ID: 30396819
DOI: doi.org/10.1016/j.pan.2018.10.004
Titolo: Tumor treating fields in combination with gemcitabine or gemcitabine plus nab-paclitaxel in pancreatic cancer: Results of the PANOVA phase 2 stud y.
Autori: Rivera F., Benavides M., Gallego J., Guillen-Ponce C., Lopez-Martin J., Küng M.
Data di Pubblicazione: 2018-11-07
Abstract: The PANOVA trial demonstrated that the combination of TTFields and systemic chemotherapy is safe and tolerable in patients with advanced PDAC. Based on the safety and preliminary efficacy results of this phase 2 study, a randomized phase 3 study (PANOVA-3) is underway.
Journal Title: Pancreatology : official journal of the International Associa tion of Pancreatology (IAP) ... [et al.]

PUBMED ID: 30392813
DOI: doi.org/10.1016/S1470-2045(18)30532-1
Titolo: Prognostic effect of whole chromosomal aberration signatures in stan dard-risk, non-WNT/non-SHH medulloblastoma: a retrospective, molecular analy sis of the HIT-SIOP PNET 4 trial.
Autori: Goschzik T., Schwalbe EC., Hicks D., Smith A., Zur Muehlen A., Figar ella-Branger D., Doz F., Rutkowski S., Lannering B., Pietsch T., Clifford SC .
Data di Pubblicazione: 2018-11-06
Abstract: Cancer Research UK, Swedish Childhood Cancer Foundation, French Mi nistry of Health/French National Cancer Institute, and the German Children's Cancer Foundation.
Journal Title: The Lancet. Oncology

PUBMED ID: 30389317
DOI: doi.org/10.1016/j.prp.2018.10.023
Titolo: Cell division cycle associated 7 like predicts unfavorable prognosis and promotes invasion in glioma.
Autori: Shen FZ., Li XS., Ma JW., Wang XY., Zhao SP., Meng L., Liang SF., Zh ao XL.
Data di Pubblicazione: 2018-11-04
Abstract: CDCA7L is highly expressed in human glioma tissues and a high CDCA 7L expression level predicts the dismal prognosis for glioma patients. Moreo ver, CDCA7L can promote glioma invasion, which can serve as an independent p otential prognostic biomarker for glioma patients.
Journal Title: Pathology, research and practice

PUBMED ID: 30366780
DOI: doi.org/10.1016/j.jocn.2018.10.084

Titolo: Glioneuronal brainstem tumor - It's all in the eyes.
Autori: Foster E., McLean C., White O.
Data di Pubblicazione: 2018-10-28
Abstract: A previously well man presented with several months' history of ne urological symptoms including diplopia and balance difficulties. Examination revealed fluctuating neurological deficits, fatigable weakness and slowed sa ccades. Extensive testing revealed mildly elevated cerebrospinal fluid prote in, strongly positive single fiber electromyography and a dorsal pontine les ion at the floor of the 4th ventricle. An autoimmune process was felt to bes t account for the myasthenic presentation while the differential diagnoses f or the brainstem lesion included glioma. Aggressive immunotherapy failed to halt clinical deterioration; over months he developed generalized weakness, aspiration pneumonia and died. Post-mortem analysis revealed glioneuronal tu mor infiltration throughout the brainstem, cerebellum and along the meningea l surface. This is an unusual case of an infiltrative brainstem lesion, with the presentation suggesting a primary diagnosis of myasthenia gravis. The pr ogressive nature of the illness, despite aggressive immune therapy, together with slow saccades, underscored a more sinister process. Cerebral imaging sh ould be performed in patients with fluctuating neurological symptoms, progre ssive deterioration, and ocular, bulbar, respiratory, or pyramidal pattern d eficits, and differentials for contrast-enhancing brain lesions should inclu de primary brain tumors. In such cases, biopsy must proceed if the disease i s of relatively recent onset, to facilitate diagnosis and maximize treatment opportunities.
Journal Title: Journal of clinical neuroscience : official journal of the Ne urosurgical Society of Australasia

PUBMED ID: 30361826
DOI: doi.org/10.1007/s13402-018-0411-7
Titolo: Molecular features unique to glioblastoma radiation resistant residu al cells may affect patient outcome - a short report.
Autori: Kaur E., Goda JS., Ghorai A., Salunkhe S., Shetty P., Moiyadi AV., S ridhar E., Mahajan A., Jalali R., Dutt S.
Data di Pubblicazione: 2018-10-27
Abstract: Our data indicate that molecular features of innately radiation re sistant GBM cells independently correlate with clinical outcome. Our study a lso highlights the relevance of using patient-derived primary GBM cultures f or the characterization of RR cells that are otherwise inaccessible for anal ysis.
Journal Title: Cellular oncology (Dordrecht)

PUBMED ID: 30351999
DOI: doi.org/10.1200/JCO.2018.78.9990
Titolo: BRAF Inhibition in
Autori: Kaley T., Touat M., Subbiah V., Hollebecque A., Rodon J., Lockhart A C., Keedy V., Bielle F., Hofheinz RD., Joly F., Blay JY., Chau I., Puzanov I ., Raje NS., Wolf J., DeAngelis LM., Makrutzki M., Riehl T., Pitcher B., Bas elga J., Hyman DM.
Data di Pubblicazione: 2018-10-24
Abstract: Vemurafenib demonstrated evidence of durable antitumor activity in some patients with
Journal Title: Journal of clinical oncology : official journal of the Americ an Society of Clinical Oncology

PUBMED ID: 30227295
DOI: doi.org/10.1016/j.clineuro.2018.09.020

Titolo: How is stereotactic brain biopsy evolving? A multicentric analysis o f a series of 421 cases treated in Rome over the last sixteen years.
Autori: Callovini GM., Telera S., Sherkat S., Sperduti I., Callovini T., Car apella CM.
Data di Pubblicazione: 2018-09-19
Abstract: Over the last sixteen years, we have witnessed a significant decre ase in SBB procedures and a modification in target selection and histologic results. Despite the significant evolution of neuroimaging, an accurate non-invasive diagnosis of intracranial expanding lesions has not yet been achiev ed. Furthermore, the most recent WHO classification of brain tumors (2016), which incorporates molecular and morphological features, has boosted the nee d for molecular processing of tissue samples in all expanding brain lesions. For these reasons, it is likely that SBBs will continue to be performed in s pecific cases, playing a significant role in diagnostic confirmation by prov iding tissue samples, so as to better assess the biology and the prognosis o f cerebral lesions, as well as their sensitivity to standard radio-chemother apy or to new molecular target therapies.
Journal Title: Clinical neurology and neurosurgery

PUBMED ID: 30220707
DOI: doi.org/10.1038/s41416-018-0251-2
Titolo: Brief Report: Potent clinical and radiological response to larotrect inib in TRK fusion-driven high-grade glioma.
Autori: Ziegler DS., Wong M., Mayoh C., Kumar A., Tsoli M., Mould E., Tyrrel l V., Khuong-Quang DA., Pinese M., Gayevskiy V., Cohn RJ., Lau LMS., Reynold s M., Cox MC., Gifford A., Rodriguez M., Cowley MJ., Ekert PG., Marshall GM. , Haber M.
Data di Pubblicazione: 2018-09-18
Abstract: Genes encoding TRK are oncogenic drivers in multiple tumour types including infantile fibrosarcoma, papillary thyroid cancer and high-grade gl iomas (HGG). TRK fusions have a critical role in tumourigenesis in 40% of in fant HGG. Here we report the first case of a TRK fusion-driven HGG treated w ith larotrectinib-the first selective pan-TRK inhibitor in clinical developm ent. This 3-year-old girl had failed multiple therapies including chemothera py and radiotherapy. Tumour profiling confirmed an ETV6-NTRK3 fusion. Treatm ent with larotrectinib led to rapid clinical improvement with near total res olution of primary and metastatic lesions on MRI imaging. This is the first report of a TRK fusion glioma successfully treated with a TRK inhibitor.
Journal Title: British journal of cancer

PUBMED ID: 30206764
DOI: doi.org/10.1007/s11060-018-2991-5
Titolo: Reirradiation and PD-1 inhibition with nivolumab for the treatment o f recurrent diffuse intrinsic pontine glioma: a single-institution experienc e.
Autori: Kline C., Liu SJ., Duriseti S., Banerjee A., Nicolaides T., Raber S. , Gupta N., Haas-Kogan D., Braunstein S., Mueller S.
Data di Pubblicazione: 2018-09-13
Abstract: Our experience demonstrates the tolerability of reRT with concurre nt PD-1 inhibition for recurrent DIPG and suggests that combination therapy may offer survival benefit. Future prospective studies are needed to confirm the benefits of this combination therapy.
Journal Title: Journal of neuro-oncology

PUBMED ID: 30203110
DOI: doi.org/10.1007/s00066-018-1358-3

Titolo: CT-guided interstitial HDR-brachytherapy for recurrent glioblastoma multiforme: a 20-year single-institute experience.
Autori: Chatzikonstantinou G., Zamboglou N., Archavlis E., Strouthos I., Zoga E., Milickovic N., Hilaris B., Baltas D., Rödel C., Tselis N.
Data di Pubblicazione: 2018-09-12
Abstract: For patients with recurrent GBM, interstitial HDR BRT is an effective re-irradiation method for even larger tumors providing palliation without excessive toxicity.
Journal Title: Strahlentherapie und Onkologie : Organ der Deutschen Rontgengesellschaft ... [et al]

PUBMED ID: 30182159
DOI: doi.org/10.1007/s11060-018-2989-z
Titolo: Bevacizumab and re-irradiation for recurrent high grade gliomas: does sequence matter?
Autori: Palmer JD., Bhamidipati D., Song A., Eldredge-Hindy HB., Siglin J., Dan TD., Champ CE., Zhang I., Bar-Ad V., Kim L., Glass J., Evans JJ., Andrews DW., Werner-Wasik M., Shi W.
Data di Pubblicazione: 2018-09-06
Abstract: The combination of FSRT and BEV for recurrent/progressive HGG provides promising results in terms of overall survival and survival from recurrence. Combining these treatment modalities appears to improve upon the historic outcomes of either treatment alone. The outcomes data from this study support the ongoing RTOG trial exploring the combination of BEV and FSRT for recurrent HGG.
Journal Title: Journal of neuro-oncology

PUBMED ID: 30137042
DOI: doi.org/10.17116/neiro201882487
Titolo: [Li-Fraumeni syndrome in a patient with multiple anaplastic oligodendrogliomas of the brain (a case report and literature review)].
Autori: Potapov AA., Abdilatipov AA., Okhlopkov VA., Gavrilov AG., Zakharova NE., Goryaynov SA., Kobyakov GL., Absalyamova OV., Kravchuk AD., Kulikov AS., Shugay SV., Nikitin PV., Batalov AI., Shelygin YA., Lyubchenko LN., Aliev MD., Spallone A.
Data di Pubblicazione: 2018-08-24
Abstract: An analysis of the literature and the clinical case indicate the success of multiple surgical interventions and chemotherapy courses performed for a long time in the patient with Li-Fraumeni syndrome manifested by colon adenocarcinoma, recurrent B-cell lymphoma, and multiple anaplastic oligodendroglioma of the brain. The patient had a good quality of life and returned to professional activity.
Journal Title: Zhurnal voprosy neirokhirurgii imeni N. N. Burdenko

PUBMED ID: 30107580
DOI: doi.org/10.1093/neuros/nyy365
Titolo: Is Visible Aminolevulinic Acid-Induced Fluorescence an Independent Biomarker for Prognosis in Histologically Confirmed (World Health Organization 2016) Low-Grade Gliomas?
Autori: Jaber M., Ewelt C., Wölfer J., Brokinkel B., Thomas C., Hasselblatt M., Grauer O., Stummer W.
Data di Pubblicazione: 2018-08-15
Abstract: This is the first report investigating the role of ALA-induced fluorescence in histologically confirmed LGG. Fluorescence appeared to be a marker for inherent malignant transformation and OS, independently of known prognostic markers. Fluorescence in LGG might be taken into account when deciding on adjuvant therapies.

Journal Title: Neurosurgery

PUBMED ID: 30097825
DOI: doi.org/10.1007/s11060-018-2972-8
Titolo: Impact of adjuvant treatments on survival in Korean patients with WHO grade II gliomas: KNOG 15-02 and KROG 16-04 intergroup study.
Autori: Koo T., Lim DH., Seol HJ., Dho YS., Kim IH., Chang JH., Lee J., Jung TY., Gwak HS., Cho KH., Hong CK., Lee IJ., Kim E., Kim JH., Hong YK., Jang HS., Kim CY., Kim IA., Kim SH., Kim YI., Kim EY., Kim WC., Hong S.
Data di Pubblicazione: 2018-08-12
Abstract: The achievement of GTR is important to improve survival in LGG patients. Adjuvant chemotherapy may enhance PFS, but adjuvant RT did not improve survival outcomes. After PSM, we observed potential impacts of adjuvant RT on PFS. Our results may reflect real-world practice and consequently may help to optimize treatment strategies for LGG.
Journal Title: Journal of neuro-oncology

PUBMED ID: 30094640
DOI: doi.org/10.1007/s00234-018-2060-y
Titolo: Glioblastoma radiomics: can genomic and molecular characteristics correlate with imaging response patterns?
Autori: Soike MH., McTyre ER., Shah N., Puchalski RB., Holmes JA., Paulsson AK., Miller LD., Cramer CK., Lesser GJ., Strowd RE., Hinson WH., Mott RT., Johnson AJ., Lo HW., Laxton AW., Tatter SB., Debinski W., Chan MD.
Data di Pubblicazione: 2018-08-11
Abstract: IR is associated with improved OS and PFS. The proneural subtype and MGMT methylated tumors had higher rates of IR.
Journal Title: Neuroradiology

PUBMED ID: 30071804
DOI: doi.org/10.4155/tde-2018-0022
Titolo: Nanotechnology-based strategies as novel therapies in gliomas.
Autori: Gaikwad PS., Banerjee R.
Data di Pubblicazione: 2018-08-04
Abstract: Gliomas are the most common malignancies of the brain and have a mean survival of 12 months with only 5-10% of the patients surviving for more than 5 years, independent of treatment after diagnosis. Conventional treatment modalities have found the modest success in reducing tumor burden and metastases. Presence of different biological barriers and drug-resistance efflux transporters are crucial for tumor recurrence and treatment failure. Nanotechnology may amend these circumstances by targeting residual infiltrating malignant cells with minimal damage to normal cells, on-demand release and an improved cellular uptake by tumor cells. This review highlights the current status and advances in nanotechnology for treatment of gliomas.
Journal Title: Therapeutic delivery

PUBMED ID: 30069427
DOI: doi.org/10.1016/j.nicl.2018.07.001
Titolo: Imaging biomarkers guided anti-angiogenic therapy for malignant gliomas.
Autori: Kong Z., Yan C., Zhu R., Wang J., Wang Y., Wang Y., Wang R., Feng F., Ma W.
Data di Pubblicazione: 2018-08-03
Abstract: Antiangiogenic therapy is a universal approach to the treatment of malignant gliomas but fails to prolong the overall survival of newly diagnosed or recurrent glioblastoma patients. Imaging biomarkers are quantitative i

maging parameters capable of objectively describing biological processes, pa
thological changes and treatment responses in some situations and have been
utilized for outcome predictions of malignant gliomas in anti-angiogenic the
rapy. Advanced magnetic resonance imaging techniques (including perfusion-we
ighted imaging and diffusion-weighted imaging), positron emission computed t
omography and magnetic resonance spectroscopy are imaging techniques that ca
n be used to acquire imaging biomarkers, including the relative cerebral blo
od volume (rCBV), K
Journal Title: NeuroImage. Clinical

PUBMED ID: 30054667
DOI: doi.org/10.1007/s00262-018-2214-0
Titolo: High-grade glioma associated immunosuppression does not prevent immu
ne responses induced by therapeutic vaccines in combination with T
Autori: Löhr M., Freitag B., Technau A., Krauss J., Monoranu CM., Rachor J.,
Lutz MB., Hagemann C., Kessler AF., Linsenmann T., Wölfl M., Ernestus RI., E
ngelhardt S., Gelbrich G., Schlegel PG., Eyrich M.
Data di Pubblicazione: 2018-07-29
Abstract: High-grade gliomas (HGG) exert systemic immunosuppression, which i
s of particular importance as immunotherapeutic strategies such as therapeut
ic vaccines are increasingly used to treat HGGs. In a first cohort of 61 HGG
patients we evaluated a panel of 30 hematological and 34 plasma biomarkers.
Then, we investigated in a second cohort of 11 relapsed HGG patients receivi
ng immunomodulation with metronomic cyclophosphamide upfront to a DC-based v
accine whether immune abnormalities persisted and whether they hampered indu
ction of IFNγ
Journal Title: Cancer immunology, immunotherapy : CII

PUBMED ID: 30035459
DOI: doi.org/10.23736/S0390-5616.18.04463-6
Titolo: The prognostic improvement of add-on bevacizumab for progressive dis
ease during concomitant temozolomide and radiation therapy in the patients w
ith glioblastoma and anaplastic astrocytoma.
Autori: Yamaguchi S., Ishi Y., Motegi H., Okamoto M., Kobayashi H., Hirata K
., Oda Y., Tanaka S., Terasaka S., Houkin K.
Data di Pubblicazione: 2018-07-24
Abstract: We found that, for patients with GBM/AAs whose tumors were continu
ously growing during radiotherapy, add-on BEV treatment resulted in survival
benefits.
Journal Title: Journal of neurosurgical sciences

PUBMED ID: 30011045
DOI: doi.org/10.1093/neuros/nyy268
Titolo: Programmed Death Ligand 1 Is a Negative Prognostic Marker in Recurre
nt Isocitrate Dehydrogenase-Wildtype Glioblastoma.
Autori: Pratt D., Dominah G., Lobel G., Obungu A., Lynes J., Sanchez V., Ada
mstein N., Wang X., Edwards NA., Wu T., Maric D., Giles AJ., Gilbert MR., Qu
ezado M., Nduom EK.
Data di Pubblicazione: 2018-07-17
Abstract: A 5% PD-L1 expression cut-off identified a subset of glioblastoma
that is associated with a worse clinical outcome. This association remained
significant within the newly defined IDH-wildtype classification. These find
ings could have implications for patient stratification in future clinical t
rials of PD-1/PD-L1 blockade.
Journal Title: Neurosurgery

PUBMED ID: 29997250
DOI: doi.org/10.1126/scitranslmed.aao3240
Titolo: CRISPR-enhanced engineering of therapy-sensitive cancer cells for self-targeting of primary and metastatic tumors.
Autori: Reinshagen C., Bhere D., Choi SH., Hutten S., Nesterenko I., Wakimoto H., Le Roux E., Rizvi A., Du W., Minicucci C., Shah K.
Data di Pubblicazione: 2018-07-13
Abstract: Tumor cells engineered to express therapeutic agents have shown promise to treat cancer. However, their potential to target cell surface receptors specific to the tumor site and their posttreatment fate have not been explored. We created therapeutic tumor cells expressing ligands specific to primary and recurrent tumor sites (receptor self-targeted tumor cells) and extensively characterized two different approaches using (i) therapy-resistant cancer cells, engineered with secretable death receptor-targeting ligands for "off-the-shelf" therapy in primary tumor settings, and (ii) therapy-sensitive cancer cells, which were CRISPR-engineered to knock out therapy-specific cell surface receptors before engineering with receptor self-targeted ligands and reapplied in autologous models of recurrent or metastatic disease. We show that both approaches allow high expression of targeted ligands that induce tumor cell killing and translate into marked survival benefits in mouse models of multiple cancer types. Safe elimination of therapeutic cancer cells after treatment was achieved by co-engineering with a prodrug-converting suicide system, which also allowed for real-time in vivo positron emission tomography imaging of therapeutic tumor cell fate. This study demonstrates self-tumor tropism of engineered cancer cells and their therapeutic potential when engineered with receptor self-targeted molecules, and it establishes a roadmap toward a safe clinical translation for different cancer types in primary, recurrent, and metastatic settings.
Journal Title: Science translational medicine

PUBMED ID: 29992434
DOI: doi.org/10.1007/s11060-018-2931-4
Titolo: Pineal region glioblastomas display features of diffuse midline and non-midline gliomas.
Autori: D'Amico RS., Zanazzi G., Wu P., Canoll P., Bruce JN.
Data di Pubblicazione: 2018-07-12
Abstract: This study expands the clinical and pathologic spectrum of pineal region GBM, and provides the first report of the genetic landscape of these tumors.
Journal Title: Journal of neuro-oncology

PUBMED ID: 29990975
DOI: doi.org/10.1159/000469681
Titolo: Novel and Prospective Molecular Targets for Therapy of Intracranial Gliomas.
Autori: Butowski N.
Data di Pubblicazione: 2018-07-11
Abstract: Multiple alterations in the expression levels of genes or proteins have been identified in gliomas, including activation of oncogenes and silencing of tumor suppressor genes. Illuminating these molecular mechanisms of tumorigenesis and treatment resistance is necessary for the development of new therapies. With the promise of better effectiveness and less toxicity, the emphasis in drug development has moved from cytotoxic, non-specific chemotherapies to molecular targeted agents. However, despite progress in other areas of oncology, targeted therapy success stories in cases of brain tumors remain all but absent. Nonetheless, experiences from previous clinical trials suggest that a small number of unselected patients may benefit from such treatment. An increasing knowledge about related factors and prospective enrichm

ent strategies now shape research and clinical trial design in neuro-oncolog y and may lead to improved outcomes after molecular targeted therapies of gl iomas.
Journal Title: Progress in neurological surgery

PUBMED ID: 29980414
DOI: doi.org/10.1016/j.ijrobp.2018.04.045
Titolo: Combining Perfusion and High B-value Diffusion MRI to Inform Prognos is and Predict Failure Patterns in Glioblastoma.
Autori: Wahl DR., Kim MM., Aryal MP., Hartman H., Lawrence TS., Schipper MJ. , Parmar HA., Cao Y.
Data di Pubblicazione: 2018-07-08
Abstract: TV
Journal Title: International journal of radiation oncology, biology, physics

PUBMED ID: 29980179
DOI: doi.org/10.1186/s12883-018-1099-z
Titolo: Clinical characteristics and short-term prognosis of LGI1 antibody e ncephalitis: a retrospective case study.
Autori: Li W., Wu S., Meng Q., Zhang X., Guo Y., Cong L., Cong S., Zheng D.
Data di Pubblicazione: 2018-07-08
Abstract: Primary symptoms of LGI1 antibody encephalitis include memory impa irments, seizures, FBDS, and mental and behavioral abnormalities. Increased titers of LGI1 antibodies are also present in the serum/CSF of patients. Pat ients often have hyponatremia, and MRIs show abnormalities in various brain regions. Finally, immunotherapy shows good efficacy and positive benefits, a lthough patients may relapse in the short-term.
Journal Title: BMC neurology

PUBMED ID: 29979390
DOI: doi.org/10.1097/MD.0000000000011254
Titolo: High-dose fotemustine in temozolomide-pretreated glioblastoma multif orme patients: A phase I/II trial.
Autori: Marinelli A., Lamberti G., Cerbone L., Cordua N., Buonerba C., Pelus o G., Di Lorenzo G., De Placido S.
Data di Pubblicazione: 2018-07-07
Abstract: We conclude that fotemustine can be safely administered at 120mg/m biweekly. The efficacy of such modified schedule and doses should be compare d to the biweekly schedule at 80mg and the standard weekly schedule at 80 to 100mg/m.
Journal Title: Medicine

PUBMED ID: 29953370
DOI: doi.org/10.1615/CritRevOncog.2018025740
Titolo: Radiation-Induced Gliomas.
Autori: Aherne NJ., Murphy BM.
Data di Pubblicazione: 2018-06-29
Abstract: Radiation therapy has been a cornerstone of cancer management for many decades and is an integral part of the multi-modality care of patients with brain tumors. The known serious side effects of radiation therapy on th e head or central nervous system are uncommon and include radiation necrosis , microangiopathy, and progressive leukencephalopathy. In addition, there ha ve been descriptions of radiation-induced tumors including sarcomas, gliomas , lymphomas, and carcinomas of the thyroid. Patients who have received radia tion therapy of the head or face may rarely develop radiation-induced tumors

, a majority of which are meningiomas, followed by radiation-induced gliomas (RIGs) and sarcomas. The increased risk of RIGs is well described in both th e pediatric and adult populations and after the use of both therapeutic and diagnostic radiations. The incidence of RIGs is estimated at approximately 0 .5-2.7% at a latent period of approximately 15 years. The risk appears to be dependent on patient age at treatment, as well as radiation dose and treatme nt volume considerations. The scope of this review focuses on the etiology, clinical features, and management of RIGs as they relate to previous radiati on therapy.
Journal Title: Critical reviews in oncogenesis

PUBMED ID: 29949160
DOI: doi.org/10.26355/eurrev_201806_15268
Titolo: MicroRNA-378 acts as a prognosis marker and inhibits cell migration, invasion and epithelial-mesenchymal transition in human glioma by targeting IRG1.
Autori: Shi HZ., Wang D., Sun XN., Sheng L.
Data di Pubblicazione: 2018-06-28
Abstract: We showed that the suppressive role of miR-378 in glioma, which wa s regulated by IRG1, suggested that the miR-378/IRG1 axis may be an effectiv e target for glioma treatment.
Journal Title: European review for medical and pharmacological sciences

PUBMED ID: 29943141
DOI: doi.org/10.1007/s10143-018-0996-3
Titolo: IDH wild-type WHO grade II diffuse low-grade gliomas. A heterogeneou s family with different outcomes. Systematic review and meta-analysis.
Autori: Di Carlo DT., Duffau H., Cagnazzo F., Benedetto N., Morganti R., Per rini P.
Data di Pubblicazione: 2018-06-27
Abstract: WHO grade II diffuse low-grade gliomas (DLGGs) were recently divid ed into sub-groups on the basis of their molecular profiles. IDH wild-type (IDH-wt) tumors seem to be associated with unfavorable prognoses due to biolo gical similarities to glioblastomas. The authors performed a systematic revi ew and meta-analysis of literature examining epidemiology, clinical characte ristics, management, and the outcome of IDH-wt grade II DLGGs. According to PRISMA guidelines, a comprehensive review of studies published from January 2009 to October 2017 was carried out. The authors identified series that exa mined the prevalence rate, clinical and radiological characteristics, treatm ent, and outcome of IDH-wt DLGGs. Variables influencing outcomes were analyz ed using a random-effects meta-analysis model. Finally, a meta-regression an alysis was performed to examine the impact of therapeutic strategies on the effect-size. Twenty-two studies were included in this systematic review. The IDH-wt prevalence rate was 22.9% (95% CI 18.4-27.4%). The hazard ratio for t his molecular subgroup in the DLGGs population was 3.46 (95% CI 2.24-5.36; p <0.001), and the heterogeneity was significant (I
Journal Title: Neurosurgical review

PUBMED ID: 29942135
DOI: doi.org/10.2147/OTT.S160685
Titolo: Effectiveness of lomustine and bevacizumab in progressive glioblasto ma: a meta-analysis.
Autori: Song J., Xue YQ., Zhao MM., Xu P.
Data di Pubblicazione: 2018-06-27
Abstract: Although treatment with CCNU plus BEV prolonged PFS, it did not co nfer OS advantage over monotherapies in patients with progressive GBM. The e

ncouraging results of the addition of CCNU to BEV warrant investigation in f urther randomized trials.
Journal Title: OncoTargets and therapy

PUBMED ID: 29879076
DOI: doi.org/10.1097/MD.0000000000011072
Titolo: Primary central nervous system lymphoma in a patient with systemic l upus erythematosus mimicking high-grade glioma: A case report and review of literature.
Autori: Su L., Ding M., Chen L., Li C., Lao M.
Data di Pubblicazione: 2018-06-08
Abstract: PCNSL in immunocompromised hosts may present heterogeneous contras t enhancement, which should be differentiated from other diseases especially high-grade glioma.
Journal Title: Medicine

PUBMED ID: 29868485
DOI: doi.org/10.3389/fonc.2018.00169
Titolo: The Integration of Biology Into the Treatment of Diffuse Intrinsic P ontine Glioma: A Review of the North American Clinical Trial Perspective.
Autori: Clymer J., Kieran MW.
Data di Pubblicazione: 2018-06-06
Abstract: Dramatic advances in the molecular analysis of diffuse intrinsic p ontine glioma have occurred over the last decade and resulted in the identif ication of potential therapeutic targets. In spite of these advances, no sig nificant improvement in the outcome has been achieved and median survival re mains approximately 10 months. An understanding of the approaches that have b een taken to date, why they failed, and how that information can lead the fi eld forward is critical if we are to change the
Journal Title: Frontiers in oncology

PUBMED ID: 29855771
DOI: doi.org/10.1007/s11060-018-2910-9
Titolo: Mono-exponential, diffusion kurtosis and stretched exponential diffu sion MR imaging response to chemoradiation in newly diagnosed glioblastoma.
Autori: Chakhoyan A., Woodworth DC., Harris RJ., Lai A., Nghiemphu PL., Liau LM., Pope WB., Cloughesy TF., Ellingson BM.
Data di Pubblicazione: 2018-06-02
Abstract: Despite increased tissue complexity following chemoradiation, adva nced diffusion models have longer acquisition times, provide largely compara ble measures of diffusivity, and do not appear to provide additional prognos tic value compared to mono-exponential ADC maps.
Journal Title: Journal of neuro-oncology

PUBMED ID: 29788980
DOI: doi.org/10.1186/s13256-018-1680-5
Titolo: Treatment of ventriculoperitoneal shunt infection and ventriculitis caused by Acinetobacter baumannii: a case report.
Autori: Demoz GT., Alebachew M., Legesse Y., Ayalneh B.
Data di Pubblicazione: 2018-05-24
Abstract: We presented our case of pandrug-resistant A. baumannii ventriculo peritoneal shunt infection and ventriculitis successfully treated with a sys temic ampicillin-sulbactam. Provision of systemic ampicillin-sulbactam shoul d not be undermined. Therefore, this case exemplifies that intravenous admin

istration of ampicillin-sulbactam can be a good therapeutic option against A . baumannii ventriculoperitoneal shunt infection and ventriculitis.
Journal Title: Journal of medical case reports

PUBMED ID: 29779086
DOI: doi.org/10.1007/s11060-018-2907-4
Titolo: Retrospective study of nivolumab for patients with recurrent high gr ade gliomas.
Autori: Mantica M., Pritchard A., Lieberman F., Drappatz J.
Data di Pubblicazione: 2018-05-21
Abstract: Treatment with nivolumab therapy was associated with a manageable safety profile. In a subset of patients, there was disease stabilization in heavily pre-treated recurrent HGG.
Journal Title: Journal of neuro-oncology

PUBMED ID: 29774180
DOI: doi.org/10.21037/qims.2018.04.05
Titolo: Survival prediction based on qualitative MRI diffusion signature in patients with recurrent high grade glioma treated with bevacizumab.
Autori: Goyal P., Tenenbaum M., Gupta S., Kochar PS., Bhatt AA., Mangla M., Kumar Y., Mangla R.
Data di Pubblicazione: 2018-05-19
Abstract: In patients with recurrent glioma treated with bevacizumab, the pr esence of homogenous dark signal (FDR
Journal Title: Quantitative imaging in medicine and surgery

PUBMED ID: 29764702
DOI: doi.org/10.1016/j.jocn.2018.04.077
Titolo: A novel neuromodulation technique for the rehabilitation of balance and gait: A case study.
Autori: Cofré Lizama LE., Bastani A., Panisset MG., Drummond K., Khan F., Ga lea MP.
Data di Pubblicazione: 2018-05-17
Abstract: Cranial-nerve non-invasive neuromodulation (CN-NINM) through the t ongue has been proposed as an adjuvant intervention to improve efficacy of r ehabilitation. However, CN-NINM effects have only been explored in multiple sclerosis and stroke populations. In this report we used CN-NINM during a 2-week (2 × 1.5 h sessions daily) physiotherapy program for the rehabilitation o f a 57 y/o woman presenting with balance and gait impairments after a surgic al resection of a fourth ventricular ependymoma. Clinical and instrumented b alance and gait assessments showed improved performance in all tests and wit hout adverse effects This study shows the beneficial effects and feasibility of combined physiotherapy and CN-NINM in this patient.
Journal Title: Journal of clinical neuroscience : official journal of the Ne urosurgical Society of Australasia

PUBMED ID: 29753958
DOI: doi.org/10.1016/j.jconrel.2018.05.008
Titolo: Drug delivery challenges and future of chemotherapeutic nanomedicine for glioblastoma treatment.
Autori: Ganipineni LP., Danhier F., Préat V.
Data di Pubblicazione: 2018-05-14
Abstract: Glioblastoma (GBM) is one of the most aggressive and deadliest cen tral nervous system tumors, and the current standard treatment is surgery fo llowed by radiotherapy with concurrent chemotherapy. Nevertheless, the survi

val period is notably low. Although ample research has been performed to dev elop an effective therapeutic strategy for treating GBM, the success of exte nding patients' survival period and quality of life is limited. This review focuses on the strategies developed to address the challenges associated wit h drug delivery in GBM, particularly nanomedicine. The first part describes major obstacles to the development of effective GBM treatment strategies. Th e second part focuses on the conventional chemotherapeutic nanomedicine stra tegies, their limitations and the novel and advanced strategies of nanomedic ine, which could be promising for GBM treatment. We also highlighted the pro minence of nanomedicine clinical translation. The near future looks bright f ollowing the beginning of clinical translation of nanochemotherapy for GBM.
Journal Title: Journal of controlled release : official journal of the Contr olled Release Society

PUBMED ID: 29752148
DOI: doi.org/10.1016/j.neuchi.2017.12.007
Titolo: Malignant primary diffuse leptomeningeal gliomatosis with histone H3 .3 K27M mutation.
Autori: Champeaux C., Drier A., Devaux B., Tauziède-Espariat A.
Data di Pubblicazione: 2018-05-13
Abstract: MPLG is a rare tumor which should be considered whenever a patient presents with diffuse or multinodular meningeal contrast-enhancing lesions. Some cases of MLPG share histological and immunophenotypical features with d iffuse midline gliomas H3-K27M-mutant, a rapidly fatal disease. The diagnosi s remains histopathological and, therefore a biopsy is obligatory without de lay. Immunohistochemistry and/or molecular analyses are now currently essent ial for a formal classification and, to provide a better prediction of clini cal outcome, particularly in this heterogeneous group of tumors.
Journal Title: Neuro-Chirurgie

PUBMED ID: 29712977
DOI: doi.org/10.1038/s41598-018-25169-2
Titolo: Concordant association validates MGMT methylation and protein expres sion as favorable prognostic factors in glioma patients on alkylating chemot herapy (Temozolomide).
Autori: Pandith AA., Qasim I., Zahoor W., Shah P., Bhat AR., Sanadhya D., Sh ah ZA., Naikoo NA.
Data di Pubblicazione: 2018-05-02
Abstract: O
Journal Title: Scientific reports

PUBMED ID: 29687258
DOI: doi.org/10.1007/s00401-018-1849-4
Titolo: Novel, improved grading system(s) for IDH-mutant astrocytic gliomas.
Autori: Shirahata M., Ono T., Stichel D., Schrimpf D., Reuss DE., Sahm F., K oelsche C., Wefers A., Reinhardt A., Huang K., Sievers P., Shimizu H., Nanjo H., Kobayashi Y., Miyake Y., Suzuki T., Adachi JI., Mishima K., Sasaki A., N ishikawa R., Bewerunge-Hudler M., Ryzhova M., Absalyamova O., Golanov A., Si nn P., Platten M., Jungk C., Winkler F., Wick A., Hänggi D., Unterberg A., P fister SM., Jones DTW., van den Bent M., Hegi M., French P., Baumert BG., St upp R., Gorlia T., Weller M., Capper D., Korshunov A., Herold-Mende C., Wick W., Louis DN., von Deimling A.
Data di Pubblicazione: 2018-04-25
Abstract: According to the 2016 World Health Organization Classification of Tumors of the Central Nervous System (2016 CNS WHO), IDH-mutant astrocytic g liomas comprised WHO grade II diffuse astrocytoma, IDH-mutant (AII
Journal Title: Acta neuropathologica

PUBMED ID: 29676695
DOI: doi.org/10.3171/2017.10.JNS171825
Titolo: Huge heterogeneity in survival in a subset of adult patients with re sected, wild-type isocitrate dehydrogenase status, WHO grade II astrocytomas .
Autori: Poulen G., Gozé C., Rigau V., Duffau H.
Data di Pubblicazione: 2018-04-21
Abstract: OBJECTIVEWorld Health Organization grade II gliomas are infiltrati ng tumors that inexorably progress to a higher grade of malignancy. However, the time to malignant transformation is quite unpredictable at the individua l patient level. A wild-type isocitrate dehydrogenase (IDH-wt) molecular pro file has been reported as a poor prognostic factor, with more rapid progress ion and a shorter survival compared with IDH-mutant tumors. Here, the oncolo gical outcomes of a series of adult patients with IDH-wt, diffuse, WHO grade II astrocytomas (AII) who underwent resection without early adjuvant therapy were investigated.METHODSA retrospective review of patients extracted from a prospective database who underwent resection between 2007 and 2013 for histo pathologically confirmed, IDH-wt, non-1p19q codeleted AII was performed. All patients had a minimum follow-up period of 2 years. Information regarding cl inical, radiographic, and surgical results and survival were collected and a nalyzed.RESULTSThirty-one consecutive patients (18 men and 13 women, median age 39.6 years) were included in this study. The preoperative median tumor v olume was 54 cm3 (range 3.5-180 cm3). The median growth rate, measured as th e velocity of diametric expansion, was 2.45 mm/year. The median residual vol ume after surgery was 4.2 cm3 (range 0-30 cm3) with a median volumetric exte nt of resection of 93.97% (8 patients had a total or supratotal resection). No patient experienced permanent neurological deficits after surgery, and al l patients resumed a normal life. No immediate postoperative chemotherapy or radiation therapy was given. The median clinical follow-up duration from dia gnosis was 74 months (range 27-157 months). In this follow-up period, 18 pat ients received delayed chemotherapy and/or radiotherapy for tumor progressio n. Five patients (16%) died at a median time from radiological diagnosis of 3.5 years (range 2.6-4.5 years). Survival from diagnosis was 77.27% at 5 yea rs. None of the 21 patients with a long-term follow-up greater than 5 years have died. There were no significant differences between the clinical, radio logical, or molecular characteristics of the survivors relative to the patie nts who died.CONCLUSIONSHuge heterogeneity in the survival data for a subset of 31 patients with resected IDH-wt AII tumors was observed. These findings suggest that IDH mutation status alone is not sufficient to predict risk of malignant transformation and survival at the individual level. Therefore, th e therapeutic management of AII tumors, in particular the decision to admini ster early adjuvant chemotherapy and/or radiation therapy following surgery, should not solely rely on routine molecular markers.
Journal Title: Journal of neurosurgery

PUBMED ID: 29637509
DOI: doi.org/10.1007/s11060-018-2847-z
Titolo: Safety, efficacy and survival of patients with primary malignant bra in tumours (PMBT) in phase I (Ph1) trials: the 12-year Royal Marsden experie nce.
Autori: Coleman N., Michalarea V., Alken S., Rihawi K., Lopez RP., Tunariu N ., Petruckevitch A., Molife LR., Banerji U., De Bono JS., Welsh L., Saran F. , Lopez J.
Data di Pubblicazione: 2018-04-12
Abstract: We report a survival benefit for patients with PMBT treated on Ph1 trials. Toxicity and efficacy outcomes were comparable to the general Ph1 po pulation. In the absence of an internationally recognized standard second li

ne treatment for patients with recurrent PMBT, more Ph1 trials should allow enrolment of patients with refractory PMBT and Ph1 trial participation shoul d be considered at an earlier stage.
Journal Title: Journal of neuro-oncology

PUBMED ID: 29632053
DOI: doi.org/10.6004/jnccn.2017.7052
Titolo: Concurrent BRAF/MEK Inhibitors in
Autori: Schreck KC., Guajardo A., Lin DDM., Eberhart CG., Grossman SA.
Data di Pubblicazione: 2018-04-11
Abstract: We report a survival benefit for patients with PMBT treated on Ph1 trials. Toxicity and efficacy outcomes were comparable to the general Ph1 po pulation. In the absence of an internationally recognized standard second li ne treatment for patients with recurrent PMBT, more Ph1 trials should allow enrolment of patients with refractory PMBT and Ph1 trial participation shoul d be considered at an earlier stage.
Journal Title: Journal of the National Comprehensive Cancer Network : JNCCN

PUBMED ID: 29619962
DOI: doi.org/10.1016/j.ijrobp.2018.01.048
Titolo: A Prospective 4π Radiation Therapy Clinical Study in Recurrent High-Grade Glioma Patients.
Autori: Yu VY., Landers A., Woods K., Nguyen D., Cao M., Du D., Chin RK., Sh eng K., Kaprealian TB.
Data di Pubblicazione: 2018-04-06
Abstract: The feasibility, safety, dosimetric benefits, delivery efficiency, and patient comfort of 4π radiation therapy have been clinically demonstrate d with a prospective clinical trial. The results elucidate the potential and challenges of wider clinical implementations.
Journal Title: International journal of radiation oncology, biology, physics

PUBMED ID: 29594657
DOI: doi.org/10.1007/s11060-018-2820-x
Titolo: A predictive value of von Willebrand factor for early response to Be vacizumab therapy in recurrent glioma.
Autori: Pace A., Mandoj C., Antenucci A., Villani V., Sperduti I., Casini B. , Carosi M., Fabi A., Vidiri A., Koudriavtseva T., Conti L.
Data di Pubblicazione: 2018-03-30
Abstract: Bevacizumab (BV), a neutralizing monoclonal antibody against the v ascular endothelial growth factor ligand, is recognized as a potent anti-ang iogenic agent with antitumor activity. The aim of this single-center, retros pective, longitudinal study was to investigate the possible predictive value of baseline demographic, clinical and laboratory parameters for early 3-mont h response to BV therapy in patients with recurrent glioma. Forty-nine patie nts with recurrent glioma received BV at 10 mg/kg intravenously every 3 week s alone or in association with chemotherapy were included in this study. Blo od samples were collected from all patients before the first (baseline), the second and the third administration of BV. After 3 months of BV therapy, pat ients with partial response were defined as responders whereas patients with stable or progressive disease were defined as non-responders. The median ove rall follow-up was 8 months (range 1-73), the median overall survival (OS) w as 8 months (95% CI 6-10) and the median progression free survival (PFS) was 4 months (95% CI 3-5). Thirty-five % of patients were responders and showed significantly lower von Willebrand factor (VWF) levels than non-responders a t all sample times ($p<.02$ for all). Also, on multivariate analysis the base line VWF value was the only predictor for an early response to BV therapy. F

urthermore, D-dimer and prothrombin fragment 1+2 were predictive factors for OS while Karnofsky performance status resulted predictive for PFS. VWF antig en value is a possible predictive biomarker for an early 3-month response to BV therapy in recurrent glioma.
Journal Title: Journal of neuro-oncology

PUBMED ID: 29572492
DOI: doi.org/10.1038/s41598-018-22739-2
Titolo: Radiomic MRI signature reveals three distinct subtypes of glioblasto ma with different clinical and molecular characteristics, offering prognosti c value beyond IDH1.
Autori: Rathore S., Akbari H., Rozycki M., Abdullah KG., Nasrallah MP., Bind er ZA., Davuluri RV., Lustig RA., Dahmane N., Bilello M., O'Rourke DM., Dava tzikos C.
Data di Pubblicazione: 2018-03-25
Abstract: The remarkable heterogeneity of glioblastoma, across patients and over time, is one of the main challenges in precision diagnostics and treatm ent planning. Non-invasive in vivo characterization of this heterogeneity us ing imaging could assist in understanding disease subtypes, as well as in ri sk-stratification and treatment planning of glioblastoma. The current study leveraged advanced imaging analytics and radiomic approaches applied to mult i-parametric MRI of de novo glioblastoma patients (n=208 discovery, n=53 re plication), and discovered three distinct and reproducible imaging subtypes of glioblastoma, with differential clinical outcome and underlying molecular characteristics, including isocitrate dehydrogenase-1 (IDH1), O
Journal Title: Scientific reports

PUBMED ID: 29559563
DOI: doi.org/10.1158/1078-0432.CCR-17-1775
Titolo: Phase I Study of MEDI3617, a Selective Angiopoietin-2 Inhibitor Alon e and Combined with Carboplatin/Paclitaxel, Paclitaxel, or Bevacizumab for A dvanced Solid Tumors.
Autori: Hyman DM., Rizvi N., Natale R., Armstrong DK., Birrer M., Recht L., Dotan E., Makker V., Kaley T., Kuruvilla D., Gribbin M., McDevitt J., Lai DW ., Dar M.
Data di Pubblicazione: 2018-03-22
Abstract: The remarkable heterogeneity of glioblastoma, across patients and over time, is one of the main challenges in precision diagnostics and treatm ent planning. Non-invasive in vivo characterization of this heterogeneity us ing imaging could assist in understanding disease subtypes, as well as in ri sk-stratification and treatment planning of glioblastoma. The current study leveraged advanced imaging analytics and radiomic approaches applied to mult i-parametric MRI of de novo glioblastoma patients (n=208 discovery, n=53 re plication), and discovered three distinct and reproducible imaging subtypes of glioblastoma, with differential clinical outcome and underlying molecular characteristics, including isocitrate dehydrogenase-1 (IDH1), O
Journal Title: Clinical cancer research : an official journal of the America n Association for Cancer Research

PUBMED ID: 29557060
DOI: doi.org/10.1007/s11060-018-2831-7
Titolo: JCOG0911 INTEGRA study: a randomized screening phase II trial of int erferonβ plus temozolomide in comparison with temozolomide alone for newly d iagnosed glioblastoma.
Autori: Wakabayashi T., Natsume A., Mizusawa J., Katayama H., Fukuda H., Sum i M., Nishikawa R., Narita Y., Muragaki Y., Maruyama T., Ito T., Beppu T., N

akamura H., Kayama T., Sato S., Nagane M., Mishima K., Nakasu Y., Kurisu K., Yamasaki F., Sugiyama K., Onishi T., Iwadate Y., Terasaki M., Kobayashi H., Matsumura A., Ishikawa E., Sasaki H., Mukasa A., Matsuo T., Hirano H., Kumabe T., Shinoura N., Hashimoto N., Aoki T., Asai A., Abe T., Yoshino A., Arakawa Y., Asano K., Yoshimoto K., Shibui S., Shibui S.
Data di Pubblicazione: 2018-03-21
Abstract: TMZ + IFNβ + RT is not considered as a candidate for the following phase III trial, and TMZ + RT remained to be a most promising treatment. This trial was registered with the UMIN Clinical Trials Registry: UMIN000003466.
Journal Title: Journal of neuro-oncology

PUBMED ID: 29551724
DOI: doi.org/10.1016/j.wneu.2018.03.069
Titolo: The Effectiveness of Salvage Treatments for Recurrent Lesions of Oligodendrogliomas Previously Treated with Upfront Chemotherapy.
Autori: Kuga D., Hata N., Akagi Y., Amemiya T., Sangatsuda Y., Hatae R., Yoshimoto K., Mizoguchi M., Iihara K.
Data di Pubblicazione: 2018-03-20
Abstract: In isocitrate dehydrogenase-mutant and 1p/19q-codeleted oligodendrogliomas, most of the tumors that demonstrated early progression appeared as local, nonlethal lesions, which have been well-controlled by salvage treatments. A precise diagnosis of oligodendrogliomas using molecular parameters is crucial to receive the best benefit from salvage treatment.
Journal Title: World neurosurgery

PUBMED ID: 29540809
DOI: doi.org/10.1038/s41598-018-22697-9
Titolo: Retrospective Analysis of Radiological Recurrence Patterns in Glioblastoma, Their Prognostic Value And Association to Postoperative Infarct Volume.
Autori: Bette S., Barz M., Huber T., Straube C., Schmidt-Graf F., Combs SE., Delbridge C., Gerhardt J., Zimmer C., Meyer B., Kirschke JS., Boeckh-Behrens T., Wiestler B., Gempt J.
Data di Pubblicazione: 2018-03-16
Abstract: Recent studies suggested that postoperative hypoxia might trigger invasive tumor growth, resulting in diffuse/multifocal recurrence patterns. Aim of this study was to analyze distinct recurrence patterns and their association to postoperative infarct volume and outcome. 526 consecutive glioblastoma patients were analyzed, of which 129 met our inclusion criteria: initial tumor diagnosis, surgery, postoperative diffusion-weighted imaging and tumor recurrence during follow-up. Distinct patterns of contrast-enhancement at initial diagnosis and at first tumor recurrence (multifocal growth/progression, contact to dura/ventricle, ependymal spread, local/distant recurrence) were recorded by two blinded neuroradiologists. The association of radiological patterns to survival and postoperative infarct volume was analyzed by uni-/multivariate survival analyses and binary logistic regression analysis. With increasing postoperative infarct volume, patients were significantly more likely to develop multifocal recurrence, recurrence with contact to ventricle and contact to dura. Patients with multifocal recurrence (Hazard Ratio (HR) 1.99, P = 0.010) had significantly shorter OS, patients with recurrent tumor with contact to ventricle (HR 1.85, P = 0.036), ependymal spread (HR 2.97, P = 0.004) and distant recurrence (HR 1.75, P = 0.019) significantly shorter post-progression survival in multivariate analyses including well-established prognostic factors like age, Karnofsky Performance Score (KPS), therapy, extent of resection and patterns of primary tumors. Postoperative infarct volume might initiate hypoxia-mediated aggressive tumor growth resulting in multifocal and diffuse recurrence patterns and impaired survival.

Journal Title: Scientific reports

PUBMED ID: 29524050
DOI: doi.org/10.1007/s12035-018-0978-z
Titolo: Role of Chimeric Antigen Receptor T Cell Therapy in Glioblastoma Multiforme.
Autori: Jindal V.
Data di Pubblicazione: 2018-03-11
Abstract: Glioblastoma multiforme (GBM) is the most common primary malignant cancer of brain, which is extremely aggressive and carries a dreadful prognosis. Current treatment protocol runs around radiotherapy, surgical resection, and temozolomide with median overall survival of around 12-15 months. Due to its heterogeneity and mutational load, immunotherapy with chimeric antigen receptor (CAR) T cell therapy can be a promising treatment option for recurrent glioblastoma. Initial phase 1 studies have shown that this therapy is safe without dose-limiting side effects and it also has a better clinical outcome. Therefore, CAR T cell therapy can be a great future tool in our armamentarium to treat advanced GBM. In this article, we have explained the structure, mechanism of action, and rationale of CAR T cell therapy in GBM; we also discussed various antigenic targets and clinical outcome of initial studies of this novel therapy.
Journal Title: Molecular neurobiology

PUBMED ID: 29522936
DOI: doi.org/10.1016/j.clineuro.2018.02.027
Titolo: Evaluation of DNA ploidy with intraoperative flow cytometry may predict long-term survival of patients with supratentorial low-grade gliomas: Analysis of 102 cases.
Autori: Suzuki A., Maruyama T., Nitta M., Komori T., Ikuta S., Chernov M., Tamura M., Kawamata T., Muragaki Y.
Data di Pubblicazione: 2018-03-10
Abstract: DNA ploidy assessed with iFC may be effectively used as prognostic indicator in cases of LGG, especially of DA. Aneuploid tumors demonstrate more aggressive clinical course translated into shorter OS of patients. Thus, their detection during surgery may be helpful for decision on the optimal EOR, and for choice of the most appropriate postoperative adjuvant therapy.
Journal Title: Clinical neurology and neurosurgery

PUBMED ID: 29492119
DOI: doi.org/10.4103/ajns.AJNS_95_17
Titolo: Significant Effect of Anti-tyrosine Kinase Inhibitor (Gefitinib) on Overall Survival of the Glioblastoma Multiforme Patients in the Backdrop of Mutational Status of Epidermal Growth Factor Receptor and
Autori: Arif SH., Pandith AA., Tabasum R., Ramzan AU., Singh S., Siddiqi MA., Bhat AR.
Data di Pubblicazione: 2018-03-02
Abstract: We conclude that
Journal Title: Asian journal of neurosurgery

PUBMED ID: 29483008
DOI: doi.org/10.1016/j.jocn.2018.02.009
Titolo: The utilization of MGMT promoter methylation testing in United States hospitals for glioblastoma and its impact on prognosis.
Autori: Lee A., Youssef I., Osborn VW., Safdieh J., Becker DJ., Schreiber D.
Data di Pubblicazione: 2018-02-28
Abstract: Multiple studies have identified O

Journal Title: Journal of clinical neuroscience : official journal of the Ne
urosurgical Society of Australasia

PUBMED ID: 29442128
DOI: doi.org/10.1007/s00066-018-1276-4
Titolo: Semantic imaging features predict disease progression and survival i
n glioblastoma multiforme patients.
Autori: Peeken JC., Hesse J., Haller B., Kessel KA., Nüsslin F., Combs SE.
Data di Pubblicazione: 2018-02-15
Abstract: We demonstrated a predictive value of several qualitative imaging
features for progression and survival. The performance of prognostic models
was increased by combining clinical, pathological, and imaging features.
Journal Title: Strahlentherapie und Onkologie : Organ der Deutschen Rontgeng
esellschaft ... [et al]

PUBMED ID: 29412012
DOI: doi.org/10.1080/10717544.2018.1436099
Titolo: Application of an assay Cascade methodology for a deep preclinical c
haracterization of polymeric nanoparticles as a treatment for gliomas.
Autori: Fornaguera C., Lázaro MÁ., Brugada-Vilà P., Porcar I., Morera I., Gu
erra-Rebollo M., Garrido C., Rubio N., Blanco J., Cascante A., Borrós S.
Data di Pubblicazione: 2018-02-08
Abstract: Glioblastoma multiforme (GBM) is the most devastating primary brai
n tumor due to its infiltrating and diffuse growth characteristics, a situat
ion compounded by the lack of effective treatments. Currently, many efforts
are being devoted to find novel formulations to treat this disease, specific
ally in the nanomedicine field. However, due to the lack of comprehensive ch
aracterization that leads to insufficient data on reproducibility, only a re
duced number of nanomedicines have reached clinical phases. In this context,
the aim of the present study was to use a cascade of assays that evaluate fr
om physical-chemical and structural properties to biological characteristics
, both in vitro and in vivo, and also to check the performance of nanopartic
les for glioma therapy. An amphiphilic block copolymer, composed of polyeste
r and poly(ethylene glycol; PEG) blocks, has been synthesized. Using a mixtu
re of this copolymer and a polymer containing an active targeting moiety to
the Blood Brain Barrier (BBB; Seq12 peptide), biocompatible and biodegradabl
e polymeric nanoparticles have been prepared and extensively characterized.
In vitro studies demonstrated that nanoparticles are safe for normal cells b
ut cytotoxic for cancer cells. In vivo studies in mice demonstrated the abil
ity of the Seq12 peptide to cross the BBB. Finally, in vivo efficacy studies
using a human tumor model in SCID mice resulted in a significant 50% life-sp
an increase, as compared with non-treated animals. Altogether, this assay ca
scade provided extensive pre-clinical characterization of our polymeric nano
particles, now ready for clinical evaluation.
Journal Title: Drug delivery

PUBMED ID: 29410102
DOI: doi.org/10.1016/j.wneu.2018.01.123
Titolo: Laser-Induced Thermal Therapy in Neuro-Oncology: A Review.
Autori: Ashraf O., Patel NV., Hanft S., Danish SF.
Data di Pubblicazione: 2018-02-08
Abstract: With the advent of real-time monitoring and damage estimation, LIT
T has gained ground in the management of intracranial tumors. Larger scale t
rials must be performed to develop standard protocols to define specific ind
ications for use. Further large clinical studies for LITT in non-oncologic c
ases are also of interest.
Journal Title: World neurosurgery

PUBMED ID: 29396437
DOI: doi.org/10.1038/s41598-018-19825-w
Titolo: Gene therapy for human glioblastoma using neurotropic JC virus-like particles as a gene delivery vector.
Autori: Chao CN., Yang YH., Wu MS., Chou MC., Fang CY., Lin MC., Tai CK., Sh en CH., Chen PL., Chang D., Wang M.
Data di Pubblicazione: 2018-02-04
Abstract: Glioblastoma multiforme (GBM), the most common malignant brain tum or, has a short period of survival even with recent multimodality treatment. The neurotropic JC polyomavirus (JCPyV) infects glial cells and oligodendroc ytes and causes fatal progressive multifocal leukoencephalopathy in patients with AIDS. In this study, a possible gene therapy strategy for GBM using JCP yV virus-like particles (VLPs) as a gene delivery vector was investigated. W e found that JCPyV VLPs were able to deliver the GFP reporter gene into tumo r cells (U87-MG) for expression. In an orthotopic xenograft model, nude mice implanted with U87 cells expressing the near-infrared fluorescent protein an d then treated by intratumoral injection of JCPyV VLPs carrying the thymidin e kinase suicide gene, combined with ganciclovir administration, exhibited s ignificantly prolonged survival and less tumor fluorescence during the exper iment compared with controls. Furthermore, JCPyV VLPs were able to protect a nd deliver a suicide gene to distal subcutaneously implanted U87 cells in nu de mice via blood circulation and inhibit tumor growth. These findings show that metastatic brain tumors can be targeted by JCPyV VLPs carrying a therap eutic gene, thus demonstrating the potential of JCPyV VLPs to serve as a gen e therapy vector for the far highly treatment-refractory GBM.
Journal Title: Scientific reports

PUBMED ID: 29393706
DOI: doi.org/10.1080/07357907.2018.1430818
Titolo: Biomarkers in Recurrent Grade III Glioma Patients Treated with Bevac izumab and Irinotecan.
Autori: Toft A., Urup T., Christensen IJ., Michaelsen SR., Lukram B., Grunne t K., Kosteljanetz M., Larsen VA., Lassen U., Broholm H., Poulsen HS.
Data di Pubblicazione: 2018-02-03
Abstract: Predictive biomarkers and prognostic models are required to identi fy recurrent grade III glioma patients who benefit from existing treatment. In this study of 62 recurrent grade III glioma patients, a range of clinical and paraclinical factors are tested for association with progression-free su rvival, overall survival, and response to bevacizumab and irinotecan therapy . Significant factors from univariate screening are included in multivariate analysis. Biomarkers previously advanced as predictive or prognostic in the first-line setting did not affect outcome in this patient cohort. Based on t he optimized model for overall survival, comprising performance status and p 53 expression, a prognostic index is established.
Journal Title: Cancer investigation

PUBMED ID: 29380489
DOI: doi.org/10.1002/hbm.23986
Titolo: Linking late cognitive outcome with glioma surgery location using re section cavity maps.
Autori: Hendriks EJ., Habets EJJ., Taphoorn MJB., Douw L., Zwinderman AH., V andertop WP., Barkhof F., Klein M., De Witt Hamer PC.
Data di Pubblicazione: 2018-01-31
Abstract: Patients with a diffuse glioma may experience cognitive decline or improvement upon resective surgery. To examine the impact of glioma location , cognitive alteration after glioma surgery was quantified and related to vo

xel-based resection probability maps. A total of 59 consecutive patients (ra nge 18-67 years of age) who had resective surgery between 2006 and 2011 for a supratentorial nonenhancing diffuse glioma (grade I-III, WHO 2007) were in cluded in this observational cohort study. Standardized neuropsychological e xamination and MRI were obtained before and after surgery. Intraoperative st imulation mapping guided resections towards neurological functions (language , sensorimotor function, and visual fields). Maps of resected regions were c onstructed in standard space. These resection cavity maps were compared betw een patients with and without new cognitive deficits (z-score difference >1. 5 SD between baseline and one year after resection), using a voxel-wise rand omization test and calculation of false discovery rates. Brain regions signi ficantly associated with cognitive decline were classified in standard corti cal and subcortical anatomy. Cognitive improvement in any domain occurred in 10 (17%) patients, cognitive decline in any domain in 25 (42%), and decline in more than one domain in 10 (17%). The most frequently affected subdomains were attention in 10 (17%) patients and information processing speed in 9 (1 5%). Resection regions associated with decline in more than one domain were predominantly located in the right hemisphere. For attention decline, no spe cific region could be identified. For decline in information speed, several regions were found, including the frontal pole and the corpus callosum. Cogn itive decline after resective surgery of diffuse glioma is prevalent, in par ticular, in patients with a tumor located in the right hemisphere without co gnitive function mapping.
Journal Title: Human brain mapping

PUBMED ID: 29374809
DOI: doi.org/10.1007/s11060-018-2775-y
Titolo: Final results of a phase I dose-escalation, dose-expansion study of adding disulfiram with or without copper to adjuvant temozolomide for newly diagnosed glioblastoma.
Autori: Huang J., Campian JL., Gujar AD., Tsien C., Ansstas G., Tran DD., De Wees TA., Lockhart AC., Kim AH.
Data di Pubblicazione: 2018-01-29
Abstract: Disulfiram has shown promising activity including proteasome inhib itory properties and synergy with temozolomide in preclinical glioblastoma (GBM) models. In a phase I study for newly diagnosed GBM after chemoradiother apy, we have previously reported our initial dose-escalation results combini ng disulfiram with adjuvant temozolomide and established the maximum tolerat ed dose (MTD) as 500 mg per day. Here we report the final results of the pha se I study including an additional dose-expansion cohort of disulfiram with concurrent copper. The phase I study consisted of an initial dose-escalation phase of disulfiram 500-1000 mg daily during adjuvant temozolomide, followed by a dose-expansion phase of disulfiram 500 mg daily with copper 2 mg three times daily. Proteasome inhibition was assessed using fluorometric 20S prote asome assay on peripheral blood cell. A total of 18 patients were enrolled: 7 patients received 500 mg disulfiram, 5 patients received 1000 mg disulfira m, and 6 patients received 500 mg disulfiram with copper. Two dose-limiting toxicities occurred with 1000 mg disulfiram. At disulfiram 500 mg with or wi thout copper, only 1 patient (7%) required dose-reduction during the first m onth of therapy. Addition of copper to disulfiram did not increase toxicity nor proteasome inhibition. The median progression-free survival was 4.5 mont hs (95% CI 0.8-8.2). The median overall survival (OS) was 14.0 months (95% C I 8.3-19.6), and the 2-year OS was 24%. The MTD of disulfiram at 500 mg dail y in combination with adjuvant temozolomide was well tolerated by GBM patien ts, but 1000 mg daily was not. Toxicity and pharmacodynamic effect of disulf iram were similar with or without concurrent copper. The clinical efficacy a ppeared to be comparable to historical data. Additional clinical trials to c ombine disulfiram and copper with chemoradiotherapy or to resensitize recurr ent GBM to temozolomide are ongoing.

Journal Title: Journal of neuro-oncology

PUBMED ID: 29374392
DOI: doi.org/10.1007/s13402-017-0361-5
Titolo: p53 expression and subcellular survivin localization improve the diagnosis and prognosis of patients with diffuse astrocytic tumors.
Autori: Faccion RS., Bernardo PS., de Lopes GPF., Bastos LS., Teixeira CL., de Oliveira JA., Fernandes PV., Dubois LG., Chimelli L., Maia RC.
Data di Pubblicazione: 2018-01-28
Abstract: Our data suggest that subcellular survivin localization and p53 expression may be employed as valuable tools to improve the accuracy of the histological sub-classification of diffuse astrocytic tumors. Patients whose tumors overexpress these proteins may benefit from radiotherapy, irrespective age and/or histological classification.
Journal Title: Cellular oncology (Dordrecht)

PUBMED ID: 29348883
DOI: doi.org/10.18632/oncotarget.22947
Titolo: Spatial habitats from multiparametric MR imaging are associated with signaling pathway activities and survival in glioblastoma.
Autori: Dextraze K., Saha A., Kim D., Narang S., Lehrer M., Rao A., Narang S., Rao D., Ahmed S., Madhugiri V., Fuller CD., Kim MM., Krishnan S., Rao G., Rao A.
Data di Pubblicazione: 2018-01-20
Abstract: Glioblastoma (GBM) show significant inter- and intra-tumoral heterogeneity, impacting response to treatment and overall survival time of 12-15 months. To study glioblastoma phenotypic heterogeneity, multi-parametric magnetic resonance images (MRI) of 85 glioblastoma patients from The Cancer Genome Atlas were analyzed to characterize tumor-derived spatial habitats for their relationship with outcome (overall survival) and to identify their molecular correlates (i.e., determine associated tumor signaling pathways correlated with imaging-derived habitat measurements). Tumor sub-regions based on four sequences (fluid attenuated inversion recovery, T1-weighted, post-contrast T1-weighted, and T2-weighted) were defined by automated segmentation. From relative intensity of pixels in the 3-dimensional tumor region, "imaging habitats" were identified and analyzed for their association to clinical and genetic data using survival modeling and Dirichlet regression, respectively. Sixteen distinct tumor sub-regions ("spatial imaging habitats") were derived, and those associated with overall survival (denoted "relevant" habitats) in glioblastoma patients were identified. Dirichlet regression implicated each relevant habitat with unique pathway alterations. Relevant habitats also had some pathways and cellular processes in common, including phosphorylation of STAT-1 and natural killer cell activity, consistent with cancer hallmarks. This work revealed clinical relevance of MRI-derived spatial habitats and their relationship with oncogenic molecular mechanisms in patients with GBM. Characterizing the associations between imaging-derived phenotypic measurements with the genomic and molecular characteristics of tumors can enable insights into tumor biology, further enabling the practice of personalized cancer treatment. The analytical framework and workflow demonstrated in this study are inherently scalable to multiple MR sequences.
Journal Title: Oncotarget

PUBMED ID: 29340013
DOI: doi.org/10.18632/oncotarget.22500
Titolo: The small molecule SI113 synergizes with mitotic spindle poisons in arresting the growth of human glioblastoma multiforme.

Autori: Abbruzzese C., Catalogna G., Gallo E., di Martino S., Mileo AM., Carosi M., Dattilo V., Schenone S., Musumeci F., Lavia P., Perrotti N., Amato R., Paggi MG.
Data di Pubblicazione: 2018-01-18
Abstract: Glioblastoma multiforme (GBM) is the deadliest brain tumor. State-of-art GBM therapy often fails to ensure control of a disease characterized by high frequency of recurrences and progression. In search for novel therapeutic approaches, we assayed the effect of compounds from a cancer drug library on the ADF GBM cell line, establishing their elevated sensitivity to mitotic spindle poisons. Our previous work showed that the effectiveness of the spindle poison paclitaxel in inhibiting cancer cell growth was dependent on the expression of RANBP1, a regulatory target of the serine/threonine kinase SGK1. Recently, we developed the small molecule SI113 to inhibit SGK1 activity. Therefore, we explored the outcome of the association between SI113 and selected spindle poisons, finding that these drugs generated a synergistic cytotoxic effect in GBM cells, drastically reducing their viability and clonogenic capabilities
Journal Title: Oncotarget

PUBMED ID: 29339090
DOI: doi.org/10.1016/j.ajpath.2017.11.019
Titolo: Patched 1 Expression Correlates with Biochemical Relapse in High-Risk Prostate Cancer Patients.
Autori: Gonnissen A., Isebaert S., Perneel C., McKee CM., Van Utterbeeck F., Lerut E., Verrill C., Bryant RJ., Joniau S., Muschel RJ., Haustermans K.
Data di Pubblicazione: 2018-01-18
Abstract: There is an unmet clinical need for adequate biomarkers to aid risk stratification and management of prostate cancer (PCa) patients. Even within the high-risk PCa category, not all patients will invariably have a poor prognosis, and improved stratification of this heterogeneous group is needed. In this context, components of the hedgehog (Hh) pathway may have promise as biomarkers, because the available evidence suggests increased Hh pathway activity may confer a poorer outcome in advanced and castrate-resistant PCa. In this study, potential associations between Hh pathway protein expression and clinicopathological factors, including time to biochemical recurrence (BCR), were investigated using a tissue microarray constructed from benign and malignant prostate samples from 75 predominantly high-risk PCa patients who underwent radical prostatectomy. Hh signaling activity was found to differ between benign and malignant prostate tissue, with a greater amount of active Hh signaling present in malignant than benign prostate epithelium. High expression of Patched 1 in malignant prostate epithelium was found to be an independent predictor of BCR in high-risk PCa patients. Glioma-associated oncogene 1 may potentially represent a clinically useful biomarker of an aggressive tumor phenotype. Evaluation of Hh signaling activity in PCa patients may be useful for risk stratification, and epithelial Patched 1 expression, in particular, may be a prognostic marker for BCR in high-risk PCa patients.
Journal Title: The American journal of pathology

PUBMED ID: 29333019
DOI: doi.org/10.4103/ijmpo.ijmpo_200_16
Titolo: Modulated Radiotherapy with Concurrent and Adjuvant Temozolomide for Anaplastic Gliomas: Indian Single-center Data.
Autori: Kataria T., Basu T., Gupta D., Goyal S., Nasreen S., Bisht SS., Abhishek A., Banerjee S., Narang K., Jha AN., Mohapatra I., Modi JA.
Data di Pubblicazione: 2018-01-16
Abstract: Modulated RT with TMZ among Grade III glioma patients resulted in minimum treatment-related toxicities and encouraging survival. Molecular prognostic markers will determine most favorable groups in future.

Journal Title: Indian journal of medical and paediatric oncology : official journal of Indian Society of Medical & Paediatric Oncology

PUBMED ID: 29309981
DOI: doi.org/10.1016/j.wneu.2017.12.159
Titolo: Surgical Treatment of Spinal Ependymomas: Experience in 49 Patients.
Autori: Wild F., Hartmann C., Heissler HE., Hong B., Krauss JK., Nakamura M.
Data di Pubblicazione: 2018-01-09
Abstract: Gross total resection is considered the first choice in treatment of spinal ependymomas. The most important predictor of clinical outcome is preoperative neurologic functioning. The role of postoperative radiation needs further clarification.
Journal Title: World neurosurgery

PUBMED ID: 29308304
DOI: doi.org/10.1080/2162402X.2017.1382792
Titolo: PD-1 related transcriptome profile and clinical outcome in diffuse gliomas.
Autori: Liu S., Wang Z., Wang Y., Fan X., Zhang C., Ma W., Qiu X., Jiang T.
Data di Pubblicazione: 2018-01-09
Abstract: Gross total resection is considered the first choice in treatment of spinal ependymomas. The most important predictor of clinical outcome is preoperative neurologic functioning. The role of postoperative radiation needs further clarification.
Journal Title: Oncoimmunology

PUBMED ID: 29294371
DOI: doi.org/10.1016/j.semcancer.2017.12.011
Titolo: Targeting the Warburg effect for cancer treatment: Ketogenic diets for management of glioma.
Autori: Poff A., Koutnik AP., Egan KM., Sahebjam S., D'Agostino D., Kumar NB.
Data di Pubblicazione: 2018-01-03
Abstract: Gliomas are a highly heterogeneous tumor, refractory to treatment and the most frequently diagnosed primary brain tumor. Although the current WHO grading system (2016) demonstrates promise towards identifying novel treatment modalities and better prediction of prognosis over time, to date, existing targeted and mono therapy approaches have failed to elicit a robust impact on disease progression and patient survival. It is possible that tumor heterogeneity as well as specifically targeted agents fail because redundant molecular pathways in the tumor make it refractory to such approaches. Additionally, the underlying metabolic pathology, which is significantly altered during neoplastic transformation and tumor progression, is unaccounted for. With several molecular and metabolic pathways implicated in the carcinogenesis of CNS tumors, including glioma, we postulate that a systemic, broad spectrum approach to produce robust targeting of relevant and multiple molecular and metabolic regulation of growth and survival pathways, critical to the modulation of hallmarks of carcinogenesis, without clinically limiting toxicity, may provide a more sustained impact on clinical outcomes compared to the modalities of treatment evaluated to date. The objective of this review is to examine the emerging hallmark of reprogramming energy metabolism of the tumor cells and the tumor microenvironment during carcinogenesis, and to provide a rationale for exploiting this hallmark and its biological capabilities as a target for secondary chemoprevention and treatment of glioma. This review will primarily focus on interventions to induce ketosis to target the glycolytic phenotype of many cancers, with specific application to secondary chemoprevention of low grade glioma- to halt the progression of lower grade tu

mors to more aggressive subtypes, as evidenced by reduction in validated int ermediate endpoints of disease progression including clinical symptoms.
Journal Title: Seminars in cancer biology

PUBMED ID: 29291003
DOI: doi.org/10.18632/oncotarget.22197
Titolo: Pseudogenes of annexin A2, novel prognosis biomarkers for diffuse gl iomas.
Autori: Li S., Zou H., Shao YY., Mei Y., Cheng Y., Hu DL., Tan ZR., Zhou HH.
Data di Pubblicazione: 2018-01-02
Abstract: Diffuse gliomas is a kind of common malignant primary brain tumor. Pseudogenes have multilayered biological function in the progression of huma n cancers. In this study, Differentially Expressed Pseudogenes (DEPs) betwee n glioblastomas and non-tumor controls were found by bioinformatics analysis , of which the annexin A2 pseudogenes (ANXA2P1, ANXA2P2 and ANXA2P3) were si gnificantly up-regulated, along with the parent gene annexin A2 (ANXA2
Journal Title: Oncotarget

PUBMED ID: 29260361
DOI: doi.org/10.1007/s11060-017-2714-3
Titolo: Sex-dependent association of preoperative hematologic markers with g lioma grade and progression.
Autori: Xu W., Wang D., Zheng X., Ou Q., Huang L.
Data di Pubblicazione: 2017-12-21
Abstract: Neutrophil-to-lymphocyte ratio (NLR), platelet-lymphocyte ratio, t he systemic immune-inflammation index (SII), and red blood cell distribution width (RDW), have been recognized as promising predictors for histological g rade and prognosis in multiple cancer types. However, few investigations ill ustrated the impacts of sex on the clinical utility of hematologic markers. Patients with primary gliomas were retrospectively reviewed. The association between grade and inflammatory markers by sex were investigated by univariat e and multivariate analysis. The discrimination ability of logistic regressi on model was evaluated by the area under the receiver-operating characterist ic curve (AUC) for high-grade glioma (HGG). Kaplan-Meier progressionfree sur vival (PFS) curves were plotted to assess the prognostic value of RDW. In su bgroup analysis, distinctively elevated NLR and SII levels were exclusively present in male HGGs group ($p = 0.001$); whereas RDW notably increased in fema le HGGs group ($p = 0.001$). On multivariate analysis, increased odds ratio of HGGs was exclusively observed for female patients with elevated RDW (odds ra tio = 1.589). Moreover, regression model developed by RDW exhibited an excell ent discriminative ability for the prediction of HGGs in female patients (AU C = 0.817). Median progression time with RDW < 13.2 versus RDW ≥ 13.2 was 62.5 v ersus 33.0 months (log rank $p = 0.017$). Older females (≥ 45 years) with increa sed RDW levels portended worse survival (HR 3.693, 95% CI 1.747-8.325, $p = 0.$ 001). Meanwhile, the significant association of RDW levels with PFS in male subgroup was not observed ($p > 0.05$). In conclusion, superior to NLR and SII, RDW would be sex-specific predictor for tumor grade and progression for HGG female patients.
Journal Title: Journal of neuro-oncology

PUBMED ID: 29258767
DOI: doi.org/10.1016/j.prp.2017.12.009
Titolo: Immunohistochemical comparative analysis of GFAP, MAP - 2, NOGO - A, OLIG - 2 and WT - 1 expression in WHO 2016 classified neuroepithelial tumour s and their prognostic value.

Autori: Schwab DE., Lepski G., Borchers C., Trautmann K., Paulsen F., Schitt enhelm J.
Data di Pubblicazione: 2017-12-21
Abstract: Immunohistochemistry is routinely used in differential diagnosis o f tumours of the central nervous system (CNS). The latest 2016 WHO 2016 revi sion now includes molecular data such as IDH mutation and 1p/19q codeletion thus restructuring glioma classification. Direct comparative information bet ween commonly used immunohistochemical markers for glial tumours GFAP, MAP - 2, NOGO - A, OLIG - 2 and WT - 1 concerning quality and quantity of expressi on and their relation to the new molecular markers are lacking. We therefore compared the immunohistochemical staining results of all five antibodies in 34 oligodendrogliomas, 106 ependymomas and 423 astrocytic tumours. GFAP expr ession was reduced in cases with higher WHO grade, oligodendroglial differen tiation and in IDH wildtype diffuse astrocytomas. By contrast MAP - 2 expres sion was significantly increased in diffuse astrocytomas with IDH mutation, while NOGO - A expression was not associated with any molecular marker. WT - 1 expression was significantly decreased in tumours with IDH mutation and AT RX loss. OLIG - 2 was increased in IDH-mutant grade II astrocytomas and in c ases with higher proliferation rate. In univariate survival analysis high WT - 1 expression was significantly associated with worse outcome in diffuse as trocytic tumours (log rank $p < 0.0001$; $n = 211$; median time: 280 days vs 562 day s). None of the markers was prognostic in multivariate survival analysis. Am ong the evaluated markers MAP - 2, OLIG - 2 and WT - 1 showed the best poten tial to separate between glioma entities and can be recommended for a standa rdized immunohistochemical panel.
Journal Title: Pathology, research and practice

PUBMED ID: 29254497
DOI: doi.org/10.1186/s40425-017-0302-x
Titolo: Retrospective review of safety and efficacy of programmed cell death -1 inhibitors in refractory high grade gliomas.
Autori: Reiss SN., Yerram P., Modelevsky L., Grommes C.
Data di Pubblicazione: 2017-12-20
Abstract: While response rates are low, a few patients had a prolonged PFS. Pembrolizumab was tolerated with few serious toxicities, even in patients re ceiving concomitant therapy.
Journal Title: Journal for immunotherapy of cancer

PUBMED ID: 29245310
DOI: doi.org/10.1097/MD.0000000000009053
Titolo: A pilot clinical study of apatinib plus irinotecan in patients with recurrent high-grade glioma: Clinical Trial/Experimental Study.
Autori: Wang L., Liang L., Yang T., Qiao Y., Xia Y., Liu L., Li C., Lu P., J iang X.
Data di Pubblicazione: 2017-12-17
Abstract: NCT02848794/Ahead-BG306.
Journal Title: Medicine

PUBMED ID: 29218626
DOI: doi.org/10.1007/s12094-017-1816-x
Titolo: Treatment-related changes in glioblastoma: a review on the controver sies in response assessment criteria and the concepts of true progression, p seudoprogression, pseudoresponse and radionecrosis.
Autori: Delgado-López PD., Riñones-Mena E., Corrales-García EM.
Data di Pubblicazione: 2017-12-09

Abstract: The assessment of response to therapy in glioblastoma remains a ch
allenge, because the surrogate measures of survival are subject to radiograp
hic misinterpretation. A solid and reliable definition of progression is nee
ded for both clinical decision-making and for evaluating response within the
clinical trials. Historically, assessment criteria have used radiologic and
clinical features aimed to correctly classify patients into progressive or n
on-progressive disease. The widely used RANO criteria are a valuable tool in
disease evaluation, both in the clinical setting and in the clinical trials.
However, assessment criteria have certain limitations that emerging image te
chniques have tried to overcome. Differentiating true progression from treat
ment-related changes (like pseudoprogression or pseudoresponse) is crucial i
n order not to prematurely discontinue adjuvant chemotherapy or redirect the
patient to second-line options. This fact underscores the need for advanced
radiologic techniques, like specific diffusion and perfusion MRI sequences,
MR spectroscopy and PET, which seem to play a role in distinguishing these p
henomena.
Journal Title: Clinical & translational oncology : official publication of t
he Federation of Spanish Oncology Societies and of the National Cancer Insti
tute of Mexico

PUBMED ID: 29207176
DOI: doi.org/10.3892/or.2017.6134
Titolo: P4HB and PDIA3 are associated with tumor progression and therapeutic
outcome of diffuse gliomas.
Autori: Zou H., Wen C., Peng Z., Shao YY., Hu L., Li S., Li C., Zhou HH.
Data di Pubblicazione: 2017-12-06
Abstract: Diffuse gliomas are the most common type of primary brain and cent
ral nervous system (CNS) tumors. Protein disulfide isomerases (PDIs) such as
P4HB and PDIA3 act as molecular chaperones for reconstructing misfolded prot
eins, and are involved in endoplasmic reticulum stress and the unfolded prot
ein response. The present study focused on the role of P4HB and PDIA3 in dif
fuse gliomas. Analysis of GEO and HPA data revealed that the expression leve
ls of P4HB and PDIA3 were upregulated in glioma datasets. their increased ex
pression was then validated in 99 glioma specimens compared with 11 non-tumo
r tissues. High expression of P4HB and PDIA3 was significantly correlated wi
th high Ki-67 and a high frequency of the TP53 mutation. Kaplan-Meier surviv
al curve and Cox regression analyses showed that glioma patients with high P
4HB and PDIA3 expression had a poor survival outcome, P4HB and PDIA3 could b
e independent prognostic biomarkers for diffuse gliomas. In vitro, knockdown
of PDIA3 suppressed cell proliferation, induced cell apoptosis, and decrease
d the migration of glioma cells. Furthermore, downregulation of P4HB and PDI
A3 may contribute to improve the survival of patients who receive chemothera
py and radiotherapy. The data suggest that high expression of P4HB and PDIA3
plays an important role in glioma progression, and could predict the surviva
l outcome and therapeutic response of glioma patients. Therefore, protein di
sulfide isomerases may be explored as prognostic biomarkers and therapeutic
targets for diffuse gliomas.
Journal Title: Oncology reports

PUBMED ID: 29195506
DOI: doi.org/10.1186/s13014-017-0924-7
Titolo: Treatment of meningioma and glioma with protons and carbon ions.
Autori: Adeberg S., Harrabi SB., Verma V., Bernhardt D., Grau N., Debus J.,
Rieken S.
Data di Pubblicazione: 2017-12-03
Abstract: The rapid rise of particle therapy across the world necessitates e
vidence to justify its ever-increasing utilization. This narrative review su
mmarizes the current status of these technologies on treatment of both menin

giomas and gliomas, the most common benign and malignant primary brain tumor s, respectively. Proton beam therapy (PBT) for meningiomas displays high rat es of long-term local control, low rates of symptomatic deterioration, along with the potential for safe dose-escalation in select (but not necessarily r outine) cases. PBT is also associated with low adverse events and maintenanc e of functional outcomes, which have implications for quality of life and co st-effectiveness measures going forward. Data on carbon ion radiation therap y (CIRT) are limited; existing series describe virtually no high-grade toxic ities and high local control. Regarding the few available data on low-grade gliomas, PBT provides opportunities to dose-escalate while affording no incr ease of severe toxicities, along with maintaining appropriate quality of lif e. Although dose-escalation for low-grade disease has been less frequently p erformed than for glioblastoma, PBT and CIRT continue to be utilized for the latter, and also have potential for safer re-irradiation of high-grade gliom as. For both neoplasms, the impact of superior dosimetric profiles with endp oints such as neurocognitive decline and neurologic funcionality, are also d iscussed to the extent of requiring more data to support the utility of part icle therapy. Caveats to these data are also described, such as the largely retrospective nature of the available studies, patient selection, and hetero geneity in patient population as well as treatment (including mixed photon/p article treatment). Nevertheless, multiple prospective trials (which may par tially attenuate those concerns) are also discussed. In light of the low qua ntity and quality of available data, major questions remain regarding econom ic concerns as well.
Journal Title: Radiation oncology (London, England)

PUBMED ID: 29179732
DOI: doi.org/10.1186/s13046-017-0642-x
Titolo: Drug repurposing for the treatment of glioblastoma multiforme.
Autori: Abbruzzese C., Matteoni S., Signore M., Cardone L., Nath K., Glickso n JD., Paggi MG.
Data di Pubblicazione: 2017-11-29
Abstract: The spiraling costs of new antineoplastic drugs and the long time required for them to reach the market demands a profoundly different approac h to keep lifesaving therapies affordable for cancer patients. In this conte xt, repurposing can represent a relatively inexpensive, safe and fast approa ch to glioblastoma treatment. To this end, pros and cons must be accurately considered.
Journal Title: Journal of experimental & clinical cancer research : CR

PUBMED ID: 29166609
DOI: doi.org/10.1016/j.celrep.2017.10.083
Titolo: GPR56/ADGRG1 Inhibits Mesenchymal Differentiation and Radioresistanc e in Glioblastoma.
Autori: Moreno M., Pedrosa L., Paré L., Pineda E., Bejarano L., Martínez J., Balasubramaniyan V., Ezhilarasan R., Kallarackal N., Kim SH., Wang J., Audia A., Conroy S., Marin M., Ribalta T., Pujol T., Herreros A., Tortosa A., Mira H., Alonso MM., Gómez-Manzano C., Graus F., Sulman EP., Piao X., Nakano I., Prat A., Bhat KP., de la Iglesia N.
Data di Pubblicazione: 2017-11-23
Abstract: A mesenchymal transition occurs both during the natural evolution of glioblastoma (GBM) and in response to therapy. Here, we report that the a dhesion G-protein-coupled receptor, GPR56/ADGRG1, inhibits GBM mesenchymal d ifferentiation and radioresistance. GPR56 is enriched in proneural and class ical GBMs and is lost during their transition toward a mesenchymal subtype. GPR56 loss of function promotes mesenchymal differentiation and radioresista nce of glioma initiating cells both in vitro and in vivo. Accordingly, a low GPR56-associated signature is prognostic of a poor outcome in GBM patients e

ven within non-G-CIMP GBMs. Mechanistically, we reveal GPR56 as an inhibitor of the nuclear factor kappa B (NF-κB) signaling pathway, thereby providing t he rationale by which this receptor prevents mesenchymal differentiation and radioresistance. A pan-cancer analysis suggests that GPR56 might be an inhib itor of the mesenchymal transition across multiple tumor types beyond GBM.
Journal Title: Cell reports

PUBMED ID: 29150792
DOI: doi.org/10.1007/s12020-017-1474-3
Titolo: Correlation between MGMT promoter methylation and response to temozo lomide-based therapy in neuroendocrine neoplasms: an observational retrospec tive multicenter study.
Autori: Campana D., Walter T., Pusceddu S., Gelsomino F., Graillot E., Prinz i N., Spallanzani A., Fiorentino M., Barritault M., Dall'Olio F., Brighi N., Biasco G.
Data di Pubblicazione: 2017-11-19
Abstract: According to our results, MGMT methylation status, evaluated with methylation specific-polymerase chain reaction or pyrosequencing, should hav e an important role in patients with metastatic NENs, in order to guide ther apeutic options. These results need further confirmation with prospective st udies.
Journal Title: Endocrine

PUBMED ID: 29143923
DOI: doi.org/10.1007/s11060-017-2668-5
Titolo: Impact of concurrent versus adjuvant chemotherapy on the severity an d duration of lymphopenia in glioma patients treated with radiation therapy.
Autori: Lin AJ., Campian JL., Hui C., Rudra S., Rao YJ., Thotala D., Hallaha n D., Huang J.
Data di Pubblicazione: 2017-11-17
Abstract: Prolonged severe lymphopenia has been shown to persist beyond a ye ar in glioma patients after radiation therapy (RT) with concurrent and adjuv ant chemotherapy. This study examines the differential impact of concurrent versus adjuvant chemotherapy on lymphopenia after RT. WHO grade II-III gliom a patients who received RT with concurrent and/or adjuvant chemotherapy from 2007 to 2016 were retrospectively analyzed. Concurrent chemotherapy was temo zolomide (TMZ), and adjuvant chemotherapy was either TMZ or procarbazine/lom ustine/vincristine (PCV). Absolute lymphocyte count (ALC) was analyzed at ba seline, 1.5, 3, 6, and 12 months after the start of RT. Univariable and mult ivariable logistic regression were used to identify the clinical variables i n predicting acute or late lymphopenia. There were 151 patients with evaluab le ALC: 91 received concurrent and adjuvant TMZ (CRT+ADJ), 32 received only concurrent TMZ (CRT), and 28 received only adjuvant TMZ or PCV (ADJ). There were 9 (10%) versus 6 (19%) versus 0 (0%) cases of grade 3 lymphopenia (ALC< 500/mm
Journal Title: Journal of neuro-oncology

PUBMED ID: 29113369
DOI: doi.org/10.18632/oncotarget.19080
Titolo: Prognostic role of Gli1 expression in breast cancer: a meta-analysis .
Autori: Wang B., Yu T., Hu Y., Xiang M., Peng H., Lin Y., Han L., Zhang L.
Data di Pubblicazione: 2017-11-09
Abstract: Glioma-associated oncogene 1 (Gli1) is a critical transcriptional factor of Sonic hedgehog pathway which has been proved to participate in the initiation and progression of tumor in mammalians. However, its clinical val

ue in breast cancer remains unknown. Thus, a meta-analysis was performed to clarify the association of Gli1 over-expression, clinic-pathological characteristics, molecular subtypes and prognosis in breast cancer. According to included criteria, 13 eligible studies containing 2816 patients all around the world were selected in this study. Our results indicated no significant association of Gli1 expression and histological grade (RR = 1.20, 95% CI: [0.98, 1.47]), T stage (RR = 1.05, 95% CI: [0.87, 1.27]), clinical stage (RR = 1.04, 95% CI: [0.93, 1.18]) and lymph node metastasis (RR = 1.12, 95% CI: [0.92, 1.37]). In addition, pooled RR showed no correlation of Gli1 expression and progesterone receptor (PR) (RR = 0.92, 95% CI: [0.70, 1.21]), estrogen receptor (ER) (RR = 1.03, 95% CI: [0.74, 1.42]), human epidermal growth factor receptor 2 (HER-2) (RR = 1.12, 95% CI: [0.90, 1.39]). Nonetheless, up-regulated Gli1 expression predicts shorter disease-free survival (DFS) (HR = 1.38, 95% CI: [1.05, 1.81]), 3-year survival (HR = 1.74, 95% CI: [1.28, 2.36]), 5-year survival (HR = 2.04, 95% CI: [1.62, 2.57]) and overall survival (OS) (HR = 2.05, 95% CI: [1.60, 2.64]). In conclusion, over-expression of Gli1 tends to progressive stages and is related to unfavorable prognosis of breast cancer, which may become a potential prognosis indicator and therapy target in breast cancer.
Journal Title: Oncotarget

PUBMED ID: 29108264
DOI: doi.org/10.18632/oncotarget.20226
Titolo: lncRNAs PVT1 and HAR1A are prognosis biomarkers and indicate therapy outcome for diffuse glioma patients.
Autori: Zou H., Wu LX., Yang Y., Li S., Mei Y., Liu YB., Zhang L., Cheng Y., Zhou HH.
Data di Pubblicazione: 2017-11-08
Abstract: Diffuse gliomas are well known malignant brain tumors. Long non-coding RNAs (lncRNAs), a type of RNA transcript with more than 200 nucleotides, involve in tumorigenesis and development of various cancers. This study focused on identifying differentially expressed lncRNAs in gliomas based on gene expression profiling, and chose certain lncRNAs PVT1, CYTOR, HAR1A and MIAT, which changed with significant differences. Further analysis of TCGA and GEO data revealed that the expressions of PVT1 and CYTOR were up-regulated, while HAR1A and MIAT expressions were down-regulated in gliomas. Their expression patterns were validated in an independent cohort containing 98 glioma specimens and 12 non-tumor tissue controls. High expression of PVT1 and CYTOR as well as low HAR1A and MIAT expression were associated with high Ki-67 level and more
Journal Title: Oncotarget

PUBMED ID: 29093005
DOI: doi.org/10.1158/0008-5472.CAN-17-0469
Titolo: Dendritic Cells Enhance Polyfunctionality of Adoptively Transferred T Cells That Target Cytomegalovirus in Glioblastoma.
Autori: Reap EA., Suryadevara CM., Batich KA., Sanchez-Perez L., Archer GE., Schmittling RJ., Norberg PK., Herndon JE., Healy P., Congdon KL., Gedeon PC., Campbell OC., Swartz AM., Riccione KA., Yi JS., Hossain-Ibrahim MK., Saraswathula A., Nair SK., Dunn-Pirio AM., Broome TM., Weinhold KJ., Desjardins A., Vlahovic G., McLendon RE., Friedman AH., Friedman HS., Bigner DD., Fecci PE., Mitchell DA., Sampson JH.
Data di Pubblicazione: 2017-11-03
Abstract: Median survival for glioblastoma (GBM) remains <15 months. Human cytomegalovirus (CMV) antigens have been identified in GBM but not normal brain, providing an unparalleled opportunity to subvert CMV antigens as tumor-specific immunotherapy targets. A recent trial in recurrent GBM patients demo

nstrated the potential clinical benefit of adoptive T-cell therapy (ATCT) of CMV phosphoprotein 65 (pp65)-specific T cells. However,
Journal Title: Cancer research

PUBMED ID: 29076150
DOI: doi.org/10.1111/bjh.14987
Titolo: A phase 1 clinical trial evaluating marizomib, pomalidomide and low-dose dexamethasone in relapsed and refractory multiple myeloma (NPI-0052-107): final study results.
Autori: Spencer A., Harrison S., Zonder J., Badros A., Laubach J., Bergin K. , Khot A., Zimmerman T., Chauhan D., Levin N., MacLaren A., Reich SD., Trikh a M., Richardson P.
Data di Pubblicazione: 2017-10-28
Abstract: Marizomib (MRZ) is an irreversible, pan-subunit proteasome inhibit or (PI) in clinical development for relapsed/refractory multiple myeloma (RR MM) and glioma. This study analysed MRZ, pomalidomide (POM) and low-dose dex amethasone (Lo-DEX) [PMD] in RRMM to evaluate safety and determine the maxim um tolerated dose (MTD) and/or recommended Phase 2 dose (RP2D). Intravenous MRZ (0·3-0·5 mg/m
Journal Title: British journal of haematology

PUBMED ID: 29076027
DOI: doi.org/10.1007/s13402-017-0355-3
Titolo: Serum exosomal miR-301a as a potential diagnostic and prognostic bio marker for human glioma.
Autori: Lan F., Qing Q., Pan Q., Hu M., Yu H., Yue X.
Data di Pubblicazione: 2017-10-28
Abstract: Our data indicate that serum exosomal miR-301a levels may reflect the cancer-bearing status and pathological changes in glioma patients. Serum exosomal miR-301a expression may serve as a novel biomarker for glioma diagn osis and as a prognostic factor for advanced grade disease.
Journal Title: Cellular oncology (Dordrecht)

PUBMED ID: 29074604
DOI: doi.org/10.1158/1078-0432.CCR-17-0963
Titolo: Prospective Feasibility Trial for Genomics-Informed Treatment in Rec urrent and Progressive Glioblastoma.
Autori: Byron SA., Tran NL., Halperin RF., Phillips JJ., Kuhn JG., de Groot JF., Colman H., Ligon KL., Wen PY., Cloughesy TF., Mellinghoff IK., Butowski NA., Taylor JW., Clarke JL., Chang SM., Berger MS., Molinaro AM., Maggiora G M., Peng S., Nasser S., Liang WS., Trent JM., Berens ME., Carpten JD., Craig DW., Prados MD.
Data di Pubblicazione: 2017-10-28
Abstract: Our data indicate that serum exosomal miR-301a levels may reflect the cancer-bearing status and pathological changes in glioma patients. Serum exosomal miR-301a expression may serve as a novel biomarker for glioma diagn osis and as a prognostic factor for advanced grade disease.
Journal Title: Clinical cancer research : an official journal of the America n Association for Cancer Research

PUBMED ID: 29056290
DOI: doi.org/10.1016/j.radonc.2017.09.024
Titolo: The extent of edema and tumor synchronous invasion into the subventr icular zone and corpus callosum classify outcomes and radiotherapy strategie s of glioblastomas.

Autori: Liang HT., Chen WY., Lai SF., Su MY., You SL., Chen LH., Tseng HM., Chen CM., Kuo SH., Tseng WI.
Data di Pubblicazione: 2017-10-24
Abstract: Our results support the need for developing individualized irradia tion strategies for glioblastomas according to EPE and sSVZCC.
Journal Title: Radiotherapy and oncology : journal of the European Society f or Therapeutic Radiology and Oncology

PUBMED ID: 29053887
DOI: doi.org/10.1111/nan.12447
Titolo: Low FoxG1 and high Olig-2 labelling indices define a prognostically favourable subset in isocitrate dehydrogenase (IDH)-mutant gliomas.
Autori: Schäfer S., Behling F., Skardelly M., Koch M., Ott I., Paulsen F., T abatabai G., Schittenhelm J.
Data di Pubblicazione: 2017-10-21
Abstract: While the combined FoxG1/Olig-2 profile may discriminate H3F3A K27 - and G34-mutant tumours and define a prognostically favourable subset in ID H-mutant gliomas, our data show that labelling indices of these transcriptio n factors overlap with adult IDH-mutant and wild-type tumour classes.
Journal Title: Neuropathology and applied neurobiology

PUBMED ID: 29037775
DOI: doi.org/10.1016/j.radonc.2017.09.034
Titolo: Neuroendocrine late effects after tailored photon radiotherapy for c hildren with low grade gliomas: Long term correlation with tumour and treatm ent parameters.
Autori: Aloi D., Belgioia L., Barra S., Giannelli F., Cavagnetto F., Gallo F ., Milanaccio C., Garrè M., Di Profio S., Di Iorgi N., Corvò R.
Data di Pubblicazione: 2017-10-18
Abstract: Radiotherapy showed excellent OS and PFS rates and acceptable late neuroendocrine toxicity profile in this population of LGG patients treated o ver a period of 13years. In our experience, the dose to the HPA was predicti ve of the risk of late endocrine toxicity.
Journal Title: Radiotherapy and oncology : journal of the European Society f or Therapeutic Radiology and Oncology

PUBMED ID: 29036345
DOI: doi.org/10.1093/neuonc/nox151
Titolo: Phase II study of cabozantinib in patients with progressive glioblas toma: subset analysis of patients with prior antiangiogenic therapy.
Autori: Cloughesy TF., Drappatz J., de Groot J., Prados MD., Reardon DA., Sc hiff D., Chamberlain M., Mikkelsen T., Desjardins A., Ping J., Holland J., W eitzman R., Wen PY.
Data di Pubblicazione: 2017-10-17
Abstract: NCT00704288 (https://www.clinicaltrials.gov/ct2/show/NCT00704288).
Journal Title: Neuro-oncology

PUBMED ID: 29025274
DOI: doi.org/10.1080/03007995.2017.1392294
Titolo: Overall survival in patients with glioblastoma before and after beva cizumab approval.
Autori: Johnson DR., Omuro AMP., Ravelo A., Sommer N., Guerin A., Ionescu-It tu R., Shi S., Macalalad A., Uhm JH.
Data di Pubblicazione: 2017-10-14
Abstract: The results of this large population-based study suggested an impr ovement in OS among patients with a GBM diagnosis in 2010-2012 compared to 2

006-2008. While the cause of this improvement cannot be proven in a retrospe ctive analysis, the timing of the survival increase coincides with the appro val of bevacizumab for the treatment of patients with progressive GBM, indic ating a possible benefit of bevacizumab in this population.
Journal Title: Current medical research and opinion

PUBMED ID: 29016998
DOI: doi.org/10.1093/neuonc/nox154
Titolo: Phase II study of cabozantinib in patients with progressive glioblas toma: subset analysis of patients naive to antiangiogenic therapy.
Autori: Wen PY., Drappatz J., de Groot J., Prados MD., Reardon DA., Schiff D ., Chamberlain M., Mikkelsen T., Desjardins A., Holland J., Ping J., Weitzma n R., Cloughesy TF.
Data di Pubblicazione: 2017-10-11
Abstract: NCT00704288 (https://www.clinicaltrials.gov/ct2/show/NCT00704288).
Journal Title: Neuro-oncology

PUBMED ID: 29016943
DOI: doi.org/10.1093/neuonc/nox162
Titolo: Radiologic progression of glioblastoma under therapy-an exploratory analysis of AVAglio.
Autori: Nowosielski M., Ellingson BM., Chinot OL., Garcia J., Revil C., Radb ruch A., Nishikawa R., Mason WP., Henriksson R., Saran F., Kickingereder P., Platten M., Sandmann T., Abrey LE., Cloughesy TF., Bendszus M., Wick W.
Data di Pubblicazione: 2017-10-11
Abstract: Progression of glioblastoma under therapy can be characterized rad iologically. These radiologic phenotypes are influenced by treatment and dev elop differently over time with differential outcomes. Complete resolution o f contrast enhancement during treatment is a favorable factor for outcome.
Journal Title: Neuro-oncology

PUBMED ID: 29016808
DOI: doi.org/10.1093/neuonc/nox160
Titolo: Molecular differences in IDH wildtype glioblastoma according to MGMT promoter methylation.
Autori: Kessler T., Sahm F., Sadik A., Stichel D., Hertenstein A., Reifenber ger G., Zacher A., Sabel M., Tabatabai G., Steinbach J., Sure U., Krex D., G rosu AL., Bewerunge-Hudler M., Jones D., Pfister SM., Weller M., Opitz C., B endszus M., von Deimling A., Platten M., Wick W.
Data di Pubblicazione: 2017-10-11
Abstract: MGMT promoter methylation status does not define a molecularly dis tinct glioblastoma subpopulation among untreated tumors. Progressive mMGMT g lioblastomas and mMGMT tumors of patients with short survival tend to have m ore unfavorable molecular profiles.
Journal Title: Neuro-oncology

PUBMED ID: 28990795
DOI: doi.org/10.2217/cns-2017-0001
Titolo: Postprogression survival in patients with glioblastoma treated with concurrent chemoradiotherapy: a routine care cohort study.
Autori: Majewska P., Ioannidis S., Raza MH., Tanna N., Bulbeck H., Williams M.
Data di Pubblicazione: 2017-10-10
Abstract: Glioblastoma is the commonest malignant brain tumor in adults. Mos t patients develop progressive disease before they die. However, survival af ter developing progressive disease is infrequently reported. We identified p

atients with histologically proven disease who were treated with concurrent chemoradiotherapy during 2006-2013. We analyzed overall survival (OS), progr ession-free survival and postprogression survival (PPS) in relation to age, O6-methylguanine-DNA methyltransferase promoter methylation and extent of su rgical resection. We identified 166 patients. Median survival was 13.5 month s; 2-year OS was 21.7%. Median progression-free survival and PPS were 7.03 a nd 4.53 months, respectively. Age and extent of surgical resection were corr elated with OS. Only the extent of surgical resection was associated with PP S. Our work suggests that the established prognostic factors for glioblastom a do not appear to help predict PPS.
Journal Title: CNS oncology

PUBMED ID: 28988377
DOI: doi.org/10.1007/s11060-017-2624-4
Titolo: Phase I study of sorafenib and tipifarnib for recurrent glioblastoma : NABTC 05-02.
Autori: Nghiemphu PL., Ebiana VA., Wen P., Gilbert M., Abrey LE., Lieberman F., DeAngelis LM., Robins HI., Yung WKA., Chang S., Drappatz J., Mehta MP., Levin VA., Aldape K., Dancey JE., Wright JJ., Prados M., Kuhn J., Cloughesy TF.
Data di Pubblicazione: 2017-10-09
Abstract: Recurrent glioblastoma (GBM) has a very low 6-month progression fr ee survival (PFS) with currently available treatments. Combination chemother apy to target multiple cell signaling pathways is currently being investigat ed in order to improve prognosis for recurrent disease. The purpose of this phase I study was to determine the maximum tolerated dose (MTD) for the comb ination of tipifarnib and sorafenib for the treatment of recurrent GBM. Pati ents with pathologically proven WHO grade IV GBM and radiographically proven tumor recurrence were eligible for this study. Treatments included sorafenib at twice daily and escalating dosages of tipifarnib. Dose-limiting toxicity (DLT) was determined over the first 28-days of treatments, and the MTD was d etermined in a 3+3 study design. We enrolled 24 patients, and 21 patients c ompleted the MTD period. The study was stopped early with no MTD determinati on for excessive toxicities. The last dose level reached was sorafenib at 20 0 mg twice a day and tipifarnib 100 mg twice a day on an alternating week sc hedule. The DLTs included diarrhea, lipase elevation, hypophosphatemia, and arthralgia. The combination of sorafenib and tipifarnib has excessive toxici ties and full single agent dosages could not be achieved in combination.
Journal Title: Journal of neuro-oncology

PUBMED ID: 28956223
DOI: doi.org/10.1007/s11060-017-2619-1
Titolo: Estimating progression-free survival in patients with glioblastoma u sing routinely collected data.
Autori: Kelly C., Majewska P., Ioannidis S., Raza MH., Williams M.
Data di Pubblicazione: 2017-09-29
Abstract: Glioblastoma (GBM) represents 80% of all primary malignant brain t umours in adults. Prognosis is poor, and there is a clear correlation betwee n disease progression and deterioration in functional status. In this pilot study we assess whether we can estimate disease progression and progression free survival (PFS) from routinely collected electronic healthcare data. We identified fifty patients with glioblastoma who had chemo-radiotherapy. For each patient we manually collected a reference data set recording demographi cs, surgery, radiotherapy, chemotherapy, follow-up and death. We also obtain ed an electronic routine data set for each patient by combining local data o n chemotherapy/radiotherapy and hospital admissions. We calculated overall s urvival (OS) and PFS using the reference data set, and estimated them using

the routine data sets using two different methods, and compared the estimate d measures with the reference measures. Overall survival was 68% at 1 year a nd median OS was 12.8 months. The routine data correctly identified progress ive disease in 37 of 40 patients and stable disease in 7 of 10 patients. PFS was 7.4 months and the estimated PFS using routine data was 9.1 and 7.8 mont hs with methods 1 and 2 respectively. There was acceptable agreement between reference and routine data in 49 of 50 patients for OS and 35 of 50 patients for PFS. The event of progression, subsequent treatment and OS are well esti mated using our approach, but PFS estimation is less accurate. Our approach could refine our understanding of the disease course and allow us to report PFS, OS and treatment nationally.
Journal Title: Journal of neuro-oncology

PUBMED ID: 28946903
DOI: doi.org/10.1186/s13046-017-0600-7
Titolo: High expression of Bruton's tyrosine kinase (BTK) is required for EG FR-induced NF-κB activation and predicts poor prognosis in human glioma.
Autori: Yue C., Niu M., Shan QQ., Zhou T., Tu Y., Xie P., Hua L., Yu R., Liu X.
Data di Pubblicazione: 2017-09-27
Abstract: Taken together, our study suggests that BTK is a novel prognostic marker and molecular therapeutic target for glioma. BTK is required for EGFR -induced NF-κB activation in glioma cells. These findings provide the basis for future clinical studies of ibrutinib for the treatment of glioma.
Journal Title: Journal of experimental & clinical cancer research : CR

PUBMED ID: 28928820
DOI: doi.org/10.3892/ol.2017.6543
Titolo: Management of supratentorial recurrent low-grade glioma: A multidisc iplinary experience in 35 adult patients.
Autori: Spitaels J., Devriendt D., Sadeghi N., Luce S., De Witte O., Goldman S., Mélot C., Lefranc F.
Data di Pubblicazione: 2017-09-21
Abstract: The management of recurrent diffuse low-grade gliomas (LGGs) is co ntroversial. In the present study, the multidisciplinary management of 35 pa tients with recurrent LGGs was retrospectively analyzed. Tumor progression o r recurrence was defined by clinical, radiological and/or metabolic pejorati ve evolution. All patients were regularly followed up by a multidisciplinary neuro-oncological group at Hôpital Erasme. Patients with histologically conf irmed supratentorial LGGs (7 astrocytoma, 22 oligodendrogliomas and 6 oligoa strocytomas) who had undergone surgery between August 2004 and November 2010 were included. A total of 3 patients exhibited no tumor progression (median follow-up (FU), 81 months; range, 68-108 months). Tumor recurrence occurred in the 32 remaining patients [progression-free survival (PFS), 26 months; ra nge, 2-104 months]. In addition, 25/29 (86%) patients who received surgery a lone underwent reoperation at the time of tumor recurrence, and high-grade t ransformation occurred in 6 of these patients (24%). Furthermore, 4/29 (14%) patients were treated with adjuvant therapy alone (3 chemotherapy and 1 radi otherapy). In the 19 patients with no high-grade transformation at reinterve ntion, 3 received adjuvant therapy and 16 were regularly followed up through multimodal imaging. The PFS time of the patients who underwent reoperation w ith close FU (n=16) and for the patients receiving adjuvant therapy with or without surgery (n=7) at first recurrence was 10 and 24 months (P=0.005), re spectively. However, no significant difference was observed for overall surv ival (P=0.403). At the time of this study, 22 of the 35 patients included we re alive following a median FU time of 109 months (range, 55-136). The resul ts of the present study could change the multidisciplinary approach used int o a more aggressive approach with adjuvant therapy, with or without surgery,

for the treatment of a select subpopulation of patients with LGGs at the fir st instance of tumor recurrence.
Journal Title: Oncology letters

PUBMED ID: 28927109
DOI: doi.org/10.3892/ol.2017.6630
Titolo: Disease progression patterns of bevacizumab responders with recurren t malignant gliomas.
Autori: Kim JH., Jung TY., Hwang EC., Jung SH., Jung S., Kim IY., Jang WY., Moon KS., Lee KH., Kim SK.
Data di Pubblicazione: 2017-09-21
Abstract: Tumor progression in patients with recurrent malignant glioma who respond to bevacizumab (BEV) is difficult to assess. The current study revie wed the clinical and radiological results of patients following a BEV-based chemotherapy regimen, and evaluated disease progression patterns in patients who responded to BEV therapy. From August 2011 to November 2015, 24 patients (18 glioblastoma cases and 6 anaplastic astrocytoma cases) were treated with BEV-based chemotherapy. In total, 6 patients were treated with BEV alone and 18 patients were treated with BEV combined with irinotecan. The male-female ratio was 10:14, and the median age was 47.5 years (range, 29-69). Patient p erformance status (PS) was classified using the Eastern Cooperative Oncology Group PS scores as follows: PS 1 (n=3), PS 2 (n=9), PS 3 (n=9) and PS 4 (n=3). Treatment-associated complications were also analyzed according to the Na tional Cancer Institute Common Terminology Criteria for Adverse Events versi on 4.0. Treatment responses were estimated using the Response Assessment in Neuro-Oncology Criteria. Progression-free survival (PFS) following treatment , patterns of disease progression and overall survival following treatment f ailure were also analyzed. The median PFS was 2.8 months (range, 0.6-10.1). In total, 2 patients did not continue treatment due to rectal bleeding and s evere hematologic toxicity. Amongst the BEV responders (n=16, 72.7%), there was clinical deterioration without significant radiological progression in 2 patients (n=2, 12.5%). Radiological progression of non-enhancing lesions wit hout enhancement flare-ups was observed in 6 patients (42.9%). A total of 3 of those lesions were diffuse and 3 were focal. Increased lesion enhancement was observed in 8 patients (57.1%). Of the non-responders (n=6, 27.3%), diff use enlargement of non-enhancing lesions was detected in 2 patients and an i ncrease in lesion enhancement occurred in 4 patients. BEV complete responder s (n=3) radiologically progressed with enlarged T2/fluid attenuation inversi on recovery lesions without enhancement, followed by enhancement flare-ups. Following BEV treatment failure, 8 patients received a number of adjuvant tr eatments and the overall survival was 4.5 months (range, 0.4-34.0). Clinical symptoms and radiological alterations of non-enhancing lesions must be evalu ated in order to assess tumor progression in the BEV responders, particularl y in patients who have achieved complete remission.
Journal Title: Oncology letters

PUBMED ID: 28901423
DOI: doi.org/10.3892/mmr.2017.7456
Titolo: A multi-targeted tyrosine kinase inhibitor lenvatinib for the treatm ent of mice with advanced glioblastoma.
Autori: Li J., Zou CL., Zhang ZM., Lv LJ., Qiao HB., Chen XJ.
Data di Pubblicazione: 2017-09-14
Abstract: Glioblastoma is the most aggressive primary brain tumor that origi nates from the glial cells in adults. Aberrant angiogenesis is essential for malignant glioblastoma tumorigenesis, development and metastasis. Lenvatinib is a multi-targeted anticancer agent that targets of receptor tyrosine kinas es including vascular endothelial growth factor receptor 1 and 2, fibroblast growth factor receptor 1, platelet-derived growth factor receptor β and v-ki

t Hardy-Zuckerman 4 feline sarcoma viral oncogene homolog. In the present st udy, the therapeutic effects of lenvatinib as a treatment for glioblastoma w ere investigated in vivo and in vitro. The maximum dose toxicity (MDT) and t reatment-associated adverse events of lenvatinib were identified by cytotoxi city assay in experimental mice. Increasing levels of the pro-apoptosis gene s caspase-3, -8, -9 and -10 following lenvatinib treatment were determined b y reverse transcription-quantitative polymerase chain reaction, and apoptosi s of the malignant gliomas cells was analyzed by FACS. In vivo treatment wit h lenvatinib for BV-2 bearing male BALC/c nude mice was assessed via tumor g rowth suppression and long-term observation of survival. Subsequent cytotoxi c T lymphocyte responses were further analyzed to determine the in vivo effi cacy of lenvatinib treatment in mice with glioblastoma. The MDT of lenvatini b was identified as 0.24 mg, with relatively few side effects and improved e fficacy in mice. Lenvatinib (0.24 mg) significantly increased apoptosis in B V-2, C6, BC3H1 and G422 glioma cell lines. Tumor growth was significantly in hibited and tumor-bearing mice demonstrated an improved survival rate follow ing treatment with lenvatinib. In conclusion, lenvatinib provided an effecti ve treatment outcome, and the results of the present study may help to achie ve a comprehensive therapeutic schedule for clinical application.
Journal Title: Molecular medicine reports

PUBMED ID: 28885120
DOI: doi.org/10.3171/2017.3.JNS162383
Titolo: Threshold of the extent of resection for WHO Grade III gliomas: retr ospective volumetric analysis of 122 cases using intraoperative MRI.
Autori: Fujii Y., Muragaki Y., Maruyama T., Nitta M., Saito T., Ikuta S., Is eki H., Hongo K., Kawamata T.
Data di Pubblicazione: 2017-09-09
Abstract: OBJECTIVE WHO Grade III gliomas are relatively rare and treated wi th multiple modalities such as surgery, chemotherapy, and radiotherapy. The impact of the extent of resection (EOR) on improving survival in patients wi th this tumor type is unclear. Moreover, because of the heterogeneous radiol ogical appearance of Grade III gliomas, the MRI sequence that best correlate s with tumor volume is unknown. In the present retrospective study, the auth ors evaluated the prognostic significance of EOR. METHODS Clinical and radio logical data from 122 patients with newly diagnosed WHO Grade III gliomas wh o had undergone intraoperative MRI-guided resection at a single institution between March 2000 and December 2011 were analyzed retrospectively. Patients were divided into 2 groups by histological subtype: 81 patients had anaplast ic astrocytoma (AA) or anaplastic oligoastrocytoma (AOA), and 41 patients ha d anaplastic oligodendroglioma (AO). EOR was calculated using pre- and posto perative T2-weighted and contrast-enhanced T1-weighted MR images. Univariate and multivariate analyses were performed to evaluate the prognostic signific ance of EOR on overall survival (OS). RESULTS The 5-, 8-, and 10-year OS rat es for all patients were 74.28%, 70.59%, and 65.88%, respectively. The 5- an d 8-year OS rates for patients with AA and AOA were 72.2% and 67.2%, respect ively, and the 10-year OS rate was 62.0%. On the other hand, the 5- and 8-ye ar OS rates for patients with AO were 79.0% and 79.0%; the 10-year OS rate i s not yet available. The median pre- and postoperative T2-weighted high-sign al intensity volumes were 56.1 cm
Journal Title: Journal of neurosurgery

PUBMED ID: 28871999
DOI: doi.org/10.1016/j.ijrobp.2017.04.007
Titolo: Multimodal Magnetic Resonance Imaging of Treatment-Induced Changes t o Diffuse Infiltrating Pontine Gliomas in Children and Correlation to Patien t Progression-Free Survival.

Autori: Calmon R., Puget S., Varlet P., Beccaria K., Blauwblomme T., Grevent D., Sainte-Rose C., Castel D., Dufour C., Dhermain F., Bolle S., Saitovitch A., Zilbovicius M., Brunelle F., Grill J., Boddaert N.
Data di Pubblicazione: 2017-09-06
Abstract: Multimodal MRI provides useful information about diffuse infiltrating pontine gliomas' response to treatment; rCBV increases following RT, and higher values are correlated with better PFS. High rCBV values following RT should not be mistaken for progression and could be an indicator of response to therapy.
Journal Title: International journal of radiation oncology, biology, physics

PUBMED ID: 28868256
DOI: doi.org/10.3389/fonc.2017.00178
Titolo: Multiparametric MRI and [
Autori: Hassanzadeh C., Rao YJ., Chundury A., Rowe J., Ponisio MR., Sharma A., Miller-Thomas M., Tsien CI., Ippolito JE.
Data di Pubblicazione: 2017-09-05
Abstract: Recurrent GBM in the molecular era is associated with highly variable outcomes. Multiparametric MR and FDG-PET biomarkers may provide a clinically relevant, non-invasive and cost-effective method of predicting prognosis and improving clinical decision making in the treatment of patients with suspected tumor recurrence.
Journal Title: Frontiers in oncology

PUBMED ID: 28842741
DOI: doi.org/10.1007/s00234-017-1899-7
Titolo: Response Assessment in Neuro-Oncology criteria, contrast enhancement and perfusion MRI for assessing progression in glioblastoma.
Autori: Tensaouti F., Khalifa J., Lusque A., Plas B., Lotterie JA., Berry I., Laprie A., Cohen-Jonathan Moyal E., Lubrano V.
Data di Pubblicazione: 2017-08-27
Abstract: In conclusion, our findings suggest that CE-3D criterion is not yet suitable to assess progression in routine clinical practice. Indeed, the accurate threshold is still not well defined. To date, in our opinion, early detection of disease progression by RANO combined with advanced MRI imaging techniques like MRI perfusion and diffusion remains the best way to assess disease progression. Further investigations that would examine the impact of treatment modifications after progression determined by different criteria on overall survival would be of great value.
Journal Title: Neuroradiology

PUBMED ID: 28836106
DOI: doi.org/10.1007/s11060-017-2599-1
Titolo: The impact of adjuvant therapy for patients with high-risk diffuse WHO grade II glioma.
Autori: Youland RS., Kreofsky CR., Schomas DA., Brown PD., Buckner JC., Laack NN.
Data di Pubblicazione: 2017-08-25
Abstract: Despite recent randomized, prospective evidence supporting use of RT and chemotherapy (CRT) for high-risk low-grade gliomas (LGG), many patients have historically received RT alone, chemotherapy alone or observation postoperatively. The purpose of this study is to evaluate outcomes for historical treatments in comparison to CRT for high-risk diffuse WHO grade II glioma patients. Records from 309 adults with WHO grade II glioma (1997-2008) eligible for RTOG 9802 (incomplete resection/biopsy or age ≥40 years) were retrospectively reviewed. Kaplan-Meier estimates were used for progression-free survival (PFS) and overall survival (OS). The Cox proportional hazards model

was used for estimates of risk ratios for univariate and multivariate analys es. Median follow-up was 10.6 years. Adjuvant treatments included radiothera py (RT) alone (45%), observation (31%), CRT (21%) and chemotherapy alone (3%). Non-astrocytic histology, TERT promoter mutation, 1p/19q codeletion and e xtensive resections were associated with improved PFS and OS on univariate a nalysis (all $p<0.05$). IDH mutations and adjuvant CRT was associated with im proved PFS (all $p<0.05$). On multivariate analysis, histology, molecular gro uping and extent of resection were significantly associated with PFS and OS. In addition, multivariate analysis revealed that CRT was associated with imp roved PFS and OS compared with RT alone, and improved PFS compared with obse rvation. This study confirms the benefit of adding chemotherapy to RT compar ed with RT alone or observation. These findings emphasize the need for aggre ssive treatment in patients with high-risk LGG.
Journal Title: Journal of neuro-oncology

PUBMED ID: 28824876
DOI: doi.org/10.3389/fonc.2017.00165
Titolo: Gliomatosis Cerebri: Current Understanding and Controversies.
Autori: Ranjan S., Warren KE.
Data di Pubblicazione: 2017-08-22
Abstract: Gliomatosis cerebri (GC) is a rare, extensively infiltrating gliom a involving multiple contiguous lobes of the brain. This lethal disease affe cts all age groups, and the majority of patients have a poor outcome despite aggressive treatment. Despite its initial recognition in 1938, GC remains a controversial entity with little consensus in its definition, histology, or treatment. The majority of GC tumors are astrocytic, although mixed phenotyp es have been identified. Treatment of GC is challenging as surgery is genera lly not an option due to the extensive areas of brain involved, the benefit of radiation therapy is unclear, and no chemotherapy has proven efficacy. Du e to the rarity of the disease and its heterogeneity, both at histopathologi cal and molecular levels, it is difficult to conduct clinical trials tailore d for this diagnosis. This review summarizes our current knowledge, examines clinical studies focusing on the treatment of GC, highlights ongoing challen ges, and discusses the recent molecular insights into adult and pediatric GC . We conclude that, although no longer recognized as a distinct pathological entity, GC represents a unique disease phenotype. Given the histologic and m olecular overlap with other diffuse gliomas, the research emphasis should be on investigating its unique invasive biology.
Journal Title: Frontiers in oncology

PUBMED ID: 28791500
DOI: doi.org/10.1007/s00701-017-3277-y
Titolo: Correlation of volumetric growth and histological grade in 50 mening iomas.
Autori: Soon WC., Fountain DM., Koczyk K., Abdulla M., Giri S., Allinson K., Matys T., Guilfoyle MR., Kirollos RW., Santarius T.
Data di Pubblicazione: 2017-08-10
Abstract: Reliable tools now exist to evaluate and monitor volumetric growth of meningiomas. Grade II meningiomas have significantly higher VGR compared with grade I meningiomas and growth of more than 3 cm
Journal Title: Acta neurochirurgica

PUBMED ID: 28747219
DOI: doi.org/10.1186/s13256-017-1373-5
Titolo: Role of eculizumab in a pediatric refractory gemcitabine-induced thr ombotic microangiopathy: a case report.

Autori: Facchini L., Lucchesi M., Stival A., Roperto RM., Melosi F., Materas si M., Farina S., Tintori V., de Martino M., Sardi I.
Data di Pubblicazione: 2017-07-28
Abstract: Eculizumab prevents serious complement-mediated vascular damage fo r chemotherapy-induced thrombotic microangiopathy in pediatric cases.
Journal Title: Journal of medical case reports

PUBMED ID: 28711289
DOI: doi.org/10.1016/j.jocn.2017.06.070
Titolo: Clinical outcomes in recurrent glioblastoma with bevacizumab therapy : An analysis of the literature.
Autori: Tipping M., Eickhoff J., Ian Robins H.
Data di Pubblicazione: 2017-07-17
Abstract: Bevacizumab (BEV) is a common treatment for recurrent glioblastoma (GBM). After progression on BEV, there is no consensus on subsequent therapy , as multiple chemotherapy trials have failed to demonstrate discernible act ivity for salvage. A previous review (995 patients) estimated a progression free survival (PFS) on BEV of 4.2months (SD±2.1) with an overall survival (O S) after progression on BEV at 3.8months (SD±1). We endeavored to establish a more rigorous historical control, both as a benchmark for efficacy, and a prognostic tool for clinical practice. A comprehensive literature review was performed utilizing PubMed and societal presentation abstracts. A total 2388 patients from 53 arms of 42 studies were analyzed in three groups: 1) thirty -two studies in which survival post-BEV was determined by subtracting PFS fr om OS (2045 patients): PFS on BEV=4.38months (95% CI 4.09-4.68); OS post-BEV =3.36months (95% CI 3.12-3.66); 2) two studies (94 patients) in which OS pos t-BEV is reported: OS=3.26 (95% CI 2.39-4.42); 3) eight studies of salvage t herapy after progression on BEV (249 patients): of OS post-BEV=4.46months (9 5% CI 3.68-5.54). These estimates provide a firm historical control for PFS on BEV, as well as OS after disease progression on BEV therapy.
Journal Title: Journal of clinical neuroscience : official journal of the Ne urosurgical Society of Australasia

PUBMED ID: 28708230
DOI: doi.org/10.5301/tj.5000672
Titolo: Short course radiotherapy concomitant with temozolomide in GBM patie nts: a phase II study.
Autori: Fariselli L., Cuppini L., Gaviani P., Marchetti M., Pinzi V., Milane si I., Simonetti G., Tramacere I., DiMeco F., Salmaggi A., Silvani A.
Data di Pubblicazione: 2017-07-15
Abstract: To improve local control and OS, a more aggressive treatment sched ule should be explored. The related higher necrosis risk and its implication s regarding local control deserve further investigation.
Journal Title: Tumori

PUBMED ID: 28702781
DOI: doi.org/10.1007/s11060-017-2550-5
Titolo: Radiographic patterns of progression with associated outcomes after bevacizumab therapy in glioblastoma patients.
Autori: Cachia D., Elshafeey NA., Kamiya-Matsuoka C., Hatami M., Alfaro-Muno z KD., Mandel JJ., Colen R., DeGroot JF.
Data di Pubblicazione: 2017-07-14
Abstract: Treatment response and survival after bevacizumab failure remains poor in patients with glioblastoma. Several recent publications examining gl ioblastoma patients treated with bevacizumab have described specific radiogr aphic patterns of disease progression as correlating with outcome. This stud y aims to scrutinize these previously reported radiographic prognostic model

s in an independent data set to inspect their reproducibility and potential for clinical utility. Sixty four patients treated at MD Anderson matched pre determined inclusion criteria. Patients were categorized based on previously published data by: (1) Nowosielski et al. into: T2-diffuse, cT1 Flare-up, no n-responders and T2 circumscribed groups (2) Modified Pope et al. criteria i nto: local, diffuse and distant groups and (3) Bahr et al. into groups with or without new diffusion-restricted and/or pre-contrast T1-hyperintense lesi ons. When classified according to Nowosielski et al. criteria, the cT1 Flare -up group had the longest overall survival (OS) from bevacizumab initiation, with non-responders having the worst outcomes. The T2 diffuse group had the longest progression free survival (PFS) from start of bevacizumab. When clas sified by modified Pope at al. criteria, most patients did not experience a shift in tumor pattern from the pattern at baseline, while the PFS and OS in patients with local-to-local and local-to-diffuse/distant patterns of progre ssion were similar. Patients developing restricted diffusion on bevacizumab had worse OS. Diffuse patterns of progression in patients treated with bevac izumab are rare and not associated with worse outcomes compared to other rad iographic subgroups. Emergence of restricted diffusion during bevacizumab tr eatment was a radiographic marker of worse OS.
Journal Title: Journal of neuro-oncology

PUBMED ID: 28693286
DOI: doi.org/10.3892/ol.2017.6251
Titolo: Bevacizumab as a last-line treatment for glioblastoma following fail ure of radiotherapy, temozolomide and lomustine.
Autori: Wenger KJ., Wagner M., You SJ., Franz K., Harter PN., Burger MC., Vo ss M., Ronellenfitsch MW., Fokas E., Steinbach JP., Bähr O.
Data di Pubblicazione: 2017-07-12
Abstract: In previous trials, bevacizumab failed to prolong the overall surv ival time in newly diagnosed glioblastoma and at the first recurrence. Rando mized clinical trials at the second or further recurrence following the fail ure of radiotherapy, temozolomide and lomustine, and retrospective analyses focusing on this specific cohort, are not yet available. A total of 62 patie nts with glioblastoma who received bevacizumab after the failure of standard care, including radiotherapy, temozolomide and lomustine, were retrospective ly identified. Patient characteristics, previous treatment details, concomit ant therapy, response based on the Response Assessment in Neuro-Oncology cri teria, and progression-free survival (PFS) and overall survival (OS) times a nd rates were evaluated. Furthermore, the PFS and OS times and rates were an alyzed for responders and non-responders. Of the patients, 54.8% (n=34) resp onded to treatment [complete response (CR) 3.2%, n=2; partial response (PR) 51.6%, n=32]. The median PFS time was 3.5 months and the median OS time was 7.5 months. The PFS rate at 6 months was 21.5% and the OS rate at 12 months was 11.5%. Responders (CR or PR) experienced a superior median PFS time comp ared with non-responders (i.e. stable or progressive disease; 5.4 vs. 1.9 mo nths; P<0.0001) and a superior PFS rate at 6 months (34.9 vs. 7.1%; P<0.0001). The median OS time (8.6 vs. 6.4 months; P<0.0001) and OS rate at 12 month s (21.3 vs. 0%; P<0.0001) were also superior in patients who exhibited a res ponse to bevacizumab treatment. In conclusion, the objective response rate a nd the PFS and OS times and rates indicate that bevacizumab has activity in patients with glioblastoma following the failure of radiotherapy, temozolomi de, and lomustine. A randomized trial comparing bevacizumab with best suppor tive care in these patients is advised.
Journal Title: Oncology letters

PUBMED ID: 28685405
DOI: doi.org/10.1007/s11060-017-2562-1

Titolo: Impact of removed tumor volume and location on patient outcome in gl
ioblastoma.
Autori: Awad AW., Karsy M., Sanai N., Spetzler R., Zhang Y., Xu Y., Mahan MA
.
Data di Pubblicazione: 2017-07-08
Abstract: Glioblastoma is an aggressive primary brain tumor with devastating
ly poor prognosis. Multiple studies have shown the benefit of wider extent o
f resection (EOR) on patient overall survival (OS) and worsened survival wit
h larger preoperative tumor volumes. However, the concomitant impact of post
operative tumor volume and eloquent location on OS has yet to be fully evalu
ated. We performed a retrospective chart review of adult patients treated fo
r glioblastoma from January 2006 through December 2011. Adherence to standar
dized postoperative chemoradiation protocols was used as an inclusion criter
ion. Detailed volumetric and location analysis was performed on immediate pr
eoperative and immediate postoperative magnetic resonance imaging. Cox propo
rtional hazard modeling approach was employed to explore the modifying effec
ts of EOR and eloquent location after adjusting for various confounders and
associated characteristics, such as preoperative tumor volume and demographi
cs. Of the 471 screened patients, 141 were excluded because they did not mee
t all inclusion criteria. The mean (±SD) age of the remaining 330 patients (
60.6% male) was 58.9±12.9 years; the mean preoperative and postoperative Ka
rnofsky performance scores (KPSs) were 76.2±10.3 and 80.0±16.6, respectivel
y. Preoperative tumor volume averaged 33.2±29.0 ml, postoperative residual
was 4.0±8.1 ml, and average EOR was 88.6±17.6%. The observed average follow
-up was 17.6±15.7 months, and mean OS was 16.7±14.4 months. Survival analys
is showed significantly shorter survival for patients with lesions in perive
ntricular (16.8±1.7 vs. 21.5±1.4 mo, p=0.03), deep nuclei/basal ganglia (1
1.6±1.7 vs. 20.6±1.2, p=0.002), and multifocal (12.0±1.4 vs. 21.3±1.3 mon
ths, p=0.0001) locations, but no significant influence on survival was seen
for eloquent cortex sites (p=0.14, range 0.07-0.9 for all individual locati
ons). OS significantly improved with EOR in univariate analysis, averaging 2
2.3, 19.7, and 13.2 months for >90, 80-90, and 70-80% resection, respectivel
y. Survival was 22.8, 19.0, and 12.7 months for 0, 0-5, and 5-10 ml postoper
ative residual, respectively. A hazard model showed that larger preoperative
tumor volume [hazard ratio (HR) 1.05, 95% CI 1.02-1.07], greater age (HR 1.0
2, 95% CI 1.01-1.03), multifocality (HR 1.44, 95% CI 1.01-2.04), and deep nu
clei/basal ganglia (HR 2.05, CI 1.27-3.3) were the most predictive of poor s
urvival after adjusting for KPS and tumor location. There was a negligible b
ut significant interaction between EOR and preoperative tumor volume (HR 0.9
995, 95% CI 0.9993-0.9998), but EOR alone did not correlate with OS after ad
justing for other factors. The interaction between EOR and preoperative tumo
r volume represented tumor volume removed during surgery. In conclusion, EOR
alone was not an important predictor of outcome during GBM treatment once pr
eoperative tumor volume, age, and deep nuclei/basal ganglia location were fa
ctored. Instead, the interaction between EOR and preoperative volume, repres
enting reduced disease burden, was an important predictor of reducing OS. Re
moval of tumor from eloquent cortex did not impact postoperative KPS. These
results suggest aggressive surgical treatment to reduce postoperative residu
al while maintaining postoperative KPS may aid patient survival outcomes for
a given tumor size and location.
Journal Title: Journal of neuro-oncology

PUBMED ID: 28685404
DOI: doi.org/10.1007/s11060-017-2537-2
Titolo: Analysis of factors influencing the access to concomitant chemo-radi
otherapy in elderly patients with high grade gliomas: role of MMSE, age and
tumor volume.

Autori: Di Cristofori A., Zarino B., Fanizzi C., Fornara GA., Bertani G., Rampini P., Carrabba G., Caroli M.
Data di Pubblicazione: 2017-07-08
Abstract: High grade gliomas (HGG) are tumors with a rapidly progressive course and the standard of care consists of surgery and chemo-radiotherapy. Elderly patients with HGG usually have a worse prognosis due to their comorbidities and difficulties in accessing or completing adjuvant treatments. The purpose of our study was to assess the influence of pre-operative factors (MMSE, age, sex, KPS, tumor volume) on the post-operative access to chemo-radiotherapy in the elderly population. In addition, the influence of the access to adjuvant therapies on overall survival (OS) was assessed. We retrospectively reviewed our consecutive case series of 117 elderly patients (≥65 years) with HGG treated in our Institution. All the clinical records regarding age, sex, tumor location, MMSE, KPS, access to adjuvant treatments and OS were analyzed. 72 males and 45 females with a median age of 71 years were analyzed. Adjuvant therapies were considered; concomitant chemo-radiotherapy with standard radiotherapy or hypofractionated radiation regimen. 84 patients had access to adjuvant therapies. Access to therapies was associated with a median age of 71(range 66-80) years, a median MMSE of 26(range 5-30), and a median tumor volume of 24 cm
Journal Title: Journal of neuro-oncology

PUBMED ID: 28683323
DOI: doi.org/10.1016/j.celrep.2017.06.036
Titolo: Identification of a Druggable Pathway Controlling Glioblastoma Invasiveness.
Autori: Pencheva N., de Gooijer MC., Vis DJ., Wessels LFA., Würdinger T., van Tellingen O., Bernards R.
Data di Pubblicazione: 2017-07-07
Abstract: Diffuse and uncontrollable brain invasion is a hallmark of glioblastoma (GBM), but its mechanism is understood poorly. We developed a 3D ex vivo organotypic model to study GBM invasion. We demonstrate that invading GBM cells upregulate a network of extracellular matrix (ECM) components, including multiple collagens, whose expression correlates strongly with grade and clinical outcome. We identify interferon regulatory factor 3 (IRF3) as a transcriptional repressor of ECM factors and show that IRF3 acts as a suppressor of GBM invasion. Therapeutic activation of IRF3 by inhibiting casein kinase 2 (CK2)-a negative regulator of IRF3-downregulated the expression of ECM factors and suppressed GBM invasion in ex vivo and in vivo models across a panel of patient-derived GBM cell lines representative of the main molecular GBM subtypes. Our data provide mechanistic insight into the invasive capacity of GBM tumors and identify a potential therapy to inhibit GBM invasion.
Journal Title: Cell reports

PUBMED ID: 28678383
DOI: doi.org/10.1002/cncr.30838
Titolo: The role of early magnetic resonance imaging in predicting survival on bevacizumab for recurrent glioblastoma: Results from a prospective clinical trial (CABARET).
Autori: Field KM., Phal PM., Fitt G., Goh C., Nowak AK., Rosenthal MA., Simes J., Barnes EH., Sawkins K., Cher LM., Hovey EJ., Wheeler H.
Data di Pubblicazione: 2017-07-06
Abstract: In this study, early progression on MRI appears to be a robust marker of a poor prognosis for patients on bevacizumab. Cancer 2017;123:3576-82. © 2017 American Cancer Society.
Journal Title: Cancer

PUBMED ID: 28675067
DOI: doi.org/10.1080/0284186X.2017.1332780
Titolo: Postoperative neoadjuvant temozolomide before radiotherapy versus st
andard radiotherapy in patients 60 years or younger with anaplastic astrocyt
oma or glioblastoma: a randomized trial.
Autori: Malmström A., Poulsen HS., Grønberg BH., Stragliotto G., Hansen S.,
Asklund T., Holmlund B., Łysiak M., Dowsett J., Kristensen BW., Söderkvist P
., Rosell J., Henriksson R., Henriksson R.
Data di Pubblicazione: 2017-07-05
Abstract: No advantage of NeoTMZ was noted for the overall study population
or subgroup of GBM, while NeoTMZ resulted in 5 years longer median survival
for patients diagnosed as AA.
Journal Title: Acta oncologica (Stockholm, Sweden)

PUBMED ID: 28666368
DOI: doi.org/10.1093/neuonc/nox121
Titolo: Cost-effectiveness of radiation and chemotherapy for high-risk low-g
rade glioma.
Autori: Qian Y., Maruyama S., Kim H., Pollom EL., Kumar KA., Chin AL., Harri
s JP., Chang DT., Pitt A., Bendavid E., Owens DK., Durkee BY., Soltys SG.
Data di Pubblicazione: 2017-07-02
Abstract: The addition of PCV to RT is a cost-effective treatment strategy f
or patients with high-risk LGG.
Journal Title: Neuro-oncology

PUBMED ID: 28647829
DOI: doi.org/10.1007/s10072-017-3036-0
Titolo: Extra central nervous system metastases from glioblastoma: a new pos
sible trigger event?
Autori: Simonetti G., Silvani A., Fariselli L., Hottinger AF., Pesce GA., Pr
ada F., Gaviani P.
Data di Pubblicazione: 2017-06-26
Abstract: Extra-cranial metastases of glioblastoma (GBM) represent a rare ev
ent, and the biological-genetic mechanisms involved in the pathogenesis have
not yet been determined. We report the case of a young patient with multiple
visceral and osseous metastases occurred after 4 years after first diagnosis
of GBM. The strangeness as well as the rarity of this event does not allow t
o identify an effective treatment for GBM metastases, making the management
of this ominous tumor an even greater challenge.
Journal Title: Neurological sciences : official journal of the Italian Neuro
logical Society and of the Italian Society of Clinical Neurophysiology

PUBMED ID: 28640702
DOI: doi.org/10.1200/JCO.2017.72.6737
Titolo: Diffuse Infiltrating Oligodendroglioma and Astrocytoma.
Autori: van den Bent MJ., Smits M., Kros JM., Chang SM.
Data di Pubblicazione: 2017-06-23
Abstract: The new 2016 WHO brain tumor classification defines different diff
use gliomas primarily according to the presence or absence of IDH mutations
(IDH-mt) and combined 1p/19q loss. Today, the diagnosis of anaplastic oligo
dendroglioma requires the presence of both IDH-mt and 1p/19q co-deletion, wh
ereas anaplastic astrocytoma is divided into IDH wild-type (IDH-wt) and IDH
-mt tumors. IDH-mt tumors have a more favorable prognosis, and tumors with l
ow-grade histology especially tend evolve slowly. IDH-wt tumors are not a ho
mogeneous entity and warrant further molecular testing because some have gli
oblastoma-like molecular features with poor clinical outcome. Treatment cons
ists of a resection that should be as extensive as safely possible, radiothe

rapy, and chemotherapy. Trials of patients with newly diagnosed grade II or III glioma have shown survival benefit from adding chemotherapy to radiotherapy compared with initial treatment using radiotherapy alone. Both temozolomide and the combination of procarbazine, lomustine, and vincristine provide survival benefit. In contrast, trials that compare single modality treatment of chemotherapy alone with radiotherapy alone did not observe survival differences. Currently, for patients with grade II or III gliomas who require postsurgical treatment, the preferred treatment consists of a combination of radiotherapy and chemotherapy. Low-grade gliomas with favorable characteristics are slow-growing tumors. When deciding on the timing of postsurgical treatment with radiotherapy and chemotherapy, both clinical and molecular factors should be taken into account, but a more conservative approach can be considered initially in some of these patients. The factor that best predicts benefit of chemotherapy in grade II and III glioma remains to be established.
Journal Title: Journal of clinical oncology : official journal of the American Society of Clinical Oncology

PUBMED ID: 28620243
DOI: doi.org/10.1038/s41598-017-03785-8
Titolo: Targeting glioma stem cells in vivo by a G-quadruplex-stabilizing synthetic macrocyclic hexaoxazole.
Autori: Nakamura T., Okabe S., Yoshida H., Iida K., Ma Y., Sasaki S., Yamori T., Shin-Ya K., Nakano I., Nagasawa K., Seimiya H.
Data di Pubblicazione: 2017-06-17
Abstract: G-quadruplex (G4) is a higher-order nucleic acid structure that is formed by guanine-rich sequences. G4 stabilization by small-molecule compounds called G4 ligands often causes cytotoxicity, although the potential medicinal impact of this effect has not been fully established. Here we demonstrate that a synthetic G4 ligand, Y2H2-6M(4)-oxazole telomestatin derivative (6OTD), limits the growth of intractable glioblastoma (grade IV glioma) and glioma stem cells (GSCs). Experiments involving a human cancer cell line panel and mouse xenografts revealed that 6OTD exhibits antitumor activity against glioblastoma. 6OTD inhibited the growth of GSCs more potently than it did the growth of differentiated non-stem glioma cells (NSGCs). 6OTD caused DNA damage, G1 cell cycle arrest, and apoptosis in GSCs but not in NSGCs. These DNA damage foci tended to colocalize with telomeres, which contain repetitive G4-forming sequences. Compared with temozolomide, a clinical DNA-alkylating agent against glioma, 6OTD required lower concentrations to exert anti-cancer effects and preferentially affected GSCs and telomeres. 6OTD suppressed the intracranial growth of GSC-derived tumors in a mouse xenograft model. These observations indicate that 6OTD targets GSCs through G4 stabilization and promotion of DNA damage responses. Therefore, G4s are promising therapeutic targets for glioblastoma.
Journal Title: Scientific reports

PUBMED ID: 28602885
DOI: doi.org/10.1016/j.wneu.2017.05.165
Titolo: High Expression of Glypican-1 Predicts Dissemination and Poor Prognosis in Glioblastomas.
Autori: Saito T., Sugiyama K., Hama S., Yamasaki F., Takayasu T., Nosaka R., Onishi S., Muragaki Y., Kawamata T., Kurisu K.
Data di Pubblicazione: 2017-06-13
Abstract: GPC-1 expression significantly correlated with OS in patients with GBM who received radiotherapy and temozolomide treatment. GPC-1 expression can help predict the occurrence of dissemination and shorter OS in patients with GBM.
Journal Title: World neurosurgery

PUBMED ID: 28574607
DOI: doi.org/10.1111/nan.12415
Titolo: Prognostic value of O-6-methylguanine-DNA methyltransferase (MGMT) p
rotein expression in glioblastoma excluding nontumour cells from the analysi
s.
Autori: Dahlrot RH., Dowsett J., Fosmark S., Malmström A., Henriksson R., Bo
ldt H., de Stricker K., Sørensen MD., Poulsen HS., Lysiak M., Söderkvist P.,
Rosell J., Hansen S., Kristensen BW.
Data di Pubblicazione: 2017-06-03
Abstract: Our data indicate that MGMT protein expression in tumour cells has
an independent prognostic significance. Exclusion of nontumour cells contrib
uted to a more exact analysis of tumour-specific MGMT protein expression. Th
is should be incorporated in future studies evaluating MGMT status before po
tential integration into clinical practice.
Journal Title: Neuropathology and applied neurobiology

PUBMED ID: 28556364
DOI: doi.org/10.1111/cas.13285
Titolo: Phase I study of glasdegib (PF-04449913), an oral smoothened inhibit
or, in Japanese patients with select hematologic malignancies.
Autori: Minami Y., Minami H., Miyamoto T., Yoshimoto G., Kobayashi Y., Munak
ata W., Onishi Y., Kobayashi M., Ikuta M., Chan G., Woolfson A., Ono C., Sha
ik MN., Fujii Y., Zheng X., Naoe T.
Data di Pubblicazione: 2017-05-31
Abstract: The hedgehog signaling pathway regulates multiple morphogenetic pr
ocesses during embryogenesis. Aberrant activation of the hedgehog pathway si
gnal transduction in adult tissues is associated with the pathogenesis of he
matologic malignancies and solid tumors. We report findings from an open-lab
el, multicenter phase I trial of the selective, small-molecule hedgehog sign
aling inhibitor glasdegib (PF-04449913) in Japanese patients with select adv
anced hematologic malignancies. Glasdegib was administered as once-daily ora
l doses (25, 50 and 100 mg) in 28-day cycles after a lead-in dose on Day -5.
The primary objectives were to determine first-cycle dose-limiting toxicitie
s, safety, vital signs and laboratory test abnormalities. Secondary objectiv
es included evaluation of pharmacokinetics, pharmacodynamics and preliminary
evidence of clinical activity of glasdegib. No dose-limiting toxicities were
noted in the 13 patients in the present study. All patients experienced at l
east one treatment-emergent, all-causality adverse event. The most frequent
treatment-related adverse events (observed in ≥3 patients) were dysgeusia (
n = 9), muscle spasms (n = 5), alopecia, decreased appetite (n = 4 each), an
d increased blood creatinine phosphokinase, constipation and diarrhea (n = 3
each). Two deaths occurred during the study and were deemed not to be treatm
ent-related due to disease progression. Glasdegib demonstrated dose-proporti
onal pharmacokinetics, marked downregulation of the glioma-associated transc
riptional regulator GLI1 expression in normal skin, and evidence of prelimin
ary clinical activity, although data are limited. Glasdegib was safe and wel
l tolerated across the dose levels tested. It is confirmed that the 100-mg d
ose is safe and tolerable in Japanese patients, and this dose level will be
examined in the future clinical trial.
Journal Title: Cancer science

PUBMED ID: 28513547
DOI: doi.org/10.3390/genes8050145
Titolo: Epigenetic Regulation of Telomere Maintenance for Therapeutic Interv
entions in Gliomas.
Autori: Naderlinger E., Holzmann K.
Data di Pubblicazione: 2017-05-18

Abstract: High-grade astrocytoma of WHO grade 4 termed glioblastoma multiforme (GBM) is a common human brain tumor with poor patient outcome. Astrocytoma demonstrates two known telomere maintenance mechanisms (TMMs) based on telomerase activity (TA) and on alternative lengthening of telomeres (ALT). ALT is associated with lower tumor grades and better outcome. In contrast to ALT, regulation of TA in tumors by direct mutation and epigenetic activation of the hTERT promoter is well established. Here, we summarize the genetic background of TMMs in non-malignant cells and in cancer, in addition to clinical and pathological features of gliomas. Furthermore, we present new evidence for epigenetic mechanisms (EMs) involved in regulation of ALT and TA with special emphasis on human diffuse gliomas as potential therapeutic drug targets. We discuss the role of TMM associated telomeric chromatin factors such as DNA and histone modifying enzymes and non-coding RNAs including microRNAs and long telomeric TERRA transcripts.
Journal Title: Genes

PUBMED ID: 28511812
DOI: doi.org/10.1016/j.pediatrneurol.2017.04.008
Titolo: Acute Management of Symptomatic Subependymal Giant Cell Astrocytoma With Everolimus.
Autori: Arroyo MS., Krueger DA., Broomall E., Stevenson CB., Franz DN.
Data di Pubblicazione: 2017-05-18
Abstract: Everolimus can effectively reduce tumor size, decrease cerebrospinal fluid protein, and allow successful ventriculoperitoneal shunt placement without the need for surgical resection of a symptomatic SEGA.
Journal Title: Pediatric neurology

PUBMED ID: 28500559
DOI: doi.org/10.1007/s11060-017-2466-0
Titolo: Nivolumab for patients with recurrent glioblastoma progressing on bevacizumab: a retrospective case series.
Autori: Chamberlain MC., Kim BT.
Data di Pubblicazione: 2017-05-14
Abstract: A single institution retrospective evaluation of nivolumab following disease progression on bevacizumab in adults with recurrent glioblastoma (GBM) with an objective of determining progression free survival (PFS). There is no accepted therapy for recurrent GBM after failure of bevacizumab. 16 adults, ages 52-72 years (median 62), with recurrent GBM were treated. All patients had previously been treated with surgery, concurrent radiotherapy and temozolomide, and post-radiotherapy temozolomide. Bevacizumab (with or without lomustine) was administered to all patients at first recurrence. Patients were treated with nivolumab only (3 mg/kg) once every 2 weeks at second recurrence. One cycle of nivolumab was defined as 2 treatments. Neurological evaluation was performed bi-weekly and neuroradiographic assessment every 4 weeks. A total of 37 treatment cycles (median 2) were administered of nivolumab in which there were 14 Grade 2 adverse events (AEs) and Grade 3 AEs in two patients. No Grade 4 or 5 AEs were seen. Following 1 month of nivolumab, seven patients demonstrated progressive disease and discontinued therapy. No patient demonstrated a response though nine patients demonstrated neuroradiographic stable response. Survival in the entire cohort ranged from 2 to 6 months with a median of 3.5 months (CI 2.8, 4.2). Median and 6-month PFS at 6 months was 2.0 months (range 1-5 months; CI 1.3, 2.7) and 0% respectively. Nivolumab salvage therapy demonstrated no survival advantage in patients with recurrent bevacizumab refractory GBM emphasizing a continued unmet need in neuro-oncology.
Journal Title: Journal of neuro-oncology

PUBMED ID: 28496000
DOI: doi.org/10.18632/oncotarget.17322
Titolo: Stratification according to recursive partitioning analysis predicts outcome in newly diagnosed glioblastomas.
Autori: Yang F., Yang P., Zhang C., Wang Y., Zhang W., Hu H., Wang Z., Qiu X., Jiang T.
Data di Pubblicazione: 2017-05-13
Abstract: Glioblastoma accounts for more than half of diffuse gliomas. The prognosis of patients with glioblastoma remains poor despite comprehensive and intensive treatments. Furthermore, the clinical significance of molecular parameters and routinely available clinical variables for the prognosis prediction of glioblastomas remains limited. The authors describe a novel model may help in prognosis prediction and clinical management of glioblastoma patients. We performed a recursive partitioning analysis to generate three independent prognostic classes of 103 glioblastomas patients from TCGA dataset. Class I (MGMT promoter methylated, age <58), class II (MGMT promoter methylation, age ≥58; MGMT promoter unmethylation, age <54, KPS ≥70; MGMT promoter unmethylation, age >59, KPS ≥70), class III (MGMT promoter unmethylation, age 54-58, KPS ≥70; MGMT promoter unmethylation, KPS <70). Age, KPS and MGMT promoter methylation were the most significant prognostic factors for overall survival. The results were validated in CGGA dataset.This was the first study to combine various molecular parameters and clinical factors into recursive partitioning analysis to predict the prognosis of patients with glioblastomas. We included MGMT promoter methylation in our study, which could give better suggestion to patients for their chemotherapy. This clinical study will serve as the backbone for the future incorporation of molecular prognostic markers currently in development. Thus, our recursive partitioning analysis model for glioblastomas may aid in clinical prognosis evaluation.
Journal Title: Oncotarget

PUBMED ID: 28485350
DOI: doi.org/10.4103/0019-509X.204774
Titolo: A case series of salvage CCNU in high-grade glioma who have previously received temozolomide from a tertiary care institute in Mumbai.
Autori: Patil VM., Abhinav R., Tonse R., Epari S., Gupta T., Jalali R.
Data di Pubblicazione: 2017-05-10
Abstract: CCNU is associated with modest treatment outcomes in recurrent/relapsed high-grade gliomas. The high rate of myelosuppression is a concern. Urgent efforts are required to improve upon these results.
Journal Title: Indian journal of cancer

PUBMED ID: 28480352
DOI: doi.org/10.21010/ajtcam.v13i6.1
Titolo: TREATMENT OF PROGRESSION OF DIFFUSE ASTROCYTOMA BY HERBAL MEDICINE: CASE REPORT.
Autori: Trogrlić I., Trogrlić D., Trogrlić Z.
Data di Pubblicazione: 2017-05-09
Abstract: The results presented in this research paper clearly indicate the potential of phytotherapy in the treatment of some types of brain tumours. A complete regression of tumour following the treatment with nothing but herbal medicine offers support for such claim. Future research should demonstrate the effectiveness of phytotherapy, as a supplementary form of brain tumour treatment, and the results of this research should be compared with the existing information on the effectiveness of the protocols currently used in the treatment of these types of tumour.
Journal Title: African journal of traditional, complementary, and alternative medicines : AJTCAM

PUBMED ID: 28429093
DOI: doi.org/10.1007/s10014-017-0285-9
Titolo: A case of glioblastoma resected immediately after administering beva cizumab: consideration on histopathological findings and safety of surgery.
Autori: Tokuda Y., Tamura R., Ohara K., Yoshida K., Sasaki H.
Data di Pubblicazione: 2017-04-22
Abstract: Surgery after administering bevacizumab should be carefully consid ered particularly because of wound healing concerns. A 27-year-old man prese nted with multiple tumor recurrences after gross total removal of a left tem poral oligodendroglioma (1p/19q-noncodeleted). Whole brain radiotherapy with concomitant temozolomide and bevacizumab was immediately prescribed; however , the patient's condition deteriorated because of brain herniation. Three da ys after administering bevacizumab, an emergency tumor removal with external decompression and a ventriculo-peritoneal shunt was performed. The surgery a nd postoperative clinical course were uneventful. On histopathological exami nation, the tumor showed findings such as tumor vessel thrombosis, numerous interstitial red blood cells, and cells with degraded, fragmented nuclei pos sibly suggesting apoptosis, which could be attributable to bevacizumab. Perf orming craniotomy shortly after administering bevacizumab is not recommended ; however, it can still be safely performed as long as surgery and wound man agement is carefully performed. Vessel thrombosis might be among the mechani sms of action of bevacizumab.
Journal Title: Brain tumor pathology

PUBMED ID: 28407030
DOI: doi.org/10.1093/annonc/mdx169
Titolo: Intratumoral heterogeneity: pathways to treatment resistance and rel apse in human glioblastoma.
Autori: Qazi MA., Vora P., Venugopal C., Sidhu SS., Moffat J., Swanton C., S ingh SK.
Data di Pubblicazione: 2017-04-14
Abstract: Intratumoral heterogeneity (ITH) has increasingly being described for multiple cancers as the root cause of therapy resistance. Recent studies have started to explore the scope of ITH in glioblastoma (GBM), a highly agg ressive and fatal form of brain tumor, to explain its inevitable therapy res istance and disease relapse. In this review, we detail the emerging data tha t explores the extensive genetic, cellular and functional ITH present in GBM . We discuss current experimental models of human GBM recurrence and suggest harnessing new technologies (CRISPR-Cas9 screening, CyTOF, cellular barcodin g, single cell analysis) to delineate GBM ITH and identify treatment-refract ory cell populations, thus opening new therapeutic windows. We will also exp lore why current therapeutics have failed in clinical trials and how ITH can inform us on developing empiric therapies for the treatment of recurrent GBM .
Journal Title: Annals of oncology : official journal of the European Society for Medical Oncology

PUBMED ID: 28382223
DOI: doi.org/10.4103/jpi.jpi_43_16
Titolo: Identification of Histological Correlates of Overall Survival in Low er Grade Gliomas Using a Bag-of-words Paradigm: A Preliminary Analysis Based on Hematoxylin & Eosin Stained Slides from the Lower Grade Glioma Cohort of The Cancer Genome Atlas.
Autori: Powell RT., Olar A., Narang S., Rao G., Sulman E., Fuller GN., Rao A .
Data di Pubblicazione: 2017-04-07

Abstract: Here, we demonstrated one potential strategy to incorporate image features derived from H and E stained slides into predictive models of OS. I n addition, we showed how these image-derived phenotypic characteristics cor relate with molecular signaling activity underlying the etiology or behavior of LGG.
Journal Title: Journal of pathology informatics

PUBMED ID: 28380636
DOI: doi.org/10.1093/neuonc/nox002
Titolo: The role of image-guided intensity modulated proton therapy in gliom a.
Autori: Grosshans DR., Mohan R., Gondi V., Shih HA., Mahajan A., Brown PD.
Data di Pubblicazione: 2017-04-06
Abstract: Gliomas represent a broad spectrum of disease with life-expectancy outcomes ranging from months to decades. As our understanding of the molecul ar profiles of gliomas expands rapidly, practitioners are now better able to identify patients with favorable versus nonfavorable prognoses. Radiation th erapy plays a key role in glioma treatment, improving disease control and of tentimes survival. However, for survivors, either long-term or short-term, r adiation-induced cognitive impairments may negatively impact their quality o f life. For patients with both favorable and unfavorable prognoses, intensit y modulated proton therapy (IMPT) may offer significant, yet unproven benefi ts. IMPT is the newest and most advanced proton delivery technique, one with substantial benefits compared with historical proton techniques. IMPT allows practitioners to maximize the physical benefits of protons, increasing norma l tissue sparing and reducing the potential for adverse effects. For more ag gressive tumors, the dose conformality and normal tissue sparing afforded by IMPT may also allow for dose escalation to target volumes. However, in order to truly maximize the clinical potential of IMPT, the field of radiation onc ology must not only implement the most advanced technologies, but also under stand and capitalize on the unique biologic aspects of proton therapy.
Journal Title: Neuro-oncology

PUBMED ID: 28373454
DOI: doi.org/10.21873/anticanres.11524
Titolo: A Retrospective Evaluation of Bevacizumab Treatment in Patients with Progressive Malignant Glioma in Northern Sweden.
Autori: Sandström M., Laudius M., Lindqvist T., Asklund T., Johansson M.
Data di Pubblicazione: 2017-04-05
Abstract: Results from this retrospective study are comparable with earlier phase-II studies and motivate randomized trials of bevacizumab-based treatme nt in the second-line setting.
Journal Title: Anticancer research

PUBMED ID: 20511183
DOI: doi.org/10.1093/neuonc/noq008
Titolo: Prolonged survival for patients with newly diagnosed, inoperable gli oblastoma with 3-times daily ultrafractionated radiation therapy.
Autori: Beauchesne P., Bernier V., Carnin C., Taillandier L., Djabri M., Mar tin L., Michel X., Maire JP., Khalil T., Kerr C., Gorlia T., Stupp R., Pedeu x R.
Data di Pubblicazione: 2010-06-01
Abstract: Ultrafractionation of radiation therapy is a novel regimen consist ing of irradiating tumors several times daily, delivering low doses (<0.75 G y) at which hyperradiosensitivity occurs. We recently demonstrated the high efficiency of ultrafractionated radiotherapy (RT) on glioma xenografts and r eport here on a phase II clinical trial to determine the safety, tolerabilit

y, and efficacy of an ultrafractionation regimen in patients with newly and inoperable glioblastoma (GBM). Thirty-one patients with histologically prove n, newly diagnosed, and unresectable supratentorial GBM (WHO grade IV) were enrolled. Three daily doses of 0.75 Gy were delivered at least 4 hours apart , 5 days per week over 6-7 consecutive weeks (90 fractions for a total of 67 .5 Gy). Conformal irradiation included the tumor bulk with a margin of 2.5 c m. The primary end points were safety, toxicity, and tolerability, and the s econdary end points were overall survival (OS) and progression-free survival (PFS). Multivariate analysis was used to compare the OS and PFS with the EOR TC-NCIC trial 26981-22981/CE.3 of RT alone vs radiation therapy and temozolo mide (TMZ). The ultrafractionation radiation regimen was safe and well toler ated. No acute Grade III and/or IV CNS toxicity was observed. Median PFS and OS from initial diagnosis were 5.1 and 9.5 months, respectively. When compar ing with the EORTC/NCIC trial, in both PFS and OS multivariate analysis, ult rafractionation showed superiority over RT alone, but not over RT and TMZ. T he ultrafractionation regimen is safe and may prolong the survival of patien ts with GBM. Further investigation is warranted and a trial associating ultr a-fractionation and TMZ is ongoing.
Journal Title: Neuro-oncology

PUBMED ID: 28347331
DOI: doi.org/10.1186/s40880-017-0201-z
Titolo: Progressive multifocal exophytic pontine glioblastoma: a case report with literature review.
Autori: Chen F., Li Z., Weng C., Li P., Tu L., Chen L., Xie W., Li L.
Data di Pubblicazione: 2017-03-29
Abstract: Multifocal pontine glioblastoma exhibiting an exophytic growth pat tern in the cerebello-pontine angle (CPA) is rare. We present a case of a 5- year-old girl with consecutive neurological imaging and other clinical findi ngs indicating progressive multifocal exophytic pontine glioblastoma. Three lesions were reported, of which two were initially presented, and one was de veloped 2 months later. One lesion demonstrated a progressing exophytic exte nsion in the cistern of the left side of the CPA. The other two lesions were located and confined within the pons. Initial magnetic resonance imaging and positron emission tomography-computed tomography indicated low-grade glioma or inflammatory disease. However, 2 and 3 months later, subsequent magnetic resonance spectroscopy (MRS) displayed elevated choline and depressed N-acet yl aspartate peaks compared with the peaks on the initial MRS, indicating a high-grade glioma. Subtotal resection was performed for the CPA lesion. Hist opathologic examination showed discrepant features of different parts of the CPA lesion. The patient received no further chemotherapy or radiotherapy and died 2 months after surgery. The multifocal and exophytic features of this c ase and the heterogeneous manifestations on neurological images were rare an d confusing for both diagnosis and surgical decision-making. Our case report may contribute knowledge and helpful guidance for other medical doctors.
Journal Title: Chinese journal of cancer

PUBMED ID: 28300718
DOI: doi.org/10.1016/j.wneu.2017.03.012
Titolo: Does Pretreatment Tumor Growth Hold Prognostic Information for Patie nts with Glioblastoma?
Autori: Stensjøen AL., Berntsen EM., Mikkelsen VE., Torp SH., Jakola AS., Sa lvesen Ø., Solheim O.
Data di Pubblicazione: 2017-03-17
Abstract: Pretreatment glioblastoma growth harbors prognostic information. P atients with slower growing tumors have higher odds of survival beyond 2 yea rs, adjusted for other prognostic factors.
Journal Title: World neurosurgery

PUBMED ID: 28274399
DOI: doi.org/10.1016/j.prro.2016.11.005
Titolo: Radiation and subsequent reirradiation outcomes in the treatment of diffuse intrinsic pontine glioma and a systematic review of the reirradiation literature.
Autori: Freese C., Takiar V., Fouladi M., DeWire M., Breneman J., Pater L.
Data di Pubblicazione: 2017-03-10
Abstract: Radiation therapy is essential in the definitive management of DIPG. With advances in treatment techniques, it is feasible to reirradiate select patients with progressive disease; however, further research is warranted to optimize dose, delivery, and patient selection in the recurrent/progressive setting. In the future, it may be reasonable to propose more focal delivery of reRT (ie, hypofractionated radiation) in select patients with the goal of reducing treatment time and providing effective palliation.
Journal Title: Practical radiation oncology

PUBMED ID: 28258444
DOI: doi.org/10.1007/s00259-017-3661-0
Titolo: Response assessment of bevacizumab therapy in GBM with integrated 11C-MET-PET/MRI: a feasibility study.
Autori: Deuschl C., Moenninghoff C., Goericke S., Kirchner J., Köppen S., Binse I., Poeppel TD., Quick HH., Forsting M., Umutlu L., Herrmann K., Hense J., Schlamann M.
Data di Pubblicazione: 2017-03-05
Abstract: This study demonstrates the potential of integrated 11C-MET-PET/MRI for response assessment of GBM and the utility of combined assessment of morphologic and metabolic information with the proposal for assessing relapsed GBM.
Journal Title: European journal of nuclear medicine and molecular imaging

PUBMED ID: 28234741
DOI: doi.org/10.1097/MPH.0000000000000806
Titolo: Concomitant Use of Panobinostat and Reirradiation in Progressive DIPG: Report of 2 Cases.
Autori: Wang ZJ., Ge Y., Altinok D., Poulik J., Sood S., Taub JW., Edwards H., Kieran MW., Steven M.
Data di Pubblicazione: 2017-02-25
Abstract: Diffuse intrinsic pontine glioma (DIPG) remains a devastating disease. Panobinostat has been shown to have therapeutic efficacy both in vitro and in DIPG orthotopic xenograft models; however, clinical data in patients with DIPG are lacking. We present 2 cases of DIPG, who were treated with panobinostat at 22 to 25 mg/m/dose, 3 times weekly for 2 weeks in 3-week cycles and concomitant reirradiation after disease progression. Two episodes of asymptomatic thrombocytopenia were observed in 1 patient. Hyperacetylation of histone H4 of peripheral blood mononuclear cells was evident following treatment. In our experience, panobinostat administered with reirradiation was well tolerated at a relatively higher dose than that used in adult studies.
Journal Title: Journal of pediatric hematology/oncology

PUBMED ID: 28228086
DOI: doi.org/10.2174/1568009617666170222125035
Titolo: Clinical Trials with Oncolytic Measles Virus: Current Status and Future Prospects.
Autori: Msaouel P., Opyrchal M., Dispenzieri A., Peng KW., Federspiel MJ., Russell SJ., Galanis E.

Data di Pubblicazione: 2017-02-24
Abstract: Attenuated Edmonston lineage measles virus (MV-Edm) vaccine strain s can preferentially infect and lyse a wide variety of cancer cells. Oncolyt ic MV-Edm derivatives are genetically engineered to express the human carcin oembryonic antigen (MV-CEA virus) or the human sodium iodide symporter (MV-N IS virus) and are currently being tested in clinical trials against ovarian cancer, glioblastoma multiforme, multiple myeloma, mesothelioma, head and ne ck cancer, breast cancer and malignant peripheral nerve sheath tumors. This review describes the basic and preclinical data that facilitated the clinica l translation of MV-Edm strains, and summarizes the clinical results of this oncolytic platform to date. Furthermore, we discuss the latest clinically re levant MV-Edm vector developments and creative strategies for future transla tional steps.
Journal Title: Current cancer drug targets

PUBMED ID: 28204914
DOI: doi.org/10.1007/s11060-016-2241-7
Titolo: Salvage therapy with bendamustine for temozolomide refractory recurr ent anaplastic gliomas: a prospective phase II trial.
Autori: Chamberlain MC., Colman H., Kim BT., Raizer J.
Data di Pubblicazione: 2017-02-17
Abstract: There is no standard therapy for recurrent anaplastic glioma (AG). Salvage therapies include alkylator-based chemotherapy, re-resection with or without carmustine implants, re-irradiation and bevacizumab. Bendamustine is a novel bifunctional alkylator with CNS penetration never previously evaluat ed in AG. Assess response and toxicity of bendamustine in recurrent AG in a phase II trial. Adults with radiation and temozolomide refractory recurrent AG were treated with bendamustine. A cycle of bendamustine was defined as tw o consecutive days of treatment (100 mg/m
Journal Title: Journal of neuro-oncology

PUBMED ID: 28204639
DOI: doi.org/10.1093/neuonc/now311
Titolo: Comparison of 2D (RANO) and volumetric methods for assessment of rec urrent glioblastoma treated with bevacizumab-a report from the BELOB trial.
Autori: Gahrmann R., van den Bent M., van der Holt B., Vernhout RM., Taal W. , Vos M., de Groot JC., Beerepoot LV., Buter J., Flach ZH., Hanse M., Jasper se B., Smits M.
Data di Pubblicazione: 2017-02-17
Abstract: In the first 12 weeks, volumetric methods did not provide signific ant improvement over the RANO criteria as a posttreatment prognostic marker.
Journal Title: Neuro-oncology

PUBMED ID: 28188088
DOI: doi.org/10.1016/j.clon.2017.01.010
Titolo: High-dose Neural Stem Cell Radiation May Not Improve Survival in Gli oblastoma.
Autori: Achari R., Arunsingh M., Badgami RK., Saha A., Chatterjee S., Shrima li RK., Mallick I., Arun B.
Data di Pubblicazione: 2017-02-12
Abstract: In this cohort, 67.2% of newly diagnosed glioblastoma patients had NSC involved with CELs at presentation and 95.9% at progression. This might be an imaging surrogate of the current notion of gliomagenesis and progressi on from NSC rests. A high radiation dose to NSC_Ipsi was significantly assoc iated with inferior survival. This could be a function of larger tumours and planning target volumes in those with pre-treatment NSC involvement. Methyla ted MGMT and good compliance to adjuvant temozolomide were independent predi

ctors of better survival. Until further evidence brings hope for glioblastom a, elective, partial NSC irradiation remains experimental.
Journal Title: Clinical oncology (Royal College of Radiologists (Great Brita in))

PUBMED ID: 28176936
DOI: doi.org/10.2147/OTT.S125587
Titolo: Add-on bevacizumab can prevent early clinical deterioration and prol ong survival in newly diagnosed partially resected glioblastoma patients wit h a poor performance status.
Autori: Hata N., Yoshimoto K., Hatae R., Kuga D., Akagi Y., Sangatsuda Y., S uzuki SO., Shono T., Mizoguchi M., Iihara K.
Data di Pubblicazione: 2017-02-09
Abstract: Our findings suggest that add-on BEV can prevent early clinical de terioration of pr-GBM patients and contribute to a prolonged survival, espec ially for those with a poor PS.
Journal Title: OncoTargets and therapy

PUBMED ID: 28176389
DOI: doi.org/10.1111/vru.12474
Titolo: IMAGING DIAGNOSIS -ANTEMORTEM DETECTION OF OLIGODENDROGLIOMA "CEREBR OSPINAL FLUID DROP METASTASES" IN A DOG BY SERIAL MAGNETIC RESONANCE IMAGING .
Autori: Vigeral M., Bentley RT., Rancilio NJ., Miller MA., Heng HG.
Data di Pubblicazione: 2017-02-09
Abstract: An English Bulldog underwent radiation therapy of an intracranial, left lateral ventricle mass. Following resolution of the primary mass, an in traventricular fourth ventricle lesion developed. Subsequently, multiple les ions developed from the cervical central canal and leptomeninges. Serial mag netic resonance imaging documented the propagation of lesions along the cere brospinal fluid (CSF) pathways, known as "CSF drop metastasis." Histopatholo gy confirmed multifocal intraventricular and leptomeningeal oligodendrogliom a. Oligodendroglioma should be included in the differential diagnosis for an intraventricular tumor exhibiting apparent CSF drop metastasis.
Journal Title: Veterinary radiology & ultrasound : the official journal of t he American College of Veterinary Radiology and the International Veterinary Radiology Association

PUBMED ID: 28169231
DOI: doi.org/10.4103/0973-1482.168988
Titolo: Palbociclib: A new hope in the treatment of breast cancer.
Autori: Palanisamy RP.
Data di Pubblicazione: 2017-02-08
Abstract: Breast cancer being one of the common cancers has high morbidity a nd mortality. Despite the conventional treatment, the burden of the disease increases year after year. There is a need for newer drugs that target the d ifferent mechanisms in the pathogenesis. The interaction of cyclins with cyc lin dependent kinases (CDKs) plays a major role in the abnormal cell cycle i n cancer and it is considered to be an important target. Palbociclib is a CD K inhibitor currently approved for the treatment of breast cancer. The precl inical studies with breast cancer lines were sensitive to palbociclib and th e clinical trials phase I, phase II (PALOMA 1), and phase III (PALOMA 2, 3, PENTELOPE, PEARL) showed that the drug was efficacious when combined other c onventional drugs for breast cancer. Palbociclib was also been tested in var ious other germ cell tumors, melanoma, multiple myeloma, glioblastoma multif orme etc., The major adverse effect of the drug includes hematological toxic ity mainly neutropenia, gastrointestinal adverse effects.

Journal Title: Journal of cancer research and therapeutics

PUBMED ID: 28161497
DOI: doi.org/10.1016/j.ejca.2016.12.007
Titolo: Survival benefit for patients with diffuse intrinsic pontine glioma (DIPG) undergoing re-irradiation at first progression: A matched-cohort analysis on behalf of the SIOP-E-HGG/DIPG working group.
Autori: Janssens GO., Gandola L., Bolle S., Mandeville H., Ramos-Albiac M., van Beek K., Benghiat H., Hoeben B., Morales La Madrid A., Kortmann RD., Hargrave D., Menten J., Pecori E., Biassoni V., von Bueren AO., van Vuurden DG., Massimino M., Sturm D., Peters M., Kramm CM.
Data di Pubblicazione: 2017-02-06
Abstract: The majority of patients with DIPG, responding to upfront radiotherapy, do benefit of re-irradiation with acceptable tolerability.
Journal Title: European journal of cancer (Oxford, England : 1990)

PUBMED ID: 28123740
DOI: doi.org/10.3892/mco.2016.1086
Titolo: Efficacy of bevacizumab therapy for unresectable malignant glioma: A retrospective analysis.
Autori: Yonezawa H., Hirano H., Uchida H., Habu M., Hanaya R., Oyoshi T., Sadamura Y., Hanada T., Tokimura H., Moinuddin F., Arita K.
Data di Pubblicazione: 2017-01-27
Abstract: Bevacizumab (BEV), an inhibitor of vascular endothelial growth factor A, has been used for primary and recurrent malignant gliomas in Japan since June, 2013. Previous randomized controlled studies demonstrated that BEV prolonged the progression-free survival, but not the overall survival (OS) of patients with newly diagnosed glioblastoma. The aim of the present study was to elucidate the effect of BEV on the OS of patients with unresectable malignant gliomas. Of the 440 cases of malignant glioma initially treated in our institute between 2000 and 2015, 88 were not suitable for maximal resection due to patient age, physical condition, tumor location and extent, or the patient's wishes. Based on the biopsy results, the pathological diagnosis was glioblastoma, anaplastic astrocytoma and anaplastic oligodendroglioma in 60, 19 and 9 patients, respectively. Kaplan-Meier and log-rank analyses were performed to investigate the effect of BEV on OS. OS was longer in the BEV group (n=24) compared with that in the non-BEV group [n=64; median survival time (MST), 566 vs. 243 days, respectively; hazard ratio (HR)=0.413; 95% confidence interval (CI): 0.216-0.787; P=0.003]. In the 41 patients who received temozolomide (TMZ) and radiotherapy and the 31 patients with glioblastoma who received TMZ and radiotherapy, OS was longer in the BEV group compared with that in the non-BEV group (MST, 568 vs. 334 days, HR=0.404, 95% CI: 0.175-0.933, P=0.016; and MST, 566 vs. 160 days, HR=0.253, 95% CI: 0.099-0.646, P=0.001, respectively). In the Cox hazard model analysis of 41 patients who underwent TMZ-based chemoradiotherapy after biopsy, the use of BEV was the strongest independent beneficial factor associated with prolonged OS (HR=0.101; P=0.0002). Our retrospective survey suggested that BEV prolongs the OS of patients with unresectable malignant gliomas. However, these results must be verified by a well-designed prospective randomized controlled trial.
Journal Title: Molecular and clinical oncology

PUBMED ID: 28110346
DOI: doi.org/10.1007/s00259-017-3618-3
Titolo: Prognostic value of molecular and imaging biomarkers in patients with supratentorial glioma.
Autori: Lopci E., Riva M., Olivari L., Raneri F., Soffietti R., Piccardo A., Bizzi A., Navarria P., Ascolese AM., Rudà R., Fernandes B., Pessina F., Grim

aldi M., Simonelli M., Rossi M., Alfieri T., Zucali PA., Scorsetti M., Bello L., Chiti A.
Data di Pubblicazione: 2017-01-23
Abstract: Bevacizumab (BEV), an inhibitor of vascular endothelial growth fac tor A, has been used for primary and recurrent malignant gliomas in Japan si nce June, 2013. Previous randomized controlled studies demonstrated that BEV prolonged the progression-free survival, but not the overall survival (OS) o f patients with newly diagnosed glioblastoma. The aim of the present study w as to elucidate the effect of BEV on the OS of patients with unresectable ma lignant gliomas. Of the 440 cases of malignant glioma initially treated in o ur institute between 2000 and 2015, 88 were not suitable for maximal resecti on due to patient age, physical condition, tumor location and extent, or the patient's wishes. Based on the biopsy results, the pathological diagnosis wa s glioblastoma, anaplastic astrocytoma and anaplastic oligodendroglioma in 6 0, 19 and 9 patients, respectively. Kaplan-Meier and log-rank analyses were performed to investigate the effect of BEV on OS. OS was longer in the BEV g roup (n=24) compared with that in the non-BEV group [n=64; median survival t ime (MST), 566 vs. 243 days, respectively; hazard ratio (HR)=0.413; 95% conf idence interval (CI): 0.216-0.787; P=0.003]. In the 41 patients who received temozolomide (TMZ) and radiotherapy and the 31 patients with glioblastoma wh o received TMZ and radiotherapy, OS was longer in the BEV group compared wit h that in the non-BEV group (MST, 568 vs. 334 days, HR=0.404, 95% CI: 0.175- 0.933, P=0.016; and MST, 566 vs. 160 days, HR=0.253, 95% CI: 0.099-0.646, P= 0.001, respectively). In the Cox hazard model analysis of 41 patients who un derwent TMZ-based chemoradiotherapy after biopsy, the use of BEV was the str ongest independent beneficial factor associated with prolonged OS (HR=0.101; P=0.0002). Our retrospective survey suggested that BEV prolongs the OS of pa tients with unresectable malignant gliomas. However, these results must be v erified by a well-designed prospective randomized controlled trial.
Journal Title: European journal of nuclear medicine and molecular imaging

PUBMED ID: 28070598
DOI: doi.org/10.1007/s00234-016-1769-8
Titolo: Advanced MRI assessment to predict benefit of anti-programmed cell d eath 1 protein immunotherapy response in patients with recurrent glioblastom a.
Autori: Qin L., Li X., Stroiney A., Qu J., Helgager J., Reardon DA., Young G S.
Data di Pubblicazione: 2017-01-11
Abstract: MRI reveals an initial increase in volumes of abnormal tissue with contrast enhancement, edema, and intermediate ADC suggesting hypercellularit y within the first 0-6 months of immunotherapy. Subsequent stabilization and improvement in IADC VOI appear to better predict ultimate therapeutic benefi t from these agents than conventional imaging.
Journal Title: Neuroradiology

PUBMED ID: 28052119
DOI: doi.org/10.1371/journal.pone.0169485
Titolo: Pre-Clinical Study of Panobinostat in Xenograft and Genetically Engi neered Murine Diffuse Intrinsic Pontine Glioma Models.
Autori: Hennika T., Hu G., Olaciregui NG., Barton KL., Ehteda A., Chitranjan A., Chang C., Gifford AJ., Tsoli M., Ziegler DS., Carcaboso AM., Becher OJ.
Data di Pubblicazione: 2017-01-05
Abstract: Our collaborative pre-clinical study confirms that panobinostat is an effective targeted agent against DIPG human and murine tumor cells in vit ro and in short-term in vivo efficacy studies in mice but does not significa ntly impact survival of mice bearing H3.3-K27M-mutant tumors. We suggest thi

s may be due to toxicity associated with systemic administration of panobino stat that necessitated dose de-escalation.
Journal Title: PloS one

PUBMED ID: 28025828
DOI: doi.org/10.1111/ane.12719
Titolo: Prognostic parameters and outcome after re-irradiation for progressi ve glioblastoma.
Autori: Zwirner K., Paulsen F., Schittenhelm J., Borchers C., Skardelly M., Zips D., Eckert F.
Data di Pubblicazione: 2016-12-28
Abstract: The favourable results regarding overall survival are probably due to patient selection for re-irradiation. If technically feasible, stereotact ic radiosurgery or hypofractionated regimes should be preferred. In this hig hly selected re-irradiation cohort, only some of the well-known prognostic f actors of the primary tumour setting were found to influence overall surviva l significantly. In contrast, also some patients presenting with unfavourabl e predictive parameters showed an encouraging course of disease and thus sho uld not be excluded from re-irradiation.
Journal Title: Acta neurologica Scandinavica

PUBMED ID: 28019637
DOI: doi.org/10.2174/0929867323666161223150242
Titolo: Recent Advances in Targeted Therapy for Glioma.
Autori: Lin L., Cai J., Jiang C.
Data di Pubblicazione: 2016-12-27
Abstract: Gliomas are the most common primary malignant brain tumors, which have a universally fatal outcome. Current standard treatment for glioma pati ents is surgical removal followed by radiotherapy and adjuvant chemotherapy. Due to therapeutic resistance and tumor recurrence, efforts are ongoing to i dentify the molecules that are fundamental to regulate the tumor progression and provide additional methods for individual treatment of glioma patients. By studying the initiation and maintenance of glioma, studies focused on the targets of tyrosine kinase receptors including EGFR, PDGFR and other crucial signal pathways such as PI3K/AKT and RAS/RAF/MAPK pathway. Furthermore, rece nt advances in targeting immunotherapy and stem cell therapy also brought nu merous strategies to glioma treatment. This article reviewed the researches focused on the advanced strategies of various target therapies for improving the glioma treatment efficacy, and discussed the challenges and future direc tions for glioma therapy.
Journal Title: Current medicinal chemistry

PUBMED ID: 27998280
DOI: doi.org/10.1186/s12987-016-0047-9
Titolo: Misleading early blood volume changes obtained using ferumoxytol-bas ed magnetic resonance imaging perfusion in high grade glial neoplasms treate d with bevacizumab.
Autori: Netto JP., Schwartz D., Varallyay C., Fu R., Hamilton B., Neuwelt EA .
Data di Pubblicazione: 2016-12-22
Abstract: Decreased perfusion after BEV significantly alters rCBV measuremen ts when using ferumoxytol. BEV treatment response hinders efforts to differe ntiate true progression from pseudoprogression using blood volume measuremen ts in malignant glioma, potentially impacting patient diagnosis and manageme nt.
Journal Title: Fluids and barriers of the CNS

PUBMED ID: 27921166
DOI: doi.org/10.1007/s00415-016-8355-1
Titolo: Outcome in unresectable glioblastoma: MGMT promoter methylation make s the difference.
Autori: Thon N., Thorsteinsdottir J., Eigenbrod S., Schüller U., Lutz J., Kr eth S., Belka C., Tonn JC., Niyazi M., Kreth FW.
Data di Pubblicazione: 2016-12-07
Abstract: In 2011, we reported a predominant prognostic/predictive role of M GMT promoter methylation status on progression-free survival (PFS) in unrese ctable glioblastoma patients undergoing upfront radiotherapy plus concomitan t and maintenance temozolomide (RTX/TMZ → TMZ). We, here, present the final results of this prospective study focussing on the prognostic/predictive val ue of MGMT promoter methylation status for death risk stratification. Overal l, 56 adult patients with unresectable, biopsy proven glioblastoma were pros pectively assigned to upfront RTX/TMZ → TMZ treatment between March 2006 and August 2008. Last follow-up was performed in June 2016. MGMT promoter methyl ation was determined using methylation-specific PCR (MSP) and sodium bisulfi te sequencing. Analyses were done by intention to treat. Prognostic factors were obtained from proportional hazard models. At the time of the final anal ysis 55 patients showed progressive disease and 53 patients had died. MGMT p romoter was methylated (unmethylated) in 30 (26) patients. Methylation of th e MGMT promoter was the strongest favorable predictor for overall survival (OS, median: 20.3 vs. 7.3 months, p < 0.001, HR 0.30, 95% CI 0.16-0.55), and PFS (median: 15.0 vs. 6.1 months, p < 0.001, HR 0.31, 95% CI 0.17-0.57) and was also associated with higher frequencies of treatment response and prolon ged post-recurrence survival (PRS, median: 4.5 vs. 1.4 months, p < 0.002, HR 0.39, 95% CI 0.21-0.71). Knowledge of MGMT promoter methylation status is es sential for patients' counseling, prognostic evaluation, and for the design of future trials dealing with unresectable glioblastomas.
Journal Title: Journal of neurology

PUBMED ID: 27893017
DOI: doi.org/10.1001/jamaneurol.2016.4226
Titolo: Evaluation of Cognitive Deficits and Structural Hippocampal Damage i n Encephalitis With Leucine-Rich, Glioma-Inactivated 1 Antibodies.
Autori: Finke C., Prüss H., Heine J., Reuter S., Kopp UA., Wegner F., Then B ergh F., Koch S., Jansen O., Münte T., Deuschl G., Ruprecht K., Stöcker W., Wandinger KP., Paul F., Bartsch T.
Data di Pubblicazione: 2016-11-29
Abstract: Anti-LGI1 encephalitis is associated with cognitive deficits and d isability as a result of structural damage to the hippocampal memory system. This damage might be prevented by early immunotherapy.
Journal Title: JAMA neurology

PUBMED ID: 27853960
DOI: doi.org/10.1007/s11060-016-2332-5
Titolo: Phase II study of tivozanib, an oral VEGFR inhibitor, in patients wi th recurrent glioblastoma.
Autori: Kalpathy-Cramer J., Chandra V., Da X., Ou Y., Emblem KE., Muzikansky A., Cai X., Douw L., Evans JG., Dietrich J., Chi AS., Wen PY., Stufflebeam S ., Rosen B., Duda DG., Jain RK., Batchelor TT., Gerstner ER.
Data di Pubblicazione: 2016-11-18
Abstract: Targeting tumor angiogenesis is a potential therapeutic strategy f or glioblastoma because of its high vascularization. Tivozanib is an oral pa n-VEGF receptor tyrosine kinase inhibitor that hits a central pathway in gli oblastoma angiogenesis. We conducted a phase II study to test the effectiven ess of tivozanib in patients with recurrent glioblastoma. Ten adult patients

were enrolled and treated with tivozanib 1.5 mg daily, 3 weeks on/1 week off in 28-day cycles. Brain MRI and blood biomarkers of angiogenesis were performed at baseline, within 24-72 h of treatment initiation, and monthly thereafter. Dynamic contrast enhanced MRI, dynamic susceptibility contrast MRI, and vessel architecture imaging were used to assess vascular effects. Resting state MRI was used to assess brain connectivity. Best RANO criteria responses were: 1 complete response, 1 partial response, 4 stable diseases, and 4 progressive disease (PD). Two patients were taken off study for toxicity and 8 patients were taken off study for PD. Median progression-free survival was 2.3 months and median overall survival was 8.1 months. Baseline abnormal tumor vascular permeability, blood flow, tissue oxygenation and plasma sVEGFR2 significantly decreased and plasma PlGF and VEGF increased after treatment, suggesting an anti-angiogenic effect of tivozanib. However, there were no clear structural changes in vasculature as vessel caliber and enhancing tumor volume did not significantly change. Despite functional changes in tumor vasculature, tivozanib had limited anti-tumor activity, highlighting the limitations of anti-VEGF monotherapy. Future studies in glioblastoma should leverage the anti-vascular activity of agents targeting VEGF to enhance the activity of other therapies.
Journal Title: Journal of neuro-oncology

PUBMED ID: 27844308
DOI: doi.org/10.1007/s11060-016-2331-6
Titolo: Impact of concurrent chemotherapy with radiation therapy for elderly patients with newly diagnosed glioblastoma: a review of the National Cancer Data Base.
Autori: Huang J., Samson P., Perkins SM., Ansstas G., Chheda MG., DeWees TA., Tsien CI., Robinson CG., Campian JL.
Data di Pubblicazione: 2016-11-16
Abstract: To investigate the utilization and overall survival (OS) impact of concurrent chemotherapy in combination with radiation therapy (RT) for elderly glioblastoma (GBM) patients. Elderly patients (age >70) with supratentorial and nonmetastatic GBM who received RT of 20-75 Gy with concurrent single-agent chemotherapy (ChemoRT) or without (RT alone) during 2004-2012 were identified from the National Cancer Data Base (NCDB). The Cochran-Armitage test was used for trend analysis. Hazard ratios (HR) and 95% confidence intervals (CIs) were determined using Cox proportional hazards. Propensity score analysis was performed to reduce selection bias in treatment allocation. A total of 5252 patients were identified (RT alone: n=1389; ChemoRT: n=3863). There was increasing utilization of chemotherapy during this period (45-80%, P<.001). A similar trend was also observed for the subset of age >80 (25-68%, P<.001). ChemoRT was associated with significantly better OS than RT alone (HR 0.79, 95% CI 0.70-0.89, P<.001) on multivariate analysis, and similar OS benefit was demonstrated with 1202 pairs of propensity-matched patients (HR 0.79, 95% CI 0.73-0.86, P<.001). For the matched pair, the median OS was 5.8 months with ChemoRT and 5.0 months with RT alone; the 2-year OS rate was 9% with ChemoRT and 4% with RT alone (P<.001). Concurrent chemotherapy has been administered with RT for the majority of elderly GBM patients. Addition of chemotherapy to RT for elderly GBM patients is associated with significantly improve OS in routine clinical practice.
Journal Title: Journal of neuro-oncology

PUBMED ID: 27840944
DOI: doi.org/10.3892/mmr.2016.5921
Titolo: Dec1 expression predicts prognosis and the response to temozolomide chemotherapy in patients with glioma.

Autori: Li XM., Lin W., Wang J., Zhang W., Yin AA., Huang Y., Zhang J., Yao L., Bian H., Zhang J., Zhang X.
Data di Pubblicazione: 2016-11-15
Abstract: Differentiated embryo chondrocyte expressed gene 1 (Dec1), a crucial cell differentiation mediator and apoptosis inhibitor, is abundantly expressed in various types of human cancer and is associated with malignant tumor progression. As poor differentiation and low apoptosis are closely associated with poor survival rates and a poor response to radio/chemotherapy in patients with cancer, the prognostic value of Dec1 expression was examined in the present study and its correlation with response to temozolomide (TMZ) chemotherapy was analyzed in patients with glioma. Dec1 expression was analyzed by immunohistochemistry in 157 samples of newly diagnosed glioma and 63 recurrent glioblastoma cases that relapsed during TMZ chemotherapy. Correlations with clinical variables, prognosis and the response to TMZ chemotherapy were analyzed in the newly diagnosed gliomas. Dec1 expression was also compared with the apoptosis index determined by TdT-mediated dUTP nick ending-labeling assay in recurrent glioblastomas. The antiglioma effect of TMZ in nude mice xenografts with Dec1 expression was examined in vivo. High expression of Dec1, which was significantly associated with high pathological tumor grade and poor response to TMZ chemotherapy, was demonstrated to be an unfavorable independent prognostic factor and predicted poor survival in patients with newly diagnosed glioma. In patients with recurrent glioblastoma, there was a negative correlation between Dec1 expression and the apoptotic index. In nude mice treated with TMZ, Dec1 overexpression potentiated proliferation, but attenuated TMZ-induced apoptosis. In conclusion, Dec1 is a prognostic factor for the clinical outcome and a predictive factor for the response to TMZ chemotherapy in patients with glioma.
Journal Title: Molecular medicine reports

PUBMED ID: 27826681
DOI: doi.org/10.1007/s11060-016-2310-y
Titolo: Role of surgical resection in recurrent glioblastoma: prognostic factors and outcome evaluation in an observational study.
Autori: Pessina F., Navarria P., Cozzi L., Tomatis S., Riva M., Ascolese AM., Santoro A., Simonelli M., Bello L., Scorsetti M.
Data di Pubblicazione: 2016-11-10
Abstract: The role of surgical resection in progressive or recurrent glioblastoma multiforme (GBM) lack of high level of evidence. The aim of this evaluation was to assess the role of surgical resection in relapsing GBM, in relation to the extent of surgical resection (EOR) and the amount of residual tumor volume (RTV). Among patients treated for newly diagnosed GBM between September 2008-December 2014, 64 patients with recurrent GBM were included in this retrospective evaluation. All patients underwent surgical resection followed by adjuvant treatments, chemotherapy and/or radiotherapy Results were evaluated in terms of local control (LC) rate, progression free survival (PFS) and patients overall survival (OS). Gross total resection (GTR) (>90%) was achieved in 48 (75%) patients and subtotal resection (STR) in 16 (25%). RTV was 0 in 40 (62.5%) patients and >0 in 24 (37.5%). No severe postoperative morbidity occurred. The median LC time was 6.0±0.1 months (95% CI 5.29-8.55), with a 1 and 2 years LC rate of 29.4±6.9%. The median PFS time was 6.8±0.8 months, with a 1 year PFS rate of 27.2±7.2% (95% CI 14.2-41.9). The median OS time was 10.3±0.5 months (95% CI 7.6-10.4) with a 1 and 2 years OS rate of 22.5±6.7% (95% CI 10.9-36.6). On univariate analysis EOR and RTV were recorded as conditioning LC and survival. These data was confirmed also in multivariate analysis only for RTV ($p<0.01$). Recurrent GBM can take advantage of repeated surgery in selected patients with younger age and good clinical status. The entity of surgical resection was confirmed as conditioning survival.

Journal Title: Journal of neuro-oncology

PUBMED ID: 27811370
DOI: doi.org/10.18632/oncotarget.13028
Titolo: IL-10 and PRKDC polymorphisms are associated with glioma patient sur
vival.
Autori: Hu M., Du J., Cui L., Huang T., Guo X., Zhao Y., Ma X., Jin T., Li G
., Song J.
Data di Pubblicazione: 2016-11-05
Abstract: Interleukin-10 (IL-10) and DNA repair gene PRKDC mutations are imp
licated in the development of multiple human cancers, including glioma. We i
nvestigated associations between IL-10 and PRKDC gene polymorphisms and prog
nosis in low- and high-grade glioma patients. We analyzed the associations o
f one IL-10 and one PRKDC single nucleotide polymorphism with patient clinic
al factors in 481 glioma patients using Cox proportional hazard models and K
aplan-Meier curves. We also assessed associations between patient clinical c
haracteristics and prognosis. Our data showed that the extent of tumor resec
tion (gross-total resection) and application of chemotherapy were associated
with improved patient outcomes in all glioma cases. Additionally, univariate
(Log-rank p = 0.019) and multivariate Cox regression analyses (p = 0.022) sh
owed that the IL-10 rs1800871 C/T genotype correlates with improved overall
survival in cases of low-grade glioma, whereas the PRKDC rs7003908 C/C genot
ype correlated with reduced overall and progression-free survival in high-gr
ade glioma patients in univariate (Log-rank p = 0.000 and p = 0.000, respect
ively) and multivariate Cox regression analyses (p = 0.001; p = 0.002, respe
ctively). These results suggest that IL-10 rs1800871 and PRKDC rs7003908 may
be useful biomarkers for predicting glioma patient outcome. Further function
al studies are needed to evaluate the mechanisms by which these polymorphism
s affect glioma progression.
Journal Title: Oncotarget

PUBMED ID: 27809808
DOI: doi.org/10.1186/s12885-016-2890-0
Titolo: Planning TTFields treatment using the NovoTAL system-clinical case s
eries beyond the use of MRI contrast enhancement.
Autori: Connelly J., Hormigo A., Mohilie N., Hu J., Chaudhry A., Blondin N.
Data di Pubblicazione: 2016-11-05
Abstract: This paper details important approaches for integrating clinical c
onsiderations, nonmeasurable disease and advanced imaging into the treatment
planning workflow for TTFields. As TTFields become integrated into standard
care pathways for glioblastoma, this case series demonstrates that treatment
planning beyond the extent of contrast enhancement is clinically feasible an
d should be prospectively compared to standard treatment planning in a clini
cal trial setting, in order to determine the impact on patient outcomes.
Journal Title: BMC cancer

PUBMED ID: 27693428
DOI: doi.org/10.1016/j.jconrel.2016.09.034
Titolo: Anticancer drug-loaded hydrogels as drug delivery systems for the lo
cal treatment of glioblastoma.
Autori: Bastiancich C., Danhier P., Préat V., Danhier F.
Data di Pubblicazione: 2016-11-07
Abstract: Among central nervous system tumors, Glioblastoma (GBM) is the mos
t common, aggressive and neurological destructive primary brain tumor in adu
lts. Standard care therapy for GBM consists in surgical resection of the acc
essible tumor (without causing neurological damage) followed by chemoradiati
on. However, several obstacles limit the assessment of tumor response and th

e delivery of cytotoxic agents at the tumor site, leading to a lack of effec tiveness of conventional treatments against GBM and fatal outcome. Despite t he efforts of the scientific community to increase the long-term benefits of GBM therapy, at the moment GBM remains incurable. Among the strategies that have been adopted in the last two decades to find new and efficacious therap ies for the treatment of GBM, the local delivery of chemotherapeutic drugs i n the tumor resection cavity emerged. In this review, our aim is to provide an overview on hydrogels loaded with anticancer drugs for the treatment of G BM recently used in preclinical and clinical studies, their advantages and m ajor limitations for clinical translation. This review is divided in three p arts: the first one describes the context of GBM and its current treatments, with a highlight on the role of local delivery in GBM treatment and the deve lopment of GBM resection murine models. Then, recent developments in the use of anticancer drug-loaded hydrogels for the treatment of GBM will be detaile d. The final section will be focused on the limitations for in vivo studies, clinical translation and the clinical perspectives to the development of hyd rogels.
Journal Title: Journal of controlled release : official journal of the Contr olled Release Society

PUBMED ID: 27744717
DOI: doi.org/10.1080/14712598.2016.1249846
Titolo: The prospect of patritumab for treating non-small cell lung cancer.
Autori: Horinouchi H.
Data di Pubblicazione: 2016-10-18
Abstract: The mutation or expression of HER family members serves as a thera peutic target for tyrosine kinase inhibitors or monoclonal antibodies in div erse cancers, such as non-small cell lung cancer, breast cancer, gastric can cer, head and neck cancer, colorectal cancer, pancreatic cancer and glioblas toma. HER3, which heterodimerizes with HER1 and HER2, has received much atte ntion as a potential target for anti-EGFR treatment. Patritumab is a novel, fully human monoclonal antibody directed against HER3. Areas covered: In thi s review article, an overview of the market, chemistry, pharmacodynamics, ph armacokinetics, efficacy, and safety of patritumab is provided based on data from phase I studies, a combination phase I trial, and a randomized phase II trial comparing two doses of patritumab. Expert opinion: The combination of patritumab plus erlotinib has shown a promising efficacy and safety in early -phase clinical trials. In a randomized phase II trial, higher mRNA expressi on of heregulin (a ligand of HER3) was associated with better progression-fr ee survival and a tendency toward improved overall survival. In the era of p recise treatment based on an appropriate target with a predictive biomarker, further studies with patritumab are needed to realize its potential in cance r treatment.
Journal Title: Expert opinion on biological therapy

PUBMED ID: 27796446
DOI: doi.org/10.1007/s00234-016-1741-7
Titolo: Prognostic value of preoperative dynamic contrast-enhanced MRI perfu sion parameters for high-grade glioma patients.
Autori: Ulyte A., Katsaros VK., Liouta E., Stranjalis G., Boskos C., Papanik olaou N., Usinskiene J., Bisdas S.
Data di Pubblicazione: 2016-11-01
Abstract: High v
Journal Title: Neuroradiology

PUBMED ID: 27645758
DOI: doi.org/10.5692/clinicalneurol.cn-000928

Titolo: A case of progressive multifocal leukoencephalopathy with chronic re nal failure, whose JC virus in cerebrospinal fluid disappeared after mefloqu ine-mirtazapine dual therapy.
Autori: Ohnuki E., Asayama S., Asayama T., Nakamichi K., Saijo M., Kosaka S.
Data di Pubblicazione: 2016-09-21
Abstract: An 83-year-old man with chronic renal failure was referred to our hospital because of subacute progressive right hemiparesis. A brain MRI show ed high-intensity lesions in bilateral middle cerebellar peduncles and white matter of the left frontal lobe on T
Journal Title: Rinsho shinkeigaku = Clinical neurology

PUBMED ID: 26558632
DOI: doi.org/10.1007/s12035-015-9525-3
Titolo: Proliferating Cell Nuclear Antigen Has an Association with Prognosis and Risks Factors of Cancer Patients: a Systematic Review.
Autori: Lv Q., Zhang J., Yi Y., Huang Y., Wang Y., Wang Y., Zhang W.
Data di Pubblicazione: 2015-11-13
Abstract: Proliferating cell nuclear antigen (PCNA) is reported as a famous marker in various tumors. A couple of articles have been published about the clinical function of PCNA on cancer progression; however, these results are conflicting in some degree. Thus, it is crucial to perform a systematic revi ew and meta-analysis to identify their real actions. Here, we took cervical cancer and glioma as example and then pooled hazard ratios (HRs) or odds rat ios (ORs) with 95 % confidence intervals (95 % CIs). In the present study, t he PCNA expression in cervical cancer and gliomas patients was both correlat ed with 5-year-overall survival (OS) (HR = 4.41, 95 % CI 2.71-7.17, p = 0.000; HR = 4.40, 95 % CI 3.00-6.47, p = 0.000; respectively). In addition, a fixed ef fect model revealed a significant association between PCNA and FIGO stage (O R = 4.48, 95 % CI 3.48-5.77, p = 0.000) or WHO grade (OR = 5.64, 95 % CI 4.15-7. 68, p = 0.000), rather than age (OR = 1.01, 95 % CI 0.71-1.43, p = 0.957; OR = 1.0 0, 95 % CI 0.80-1.24, p = 0.989; respectively). No heterogeneity was observed across all studies. According to funnel plot, no publication bias was report ed. In conclusion, our systematic review suggests that PCNA expression is si gnificantly associated with poor 5-year survival, advanced stage or higher W HO grade, which might be suggested as a useful prognostic and diagnostic bio marker, or an effective therapy target in cervical cancer, gliomas, or even more cancers.
Journal Title: Molecular neurobiology

PUBMED ID: 27486853
DOI: doi.org/10.1111/cas.13027
Titolo: Oncolytic virus therapy: A new era of cancer treatment at dawn.
Autori: Fukuhara H., Ino Y., Todo T.
Data di Pubblicazione: 2016-08-04
Abstract: Oncolytic virus therapy is perhaps the next major breakthrough in cancer treatment following the success in immunotherapy using immune checkpo int inhibitors. Oncolytic viruses are defined as genetically engineered or n aturally occurring viruses that selectively replicate in and kill cancer cel ls without harming the normal tissues. T-Vec (talimogene laherparepvec), a s econd-generation oncolytic herpes simplex virus type 1 (HSV-1) armed with GM -CSF, was recently approved as the first oncolytic virus drug in the USA and Europe. The phase III trial proved that local intralesional injections with T-Vec in advanced malignant melanoma patients can not only suppress the grow th of injected tumors but also act systemically and prolong overall survival . Other oncolytic viruses that are closing in on drug approval in North Amer ica and Europe include vaccinia virus JX-594 (pexastimogene devacirepvec) fo r hepatocellular carcinoma, GM-CSF-expressing adenovirus CG0070 for bladder

cancer, and Reolysin (pelareorep), a wild-type variant of reovirus, for head and neck cancer. In Japan, a phase II clinical trial of G47Δ, a third-generation oncolytic HSV-1, is ongoing in glioblastoma patients. G47Δ was recently designated as a "Sakigake" breakthrough therapy drug in Japan. This new system by the Japanese government should provide G47Δ with priority reviews and a fast-track drug approval by the regulatory authorities. Whereas numerous oncolytic viruses have been subjected to clinical trials, the common feature that is expected to play a major role in prolonging the survival of cancer patients is an induction of specific antitumor immunity in the course of tumor-specific viral replication. It appears that it will not be long before oncolytic virus therapy becomes a standard therapeutic option for all cancer patients.
Journal Title: Cancer science

PUBMED ID: 27334276
DOI: doi.org/10.1007/s00066-016-1007-7
Titolo: Intensity-modulated proton therapy, volumetric-modulated arc therapy, and 3D conformal radiotherapy in anaplastic astrocytoma and glioblastoma : A dosimetric comparison.
Autori: Adeberg S., Harrabi SB., Bougatf N., Bernhardt D., Rieber J., Koerber SA., Syed M., Sprave T., Mohr A., Abdollahi A., Haberer T., Combs SE., Herfarth K., Debus J., Rieken S.
Data di Pubblicazione: 2016-06-24
Abstract: Essential dose reduction while maintaining equal target volume coverage was observed using PRT, particularly in contralaterally located critical neuronal structures, areas of neurogenesis, and structures of neurocognitive functions. These findings were supported by preliminary clinical results confirming the safety and feasibility of PRT in HGG.
Journal Title: Strahlentherapie und Onkologie : Organ der Deutschen Rontgengesellschaft ... [et al]

PUBMED ID: 27770279
DOI: doi.org/10.1007/s11060-016-2288-5
Titolo: NRG oncology RTOG 0625: a randomized phase II trial of bevacizumab with either irinotecan or dose-dense temozolomide in recurrent glioblastoma.
Autori: Gilbert MR., Pugh SL., Aldape K., Sorensen AG., Mikkelsen T., Penas-Prado M., Bokstein F., Kwok Y., Lee RJ., Mehta M.
Data di Pubblicazione: 2016-10-23
Abstract: Angiogenesis, a hallmark of glioblastoma, can potentially be targeted by inhibiting the VEGF pathway using bevacizumab, a humanized monoclonal antibody against VEGF-A. This study was designed to determine the efficacy and safety of these regimens in the cooperative group setting. Eligibility included age ≥18, recurrent or progressive GBM after standard chemoradiation. Treatment was intravenous bevacizumab 10 mg/kg and either irinotecan (CPT) 125 mg/m
Journal Title: Journal of neuro-oncology

PUBMED ID: 27695068
DOI: doi.org/10.1371/journal.pone.0164051
Titolo: Enhancing Predicted Efficacy of Tumor Treating Fields Therapy of Glioblastoma Using Targeted Surgical Craniectomy: A Computer Modeling Study.
Autori: Korshoej AR., Saturnino GB., Rasmussen LK., von Oettingen G., Sørensen JC., Thielscher A.
Data di Pubblicazione: 2016-10-04
Abstract: Our results provide theoretical evidence that small and clinically feasible craniectomies may provide significant enhancement of TTFields intensity in cerebral hemispheric tumors without severely compromising brain prot

ection or causing unacceptable heating in healthy tissues. A clinical trial is being planned to validate safety and efficacy.
Journal Title: PloS one

PUBMED ID: 27690657
DOI: doi.org/10.3171/2016.7.FOCUS16234
Titolo: Laser interstitial thermal therapy for newly diagnosed and recurrent glioblastoma.
Autori: Thomas JG., Rao G., Kew Y., Prabhu SS.
Data di Pubblicazione: 2016-10-04
Abstract: OBJECTIVE Glioblastoma (GBM) is the most common and deadly malignant primary brain tumor. Better surgical therapies are needed for newly diagnosed GBMs that are difficult to resect and for GBMs that recur despite standard therapies. The authors reviewed their institutional experience of using laser interstitial thermal therapy (LITT) for the treatment of newly diagnosed or recurrent GBMs. METHODS This study reports on the pre-LITT characteristics and post-LITT outcomes of 8 patients with newly diagnosed GBMs and 13 patients with recurrent GBM who underwent LITT. RESULTS Compared with the group with recurrent GBMs, the patients with newly diagnosed GBMs who underwent LITT tended to be older (60.8 vs 48.9 years), harbored larger tumors (22.4 vs 14.6 cm
Journal Title: Neurosurgical focus

PUBMED ID: 27690656
DOI: doi.org/10.3171/2016.7.FOCUS16236
Titolo: Stereotactic laser ablation for hypothalamic and deep intraventricular lesions.
Autori: Buckley RT., Wang AC., Miller JW., Novotny EJ., Ojemann JG.
Data di Pubblicazione: 2016-10-04
Abstract: OBJECTIVE Laser ablation is a novel, minimally invasive procedure that utilizes MRI-guided thermal energy to treat epileptogenic and other brain lesions. In addition to treatment of mesial temporal lobe epilepsy, laser ablation is increasingly being used to target deep or inoperable lesions, including hypothalamic hamartoma (HH), subependymal giant cell astrocytoma (SEGA), and exophytic intrinsic hypothalamic/third ventricular tumors. The authors reviewed their early institutional experience with these patients to characterize clinical outcomes in patients undergoing this procedure. METHODS A retrospective cohort (n = 12) of patients undergoing laser ablation at a single institution was identified, and clinical and radiographic records were reviewed. RESULTS Laser ablation was successfully performed in all patients. No permanent neurological or endocrine complications occurred; 2 (17%) patients developed acute obstructive hydrocephalus or shunt malfunction following treatment. Laser ablation of HH resulted in seizure freedom (Engel Class I) in 67%, with the remaining patients having a clinically significant reduction in seizure frequency of greater than 90% compared with preoperative baseline (Engel Class IIB). Treatment of SEGAs resulted in durable clinical and radiographic tumor control in 2 of 3 cases, with one patient receiving adjuvant everolimus and the other receiving no additional therapy. Palliative ablation of hypothalamic/third ventricular tumors resulted in partial tumor control in 1 of 3 patients. CONCLUSIONS Early experience suggests that laser ablation is a generally safe, durable, and effective treatment for patients harboring HHs. It also appears effective for local control of SEGAs, especially in combination therapy with everolimus. Its use as a palliative treatment for intrinsic hypothalamic/deep intraventricular tumors was less successful and associated with a higher risk of serious complications. Additional experience and long-term follow-up will be beneficial in further characterizing the effectiveness and risk profile of laser ablation in treating these lesions i

n comparison with conventional resective surgery or stereotactic radiosurger
y.
Journal Title: Neurosurgical focus

PUBMED ID: 27686946
DOI: doi.org/10.1016/S1470-2045(16)30313-8
Titolo: Temozolomide chemotherapy versus radiotherapy in high-risk low-grade
glioma (EORTC 22033-26033): a randomised, open-label, phase 3 intergroup stu
dy.
Autori: Baumert BG., Hegi ME., van den Bent MJ., von Deimling A., Gorlia T.,
Hoang-Xuan K., Brandes AA., Kantor G., Taphoorn MJB., Hassel MB., Hartmann C
., Ryan G., Capper D., Kros JM., Kurscheid S., Wick W., Enting R., Reni M.,
Thiessen B., Dhermain F., Bromberg JE., Feuvret L., Reijneveld JC., Chinot O
., Gijtenbeek JMM., Rossiter JP., Dif N., Balana C., Bravo-Marques J., Cleme
nt PM., Marosi C., Tzuk-Shina T., Nordal RA., Rees J., Lacombe D., Mason WP.
, Stupp R.
Data di Pubblicazione: 2016-10-01
Abstract: Merck Sharpe & Dohme-Merck & Co, Canadian Cancer Society, Swiss Ca
ncer League, UK National Institutes of Health, Australian National Health an
d Medical Research Council, US National Cancer Institute, European Organisat
ion for Research and Treatment of Cancer Cancer Research Fund.
Journal Title: The Lancet. Oncology

PUBMED ID: 27680966
DOI: doi.org/10.23736/S0390-5616.16.03874-1
Titolo: Second line treatment of recurrent glioblastoma with sunitinib: resu
lts of a phase II study and systematic review of literature.
Autori: Grisanti S., Ferrari VD., Buglione M., Agazzi GM., Liserre R., Polia
ni L., Buttolo L., Gipponi S., Pedersini R., Consoli F., Panciani P., Roca E
., Spena G., Triggiani L., Berruti A., Berruti A.
Data di Pubblicazione: 2016-09-30
Abstract: Results of this trial and those of the systematic review indicate
that, compared to conventional chemotherapy or bevacizumab, sunitinib has in
sufficient activity in the setting of recurrent GBM. Better patient's molecu
lar stratification for second-line treatment in GBM is warranted.
Journal Title: Journal of neurosurgical sciences

PUBMED ID: 27590514
DOI: doi.org/10.18632/oncotarget.11756
Titolo: Radiation combined with temozolomide contraindicated for young adult
s diagnosed with anaplastic glioma.
Autori: Yang P., Zhang C., Cai J., You G., Wang Y., Qiu X., Li S., Wu C., Ya
o K., Li W., Peng X., Zhang W., Jiang T.
Data di Pubblicazione: 2016-09-04
Abstract: We observed no survival benefit in young adults (age < 50) with an
aplastic glioma when treated with TMZ combined with RT. Our findings warrant
further investigation of younger patients diagnosed with anaplastic glioma t
reated with radiotherapy plus TMZ chemotherapy.
Journal Title: Oncotarget

PUBMED ID: 27573687
DOI: doi.org/10.1007/s00401-016-1611-8
Titolo: Prognostic impact of the 2016 WHO classification of diffuse gliomas
in the French POLA cohort.
Autori: Tabouret E., Nguyen AT., Dehais C., Carpentier C., Ducray F., Idbaih
A., Mokhtari K., Jouvet A., Uro-Coste E., Colin C., Chinot O., Loiseau H., M

oyal E., Maurage CA., Polivka M., Lechapt-Zalcman E., Desenclos C., Meyronet D., Delattre JY., Figarella-Branger D., Figarella-Branger D.
Data di Pubblicazione: 2016-08-31
Abstract: The new WHO classification of diffuse gliomas has been refined and now includes the 1p/19q codeletion, IDH1/2 mutation, and histone H3-K27M mut ation. Our objective was to assess the prognostic value of the updated 2016 WHO classification in the French POLA cohort. All cases of high-grade oligod endroglial tumors sent for central pathological review and included into the French nationwide POLA cohort were reclassified according to the updated 4th WHO classification. In total, 1041 patients were included, with a median age at diagnosis of 50.4 years (range 17.1-84.4). Based on the new histomolecula r classification, diagnoses included anaplastic oligodendroglioma IDH mutant and 1p/19q-codeleted (32.5 %), anaplastic astrocytoma IDH mutant (IDH (mut)) (11.0 %), anaplastic astrocytoma IDH wild type (IDH (wt)) (5.3 %), glioblast oma IDH (mut) (17.1 %), and glioblastoma IDH (wt) (33.2 %). Ten patients pre sented with a diffuse midline tumor, H3 K27M mutant. The new WHO classificat ion was prognostic for progression-free survival (PFS) and overall survival (OS) ($p < 0.001$). We did not find prognosis differences between grades III a nd IV for IDH (mut) 1p/19q intact and IDH (wt) gliomas in univariate and mul tivariate analyses. Among anaplastic astrocytoma IDH (wt), cases with chromo some arm 7p gain and 10q loss (55 %) had shorter PFS than the others ($p = 0.$ 027). In conclusion, the new WHO histomolecular classification of diffuse gl iomas presented with high prognostic value. Grading was not discriminant bet ween grade III and IV high-grade gliomas.
Journal Title: Acta neuropathologica

PUBMED ID: 27515827
DOI: doi.org/10.1093/neuonc/now091
Titolo: Evaluation of pseudoprogression rates and tumor progression patterns in a phase III trial of bevacizumab plus radiotherapy/temozolomide for newly diagnosed glioblastoma.
Autori: Wick W., Chinot OL., Bendszus M., Mason W., Henriksson R., Saran F., Nishikawa R., Revil C., Kerloeguen Y., Cloughesy T.
Data di Pubblicazione: 2016-08-13
Abstract: Pseudoprogression complicated progression assessment in a small bu t relevant number of patients but had negligible impact on PFS. Bevacizumab did not appear to adversely impact tumor progression patterns.
Journal Title: Neuro-oncology

PUBMED ID: 27503138
DOI: doi.org/10.1186/s40478-016-0351-2
Titolo: A combination of TERT promoter mutation and MGMT methylation status predicts clinically relevant subgroups of newly diagnosed glioblastomas.
Autori: Arita H., Yamasaki K., Matsushita Y., Nakamura T., Shimokawa A., Tak ami H., Tanaka S., Mukasa A., Shirahata M., Shimizu S., Suzuki K., Saito K., Kobayashi K., Higuchi F., Uzuka T., Otani R., Tamura K., Sumita K., Ohno M., Miyakita Y., Kagawa N., Hashimoto N., Hatae R., Yoshimoto K., Shinojima N., Nakamura H., Kanemura Y., Okita Y., Kinoshita M., Ishibashi K., Shofuda T., Kodama Y., Mori K., Tomogane Y., Fukai J., Fujita K., Terakawa Y., Tsuyuguch i N., Moriuchi S., Nonaka M., Suzuki H., Shibuya M., Maehara T., Saito N., N agane M., Kawahara N., Ueki K., Yoshimine T., Miyaoka E., Nishikawa R., Komo ri T., Narita Y., Ichimura K.
Data di Pubblicazione: 2016-08-10
Abstract: The prognostic impact of TERT mutations has been controversial in IDH-wild tumors, particularly in glioblastomas (GBM). The controversy may be attributable to presence of potential confounding factors such as MGMT methy lation status or patients' treatment. This study aimed to evaluate the impac t of TERT status on patient outcome in association with various factors in a

large series of adult diffuse gliomas. We analyzed a total of 951 adult diff use gliomas from two cohorts (Cohort 1, n=758; Cohort 2, n=193) for IDH1/2, 1p/19q, and TERT promoter status. The combined IDH/TERT classification divid ed Cohort 1 into four molecular groups with distinct outcomes. The overall s urvival (OS) was the shortest in IDH wild-type/TERT mutated groups, which mo stly consisted of GBMs (P<0.0001). To investigate the association between T ERT mutations and MGMT methylation on survival of patients with GBM, samples from a combined cohort of 453 IDH-wild-type GBM cases treated with radiation and temozolomide were analyzed. A multivariate Cox regression model revealed that the interaction between TERT and MGMT was significant for OS (P=0.0064). Compared with TERT mutant-MGMT unmethylated GBMs, the hazard ratio (HR) f or OS incorporating the interaction was the lowest in the TERT mutant-MGMT m ethylated GBM (HR, 0.266), followed by the TERT wild-type-MGMT methylated (H R, 0.317) and the TERT wild-type-MGMT unmethylated GBMs (HR, 0.542). Thus, p atients with TERT mutant-MGMT unmethylated GBM have the poorest prognosis. O ur findings suggest that a combination of IDH, TERT, and MGMT refines the cl assification of grade II-IV diffuse gliomas.
Journal Title: Acta neuropathologica communications

PUBMED ID: 27502586
DOI: doi.org/10.1186/s12883-016-0658-4
Titolo: EFFECTS: an expanded access program of everolimus for patients with subependymal giant cell astrocytoma associated with tuberous sclerosis compl ex.
Autori: Fogarasi A., De Waele L., Bartalini G., Jozwiak S., Laforgia N., Ver helst H., Petrak B., Pedespan JM., Witt O., Castellana R., Crippa S., Gislim berti G., Gyorsok Z.
Data di Pubblicazione: 2016-08-10
Abstract: This study confirms the acceptable safety profile of everolimus in patients with SEGA associated with TSC in a real-world setting. The results further support the efficacy of everolimus in the treatment of SEGA associat ed with TSC. (EudraCT: 2010-022583-13).
Journal Title: BMC neurology

PUBMED ID: 27501915
DOI: doi.org/10.1007/s11864-016-0430-4
Titolo: The Role of Molecular Diagnostics in the Management of Patients with Gliomas.
Autori: Wirsching HG., Weller M.
Data di Pubblicazione: 2016-08-10
Abstract: The revised World Health Organization (WHO) classification of tumo rs of the central nervous system of 2016 combines biology-driven molecular m arker diagnostics with classical histological cancer diagnosis. Reclassifica tion of gliomas by molecular similarity beyond histological boundaries impro ves outcome prediction and will increasingly guide treatment decisions. This change in paradigms implies more personalized and eventually more efficient therapeutic approaches, but the era of molecular targeted therapies for glio mas is yet at its onset. Promising results of molecularly targeted therapies in genetically less complex gliomas with circumscribed growth such as subepe ndymal giant cell astrocytoma or pilocytic astrocytoma support further devel opment of molecularly targeted therapies. In diffuse gliomas, several molecu lar markers that predict benefit from alkylating agent chemotherapy have bee n identified in recent years. For example, co-deletion of chromosome arms 1p and 19q predicts benefit from polychemotherapy with procarbazine, CCNU (lomu stine), and vincristine (PCV) in patients with anaplastic oligodendroglioma, and the presence of 1p/19q co-deletion was integrated as a defining feature of oligodendroglial tumors in the revised WHO classification. However, the t

remendous increase in knowledge of molecular drivers of diffuse gliomas on g enomic, epigenetic, and gene expression levels has not yet translated into e ffective molecular targeted therapies. Multiple reasons account for the fail ure of early clinical trials of molecularly targeted therapies in diffuse gl iomas, including the lack of molecular entry controls as well as pharmacokin etic and pharmacodynamics issues, but the key challenge of specifically targ eting the molecular backbone of diffuse gliomas is probably extensive clonal heterogeneity. A more profound understanding of clonal selection, alternativ e activation of oncogenic signaling pathways, and genomic instability is war ranted to identify effective combination treatments and ultimately improve s urvival.
Journal Title: Current treatment options in oncology

PUBMED ID: 27475318
DOI: doi.org/10.1016/j.jocn.2016.06.014
Titolo: The survival significance of a measurable enhancing lesion after com pleting standard treatment for newly diagnosed glioblastoma.
Autori: Kim SK., Kim TM., Lee ST., Lee SH., Heo DS., Kim IH., Kim DG., Jung HW., Choi SH., Lee SH., Park CK.
Data di Pubblicazione: 2016-08-01
Abstract: The goal of this study was to analyze the survival outcome accordi ng to the treatment response after completing standard treatment protocol fo r newly diagnosed glioblastoma (GBM) and to suggest a patient who should be considered for further treatment. After approving by our Institutional Revie w Board, 57 patients (38 male, 19 female; median age, 52years; age range, 16 -81years) with newly diagnosed GBM who completed standard treatment protocol were examined retrospectively. According to the treatment response using the RANO criteria, there were 20 patients with complete response (CR), five pati ents with partial response (PR), 13 patients with stable disease (SD) and 19 patients with progressive disease (PD) after the completion of standard trea tment. Patients (PR+SD+PD) with a measurable enhancing lesion were categoriz ed the MEL group (n=37). We analyzed the difference of survival outcome betw een CR group and MEL group. The median progression-free survival (PFS) in th e CR group was significantly better than that of the MEL group (18.0months v s. 3.0months, p=0.004). The median overall survival (OS) was also significan tly longer in the CR group (25.0months vs. 15.0months, p=0.005). However, th ere was no significant difference in the survival outcome of the CR group co mpared with that of the subset of MEL group patients who showed PR or SD. Po or survival outcome was found only in MEL group patients who exhibited progr ession. Patients with a measurable enhancing lesion showing progression afte r completion of standard treatment protocol are appropriate candidates for f urther treatment.
Journal Title: Journal of clinical neuroscience : official journal of the Ne urosurgical Society of Australasia

PUBMED ID: 27473815
DOI: doi.org/10.1016/j.ijrobp.2016.05.009
Titolo: Phase 1 Study of Preoperative Chemoradiation Therapy With Temozolomi de and Capecitabine in Patients With Locally Advanced Rectal Cancer.
Autori: Jeong JH., Hong YS., Park Y., Kim J., Kim JE., Kim KP., Kim SY., Par k JH., Kim JH., Park IJ., Lim SB., Yu CS., Kim JC., Kim TW.
Data di Pubblicazione: 2016-07-31
Abstract: There was a tendency toward higher pCR rates in patients with hype rmethylated MGMT. Future randomized studies are therefore warranted.
Journal Title: International journal of radiation oncology, biology, physics

PUBMED ID: 27466078

DOI: doi.org/10.1620/tjem.239.269
Titolo: Expression of ADP-ribosyltransferase 1 Is Associated with Poor Prognosis of Glioma Patients.
Autori: Li Z., Yan X., Sun Y., Yang X.
Data di Pubblicazione: 2016-07-29
Abstract: Glioma has a poor prognosis due to its rapid overgrowth, diffuse invasion, and chemotherapy resistance. The improvements in clinical outcome are still limited and the identification of novel biomarkers involved in the progression of gliomas is still under critical demands. Amino acid ADP-ribosyltransferase 1 (ART1) is an enzyme that catalyzes the mono-ADP-ribosylation, a reversible post-translational modification. For example, the mono-ADP-ribosylation of transcription factors can affect their binding to target gene promoters. However, the functional significance of ART1 in glioma has not been reported. We collected 107 glioma cases from Qianfoshan Hospital and Yidu Central Hospital of Weifang between April 2008 and September 2015 to analyze the prognosis value of ART1 in gliomas. RT-qPCR analysis showed that the expression level of ART1 mRNA in glioma tissues was 4-fold higher than that in normal brain tissues. According to the immunohistochemical staining results, 44 patients (41.1%) were categorized as ART1 positive (≥ 20% of stained glioma cells), while the other 63 patients (58.9%) categorized as ART1 negative (< 20% of stained glioma cells). Moreover, the mean percentage of ART1-positive cells was 43.7%, 53.6% and 64.2% in WHO grade II, III and IV specimens, respectively. Through univariate and multivariate analyses, we identified ART1 as an independent prognostic factor. We also found that ART1 overexpression in U251 glioblastoma cells could significantly decrease the susceptibility to vincristine, one of tubulin-targeted drugs, which is widely used in clinical treatment for glioma. Taken together, we propose that up-regulation of ART1 expression is associated with the aggressiveness of glioma.
Journal Title: The Tohoku journal of experimental medicine

PUBMED ID: 27461038
DOI: doi.org/10.1007/s11864-016-0422-4
Titolo: Relapsed Glioblastoma: Treatment Strategies for Initial and Subsequent Recurrences.
Autori: Tosoni A., Franceschi E., Poggi R., Brandes AA.
Data di Pubblicazione: 2016-07-28
Abstract: At the time of glioblastoma (GBM) recurrence, a sharp analysis of prognostic factors, disease characteristics, response to adjuvant treatment, and clinical conditions should be performed. A prognostic assessment could allow a careful selection between patients that could be proposed to intensified approaches or palliative setting. Participation in clinical trials aims to improve outcome, and should be encouraged due to dismal prognosis of GBM patients after recurrence. Reoperation should be proposed if the tumor is amenable to a complete resection and if prognostic factors suggest that patient could benefit from a second surgery. Second-line chemotherapy should be chosen based on MGMT status, time to disease recurrence, and toxicity profile. If enrollment into a clinical trial is not possible, a nitrosourea-based regimen is the preferred choice, carefully evaluating any previous temozolomide (TMZ)-related toxicity. In MGMT-methylated patients relapsing after TMZ completion, a rechallenge could be proposed. After second progression, the clinical advantage of subsequent lines of chemotherapy still needs to be clarified. However, based on performance status, patients' preference, and disease behavior, a third-line treatment could be considered. Available treatments include nitrosoureas, bevacizumab, or carboplatin plus etoposide. However, more effective therapeutic options are needed.
Journal Title: Current treatment options in oncology

PUBMED ID: 27423645

DOI: doi.org/10.1007/s11060-016-2202-1
Titolo: Relapse patterns and outcome after relapse in standard risk medullob lastoma: a report from the HIT-SIOP-PNET4 study.
Autori: Sabel M., Fleischhack G., Tippelt S., Gustafsson G., Doz F., Kortman n R., Massimino M., Navajas A., von Hoff K., Rutkowski S., Warmuth-Metz M., Clifford SC., Pietsch T., Pizer B., Lannering B., Lannering B.
Data di Pubblicazione: 2016-07-18
Abstract: The HIT-SIOP-PNET4 randomised trial for standard risk medulloblast oma (MB) (2001-2006) included 338 patients and compared hyperfractionated an d conventional radiotherapy. We here report the long-term outcome after a me dian follow up of 7.8 years, including detailed information on relapse and t he treatment of relapse. Data were extracted from the HIT Group Relapsed MB database and by way of a specific case report form. The event-free and overa ll (OS) survival at 10 years were 76±2% and 78±2% respectively with no sig nificant difference between the treatment arms. Seventy-two relapses and thr ee second malignant neoplasms were reported. Thirteen relapses (18%) were is olated local relapses in the posterior fossa (PF) and 59 (82%) were craniosp inal, metastatic relapses (isolated or multiple) with or without concurrent PF disease. Isolated PF relapse vs all other relapses occurred at mean/media n of 38/35 and 28/26 months respectively (p=0.24). Late relapse, i.e. >5 ye ars from diagnosis, occurred in six patients (8%). Relapse treatment consist ed of combinations of surgery (25%), focal radiotherapy (RT 22%), high dose chemotherapy with stem cell rescue (HDSCR 21%) and conventional chemotherapy (90%). OS at 5 years after relapse was 6.0±4%. In multivariate analysis; is olated relapse in PF, and surgery were significantly associated with prolong ed survival whereas RT and HDSCR were not. Survival after relapse was not re lated to biological factors and was very poor despite several patients recei ving intensive treatments. Exploration of new drugs is warranted, preferably based on tumour biology from biopsy of the relapsed tumour.
Journal Title: Journal of neuro-oncology

PUBMED ID: 27422128
DOI: doi.org/10.1007/s11060-016-2206-x
Titolo: Impact of tapering and discontinuation of bevacizumab in patients wi th progressive glioblastoma.
Autori: Hertenstein A., Hielscher T., Menn O., Wiestler B., Winkler F., Plat ten M., Wick W., Wick A.
Data di Pubblicazione: 2016-07-17
Abstract: Bevacizumab is frequently used in patients with progressive gliobl astoma raising questions regarding frequency of treatments, dosage, duration of therapy and the possibility of tapering and discontinuation for selected patient groups. We retrospectively assessed the safety and outcome of taperi ng and discontinuation of bevacizumab therapy for reasons other than disease progression and toxicity in 19 patients with progressive glioblastoma receiv ing bevacizumab for at least 6 months. In 10 of the 19 patients tapering bev acizumab resulted in complete discontinuation and reinitiation after disease progression during halted treatment. As a comparison group 33 patients with bevacizumab for at least 6 months continuously dosed at 10 mg/kg every 2 wee ks were selected. Age and Karnofsky performance status at start of bevacizum ab were similar in both groups. Influenced by the selection process, progres sion-free survival (PFS) and overall survival (OS) were longer in the group receiving a tapered and discontinued bevacizumab regimen (PFS 22.7 versus 11 .2 months, HR 0.33, p-value=0.01; OS 29.9 versus 15.5 months, HR 0.22, p-va lue=0.001) with a median time of discontinuation of 4.5 months (range: 1.9- 44.2 months). Stable disease or partial response according to RANO at ≥3 mon ths was achieved in 89% of patients with reinitiated bevacizumab therapy aft er discontinuation. These data indicate that tapering and discontinuation of

bevacizumab therapy for other reasons than progression is feasible without a n increased risk for tumor rebound or unresponsiveness to reinitiated bevaci zumab therapy.
Journal Title: Journal of neuro-oncology

PUBMED ID: 27411023
DOI: doi.org/10.1080/14712598.2016.1212012
Titolo: Recent advances and future of immunotherapy for glioblastoma.
Autori: Kamran N., Calinescu A., Candolfi M., Chandran M., Mineharu Y., Asad AS., Koschmann C., Nunez FJ., Lowenstein PR., Castro MG.
Data di Pubblicazione: 2016-07-14
Abstract: Encouraging results have been observed with immunotherapeutic stra tegies; some clinical trials are reaching phase III. Significant progress ha s been made in unraveling the molecular and genetic heterogeneity of GBM and its implications to disease prognosis. There is now consensus related to the critical need to incorporate tumor heterogeneity into the design of therapeu tic approaches. Recent data also indicates that an efficacious treatment str ategy will need to be combinatorial and personalized to the tumor genetic si gnature.
Journal Title: Expert opinion on biological therapy

PUBMED ID: 27393350
DOI: doi.org/10.1007/s11060-016-2188-8
Titolo: The effects of sequential treatments on hippocampal volumes in malig nant glioma patients.
Autori: Nolen SC., Lee B., Shantharam S., Yu HJ., Su L., Billimek J., Bota D A.
Data di Pubblicazione: 2016-07-10
Abstract: Malignant gliomas (MG) are very aggressive tumors. In an effort to improve the outcome, the patients receive multi-modal therapies such as surg ery, radiation and chemotherapy (temozolomide followed in many cases by beva cizumab). The survivors are affected by multiple learning and memory deficit s. Greater deterioration over time in hippocampal specific cognitive tasks w as shown in patients receiving bevacizumab in addition to radiation and temo zolomide for a longer period of time (RTOG 0825). The rate of hippocampal at rophy in patients treated with radiation and temozolomide followed by bevaci zumab is not yet determined, and is the goal of the present study. We used t he serial MRIs obtained as parts of standard clinical care in patients with MG. Measurements were done using the Medical Image Processing, Analysis and Visualization (MIPAV) software. The hippocampus in the contralateral hemisph ere was manually traced and measured, to avoid morphological structure chang es induced by the tumor, radiation fields or surgical markers. We determined a longitudinal progression of hippocampal atrophy-with the maximum volume lo ss (33.26%) for the patients that were on treatment for 5 years. There was n o detectable hippocampal atrophy during the chemo-radiation followed by adju vant temozolomide. A significant decrease in the absolute hippocampus volume was noted after 6 months of continuous bevacizumab treatment ($p < 0.05$). The hippocampal volume loss progressed over the next 3 years, and was higher tha n the one previously reported in Alzheimer disease patients. The hippocampal volume loss is minimal during the 1 month after diagnosis, when the patients receive chemo-radiation and adjuvant temozolomide. However, prolonged treatm ent including bevacizumab is associated with a significant rate of hippocamp al volume loss.
Journal Title: Journal of neuro-oncology

PUBMED ID: 27371575

DOI: doi.org/10.1158/2159-8290.CD-16-0563
Titolo: CDK4/6 Inhibitors: Promising Opportunities beyond Breast Cancer.
Autori: Lim JS., Turner NC., Yap TA.
Data di Pubblicazione: 2016-07-03
Abstract: Patnaik and colleagues report on the safety, pharmacokinetics, pha rmacodynamics, and preliminary efficacy of abemaciclib for the treatment of advanced solid cancers, demonstrating antitumor activity in advanced breast cancers as well as glioblastoma, melanoma, non-small cell lung cancer, color ectal cancer, and ovarian cancer. The development of abemaciclib and other C DK4/6 inhibitors should now be fully optimized through the use of novel pred ictive biomarkers of response and rational combinations. Cancer Discov; 6(7) ; 697-9. ©2016 AACRSee related article by Patnaik et al., p. 740.
Journal Title: Cancer discovery

PUBMED ID: 27353036
DOI: doi.org/10.1530/ERC-16-0117
Titolo: MGMT expression predicts response to temozolomide in pancreatic neur oendocrine tumors.
Autori: Cros J., Hentic O., Rebours V., Zappa M., Gille N., Theou-Anton N., Vernerey D., Maire F., Lévy P., Bedossa P., Paradis V., Hammel P., Ruszniews ki P., Couvelard A.
Data di Pubblicazione: 2016-06-30
Abstract: Temozolomide (TEM) showed encouraging results in well-differentiat ed pancreatic neuroendocrine tumors (WDPNETs). Low O(6)-methylguanine-DNA me thyltransferase (MGMT) expression and MGMT promoter methylation within tumor s correlate with a better outcome under TEM-based chemotherapy in glioblasto ma. We aimed to assess whether MGMT expression and MGMT promoter methylation could help predict the efficacy of TEM-based chemotherapy in patients with W DPNET. Consecutive patients with progressive WDPNET and/or liver involvement over 50% who received TEM between 2006 and 2012 were retrospectively studied . Tumor response was assessed according to Response Evaluation Criteria in S olid Tumors (RECIST) 1.1 guidelines. Nuclear expression of MGMT was assessed by immunochemistry (H-score, 0-300) and MGMT promoter methylation by pyroseq uencing. Forty-three patients (21 men, 58years (27-84)) with grade 1 WDPNET (n=6) or 2 (n=36) were analyzed. Objective response, stable disease, and pro gression rates were seen in 17 patients (39.5%), 18 patients (41.9%), and 8 patients (18.6%), respectively. Low MGMT expression (≤50) was associated wit h radiological objective response (P=0.04) and better progression-free survi val (PFS) (HR=0.35 (0.15-0.81), P=0.01). Disease control rate at 18months of treatment remained satisfying with an MGMT score up to 100 (74%) but dropped with a higher expression. High MGMT promoter methylation was associated with a low MGMT expression and longer PFS (HR=0.37 (0.29-1.08), P=0.05). Low MGMT score (≤50) appears to predict an objective tumor response, whereas an inter mediate MGMT score (50-100) seems to be associated with prolonged stable dis ease.
Journal Title: Endocrine-related cancer

PUBMED ID: 27334978
DOI: doi.org/10.1007/s11864-016-0418-0
Titolo: Targeted Therapeutics in Patients With High-Grade Gliomas: Past, Pre sent, and Future.
Autori: Chen R., Cohen AL., Colman H.
Data di Pubblicazione: 2016-06-24
Abstract: High-grade gliomas remain incurable despite current therapies, whi ch are plagued by high morbidity and mortality. Molecular categorization of glioma subtypes using mutations in isocitrate dehydrogenase 1/2 (IDH1/2), TP 53, and ATRX; codeletion of chromosomes 1p and 19q; DNA methylation; and amp lification of genes such as epidermal growth factor receptor (EGFR) and plat

elet-derived growth factor receptor, alpha polypeptide provides a more accur
ate prognostication and biologic classification than classical histopatholog
ical diagnoses, and a number of molecular markers are being incorporated in
the new World Health Organization classification of gliomas. However, despit
e the improved understanding of the molecular subtypes of gliomas and the un
derlying alterations in specific signaling pathways, these observations have
so far failed to result in the successful application of targeted therapies,
as has occurred in other solid tumors. To date, the only targeted therapy fo
r gliomas approved by the US Food and Drug Administration is bevacizumab, wh
ich targets vascular endothelial growth factor. EGFR remains a dominant mole
cular alteration in specific glioma subtypes and represents a potentially pr
omising target, with drugs of multiple types targeting EGFR in development i
ncluding vaccines, antibody drug conjugates, and chimeric antigen receptor (
CAR) T cells, despite the prior failures of EGFR tyrosine kinase inhibitors.
Immune therapies under investigation include checkpoint inhibitors, vaccines
against tumor-associated antigens and tumor-specific antigens, pulsed dendri
tic cells, heat shock protein-tumor conjugates, and CAR T cells. Mutations i
n the IDH1/2 genes are central to gliomagenesis in a high proportion of grad
e II and III gliomas, and ongoing trials are examining vaccines against IDH1
, small molecular inhibitors of IDH1 and IDH2, and metabolic components incl
uding NAD+ depletion to target IDH-mutated gliomas. The central role of DNA
methylation in a subset of gliomas may be targetable, but better understandi
ng of the relation between epigenetic alterations and resulting tumor biolog
y appears necessary. Ultimately, given the prior failure of single-agent tar
geted therapy in high-grade gliomas, it appears that novel combinatorial the
rapy or targeted drugs with immunomodulatory or epigenetic approaches will l
ikely be necessary to successfully combat these challenging tumors.
Journal Title: Current treatment options in oncology

PUBMED ID: 27318492
DOI: doi.org/10.1007/s00432-016-2187-3
Titolo: The earlier the better? Bevacizumab in the treatment of recurrent MG
MT-non-methylated glioblastoma.
Autori: Schaub C., Schäfer N., Mack F., Stuplich M., Kebir S., Niessen M., T
zaridis T., Banat M., Vatter H., Waha A., Herrlinger U., Glas M.
Data di Pubblicazione: 2016-06-20
Abstract: Our findings suggest that early treatment with BEV in patients wit
h MGMT-non-methylated relapsed GBM is associated with a better PFS, but not
with superior OS, possibly implicating that the early, i.e., second-line, us
e of BEV is not mandatory and BEV treatment may safely be delayed to third-l
ine therapy in this subgroup of patients.
Journal Title: Journal of cancer research and clinical oncology

PUBMED ID: 27311324
DOI: doi.org/10.1186/s40478-016-0331-6
Titolo: ATRX immunostaining predicts IDH and H3F3A status in gliomas.
Autori: Ebrahimi A., Skardelly M., Bonzheim I., Ott I., Mühleisen H., Eckert
F., Tabatabai G., Schittenhelm J.
Data di Pubblicazione: 2016-06-18
Abstract: Gliomas are the most frequent intraaxial CNS neoplasms with a hete
rogeneous molecular background. Recent studies on diffuse gliomas have shown
frequent alterations in the genes involved in chromatin remodelling pathways
such as α-thalassemia/mental-retardation-syndrome-X-linked gene (ATRX). Yet,
the reliability of ATRX in predicting isocitrate dehydrogenase (IDH) and H3
histone, family 3A (H3F3A) mutations in gliomas, is unclear.We analysed the
ATRX expression status by immunohistochemistry, in a large series of 1064 gl
iomas and analysed the results in correlation to IDH, H3F3A and loss of hete
rozygosity (LOH) 1p/19q status in these tumors. We also investigated the pro

gnostic potential of ATRX concerning the clinical outcome of patients with diffuse gliomas.According to our results, loss of nuclear ATRX expression was accompanied with an astrocytic tumor lineage and a younger age of onset. ATRX loss in astrocytomas was also strongly associated with IDH1/2 and H3F3A mutation ($p < 0.0001$). Among 196 glial tumors with nuclear ATRX loss, 173 (89 %) had an IDH1 or IDH2 mutation. Among the remaining 23 cases (11 %) with ATRX loss and IDH wild type status, 7 cases had a H3F3A G34R mutation (3 %) and 2 cases had a H3F3A K27M mutation (1 %). ATRX retention in IDH1/2 mutant tumors was strongly associated with LOH 1p/19q and oligodendroglioma histology ($p < 0.0001$). We also confirmed the significant prognostic role of ATRX. Diffuse gliomas with ATRX loss ($n = 137$, median 1413 days, 95 % CI: 1065-1860 days) revealed a significantly better clinical outcome compared with tumors with ATRX retention ($n = 335$, median: 609, 95 % CI: 539-760 days, HR = 1.81, $p < 0.0001$).In conclusion, ATRX is a potential marker for prediction of IDH/H3F3A mutations and substratification of diffuse gliomas into survival relevant tumor groups. Such classification is of great importance for further clinical decision making especially concerning the therapeutic options available for diffuse gliomas.
Journal Title: Acta neuropathologica communications

PUBMED ID: 27306443
DOI: doi.org/10.1007/s11060-016-2167-0
Titolo: Myxopapillary ependymoma: a SEER analysis of epidemiology and outcomes.
Autori: Bates JE., Choi G., Milano MT.
Data di Pubblicazione: 2016-06-17
Abstract: Myxopapillary ependymoma (MPE) is an exceedingly rare tumor histology. While surgery is clearly the treatment of choice, controversy exists regarding the role of adjuvant radiotherapy (RT). Using the Surveillence, epidemiology, and end results (SEER) database, we aimed to determine the epidemiology, prognostic factors, and treatment-related outcomes for MPE. A total of 773 cases were found in the SEER database. The incidence in the American population was found to be 1.00 per million person-years. On multivariate analysis, receipt of surgery (HR = 0.14, CI = 0.06-0.35, $p < 0.001$), receipt of RT (HR = 4.06, CI = 1.87-8.81, $p < 0.001$), age less than 30 (HR = 0.24, CI = 0.08-0.72, $p = 0.01$), and Caucasian race (HR = 0.37, CI = 0.13-0.996, $p = 0.049$) were statistically significant prognostic factors. The mean tumor size among those receiving RT (4.6 cm) was significantly larger than among those not receiving RT (3.2 cm, $p = 0.0002$). Those who lived in metropolitan areas were more likely to receive RT than those who did not. Given multiple previous studies show that RT improves PFS and the discrepancy in tumor size, selection bias is likely a significant contributor to the apparent negative impact of RT on OS. Regardless, surgery remains the most crucial aspect in the care of patients with MPE.
Journal Title: Journal of neuro-oncology

PUBMED ID: 27287048
DOI: doi.org/10.1186/s12885-016-2399-6
Titolo: Can advanced new radiation therapy technologies improve outcome of high grade glioma (HGG) patients? analysis of 3D-conformal radiotherapy (3DCRT) versus volumetric-modulated arc therapy (VMAT) in patients treated with surgery, concomitant and adjuvant chemo-radiotherapy.
Autori: Navarria P., Pessina F., Cozzi L., Ascolese AM., Lobefalo F., Stravato A., D'Agostino G., Franzese C., Caroli M., Bello L., Scorsetti M.
Data di Pubblicazione: 2016-06-12
Abstract: VMAT resulted superior to 3DCRT in terms of dosimetric findings and clinical results.

Journal Title: BMC cancer

PUBMED ID: 27285546
DOI: doi.org/10.3171/2016.4.JNS152771
Titolo: Eosinophilic meningitis triggered by implanted Gliadel wafers: case report.
Autori: Saito K., Yamasaki K., Yokogami K., Ivanova A., Takeishi G., Sato Y., Takeshima H.
Data di Pubblicazione: 2016-06-11
Abstract: Although carmustine (Gliadel) wafers improve local tumor control and extend the overall survival in patients with malignant glioma, adverse effects have been documented. The authors report the first case of eosinophilic meningitis triggered by the placement of Gliadel wafers. A 61-year-old man with a history of alimentary allergy and glioblastoma in the right frontal lobe underwent resection followed by the implantation of Gliadel wafers. Three weeks later he suffered the sudden onset of headache, vomiting, and progressive consciousness disturbance. Computed tomography revealed enlargement of the ventricular system and subdural space on the side of the tumor. His CSF leukocyte count increased up to 3990 cells/mm
Journal Title: Journal of neurosurgery

PUBMED ID: 27269943
DOI: doi.org/10.1200/JCO.2015.65.7825
Titolo: Therapeutic Impact of Cytoreductive Surgery and Irradiation of Posterior Fossa Ependymoma in the Molecular Era: A Retrospective Multicohort Analysis.
Autori: Ramaswamy V., Hielscher T., Mack SC., Lassaletta A., Lin T., Pajtler KW., Jones DT., Luu B., Cavalli FM., Aldape K., Remke M., Mynarek M., Rutkowski S., Gururangan S., McLendon RE., Lipp ES., Dunham C., Hukin J., Eisenstat DD., Fulton D., van Landeghem FK., Santi M., van Veelen ML., Van Meir EG., Osuka S., Fan X., Muraszko KM., Tirapelli DP., Oba-Shinjo SM., Marie SK., Carlotti CG., Lee JY., Rao AA., Giannini C., Faria CC., Nunes S., Mora J., Hamilton RL., Hauser P., Jabado N., Petrecca K., Jung S., Massimi L., Zollo M., Cinalli G., Bognár L., Klekner A., Hortobágyi T., Leary S., Ermoian RP., Olson JM., Leonard JR., Gardner C., Grajkowska WA., Chambless LB., Cain J., Eberhart CG., Ahsan S., Massimino M., Giangaspero F., Buttarelli FR., Packer RJ., Emery L., Yong WH., Soto H., Liau LM., Everson R., Grossbach A., Shalaby T., Grotzer M., Karajannis MA., Zagzag D., Wheeler H., von Hoff K., Alonso MM., Tuñon T., Schüller U., Zitterbart K., Sterba J., Chan JA., Guzman M., Elbabaa SK., Colman H., Dhall G., Fisher PG., Fouladi M., Gajjar A., Goldman S., Hwang E., Kool M., Ladha H., Vera-Bolanos E., Wani K., Lieberman F., Mikkelsen T., Omuro AM., Pollack IF., Prados M., Robins HI., Soffietti R., Wu J., Metellus P., Tabori U., Bartels U., Bouffet E., Hawkins CE., Rutka JT., Dirks P., Pfister SM., Merchant TE., Gilbert MR., Armstrong TS., Korshunov A., Ellison DW., Taylor MD.
Data di Pubblicazione: 2016-06-09
Abstract: The most impactful biomarker for posterior fossa ependymoma is molecular subgroup affiliation, independent of other demographic or treatment variables. However, both EPN_PFA and EPN_PFB still benefit from increased extent of resection, with the survival rates being particularly poor for subtotally resected EPN_PFA, even with adjuvant radiation therapy. Patients with EPN_PFB who undergo gross total resection are at lower risk for relapse and should be considered for inclusion in a randomized clinical trial of observation alone with radiation reserved for those who experience recurrence.
Journal Title: Journal of clinical oncology : official journal of the American Society of Clinical Oncology

PUBMED ID: 27253224
DOI: doi.org/10.1371/journal.pone.0155315
Titolo: Addition of Anti-Angiogenetic Therapy with Bevacizumab to Chemo- and Radiotherapy for Leptomeningeal Metastases in Primary Brain Tumors.
Autori: Burger MC., Zeiner PS., Jahnke K., Wagner M., Mittelbronn M., Steinbach JP.
Data di Pubblicazione: 2016-06-03
Abstract: Leptomeningeal dissemination of a primary brain tumor is a condition which is challenging to treat, as it often occurs in rather late disease stages in highly pretreated patients. Its prognosis is dismal and there is still no accepted standard of care. We report here a good clinical effect with a partial response in three out of nine patients and a stable disease with improvement on symptoms in two more patients following systemic anti-angiogenic treatment with bevacizumab (BEV) alone or in combination with chemo- and/or radiotherapy in a series of patients with leptomeningeal dissemination from primary brain tumors (diffuse astrocytoma WHO°II, anaplastic astrocytoma WHO°III, anaplastic oligodendroglioma WHO°III, primitive neuroectodermal tumor and glioblastoma, both WHO°IV). This translated into effective symptom control in five out of nine patients, but only moderate progression-free and overall survival times were reached. Partial responses as assessed by RANO criteria were observed in three patients (each one with anaplastic oligodendroglioma, primitive neuroectodermal tumor and glioblastoma). In these patients progression-free survival (PFS) intervals of 17, 10 and 20 weeks were achieved. In three patients (each one with diffuse astrocytoma, anaplastic astrocytoma and primitive neuroectodermal tumor) stable disease was observed with PFS of 13, 30 and 8 weeks. Another three patients (all with glioblastoma) were primary non-responders and deteriorated rapidly with PFS of 3 to 4 weeks. No severe adverse events were seen. These experiences suggest that the combination of BEV with more conventional therapy schemes with chemo- and/or radiotherapy may be a palliative treatment option for patients with leptomeningeal dissemination of brain tumors.
Journal Title: PloS one

PUBMED ID: 27252150
DOI: doi.org/10.1002/cam4.734
Titolo: Prognostic value of health-related quality of life for death risk stratification in patients with unresectable glioblastoma.
Autori: Paquette B., Vernerey D., Chauffert B., Dabakuyo S., Feuvret L., Taillandier L., Frappaz D., Taillia H., Schott R., Ducray F., Fabbro M., Tennevet I., Ghiringhelli F., Guillamo JS., Durando X., Castera D., Frenay M., Campello C., Dalban C., Skrzypski J., Chinot O., Anota A., Bonnetain F.
Data di Pubblicazione: 2016-06-03
Abstract: Glioblastoma is the most common malignant brain tumor in adults. Baseline health-related quality of life (HRQoL) is a major subject of concern for these patients. We aimed to assess the independent prognostic value of HRQoL in unresectable glioblastoma (UGB) patients for death risk stratification. One hundred and thirty-four patients with UGB were enrolled from the TEMAVIR trial. HRQoL was evaluated at baseline using the EORTC QLQ-C30 and BN20 brain cancer module. Clinical and HRQoL parameters were evaluated in univariable and multivariable Cox analysis as prognostic factors for overall survival (OS). Performance assessment and internal validation of the final model were evaluated with Harrel's C-index, calibration plot, and bootstrap sample procedure. Two OS independent predictors were identified: future uncertainty and sensitivity deficit. The final model exhibited good calibration and acceptable discrimination (C statistic = 0.63). The internal validity of the model was verified with robust uncertainties around the hazard ratio. The prognostic score identified three groups of patients with distinctly different risk profiles with median OS estimated at 16.2, 9.2, and 4.5 months. We demonstrated the additional prognostic value of HRQoL in UGB for death risk strati

fication and provided a score that may help to guide clinical management and stratification in future clinical trials.
Journal Title: Cancer medicine

PUBMED ID: 27245820
DOI: doi.org/10.1007/s00066-016-0987-7
Titolo: Clinically significant CMV (re)activation during or after radiotherapy/chemotherapy of the brain : Correlation with neurological deterioration and improvement upon antiviral treatment.
Autori: Goerig N., Semrau S., Frey B., Korn K., Fleckenstein B., Überla K., Dörfler A., Putz F., Gaipl US., Fietkau R.
Data di Pubblicazione: 2016-06-02
Abstract: Further prospective studies verifying and investigating this observation in terms of frequency and clinical relevance seem indicated.
Journal Title: Strahlentherapie und Onkologie : Organ der Deutschen Rontgenesellschaft ... [et al]

PUBMED ID: 27232884
DOI: doi.org/10.1371/journal.pone.0156369
Titolo: Multi-Center Randomized Phase II Study Comparing Cediranib plus Gefitinib with Cediranib plus Placebo in Subjects with Recurrent/Progressive Glioblastoma.
Autori: Brown N., McBain C., Nash S., Hopkins K., Sanghera P., Saran F., Phillips M., Dungey F., Clifton-Hadley L., Wanek K., Krell D., Jeffries S., Khan I., Smith P., Mulholland P.
Data di Pubblicazione: 2016-05-28
Abstract: ClinicalTrials.gov NCT01310855.
Journal Title: PloS one

PUBMED ID: 27193554
DOI: doi.org/10.1007/s11060-016-2144-7
Titolo: Prognostic factors in recurrent glioblastoma patients treated with bevacizumab.
Autori: Schaub C., Tichy J., Schäfer N., Franz K., Mack F., Mittelbronn M., Kebir S., Thiepold AL., Waha A., Filmann N., Banat M., Fimmers R., Steinbach JP., Herrlinger U., Rieger J., Glas M., Bähr O.
Data di Pubblicazione: 2016-05-20
Abstract: The value of bevacizumab (BEV) in recurrent glioblastoma is unclear. Imaging parameters and progression-free survival (PFS) are problematic endpoints. Few data exist on clinical factors influencing overall survival (OS) in unselected patients with recurrent glioblastoma exposed to BEV. We retrospectively analyzed 174 patients with recurrent glioblastoma treated with BEV at two German brain tumor centers. We evaluated general patient characteristics, MGMT status, pretreatment, concomitant oncologic treatment and overall survival. Karnofsky performance score, number of prior chemotherapies, number of prior recurrences and combined treatment with irinotecan (IRI) were significantly associated with OS in univariate analysis. We did not find differences in OS related to sex, age, histology, MGMT status, prior surgical treatment or number of prior radiotherapies. Combined treatment with IRI and higher KPS both remained significantly associated with prolonged survival in multivariate analysis, but patients receiving IRI co-treatment had less advanced disease. Grouping into clinically relevant categories revealed an OS of 16.9 months from start of BEV in patients with first recurrence and KPS ≥ 80 % (n = 25). In contrast, in patients with second recurrence and KPS < 80 %, OS was 3.6 months (n = 27). Our observational data support an early use of BEV in patients with good performance status. The benefit of co-treatment with IRI in our cohort seems to be the result of biased patient recruitment.

Journal Title: Journal of neuro-oncology

PUBMED ID: 27189273
DOI: doi.org/10.3349/ymj.2016.57.4.824
Titolo: Re-Irradiation for Recurrent Gliomas: Treatment Outcomes and Prognostic Factors.
Autori: Lee J., Cho J., Chang JH., Suh CO.
Data di Pubblicazione: 2016-05-19
Abstract: Re-irradiation in conjunction with surgery could be a salvage treatment for selected recurrent glioma patients with good performance status and recurrence over a long time.
Journal Title: Yonsei medical journal

PUBMED ID: 27165580
DOI: doi.org/10.1007/s11060-016-2136-7
Titolo: Clinical outcome of an alternative fotemustine schedule in elderly patients with recurrent glioblastoma: a mono-institutional retrospective study.
Autori: Lombardi G., Bellu L., Pambuku A., Della Puppa A., Fiduccia P., Farina M., D'Avella D., Zagonel V.
Data di Pubblicazione: 2016-05-12
Abstract: The optimal treatment of recurrent glioblastoma (GBM) in elderly patients is unclear. Fotemustine (FTM) is a third-generation nitrosourea showing efficacy in gliomas and it has been used with different schedules in adult patients. We performed, for the first time anywhere, a mono-institutional retrospective study to analyze the clinical outcome of an alternative fotemustine schedule in elderly patients with recurrent GBM. Retrospectively, we analyzed all GBM patients 65 years or older previously treated with the combination of radiation therapy and temozolomide (TMZ), receiving an alternative FTM schedule as second-line treatment at our Oncological Center from October 2011 to October 2014 with an ECOG PS ≤ 2. FTM was administrated at 80 mg/m(2) every 2 weeks for five consecutive administrations (induction phase), and then every 4 weeks at 80 mg/m(2) as maintenance. We enrolled 44 patients, 33 males and 11 females; average age was 70 years. ECOG PS was 0-1 in 80 % of the patients. 38 patients relapsed during temozolomide (TMZ) therapy. MGMT methylation status was analyzed in 34 patients and MGMT was methylated in 53 % of the patients. The median progression free survival (PFS) and overall survival (OS) from FTM treatment was 4.1 months (95 % CI 3.1-5.2) and 7 months (95 % CI 5.2-8.4), respectively. Patients with MGMT methylated status and patients who relapsed after completing TMZ therapy had a longer PFS and OS from the beginning of FTM. Thrombocytopenia was the most frequent grade 3-4 haematological toxicity (9 %). The alternative schedule of FTM may be an active and safe treatment for elderly patients with recurrent glioblastoma, especially patients with methylated MGMT and who relapsed after completing temozolomide therapy.
Journal Title: Journal of neuro-oncology

PUBMED ID: 27154166
DOI: doi.org/10.1007/s11060-016-2137-6
Titolo: Update on the evidence-based clinical practice parameter guidelines for the treatment of adults with diffuse low grade glioma: the role of initial chemotherapy.
Autori: Ziu M., Olson JJ.
Data di Pubblicazione: 2016-05-08
Abstract:
Journal Title: Journal of neuro-oncology

PUBMED ID: 27108796
DOI: doi.org/10.1016/j.wneu.2016.04.030
Titolo: Progressive Low-Grade Glioma: Assessment of Prognostic Importance of Histologic Reassessment and MRI Findings.
Autori: Narang AK., Chaichana KL., Weingart JD., Redmond KJ., Lim M., Olivi A., Quinones-Hinojosa A., Kleinberg LR.
Data di Pubblicazione: 2016-04-26
Abstract: In patients with progressive LGG, new MRI enhancement and patholog ic grade were discordant in greater than 20% of cases. Pathologic confirmati on of grade should therefore be attempted, when safe, to dictate management. Beyond functioning as a surrogate for pathologic grade, new MRI enhancement may predict for worse outcomes, a concept that merits prospective investigat ion.
Journal Title: World neurosurgery

PUBMED ID: 27106406
DOI: doi.org/10.1093/neuonc/now063
Titolo: Restriction spectrum imaging predicts response to bevacizumab in pat ients with high-grade glioma.
Autori: McDonald CR., Delfanti RL., Krishnan AP., Leyden KM., Hattangadi-Glu th JA., Seibert TM., Karunamuni R., Elbe P., Kuperman JM., Bartsch H., Picci oni DE., White NS., Dale AM., Farid N.
Data di Pubblicazione: 2016-04-24
Abstract: RSI is less influenced by changes in edema, conferring an advantag e of RSI over ADC for evaluating response to anti-angiogenic therapy in pati ents with HGG.
Journal Title: Neuro-oncology

PUBMED ID: 27083133
DOI: doi.org/10.1016/j.jocn.2015.12.028
Titolo: A national perspective of adult gangliogliomas.
Autori: Varshneya K., Sarmiento JM., Nuño M., Lagman C., Mukherjee D., Nuño K., Babu H., Patil CG.
Data di Pubblicazione: 2016-04-17
Abstract: Gangliogliomas (GG) are rare tumors of the nervous system. Patient characteristics and clinical outcomes of low and high-grade GG have been dif ficult to elucidate in the adult population. This study aims to further elab orate on GG treatment and overall survival utilizing a larger cohort than pr eviously published. The USA National Cancer Database was utilized to evaluat e adult (age 18years and older) patients diagnosed with GG between 2004 and 2006. Descriptive statistics and Kaplan-Meier overall survival estimates wer e provided. A total of 198 adult GG patients were diagnosed between 2004 and 2006. Of these, 181 (91.4%) were low-grade and 17 (8.6%) high-grade GG. Over all, the median age was 36years; approximately 50% of patients were female, and 86.5% Caucasian. Most patients (59%) had near/gross total resection. Rad iation and chemotherapy were prescribed in 18 (9.1%) and 11 (5.7%) patients, respectively. Radiation (64.7% versus 3.9%, p<.0001) and chemotherapy (47.1% versus 1.7%, p<.0001) were more frequently given to patients with high-grade tumors than low-grade. The median overall survival of high-grade GG was 44.4 months (95% confidence interval [CI]: 10.5-92.5) while the corresponding est imate for low-grade tumors was not reached. Older age (hazard ratio [HR] 1.7 2, 95% CI: 1.26-2.34) and high tumor grade (HR 3.91, 95% CI: 1.43-10.8) were found to be associated with poor survival. Adult GG have a temporal lobe pre dilection and overall gross total resection rate of 59%. Older patients with high-grade tumors had an increased hazard of mortality. High-grade GG were s ignificantly more likely to be treated with radiation therapy and chemothera py.

Journal Title: Journal of clinical neuroscience : official journal of the Ne
urosurgical Society of Australasia

PUBMED ID: 27069431
DOI: doi.org/10.1016/j.jcm.2016.02.004
Titolo: Previously Undiagnosed Malignant Brain Tumor Discovered During Exami
nation of a Patient Seeking Chiropractic Care.
Autori: Anderson B.
Data di Pubblicazione: 2016-04-13
Abstract: This report describes the clinical presentation, examination, and
medical management of a 30-year-old man presenting to a chiropractic practic
e with an unsuspected malignant brain tumor.
Journal Title: Journal of chiropractic medicine

PUBMED ID: 27057742
DOI: doi.org/10.1159/000443719
Titolo: Clinical Impact of Bevacizumab in Patients with Relapsed Glioblastom
a: Focus on a Real-Life Monocentric SurVey (SV1 Study).
Autori: Rivoirard R., Chargari C., Guy JB., Nuti C., Peoc'h M., Forest F., F
alk AT., Garin C., Adjabi A., Hoarau D., Fotso MJ., Langrand Escure J., Mori
ceau G., Fournel P., Boutet C., Magné N.
Data di Pubblicazione: 2016-04-09
Abstract: The results of the SV1 study are consistent with those found in ph
ase II studies evaluating the same treatment. The irinotecan-BVZ combination
is effective in relapsed glioblastoma with acceptable toxicity. Biomarkers p
redictive of response to BVZ should help in the selection of patients who co
uld benefit from treatment.
Journal Title: Chemotherapy

PUBMED ID: 27008208
DOI: doi.org/10.1088/0031-9155/61/8/3084
Titolo: Precise image-guided irradiation of small animals: a flexible non-pr
ofit platform.
Autori: Tillner F., Thute P., Löck S., Dietrich A., Fursov A., Haase R., Luk
as M., Rimarzig B., Sobiella M., Krause M., Baumann M., Bütof R., Enghardt W
.
Data di Pubblicazione: 2016-03-24
Abstract: Preclinical in vivo studies using small animals are essential to d
evelop new therapeutic options in radiation oncology. Of particular interest
are orthotopic tumour models, which better reflect the clinical situation in
terms of growth patterns and microenvironmental parameters of the tumour as
well as the interplay of tumours with the surrounding normal tissues. Such o
rthotopic models increase the technical demands and the complexity of precli
nical studies as local irradiation with therapeutically relevant doses requi
res image-guided target localisation and accurate beam application. Moreover
, advanced imaging techniques are needed for monitoring treatment outcome. W
e present a novel small animal image-guided radiation therapy (SAIGRT) syste
m, which allows for precise and accurate, conformal irradiation and x-ray im
aging of small animals. High accuracy is achieved by its robust construction
, the precise movement of its components and a fast high-resolution flat-pan
el detector. Field forming and x-ray imaging is accomplished close to the an
imal resulting in a small penumbra and a high image quality. Feasibility for
irradiating orthotopic models has been proven using lung tumour and glioblas
toma models in mice. The SAIGRT system provides a flexible, non-profit acade
mic research platform which can be adapted to specific experimental needs an
d therefore enables systematic preclinical trials in multicentre research ne
tworks.

Journal Title: Physics in medicine and biology

PUBMED ID: 27006178
DOI: doi.org/10.1093/neuonc/now046
Titolo: Upfront bevacizumab may extend survival for glioblastoma patients wh o do not receive second-line therapy: an exploratory analysis of AVAglio.
Autori: Chinot OL., Nishikawa R., Mason W., Henriksson R., Saran F., Cloughe sy T., Garcia J., Revil C., Abrey L., Wick W.
Data di Pubblicazione: 2016-03-24
Abstract: This exploratory analysis suggests that the addition of bevacizuma b to standard glioblastoma treatment prolongs PFS and OS for patients with P D who receive only one line of therapy.
Journal Title: Neuro-oncology

PUBMED ID: 26970559
DOI: doi.org/10.1002/cncr.29907
Titolo: Clinical and treatment factors determining long-term outcomes for ad ult survivors of childhood low-grade glioma: A population-based study.
Autori: Krishnatry R., Zhukova N., Guerreiro Stucklin AS., Pole JD., Mistry M., Fried I., Ramaswamy V., Bartels U., Huang A., Laperriere N., Dirks P., N athan PC., Greenberg M., Malkin D., Hawkins C., Bandopadhayay P., Kieran MW. , Manley PE., Bouffet E., Tabori U.
Data di Pubblicazione: 2016-03-13
Abstract: The course of PLGG is associated with excellent long-term survival , but this is hampered by increased delayed mortality in patients receiving upfront radiotherapy. These observations should be considered when treatment options are being weighed for these patients.
Journal Title: Cancer

PUBMED ID: 26947725
DOI: doi.org/10.1016/j.wneu.2016.02.095
Titolo: Primary Intracranial Extra-Axial Anaplastic Ependymomas.
Autori: Yang Y., Tian KB., Hao SY., Wu Z., Li D., Zhang JT.
Data di Pubblicazione: 2016-03-08
Abstract: IEAEs are rare and have a wide spectrum of clinical and radiologic al phenotypes. Preoperative diagnosis is difficult. Favorable outcomes for I EAEs can be achieved by GTR plus radiotherapy. Multiple IEAEs benefit from t ailored staged surgical resection plus radiotherapy.
Journal Title: World neurosurgery

PUBMED ID: 26944115
DOI: doi.org/10.1016/j.jns.2016.01.006
Titolo: Autoimmune atypical parkinsonism - A group of treatable parkinsonism .
Autori: Kannoth S., Anandakkuttan A., Mathai A., Sasikumar AN., Nambiar V.
Data di Pubblicazione: 2016-03-06
Abstract: Autoimmune atypical parkinsonism is characterized by atypical park insonism with neuronal specific antibodies, sometimes associated with abnorm al CSF and significant response to immunotherapy.
Journal Title: Journal of the neurological sciences

PUBMED ID: 26939704
DOI: doi.org/10.1158/1535-7163.MCT-15-0758
Titolo: Entrectinib, a Pan-TRK, ROS1, and ALK Inhibitor with Activity in Mul tiple Molecularly Defined Cancer Indications.

Autori: Ardini E., Menichincheri M., Banfi P., Bosotti R., De Ponti C., Pulc i R., Ballinari D., Ciomei M., Texido G., Degrassi A., Avanzi N., Amboldi N. , Saccardo MB., Casero D., Orsini P., Bandiera T., Mologni L., Anderson D., Wei G., Harris J., Vernier JM., Li G., Felder E., Donati D., Isacchi A., Pes enti E., Magnaghi P., Galvani A.
Data di Pubblicazione: 2016-03-05
Abstract: Activated ALK and ROS1 tyrosine kinases, resulting from chromosoma l rearrangements, occur in a subset of non-small cell lung cancers (NSCLC) a s well as other tumor types and their oncogenic relevance as actionable targ ets has been demonstrated by the efficacy of selective kinase inhibitors suc h as crizotinib, ceritinib, and alectinib. More recently, low-frequency rear rangements of TRK kinases have been described in NSCLC, colorectal carcinoma , glioblastoma, and Spitzoid melanoma. Entrectinib, whose discovery and prec linical characterization are reported herein, is a novel, potent inhibitor o f ALK, ROS1, and, importantly, of TRK family kinases, which shows promise fo r therapy of tumors bearing oncogenic forms of these proteins. Proliferation profiling against over 200 human tumor cell lines revealed that entrectinib is exquisitely potent in vitro against lines that are dependent on the drug' s pharmacologic targets. Oral administration of entrectinib to tumor-bearing mice induced regression in relevant human xenograft tumors, including the TR KA-dependent colorectal carcinoma KM12, ROS1-driven tumors, and several ALK- dependent models of different tissue origins, including a model of brain-loc alized lung cancer metastasis. Entrectinib is currently showing great promis e in phase I/II clinical trials, including the first documented objective re sponses to a TRK inhibitor in colorectal carcinoma and in NSCLC. The drug is , thus, potentially suited to the therapy of several molecularly defined can cer settings, especially that of TRK-dependent tumors, for which no approved drugs are currently available. Mol Cancer Ther; 15(4); 628-39. ©2016 AACR.
Journal Title: Molecular cancer therapeutics

PUBMED ID: 26934681
DOI: doi.org/10.1002/ijc.30069
Titolo: LOC283731 promoter hypermethylation prognosticates survival after ra diochemotherapy in IDH1 wild-type glioblastoma patients.
Autori: Mock A., Geisenberger C., Orlik C., Warta R., Schwager C., Jungk C., Dutruel C., Geiselhart L., Weichenhan D., Zucknick M., Nied AK., Friauf S., Exner J., Capper D., Hartmann C., Lahrmann B., Grabe N., Debus J., von Deiml ing A., Popanda O., Plass C., Unterberg A., Abdollahi A., Schmezer P., Herol d-Mende C.
Data di Pubblicazione: 2016-03-03
Abstract: MGMT promoter methylation status is currently the only established molecular prognosticator in IDH wild-type glioblastoma multiforme (GBM). The refore, we aimed to discover novel therapy-associated epigenetic biomarkers. After enrichment for hypermethylated fractions using methyl-CpG-immunoprecip itation (MCIp), we performed global DNA methylation profiling for 14 long-te rm (LTS; >36 months) and 15 short-term (STS; 6-10 months) surviving GBM pati ents. Even after exclusion of the G-CIMP phenotype, we observed marked diffe rences between the LTS and STS methylome. A total of 1,247 probes in 706 gen es were hypermethylated in LTS and 463 probes in 305 genes were found to be hypermethylated in STS patients (p values < 0.05, log2 fold change ± 0.5). We i dentified 13 differentially methylated regions (DMRs) with a minimum of four differentially methylated probes per gene. Indeed, we were able to validate a subset of these DMRs through a second, independent method (MassARRAY) in o ur LTS/STS training set (ADCY1, GPC3, LOC283731/ISLR2). These DMRs were furt her assessed for their prognostic capability in an independent validation co hort ($n = 62$) of non-G-CIMP GBMs from the TCGA. Hypermethylation of multiple CpGs mapping to the promoter region of LOC283731 correlated with improved pa tient outcome ($p = 0.03$). The prognostic performance of LOC283731 promoter hy

permethylation was confirmed in a third independent study cohort (n=89), an d was independent of gender, performance (KPS) and MGMT status (p=0.0485, H R=0.63). Intriguingly, the prediction was most pronounced in younger GBM pa tients (<60 years). In conclusion, we provide compelling evidence that promo ter methylation status of this novel gene is a prognostic biomarker in IDH1 wild-type/non-G-CIMP GBMs.
Journal Title: International journal of cancer

PUBMED ID: 26929887
DOI: doi.org/10.7759/cureus.460
Titolo: Long-term Remission Over Six Years for a Patient with Recurrent Glio blastoma Treated with Cediranib/Lomustine.
Autori: Drazin D., Al-Khouja L., Patel A., Hu J., Phuphanich S.
Data di Pubblicazione: 2016-03-02
Abstract: Cediranib is an orally available, pan-VEGFR tyrosine kinase inhibi tor. A previous Phase III study of patients with recurrent glioblastoma trea ted with this drug did not meet the primary end of progressive-free survival (PFS). We identified one patient, a 57-year-old Caucasian female who, follow ing surgery in October 2008 and concurrent temozolomide and radiation therap y from November 8, 2008, to January 6, 2009, developed a tumor progression o f the left posterior frontal measuring 1.2 x 1.5 cm in February 2009. She wa s enrolled in a randomized, Phase III, placebo-controlled, partially-blinded clinical trial of cediranib as either monotherapy or in combination with lom ustine (CCNU) versus CCNU. She was randomized to receive a combination thera py with 1st cycle CCNU 190 mg and cediranib 20 mg per day on April 15, 2009. However, she developed nephrotic syndrome and uncontrolled hypertension and was taken off this study in May 2010. Her six-week MRI showed a 50% tumor re gression and a complete response at twenty-four weeks. With no enhancement s een on MRI on June 4, 2015, she has been off therapy and in clinical remissi on over five years with high functional level and good quality of life (KPS-90%). This is a case report of successful therapy for recurrent glioblastoma with long-term remission despite termination of therapy greater than six yea rs from cediranib and limited CCNU dosage.
Journal Title: Cureus

PUBMED ID: 26904576
DOI: doi.org/10.3978/j.issn.2305-5839.2016.01.25
Titolo: Concurrent therapy to enhance radiotherapeutic outcomes in glioblast oma.
Autori: Khosla D.
Data di Pubblicazione: 2016-02-24
Abstract: Glioblastoma is one of the most fatal and incurable human cancers characterized by nuclear atypia, mitotic activity, intense microvascular pro liferation and necrosis. The current standard of care includes maximal safe surgical resection followed by radiation therapy (RT) with concurrent and ad juvant temozolomide (TMZ). The prognosis remains poor with median survival o f 14.6 months with RT plus TMZ. Majority will have a recurrence within 2 yea rs from diagnosis despite adequate treatment. Radiosensitizers, radiotherapy dose escalation and altered fractionation have failed to improve outcome. Th e molecular biology of glioblastoma is complex and poses treatment challenge s. High rate of mutation, genotypic and phenotypic heterogeneity, rapid deve lopment of resistance, existence of blood-brain barrier (BBB), multiple intr acellular and intercellular signalling pathways, over-expression of growth f actor receptors, angiogenesis and antigenic diversity renders the tumor cell s differentially susceptible to various treatment modalities. Thus, the trea tment strategies require personalised or individualized approach based on th e characteristics of tumor. Several targeted agents have been evaluated in c

linical trials but the results have been modest despite these advancements. This review summarizes the current standard of care, results of concurrent c hemoradiation trials, evolving innovative treatments that use targeted thera py with standard chemoradiation or RT alone, outcome of various recent trial s and future outlook.
Journal Title: Annals of translational medicine

PUBMED ID: 26885645
DOI: doi.org/10.1371/journal.pone.0149244
Titolo: Safety and Efficacy of 5-Aminolevulinic Acid for High Grade Glioma i n Usual Clinical Practice: A Prospective Cohort Study.
Autori: Teixidor P., Arráez MÁ., Villalba G., Garcia R., Tardáguila M., Gonz ález JJ., Rimbau J., Vidal X., Montané E.
Data di Pubblicazione: 2016-02-18
Abstract: In clinical practice, the 5-ALA showed a good safety profile, but the benefits related to 5-ALA have not been yet clearly shown. The improved differentiation expected by fluorescence between normal and tumor cerebral t issue was suboptimal in a relevant number of patients; in addition, the expe cted higher degree of resection was lower than in clinical trials as well as incomplete resection was not identified as a prognostic factor risk for deat h. Because optimal fluorescence was correlated to higher complete resection rate, further research is needed to identify patients (or tumors) with more surgery benefits when using the 5-ALA.
Journal Title: PloS one

PUBMED ID: 26879084
DOI: doi.org/10.1007/s11060-016-2074-4
Titolo: Small increases in enhancement on MRI may predict survival post radi otherapy in patients with glioblastoma.
Autori: Gzell CE., Wheeler HR., McCloud P., Kastelan M., Back M.
Data di Pubblicazione: 2016-02-17
Abstract: To assess impact of volumetric changes in tumour volume post chemo radiotherapy in glioblastoma. Patients managed with chemoradiotherapy betwee n 2008 and 2011 were included. Patients with incomplete MRI sets were exclud ed. Analyses were performed on post-operative MRI, and MRIs at 1 month (M+1) , 3 months (M+3), 5 months (M+5), 7 months (M+7), and 12 months (M+12) post completion of RT. RANO definitions of response were used for all techniques. Modified RANO criteria and two volumetric analysis techniques were used. The two volumetric analysis techniques involved utility of the Eclipse treatment planning software to calculate the volume of delineated tissue: surgical cav ity plus all surrounding enhancement (Volumetric) versus surrounding enhance ment only (Rim). Retrospective analysis of 49 patients with median survival of 18.4 months. Using Volumetric analysis the difference in MS for patients who had a <5 % increase versus ≥5 % at M+3 was 23.1 versus 15.1 months (p = 0.006), and M+5 was 26.3 versus 15.1 months (p = 0.006). For patients wh o were classified as progressive disease using modified RANO criteria at M+1 and M+3 there was a difference in MS compared with those who were not (M+1: 13.1 vs. 19.4 months, p = 0.017, M+3: 13.2 vs. 20.1 months, p = 0.096). An i ncrease in the volume of cavity and enhancement of ≥5 % at M+3 and M+5 post RT was associated with reduced survival, suggesting that increases in radiol ogical abnormality of <25 % may predict survival.
Journal Title: Journal of neuro-oncology

PUBMED ID: 26865253
DOI: doi.org/10.1186/s12885-016-2131-6
Titolo: Chemotherapy with BCNU in recurrent glioma: Analysis of clinical out come and side effects in chemotherapy-naïve patients.

Autori: Jungk C., Chatziaslanidou D., Ahmadi R., Capper D., Bermejo JL., Exner J., von Deimling A., Herold-Mende C., Unterberg A.
Data di Pubblicazione: 2016-02-12
Abstract: In this study, BCNU was rarely associated with severe side effects, particularly pulmonary toxicity, and, in case of recurrent glioblastoma, even conferred a favorable outcome. Therefore BCNU appears to be an appropriate alternative to other nitrosoureas although the efficacy against newer drugs needs further evaluation.
Journal Title: BMC cancer

PUBMED ID: 26853339
DOI: doi.org/10.1016/j.ijrobp.2015.10.032
Titolo: Gemcitabine Plus Radiation Therapy for High-Grade Glioma: Long-Term Results of a Phase 1 Dose-Escalation Study.
Autori: Kim MM., Camelo-Piragua S., Schipper M., Tao Y., Normolle D., Junck L., Mammoser A., Betz BL., Cao Y., Kim CJ., Heth J., Sagher O., Lawrence TS., Tsien CI.
Data di Pubblicazione: 2016-02-09
Abstract: Gemcitabine concurrent with RT is well-tolerated and yields promising outcomes, including in patients with adverse molecular features. It is a candidate for further study, particularly for poor-prognosis patient subgroups with HGG.
Journal Title: International journal of radiation oncology, biology, physics

PUBMED ID: 26803410
DOI: doi.org/10.1016/j.biomaterials.2016.01.007
Titolo: Fibrin matrices enhance the transplant and efficacy of cytotoxic stem cell therapy for post-surgical cancer.
Autori: Bagó JR., Pegna GJ., Okolie O., Hingtgen SD.
Data di Pubblicazione: 2016-01-25
Abstract: Tumor-homing cytotoxic stem cell (SC) therapy is a promising new approach for treating the incurable brain cancer glioblastoma (GBM). However, problems of retaining cytotoxic SCs within the post-surgical GBM resection cavity are likely to significantly limit the clinical utility of this strategy. Here, we describe a new fibrin-based transplant approach capable of increasing cytotoxic SC retention and persistence within the resection cavity, yet remaining permissive to tumoritropic migration. This fibrin-based transplant can effectively treat both solid and post-surgical human GBM in mice. Using our murine model of image-guided model of GBM resection, we discovered that suspending human mesenchymal stem cells (hMSCS) in a fibrin matrix increased initial retention in the surgical resection cavity 2-fold and prolonged persistence in the cavity 3-fold compared to conventional delivery strategies. Time-lapse motion analysis revealed that cytotoxic hMSCs in the fibrin matrix remain tumoritropic, rapidly migrating from the fibrin matrix to co-localize with cultured human GBM cells. We encapsulated hMSCs releasing the cytotoxic agent TRAIL (hMSC-sTR) in fibrin, and found hMSC-sTR/fibrin therapy reduced the viability of multiple 3-D human GBM spheroids and regressed established human GBM xenografts 3-fold in 11 days. Mimicking clinical therapy of surgically resected GBM, intra-cavity seeding of therapeutic hMSC-sTR encapsulated in fibrin reduced post-surgical GBM volumes 6-fold, increased time to recurrence 4-fold, and prolonged median survival from 15 to 36 days compared to control-treated animals. Fibrin-based SC therapy could represent a clinically compatible, viable treatment to suppress recurrence of post-surgical GBM and other lethal cancer types.
Journal Title: Biomaterials

PUBMED ID: 26792581

DOI: doi.org/10.1007/s10637-015-0320-9
Titolo: A dose escalating phase I study of GLPG0187, a broad spectrum integr in receptor antagonist, in adult patients with progressive high-grade glioma and other advanced solid malignancies.
Autori: Cirkel GA., Kerklaan BM., Vanhoutte F., Van der Aa A., Lorenzon G., Namour F., Pujuguet P., Darquenne S., de Vos FY., Snijders TJ., Voest EE., S chellens JH., Lolkema MP.
Data di Pubblicazione: 2016-01-22
Abstract: GLPG0187 was well tolerated with a dose-proportional PK profile up on continuous infusion. No formal maximal tolerated dose could be establishe d. GLPG0187 showed signs of target engagement with a favourable toxicity pro file. However, continuous infusion of GLPG0187 failed to show signs of monot herapy efficacy.
Journal Title: Investigational new drugs

PUBMED ID: 26750130
DOI: doi.org/10.1007/s11910-015-0615-4
Titolo: Current Management of Adult Diffuse Infiltrative Low Grade Gliomas.
Autori: Le Rhun E., Taillibert S., Chamberlain MC.
Data di Pubblicazione: 2016-01-12
Abstract: Diffuse infiltrative low grade gliomas (LGG) account for approxima tely 15 % of all gliomas. The prognosis of LGG differs between high-risk and low-risk patients notwithstanding varying definitions of what constitutes a high-risk patient. Maximal safe resection optimally is the initial treatment . Surgery that achieves a large volume resection improves both progression-f ree and overall survival. Based on results of three randomized clinical tria ls (RCT), radiotherapy (RT) may be deferred in patients with low-risk LGG (d efined as age <40 years and having undergone a complete resection), although combined chemoradiotherapy has never been prospectively evaluated in the low -risk population. The recent RTOG 9802 RCT established a new standard of car e in high-risk patients (defined as age >40 years or incomplete resection) b y demonstrating a nearly twofold improvement in overall survival with the ad dition of PCV (procarbazine, CCNU, vincristine) chemotherapy following RT as compared to RT alone. Chemotherapy alone as a treatment of LGG may result in less toxicity than RT; however, this has only been prospectively studied onc e (EORTC 22033) in high-risk patients. A challenge remains to define when an aggressive treatment improves survival without impacting quality of life (Qo L) or neurocognitive function and when an effective treatment can be delayed in order to preserve QoL without impacting survival. Current WHO histopathol ogical classification is poorly predictive of outcome in patients with LGG. The integration of molecular biomarkers with histology will lead to an impro ved classification that more accurately reflects underlying tumor biology, p rognosis, and hopefully best therapy.
Journal Title: Current neurology and neuroscience reports

PUBMED ID: 26711384
DOI: Mancante
Titolo: [Randomized controlled study of limited margins IMRT and temozolomid e chemotherapy in patients with malignant glioma].
Autori: Zhang W., Sun J., Cao Y., Yang X.
Data di Pubblicazione: 2015-12-30
Abstract: Both groups gained favorable results, and limited margins doesn't increase local failures. Surgery results are important prognostic factors to immediate-term prognosis and PFS-1.
Journal Title: Zhonghua yi xue za zhi

PUBMED ID: 26671314

DOI: doi.org/10.1016/j.jocn.2015.05.047
Titolo: Multiple resections and survival of recurrent glioblastoma patients in the temozolomide era.
Autori: Ortega A., Sarmiento JM., Ly D., Nuño M., Mukherjee D., Black KL., Patil CG.
Data di Pubblicazione: 2015-12-17
Abstract: Glioblastoma (GBM) is the most prevalent and aggressive primary brain tumor in adults for which recurrence is inevitable and surgical resection is often recommended. We investigated the relationship between multiple tumor resections and overall survival (OS) in adult glioblastoma patients who received adjuvant radiotherapy and temozolomide following initial surgery. We retrospectively reviewed the records of all newly diagnosed adult GBM patients with tumor recurrence at our institution from March 2003 to October 2012. Kaplan-Meier survival estimates and multivariate analysis using Cox's proportional hazards model were utilized to evaluate the impact of multiple resections on OS. A total of 202 GBM patients were analyzed; 83 (41.1%), 94 (46.5%), and 25 (12.4%) patients underwent one, two, and three or more total resections, respectively. Patients who underwent multiple resections were significantly younger ($p<0.0001$) and had higher perioperative Karnofsky Performance Status scores ($p<0.0001$) than single resection patients. The median OS in months was 21.1, 25.5, and 29.0 for patients who had one, two, and three or more resections, respectively (Wilcoxon $p=0.03$). In a confounder-adjusted multivariate model, patients with multiple resections did not have significantly improved survival ($p=0.55$). Older age was strongly associated with poorer OS (hazard ratio 1.34, $p<0.0001$). Age at diagnosis was the only predictor of survival for recurrent GBM patients. After adjusting for age at diagnosis, multiple resections were not an independent predictor of OS in our glioblastoma cohort treated in the temozolomide era.
Journal Title: Journal of clinical neuroscience : official journal of the Neurosurgical Society of Australasia

PUBMED ID: 26659583
DOI: doi.org/10.1007/s00280-015-2927-0
Titolo: Hydroxyurea with or without imatinib in the treatment of recurrent or progressive meningiomas: a randomized phase II trial by Gruppo Italiano Cooperativo di Neuro-Oncologia (GICNO).
Autori: Mazza E., Brandes A., Zanon S., Eoli M., Lombardi G., Faedi M., Franceschi E., Reni M.
Data di Pubblicazione: 2015-12-15
Abstract: The conduction of a study in recurrent or progressive meningioma remains a challenge. Given the limited number of patients enrolled, no firm conclusions can be drawn about the combination of imatinib and HU. The optimal systemic therapy for meningioma failing surgery and radiation has yet to be identified.
Journal Title: Cancer chemotherapy and pharmacology

PUBMED ID: 26632856
DOI: doi.org/10.1667/RR14185.1
Titolo: MicroRNA-145 Modulates Tumor Sensitivity to Radiation in Prostate Cancer.
Autori: Gong P., Zhang T., He D., Hsieh JT.
Data di Pubblicazione: 2015-12-04
Abstract: Radiation therapy prior to surgery has increasingly become the standard of care for locally advanced prostate cancer, however tumor radioresistance remains a major clinical problem. While restoration of microRNA-145 (miR-145) expression reduces chemoradioresistance in glioblastoma and suppress prostate cancer proliferation, migration and invasion, the role of miR-145 in response to radiation therapy for prostate cancer is still unknown. The ai

m of this study was to investigate the role of miR-145 in determining the tu mor response to radiation treatment in prostate cancer. Human prostate cance r cells LNCAP and PC3 were transfected with miR-145 mimic. Clonogenic assay was used to determine whether overexpression of miR-145 could alter radiatio n response in vitro. Immunofluorescence of γ-H2AX and flow cytometric analys is of phosphorylated histone H3 were performed to investigate the potential mechanisms contributing to the enhanced radiation-induced cell killing induc ed by miR-145. In addition, a qPCR-based array was used to detect the possib le miR-145-mediated regulated genes involved. Tumor growth delay assays and survival curves were then analyzed in an animal model to investigate whether miR-145 induced radiosensitivity in vivo. Furthermore, miR-145 expression wa s assessed in 30 prostate tumor tissue biopsies taken prior to neoadjuvant r adiotherapy using miRNA arrays. Our current study suggested that ectopic exp ression of miR-145 significantly sensitized prostate cancer cells to radiati on and we used γ-H2AX phosphorylation as a surrogate marker of radiotherapy response versus miR-145 expression levels. We observed significantly more fo ci per cell in the group treated with miR-145 and radiation. In addition, mi totic catastrophe was significantly increased in cells receiving miR-145 and radiation. The above results suggest that miR-145 appears to reduced the eff iciency of the repair of radiation-induced DNA double-strand breaks in cells . A detailed examination of the involvement of the DNA repair pathway showed that miR-145 reduced the expression of 10 genes involved in DNA repair accor ding to a qPCR-based array data. Irradiation of subcutaneous PC3 tumors in m ice treated with R11-miR-145 (a cellular permeable peptide, previously repor ted) resulted in an increase in radiation-induced tumor growth delay and liv ed the longest after combination treatment. Moreover, miR-145 expression was significantly increased in patients demonstrating good response (PSA < 2.0 n g/ml/year) to neoadjuvant radiotherapy, while expression of the miR-145-regu lated DNA repair genes was significantly decreased. In conclusion, these dat a suggest a possible mechanism for miR-145 radiosensitivity, potentially thr ough down regulating of DNA repair. This novel study shows a role for miR-14 5 in modulating radiosensitivity in vivo and highlights the need for further study investigating the potential role of miR-145 as both a predictive marke r of response and a novel therapeutic agent with which to enhance the effica cy of radiation therapy.
Journal Title: Radiation research

PUBMED ID: 26626490
DOI: doi.org/10.1007/s11060-015-2008-6
Titolo: A pilot study of bevacizumab-based therapy in patients with newly di agnosed high-grade gliomas and diffuse intrinsic pontine gliomas.
Autori: Hummel TR., Salloum R., Drissi R., Kumar S., Sobo M., Goldman S., Pa i A., Leach J., Lane A., Pruitt D., Sutton M., Chow LM., Grimme L., Doughman R., Backus L., Miles L., Stevenson C., Fouladi M., DeWire M.
Data di Pubblicazione: 2015-12-03
Abstract: Although bevacizumab has not proven effective in adults with newly diagnosed high-grade gliomas (HGG), feasibility in newly diagnosed children with diffuse intrinsic pontine gliomas (DIPG) or HGG has not been reported i n a prospective study. In a safety and feasibility study, children and young adults with newly diagnosed HGG received radiotherapy (RT) with bevacizumab (10 mg/kg: days 22, 36) and temozolomide (75-90 mg/m(2)/day for 42 days) fol lowed by bevacizumab (10 mg/kg, days 1, 15), irinotecan (125 mg/m(2), days 1 , 15) and temozolomide (150 mg/m(2)/day days 1-5). DIPG patients did not rec eive temozolomide. Telomerase activity, quality of life (QOL), and functiona l outcomes were assessed. Among 27 eligible patients (15 DIPG, 12 HGG), medi an age 10 years (range 3-29 years), 6 discontinued therapy for toxicity: 2 d uring RT (grade 4 thrombocytopenia, grade 3 hepatotoxicity) and 4 during mai ntenance therapy (grade 3: thrombosis, hypertension, skin ulceration, and wo und dehiscence). Commonest ≥grade 3 toxicities included lymphopenia, neutrop

enia and leukopenia. Grade 3 hypertension occurred in 2 patients. No intracr anial hemorrhages occurred. For DIPG patients, median overall survival (OS) was 10.4 months. For HGG patients, 3-year progression free survival and OS w ere 33 % (SE ± 14 %) and 50 % (SE ± 14 %), respectively. All 3 tested tumor samples, demonstrated histone H3.3K27M (n = 2 DIPG) or G34R (n = 1 HGG) muta tions. QOL scores improved over the course of therapy. A bevacizumab-based r egimen is feasible and tolerable in newly diagnosed children and young adult s with HGG and DIPG.
Journal Title: Journal of neuro-oncology

PUBMED ID: 26617320
DOI: doi.org/10.1016/j.jneumeth.2015.11.008
Titolo: Chronic, intermittent convection-enhanced delivery devices.
Autori: Lewis O., Woolley M., Johnson D., Rosser A., Barua NU., Bienemann AS ., Gill SS., Evans S.
Data di Pubblicazione: 2015-12-01
Abstract: Here we review the improvements that have been made to CED devices over recent years and current state of the art for chronic infusion systems.
Journal Title: Journal of neuroscience methods

PUBMED ID: 26574999
DOI: doi.org/10.1097/CAD.0000000000000314
Titolo: Phase II trial of irinotecan and metronomic temozolomide in patients with recurrent glioblastoma.
Autori: Reynés G., Martínez-Sales V., Vila V., Balañá C., Pérez-Segura P., V az MA., Benavides M., Gallego O., Palomero I., Gil-Gil M., Fleitas T., Reche E.
Data di Pubblicazione: 2015-11-18
Abstract: This phase II study was conducted to determine the efficacy and sa fety of metronomic temozolomide (TMZ) in combination with irinotecan in glio blastoma (GB) at first relapse. Patients with GB at first relapse received T MZ 50 mg/m/2day divided into three doses, except for a single 100 mg/m2 dose , administered between 3 and 6 h before every irinotecan infusion. Irinoteca n was given intravenously at the previously established dose of 100 mg/m2 on days 8 and 22 of 28-day cycles. Treatment was given for a maximum of nine cy cles or until progression or unacceptable toxicity occurred. Vascular endoth elial growth factor and its soluble receptor 1, thrombospondin-1, microparti cles, and microparticle-dependent procoagulant activity were measured in blo od before treatment. The primary objective was 6-month progression-free surv ival (PFS). Twenty-seven evaluable patients were enrolled. Six-month PFS was 20.8%. Median PFS was 11.6 weeks (95% confidence interval: 7.5-15.7). Stable disease was the best response for nine (37.5%) patients, with a median durat ion of 11.2 weeks (4.2-35.85 weeks). No differences in PFS or response were observed among patients who relapsed during or after completion of adjuvant TMZ. Grade 3/4 adverse events included lymphopenia (15%), fatigue, diarrhea and febrile neutropenia (3.7% each), lymphopenia, neutropenia, and nausea/vo miting (11.1% each). One patient died from pneumonia and one patient died fr om pulmonary thromboembolism. Pretreatment levels of angiogenesis biomarkers , microparticles, and microparticle-related procoagulant activity were eleva ted in patients compared with healthy volunteers. This regimen is feasible, but failed to improve the results obtained with other second-line therapies in recurrent GB.
Journal Title: Anti-cancer drugs

PUBMED ID: 26547911
DOI: doi.org/10.1007/s11060-015-1975-y

Titolo: Seizure reduction is a prognostic marker in low-grade glioma patient s treated with temozolomide.
Autori: Koekkoek JA., Dirven L., Heimans JJ., Postma TJ., Vos MJ., Reijnevel d JC., Taphoorn MJ.
Data di Pubblicazione: 2015-11-09
Abstract: We aimed to analyze the value of seizure reduction and radiologica l response as prognostic markers of survival in patients with low-grade glio ma (LGG) treated with temozolomide (TMZ) chemotherapy. We retrospectively re viewed adult patients with a progressive LGG and uncontrolled epilepsy in tw o hospitals (VUmc Amsterdam; MCH The Hague), who received chemotherapy with TMZ between 2002 and 2014. End points were a ≥50 % seizure reduction and MRI response 6, 12 and 18 months (mo) after the start of TMZ, and their relation with progression-free survival (PFS) and overall survival (OS). We identifie d 53 patients who met the inclusion criteria. Seizure reduction was an indep endent prognostic factor for both PFS (HR 0.38; 95 % CI 0.19-0.73; p = 0.004) and OS (HR 0.39; 95 % CI 0.18-0.85; p = 0.018) after 6mo, adjusting for ag e and histopathological diagnosis, as well as after 12 and 18mo. Patients wi th an objective radiological response showed a better OS (median 87.5mo; 95 % CI 62.0-112.9) than patients without a response (median 34.4mo; 95 % CI 26 .1-42.6; p = 0.046) after 12mo. However, after 6 and 18mo OS was similar in patients with and without a response on MRI. Seizure reduction is an early a nd consistent prognostic marker for survival after treatment with TMZ, that seems to precede the radiological response. Therefore, seizure reduction may serve as a surrogate marker for tumor response.
Journal Title: Journal of neuro-oncology

PUBMED ID: 26530266
DOI: doi.org/10.1007/s11060-015-1948-1
Titolo: The role of radiotherapy in the management of patients with diffuse low grade glioma: A systematic review and evidence-based clinical practice g uideline.
Autori: Ryken TC., Parney I., Buatti J., Kalkanis SN., Olson JJ.
Data di Pubblicazione: 2015-11-05
Abstract: OUTCOMES IN ADULT PATIENTS WITH NEWLY DIAGNOSED LOW GRADE GLIOMA T REATED WITH RADIOTHERAPY: Level I Radiotherapy is recommended in the managem ent of newly diagnosed low-grade glioma in adults to prolong progression fre e survival, irrespective of extent of resection. Level II Radiotherapy is re commended in the management of newly diagnosed low grade glioma in adults as an equivalent alternative to observation in preserving cognitive function, i rrespective of extent of resection. Level III Radiotherapy is recommended in the management of newly diagnosed low grade glioma in adults to improve seiz ure control in patients with epilepsy and subtotal resection. Level III Radi otherapy is recommended in the management of newly diagnosed low-grade gliom a in adults to prolong overall survival in patients with subtotal resection. Level III Consideration of the risk of radiation induced morbidity, includin g cognitive decline, imaging abnormalities, metabolic dysfunction and malign ant transformation, is recommended when the delivery of radiotherapy is sele cted in the management of newly diagnosed low-grade glioma in adults. STRATE GIES OF RADIOTHERAPY IN ADULT PATIENTS WITH NEWLY DIAGNOSED LOW GRADE GLIOMA : Level I Lower dose radiotherapy is recommended as an equivalent alternativ e to higher dose immediate postoperative radiotherapy (45-50.4 vs. 59.4-64.8 Gy) in the management of newly diagnosed low-grade glioma in adults with red uced toxicity. Level III Delaying radiotherapy until recurrence or progressi on is recommended as an equivalent alternative to immediate postoperative ra diotherapy in the management of newly diagnosed low-grade glioma in adults b ut may result in shorter time to progression. Level III The addition of chem otherapy to radiotherapy is not recommended over whole brain radiotherapy al one in the management of low-grade glioma, as it provides no additional surv ival benefit. Level III Limited-field radiotherapy is recommended over whole

brain radiotherapy in the management of low-grade glioma. Level III Either s tereotactic radiosurgery or brachytherapy are recommended as acceptable alte rnatives to external radiotherapy in selected patients. PROGNOSTIC FACTORS I N ADULT PATIENTS WITH NEWLY DIAGNOSED LOW GRADE GLIOMA TREATED WITH RADIOTHE RAPY: Level II It is recommended that age greater than 40 years, astrocytic pathology, diameter greater than 6 cm, tumor crossing the midline and preope rative neurological deficit be considered as negative prognostic indicators when predicting overall survival in adult low grade glioma patients treated with radiotherapy. Level II It is recommended that smaller tumor size, exten t of surgical resection and higher mini-mental status exam be considered as positive prognostic indicators when predicting overall survival and progress ion free survival in patients in adult low grade glioma patients treated wit h radiotherapy. Level III It is recommended that seizures at presentation, p resence of oligodendroglial histological component and 1p19q deletion (along with additional relevant factors-see Table 1) be considered as positive prog nostic indicators when predicting response to radiotherapy in adults with lo w grade gliomas. Level III It is recommended that increasing age, decreasing performance status, decreasing cognition, presence of astrocytic histologica l component (along with additional relevant factors (see Tables 1, 2) be con sidered as negative prognostic indicators when predicting response to radiot herapy.
Journal Title: Journal of neuro-oncology

PUBMED ID: 26530265
DOI: doi.org/10.1007/s11060-015-1867-1
Titolo: The role of surgery in the management of patients with diffuse low g rade glioma: A systematic review and evidence-based clinical practice guidel ine.
Autori: Aghi MK., Nahed BV., Sloan AE., Ryken TC., Kalkanis SN., Olson JJ.
Data di Pubblicazione: 2015-11-05
Abstract: Intraoperative mapping is recommended for patients with diffuse LG Gs in eloquent locations compared to patients with non-eloquently located di ffuse LGGs as a way of preserving function.
Journal Title: Journal of neuro-oncology

PUBMED ID: 26530264
DOI: doi.org/10.1007/s11060-015-1910-2
Titolo: Management of patients with recurrence of diffuse low grade glioma: A systematic review and evidence-based clinical practice guideline.
Autori: Nahed BV., Redjal N., Brat DJ., Chi AS., Oh K., Batchelor TT., Ryken TC., Kalkanis SN., Olson JJ.
Data di Pubblicazione: 2015-11-05
Abstract: There is insufficient evidence to make any specific recommendation s. It is recommended that individuals with recurrent LGGs be enrolled in a p roperly designed clinical trial to assess the role of surgery at recurrence.
Journal Title: Journal of neuro-oncology

PUBMED ID: 26530261
DOI: doi.org/10.1007/s11060-015-1931-x
Titolo: The role of initial chemotherapy for the treatment of adults with di ffuse low grade glioma : A systematic review and evidence-based clinical pra ctice guideline.
Autori: Ziu M., Kalkanis SN., Gilbert M., Ryken TC., Olson JJ.
Data di Pubblicazione: 2015-11-05
Abstract: Level II: It is recommended that chemotherapy be added to the RT i n patients with unfavorable LGG to improve their progression free survival.
Journal Title: Journal of neuro-oncology

PUBMED ID: 26526984
DOI: doi.org/10.1007/s00280-015-2895-4
Titolo: Phase 1 study of galunisertib, a TGF-beta receptor I kinase inhibito
r, in Japanese patients with advanced solid tumors.
Autori: Fujiwara Y., Nokihara H., Yamada Y., Yamamoto N., Sunami K., Utsumi
H., Asou H., TakahashI O., Ogasawara K., Gueorguieva I., Tamura T.
Data di Pubblicazione: 2015-11-04
Abstract: NCT01722825.
Journal Title: Cancer chemotherapy and pharmacology

PUBMED ID: 26501997
DOI: doi.org/10.1002/ijc.29898
Titolo: A concurrent ultra-fractionated radiation therapy and temozolomide t
reatment: A promising therapy for newly diagnosed, inoperable glioblastoma.
Autori: Beauchesne P., Quillien V., Faure G., Bernier V., Noel G., Quetin P.
, Gorlia T., Carnin C., Pedeux R.
Data di Pubblicazione: 2015-10-27
Abstract: We report on a phase II clinical trial to determine the effect of
a concurrent ultra-fractionated radiotherapy and temozolomide treatment in i
noperable glioblastoma patients. A phase II study opened; patients over 18 y
ears of age who were able to give informed consent and had histologically pr
oven, newly diagnosed inoperable diagnosed and supratentorial glioblastoma w
ere eligible. Three doses of 0.75 Gy spaced apart by at least 4 hr were deli
vered daily, 5 days a week for six consecutive weeks for a total of 67.5 Gy.
Chemotherapy was administered during the same period, which consisted of tem
ozolomide given at a dose of 75 mg/m(2) for 7 days a week. After a 4-week br
eak, chemotherapy was resumed for up to six cycles of adjuvant temozolomide
treatment, given every 28 days, according to the standard 5-day regimen. Tol
erance and toxicity were the primary endpoints; survival and progression-fre
e survival were the secondary endpoints. In total, 40 patients were enrolled
in this study, 29 men and 11 women. The median age was 58 years, and the med
ian Karnofsky performance status was 80. The concomitant ultra-fractionated
radiotherapy and temozolomide treatment was well tolerated. Complete respons
es were seen in four patients, and partial responses were reported in seven
patients. The median survival from the initial diagnosis was 16 months. Seve
ral long-term survivors were noted. Concurrent ultra-fractionated radiation
therapy and temozolomide treatment are well accepted by the patients. The re
sults showed encouraging survival rates for these unfavorable patients.
Journal Title: International journal of cancer

PUBMED ID: 26496463
DOI: doi.org/10.1159/000440678
Titolo: Carboplatin and Etoposide in Heavily Pretreated Patients with Progre
ssive High-Grade Glioma.
Autori: Tonder M., Weller M., Eisele G., Roth P.
Data di Pubblicazione: 2015-10-27
Abstract: Carboplatin in combination with etoposide has an unfavorable risk-
benefit profile in heavily pretreated glioma patients.
Journal Title: Chemotherapy

PUBMED ID: 26451615
DOI: doi.org/10.18632/oncotarget.5437
Titolo: The radiosensitivity index predicts for overall survival in glioblas
toma.

Autori: Ahmed KA., Chinnaiyan P., Fulp WJ., Eschrich S., Torres-Roca JF., Caudell JJ.
Data di Pubblicazione: 2015-10-10
Abstract: We have previously developed a multigene expression model of tumor radiosensitivity (RSI) with clinical validation in multiple cohorts and disease sites. We hypothesized RSI would identify glioblastoma patients who would respond to radiation and predict treatment outcomes. Clinical and array based gene expression (Affymetrix HT Human Genome U133 Array Plate Set) level 2 data was downloaded from the cancer genome atlas (TCGA). A total of 270 patients were identified for the analysis: 214 who underwent radiotherapy and temozolomide and 56 who did not undergo radiotherapy. Median follow-up for the entire cohort was 9.1 months (range: 0.04-92.2 months). Patients who did not receive radiotherapy were more likely to be older ($p < 0.001$) and of poorer performance status ($p < 0.001$). On multivariate analysis, RSI is an independent predictor of OS (HR = 1.64, 95% CI 1.08-2.5; $p = 0.02$). Furthermore, on subset analysis, radiosensitive patients had significantly improved OS in the patients with high MGMT expression (unmethylated MGMT), 1 year OS 84.1% vs. 53.7% ($p = 0.005$). This observation held on MVA (HR = 1.94, 95% CI 1.19-3.31; $p = 0.008$), suggesting that RT has a larger therapeutic impact in these patients. In conclusion, RSI predicts for OS in glioblastoma. These data further confirm the value of RSI as a disease-site independent biomarker.
Journal Title: Oncotarget

PUBMED ID: 26448943
DOI: doi.org/10.1155/2015/641023
Titolo: The Diagnostic Ability of Follow-Up Imaging Biomarkers after Treatment of Glioblastoma in the Temozolomide Era: Implications from Proton MR Spectroscopy and Apparent Diffusion Coefficient Mapping.
Autori: Bulik M., Kazda T., Slampa P., Jancalek R.
Data di Pubblicazione: 2015-10-09
Abstract: Institutional validation of cut-off values obtained from advanced MRI methods is warranted not only for diagnosis of GBM recurrence, but also as enrollment criteria in salvage clinical trials and for reporting of outcomes of initial treatment.
Journal Title: BioMed research international

PUBMED ID: 26399631
DOI: doi.org/10.1007/s00401-015-1478-0
Titolo: Histone H3F3A and HIST1H3B K27M mutations define two subgroups of diffuse intrinsic pontine gliomas with different prognosis and phenotypes.
Autori: Castel D., Philippe C., Calmon R., Le Dret L., Truffaux N., Boddaert N., Pagès M., Taylor KR., Saulnier P., Lacroix L., Mackay A., Jones C., Sainte-Rose C., Blauwblomme T., Andreiuolo F., Puget S., Grill J., Varlet P., Debily MA.
Data di Pubblicazione: 2015-09-25
Abstract: Diffuse intrinsic pontine glioma (DIPG) is the most severe paediatric solid tumour, with no significant therapeutic progress made in the past 50 years. Recent studies suggest that diffuse midline glioma, H3-K27M mutant, may comprise more than one biological entity. The aim of the study was to determine the clinical and biological variables that most impact their prognosis. Ninety-one patients with classically defined DIPG underwent a systematic stereotactic biopsy and were included in this observational retrospective study. Histone H3 genes mutations were assessed by immunochemistry and direct sequencing, whilst global gene expression profiling and chromosomal imbalances were determined by microarrays. A full description of the MRI findings at diagnosis and at relapse was integrated with the molecular profiling data and clinical outcome. All DIPG but one were found to harbour either a somatic H3-K27M mutation and/or loss of H3K27 trimethylation. We also discovered a

novel K27M mutation in HIST2H3C, and a lysine-to-isoleucine substitution (K27I) in H3F3A, also creating a loss of trimethylation. Patients with tumours harbouring a K27M mutation in H3.3 (H3F3A) did not respond clinically to radiotherapy as well, relapsed significantly earlier and exhibited more metastatic recurrences than those in H3.1 (HIST1H3B/C). H3.3-K27M-mutated DIPG have a proneural/oligodendroglial phenotype and a pro-metastatic gene expression signature with PDGFRA activation, while H3.1-K27M-mutated tumours exhibit a mesenchymal/astrocytic phenotype and a pro-angiogenic/hypoxic signature supported by expression profiling and radiological findings. H3K27 alterations appear as the founding event in DIPG and the mutations in the two main histone H3 variants drive two distinct oncogenic programmes with potential specific therapeutic targets.
Journal Title: Acta neuropathologica

PUBMED ID: 26384811
DOI: doi.org/10.1007/s11060-015-1883-1
Titolo: The use of (18)F-FDG PET to differentiate progressive disease from treatment induced necrosis in high grade glioma.
Autori: Dankbaar JW., Snijders TJ., Robe PA., Seute T., Eppinga W., Hendrikse J., De Keizer B.
Data di Pubblicazione: 2015-09-20
Abstract: In the follow-up of patients treated for high grade glioma, differentiation between progressive disease (PD) and treatment-induced necrosis (TIN) is challenging. The purpose of this study is to evaluate the diagnostic accuracy of FDG PET for the differentiation between TIN and PD after high grade glioma treatment. We retrospectively identified patients between January 2011 and July 2013 that met the following criteria: age >18; glioma grade 3 or 4; treatment with radiotherapy or chemoradiotherapy; new or progressive enhancement on post treatment MRI; FDG PET within 4 weeks of MRI. Absolute and relative (to contralateral white matter) values of SUVmax and SUVpeak were determined in new enhancing lesions on MRI. The outcome of PD or TIN was determined by neurosurgical biopsy/resection, follow-up MRI, or clinical deterioration. The association between FDG PET and outcome was analyzed with univariate logistic regression and ROC analysis for: all lesions, lesions >10, >15, and >20 mm. We included 30 patients (5 grade 3 and 25 grade 4), with 39 enhancing lesions on MRI. Twenty-nine lesions represented PD and 10 TIN. Absolute and relative values of SUVmax and SUVpeak showed no significant differences between PD and TIN. ROC analysis showed highest AUCs for relative SUVpeak in all lesion sizes. Relative SUVpeak for lesions >20 mm showed reasonable discriminative properties [AUC 0.69 (0.41-0.96)]. FDG PET has reasonable discriminative properties for differentiation of PD from TIN in high grade gliomas larger than 20 mm. Overall diagnostic performance is insufficient to guide clinical decision-making.
Journal Title: Journal of neuro-oncology

PUBMED ID: 26364181
DOI: doi.org/10.1007/s00234-015-1582-9
Titolo: Early biomarkers from dynamic contrast-enhanced magnetic resonance imaging to predict the response to antiangiogenic therapy in high-grade gliomas.
Autori: Piludu F., Marzi S., Pace A., Villani V., Fabi A., Carapella CM., Terrenato I., Antenucci A., Vidiri A.
Data di Pubblicazione: 2015-09-14
Abstract: Tumor subvolumes with increased nIAUGC and K(trans) showed the potential for improving the diagnostic accuracy of DCE. Early assessments of the entire tumor volume, including necrotic areas, may provide complementary information of tumor behavior in response to anti-VEGF therapies and is worth further investigation.

Journal Title: Neuroradiology

PUBMED ID: 26354927
DOI: doi.org/10.1093/neuonc/nov182
Titolo: Molecular classification of anaplastic oligodendroglioma using next-generation sequencing: a report of the prospective randomized EORTC Brain Tumor Group 26951 phase III trial.
Autori: Dubbink HJ., Atmodimedjo PN., Kros JM., French PJ., Sanson M., Idbaih A., Wesseling P., Enting R., Spliet W., Tijssen C., Dinjens WN., Gorlia T., van den Bent MJ.
Data di Pubblicazione: 2015-09-11
Abstract: Targeted NGS allows a clinically relevant classification of diffuse glioma into groups with very different outcomes. The diagnosis of diffuse glioma should be primarily based on a molecular classification, with the histopathological grade added to it. Future discussion should primarily aim at establishing the minimum requirements for molecular classification of diffuse glioma.
Journal Title: Neuro-oncology

PUBMED ID: 26352098
DOI: doi.org/10.1227/NEU.0000000000001019
Titolo: Spinal Anaplastic Oligodendroglioma With Oligodendrogliomatosis: Molecular Markers and Management: Case Report.
Autori: Strickland BA., Cachia D., Jalali A., Cykowski MD., Penas-Prado M., Langford LA., Li J., Shah K., Weinberg JS.
Data di Pubblicazione: 2015-09-10
Abstract: Management, prognosis, and use of molecular data in the decision-making algorithm for these patients are discussed, together with a review of all cases of primary intradural intramedullary spinal anaplastic oligodendrogliomas reported to date. Our study indicates that the combination of sequential treatment with radiation and temozolomide might provide a favorable outcome in the case of 1p/19q-codeleted spinal anaplastic oligodendrogliomas and that molecular analysis can be beneficial in guiding treatment strategies, although the impact of IDH mutations on these tumors is still unclear.
Journal Title: Neurosurgery

PUBMED ID: 26323606
DOI: doi.org/10.1093/neuonc/nov167
Titolo: Temozolomide as salvage treatment for recurrent intracranial ependymomas of the adult: a retrospective study.
Autori: Rudà R., Bosa C., Magistrello M., Franchino F., Pellerino A., Fiano V., Trevisan M., Cassoni P., Soffietti R.
Data di Pubblicazione: 2015-09-02
Abstract: TMZ has a role in recurrent chemo-naïve adult patients with intracranial ependymoma, regardless of tumor grade and MGMT methylation. We suggest that, after failure of surgery and radiotherapy, TMZ should be considered as a possible first-line treatment for recurrent ependymoma.
Journal Title: Neuro-oncology

PUBMED ID: 26314843
DOI: doi.org/10.18632/oncotarget.4549
Titolo: TERT promoter mutations contribute to IDH mutations in predicting differential responses to adjuvant therapies in WHO grade II and III diffuse gliomas.

Autori: Zhang ZY., Chan AK., Ding XJ., Qin ZY., Hong CS., Chen LC., Zhang X. , Zhao FP., Wang Y., Wang Y., Zhou LF., Zhuang Z., Ng HK., Yan H., Yao Y., M ao Y.
Data di Pubblicazione: 2015-08-29
Abstract: IDH mutations frequently occur in WHO grade II and III diffuse gli omas and have favorable prognosis compared to wild-type tumors. However, whe ther IDH mutations in WHO grade II and II diffuse gliomas predict enhanced s ensitivity to adjuvant radiation (RT) or chemotherapy (CHT) is still being d ebated. Recent studies have identified recurrent mutations in the promoter r egion of telomerase reverse transcriptase (TERT) in gliomas. We previously d emonstrated that TERT promoter mutations may be promising biomarkers in glio ma survival prognostication when combined with IDH mutations. This study ana lyzed IDH and TERT promoter mutations in 295 WHO grade II and III diffuse gl iomas treated with or without adjuvant therapies to explore their impact on the sensitivity of tumors to genotoxic therapies. IDH mutations were found i n 216 (73.2%) patients and TERT promoter mutations were found in 112 (38%) p atients. In multivariate analysis, IDH mutations ($p < 0.001$) were independen t prognostic factors for PFS and OS in patients receiving genotoxic therapie s while TERT promoter mutations were not. In univariate analysis, IDH and TE RT promoter mutations were not significant prognostic factors in patients wh o did not receive genotoxic therapies. Adjuvant RT and CHT were factors inde pendently impacting PFS (RT $p = 0.001$, CHT $p = 0.026$) in IDH mutated WHO gra de II and III diffuse gliomas but not in IDH wild-type group. Univariate and multivariate analyses demonstrated TERT promoter mutations further stratifie d IDH wild-type WHO grade II and III diffuse gliomas into two subgroups with different responses to genotoxic therapies. Adjuvant RT and CHT were signifi cant parameters influencing PFS in the IDH wt/TERT mut subgroup (RT $p = 0.01$ 5, CHT $p = 0.015$) but not in the IDH wt/TERT wt subgroup. Our data demonstra ted that IDH mutated WHO grade II and III diffuse gliomas had better PFS and OS than their IDH wild-type counterparts when genotoxic therapies were admin istered after surgery. Importantly, we also found that TERT promoter mutatio ns further stratify IDH wild-type WHO grade II and III diffuse gliomas into two subgroups with different responses to adjuvant therapies. Taken together , TERT promoter mutations may predict enhanced sensitivity to genotoxic ther apies in IDH wild-type WHO grade II and III diffuse gliomas and may justify intensified treatment in this subgroup.
Journal Title: Oncotarget

PUBMED ID: 26308501
DOI: doi.org/10.1080/21645515.2015.1081727
Titolo: The progress of immunotherapy for glioblastoma.
Autori: Zhou Q., Wang Y., Ma W.
Data di Pubblicazione: 2015-08-27
Abstract: Glioblastoma is the most common primary brain tumor in adults, acc ounting for about half of all primary brain tumors. Despite multiple therape utic interventions such as surgical resection, radiotherapy, and systemic ch emotherapy, the prognosis for glioblastoma remains poor. Due to the scientif ic community's enhanced understanding of the CNS immune system and significa nt achievements in tumor immunotherapy in recent years, immunotherapy has be come a promising GBM treatment. In vaccine therapy, a number of clinical tri als have achieved encouraging results. In antibody therapy, antibodies are u sed to target immune checkpoints such as ipilimumab and nivolumab. Bioengine ering technology has also lead to a new field of tumor immunotherapy, whereb y genetically modified tumor-specific T cells are reintroduced into a patien t's body.
Journal Title: Human vaccines & immunotherapeutics

PUBMED ID: 26294320

DOI: doi.org/10.1007/s00520-015-2897-0
Titolo: Validating self-report and proxy reports of the Dexamethasone Sympto m Questionnaire -Chronic for the evaluation of longer-term corticosteroid to xicity.
Autori: Agar M., Koh ES., Gibbs E., Barnes EH., Hovey E., Livingstone A., Sa wkins K., Chye R., Lovell MR., Clark K., Vardy J., King M., King M.
Data di Pubblicazione: 2015-08-22
Abstract: The DSQ-Chronic is feasible when the patient is relatively well. A s capacity to complete the DSQ-Chronic diminishes, caregivers can be proxy-r aters. Clinicians capture corticosteroid toxicities, which may not be obviou s to the patient. The DSQ-Chronic, patient and caregiver versions, are usefu l tools to be used with clinician assessment.
Journal Title: Supportive care in cancer : official journal of the Multinati onal Association of Supportive Care in Cancer

PUBMED ID: 26289591
DOI: doi.org/10.1093/neuonc/nov152
Titolo: Differentiating the mTOR inhibitors everolimus and sirolimus in the treatment of tuberous sclerosis complex.
Autori: MacKeigan JP., Krueger DA.
Data di Pubblicazione: 2015-08-21
Abstract: Tuberous sclerosis complex (TSC) is a genetic autosomal dominant d isorder characterized by benign tumor-like lesions, called hamartomas, in mu ltiple organ systems, including the brain, skin, heart, kidneys, and lung. T hese hamartomas cause a diverse set of clinical problems based on their loca tion and often result in epilepsy, learning difficulties, and behavioral pro blems. TSC is caused by mutations within the TSC1 or TSC2 genes that inactiv ate the genes' tumor-suppressive function and drive hamartomatous cell growt h. In normal cells, TSC1 and TSC2 integrate growth signals and nutrient inpu ts to downregulate signaling to mammalian target of rapamycin (mTOR), an evo lutionarily conserved serine-threonine kinase that controls cell growth and cell survival. The molecular connection between TSC and mTOR led to the clin ical use of allosteric mTOR inhibitors (sirolimus and everolimus) for the tr eatment of TSC. Everolimus is approved for subependymal giant cell astrocyto mas and renal angiomyolipomas in patients with TSC. Sirolimus, though not ap proved for TSC, has undergone considerable investigation to treat various as pects of the disease. Everolimus and sirolimus selectively inhibit mTOR sign aling with similar molecular mechanisms, but with distinct clinical profiles . This review differentiates mTOR inhibitors in TSC while describing the mol ecular mechanisms, pathogenic mutations, and clinical trial outcomes for man aging TSC.
Journal Title: Neuro-oncology

PUBMED ID: 26282642
DOI: doi.org/10.1200/JCO.2015.61.1525
Titolo: Evaluation of the Safety and Benefit of Phase I Oncology Trials for Patients With Primary CNS Tumors.
Autori: Gounder MM., Nayak L., Sahebjam S., Muzikansky A., Sanchez AJ., Desi deri S., Ye X., Ivy SP., Nabors LB., Prados M., Grossman S., DeAngelis LM., Wen PY.
Data di Pubblicazione: 2015-08-19
Abstract: Patients with HGG who meet standard eligibility criteria may be go od candidates for solid tumor phase I studies with single-agent molecular or cytotoxic drugs with favorable preclinical rationale and pharmacokinetic pro perties in this population.
Journal Title: Journal of clinical oncology : official journal of the Americ an Society of Clinical Oncology

PUBMED ID: 26254812
DOI: doi.org/10.1016/j.ejca.2015.06.124
Titolo: Metastatic medulloblastoma in adults: outcome of patients treated ac
cording to the HIT2000 protocol.
Autori: von Bueren AO., Friedrich C., von Hoff K., Kwiecien R., Müller K., P
ietsch T., Warmuth-Metz M., Hau P., Benesch M., Kuehl J., Kortmann RD., Rutk
owski S.
Data di Pubblicazione: 2015-08-10
Abstract: Treatment of adults with metastatic medulloblastoma according to t
he intensified paediatric HIT2000 protocol was feasible with acceptable toxi
cities. EFS rates achieved by both chemotherapeutic protocols were favourabl
e and appear to be inferior to those obtained in older children/adolescents
with metastatic disease.
Journal Title: European journal of cancer (Oxford, England : 1990)

PUBMED ID: 26243269
DOI: doi.org/10.1007/s11060-015-1863-5
Titolo: IDH1 mutation is prognostic for diffuse astrocytoma but not low-grad
e oligodendrogliomas in patients not treated with early radiotherapy.
Autori: Iwadate Y., Matsutani T., Hirono S., Ikegami S., Shinozaki N., Saeki
N.
Data di Pubblicazione: 2015-08-06
Abstract: Despite accumulating knowledge regarding molecular backgrounds, th
e optimal management strategy for low-grade gliomas remains controversial. O
ne reason is the marked heterogeneity in the clinical course. To establish a
n accurate subclassification of low-grade gliomas, we retrospectively evalua
ted isocitrate dehydrogenase-1 (IDH1) mutation in clinical specimens of diff
use astrocytomas (DA) and oligodendroglial tumors separately. No patients we
re treated with early radiotherapy, and modified PCV chemotherapy was used f
or postoperative residual tumors or recurrence in oligodendroglial tumors. I
mmunohistochemical evaluation of IDH status, p53 status, O(6)-methylguanine
methyltransferase expression, and the MIB-1 index were performed. The 1p and
19q status was analyzed with fluorescence in situ hybridization. Ninety-four
patients were followed for a median period of 8.5 years. For DAs, p53 was pr
ognostic for progression- free survival (PFS) and IDH1 was significant for o
verall survival (OS) with multivariate analysis. In contrast, for oligodendr
oglial tumors, none of the parameters was significant for PFS or OS. Thus, t
he significance of IDH1 mutation is not clear in oligodendroglial tumors tha
t are homogeneously indolent and chemosensitive. In contrast, DAs are hetero
geneous tumors including some potentially malignant tumors that can be predi
cted by examining the IDH1 mutation status.
Journal Title: Journal of neuro-oncology

PUBMED ID: 26235882
DOI: doi.org/10.1016/j.anndiagpath.2015.07.003
Titolo: Coexistent ganglioglioma, focal cortical dysplasia, and hippocampal
sclerosis (triple pathology) in chronic epilepsy.
Autori: Prayson RA., Gales JM.
Data di Pubblicazione: 2015-08-04
Abstract: The most commonly identified pathologies in patients with medicall
y intractable epilepsy include focal cortical dysplasia, hippocampal scleros
is, tumors, and remote ischemic damage. Surgery has proven to be an effectiv
e therapeutic modality in most of such patients. The coexistence of multiple
pathologies in resected tissues is well documented, particularly ganglioglio
ma and focal cortical dysplasia. Cases of triple pathology are, however, ext
raordinarily unusual. We report 2 cases of triple pathology including hippoc
ampal sclerosis, ganglioglioma, and focal cortical dysplasia. Cases of patho

logically confirmed hippocampal sclerosis diagnosed between January 2000 to December 2012 (n= 349) were reviewed, and only 2 cases (0.6%) with triple pathology were identified. The histopathologic and clinical features of these 2 cases are reviewed. The patients included a 6-year-old girl and 10-year-old boy. The former patient presented with a 4-year history of epilepsy and oppositional defiant disorder. Imaging identified a lesion in the left parahippocampal gyrus and posterior hippocampus. The latter patient presented with an 8-year history of epilepsy, attention deficient hyperactivity disease, and a pervasive developmental disorder. Imaging identified a lesion in the left posterior temporal and occipital region. Resected tissues in both patients showed a ganglioglioma (World Health Organization grade I) with accompanying focal cortical dysplasia and hippocampal sclerosis. Both patients were seizure free on antiepileptic medication at last follow-up at 20 and 38 months, respectively. The prevalence of triple pathology including hippocampal sclerosis is low (<1% in the current study). Surgical intervention for triple pathology cases anecdotally appears effective in achieving seizure control.
Journal Title: Annals of diagnostic pathology

PUBMED ID: 26230475
DOI: doi.org/10.3171/2015.1.JNS141577
Titolo: Downregulation of serum microRNA-205 as a potential diagnostic and prognostic biomarker for human glioma.
Autori: Yue X., Lan F., Hu M., Pan Q., Wang Q., Wang J.
Data di Pubblicazione: 2015-08-01
Abstract: OBJECT Circulating microRNAs (miRNAs) are a new class of highly promising cancer biomarkers. Malignant glioma is one of the most devastating and lethal forms of intrinsic CNS tumor. Here, the authors evaluated serum miRNA 205 (miR-205) levels in patients with glioma. METHODS Sixty-four patients in whom glioma was diagnosed and 45 healthy controls were recruited between October 2011 and March 2012 and randomly assigned to the screening cohort or the validation cohort. Cohorts of patients with other brain tumors, including meningioma (n = 8), primary diffuse large B-cell lymphoma of the CNS (n = 6), and pituitary adenoma (n = 5), were investigated and compared. miR-205 extraction from serum was detected by real-time quantitative reverse-transcription polymerase chain reaction. The Kaplan-Meier method was applied to perform survival analysis, the risk factors were analyzed by using a Cox regression model, and the receiver operating characteristic working curve was used to analyze the value of miR-205 in the prognostic evaluation of the patients. RESULTS The authors first demonstrated that serum miR-205 expression was significantly lower in patients with glioma than in healthy controls ($p < 0.001$). It is important to note that serum miR-205 expression demonstrated a stepwise decrease with ascending pathological grades. The serum miR-205 biomarker had high sensitivity, specificity, and accuracy in patients with glioma. Serum levels of miR-205 were identified as an individual diagnostic marker and were significantly lower in the glioma cohort than in the other brain tumor cohorts. Serum miR-205 levels were significantly increased in postoperative samples over those in the preoperative samples and were reduced again during glioblastoma recurrences. Statistical analysis revealed a significant correlation between low serum miR-205 expression and both ascending pathological grades ($p = 0.002$) and low Karnofsky Performance Scale scores ($p = 0.01$). Patients with glioma at an advanced pathological grade (Grade III or IV) and a higher miR-205 serum level showed longer overall survival than those with a lower miR-205 serum concentration ($p < 0.01$). Furthermore, Cox regression analysis revealed that miR-205 serum levels were independently associated with overall survival. CONCLUSIONS These data indicate that serum miR-205 expression is a novel and valuable biomarker for the diagnosis of glioma and a prognostic factor for those with a tumor at an advanced pathological grade.
Journal Title: Journal of neurosurgery

PUBMED ID: 26227256
DOI: doi.org/10.5414/NP300864
Titolo: Well-differentiated and anaplastic astroblastoma in the same patient : a case report and review of the literature.
Autori: Samkari A., Hmoud M., Al-Mehdar A., Abdullah S.
Data di Pubblicazione: 2015-08-01
Abstract: Astroblastoma is a rare brain tumor occurring in children and adults, rarely in the elderly. It constitutes up to 3% of all brain tumors. We report a case of a 14-year-old girl who presented with recurrent seizures and minimal right hemiparesis. Magnetic resonance imaging (MRI) revealed a left fronto-parietal brain tumor. It was managed with subtotal resection in a local hospital. Subsequently, she was referred to Princess Nora Oncology Center for further characterization and management. Pathology slide revision revealed well-differentiated astroblastoma. Upon follow up, the patient had multiple recurrences of the same tumor and emergence of a new lesion at the area of Sylvian fissure. Excision of the emerging tumor revealed anaplastic astroblastoma. Astroblastoma is a glial tumor that predominantly affects females. Its clinical progression is unpredictable, with high recurrence rate. Surgical intervention is considered the mainstay of treatment, while radiotherapy and chemotherapy effectiveness is debatable. To our knowledge, this is the first reported case of well-differentiated and anaplastic astroblastoma as two separate neoplastic lesions in the same patient with its clinical, radiological, and pathological features.
Journal Title: Clinical neuropathology

PUBMED ID: 26207600
DOI: doi.org/10.3171/2015.1.JNS142349
Titolo: Magnetic resonance susceptibility weighted imaging in neurosurgery: current applications and future perspectives.
Autori: Di Ieva A., Lam T., Alcaide-Leon P., Bharatha A., Montanera W., Cusimano MD.
Data di Pubblicazione: 2015-07-25
Abstract: Susceptibility weighted imaging (SWI) is a relatively new imaging technique. Its high sensitivity to hemorrhagic components and ability to depict microvasculature by means of susceptibility effects within the veins allow for the accurate detection, grading, and monitoring of brain tumors. This imaging modality can also detect changes in blood flow to monitor stroke recovery and reveal specific subtypes of vascular malformations. In addition, small punctate lesions can be demonstrated with SWI, suggesting diffuse axonal injury, and the location of these lesions can help predict neurological outcome in patients. This imaging technique is also beneficial for applications in functional neurosurgery given its ability to clearly depict and differentiate deep midbrain nuclei and close submillimeter veins, both of which are necessary for presurgical planning of deep brain stimulation. By exploiting the magnetic susceptibilities of substances within the body, such as deoxyhemoglobin, calcium, and iron, SWI can clearly visualize the vasculature and hemorrhagic components even without the use of contrast agents. The high sensitivity of SWI relative to other imaging techniques in showing tumor vasculature and microhemorrhages suggests that it is an effective imaging modality that provides additional information not shown using conventional MRI. Despite SWI's clinical advantages, its implementation in MRI protocols is still far from consistent in clinical usage. To develop a deeper appreciation for SWI, the authors here review the clinical applications in 4 major fields of neurosurgery: neurooncology, vascular neurosurgery, neurotraumatology, and functional neurosurgery. Finally, they address the limitations of and future perspectives on SWI in neurosurgery.
Journal Title: Journal of neurosurgery

PUBMED ID: 26191506
DOI: doi.org/10.3389/fonc.2015.00148
Titolo: Future Clinical Trials in DIPG: Bringing Epigenetics to the Clinic.
Autori: Morales La Madrid A., Hashizume R., Kieran MW.
Data di Pubblicazione: 2015-07-21
Abstract: In spite of major recent advances in diffuse intrinsic pontine gli oma (DIPG) molecular characterization, this body of knowledge has not yet tr anslated into better treatments. To date, more than 250 clinical trials eval uating radiotherapy along with conventional cytotoxic chemotherapy as well a s newer biologic agents have failed to improve the dismal outcome when compa red to palliative radiation alone. The biology of DIPG remained unknown unti l recently when the neurosurgical expertise along with the recognition by th e scientific and clinical community of the importance of tissue sampling at diagnosis; ideally, in the context of a clinical trial and by trained neuros urgical teams to maximize patient safety. These pre-treatment tumor samples, and others coming from tissue obtained post-mortem, have yielded new insight s into DIPG molecular pathogenesis. We now know that DIPG comprises a hetero geneous disease with variable molecular phenotypes, different from adult hig h-grade glioma, other non-pontine pediatric high-grade gliomas, and even bet ween pontine gliomas. The discovery of histone H3.3 or H3.1 mutations has be en an important step forward in understanding tumor formation, maintenance, and progression. Pharmacologic reversal of DIPG histone demethylation theref ore offers an important potential intervention strategy for the treatment of DIPG. To date, clinical trials of newly diagnosed or progressive DIPG with e pigenetic (histone) modifiers have been unsuccessful. Whether this failure r epresents limited activity of the agents used, their CNS penetration, redund ant pathways within the tumor, or the possibility that histone mutations are necessary only to initiate DIPGs but not maintain their growth, suggest that a great deal still needs to be elucidated in both the underlying biology of these pathways and the drugs designed to target them. In this review, we wil l discuss the role of both epigenetic and genetic mutations within DIPG and the development of treatment strategies directed against the unique abnormal ities present in this disease.
Journal Title: Frontiers in oncology

PUBMED ID: 26178621
DOI: doi.org/10.1007/s11940-015-0369-y
Titolo: Novel Surgical Approaches to High-Grade Gliomas.
Autori: Rasul FT., Watts C.
Data di Pubblicazione: 2015-07-17
Abstract: Treatment of patients with high-grade glioma (HGG) should begin wi th thorough evaluation by a specialized multidisciplinary team to determine whether or not the patient is appropriate for surgery, chemotherapy and radi otherapy. Particular attention should be paid to the performance status and neurological function. Surgery is the first step in therapeutic intervention . Patients undergo either biopsy, debulking surgery or maximal resection dep ending on the anatomical location of the tumour and the patient's clinical c ondition. Extent of resection has a prognostic value. In patients who are 'f it for surgery', the aim is to remove all contrast-enhancing tumour without causing neurological deficit. If microsurgical resection is not feasible, th en a biopsy, either open or stereotactic, should be performed to confirm hig h-grade glioma diagnosis and to perform molecular genetic analyses (MGMT met hylation status, loss of heterozygosity in 1p/19q, IDH1 status) as this has treatment implications. Over the past decade, much glioma research has focus sed on novel surgical approaches to improve long-term outcomes. The evidence to support the benefit of maximizing extent of resection is growing. Advance s in neurosurgical techniques allow safer, more aggressive surgery to maximi ze tumour resection whilst minimizing neurological deficit. Surgical adjunct

s including advanced neuronavigation, intraoperative magnetic resonance imag ing, high-frequency ultrasonography, fluorescence-guided microsurgery using intraoperative fluorescence, functional mapping of motor and language pathwa ys, and locally delivered therapies are extending the armamentarium of the n eurosurgeon to provide patients with the best outcome. Operating on elderly patients and those with recurrent disease, although controversial, is becomi ng more common due to emerging neurosurgical approaches. Here, we discuss th e emerging surgical techniques and comment on the future of HGG surgery.
Journal Title: Current treatment options in neurology

PUBMED ID: 26175405
DOI: Mancante
Titolo: One size should not fit all: advancing toward personalized glioblast oma therapy.
Autori: Reardon DA., Ligon KL., Chiocca EA., Wen PY.
Data di Pubblicazione: 2015-07-16
Abstract: Over the past few years, understanding the genetic abnormalities a ssociated with glioblastoma, the most common malignant primary tumor of the central nervous system, has increased dramatically. Mutation types and frequ encies have been comprehensively assessed, glioblastoma subclasses have been defined based on gene expression and methylation analyses, and novel mutatio ns implicated in gliomagenesis have been identified. Nonetheless, a critical disconnect exists between achieved scientific advances and failure to improv e patient outcome. Currently, standard therapy incorporating surgery, crania l irradiation, and temozolomide chemotherapy is uniformly applied for all pa tients. With this approach, median survival remains unacceptably poor includ ing fewer than 10% of patients surviving 5 years after diagnosis. Salvage th erapies are ineffective with PFS-6 rates under 10% for non-bevacizumab regim ens and 40% for bevacizumab. Furthermore, all patients ultimately progress o n bevacizumab, and then typically die from rapidly progressive tumor. Innova tive treatment strategies directed to distinct patient subsets defined by sp ecific genetic and gene expression analyses represent an attractive therapeu tic paradigm shift for this highly challenging complex tumor, offering promi se to ultimately improve outcome.
Journal Title: Discovery medicine

PUBMED ID: 26162036
DOI: doi.org/10.3171/2014.12.JNS141851
Titolo: Acute progression of untreated incidental WHO Grade II glioma to gli oblastoma in an asymptomatic patient.
Autori: Cochereau J., Herbet G., Rigau V., Duffau H.
Data di Pubblicazione: 2015-07-11
Abstract: WHO Grade II glioma (low-grade glioma [LGG]) is increasingly diagn osed as an incidental finding in patients undergoing MRI for many conditions . Recent data have demonstrated that such incidental LGGs are progressive tu mors that undergo clinical transformation and ultimately become malignant. A lthough asymptomatic LGG seems to represent an earlier step in the natural c ourse of a glioma than the symptomatic LGG, it is nonetheless impossible to predict at the individual level when the tumor will become malignant. The au thors report the case of a 43-year-old woman with a right operculo-insular L GG that was incidentally diagnosed because of headaches. No treatment was pr oposed, and repeated MRI scans were performed for 6 years in another institu tion. Due to a slow but continuous growth of the lesion, the patient was fin ally referred to our center to undergo surgery. Interestingly, objective cal culation of the velocity of the tumor's diametric expansion demonstrated a s udden acceleration of the growth rate within the 5 months preceding surgery, with the development of contrast enhancement. Remarkably, the patient was st ill asymptomatic. An awake resection was performed with intraoperative elect

rical mapping. There was no functional worsening following surgery, as asses sed on postoperative neuropsychological examination. Removal of 92% of signa l abnormality on FLAIR MRI was achieved, with complete resection of the area of contrast enhancement. Neuropathological examination revealed a glioblasto ma, and the patient was subsequently treated with concomitant radiotherapy a nd chemotherapy. Although a "wait and see" attitude has been advocated by so me authors with respect to incidental LGG, our original case demonstrates th at acute transformation to glioblastoma may nonetheless occur, even before t he onset of any symptoms. Therefore, because the lack of symptoms does not p rotect from malignant transformation, we propose consideration of earlier re section in a more systematic manner in cases of incidental LGG.
Journal Title: Journal of neurosurgery

PUBMED ID: 26155413
DOI: doi.org/10.1080/2162402X.2015.1008339
Titolo: Are BiTEs the "missing link" in cancer therapy?
Autori: Suryadevara CM., Gedeon PC., Sanchez-Perez L., Verla T., Alvarez-Bre ckenridge C., Choi BD., Fecci PE., Sampson JH.
Data di Pubblicazione: 2015-07-09
Abstract: Conventional treatment for cancer routinely includes surgical rese ction and some combination of chemotherapy and radiation. These approaches a re frequently accompanied by unintended and highly toxic collateral damage t o healthy tissues, which are offset by only marginal prognostic improvements in patients with advanced cancers. This unfortunate balance has driven the d evelopment of novel therapies that aim to target tumors both safely and effi ciently. Over the past decade, mounting evidence has supported the therapeut ic utility of T-cell-centered cancer immunotherapy, which, in its various it erations, has been shown capable of eliciting highly precise and robust anti tumor responses both in animal models and human trials. The identification o f tumor-specific targets has further fueled a growing interest in T-cell the rapies given their potential to circumvent the non-specific nature of tradit ional treatments. Of the several strategies geared toward achieving T-cell r ecognition of tumor, bispecific antibodies (bsAbs) represent a novel class o f biologics that have garnered enthusiasm in recent years due to their versa tility, specificity, safety, cost, and ease of production. Bispecific T-cell Engagers (BiTEs) are a subclass of bsAbs that are specific for CD3 on one ar m and a tumor antigen on the second. As such, BiTEs function by recruiting a nd activating polyclonal populations of T-cells at tumor sites, and do so wi thout the need for co-stimulation or conventional MHC recognition. Blinatumo mab, a well-characterized BiTE, has emerged as a promising recombinant bscCD 19×CD3 construct that has demonstrated remarkable antitumor activity in pati ents with B-cell malignancies. This clinical success has resulted in the rap id extension of BiTE technology against a greater repertoire of tumor antige ns and the recent US Food and Drug Administration's (FDA) accelerated approv al of blinatumomab for the treatment of a rare form of acute lymphoblastic l eukemia (ALL). In this review, we dissect the role of T-cell therapeutics in the new era of cancer immunotherapy, appraise the value of CAR T-cells in th e context of solid tumors, and discuss why the BiTE platform may rescue seve ral of the apparent deficits and shortcomings of competing immunotherapies t o support its widespread clinical application.
Journal Title: Oncoimmunology

PUBMED ID: 26143265
DOI: doi.org/10.1007/s11864-015-0353-5
Titolo: An Evidence-Based Review of Alternating Electric Fields Therapy for Malignant Gliomas.
Autori: Wong ET., Lok E., Swanson KD.
Data di Pubblicazione: 2015-07-06

Abstract: Glioblastoma is a deadly disease and even aggressive neurosurgical resection followed by radiation and chemotherapy only extends patient surviv al to a median of 1.5 years. The challenge in treating this type of tumor st ems from the rapid proliferation of the malignant glioma cells, the diffuse infiltrative nature of the disease, multiple activated signal transduction p athways within the tumor, development of resistant clones during treatment, the blood brain barrier that limits the delivery of drugs into the central n ervous system, and the sensitivity of the brain to treatment effect. Therefo re, new therapies that possess a unique mechanism of action are needed to tr eat this tumor. Recently, alternating electric fields, also known as tumor t reating fields (TTFields), have been developed for the treatment of glioblas toma. TTFields use electromagnetic energy at an intermediate frequency of 20 0 kHz as a locoregional intervention and act to disrupt tumor cells as they undergo mitosis. In a phase III clinical trial for recurrent glioblastoma, T TFields were shown to have equivalent efficacy when compared to conventional chemotherapies, while lacking the typical side effects associated with chemo therapies. Furthermore, an interim analysis of a recent clinical trial in th e upfront setting demonstrated superiority to standard of care cytotoxic che motherapy, most likely because the subjects' tumors were at an earlier stage of clonal evolution, possessed less tumor-induced immunosuppression, or both . Therefore, it is likely that the efficacy of TTFields can be increased by combining it with other anti-cancer treatment modalities.
Journal Title: Current treatment options in oncology

PUBMED ID: 26142814
DOI: doi.org/10.1016/j.wneu.2015.06.058
Titolo: Synchronous Subarachnoid Aneurysmal Hemorrhage and Medulloblastoma i n a 6-Year-Old Girl.
Autori: Foley RW., Ndoro S., Crimmins D., Caird J.
Data di Pubblicazione: 2015-07-06
Abstract: Intraoperative hemorrhage in MB is a very rare occurrence. We desc ribe the first case of hemorrhage in MB secondary to an intracranial aneurys m. MB has a predisposition to bleed spontaneously that can have catastrophic repercussions. Sudden clinical deterioration after insertion of external ven tricular drainage should be susceptive of intracerebral hemorrhage. In cases of uncertain etiology, investigation of SAH with cerebral angiography is rec ommended.
Journal Title: World neurosurgery

PUBMED ID: 26070556
DOI: doi.org/10.1007/s11060-015-1844-8
Titolo: Re-irradiation or re-operation followed by dendritic cell vaccinatio n? Comparison of two different salvage strategies for relapsed high-grade gl iomas by means of a new prognostic model.
Autori: Müller K., Henke G., Pietschmann S., van Gool S., De Vleeschouwer S. , von Bueren AO., Compter I., Friedrich C., Matuschek C., Klautke G., Kortma nn RD., Hundsberger T., Baumert BG.
Data di Pubblicazione: 2015-06-14
Abstract: We aimed to compare two different salvage treatment strategies for relapsed high-grade glioma (HGG) patients by means of a new prognostic model . A simplified version of the so-called HGG-Immuno RPA model estimates the p rognosis of relapsed HGG patients and distinguishes three different prognost ic classes (I = good, II = intermediate, III = poor). The model has been con structed with a cohort of 117 patients whose salvage treatment consisted of re-operation followed by dendritic cell vaccination (ReOP + DCV). However, u sing only the predictors histology, age and performance status, the simplifi ed HGG-Immuno RPA model is basically independent from treatment. In the pres ent study we applied the simplified model to the cohort used to construct th

e original HGG-Immuno RPA model and another cohort of 165 patients who under went re-irradiation (ReRT) at relapse. Then, we compared the outcomes achiev ed by the two different salvage treatments in each prognostic class. The mod el predicted good, intermediate and poor prognosis for 11, 31 and 75 patient s of the ReOP + DCV cohort and for 20, 39 and 106 patients of the ReRT cohor t, respectively. Neither of the two strategies was superior to the other. In the groups with good, intermediate and poor prognosis 12-months survival rat es were 73, 59 and 25 % after ReOP + DCV and 72, 36 and 23 % after ReRT, res pectively. Being easy to handle and independent from treatment, the aforemen tioned model is useful for therapeutic decisions. ReRT and ReOP + DVC seem t o be equally effective. The choice of salvage treatment should be based on t he expected side effects.
Journal Title: Journal of neuro-oncology

PUBMED ID: 26034641
DOI: doi.org/10.1093/nop/npu031
Titolo: Large volume re-irradiation with bevacizumab is a feasible salvage o ption for patients with refractory high-grade glioma.
Autori: Back M., Gzell CE., Kastelan M., Guo L., Wheeler HR.
Data di Pubblicazione: 2015-06-03
Abstract: ReRT combined with BEV is a feasible salvage treatment option for diffuse refractory HGG.
Journal Title: Neuro-oncology practice

PUBMED ID: 26029663
DOI: doi.org/10.3389/fonc.2015.00106
Titolo: Salvage Fractionated Stereotactic Radiotherapy with or without Chemo therapy and Immunotherapy for Recurrent Glioblastoma Multiforme: A Single In stitution Experience.
Autori: Hasan S., Chen E., Lanciano R., Yang J., Hanlon A., Lamond J., Arrig o S., Ding W., Mikhail M., Ghaneie A., Brady L.
Data di Pubblicazione: 2015-06-02
Abstract: Radiation Therapy Oncology Group (RTOG) 1205 will establish the ro le of re-irradiation for recurrent GBM, however our study suggests that Cybe rKnife with chemotherapy can be safely delivered, and is most effective in p atients with smaller frontal lobe tumors, good performance status, or long i nterval from diagnosis.
Journal Title: Frontiers in oncology

PUBMED ID: 26026859
DOI: doi.org/10.1007/s11060-015-1808-z
Titolo: Prognostic implication of progression pattern after anti-VEGF bevaci zumab treatment for recurrent malignant gliomas.
Autori: Kim BS., Kim SK., Choi SH., Lee SH., Seol HJ., Nam DH., Lee JI., Par k CK., Kong DS.
Data di Pubblicazione: 2015-06-01
Abstract: Malignant glioma treated with anti-vascular endothelial growth fac tor (VEGF) bevacizumab show progression patterns that vary with different me chanisms of resistance. We evaluated the clinico-radiological data of 71 pat ients with progressive malignant glioma treated with bevacizumab to determin e the prognostic value of the differential outcome of each progression patte rn. Progression patterns were categorized as three types based on the initia l response to bevacizumab and serious changes of MR images i.e., non-enhanci ng infiltration, flare-up of contrast enhancement (CE) and primary non-respo nder progression. We analyzed the clinical outcome in each type of progressi on using Kaplan-Meier survival analysis. Analysis of progression patterns sh owed that incidence of non-enhancing infiltration progression (28.1 %) was l

ess common than flare-up of CE or primary non-responder pattern. The time fr
om initiation of bevacizumab to development of non-enhancing infiltration or
flare-up of CE progression was longer than for progression in primary non-re
sponders. There was no significant difference of overall survival, progressi
on-free survival from start of bevacizumab therapy, survival after bevacizum
ab failure between non-enhancing infiltration and flare-up of CE patterns. H
owever, in the non-enhancing infiltration pattern, early appearance of enhan
cement was observed after bevacizumab was discontinued, resulting in poor su
rvival, as compared to flare-up of CE pattern (P = 0.01). Although the appea
rance of non-enhancing infiltration after bevacizumab does not imply a worse
prognosis, discontinuation of therapy can aggravate the clinical course.
Journal Title: Journal of neuro-oncology

PUBMED ID: 26025933
DOI: doi.org/10.1634/theoncologist.2015-0135
Titolo: Phase II Trial of Upfront Bevacizumab, Irinotecan, and Temozolomide
for Unresectable Glioblastoma.
Autori: Peters KB., Lou E., Desjardins A., Reardon DA., Lipp ES., Miller E.,
Herndon JE., McSherry F., Friedman HS., Vredenburgh JJ.
Data di Pubblicazione: 2015-05-31
Abstract: Upfront treatment with BV, TMZ, and CPT-11 is tolerable and can le
ad to radiographic response in unresectable and/or subtotally resected GBM.
Journal Title: The oncologist

PUBMED ID: 26024653
DOI: doi.org/10.1007/s11060-015-1825-y
Titolo: Re-resection for recurrent high-grade glioma in the setting of re-ir
radiation: more is not always better.
Autori: Palmer JD., Siglin J., Yamoah K., Dan T., Champ CE., Bar-Ad V., Wern
er-Wasik M., Evans JJ., Kim L., Glass J., Farrell C., Andrews DW., Shi W.
Data di Pubblicazione: 2015-05-31
Abstract: The optimal treatment for patients with recurrent high grade gliom
a (HGG) remains controversial. Available therapies include surgery, re-irrad
iation, alternating electric fields or systemic therapy. Here we investigate
whether re-resection will improve survival in patients receiving repeat radi
otherapy for tumor recurrence. 231 consecutive patients with recurrent HGG t
reated with re-irradiation between 1994 and 2012 were analyzed. 105 patients
underwent re-resection. Re-irradiation was delivered using daily fractions o
f 3.5 Gy to a median total dose of 35 Gy. Survival was then analyzed compari
ng patients with and without re-resection. Overall survival (OS) and surviva
l from the first recurrence are reported. Univariate and cox-proportional ha
zard modeling was performed in a step-wise multivariate analysis using known
prognostic factors. The median follow-up time from initial diagnosis was 25.
7 months. The median OS from initial diagnosis of the entire group was 22.
5 months. There was no significant difference in median overall survival bet
ween patients who received re-resection versus no re-resection, 23 versus 21
.9 months respectively (p = 0.6). Additionally, there was no difference in m
edian survival from the time of first recurrence 10.5 months without re-rese
ction versus 11.1 months with re-resection (p = 0.09). After adjusting for k
nown prognostic variables, only age remained significant. Re-irradiation is
an effective salvage therapy for patients with localized, progressive high g
rade glioma, achieving a median survival of 10-11 months from re-irradiation
. Our data reveals no significant improvement in survival with the addition
of re-resection to re-irradiated patients with HGG.
Journal Title: Journal of neuro-oncology

PUBMED ID: 26012492

DOI: doi.org/10.1016/j.neuroscience.2015.05.037
Titolo: Imaging of autoimmune encephalitis--Relevance for clinical practice and hippocampal function.
Autori: Heine J., Prüss H., Bartsch T., Ploner CJ., Paul F., Finke C.
Data di Pubblicazione: 2015-05-28
Abstract: The field of autoimmune encephalitides associated with antibodies targeting cell-surface antigens is rapidly expanding and new antibodies are discovered frequently. Typical clinical presentations include cognitive defi cits, psychiatric symptoms, movement disorders and seizures and the majority of patients respond well to immunotherapy. Pathophysiological mechanisms and clinical features are increasingly recognized and indicate hippocampal dysfu nction in most of these syndromes. Here, we review the neuroimaging characte ristics of autoimmune encephalitides, including N-methyl-d-aspartate (NMDA) receptor, leucine-rich glioma inactivated 1 (LGI1), contactin-associated pro tein-like 2 (CASPR2) encephalitis as well as more recently discovered and le ss frequent forms such as dipeptidyl-peptidase-like protein 6 (DPPX) or glyc ine receptor encephalitis. We summarize findings of routine magnetic resonan ce imaging (MRI) investigations as well as (18)F-fluoro-2-deoxy-d-glucose (F DG)-positron emission tomography (PET) and single photon emission tomography (SPECT) imaging and relate these observations to clinical features and disea se outcome. We furthermore review results of advanced imaging analyses such as diffusion tensor imaging, volumetric analyses and resting-state functiona l MRI. Finally, we discuss contributions of these neuroimaging observations to the understanding of the pathophysiology of autoimmune encephalitides.
Journal Title: Neuroscience

PUBMED ID: 25977905
DOI: doi.org/10.14791/btrt.2015.3.1.34
Titolo: Primary diffuse leptomeningeal gliosarcomatosis.
Autori: Moon JH., Kim SH., Kim EH., Kang SG., Chang JH.
Data di Pubblicazione: 2015-05-16
Abstract: Primary diffuse leptomeningeal gliomatosis (PDLG) is a rare condit ion with a fatal outcome, characterized by diffuse infiltration of the lepto meninges by neoplastic glial cells without evidence of primary tumor in the brain or spinal cord parenchyma. In particular, PDLG histologically diagnose d as gliosarcoma is extremely rare, with only 2 cases reported to date. We r eport a case of primary diffuse leptomeningeal gliosarcomatosis. A 68-year-o ld man presented with fever, chilling, headache, and a brief episode of ment al deterioration. Initial T1-weighted post-contrast brain magnetic resonance imaging (MRI) showed diffuse leptomeningeal enhancement without a definite i ntraparenchymal lesion. Based on clinical and imaging findings, antiviral tr eatment was initiated. Despite the treatment, the patient's neurologic sympt oms and mental status progressively deteriorated and follow-up MRI showed ra pid progression of the disease. A meningeal biopsy revealed gliosarcoma and was conclusive for the diagnosis of primary diffuse leptomeningeal gliosarco matosis. We suggest the inclusion of PDLG in the potential differential diag nosis of patients who present with nonspecific neurologic symptoms in the pr esence of leptomeningeal involvement on MRI.
Journal Title: Brain tumor research and treatment

PUBMED ID: 25949228
DOI: doi.org/10.1016/j.rpor.2015.01.004
Titolo: Fractionated stereotactic radiotherapy plus bevacizumab after respon se to bevacizumab plus irinotecan as a rescue treatment for high-grade gliom as.
Autori: Conde-Moreno AJ., García-Gómez R., Albert-Antequera M., Almendros-Bl anco P., De Las Peñas-Bataller R., González-Vidal V., López-Torrecilla JL., Ferrer-Albiach C.

Data di Pubblicazione: 2015-05-08
Abstract: The combination of BVZ+FSRT as a second-line HGG relapse rescue tr eatment is well-tolerated and seems to offer promising results. We believe t hat multi-centre prospective studies are needed to determine the long-term e fficacy and toxicity of this therapeutic approach.
Journal Title: Reports of practical oncology and radiotherapy : journal of G reatpoland Cancer Center in Poznan and Polish Society of Radiation Oncology

PUBMED ID: 25907866
DOI: doi.org/10.1016/j.humpath.2015.01.023
Titolo: MicroRNA-144 suppresses tumorigenesis and tumor progression of astro cytoma by targeting EZH2.
Autori: Lin L., Zheng Y., Tu Y., Wang Z., Liu H., Lu X., Xu L., Yuan J.
Data di Pubblicazione: 2015-04-25
Abstract: Our previous study demonstrated that enhancer of zeste homolog 2 (EZH2) overexpression may be associated with aggressive tumor progression and poor prognosis in human astrocytoma. The aim of this study was to investigat e the underlying mechanisms of EZH2 on astrocytoma tumorigenesis. An online program miRWalk (http://www.umm.uni-heidelberg.de/apps/zmf/mirwalk/) was use d to predict possible microRNAs (miRNAs) that might target EZH2 messenger RN A (mRNA). Then the functions of the miRNA-EZH2 mRNA axis in astrocytoma cell proliferation, invasion, and migration were also assessed. We further evalua ted the clinical value of the miRNA-EZH2 mRNA axis in astrocytomas. As a res ult, we identified EZH2 as a target gene of miR-144. In addition, forced exp ression of miR-144 suppressed astrocytoma cell proliferation, invasion, and migration by down-regulating EZH2. Moreover, miR-144 down-regulation and EZH 2 mRNA up-regulation were both significantly associated with advanced World Health Organization grades and low Karnofsky performance status score of ast rocytoma patients. Importantly, survival analysis identified the combined ex pression of miR-144 and EZH2 (miR-144/EZH2) as an independent prognostic fac tor for overall survival in astrocytoma patients. In conclusion, miR-144 may function as a tumor suppressor by regulating EZH2 expression, and miR-144/EZ H2 expression may be a highly sensitive marker for the prognosis in astrocyt oma patients.
Journal Title: Human pathology

PUBMED ID: 25894594
DOI: doi.org/10.1007/s11060-015-1774-5
Titolo: Characterization of pseudoprogression in patients with glioblastoma: is histology the gold standard?
Autori: Melguizo-Gavilanes I., Bruner JM., Guha-Thakurta N., Hess KR., Puduv alli VK.
Data di Pubblicazione: 2015-04-21
Abstract: Pseudoprogression (psPD) refers to an increase in size or appearan ce of new areas of MRI contrast enhancement soon after completing chemoradia tion, timely diagnosis of which has been a challenge. Given that tissue samp ling of the MRI changes would be expected to accurately distinguish psPD fro m true progression when MRI changes are first seen, we examined the utility of surgery in diagnosing psPD and influencing patient outcome. We retrospect ively reviewed data from adults with GBM who had MRI changes suggestive of p rogression within 3 months of chemoRT; of these, 34 underwent surgical resec tion. Three subsets-tumor, psPD or mixed-were identified based on histology and immunohistochemistry in the surgical group and by imaging characteristic s in the nonsurgical group. A cohort of patients with stable disease post-ch emoRT served as control. PFS and OS were determined using the Kaplan-Meier m ethod and log rank analysis. Concordance for psPD between radiological inter pretation and subsequent histological diagnosis was seen in only 32% of case s (11/34) 95%CI 19-49%. A large proportion of patients had a histologically

"mixed" pattern with tumor and treatment effect. No significant differences in PFS or OS were seen among the three subtypes. Surgical sampling and histo logic review of MRI changes after chemoRT may not serve as a gold standard t o distinguish psPD from true progression in GBM patients. Refinement of the histological criteria, careful intraoperative selection of regions of intere st and advanced imaging modalities are needed for early differentiation of P sPD from progression to guide clinical management.
Journal Title: Journal of neuro-oncology

PUBMED ID: 25823657
DOI: doi.org/10.18632/oncotarget.3229
Titolo: HOTAIR is a therapeutic target in glioblastoma.
Autori: Zhou X., Ren Y., Zhang J., Zhang C., Zhang K., Han L., Kong L., Wei J., Chen L., Yang J., Wang Q., Zhang J., Yang Y., Jiang T., Li M., Kang C.
Data di Pubblicazione: 2015-04-01
Abstract: HOTAIR is a negative prognostic factor and is overexpressed in mul tiple human cancers including glioblastoma multiform (GBM). Survival analysi s of Chinese Glioma Genome Atlas (CGGA) patient data indicated that high HOT AIR expression was associated with poor outcome in GBM patients. NLK (Nemo-l ike kinase), a negative regulator of the β-catenin pathway, was negatively c orrelated with HOTAIR expression. When the β-catenin pathway was inhibited, GBM cells became susceptible to cell cycle arrest and inhibition of invasion . Introduction of the HOTAIR 5' domain in human glioma-derived astrocytoma i nduced β-catenin. An intracranial animal model was used to confirm that HOTA IR depletion inhibited GBM cell migration/invasion. In the orthotopic model, HOTAIR was required for GBM formation in vivo. In summary, HOTAIR is a poten tial therapeutic target in GBM.
Journal Title: Oncotarget

PUBMED ID: 25797780
DOI: doi.org/10.2176/nmc.ra.2014-0348
Titolo: Trends and outcomes in the treatment of gliomas based on data during 2001-2004 from the Brain Tumor Registry of Japan.
Autori: Narita Y., Shibui S., Shibui S.
Data di Pubblicazione: 2015-03-24
Abstract: The committee of Brain Tumor Registry of Japan (BTRJ) was founded in 1973 and conducts surveys and analyses of incidence, therapeutic methods, and treatment outcomes of primary and metastatic brain tumors with the coope ration of the Japan Neurosurgical Society members. Newly diagnosed 3,000-4,0 00 primary brain tumors and 600-1,000 brain metastases patients were enrolle d in each year. This report describes the trends and treatment outcomes of g liomas from BTRJ volume 13, including 13,431 patients with primary brain tum ors who newly started treatment from 2001 to 2004. Data from 382 diffuse ast rocytomas (DAs), 121 oligodendrogliomas (OLs), 90 oligoastrocytomas (OAs), 5 13 anaplastic astrocytomas (AAs), 126 anaplastic oligodendrogliomas (AOs), 1 06 anaplastic oligoastrocytomas (AOAs), and 1,489 glioblastomas (GBMs) were analyzed for overall survival (OS) and progression free survival (PFS) depen ding on age, symptoms, Karnofsky performance status, location of the tumor, extent of resection (EOR), initial radiotherapy and chemotherapy. The 5-year PFS rates of the patients with DA, OL+OA, AA, AO+AOA, and GBM were 57.0%, 74 .6%, 28.7%, 54.0%, and 9.2%, and the 5-year OS rates were 75.0%, 90.0%, 41.1 %, 68.2%, and 10.1%, respectively. Higher EOR≥75% in DA and OL+OA and that ≥ 50% in AA, AO+AOA, and GBM significantly prolonged OS. Complications and cau se of death were also reported. BTRJ had been edited for all the patients, r esearchers, and especially for clinicians at bedside to give useful informat ion about brain tumors and to contribute to the advances in brain tumor trea tment. This report revealed various clinical problematic issues pertaining t o the diagnosis and treatment of gliomas.

Journal Title: Neurologia medico-chirurgica

PUBMED ID: 25797075
DOI: doi.org/10.1016/j.wneu.2015.03.018
Titolo: Efficacy of Surgery and Further Treatment of Progressive Glioblastoma.
Autori: Woernle CM., Péus D., Hofer S., Rushing EJ., Held U., Bozinov O., Krayenbühl N., Weller M., Regli L.
Data di Pubblicazione: 2015-03-24
Abstract: Surgery of progressive glioblastoma and postoperative treatment at the time of progression is associated with improved OS in some patients. The addition of age may improve survival prediction of the NIH recurrent glioblastoma scale.
Journal Title: World neurosurgery

PUBMED ID: 25773883
DOI: doi.org/10.1016/j.ejmp.2015.02.011
Titolo: Microbeam radiation therapy: Clinical perspectives.
Autori: Grotzer MA., Schültke E., Bräuer-Krisch E., Laissue JA.
Data di Pubblicazione: 2015-03-17
Abstract: Microbeam radiation therapy (MRT), a novel form of spatially fractionated radiotherapy (RT), uses arrays of synchrotron-generated X-ray microbeams (MB). MRT has been identified as a promising treatment concept that might be applied to patients with malignant central nervous system (CNS) tumours for whom, at the current stage of development, no satisfactory therapy is available yet. Preclinical experimental studies have shown that the CNS of healthy rodents and piglets can tolerate much higher radiation doses delivered by spatially separated MBs than those delivered by a single, uninterrupted, macroscopically wide beam. High-dose, high-precision radiotherapies such as MRT with reduced probabilities of normal tissue complications offer prospects of improved therapeutic ratios, as extensively demonstrated by results of experiments published by many international groups in the last two decades. The significance of developing MRT as a new RT approach cannot be understated. Up to 50% of cancer patients receive conventional RT, and any new treatment that provides better tumour control whilst preserving healthy tissue is likely to significantly improve patient outcomes.
Journal Title: Physica medica : PM : an international journal devoted to the applications of physics to medicine and biology : official journal of the Italian Association of Biomedical Physics (AIFB)

PUBMED ID: 25762141
DOI: doi.org/10.1038/nature14320
Titolo: Tetanus toxoid and CCL3 improve dendritic cell vaccines in mice and glioblastoma patients.
Autori: Mitchell DA., Batich KA., Gunn MD., Huang MN., Sanchez-Perez L., Nair SK., Congdon KL., Reap EA., Archer GE., Desjardins A., Friedman AH., Friedman HS., Herndon JE., Coan A., McLendon RE., Reardon DA., Vredenburgh JJ., Bigner DD., Sampson JH.
Data di Pubblicazione: 2015-03-13
Abstract: After stimulation, dendritic cells (DCs) mature and migrate to draining lymph nodes to induce immune responses. As such, autologous DCs generated ex vivo have been pulsed with tumour antigens and injected back into patients as immunotherapy. While DC vaccines have shown limited promise in the treatment of patients with advanced cancers including glioblastoma, the factors dictating DC vaccine efficacy remain poorly understood. Here we show that pre-conditioning the vaccine site with a potent recall antigen such as tetanus/diphtheria (Td) toxoid can significantly improve the lymph node homing

and efficacy of tumour-antigen-specific DCs. To assess the effect of vaccine site pre-conditioning in humans, we randomized patients with glioblastoma to pre-conditioning with either mature DCs or Td unilaterally before bilateral vaccination with DCs pulsed with Cytomegalovirus phosphoprotein 65 (pp65) RN A. We and other laboratories have shown that pp65 is expressed in more than 90% of glioblastoma specimens but not in surrounding normal brain, providing an unparalleled opportunity to subvert this viral protein as a tumour-specif ic target. Patients given Td had enhanced DC migration bilaterally and signi ficantly improved survival. In mice, Td pre-conditioning also enhanced bilat eral DC migration and suppressed tumour growth in a manner dependent on the chemokine CCL3. Our clinical studies and corroborating investigations in mic e suggest that pre-conditioning with a potent recall antigen may represent a viable strategy to improve anti-tumour immunotherapy.
Journal Title: Nature

PUBMED ID: 25732040
DOI: doi.org/10.1093/annonc/mdv127
Titolo: Glioblastoma adaptation traced through decline of an IDH1 clonal dri ver and macro-evolution of a double-minute chromosome.
Autori: Favero F., McGranahan N., Salm M., Birkbak NJ., Sanborn JZ., Benz SC ., Becq J., Peden JF., Kingsbury Z., Grocok RJ., Humphray S., Bentley D., Sp encer-Dene B., Gutteridge A., Brada M., Roger S., Dietrich PY., Forshew T., Gerlinger M., Rowan A., Stamp G., Eklund AC., Szallasi Z., Swanton C.
Data di Pubblicazione: 2015-03-04
Abstract: This case sheds light on the dynamic evolution of a GBM tumour, de fining the origins of the lethal sub-clone, the macro-evolutionary genomic e vents dominating the disease at recurrence and the loss of a clonal driver. Even in the era of rapid WGS analysis, cases such as this illustrate the sig nificant hurdles for precision medicine success.
Journal Title: Annals of oncology : official journal of the European Society for Medical Oncology

PUBMED ID: 25702676
DOI: doi.org/10.5301/tj.5000210
Titolo: The added value of bevacizumab concomitantly administered with carbo platin versus carboplatin alone in patients with recurrent glioblastomas.
Autori: Kaloshi G., Diamandi P., Cakani B., Brace G., Rroji A., Petrela M.
Data di Pubblicazione: 2015-02-24
Abstract: The combination of BEV and CBDCA is associated with improved respo nse rates and survival compared with CBDCA alone. These results highlight th e value of BEV in recurrent GBM. However, the clinical benefit of this inter esting approach needs validation in a larger patient cohort.
Journal Title: Tumori

PUBMED ID: 25702193
DOI: doi.org/10.1007/s11060-015-1745-x
Titolo: Hypofractionated stereotactic radiotherapy in combination with bevac izumab or fotemustine for patients with progressive malignant gliomas.
Autori: Minniti G., Agolli L., Falco T., Scaringi C., Lanzetta G., Caporello P., Osti MF., Esposito V., Enrici RM.
Data di Pubblicazione: 2015-02-23
Abstract: To evaluate the efficacy of hypofractionated stereotactic radiothe rapy performed as reirradiation in combination with fotemustine or bevacizum ab as salvage treatment in patients with recurrent malignant glioma. Between May 2006 and December 2013, 54 patients with recurrent malignant glioma rece ived hypofractionated stereotactic radiotherapy (HSRT, 25 Gy in 5-Gy fractio ns) plus either fotemustine or bevacizumab at University of Rome Sapienza, S

ant'Andrea Hospital. All patients had Karnofsky performance score (KPS) ≥ 60 and were previously treated with standard chemoradiotherapy. Forty-two patients had a GBM and 12 patients had an anaplastic astrocytoma (AA). The median overall survival (OS) time and 12-month OS rates after HSRT was 11 months and 30 % for patients treated with HSRT plus bevacizumab and 8.3 months and 5 % for those treated with HSRT plus fotemustine (p = 0.01). Median PFS times were 4 and 6 months for patients treated with HSRT plus fotemustine or bevacizumab, respectively (p = 0.01). KPS > 70 (p = 0.04), AA histology, and the treatment with bevacizumab were independent favourable prognostic factors for OS. In general, both treatments were well tolerated with relatively low treatment-related toxicity. HSRT combined with bevacizumab or fotemustine may represent a feasible treatment option for patients with progressive malignant gliomas, although most of the tumors recur in a few months. Efficacy of bevacizumab or alkylating agents in combination with different radiation schedules needs to be evaluated in prospective studies.
Journal Title: Journal of neuro-oncology

PUBMED ID: 25688497
DOI: doi.org/10.1700/1778.19268
Titolo: Impact of 11C-methionine positron emission tomography/computed tomography on radiation therapy planning and prognosis in patients with primary brain tumors.
Autori: Schinkelshoek M., Lopci E., Clerici E., Alongi F., Mancosu P., Rodari M., Navarria P., van der Hiel B., Scorsetti M., Chiti A.
Data di Pubblicazione: 2015-02-18
Abstract: Despite the limited study population, our data indicate that MET-PET/CT can have a significant impact on radiation therapy planning in patients with primary brain tumors. Moreover, treatment modification according to PET appears to be a predictor of clinical outcome in this group of patients.
Journal Title: Tumori

PUBMED ID: 25655102
DOI: doi.org/10.1158/1078-0432.CCR-14-2737
Titolo: MGMT Promoter Methylation Is a Strong Prognostic Biomarker for Benefit from Dose-Intensified Temozolomide Rechallenge in Progressive Glioblastoma: The DIRECTOR Trial.
Autori: Weller M., Tabatabai G., Kästner B., Felsberg J., Steinbach JP., Wick A., Schnell O., Hau P., Herrlinger U., Sabel MC., Wirsching HG., Ketter R., Bähr O., Platten M., Tonn JC., Schlegel U., Marosi C., Goldbrunner R., Stupp R., Homicsko K., Pichler J., Nikkhah G., Meixensberger J., Vajkoczy P., Kollias S., Hüsing J., Reifenberger G., Wick W., Wick W.
Data di Pubblicazione: 2015-02-07
Abstract: Temozolomide rechallenge is a treatment option for MGMT promoter-methylated recurrent glioblastoma. Alternative strategies need to be considered for patients with progressive glioblastoma without MGMT promoter methylation.
Journal Title: Clinical cancer research : an official journal of the American Association for Cancer Research

PUBMED ID: 25609769
DOI: doi.org/10.1212/WNL.0000000000001262
Titolo: Biological tumor volume in 18FET-PET before radiochemotherapy correlates with survival in GBM.
Autori: Suchorska B., Jansen NL., Linn J., Kretzschmar H., Janssen H., Eigenbrod S., Simon M., Pöpperl G., Kreth FW., la Fougere C., Weller M., Tonn JC., Tonn JC.
Data di Pubblicazione: 2015-01-23

Abstract: BTV(preRCx) and TAC represent important (18)FET-PET-derived imagin g biomarkers in GBM. Increasing TACs are associated with prolonged OS. The B TV(preRCx) is a strong prognostic factor for progression-free survival and O S independent of the mode of surgery. Our data furthermore suggest that pati ents harboring resectable GBM might benefit from maximal PET-guided tumor re section.
Journal Title: Neurology

PUBMED ID: 25601471
DOI: doi.org/10.2174/1566524015666150114115427
Titolo: Targeting the PI3K/AKT/mTOR signaling pathway in medulloblastoma.
Autori: Dimitrova V., Arcaro A.
Data di Pubblicazione: 2015-01-21
Abstract: Medulloblastoma is the most common malignant childhood brain tumor and is associated with a poor outcome. There is an urgent need to develop no vel targeted therapeutic approaches for medulloblastoma, which will arise fr om an enhanced understanding of the disease at the molecular level. Medullob lastoma has been recognized to be a heterogeneous disease, and no recurrent cancer gene mutations have been found, although many of the mutations descri bed so far affect key intracellular signaling pathways, such as sonic hedgeh og (SHH) and Wnt/β-catenin. The PI3K/AKT/mTOR (PAM) signaling pathway contro ls key cellular responses, such as cell growth and proliferation, survival, migration and metabolism. Over the last decades, it has been recognized that this intracellular signaling pathway is frequently activated by genetic and epigenetic alterations in malignant brain tumors, including medulloblastoma. Clinical trials have started to evaluate the safety and efficacy of agents t argeting this pathway in malignant brain tumors. Due to the complexity of th e PAM signaling pathway, there remain significant difficulties in the develo pment of novel therapeutic approaches. The future challenges in developing e ffective treatments for cancer patients include the development of predictiv e biomarkers and combinatorial approaches to effectively target multiple sig nal transduction pathways. In this review article, we will summarize the cur rent knowledge about the role of PAM signaling in medulloblastoma and discus s the strategies that are currently being evaluated with targeted agents aga inst this pathway.
Journal Title: Current molecular medicine

PUBMED ID: 20464625
DOI: doi.org/10.1007/s11060-010-0197-6
Titolo: Nitrosourea-based chemotherapy for low grade gliomas failing initial treatment with temozolomide.
Autori: Kaloshi G., Sierra del Rio M., Ducray F., Psimaras D., Idbaih A., La igle-Donadey F., Taillibert S., Houillier C., Dehais C., Omuro A., Sanson M. , Delattre JY., Hoang-Xuan K.
Data di Pubblicazione: 2010-05-14
Abstract: There is a growing evidence of using Temozolomide as upfront thera py for progressive low grade gliomas. No data exist on the efficacy of nitro soureas as an alternative to radiotherapy in those patients who progress aft er Temozolomide. We retrospectively reviewed 30 patients with median age of 46 years. Twenty-one patients had pure oligodendrogliomas. Thirteen patients had a non-enhancing tumor at progression after Temozolomide. The chromosomes 1p/19q were co-deleted in 5 cases and retained in 10 cases. Response rate wa s 10% (3 minor responses achieved in non-enhancing tumors). Tolerance was ac ceptable (17% grade III and IV myelosupression). Median PFS was 6.5 months. Median OS from start of salvage treatment was 23.4 months. Tumors without co ntrast enhancement demonstrated a better prognosis than those with contrast enhancement both in term of PFS (P = 0.0003) and OS (P = 0.0006). Chromosome s 1p/19q codeletion was not predictive for objective response to salvage tre

atment but correlated with a better PFS (P = 0.02). In conclusion, salvage N U chemotherapy provide disappointing results in TMZ-pretreated low grade gli omas (LGG), which should be treated in priority by conventional radiotherapy especially in LGG that display contrast enhancement at progression.
Journal Title: Journal of neuro-oncology

PUBMED ID: 20458050
DOI: doi.org/10.1200/JCO.2009.26.3988
Titolo: Phase II study of cediranib, an oral pan-vascular endothelial growth factor receptor tyrosine kinase inhibitor, in patients with recurrent gliobl astoma.
Autori: Batchelor TT., Duda DG., di Tomaso E., Ancukiewicz M., Plotkin SR., Gerstner E., Eichler AF., Drappatz J., Hochberg FH., Benner T., Louis DN., C ohen KS., Chea H., Exarhopoulos A., Loeffler JS., Moses MA., Ivy P., Sorense n AG., Wen PY., Jain RK.
Data di Pubblicazione: 2010-05-12
Abstract: Cediranib monotherapy for recurrent glioblastoma is associated wit h encouraging proportions of radiographic response, 6-month progression-free survival, and a steroid-sparing effect with manageable toxicity. We identifi ed early changes in circulating molecules as potential biomarkers of respons e to cediranib. The efficacy of cediranib and the predictive value of these candidate biomarkers will be explored in prospective trials.
Journal Title: Journal of clinical oncology : official journal of the Americ an Society of Clinical Oncology

PUBMED ID: 25599276
DOI: doi.org/10.3171/2014.10.FOCUS14651
Titolo: Proposed therapeutic strategy for adult low-grade glioma based on ag gressive tumor resection.
Autori: Nitta M., Muragaki Y., Maruyama T., Ikuta S., Komori T., Maebayashi K., Iseki H., Tamura M., Saito T., Okamoto S., Chernov M., Hayashi M., Okada Y.
Data di Pubblicazione: 2015-01-20
Abstract: OBJECT There is no standard therapeutic strategy for low-grade gli oma (LGG). The authors hypothesized that adjuvant therapy might not be neces sary for LGG cases in which total radiological resection was achieved. Accor dingly, they established a treatment strategy based on the extent of resecti on (EOR) and the MIB-1 index: patients with a high EOR and low MIB-1 index w ere observed without postoperative treatment, whereas those with a low EOR a nd/or high MIB-1 index received radiotherapy (RT) and/or chemotherapy. In th e present retrospective study, the authors reviewed clinical data on patient s with primarily diagnosed LGGs who had been treated according to the above- mentioned strategy, and they validated the treatment policy. Given their res ults, they will establish a new treatment strategy for LGGs stratified by EO R, histological subtype, and molecular status. METHODS One hundred fifty-thr ee patients with diagnosed LGG who had undergone resection or biopsy at Toky o Women's Medical University between January 2000 and August 2010 were analy zed. The patients consisted of 84 men and 69 women, all with ages ≥ 15 years . A total of 146 patients underwent surgical removal of the tumor, and 7 pat ients underwent biopsy. RESULTS Postoperative RT and nitrosourea-based chemo therapy were administered in 48 and 35 patients, respectively. Extent of res ection was significantly associated with both overall survival (OS; p = 0.00 96) and progression-free survival (PFS; p = 0.0007) in patients with diffuse astrocytoma but not in those with oligodendroglial subtypes. Chemotherapy si gnificantly prolonged PFS, especially in patients with oligodendroglial subt ypes (p = 0.0009). Patients with a mutant IDH1 gene had significantly longer OS (p = 0.034). Multivariate analysis did not identify MIB-1 index or RT as prognostic factors, but it did identify chemotherapy as a prognostic factor

for PFS and EOR as a prognostic factor for OS and PFS. CONCLUSIONS The findings demonstrated that EOR was significantly correlated with patient survival ; thus, one should aim for maximum tumor resection. In addition, patients with a higher EOR can be safely observed without adjuvant therapy. For patients with partial resection, postoperative chemotherapy should be administered for those with oligodendroglial subtypes, and repeat resection should be considered for those with astrocytic tumors. More aggressive treatment with RT and chemotherapy may be required for patients with a poor prognosis, such as those with diffuse astrocytoma, 1p/19q nondeleted tumors, or IDH1 wild-type oligodendroglial tumors with partial resection.
Journal Title: Neurosurgical focus

PUBMED ID: 25594327
DOI: doi.org/10.3171/2014.11.JNS13295
Titolo: Role of adjuvant or salvage radiosurgery in the management of unresected residual or progressive glioblastoma multiforme in the pre-bevacizumab era.
Autori: Niranjan A., Kano H., Iyer A., Kondziolka D., Flickinger JC., Lunsford LD.
Data di Pubblicazione: 2015-01-17
Abstract: In this analysis 30% of a heterogeneous cohort of GBM patients eligible for SRS had an OS of 2 years. Radiosurgery at the time of tumor progression was associated with a median survival of 21.8 months. The role of radiosurgery for GBMs remains controversial. The findings in this study support the need for a funded and appropriately designed clinical trial that will provide a higher level of evidence regarding the future role of SRS for glioblastoma patients in whom disease has progressed despite standard management.
Journal Title: Journal of neurosurgery

PUBMED ID: 25575937
DOI: doi.org/10.1007/s11060-014-1693-x
Titolo: Impact of bevacizumab administered dose on overall survival of patients with progressive glioblastoma.
Autori: Levin VA., Mendelssohn ND., Chan J., Stovall MC., Peak SJ., Yee JL., Hui RL., Chen DM.
Data di Pubblicazione: 2015-01-11
Abstract: Bevacizumab (BEV, Avastin(®)) produces durable objective radiological responses of 20-26 %, median response durations of 16-18 weeks, and median overall survival (mOS) of 31-40 weeks. While the use of BEV is well-established, the lack of dose-response studies in glioblastoma (GBM) patients raises the question whether current dosing practice is optimal. As a result of differing approaches to BEV dosing that ranged from the FDA approved package insert dose of 10 mg/kg every 2 weeks to 7.5 mg/kg every 3-4 weeks, among physicians within Northern California Kaiser Permanente hospitals over 4+ years, we did an IRB-approved retrospective analysis of patients seen in Northern California Kaiser Permanente facilities and treated with BEV. Between September 1, 2008 and August 31, 2013, 181 patients received BEV for tumor progression/recurrence starting 2.6 weeks after completion of chemoradiation. The integrated BEV administered dose-week (AUCBEV) for all patients had a median AUCBEV of 3.6 mg·wk/kg). Maximum likelihood analysis found patients over 65 years did worse than younger patients (p = 0.004), women lived longer (p = 0.002), and patients treated below the AUCBEV did better than those treated above the median AUCBEV (p = 0.003). mOS for BEV starting 1 month after chemoradiation was 45 versus 68 weeks (p = 0.012) and BEV starting 3 months after chemoradiation was 40 versus 74 weeks (p = 0.0085). Dosing BEV at half the standard dose for progressive/recurrent GBM was at least equivalent to or, maybe better than standard dosing. Unexplained was the observation that females had longer OS with BEV than males.

Journal Title: Journal of neuro-oncology

PUBMED ID: 25572814
DOI: doi.org/10.1007/s12032-014-0460-3
Titolo: Single-agent bevacizumab is an effective treatment in recurrent glio blastoma.
Autori: Hacibekiroglu I., Kodaz H., Erdogan B., Turkmen E., Ozcelik M., Esen kaya A., Saygi HM., Uzunoglu S., Cicin I.
Data di Pubblicazione: 2015-01-10
Abstract: The aim of this study was to evaluate the efficiency and safety of single-agent bevacizumab therapy for recurrent glioblastoma multiforme (GBM) . We identified patients with histologically confirmed glioblastoma and Worl d Health Organization Grade III glioma who were previously treated with temo zolomide plus radiotherapy and received 10 mg/kg bevacizumab intravenous inf usion every 2 weeks until disease progression for recurrent disease. A total 24 patients included to this study. Twenty-two patients had GBM, and two pat ients had WHO grade III glioma. No complete response was observed, five pati ents (20.8 %) had partial response, nine patients (37.5 %) had stable diseas es, and ten patients (41.7 %) had progressive diseases. The overall response rate was 20.8 %. The 6-month PFS rate (PFS6) and median PFS were determined as 37.5 % and 4.1 months, respectively. Median OS was 6.4 months. Performanc e status of 17 (70.8 %) patients was improved following bevacizumab regimen. Univariate analysis showed that improvement in performance status (IPS) foll owing bevacizumab therapy was a significant predictor of both PFS ($p < 0.001$) and OS ($p < 0.020$). Bevacizumab-related adverse effects were observed in 1 3 (54.1 %) patients. Grade 3-4 toxicity was observed in 4 (16.6 %) patients. Therapy interruptions were experienced in two patients due to adverse effect s. Single-agent bevacizumab is an effective and safe treatment alternative i n recurrent GBM. IPS following bevacizumab therapy was a significant predict or of both PFS and OS.
Journal Title: Medical oncology (Northwood, London, England)

PUBMED ID: 25569296
DOI: doi.org/10.1016/j.clineuro.2014.12.006
Titolo: Gliomatosis cerebri having a poor performance status without recurre nce after radiotherapy: a single institutional experience.
Autori: Jung TY., Yoon MS., Kim YH., Jung S., Kim IY., Jang WY., Moon KS., L ee KH., Kim SK.
Data di Pubblicazione: 2015-01-09
Abstract: Some GC patients, especially the elderly, might have a poor perfor mance status without recurrence after RT of a larger radiation field.
Journal Title: Clinical neurology and neurosurgery

PUBMED ID: 25563816
DOI: doi.org/10.1007/s11060-014-1714-9
Titolo: Salvage therapy with lomustine for temozolomide refractory recurrent anaplastic astrocytoma: a retrospective study.
Autori: Chamberlain MC.
Data di Pubblicazione: 2015-01-08
Abstract: There is no standard therapy for recurrent anaplastic astrocytoma (AA). Assess response and toxicity of lomustine (CCNU) in recurrent AA follo wing prior surgery, radiotherapy and TMZ in a retrospective case series. Thi rty-five adults (18 males; 17 females: median age 42.5 years) with TMZ refra ctory recurrent AA were treated with lomustine. Seven patients were treated at 1st recurrence and 28 patients were treated at 2nd recurrence. Prior salv age therapy included re-resection in 19, TMZ in 20 and radiotherapy in 7. A cycle of lomustine was defined as 110 mg/m(2) on day 1 only administered onc

e every 6-8 weeks. Success of treatment was defined as progression free surv ival at 6 months of 40 % or better. Grade 3 or 4 toxicities included anemia (14 patients), constipation (1), fatigue (4), lymphopenia (5), nausea/vomiti ng (2), neutropenia (8) and thrombocytopenia (10). No grade five toxicities were seen. The median number of cycles of therapy was 3 (range 1-6). Best ra diographic response was progressive disease in 14 (40 %), stable disease in 19 (54 %) and partial response in 2 (5.7 %). Median progression free surviva l (PFS) was 4.5 months (range 1.5-12 months), 6-month PFS was 40 % and 12 mo nth PFS was 11.4 %. Median survival after onset of CCNU was 9.5 months (rang e 2.5-15 months). Median overall survival was 2.7 years (range 1.7-4.3). In this small retrospective series of patients with recurrent AA refractory to TMZ, lomustine appears to have modest single agent with manageable toxicity. Confirmation in a larger series of similar patients is required.
Journal Title: Journal of neuro-oncology

PUBMED ID: 27158638
DOI: doi.org/10.14800/ccm.747
Titolo: Temozolomide resistance and tumor recurrence: Halting the Hedgehog.
Autori: Munoz JL., Rodriguez-Cruz V., Walker ND., Greco SJ., Rameshwar P.
Data di Pubblicazione: 2016-05-10
Abstract: Chemotherapy with Temozolomide (TMZ), radiation and surgery are th e primary methods to treat Glioblastoma Multiforme (GBM), the most common ad ult intracranial tumor with dismal outcome. GBM resistance to therapy is the main reason of poor patient outcomes. Thus, methods to overcome the resistan ce are an area of extensive research. This highlight focuses on three recent ly published articles on the mechanism of resistance and possible therapeuti c intervention, including RNA treatment with stem cells. We showed a crucial role of the developmental Sonic Hedgehog (SHH) pathway in the acquisition an d maintenance of TMZ resistance. SHH signaling caused TMZ resistance in GBM cells through an increase in the multiple drug resistance gene (MDR1). The S HH receptor, Patched-1 (PTCH1), negatively regulate SHH signaling. In GBM, m iR-9 suppressed PTCH1 levels, resulting in the activation of SHH pathway. Th us, SHH signaling is independent of the ligand in resistant GBM cells. MiR-9 was also increased in chemoresistance CD133+ GBM cells. A potential method t o reverse resistance was tested by delivering the anti-miR in bone marrow-de rived Mesenchymal Stem Cells (MSCs). The anti-miR-9 was transferred into the resistant GBM cells through exosomes and gap junctional intercellular commun ication. We also review on-going clinical trials with inhibitor of SHH signa ling, and also discuss drug delivery by cell therapy for GBM. While GBM trea tment has proven to be a challenge, there are a number of novel approaches w e are currently developing to manage this malignancy.
Journal Title: Cancer cell & microenvironment

PUBMED ID: 25542442
DOI: doi.org/10.1016/j.jfo.2014.06.011
Titolo: [Apropos of 5 cases of optic nerve tumors diagnosed during a 6-year-period].
Autori: Rebika S., Bonnin N., Kémény JL., Chiambaretta F., Bacin F.
Data di Pubblicazione: 2014-12-28
Abstract: The diagnosis of optic nerve tumors must be considered in cases of anterior or posterior progressive optic neuropathy. Treatment must be a comp romise between effective treatment of the tumor and preservation of visual f unction. Decisions are made through multidisciplinary consultations, in whic h the role of the ophthalmologist is crucial for the diagnosis and success o f the treatment.
Journal Title: Journal francais d'ophtalmologie

PUBMED ID: 25534576
DOI: doi.org/10.1007/s11060-014-1684-y
Titolo: Efficacy and patient-reported outcomes with dose-intense temozolomide in patients with newly diagnosed pure and mixed anaplastic oligodendroglioma: a phase II multicenter study.
Autori: Ahluwalia MS., Xie H., Dahiya S., Hashemi-Sadraei N., Schiff D., Fisher PG., Chamberlain MC., Pannullo S., Newton HB., Brewer C., Wood L., Prayson R., Elson P., Peereboom DM.
Data di Pubblicazione: 2014-12-24
Abstract: Standard initial therapy for patients with pure and mixed anaplastic oligodendrogliomas (AO/MAO) includes chemotherapy and radiation therapy. Anaplastic oligodendrogliomas with 1p/19q co-deletion are more responsive to chemotherapy. There is concern for potential long-term CNS toxicity of radiation. Hence an approach using chemotherapy initially and reserving radiation for progressive disease is attractive. This multicenter phase II trial included patients with newly diagnosed AO/MAO with central pathology review and 1p/19q assay. Temozolomide was given 150 mg/m(2) days 1-7 and 15-21, every 28 days for 8 cycles. The primary endpoint was progression free survival (PFS). Secondary endpoints included response rate, overall survival (OS), treatment toxicity and health-related quality of life (HRQL). Data from 62 patients enrolled between December 2001 and April 2007 at seven centers were analyzed. Among patients with measurable disease, 8 % achieved complete remission, 56 % had stable disease and 36 % had progression. The median PFS and OS were 27.2 months (95 % CI 11.9-36.3) and 105.8 months (95 % CI 51.5-N/A), respectively. Both 1p loss and 1p/19q co-deletion were positive prognostic factors for PFS ($p < 0.001$) and OS ($p < 0.001$); and there was some suggestion that 1p/19q co-deletion also predicted better response to chemotherapy ($p = 0.007$). Grade 3/4 toxicities were mainly hematological. Significantly improved HRQL in the future uncertainty domain of the brain cancer module was seen after cycle 4 ($p < 0.001$). This trial achieved outcomes similar to those reported previously. Toxicities from dose-intense temozolomide were manageable. Improvement in at least one HRQL domain increased over time. This trial supports the further study of first-line temozolomide monotherapy as an alternative to radiation therapy for patients with newly diagnosed AO/MAO with 1p 19q co-deleted tumors.
Journal Title: Journal of neuro-oncology

PUBMED ID: 25523732
DOI: doi.org/12.2014/JCPSP.935939
Titolo: Treatment updates regarding anaplastic oligodendroglioma and anaplastic oligoastrocytoma.
Autori: Khan KA., Abbasi AN., Ali N.
Data di Pubblicazione: 2014-12-20
Abstract: Anaplastic Oligodendroglioma / Anaplastic Oligoastrocytoma (AO/AOA) is a WHO Grade-III primary brain tumor. These tumors comprise about 5 - 10 % of all gliomas, which make them the third most common primary brain tumors after glioblastoma multiforme and astrocytomas. For many years standard of treatment remained Maximum Safe Resection (MSR) followed by Radiotherapy (RT). These tumors have also been known to be sensitive to alkylator-based chemotherapy particularly the subset having 1p/19q co-deletion signature. There is robust data showing that these tumors are responsive to chemotherapy in recurrent or progressive setting. Recently, up front chemotherapy has been added to standard post-surgery RT. It has been found that subset of AO/AOA having 1p/19q co-deletion responded very well to the addition of chemotherapy. This substantial benefit in terms of median Overall Survival (OS) and median Progression Free Survival (PFS) have intrigued the personalized treatment of AO/AOA on the basis of molecular signature markers.
Journal Title: Journal of the College of Physicians and Surgeons--Pakistan : JCPSP

PUBMED ID: 25493242
DOI: doi.org/10.5306/wjco.v5.i5.1060
Titolo: Clinicopathological features and treatment outcomes of brain stem gl iomas in Saudi population.
Autori: Bayoumi Y., Sabbagh AJ., Mohamed R., ElShokhaiby UM., Maklad AM., Tu nio MA., Balbaid AA.
Data di Pubblicazione: 2014-12-11
Abstract: BSG, especially the DIPG subgroup, had a dismal prognosis, needing more aggressive neurosurgical, radiation and chemotherapy techniques, while focal and tectal tumors were found to have a better prognosis.
Journal Title: World journal of clinical oncology

PUBMED ID: 25462098
DOI: doi.org/10.1016/j.clineuro.2014.11.006
Titolo: Treatment results and outcome in elderly patients with glioblastoma multiforme--a retrospective single institution analysis.
Autori: Hoffermann M., Bruckmann L., Kariem Mahdy A., Asslaber M., Payer F., von Campe G.
Data di Pubblicazione: 2014-12-03
Abstract: It appears that more aggressive treatment regimens can lead to lon ger overall survival in elderly glioblastoma multiforme patients. Gross tota l resection should be offered whenever safely possible; otherwise, biopsy ma y be preferred. Non-surgical treatment should consist of postoperative radio therapy and concomitant and/or adjuvant chemotherapy. Possibly higher rates of hematological side effects in concomitant chemotherapy need to be further investigated.
Journal Title: Clinical neurology and neurosurgery

PUBMED ID: 25441707
DOI: doi.org/10.1016/j.neuchi.2013.12.007
Titolo: Tectal plate tumours. Our experience with a paediatric surgical seri es.
Autori: Mottolese C., Szathmari A., Beuriat PA., Frappaz D., Jouvet A., Herm ier M.
Data di Pubblicazione: 2014-12-03
Abstract: Exophytic tectal plate tumours can be treated based on a microsurg ical approach in paediatric patients. In experienced hands surgery can be pe rformed with an acceptable morbidity and with zero percent mortality. In our experience, the sub-occipital transtentorial approach permits a wide view of the region and safe surgical removal.
Journal Title: Neuro-Chirurgie

PUBMED ID: 25434384
DOI: doi.org/10.3171/2014.9.FOCUS14519
Titolo: Molecularly targeted therapies for recurrent glioblastoma: current a nd future targets.
Autori: Lau D., Magill ST., Aghi MK.
Data di Pubblicazione: 2014-12-02
Abstract: Recurrent glioblastoma remains very difficult to treat, even with molecular targeted therapies and anticancer agents. The currently available targeted therapy regimens have poor to modest activity against recurrent gli oblastoma. As newer agents are actively being developed, combination regimen s have provided the most promising results for improving outcomes. Targeted therapies matched to molecular profiles of individual tumors are predicted t o be a critical component necessary for improving efficacy in future trials.

Journal Title: Neurosurgical focus

PUBMED ID: 25428586
DOI: doi.org/10.1007/s00234-014-1468-2
Titolo: ^{23}Na-MRI of recurrent glioblastoma multiforme after intraoperative radiotherapy: technical note.
Autori: Haneder S., Giordano FA., Konstandin S., Brehmer S., Buesing KA., Schmiedek P., Schad LR., Wenz F., Schoenberg SO., Ong MM.
Data di Pubblicazione: 2014-11-28
Abstract: (23)Na-MRI provided similar information in the suspicious area compared to (18)F-FET-PET, exceeding conventional (1)H-MRI. Still, (23)Na-MRI remains an investigational technique, which is worth to be further evaluated.
Journal Title: Neuroradiology

PUBMED ID: 25424852
DOI: doi.org/10.1158/1078-0432.CCR-14-1380
Titolo: First-in-human dose study of the novel transforming growth factor-β receptor I kinase inhibitor LY2157299 monohydrate in patients with advanced cancer and glioma.
Autori: Rodon J., Carducci MA., Sepulveda-Sánchez JM., Azaro A., Calvo E., Seoane J., Braña I., Sicart E., Gueorguieva I., Cleverly AL., Pillay NS., Desaiah D., Estrem ST., Paz-Ares L., Holdhoff M., Blakeley J., Lahn MM., Baselga J.
Data di Pubblicazione: 2014-11-27
Abstract: On the basis of the safety, pharmacokinetics, and antitumor activity in patients with glioma, the intermittent administration of LY2157299 at 300 mg/day is safe for future clinical investigation.
Journal Title: Clinical cancer research : an official journal of the American Association for Cancer Research

PUBMED ID: 25375042
DOI: Mancante
Titolo: Multidisciplinary management of adult low grade gliomas.
Autori: Mariş D., Nica D., Mohan D., Moisa H., Ciurea AV.
Data di Pubblicazione: 2014-11-07
Abstract: LGG: low grade gliomas, WHO: World Health Organization, OS: overall survival, PFS: progression-free survival, MRI: Magnetic resonance imaging, MRS: Magnetic resonance spectroscopy, MPFS: malignant progression-free survival, rCBV: Relative Cerebral Blood Volume, QOL: quality of life, FLAIR: Fluid attenuated inversion recovery, MGMT: O6-methylguanine DNA methyltransferase enzyme, DSC MR imaging: Dynamic Susceptibility Contrast Perfusion MR imaging, 1H-MRS: Proton Magnetic Resonance Spectroscopy, IDH1: isocitrate dehydrogenase 1 gene, SPECT: Single-photon emission computed tomography, PET: Positron emission tomography, DTI-FT: Diffuse Tensor Imaging-fiber tracking technique, DES: direct electrical stimulation, EEG: Electroencephalography, EcoG: Electrocorticography, MEP: motor evoked potentials, EMG: Electromyography, AED: anti-epileptic drugs, TMZ: Temozolomide, EORTC: European Organization for Research and Treatment of Cancer, NCCTG: North Central Cancer Treatment Group, RTOG: Radiation Therapy Oncology Group, ECOG: Eastern Cooperative Oncology Group, EOR: extent of resection, Gy: Gray (unit), GyE: gray equivalent, RT: radiation therapy, IMRT: image-guided intensity modulated radiotherapy, FSRT: fractionated stereotactic radiotherapy, SRS: proton therapy or stereotactic radiosurgery, LET: high-linear energy transfer beams, RBE: relative biological effectiveness, CTCAE: Common Terminology Criteria for Adverse Events, PCV: procarbazine, lomustine, and vincristine chemotherapy.
Journal Title: Chirurgia (Bucharest, Romania : 1990)

PUBMED ID: 25366336
DOI: doi.org/10.1093/neuonc/nou303
Titolo: Preclinical antitumor efficacy of selective exportin 1 inhibitors in glioblastoma.
Autori: Green AL., Ramkissoon SH., McCauley D., Jones K., Perry JA., Hsu JH., Ramkissoon LA., Maire CL., Hubbell-Engler B., Knoff DS., Shacham S., Ligon KL., Kung AL.
Data di Pubblicazione: 2014-11-05
Abstract: SINE compounds show preclinical efficacy utilizing in vitro and in vivo models of GBM, with induction of apoptosis as the mechanism of action. Selinexor is now in early clinical trials in solid and hematological malignancies. Based on these preclinical data and excellent brain penetration, we have initiated clinical trials of Selinexor in patients with relapsed GBM.
Journal Title: Neuro-oncology

PUBMED ID: 25355680
DOI: doi.org/10.1093/neuonc/nou297
Titolo: Practice changing mature results of RTOG study 9802: another positive PCV trial makes adjuvant chemotherapy part of standard of care in low-grade glioma.
Autori: van den Bent MJ.
Data di Pubblicazione: 2014-10-31
Abstract: The long-term follow-up of the RTOG 9802 trial that compared 54 Gy of radiotherapy (RT) with the same RT followed by adjuvant procarbazine, CCNU, and vincristine (PCV) chemotherapy in high-risk low-grade glioma shows a major increase in survival after adjuvant PCV chemotherapy. Median overall survival increased from 7.8 years to 13.3 years, with a hazard ratio of death of 0.59 (log rank: P = .002). This increase in survival was observed despite the fact that 77% of patients who progressed after RT alone received salvage chemotherapy. With this outcome, RT + PCV is now to be considered standard of care for low-grade glioma requiring postsurgical adjuvant treatment. Unfortunately, studies on molecular correlates associated with response are still lacking. This is now the third trial showing benefit from the addition of PCV to RT in grade II or III diffuse glioma. The optimal parameter for selecting patients for adjuvant PCV has not yet been fully elucidated, but several candidate markers have so far emerged. It is still unclear whether temozolomide can replace PCV and whether initial management with chemotherapy only is a safe initial treatment. Potentially, that may adversely affect overall survival, but concerns for delayed RT-induced neurotoxicity may limit acceptance of early RT in patients with expected long term survival. The current evidence supports that in future trials, grades II and III tumors with similar molecular backgrounds should be combined, and trials should focus on molecular glial subtype regardless of grade.
Journal Title: Neuro-oncology

PUBMED ID: 25342602
DOI: doi.org/10.1093/neuonc/nou232
Titolo: Targeted molecular therapies against epidermal growth factor receptor: past experiences and challenges.
Autori: Reardon DA., Wen PY., Mellinghoff IK.
Data di Pubblicazione: 2014-10-25
Abstract: Epidermal growth factor receptor (EGFR) has emerged as a highly attractive therapeutic target in glioblastoma (GBM) based on its high frequency of gene amplification and mutation and its identification as an upstream trigger of dysregulated cell signaling cascades that drive GBM pathophysiology. Extensive investment has been committed in an attempt to exploit EGFR therapeutically to improve outcome for GBM patients, including the development

of a variety of EGFR-targeting therapeutics as well as the participation of hundreds of participants in multiple, carefully constructed clinical trials. In this review, we summarize the design and results of clinical trials evaluating EGFR tyrosine kinase inhibitors in recurrent and newly diagnosed GBM patients. While overall results thus far have been disappointing, it is premature to discount EGFR as a therapeutic target in GBM on the basis of these studies given the limitations in study design and the pharmacology of first-generation EGFR kinase inhibitors. Although important lessons have been learned, critical questions remain unanswered and warrant further study.
Journal Title: Neuro-oncology

PUBMED ID: 25338498
DOI: doi.org/10.1158/1078-0432.CCR-14-0951-T
Titolo: A phase II, randomized, study of weekly APG101+reirradiation versus reirradiation in progressive glioblastoma.
Autori: Wick W., Fricke H., Junge K., Kobyakov G., Martens T., Heese O., Wiestler B., Schliesser MG., von Deimling A., Pichler J., Vetlova E., Harting I., Debus J., Hartmann C., Kunz C., Platten M., Bendszus M., Combs SE.
Data di Pubblicazione: 2014-10-24
Abstract: CD95 pathway inhibition in combination with rRT is an innovative concept with clinical efficacy. It warrants further clinical development. CD95L promoter methylation in the tumor may be developed as a biomarker.
Journal Title: Clinical cancer research : an official journal of the American Association for Cancer Research

PUBMED ID: 25286037
DOI: doi.org/10.2217/cns.14.29
Titolo: Retrospective analysis of safety and feasibility of a 3 days on/11 days off temozolomide dosing regimen in recurrent adult malignant gliomas.
Autori: van Vugt VA., Piccioni DE., Brown BD., Brown T., Saria MG., Juarez T., Kesari S.
Data di Pubblicazione: 2014-10-07
Abstract: The '3 on/11 off' temozolomide regimen for recurrent high-grade gliomas was tolerable and warrants further study in a larger, prospective study.
Journal Title: CNS oncology

PUBMED ID: 25268364
DOI: doi.org/10.1371/journal.pone.0108861
Titolo: Human cytomegalovirus tegument protein pp65 is detected in all intra- and extra-axial brain tumours independent of the tumour type or grade.
Autori: Libard S., Popova SN., Amini RM., Kärjä V., Pietiläinen T., Hämäläinen KM., Sundström C., Hesselager G., Bergqvist M., Ekman S., Zetterling M., Smits A., Nilsson P., Pfeifer S., de Ståhl TD., Enblad G., Ponten F., Alafuzoff I.
Data di Pubblicazione: 2014-10-01
Abstract: Human cytomegalovirus (HCMV) has been indicated being a significant oncomodulator. Recent reports have suggested that an antiviral treatment alters the outcome of a glioblastoma. We analysed the performance of commercial HCMV-antibodies applying the immunohistochemical (IHC) methods on brain sample obtained from a subject with a verified HCMV infection, on samples obtained from 14 control subjects, and on a tissue microarray block containing cores of various brain tumours. Based on these trials, we selected the best performing antibody and analysed a cohort of 417 extra- and intra-axial brain tumours such as gliomas, medulloblastomas, primary diffuse large B-cell lymphomas, and meningiomas. HCMV protein pp65 immunoreactivity was observed in all types of tumours analysed, and the IHC expression did not depend on the

patient's age, gender, tumour type, or grade. The labelling pattern observed in the tumours differed from the labelling pattern observed in the tissue wi th an active HCMV infection. The HCMV protein was expressed in up to 90% of all the tumours investigated. Our results are in accordance with previous re ports regarding the HCMV protein expression in glioblastomas and medulloblas tomas. In addition, the HCMV protein expression was seen in primary brain ly mphomas, low-grade gliomas, and in meningiomas. Our results indicate that th e HCMV protein pp65 expression is common in intra- and extra-axial brain tum ours. Thus, the assessment of the HCMV expression in tumours of various orig ins and pathologically altered tissue in conditions such as inflammation, in fection, and even degeneration should certainly be facilitated.
Journal Title: PloS one

PUBMED ID: 25261556
DOI: doi.org/10.1158/1078-0432.CCR-14-1143
Titolo: An open-label phase Ib dose-escalation study of TRC105 (anti-endogli n antibody) with bevacizumab in patients with advanced cancer.
Autori: Gordon MS., Robert F., Matei D., Mendelson DS., Goldman JW., Chiorea n EG., Strother RM., Seon BK., Figg WD., Peer CJ., Alvarez D., Adams BJ., Th euer CP., Rosen LS.
Data di Pubblicazione: 2014-09-28
Abstract: TRC105 was well tolerated with bevacizumab and clinical activity w as observed in a VEGF inhibitor-refractory population. Ongoing clinical tria ls are testing TRC105 in combination with bevacizumab in glioblastoma and wi th VEGFR TKIs in renal cell carcinoma, hepatocellular carcinoma, and soft ti ssue sarcoma.
Journal Title: Clinical cancer research : an official journal of the America n Association for Cancer Research

PUBMED ID: 25247196
DOI: doi.org/10.1155/2014/952128
Titolo: Interleukin-13 receptor alpha 2-targeted glioblastoma immunotherapy.
Autori: Sengupta S., Thaci B., Crawford AC., Sampath P.
Data di Pubblicazione: 2014-09-24
Abstract: Glioblastoma (GBM) is the most lethal primary brain tumor, and des pite several refinements in its multimodal management, generally has very po or prognosis. Targeted immunotherapy is an emerging field of research that s hows great promise in the treatment of GBM. One of the most extensively stud ied targets is the interleukin-13 receptor alpha chain variant 2 (IL13Rα2). Its selective expression on GBM, discovered almost two decades ago, has been a target for therapy ever since. Immunotherapeutic strategies have been deve loped targeting IL13Rα2, including monoclonal antibodies as well as cell-bas ed strategies such as IL13Rα2-pulsed dendritic cells and IL13Rα2-targeted ch imeric antigen receptor-expressing T cells. Advanced therapeutic development has led to the completion of several clinical trials with promising outcomes . In this review, we will discuss the recent advances in the IL13Rα2-targete d immunotherapy and evaluate the most promising strategy for targeted GBM im munotherapy.
Journal Title: BioMed research international

PUBMED ID: 25242542
DOI: doi.org/10.1002/14651858.CD008218.pub3
Titolo: Antiangiogenic therapy for high-grade glioma.
Autori: Khasraw M., Ameratunga MS., Grant R., Wheeler H., Pavlakis N.
Data di Pubblicazione: 2014-09-23
Abstract: In patients with newly diagnosed GBM, the use of antiangiogenic th erapy does not improve survival, despite evidence of improved progression-fr

ee survival. Thus at this time, evidence is insufficient to support the use of antiangiogenic therapy in patients with newly diagnosed GBM on the basis of effects on survival.Bevacizumab may confer a progression-free survival benefit in GBM; however evidence in favour of using other antiangiogenic therapies in recurrent GBM is insufficient.Although bevacizumab appears to prolong progression-free survival in newly diagnosed and recurrent GBM, the impact of this on quality of life remains unclear.Adequately powered, randomised, placebo-controlled studies of bevacizumab in recurrent GBM (or HGG) are needed.Not addressed here is whether subsets of patients with newly diagnosed GBM may benefit from antiangiogenic therapies and whether these therapies are useful in other high-grade glioma histologies.
Journal Title: The Cochrane database of systematic reviews

PUBMED ID: 25228535
DOI: doi.org/10.1177/1534735414550037
Titolo: Spinal cord stimulation as adjuvant during chemotherapy and reirradiation treatment of recurrent high-grade gliomas.
Autori: Clavo B., Robaina F., Jorge IJ., Cabrera R., Ruiz-Egea E., Szolna A., Otermin E., Llontop P., Carames MA., Santana-Rodríguez N., Sminia P.
Data di Pubblicazione: 2014-09-18
Abstract: Spinal cord stimulation during reirradiation and chemotherapy is feasible and well tolerated. In our study, spinal cord stimulation was associated with clinical improvement and longer survival than previously reported in recurrent anaplastic gliomas. Spinal cord stimulation as adjuvant during chemotherapy and reirradiation in relapsed HGGs merits further research.
Journal Title: Integrative cancer therapies

PUBMED ID: 25192475
DOI: doi.org/10.3171/2014.7.JNS132449
Titolo: Residual tumor volume versus extent of resection: predictors of survival after surgery for glioblastoma.
Autori: Grabowski MM., Recinos PF., Nowacki AS., Schroeder JL., Angelov L., Barnett GH., Vogelbaum MA.
Data di Pubblicazione: 2014-09-06
Abstract: CE-RTV and EOR were found to be significant predictors of survival after GBM resection. CERTV was the more significant predictor of survival compared with EOR, suggesting that the volume of residual contrast-enhancing tumor may be a more accurate and meaningful reflection of the pathobiology of GBM.
Journal Title: Journal of neurosurgery

PUBMED ID: 25151509
DOI: doi.org/10.1007/s11060-014-1595-y
Titolo: Low-dose rate stereotactic iodine-125 brachytherapy for the treatment of inoperable primary and recurrent glioblastoma: single-center experience with 201 cases.
Autori: Kickingereder P., Hamisch C., Suchorska B., Galldiks N., Visser-Vandewalle V., Goldbrunner R., Kocher M., Treuer H., Voges J., Ruge MI.
Data di Pubblicazione: 2014-08-25
Abstract: Treatment options for inoperable glioblastoma are limited. Low-dose-rate stereotactic iodine-125 brachytherapy (SBT) has been reported as an effective and low-risk treatment option for circumscribed low-grade gliomas and brain metastases. The present study evaluates this treatment approach for patients with inoperable glioblastoma. Between 1990 and 2012, 201 patients with histologically proven glioblastoma were treated with SBT (iodine-125 seeds; median cumulative surface dose, 60 Gy; median dose-rate, 6 cGy/h; median gross-tumor-volume, 17 ml) either as primary treatment (n = 103) or at recur

rence (n = 98). In addition to SBT, 90.3 % of patients in the primary treatment group received external boost radiotherapy (median dose, 25.2 Gy). Adjuvant chemotherapy was added for 30.8 % of patients following SBT and consisted of temozolomide for the majority of cases (88.7 %). Procedure-related complications, clinical outcome, progression-free and overall survival (PFS, OS) were evaluated. Median follow-up was 9.8 months. The procedure-related mortality was zero. During follow-up, transient and permanent procedure-related morbidity was observed in 7.5 and 2.0 %, respectively. Calculated from the time of SBT, median OS and PFS rates were 10.5 and 6.2 months, with no significant differences among primary and recurrent tumors (11.1 vs.10.4 months for OS and 6.2 vs. 5.9 months for PFS). For OS, multivariate analysis revealed Karnofsky performance score, age, and adjuvant chemotherapy as independent prognostic factors (all p < 0.01). Low-dose-rate SBT is a relatively safe and potentially effective local treatment option for patients with circumscribed inoperable glioblastoma initially or at recurrence. It deserves prospective validation since it may improve the outcome for a subset of patients with inoperable GBM.
Journal Title: Journal of neuro-oncology

PUBMED ID: 25139026
DOI: doi.org/10.1007/s11060-014-1589-9
Titolo: Temozolomide after radiotherapy in recurrent "low grade" diffuse brainstem glioma in adults.
Autori: Reyes-Botero G., Laigle-Donadey F., Mokhtari K., Martin-Duverneuil N., Delattre JY.
Data di Pubblicazione: 2014-08-21
Abstract: Diffuse brainstem glioma is a rare disease in adults. Radiotherapy (RT) is usually considered to be the standard treatment. However, the role of chemotherapy in treating relapses after RT is unclear, and this study aimed to assess the use of temozolomide (TMZ) in this situation. We conducted a retrospective analysis of patients from our database with "low grade" adult diffuse infiltrating brainstem glioma who received TMZ at relapse after failing RT. The patients were diagnosed by histology or MRI criteria compatible with a low-grade glioma. The tumors were localized in the pons, medulla oblongata or midbrain, excluding supratentorial or infratentorial tumors that had infiltrated the brainstem secondarily. The patients' clinical and radiological responses were assessed, and their progression free survival (PFS) and overall survival (OS) time were estimated. Fifteen adult patients (median age 34 years) fulfilled the inclusion criteria. Histological analysis was available in 5 cases and showed grade II oligodendroglioma (2 cases), grade II oligoastrocytoma (2 cases), and grade II astrocytoma (1 case). Ten patients were selected by MRI criteria only. All patients received RT as initial treatment and had a median PFS of 34.2 months (95 % CI 24.1-44.2). The median KPS at the time of relapse was 80. TMZ was administered orally at 150-200 mg/m(2) for 5 days, every 28 days. Clinical improvement after TMZ was observed in 9 cases (60 %), whereas radiological assessment detected responses in 6/15 cases, including 4 partial and 2 minor responses. The estimated median PFS after TMZ was 9.5 months (95 % CI 7.9-11), and the median OS was 14.4 months (95 % CI 10.5-18.2). Grade 3 thrombopenia was observed in 26 % of cases. TMZ could be useful after RT failure in adult patients with recurrent diffuse "low grade" brainstem glioma.
Journal Title: Journal of neuro-oncology

PUBMED ID: 25137883
DOI: Mancante
Titolo: Clinical outcome of postoperative radiotherapy with or without chemotherapy in adult glioblastoma multiforme in Ramathibodi Hospital: a retrospective study.

Autori: Puddhikarant P., Swangsilpa T., Dhanachai M., Narkwong L., Sitathane e C., Puataweepong P., Jiarpinitnun C., Witoonpanich P., Ruangkanchanasetr R .
Data di Pubblicazione: 2014-08-21
Abstract: Proper management of GBM patient was surgical removal and postoper ative radiotherapy with or without chemotherapy. Proper palliative treatment modality was considered in selected cases of recurrent or progressive diseas e.
Journal Title: Journal of the Medical Association of Thailand = Chotmaihet t hangphaet

PUBMED ID: 25107913
DOI: doi.org/10.1158/1078-0432.CCR-14-0822
Titolo: Phase II study of bevacizumab, temozolomide, and hypofractionated st ereotactic radiotherapy for newly diagnosed glioblastoma.
Autori: Omuro A., Beal K., Gutin P., Karimi S., Correa DD., Kaley TJ., DeAng elis LM., Chan TA., Gavrilovic IT., Nolan C., Hormigo A., Lassman AB., Melli nghoff I., Grommes C., Reiner AS., Panageas KS., Baser RE., Tabar V., Pentso va E., Sanchez J., Barradas-Panchal R., Zhang J., Faivre G., Brennan CW., Ab rey LE., Huse JT.
Data di Pubblicazione: 2014-08-10
Abstract: This aggressive radiotherapy schedule was safe and more convenient for patients, achieving an OS that is comparable with historical controls. A nalysis of advanced neuroimaging parameters suggests ADC and FDG-PET as pote ntially useful biomarkers, whereas tissue correlatives uncovered the poor pr ognosis associated with the proneural signature in non-IDH-1-mutated gliobla stoma.
Journal Title: Clinical cancer research : an official journal of the America n Association for Cancer Research

PUBMED ID: 25087230
DOI: doi.org/10.1093/neuonc/nou153
Titolo: New concepts in the management of diffuse low-grade glioma: Proposal of a multistage and individualized therapeutic approach.
Autori: Duffau H., Taillandier L.
Data di Pubblicazione: 2014-08-04
Abstract: Diffuse low-grade glioma grows, migrates along white matter tracts , and progresses to high-grade glioma. Rather than a "wait and see" policy, an aggressive attitude is now recommended, with early surgery as the first t herapy. Intraoperative mapping, with maximal resection according to function al boundaries, is associated with a longer overall survival (OS) while minim izing morbidity. However, most studies have investigated the role of only on e specific treatment (surgery, radiotherapy, chemotherapy) without taking a global view of managing the cumulative time while preserving quality of life (QoL) versus time to anaplastic transformation. Our aim is to switch towards a more holistic concept based upon the anticipation of a personalized and lo ng-term multistage therapeutic approach, with online adaptation of the strat egy over the years using feedback from clinical, radiological, and histomole cular monitoring. This dynamic strategy challenges the traditional approach by proposing earlier therapy, by repeating treatments, and by reversing the classical order of therapies (eg, neoadjuvant chemotherapy when maximal rese ction is impossible, no early radiotherapy) to improve OS and QoL. New indiv idualized management strategies should deal with the interactions between th e course of this chronic disease, reaction brain remapping, and oncofunction al modulation elicited by serial treatments. This philosophy supports a pers onalized, functional, and preventive neuro-oncology.
Journal Title: Neuro-oncology

PUBMED ID: 25080363
DOI: doi.org/10.1002/cncr.28907
Titolo: Reirradiation of recurrent medulloblastoma: does clinical benefit ou tweigh risk for toxicity?
Autori: Wetmore C., Herington D., Lin T., Onar-Thomas A., Gajjar A., Merchan t TE.
Data di Pubblicazione: 2014-08-01
Abstract: The use of irradiation as a component of salvage therapy for relap sed MB may prolong survival. The benefit appears to be greatest for relapsed standard-risk patients.
Journal Title: Cancer

PUBMED ID: 25078721
DOI: doi.org/10.1016/j.addr.2014.07.010
Titolo: Multimodal imaging of gliomas in the context of evolving cellular an d molecular therapies.
Autori: Keunen O., Taxt T., Grüner R., Lund-Johansen M., Tonn JC., Pavlin T. , Bjerkvig R., Niclou SP., Thorsen F.
Data di Pubblicazione: 2014-08-01
Abstract: The vast majority of malignant gliomas relapse after surgery and s tandard radio-chemotherapy. Novel molecular and cellular therapies are thus being developed, targeting specific aspects of tumor growth. While histopath ology remains the gold standard for tumor classification, neuroimaging has o ver the years taken a central role in the diagnosis and treatment follow up of brain tumors. It is used to detect and localize lesions, define the targe t area for biopsies, plan surgical and radiation interventions and assess tu mor progression and treatment outcome. In recent years the application of no vel drugs including anti-angiogenic agents that affect the tumor vasculature , has drastically modulated the outcome of brain tumor imaging. To properly evaluate the effects of emerging experimental therapies and successfully sup port treatment decisions, neuroimaging will have to evolve. Multi-modal imag ing systems with existing and new contrast agents, molecular tracers, techno logical advances and advanced data analysis can all contribute to the establ ishment of disease relevant biomarkers that will improve disease management and patient care. In this review, we address the challenges of glioma imagin g in the context of novel molecular and cellular therapies, and take a prosp ective look at emerging experimental and pre-clinical imaging techniques tha t bear the promise of meeting these challenges.
Journal Title: Advanced drug delivery reviews

PUBMED ID: 25065849
DOI: doi.org/10.1016/j.jocn.2014.03.034
Titolo: Spinal metastasis of gliosarcoma: array-based comparative genomic hy bridization for confirmation of metastatic spread.
Autori: Schindler G., Capper D., Korshunov A., Schmieder K., Brenke C.
Data di Pubblicazione: 2014-07-29
Abstract: We report a 64-year-old woman who underwent craniotomy and gross t otal resection of a left frontal lobe tumor initially diagnosed as glioblast oma. Multiple wound revisions were necessary due to repeated wound healing d isorders under concomitant radio-chemotherapy. After 9 months there was loca l cranial tumor recurrence, requiring re-operation. Thereafter, temozolomide monotherapy was implemented. Histologically, a shift from glial to mesenchym al differentiation was observed in the recurrent tumor, resulting in the dia gnosis of gliosarcoma. A further 9 months later a thoracic spinal tumor occu rred requiring emergency tumor resection. Analysis showed a mesenchymal tumo r without definite glial component. Being resistant to local radiation thera py, symptomatic local spinal tumor progression was observed within 1 month r

equiring re-resection. There was no response to chemotherapy with bevacizuma b and irinotecan. Considering the pronounced sarcoma-like differentiation, a sarcoma chemotherapy regime with doxorubicin was initiated. This was also to no avail; the disease progressed and recurred at both the spinal and cerebra l locations, respectively. This ambiguous tumor characteristic and therapy r esistance encouraged us to retrospectively perform molecular and array-based comparative genomic hybridization (aCGH) analysis on the extirpated cerebral and spinal tumors. Tumors from both locations showed a consistent cytogeneti c signature of gain of chromosome 7, and losses of chromosomes 10 and 13. Th is novel report of aCGH analysis of spinal gliosarcoma metastasis and the co rrelation to the clinical disease course shows that genotypic profiling may serve as a supplementary diagnostic tool in improving our knowledge of the b iologic behavior of rare tumor variants.
Journal Title: Journal of clinical neuroscience : official journal of the Ne urosurgical Society of Australasia

PUBMED ID: 25055819
DOI: doi.org/10.1136/jnnp-2014-308136
Titolo: Seizure reduction in a low-grade glioma: more than a beneficial side effect of temozolomide.
Autori: Koekkoek JA., Dirven L., Heimans JJ., Postma TJ., Vos MJ., Reijnevel d JC., Taphoorn MJ.
Data di Pubblicazione: 2014-07-25
Abstract: TMZ may contribute to an important reduction in seizure frequency in patients with LGG. Seizure reduction following TMZ treatment has prognost ic significance and may serve as an important clinical outcome measure in pa tients with LGG.
Journal Title: Journal of neurology, neurosurgery, and psychiatry

PUBMED ID: 25046485
DOI: doi.org/10.4161/cbt.29926
Titolo: Potential novel role of bevacizumab in glioblastoma and cervical can cer.
Autori: Goey AK., Figg WD.
Data di Pubblicazione: 2014-07-22
Abstract: The VEGF-A binding monoclonal antibody bevacizumab is a widely pre scribed angiogenesis inhibitor and indicated for many types of cancer. As sh own by three randomized phase 3 trials recently published in the New England Journal of Medicine, novel indications for this drug are still being explore d. In the RTOG 0825 and AVAglio trials the effect of bevacizumab addition to standard therapy in newly diagnosed glioblastoma (radiotherapy plus temozolo mide) was investigated, while in GOG 240 the combination of platinum-based c hemotherapy plus bevacizumab was explored in advanced cervical cancer. In RT OG 0825, addition of bevacizumab to standard therapy did not result in survi val benefit, and moreover, quality of life was more deteriorated in the beva cizumab arm. In AVAglio, however, progression-free survival (PFS) was signif icantly increased in the bevacizumab group and these patients also experienc ed a longer deterioration-free survival. These conflicting results do not fu lly support the incorporation of bevacizumab in the first-line treatment of glioblastoma. In contrast, in GOG 240 the bevacizumab group (including pacli taxel plus topotecan or paclitaxel) experienced a significant longer PFS and overall survival, and quality of life was not negatively affected in these p atients. Thus, these results favor the use of bevacizumab in the treatment o f advanced cervical cancer.
Journal Title: Cancer biology & therapy

PUBMED ID: 25038253

DOI: doi.org/10.1093/neuonc/nou129
Titolo: Pseudoprogression in patients with glioblastoma: clinical relevance despite low incidence.
Autori: Radbruch A., Fladt J., Kickingereder P., Wiestler B., Nowosielski M., Bäumer P., Schlemmer HP., Wick A., Heiland S., Wick W., Bendszus M.
Data di Pubblicazione: 2014-07-20
Abstract: This series challenges the current concept of PsP. Even though we could confirm a prolonged OS of patients with PsP, the incidence of PsP was lower than reported previously and extended beyond 12 weeks.
Journal Title: Neuro-oncology

PUBMED ID: 24995786
DOI: doi.org/10.3171/2014.5.JNS132392
Titolo: Phase I/IIa trial of fractionated radiotherapy, temozolomide, and autologous formalin-fixed tumor vaccine for newly diagnosed glioblastoma.
Autori: Ishikawa E., Muragaki Y., Yamamoto T., Maruyama T., Tsuboi K., Ikuta S., Hashimoto K., Uemae Y., Ishihara T., Matsuda M., Matsutani M., Karasawa K., Nakazato Y., Abe T., Ohno T., Matsumura A.
Data di Pubblicazione: 2014-07-05
Abstract: The treatment regimen was well tolerated and resulted in favorable PFS and OS for newly diagnosed GBM patients. Clinical trial registration no.: UMIN000001426 (UMIN clinical trials registry, Japan).
Journal Title: Journal of neurosurgery

PUBMED ID: 24975917
DOI: doi.org/10.1111/1754-9485.12185
Titolo: Hypofractionated intensity-modulated radiotherapy with temozolomide chemotherapy may alter the patterns of failure in patients with glioblastoma multiforme.
Autori: Reddy K., Gaspar LE., Kavanagh BD., Chen C.
Data di Pubblicazione: 2014-07-01
Abstract: A 60-Gy hypo-IMRT treatment delivered in 6-Gy fractions with TMZ altered the patterns of failure in GBM, with more distant failures.
Journal Title: Journal of medical imaging and radiation oncology

PUBMED ID: 24928248
DOI: doi.org/10.1007/s00066-014-0693-2
Titolo: FET-PET-based reirradiation and chloroquine in patients with recurrent glioblastoma: first tolerability and feasibility results.
Autori: Bilger A., Bittner MI., Grosu AL., Wiedenmann N., Meyer PT., Firat E., Niedermann G., Weber WA., Milanović D.
Data di Pubblicazione: 2014-06-15
Abstract: In this case series, we observed encouraging responses to CQ and re-RT. We plan to conduct a CQ dose escalation study combined with re-RT.
Journal Title: Strahlentherapie und Onkologie : Organ der Deutschen Rontgengesellschaft ... [et al]

PUBMED ID: 24882149
DOI: doi.org/10.1016/j.clon.2014.04.001
Titolo: Current concepts in the surgical management of glioma patients.
Autori: Watts C., Price SJ., Santarius T.
Data di Pubblicazione: 2014-06-03
Abstract: The scientific basis for the surgical management of patients with glioma is rapidly evolving. The infiltrative nature of these cancers precludes a surgical cure, but despite this, cytoreductive surgery remains central to high-quality patient care. In addition to tissue sampling for accurate hi

stopathological diagnosis and molecular genetic characterisation, clinical b
enefit from decompression of space-occupying lesions and microsurgical cytor
eduction has been reported in patients with different grades of glioma. By i
ntegrating advanced surgical techniques with molecular genetic characterisat
ion of the disease and targeted radiotherapy and chemotherapy, it is possibl
e to construct a programme of personalised surgical therapy throughout the p
atient journey. The goal of therapeutic packages tailored to each patient is
to optimise patient safety and clinical outcome and must be delivered in a m
ultidisciplinary setting. Here we review the current concepts that underlie
surgical subspecialisation in the management of patients with glioma.
Journal Title: Clinical oncology (Royal College of Radiologists (Great Brita
in))

PUBMED ID: 24857153
DOI: doi.org/10.14694/EdBook_AM.2014.34.e95
Titolo: For the next trick: new discoveries in radiobiology applied to gliob
lastoma.
Autori: Debus J., Abdollahi A.
Data di Pubblicazione: 2014-05-27
Abstract: Glioblastoma (GBM) is the most common malignant brain tumor. Radio
therapy post surgical resection remained the mainstay of the management of G
BM for decades until the addition of temozolomide was shown to prolong the m
edian overall survival (OS) by 2.5 months to 14.6 months in 2005. Infiltrati
ve growth to surrounding normal brain tissue and cooption of vascular niches
, peripheral microvasuclar hyperplasia, and central hypoxic regions with pse
udopalisading necrosis are characteristics of GBM and are causally linked to
their exceptional radio- and chemo-resistant phenotype. An intratumoral hier
archy is postulated consisting of tumor stem cells in the apex with high DNA
-repair proficiency resisting radiotherapy. It is conceivable that the stem
cell property is more dynamic than originally anticipated. Niche effects suc
h as exposure to hypoxia and intercellular communication in proximities to e
ndothelial or bone marrow-derived cells (BMDC), for example, may activate su
ch "stem cell" programs. GBM are exceptionally stroma-rich tumors and may co
nsist of more than 70% stroma components, such as microglia and BMDC. It bec
omes increasingly apparent that treatment of GBM needs to integrate therapie
s targeting all above-mentioned distinct pathophysiological features. Accord
ingly, recent approaches in GBM therapy include inhibition of invasion (e.g.
, integrin, EGFR, CD95, and mTOR inhibition), antiangiogenesis and stroma mo
dulators (TGFbeta, VEGF, angiopoetin, cMET inhibitors) and activation of imm
une response (vaccination and blockage of negative co-stimulatory signals).
In addition, high LET-radiotherapy, for example with carbon ions, is postula
ted to ablate tumor stem cell and hypoxic cells more efficiently as compared
with conventional low-LET photon irradiation. We discuss current key concept
s, their limitations, and potentials to improve the outcome in this rapidly
progressive and devastating disease.
Journal Title: American Society of Clinical Oncology educational book. Ameri
can Society of Clinical Oncology. Annual Meeting

PUBMED ID: 24842754
DOI: doi.org/10.1001/jamaneurol.2014.463
Titolo: Effect of rituximab in patients with leucine-rich, glioma-inactivate
d 1 antibody-associated encephalopathy.
Autori: Irani SR., Gelfand JM., Bettcher BM., Singhal NS., Geschwind MD.
Data di Pubblicazione: 2014-05-21
Abstract: Rituximab was well tolerated in this predominantly older adult pat
ient population and may be an effective option for some patients with LGI1 a
ntibody-associated encephalopathy. Glucocorticoid therapy appears particular

ly efficacious. Earlier rituximab administration and randomized trials are r
equired to formally assess efficacy.
Journal Title: JAMA neurology

PUBMED ID: 24811110
DOI: doi.org/10.1021/nn5014484
Titolo: A nanoparticle carrying the p53 gene targets tumors including cancer
stem cells, sensitizes glioblastoma to chemotherapy and improves survival.
Autori: Kim SS., Rait A., Kim E., Pirollo KF., Nishida M., Farkas N., Dagata
JA., Chang EH.
Data di Pubblicazione: 2014-05-10
Abstract: Temozolomide (TMZ)-resistance in glioblastoma multiforme (GBM) has
been linked to upregulation of O(6)-methylguanine-DNA methyltransferase (MGM
T). Wild-type (wt) p53 was previously shown to down-modulate MGMT. However,
p53 therapy for GBM is limited by lack of efficient delivery across the bloo
d brain barrier (BBB). We have developed a systemic nanodelivery platform (s
cL) for tumor-specific targeting (primary and metastatic), which is currentl
y in multiple clinical trials. This self-assembling nanocomplex is formed by
simple mixing of the components in a defined order and a specific ratio. Her
e, we demonstrate that scL crosses the BBB and efficiently targets GBM, as w
ell as cancer stem cells (CSCs), which have been implicated in recurrence an
d treatment resistance in many human cancers. Moreover, systemic delivery of
scL-p53 down-modulates MGMT and induces apoptosis in intracranial GBM xenogr
afts. The combination of scL-p53 and TMZ increased the antitumor efficacy of
TMZ with enhanced survival benefit in a mouse model of highly TMZ-resistant
GBM. scL-p53 also sensitized both CSCs and bulk tumor cells to TMZ, increasi
ng apoptosis. These results suggest that combining scL-p53 with standard TMZ
treatment could be a more effective therapy for GBM.
Journal Title: ACS nano

PUBMED ID: 24809637
DOI: doi.org/10.1016/j.ejrad.2014.03.026
Titolo: Differentiation between vasogenic-edema versus tumor-infiltrative ar
ea in patients with glioblastoma during bevacizumab therapy: a longitudinal
MRI study.
Autori: Artzi M., Bokstein F., Blumenthal DT., Aizenstein O., Liberman G., C
orn BW., Ben Bashat D.
Data di Pubblicazione: 2014-05-10
Abstract: Characterization of non-enhancing hyperintense FLAIR lesion area i
n GB patients can provide an MR-based biomarker, indicating a shift to an in
filtrative progression pattern, and may improve therapy response assessment
in patients following bevacizumab therapy.
Journal Title: European journal of radiology

PUBMED ID: 24803676
DOI: doi.org/10.1093/neuonc/nou059
Titolo: Phase II study of sorafenib in children with recurrent or progressiv
e low-grade astrocytomas.
Autori: Karajannis MA., Legault G., Fisher MJ., Milla SS., Cohen KJ., Wisoff
JH., Harter DH., Goldberg JD., Hochman T., Merkelson A., Bloom MC., Sievert
AJ., Resnick AC., Dhall G., Jones DT., Korshunov A., Pfister SM., Eberhart C
G., Zagzag D., Allen JC.
Data di Pubblicazione: 2014-05-08
Abstract: Sorafenib produced unexpected and unprecedented acceleration of tu
mor growth in children with PLGA, irrespective of NF1 or tumor BRAF status.
In vitro studies with sorafenib indicate that this effect is likely related
to paradoxical ERK activation. Close monitoring for early tumor progression

should be included in trials of novel agents that modulate signal transducti
on.
Journal Title: Neuro-oncology

PUBMED ID: 24786603
DOI: doi.org/10.1038/bjc.2014.209
Titolo: Phase I study of sorafenib combined with radiation therapy and temoz
olomide as first-line treatment of high-grade glioma.
Autori: Hottinger AF., Ben Aissa A., Espeli V., Squiban D., Dunkel N., Varga
s MI., Hundsberger T., Mach N., Schaller K., Weber DC., Bodmer A., Dietrich
PY.
Data di Pubblicazione: 2014-05-03
Abstract: Although Sb can be combined with RT and TMZ, significant side effe
cts and moderate outcome results do not support further clinical development
in malignant gliomas. The robust PK data of the TMZ/Sb combination could be
useful in other cancer settings.
Journal Title: British journal of cancer

PUBMED ID: 24758192
DOI: doi.org/10.1186/1748-717X-9-95
Titolo: A comparison of long-term survivors and short-term survivors with gl
ioblastoma, subventricular zone involvement: a predictive factor for surviva
l?
Autori: Adeberg S., Bostel T., König L., Welzel T., Debus J., Combs SE.
Data di Pubblicazione: 2014-04-25
Abstract: Our findings underline that survival in GBM patients is heterogene
ous and influenced by multiple factors. This study confirms that tumor locat
ion with regard to the SVZ is significantly associated with survival.
Journal Title: Radiation oncology (London, England)

PUBMED ID: 24736829
DOI: doi.org/10.1007/s11060-014-1434-1
Titolo: Clinical management and outcome of histologically verified adult bra
instem gliomas in Switzerland: a retrospective analysis of 21 patients.
Autori: Hundsberger T., Tonder M., Hottinger A., Brügge D., Roelcke U., Puto
ra PM., Stupp R., Weller M.
Data di Pubblicazione: 2014-04-17
Abstract: Because of low incidence, mixed study populations and paucity of c
linical and histological data, the management of adult brainstem gliomas (BS
Gs) remains non-standardized. We here describe characteristics, treatment an
d outcome of patients with exclusively histologically confirmed adult BSGs.
A retrospective chart review of adults (age >18 years) was conducted. BSG wa
s defined as a glial tumor located in the midbrain, pons or medulla. Charact
eristics, management and outcome were analyzed. Twenty one patients (17 male
s; median age 41 years) were diagnosed between 2004 and 2012 by biopsy (n =
15), partial (n = 4) or complete resection (n = 2). Diagnoses were glioblast
oma (WHO grade IV, n = 6), anaplastic astrocytoma (WHO grade III, n = 7), di
ffuse astrocytoma (WHO grade II, n = 6) and pilocytic astrocytoma (WHO grade
I, n = 2). Diffuse gliomas were mainly located in the pons and frequently sh
owed MRI contrast enhancement. Endophytic growth was common (16 vs. 5). Post
operative therapy in low-grade (WHO grade I/II) and high-grade gliomas (WHO
grade III/IV) consisted of radiotherapy alone (three in each group), radioch
emotherapy (2 vs. 6), chemotherapy alone (0 vs. 2) or no postoperative thera
py (3 vs. 1). Median PFS (24.1 vs. 5.8 months; log-rank, p = 0.009) and mOS
(30.5 vs. 11.5 months; log-rank, p = 0.028) was significantly better in WHO
grade II than in WHO grade III/IV tumors. Second-line therapy considerably v
aried. Histologically verification of adult BSGs is feasible and has an impa

ct on postoperative treatment. Low-grade gliomas can simple be followed or t
reated with radiotherapy alone. Radiochemotherapy with temozolomide can safe
ly be prescribed for high-grade gliomas without additional CNS toxicities.
Journal Title: Journal of neuro-oncology

PUBMED ID: 24729041
DOI: doi.org/10.1093/ndt/gfu013
Titolo: The effect of everolimus on renal angiomyolipoma in patients with tu
berous sclerosis complex being treated for subependymal giant cell astrocyto
ma: subgroup results from the randomized, placebo-controlled, Phase 3 trial
EXIST-1.
Autori: Kingswood JC., Jozwiak S., Belousova ED., Frost MD., Kuperman RA., B
ebin EM., Korf BR., Flamini JR., Kohrman MH., Sparagana SP., Wu JY., Brechen
macher T., Stein K., Berkowitz N., Bissler JJ., Franz DN.
Data di Pubblicazione: 2014-04-15
Abstract: Everolimus showed efficacy in reducing angiomyolipoma lesion volum
e in patients with SEGA associated with TSC.The trial is registered with Cli
nicalTrials.gov, number NCT00789828; http://clinicaltrials.gov/ct2/show/NCT0
0789828?term=EXIST-1&rank=1.
Journal Title: Nephrology, dialysis, transplantation : official publication
of the European Dialysis and Transplant Association - European Renal Associa
tion

PUBMED ID: 24728785
DOI: doi.org/10.1007/s11060-013-1337-6
Titolo: The role of radiotherapy in the management of progressive glioblasto
ma : a systematic review and evidence-based clinical practice guideline.
Autori: Ryu S., Buatti JM., Morris A., Kalkanis SN., Ryken TC., Olson JJ., O
lson JJ.
Data di Pubblicazione: 2014-04-15
Abstract: Re-irradiation is recommended in order to maintain or improve a pa
tient's neurological status and quality of life prior to any further tumor p
rogression.
Journal Title: Journal of neuro-oncology

PUBMED ID: 24727314
DOI: doi.org/10.1212/WNL.0000000000000402
Titolo: Progression types after antiangiogenic therapy are related to outcom
e in recurrent glioblastoma.
Autori: Nowosielski M., Wiestler B., Goebel G., Hutterer M., Schlemmer HP.,
Stockhammer G., Wick W., Bendszus M., Radbruch A.
Data di Pubblicazione: 2014-04-15
Abstract: Radiologic PTs following bevacizumab treatment failure show differ
ences in time to development and are related to outcome. We therefore hypoth
esize that these PTs reflect a different glioma biology, including different
ial resistance mechanisms to bevacizumab, and may be associated with differe
nt responses to postprogression therapy.
Journal Title: Neurology

PUBMED ID: 24723564
DOI: doi.org/10.1093/neuonc/nou045
Titolo: Significance of interleukin-13 receptor alpha 2-targeted glioblastom
a therapy.
Autori: Thaci B., Brown CE., Binello E., Werbaneth K., Sampath P., Sengupta
S.
Data di Pubblicazione: 2014-04-12

Abstract: Glioblastoma multiforme (GBM) remains one of the most lethal prima ry brain tumors despite surgical and therapeutic advancements. Targeted ther apies of neoplastic diseases, including GBM, have received a great deal of i nterest in recent years. A highly studied target of GBM is interleukin-13 re ceptor α chain variant 2 (IL13Rα2). Targeted therapies against IL13Rα2 in GB M include fusion chimera proteins of IL-13 and bacterial toxins, nanoparticl es, and oncolytic viruses. In addition, immunotherapies have been developed using monoclonal antibodies and cell-based strategies such as IL13Rα2-pulsed dendritic cells and IL13Rα2-targeted chimeric antigen receptor-modified T ce lls. Advanced therapeutic development has led to the completion of phase I c linical trials for chimeric antigen receptor-modified T cells and phase III clinical trials for IL-13-conjugated bacterial toxin, with promising outcome s. Selective expression of IL13Rα2 on tumor cells, while absent in the surro unding normal brain tissue, has motivated continued study of IL13Rα2 as an i mportant candidate for targeted glioma therapy. Here, we review the preclini cal and clinical studies targeting IL13Rα2 in GBM and discuss new advances a nd promising applications.
Journal Title: Neuro-oncology

PUBMED ID: 24723487
DOI: doi.org/10.1093/annonc/mdu148
Titolo: Randomized phase II trial of irinotecan and bevacizumab as neo-adjuv ant and adjuvant to temozolomide-based chemoradiation compared with temozolo mide-chemoradiation for unresectable glioblastoma: final results of the TEMA VIR study from ANOCEF†.
Autori: Chauffert B., Feuvret L., Bonnetain F., Taillandier L., Frappaz D., Taillia H., Schott R., Honnorat J., Fabbro M., Tennevet I., Ghiringhelli F., Guillamo JS., Durando X., Castera D., Frenay M., Campello C., Dalban C., Skr zypski J., Chinot O.
Data di Pubblicazione: 2014-04-12
Abstract: Clinical trial registered under EUDRACT number 2008-002775-28 (NCT 01022918).
Journal Title: Annals of oncology : official journal of the European Society for Medical Oncology

PUBMED ID: 24661654
DOI: doi.org/10.1016/j.ijrobp.2014.01.013
Titolo: Postponed is not canceled: role of craniospinal radiation therapy in the management of recurrent infant medulloblastoma--an experience from the H IT-REZ 1997 & 2005 studies.
Autori: Müller K., Mynarek M., Zwiener I., Siegler N., Zimmermann M., Christ iansen H., Budach W., Henke G., Warmuth-Metz M., Pietsch T., von Hoff K., vo n Bueren A., Bode U., Rutkowski S., Kortmann RD., Fleischhack G., Tippelt S.
Data di Pubblicazione: 2014-03-26
Abstract: Our results suggest that salvage treatment of relapsed medulloblas tomas consisting of CSI and chemotherapy offers a second chance for cure, ev en for patients with classic histological findings. Metastatic disease at re lapse did not have an impact on survival. However, this may be explained by the small number of patients.
Journal Title: International journal of radiation oncology, biology, physics

PUBMED ID: 24652192
DOI: doi.org/10.1007/s12032-014-0924-5
Titolo: STAT3 Tyr705 phosphorylation affects clinical outcome in patients wi th newly diagnosed supratentorial glioblastoma.
Autori: Lin GS., Yang LJ., Wang XF., Chen YP., Tang WL., Chen L., Lin ZX.
Data di Pubblicazione: 2014-03-22

Abstract: STAT3 tyrosine705 phosphorylation (p-STAT3, Tyr705), a molecular h
ub for several signal transduction pathways of glioma, plays a central role
in glioblastoma (GBM) carcinogenesis and progression. However, it is still c
ontroversial whether p-STAT3 expression is associated with the clinical outc
ome of patients with glioblastoma. Such evidence would contribute to further
illustrate whether STAT3 inhibition is suitable for clinical treatment. Here
, we examined the expression of p-STAT3 in the tumor tissues from 90 patient
s with newly diagnosed supratentorial GBM via immunohistochemical technique
and evaluated the influences of its expression on progression-free survival
(PFS) and overall survival (OS) using the Kaplan-Meier curve and COX proport
ional hazards regression model. Immunohistochemical assay indicated increase
d expression of p-STAT3 in GBM tissue compared to adjacent normal brain tiss
ue without p-STAT3 expression. There were no observed associations between p
-STAT3 expression and patients' gender (P = 0.660), age (P = 0.867) or preop
erative Karnofsky Performance Status (KPS) (P = 0.121). Univariate survival
analysis revealed significant correlations of high p-STAT3 expression with s
horter PFS (P = 0.012) and OS (P = 0.009). Multivariate survival analysis co
nfirmed high p-STAT3 expression as a significant prognostic indicator for sh
orter PFS (HR 2.158, P = 0.019) and OS (HR 2.120, P = 0.031), independent of
age, KPS and chemoradiotherapy. In summary, the high percentage of p-STAT3 p
ositive tumor cells is a significant independent prognostic indicator for po
or clinical outcome in patients with GBM, in addition to advanced age, poor
performance status and nonstandard chemoradiotherapy, suggesting that STAT3
might be as a promising therapeutic target in GBM.
Journal Title: Medical oncology (Northwood, London, England)

PUBMED ID: 24637230
DOI: doi.org/10.1093/neuonc/nou029
Titolo: A single-institution phase II trial of radiation, temozolomide, erlo
tinib, and bevacizumab for initial treatment of glioblastoma.
Autori: Clarke JL., Molinaro AM., Phillips JJ., Butowski NA., Chang SM., Per
ry A., Costello JF., DeSilva AA., Rabbitt JE., Prados MD.
Data di Pubblicazione: 2014-03-19
Abstract: The combination of bevacizumab, erlotinib, TMZ, and radiotherapy a
ppears to be well tolerated and improved progression-free survival but did n
ot reach the primary endpoint of improved OS.
Journal Title: Neuro-oncology

PUBMED ID: 24616497
DOI: doi.org/10.1073/pnas.1323855111
Titolo: In vivo chemical exchange saturation transfer imaging allows early d
etection of a therapeutic response in glioblastoma.
Autori: Sagiyama K., Mashimo T., Togao O., Vemireddy V., Hatanpaa KJ., Maher
EA., Mickey BE., Pan E., Sherry AD., Bachoo RM., Takahashi M.
Data di Pubblicazione: 2014-03-12
Abstract: Glioblastoma multiforme (GBM), which account for more than 50% of
all gliomas, is among the deadliest of all human cancers. Given the dismal p
rognosis of GBM, it would be advantageous to identify early biomarkers of a
response to therapy to avoid continuing ineffective treatments and to initia
te other therapeutic strategies. The present in vivo longitudinal study in a
n orthotopic mouse model demonstrates quantitative assessment of early treat
ment response during short-term chemotherapy with temozolomide (TMZ) by amid
e proton transfer (APT) imaging. In a GBM line, only one course of TMZ (3 d
exposure and 4 d rest) at a dose of 80 mg/kg resulted in substantial reducti
on in APT signal compared with untreated control animals, in which the APT s
ignal continued to increase. Although there were no detectable differences i
n tumor volume, cell density, or apoptosis rate between groups, levels of Ki
67 (index of cell proliferation) were substantially reduced in treated tumor

s. In another TMZ-resistant GBM line, the APT signal and levels of Ki67 incr eased despite the same course of TMZ treatment. As metabolite changes are kn own to occur early in the time course of chemotherapy and precede morphologi c changes, these results suggest that the APT signal in glioma may be a usef ul functional biomarker of treatment response or degree of tumor progression . Thus, APT imaging may serve as a sensitive biomarker of early treatment re sponse and could potentially replace invasive biopsies to provide a definiti ve diagnosis. This would have a major impact on the clinical management of p atients with glioma.
Journal Title: Proceedings of the National Academy of Sciences of the United States of America

PUBMED ID: 24608453
DOI: doi.org/10.4103/0028-3886.128280
Titolo: Sulfasalazine and temozolomide with radiation therapy for newly diag nosed glioblastoma.
Autori: Takeuchi S., Wada K., Nagatani K., Otani N., Osada H., Nawashiro H.
Data di Pubblicazione: 2014-03-11
Abstract: Sulfasalazine treatment with temozolomide plus radiotherapy for ne wly diagnosed primary GBM is associated with a high rate of discontinuation due to hematologic toxic effects. This treatment may have no effect on OS or PFS, although it may improve seizure control if an adequate dose can be admi nistered.
Journal Title: Neurology India

PUBMED ID: 24604590
DOI: doi.org/10.1007/s00259-013-2678-2
Titolo: ^{18}F-FLT and ^{18}F-FDOPA PET kinetics in recurrent brain tumors.
Autori: Wardak M., Schiepers C., Cloughesy TF., Dahlbom M., Phelps ME., Huan g SC.
Data di Pubblicazione: 2014-03-08
Abstract: For recurrent malignant glioma treated with bevacizumab and irinot ecan, FLT kinetic parameters obtained early after the start of treatment (ab solute values and their associated changes) can provide sufficient informati on to predict OS with reasonable confidence using MLR. The slight increase i n accuracy for predicting OS with a combination of FLT and FDOPA PET informa tion may not warrant the additional acquisition of FDOPA PET for therapy mon itoring in patients with recurrent glioma.
Journal Title: European journal of nuclear medicine and molecular imaging

PUBMED ID: 24498562
DOI: doi.org/10.4161/onci.26968
Titolo: CSF1R inhibition delays cervical and mammary tumor growth in murine models by attenuating the turnover of tumor-associated macrophages and enhan cing infiltration by CD8
Autori: Strachan DC., Ruffell B., Oei Y., Bissell MJ., Coussens LM., Pryer N ., Daniel D.
Data di Pubblicazione: 2014-02-06
Abstract: Increased numbers of tumor-infiltrating macrophages correlate with poor disease outcome in patients affected by several types of cancer, includ ing breast and prostate carcinomas. The colony stimulating factor 1 receptor (CSF1R) signaling pathway drives the recruitment of tumor-associated macroph ages (TAMs) to the neoplastic microenvironment and promotes the differentiat ion of TAMs toward a pro-tumorigenic phenotype. Twelve clinical trials are c urrently evaluating agents that target the CSF1/CSF1R signaling pathway as a treatment against multiple malignancies, including breast carcinoma, leukemi

a, and glioblastoma. The blockade of CSF1R signaling has been shown to great
ly decrease the number of macrophages in a tissue-specific manner. However,
additional mechanistic insights are needed in order to understand how macrop
hages are depleted and the global effects of CSF1R inhibition on other tumor
-infiltrating immune cells. Using BLZ945, a highly selective small molecule
inhibitor of CSF1R, we show that CSF1R inhibition attenuates the turnover ra
te of TAMs while increasing the number of CD8
Journal Title: Oncoimmunology

PUBMED ID: 24469854
DOI: doi.org/10.1007/s11060-014-1366-9
Titolo: Factors impacting survival following second surgery in patients with
glioblastoma in the temozolomide treatment era, incorporating neutrophil/lym
phocyte ratio and time to first progression.
Autori: McNamara MG., Lwin Z., Jiang H., Templeton AJ., Zadeh G., Bernstein
M., Chung C., Millar BA., Laperriere N., Mason WP.
Data di Pubblicazione: 2014-01-29
Abstract: Patients with progressive glioblastoma (GBM) have a poor prognosis
. Neutrophil/lymphocyte ratio (NLR), a host inflammatory marker, is prognost
ic in several solid tumors. The prognostic impact of either NLR, or time fro
m first surgery for GBM to first progression (TTP), in patients undergoing s
econd surgery, has not been assessed. Patients undergoing second surgery for
GBM were retrospectively reviewed. Primary outcome was overall survival (OS)
and Cox proportional hazard models were used to assess the prognostic value
of baseline characteristics including TTP and NLR. Univariable and multivari
able analysis (MVA) of OS from second surgery were performed using accelerat
ed failure time Weibull model. Of 584 patients with GBM, 107 (18 %) underwen
t second surgery between 01/04 and 12/11. Patients who underwent second surg
ery had longer OS versus those having primary surgery alone; 20.9 versus 9.9
months (P < 0.001). Median OS from second surgery in patients with NLR ≤ 4 v
ersus NLR > 4 was 9.7 versus 5.9 months (log rank P = 0.02). The NLR retaine
d its prognostic significance for survival on MVA (time ratio [TR] 1.65, 95
% confidence interval [CI] 1.15-2.35, P < 0.01). No chemotherapy post second
surgery (TR 0.23, 95 % CI 0.16-0.33, P < 0.001) portended worse survival. In
patients undergoing second surgery, when TTP was ≤ 12 months, 12-24 months,
or >24 months, median OS from second surgery was 7.2, 7.0 and 6.3 months, re
spectively (P = 0.6). A NLR > 4 prior to second surgery is a poor prognostic
factor in GBM and later progression is associated with longer survival in pa
tients but not in longer survival after second surgery.
Journal Title: Journal of neuro-oncology

PUBMED ID: 24441743
DOI: doi.org/10.1097/CAD.0000000000000077
Titolo: Sorafenib for patients with pretreated recurrent or progressive high
-grade glioma: a retrospective, single-institution study.
Autori: Hassler MR., Ackerl M., Flechl B., Sax C., Wöhrer A., Widhalm G., Di
eckmann K., Hainfellner J., Preusser M., Marosi C.
Data di Pubblicazione: 2014-01-21
Abstract: Therapeutic options for patients with pretreated advanced high-gra
de glioma (HGG) are limited. Sorafenib, a small molecule with multiple poten
tial beneficial actions, appears particularly promising. We reviewed the out
comes of 30 patients with recurrent or progressive HGG treated with sorafeni
b within a named patient program. Overall, 16 patients suffered from recurre
nt or progressive glioblastoma multiforme and 14 patients had grade 3 glioma
s. All but four patients had previously undergone surgical debulking; all bu
t one patient had received previous standard multimodal treatment; and 18 pa
tients (60%) had received more than one line of chemotherapy, in median thre
e. Progression-free survival (PFS), defined as the time from initiation of s

orafenib to treatment discontinuation because of tumor progression or death, was selected as the endpoint. The use of sorafenib resulted in a median PFS of 3 months [95% confidence interval (CI) 1.9-4.1 months] in patients with g lioblastoma and of 3.1 months (95% CI 1.4-4.8 months) in patients with other HGG. The PFS-6 for the whole cohort was 23%. Sixteen patients reported adver se events, mostly moderate, with hypertension as the most frequently reporte d toxicity (seven patients). One patient died of cerebral bleeding (grade 5 toxicity). The overall survival after initiation of sorafenib was 6 months (95% CI 3.9-8.0 months) for patients with glioblastoma multiforme and 10 mont hs (95% CI 3.1-16.9 months) for patients with HGG. In this retrospective ana lysis of heavily pretreated patients with HGG, sorafenib monotherapy was ass ociated with tumor stabilization in a small subset of patients. The risk-ben efit ratio was acceptable in the context of an apparent clinical benefit in patients with a fatal disease.
Journal Title: Anti-cancer drugs

PUBMED ID: 24429479
DOI: doi.org/10.1007/s00066-013-0506-z
Titolo: Low-dose fractionated radiotherapy and concomitant chemotherapy for recurrent or progressive glioblastoma: final report of a pilot study.
Autori: Balducci M., Diletto B., Chiesa S., D'Agostino GR., Gambacorta MA., Ferro M., Colosimo C., Maira G., Anile C., Valentini V.
Data di Pubblicazione: 2014-01-17
Abstract: LD-FRT and chemotherapy for recurrent/progressive GBM have a good toxicity profile and clinical outcomes, even though further investigation of this novel palliative treatment approach is warranted.
Journal Title: Strahlentherapie und Onkologie : Organ der Deutschen Rontgeng esellschaft ... [et al]

PUBMED ID: 24410308
DOI: doi.org/10.2174/157488630866614010615434 3
Titolo: A fatal case of acute interstitial pneumonia (AIP) in a woman affect ed by glioblastoma.
Autori: Balzarini L., Mancini C., Marvisi M.
Data di Pubblicazione: 2014-01-14
Abstract: This report presents the case of a 67-year-old woman affected by g lioblastoma. After a few days of adjuvant therapy with temozolomide and prop hylaxis with trimetrophin-sulfamethoxazolo to prevent Pneumocystis Jiroveci, she had progressive and rapid worsening of symptoms with weakness, dyspnea a nd orthopnea. She had peripheral edema and proximal hyposthenia of the lower limbs. Chest CT showed bilateral ground-glass opacities and laboratory exams revealed hypoxemia and hypocapnia, an initial reduction in platelet and whit e blood cells, and an elevation of LDH, AST, ALT, and active urinary sedimen t. Blood cultures, bronchoalveolar lavage (BAL) data and transbronchial biop sy showed no infections, and in particular no evidence of Pneumocystis Jirov eci pneumonia. Histological examination revealed a typical pattern of AIP. S he was treated with broad-spectrum antibiotics and high-dose steroids. The s ymptoms worsened and respiratory failure required mechanical ventilation. Th e pneumonia was not responsive to medical or invasive care. She died after t en days of hospitalization. At present very little can be found in the liter ature about lung toxicity caused by temozolomide. This case can be added as a new report describing this risk. The combination therapy with temozolamide and trimetophin-sulfamethoxazolo could have a synergistic action inducing va rious forms of pulmonary toxicity. ESTABLISHED FACTS: Acute interstitial pne umonia is a common manifestation of lung toxicity caused by drugs. The clini cal course is favorable with a good response to corticosteroids. NOVEL INSIG HT: This is the first fatal case of lung toxicity caused by Temozolomide. Cl

inicians must be aware that a combination therapy including trimetophin-sulf amethoxazolo could have a synergistic action in inducing pulmonary toxicity.
Journal Title: Current drug safety

PUBMED ID: 24403268
DOI: doi.org/10.1002/cam4.154
Titolo: Efficacy of salvage stereotactic radiotherapy for recurrent glioma: impact of tumor morphology and method of target delineation on local control .
Autori: Ogura K., Mizowaki T., Arakawa Y., Sakanaka K., Miyamoto S., Hiraoka M.
Data di Pubblicazione: 2014-01-10
Abstract: In this study, we assessed the efficacy of salvage stereotactic ra diotherapy (SRT) for recurrent glioma. From August 2008 to December 2012, 30 patients with recurrent glioma underwent salvage SRT. The initial histologic al diagnoses were World Health Organization (WHO) grades II, III, and IV in 6, 9, and 15 patients, respectively. Morphologically, the type of recurrence was classified as diffuse or other. Two methods of clinical target delineati on were used: A, a contrast-enhancing tumor; or B, a contrast-enhancing tumo r with a 3-10-mm margin and/or surrounding fluid attenuation inversion recov ery (FLAIR) high-intensity areas. The prescribed dose was 22.5-35 Gy deliver ed in five fractions at an isocenter using a dynamic conformal arc technique . The overall survival (OS) and local control probability (LCP) after SRT we re calculated using the Kaplan-Meier method. A univariate analysis was used to test the effect of clinical variables on OS/LCP. The median follow-up per iod was 272 days after SRT. The OS and LCP were 83% and 56% at 6 months afte r SRT, respectively. Morphologically, the tumor type correlated significantl y with both OS and LCP (P = 0.006 and <0.001, respectively). The method of t arget delineation also had a significant influence on LCP (P = 0.016). Grade 3 radiation necrosis was observed in two patients according to Common Termin ology Criteria for Adverse Events, version 3. Salvage SRT was safe and effec tive for recurrent glioma, especially non-diffuse recurrences. Improved loca l control might be obtained by adding a margin to contrast-enhancing tumors or including increased FLAIR high-intensity areas.
Journal Title: Cancer medicine

PUBMED ID: 24395350
DOI: doi.org/10.1007/s11060-013-1352-7
Titolo: Neoadjuvant cisplatin plus temozolomide versus standard treatment in patients with unresectable glioblastoma or anaplastic astrocytoma: a differe ntial effect of MGMT methylation.
Autori: Capdevila L., Cros S., Ramirez JL., Sanz C., Carrato C., Romeo M., E txaniz O., Hostalot C., Massuet A., Cuadra JL., Villà S., Balañà C.
Data di Pubblicazione: 2014-01-08
Abstract: Patients with unresectable glioblastoma or anaplastic astrocytoma have a dismal prognosis. The role of neoadjuvant chemotherapy prior to irrad iation in these patients has been studied primarily in non-randomized studie s. We have compared the effect of neoadjuvant chemotherapy plus radiotherapy versus concomitant radiotherapy plus temozolomide in a retrospective analysi s of two consecutive series of patients in whom surgery consisted of biopsy only. From 2003 to 2005, 23 patients received two cycles of temozolomide plu s cisplatin followed by radiotherapy (Cohort 1), and from 2006 to 2010, 23 a dditional patients received concomitant radiotherapy and temozolomide follow ed by adjuvant temozolomide (Cohort 2). In Cohort 1, 91.3 % of patients rece ived all planned chemotherapy cycles. Progression-free and overall survival were 3.3 and 8.5 months, respectively. In Cohort 2, progression-free and ove rall survival were 5.1 and 11.2 months, respectively. No differences between the two groups were observed in rate of completion of radiotherapy, progress

ion-free or overall survival. MGMT methylation was assessed in 91.3 % of pat ients. In Cohort 1, patients without MGMT methylation showed a trend towards shorter progression-free survival (P = 0.09), while in Cohort 2, patients wi thout MGMT methylation had longer progression-free survival (P = 0.04). In t he overall patient population, neoadjuvant temozolomide plus cisplatin had n either a positive nor negative influence on outcome. However, our findings i ndicate that patients with methylated MGMT may derive greater benefit from n eoadjuvant temozolomide than those with unmethylated MGMT.
Journal Title: Journal of neuro-oncology

PUBMED ID: 24390814
DOI: doi.org/10.1007/s11940-013-0273-2
Titolo: Gliomatosis cerebri: a review.
Autori: Rudà R., Bertero L., Sanson M.
Data di Pubblicazione: 2014-01-07
Abstract: Gliomatosis cerebri (GC) is an intriguing disease for several reas ons. First, it is difficult to draw the border between GC and diffuse glioma s. In this regard, GC could represent the most invasive form of diffuse glio mas. Second, both in terms of histologic grading and clinical course, GC is a heterogeneous disease, ranging from rapidly evolving to slowly and somewha t indolent forms. Because of the extensive spread of the disease, surgery-ou tside a biopsy for diagnosis-is rarely indicated in gliomatosis cerebri. The rapeutic options include radiotherapy, generally involving the whole brain, and chemotherapy with temozolomide or nitrosoureas. Because of the rarity of the disease, no trial comparing these two modalities has been undertaken so far. Decision is, therefore, based on small retrospective noncomparative stu dies and expert opinions. On one hand, there is a rationale to postpone the whole brain radiotherapy because of late neurotoxicity, but on the other han d, there is also the risk that an aggressive disease evolves to intracranial hypertension making the radiotherapy hazardous or even impossible. As a cons equence, the patient would lose the opportunity to receive a potentially eff ective treatment. In this decision, the evaluation of histologic data togeth er with clinical and radiologic features, performance status, and molecular profile may be of help. Because radiotherapy usually involves large volumes of the brain, chemotherapy is generally preferred up front in patients with a slowly evolving disease. Conversely, in patients with rapidly (ie, over fe w weeks) evolving disease with neurologic deficits or when histologic featur es of glioblastoma are evident, whole brain radiotherapy (45 Gy with 1.8 Gy fractions), alone or associated with concomitant temozolomide, is often pref erred. The value of advanced of magnetic resonance imaging and positron emis sion tomography techniques to predict outcome and monitoring the treatment s till remains to be defined.
Journal Title: Current treatment options in neurology

PUBMED ID: 24353988
DOI: doi.org/MagyOnkol.2013.57.4.232
Titolo: [Results of postoperative radiochemotherapy of glioblastoma multifor me].
Autori: Lövey J., Fedorcsák I., Bajcsay A., Sipos L., Mangel L., Kásler M., Bagó A.
Data di Pubblicazione: 2013-12-20
Abstract: Glioblastoma multiforme has one of the worst prognoses of all canc ers. A substantial progression in its treatment has been achieved only eight years ago when a new adjuvant radiochemotherapy regimen containing temozolom id has been introduced to the clinical practice. In this paper we evaluate t he treatment results in adjuvant radiochemotherapy of glioblastoma carried o ut by two neurosurgery and oncology centers in Budapest, Hungary and we comp ared our results to the data of the reference phase III registration trial o

f the EORTC/NCIC. We analyzed the data of 210 patients treated for glioblast oma between 2005 and 2013. The primary endpoints of our study were overall s urvival and side effects. We studied and statistically analyzed the influenc e of multiple factors on survival. We compared our results with the data of the reference study and other results published in the literature. The media n follow-up for the surviving patients in our study was 52 months. The media n age of our patients was 58 (18-79) years. Seventy-two women and 138 men ha ve been treated. The median overall survival was 17 (3-96) months, the progr ession-free survival 11 (3-96) months. The radiochemotherapy phase was compl eted in 95.2% and the monotherapy phase in 68% of all cases.Univariate analy sis showed that age, ECOG status and RPA class had significant influence on survival. In multivariate analysis only RPA class remained statistically sig nificant (RR 1.86, 95% CI 1.14-3.05). The proportion of grade III and worse side effects during the chemoradiation phase was 3.8% and in the monotherapy phase 1.9%. These were hematological side effects only. Serious hematologica l sequelae occurred nearly exclusively in women. Comparing to the reference study the demographic distribution of the patients was similar in our study but among our patients there were less patients with unfavorable prognosis (ECOG 2 or RPA V), and it resulted in a longer median survival than in the or iginal trial (17 vs. 14.6 months). With this analysis of our patients treate d according to the Stupp-protocol for glioblastoma multiforme we validated t he results of the original EORTC/NCIC study in a Hungarian patient populatio n. Moreover, this comparison proves that the comprehensive Hungarian neuro-o ncology service is not at all inferior when compared to any of the developed countries in Europe.
Journal Title: Magyar onkologia

PUBMED ID: 24352766
DOI: doi.org/10.1007/s11060-013-1316-y
Titolo: Efficacy of erlotinib in patients with relapsed gliobastoma multifor me who expressed EGFRVIII and PTEN determined by immunohistochemistry.
Autori: Gallego O., Cuatrecasas M., Benavides M., Segura PP., Berrocal A., E rill N., Colomer A., Quintana MJ., Balaña C., Gil M., Gallardo A., Murata P. , Barnadas A.
Data di Pubblicazione: 2013-12-20
Abstract: Epidermal growth factor receptor gene (EGFR) alteration is a commo n feature in most of glioblastoma multiforme (GBM). Robust response of anti-EGFR treatments has been mostly associated with the EGFR deletion mutant var iant III (EGFRvIII) and expression of PTEN. We have performed a prospective trial in order to confirm the efficacy of erlotinib treatment in patients wi th relapsed GBM who expressed EGFRvIII and PTEN. All patients included in th e trial were required to be PTEN (+++), EGFR (+++) and EGFRvIII (+++) positi ves by immunohistochemistry. This new phase II trial enrolled 40 patients an d was design to be stopped in case of fewer than two responses in the first 13 patients. Patient eligibility included histopathology criteria, radiologi cal progression, more than 18 years old, Karnofsky performed status, KPS > 5 0, and adequate bone marrow and organ function. There was no limit to the nu mber of prior treatments for relapses. No enzyme-inducing antiepileptic drug s were allowed. The primary endpoints were response and progression-free sur vival at 6 months (PFS6). Thirteen patients (6 men, 7 women) with recurrent GBM received erlotinib 150 mg/day. Median age was 53 years, median KPS was 8 0, and median prior treatments for relapses were 2. There was one partial re sponse and three stable diseases (one at 18 months). PFS at 6 months was 20 %. Dose reduction for toxicity was not needed in any patient. Dermatitis was the main treatment-related toxicity, grade 1 in 8 patients and grade 2 in 5 patients. No grade 3 toxicity was observed. Median survival was 7 months (95 % IC 1.41-4.7). As conclusion, monotherapy with erlotinib in GBM relapses pa tients with high protein expression for PTEN (+++), EGFR (+++), and EGFRvlII (+++) showed low toxicity but minimal efficacy and the trial stopped.

Journal Title: Journal of neuro-oncology

PUBMED ID: 24347182
DOI: doi.org/10.1177/1352458513516891
Titolo: How to treat tumefactive demyelinating disease?
Autori: Siffrin V., Müller-Forell W., von Pein H., Zipp F.
Data di Pubblicazione: 2013-12-19
Abstract: Glioma-like inflammatory demyelinating lesions can be found in pat ients with pre-diagnosed multiple sclerosis, but they have also been describ ed as an isolated disease entity. The initial diagnostic work-up usually inc ludes a biopsy for histopathological analysis. However, even after unambiguo us histopathologic classification, tumefactive lesions pose a therapeutic ch allenge. Until now, there have been no guidelines on how to treat patients w ith these rare and extreme lesion phenotypes. Here we report a patient with a relapsing unifocal tumefactive demyelinating lesion. The patient initially showed a good response to steroid treatment, with full clinical recovery. Ho wever, after relapse of the same lesion, recovery was incomplete. Although i mmunosuppression was initiated, the patient presented with subsequent furthe r deterioration. Only maximal escalation of immunosuppression was able to st op the inflammatory activity. Due to the length of time of the step-wise esc alation treatment however, the lengthy lesion activity led to irreversible t issue destruction and residual non-remitting disability. Early aggressive tr eatment with an induction therapy regimen might be more appropriate for thes e rare and often strongly disabling lesion subtypes.
Journal Title: Multiple sclerosis (Houndmills, Basingstoke, England)

PUBMED ID: 24339289
DOI: doi.org/10.3349/ymj.2014.55.1.70
Titolo: Feasibility and outcomes of hypofractionated simultaneous integrated boost-intensity modulated radiotherapy for malignant gliomas: a preliminary report.
Autori: Cha J., Suh CO., Park K., Chang JH., Lee KS., Kim SH., Chang JS., Ki m JH., Suh YG., Kim JW., Cho J.
Data di Pubblicazione: 2013-12-17
Abstract: An escalated dose of hypofractionated SIB-IMRT using three-layered PTVs can be safely performed in patients with malignant glioma, and might co ntribute to better tumor control and survival.
Journal Title: Yonsei medical journal

PUBMED ID: 24321226
DOI: doi.org/10.1016/j.ejrad.2013.06.033
Titolo: Molecular and metabolic pattern classification for detection of brai n glioma progression.
Autori: Imani F., Boada FE., Lieberman FS., Davis DK., Mountz JM.
Data di Pubblicazione: 2013-12-11
Abstract: National Cancer Institute, Cancer Center Support Grant Supplement Award, Imaging Response Assessment Teams.
Journal Title: European journal of radiology

PUBMED ID: 24311637
DOI: doi.org/10.1093/neuonc/not161
Titolo: A single-arm phase II Austrian/German multicenter trial on continuou s daily sunitinib in primary glioblastoma at first recurrence (SURGE 01-07).
Autori: Hutterer M., Nowosielski M., Haybaeck J., Embacher S., Stockhammer F ., Gotwald T., Holzner B., Capper D., Preusser M., Marosi C., Oberndorfer S.

, Moik M., Buchroithner J., Seiz M., Tuettenberg J., Herrlinger U., Wick A., Vajkoczy P., Stockhammer G.
Data di Pubblicazione: 2013-12-07
Abstract: Continuous daily sunitinib showed minimal antiglioblastoma activity and substantial toxicity when given at higher doses. High endothelial c-KIT expression may define a subgroup of patients who will benefit from sunitinib treatment by achieving prolonged PFS. ClinicalTrials.gov Identifier: NCT00535379.
Journal Title: Neuro-oncology

PUBMED ID: 24305706
DOI: doi.org/10.1093/neuonc/not169
Titolo: Clinical and prognostic features of adult patients with gangliogliomas.
Autori: Yust-Katz S., Anderson MD., Liu D., Wu J., Yuan Y., Olar A., Fuller GN., Brown PD., de-Groot JF.
Data di Pubblicazione: 2013-12-06
Abstract: While GG has excellent prognosis, malignant histologic grade, older age, and diagnosis with biopsy could indicate worse prognosis. The late nature and high rate of progression emphasize the importance of long-term follow-up. The role of chemotherapy and radiation therapy for incompletely resected low-grade GG remains unclear.
Journal Title: Neuro-oncology

PUBMED ID: 24293233
DOI: doi.org/10.1007/s11060-013-1317-x
Titolo: Bevacizumab and fotemustine for recurrent glioblastoma: a phase II study of AINO (Italian Association of Neuro-Oncology).
Autori: Soffietti R., Trevisan E., Bertero L., Cassoni P., Morra I., Fabrini MG., Pasqualetti F., Lolli I., Castiglione A., Ciccone G., Rudà R.
Data di Pubblicazione: 2013-12-03
Abstract: The optimal combination of bevacizumab with cytotoxic or cytostatic drugs in recurrent glioblastoma is unknown. We performed a phase 2 trial of combined bevacizumab and fotemustine for patients with glioblastoma at first relapse after radiotherapy and temozolomide. The primary endpoint was 6-month progression-free survival (PFS), while secondary endpoints were overall survival (OS), response rate based on RANO criteria and toxicity. Fifty-four patients with recurrent GBM were enrolled. The authors observed a 6-month PFS rate of 42.6% (95% CI 29.3-55.2) and a median PFS of 5.2 months (95% CI 3.8-6.6). The median OS was 9.1 months (95% CI 7.3-10.3). Twenty-eight patients (52%) had a radiographic response, and a significant neurological improvement with steroid reduction was observed in 25/42 symptomatic patients (60%). MGMT promoter methylation was significantly associated with improved PFS in univariate analysis. Most unifocal tumors at baseline had a focal enhancing progression (76%), while the diffuse non-enhancing progression accounted for 9.5%. Response or survival were not associated with any pattern of progression. Survival after failure of treatment was short. Twelve out of 54 patients (22%) discontinued fotemustine for grade 3/4 myelotoxicity, while 4/54 (7.4%) discontinued bevacizumab. This study failed to demonstrate a superiority of the combination of bevacizumab and fotemustine over either bevacizumab or fotemustine alone as historical controls. Future studies should explore alternative regimens of combination of the two drugs.
Journal Title: Journal of neuro-oncology

PUBMED ID: 24286144
DOI: doi.org/10.3171/2013.10.JNS131512

Titolo: Delayed leptomeningeal and subependymal seeding after multiple surgeries for supratentorial diffuse low-grade gliomas in adults.
Autori: Alvarez de Eulate-Beramendi S., Rigau V., Taillandier L., Duffau H.
Data di Pubblicazione: 2013-11-30
Abstract: Cerebrospinal fluid dissemination of DLGG is a rare but possible event. It can occur throughout the progression of WHO Grade II oligodendrogliomas, oligoastrocytomas, and astrocytomas, regardless of 1p19q status. This complication seems to appear in patients who have undergone multiple incomplete resections. Salvage therapy can be considered in patients with good neurological status. However, LMSS is associated with a decreased overall survival. Therefore, this rare entity deserves further multicenter studies to better understand its pathophysiology and to adapt therapeutic strategies.
Journal Title: Journal of neurosurgery

PUBMED ID: 24218181
DOI: doi.org/10.1007/s11060-013-1284-2
Titolo: Favorable survival and metabolic outcome for children with diencephalic syndrome using a radiation-sparing approach.
Autori: Kilday JP., Bartels U., Huang A., Barron M., Shago M., Mistry M., Zhukova N., Laperriere N., Dirks P., Hawkins C., Bouffet E., Tabori U.
Data di Pubblicazione: 2013-11-13
Abstract: Diencephalic syndrome (DS) is a clinical disorder of metabolism associated with poor outcome in children with low-grade gliomas (LGGs). Since survival has been primarily reported with aggressive therapy, we report outcome data for these patients using a current, contrasting chemotherapy-driven approach. We performed a population-based review of DS patients treated with chemotherapy from 1997-2012. Metabolic rate was assessed in selected cases using open-circuit calorimetry to generate resting energy expenditure (REE) data. Tumor tissue was analyzed for BRAF alterations. Survival was compared with an age-related, radiotherapy naïve cohort of non-DS children with location-matched LGGs. Nine children (1.7% of 520 LGG diagnoses) fulfilled DS criteria. The median diagnostic age was 1.49 years (0.55-2.69 years), although neurofibromatosis Type-I patients were older (p = 0.005). All tumors analyzed exhibited either NF1 mutation or BRAF fusion. Seven tumors were histologically confirmed as low grade astrocytomas, one demonstrated neurocytic features, and one NF1 case was diagnosed using imaging and clinical criteria. All patients received chemotherapy, with seven cases also receiving initial nutritional supplementation. All nine gained weight after only 6 months of treatment. Two DS patients had serial REE measurements, revealing a hypermetabolic state (over 200% of predicted REE) at diagnosis which reduced to normal range with therapy. First-line chemotherapy treatment resulted in one minor response, stable disease in four cases, with progression in the remaining four patients. Although DS patients demonstrated inferior initial progression-free survival when compared to non-DS counterparts (5 years: 22 versus 60%, p = 0.015), all DS children remain alive at a median follow up of 5.3 years (1.2-14.9 years) with none requiring radiotherapy. Long-term sequelae included pituitary and visual dysfunction, learning difficulties and paradoxical, inappropriate weight gain. DS can be managed with non-aggressive chemotherapeutic, radiation-sparing strategies supplemented by temporary nutritional support. Multiple lines of therapy may be required to overcome disease progression but excellent survival and metabolic outcomes can be achieved. Continued surveillance is mandatory to prevent significant weight gain and support affected children with clinical sequelae.
Journal Title: Journal of neuro-oncology

PUBMED ID: 24202340
DOI: doi.org/10.3390/cancers5031177

Titolo: Outcomes in newly diagnosed elderly glioblastoma patients after conc omitant temozolomide administration and hypofractionated radiotherapy.
Autori: Nguyen LT., Touch S., Nehme-Schuster H., Antoni D., Eav S., Clavier JB., Bauer N., Vigneron C., Schott R., Kehrli P., Noël G.
Data di Pubblicazione: 2013-11-09
Abstract: This study aimed to analyze the treatment and outcomes of older gl ioblastoma patients. Forty-four patients older than 70 years of age were ref erred to the Paul Strauss Center for chemotherapy and radiotherapy. The medi an age was 75.5 years old (range: 70-84), and the patients included 18 femal es and 26 males. The median Karnofsky index (KI) was 70%. The Charlson indic es varied from 4 to 6. All of the patients underwent surgery. O6-methylguani ne-DNA methyltransferase (MGMT) methylation status was determined in 25 pati ents. All of the patients received radiation therapy. Thirty-eight patients adhered to a hypofractionated radiation therapy schedule and six patients to a normofractionated schedule. Neoadjuvant, concomitant and adjuvant chemothe rapy regimens were administered to 12, 35 and 20 patients, respectively. At the time of this analysis, 41 patients had died. The median time to relapse was 6.7 months. Twenty-nine patients relapsed, and 10 patients received chem otherapy upon relapse. The median overall survival (OS) was 7.2 months and t he one- and two-year OS rates were 32% and 12%, respectively. In a multivari ate analysis, only the Karnofsky index was a prognostic factor. Hypofraction ated radiotherapy and chemotherapy with temozolomide are feasible and accept ably tolerated in older patients. However, relevant prognostic factors are n eeded to optimize treatment proposals.
Journal Title: Cancers

PUBMED ID: 24190997
DOI: doi.org/10.1073/pnas.1318022110
Titolo: Improved tumor oxygenation and survival in glioblastoma patients who show increased blood perfusion after cediranib and chemoradiation.
Autori: Batchelor TT., Gerstner ER., Emblem KE., Duda DG., Kalpathy-Cramer J ., Snuderl M., Ancukiewicz M., Polaskova P., Pinho MC., Jennings D., Plotkin SR., Chi AS., Eichler AF., Dietrich J., Hochberg FH., Lu-Emerson C., Iafrate AJ., Ivy SP., Rosen BR., Loeffler JS., Wen PY., Sorensen AG., Jain RK.
Data di Pubblicazione: 2013-11-06
Abstract: Antiangiogenic therapy has shown clear activity and improved survi val benefit for certain tumor types. However, an incomplete understanding of the mechanisms of action of antiangiogenic agents has hindered optimization and broader application of this new therapeutic modality. In particular, the impact of antiangiogenic therapy on tumor blood flow and oxygenation status (i.e., the role of vessel pruning versus normalization) remains controversia l. This controversy has become critical as multiple phase III trials of anti -VEGF agents combined with cytotoxics failed to show overall survival benefi t in newly diagnosed glioblastoma (nGBM) patients and several other cancers. Here, we shed light on mechanisms of nGBM response to cediranib, a pan-VEGF receptor tyrosine kinase inhibitor, using MRI techniques and blood biomarker s in prospective phase II clinical trials of cediranib with chemoradiation v s. chemoradiation alone in nGBM patients. We demonstrate that improved perfu sion occurs only in a subset of patients in cediranib-containing regimens, a nd is associated with improved overall survival in these nGBM patients. More over, an increase in perfusion is associated with improved tumor oxygenation status as well as with pharmacodynamic biomarkers, such as changes in plasma placenta growth factor and sVEGFR2. Finally, treatment resistance was associ ated with elevated plasma IL-8 and sVEGFR1 posttherapy. In conclusion, tumor perfusion changes after antiangiogenic therapy may distinguish responders vs . nonresponders early in the course of this expensive and potentially toxic form of therapy, and these results may provide new insight into the selectio n of glioblastoma patients most likely to benefit from anti-VEGF treatments.

Journal Title: Proceedings of the National Academy of Sciences of the United States of America

PUBMED ID: 24105052
DOI: Mancante
Titolo: [Chemotherapy for malignant gliomas: an update].
Autori: Wakabayashi T., Natsume A., Fujii M.
Data di Pubblicazione: 2013-10-10
Abstract: Gliomas account for approximately 30% of all brain tumors and are thus the most common primary tumors of the central nervous system (CNS). Despite treatment with aggressive surgical resection, chemotherapy, and radiotherapy, high-grade (WHO grades III and IV) malignant gliomas, especially glioblastoma (GBM), the most common glioma in adults, kill patients within a median time span of a year after diagnosis. In Japan, alkylating agents such as 1-(4-amino-2-methyl-5-pyridiminyl) methyl-3-(2-chloroethyl)-3-nitrosourea (ACNU) and methyl-6-[3-(2-chloroethyl)-3-nitrosoureido]-6-deoxy-alpha-D-glucopyranoside (MCNU) have been used to treat malignant gliomas for a long time; however, this treatment provides few clinical benefits. Temozolomide (TMZ), an oral alkylating agent, has been demonstrated to possess antitumor activity against malignant gliomas with minimal additional toxicity; furthermore, a previous study found that treatment with TMZ significantly prolonged median survival time. In 2006, TMZ was certified as the treatment agent for malignant gliomas by the National Ministry of Health and Welfare of Japan. It is now used as first-line therapy. However, its clinical outcomes depend on the O6-methylguanine-DNA methyltransferase (MGMT) status, and MGMT modification is one of the key factors to deriving greater clinical benefits in the future. Combination therapy with TMZ and other antitumor drugs, especially anti-vascular endothelial growth factor (VEGF) antibody (Avascin), has been aggressively investigated for treating gliomas. Some of these drugs have been studied in experimental animal models and advanced to clinical trials. These studies suggest that combination therapy with TMZ and other antitumor drugs might further improve the clinical outcome of malignant gliomas as compared to TMZ plus radiotherapy. Based on these data, the next step will be to carry out phase II to III clinical studies to improve treatment of malignant brain tumors further.
Journal Title: Gan to kagaku ryoho. Cancer & chemotherapy

PUBMED ID: 24076268
DOI: doi.org/10.1016/j.pharmthera.2013.09.003
Titolo: Bevacizumab and micrometastases: revisiting the preclinical and clinical rollercoaster.
Autori: Mountzios G., Pentheroudakis G., Carmeliet P.
Data di Pubblicazione: 2013-10-01
Abstract: The use of bevacizumab, a monoclonal antibody against vascular endothelial growth factor (VEGF), in combination with standard therapeutic approaches, has offered clinical benefit for patients with advanced colorectal, breast, ovarian, renal, non small-cell lung cancer and glioblastoma. However, the strategy of administering bevacizumab until disease progression has been challenged by certain preclinical evidence, suggesting that prolonged exposure to anti-VEGF treatment may elicit an adaptive-evasive response, resulting in a more aggressive tumor phenotype. Moreover, the use of bevacizumab in adjuvant chemotherapeutic regimens has led to less promising results than expected. Despite our poor understanding of how bevacizumab acts in micrometastatic disease, numerous clinical trials (involving >20,000 cancer patients) are ongoing or are planned to test the therapeutic benefit in the adjuvant setting. The discrepancy of bevacizumab's efficiency in the two settings calls into question the validity of current strategies that use similar treatment regimens for early and advanced diseases. Herein, we review the mechanism

s of bevacizumab activity in the macro- as compared to the micrometastatic e nvironment and discuss possible alternative strategies in the adjuvant setti ng that might spur attention for future clinical trials. Rather than providi ng an encyclopedic survey of the literature, we highlight exemplary principl es.
Journal Title: Pharmacology & therapeutics

PUBMED ID: 24066926
DOI: doi.org/10.1186/1748-717X-8-222
Titolo: Hypofractionated stereotactic radiation therapy for recurrent gliobl astoma: single institutional experience.
Autori: Ciammella P., Podgornii A., Galeandro M., D'Abbiero N., Pisanello A. , Botti A., Cagni E., Iori M., Iotti C.
Data di Pubblicazione: 2013-09-27
Abstract: Our results suggest that hypofractionated stereotactic radiation t herapy is effective and safe in recurrent GBM. However, until prospective ra ndomized trials will confirm these results, the decision for salvage treatme nt should remain individual and based on a multidisciplinary evaluation of e ach patient.
Journal Title: Radiation oncology (London, England)

PUBMED ID: 24046261
DOI: doi.org/10.1093/neuonc/not126
Titolo: Stereotactic iodine-125 brachytherapy for the treatment of WHO grade s II and III gliomas located in the central sulcus region.
Autori: Ruge MI., Kickingereder P., Grau S., Dorn F., Galldiks N., Treuer H. , Sturm V.
Data di Pubblicazione: 2013-09-19
Abstract: Compared with microsurgical resection, SBT harbors a low risk of p rocedural complications, is minimally invasive, and seems to be an effective local treatment option for patients with inoperable, eloquent WHO grade II a nd III gliomas in the CSR. However, the value of SBT for treating gliomas st ill needs to be determined in prospective, randomized studies.
Journal Title: Neuro-oncology

PUBMED ID: 24011536
DOI: doi.org/10.1016/j.ejca.2013.08.006
Titolo: Diffuse intrinsic pontine glioma treated with prolonged temozolomide and radiotherapy--results of a United Kingdom phase II trial (CNS 2007 04).
Autori: Bailey S., Howman A., Wheatley K., Wherton D., Boota N., Pizer B., F isher D., Kearns P., Picton S., Saran F., Gibson M., Glaser A., Connolly DJ. , Hargrave D.
Data di Pubblicazione: 2013-09-10
Abstract: Diffuse intrinsic pontine glioma (DIPG) has a dismal prognosis wit h no chemotherapy regimen so far resulting in any significant improvement ov er standard radiotherapy. In this trial, a prolonged regimen (21/28d) of tem ozolomide was studied with the aim of overcoming O(6)-methylguanine methyltr ansferase (MGMT) mediated resistance. Forty-three patients with a defined cl inico-radiological diagnosis of DIPG received radiotherapy and concomitant t emozolomide (75 mg/m(2)) after which up to 12 courses of 21d of adjuvant tem ozolomide (75-100mg/m(2)) were given 4 weekly. The trial used a 2-stage desi gn and passed interim analysis. At diagnosis median age was 8 years (2-20 ye ars), 81% had cranial nerve abnormalities, 76% ataxia and 57% long tract sig ns. Median Karnofsky/Lansky score was 80 (10-100). Patients received a media n of three courses of adjuvant temozolomide, five received all 12 courses an d seven did not start adjuvant treatment. Three patients were withdrawn from study treatment due to haematological toxicity and 10 had a dose reduction.

No other significant toxicity related to temozolomide was noted. Overall sur vival (OS) (95% confidence interval (CI)) was 56% (40%, 69%) at 9 months, 35 % (21%, 49%) at 1 year and 17% (7%, 30%) at 2 years. Median survival was 9.5 months (range 7.5-11.4 months). There were five 2-year survivors with a medi an age of 13.6 years at diagnosis. This trial demonstrated no survival benef it of the addition of dose dense temozolomide, to standard radiotherapy in c hildren with classical DIPG. However, a subgroup of adolescent DIPG patients did have a prolonged survival, which needs further exploration.
Journal Title: European journal of cancer (Oxford, England : 1990)

PUBMED ID: 24008924
DOI: doi.org/10.1159/000354692
Titolo: FLAIR-only progression in bevacizumab-treated relapsing glioblastoma does not predict short survival.
Autori: Schaub C., Greschus S., Seifert M., Waha A., Blasius E., Rasch K., L andwehr C., Mack F., Schäfer N., Stuplich M., Kebir S., Vilz B., Scheffler B ., Boström J., Simon M., Urbach H., Glas M., Herrlinger U.
Data di Pubblicazione: 2013-09-07
Abstract: FLAIR-only progression is not an independent prognostic factor neg atively influencing OS in recurrent glioblastoma treated with bevacizumab an d should not lead to discontinuation of bevacizumab therapy.
Journal Title: Oncology

PUBMED ID: 23957780
DOI: doi.org/10.3109/02688697.2013.829554
Titolo: Stupp-treated glioblastoma accompanied by EBV-positive primary CNS l ymphoma.
Autori: Zakaria Z., Fenton E., Khalil A., Sattar MT., Molnar P.
Data di Pubblicazione: 2013-08-21
Abstract: We describe a patient who within 2 months of undergoing radio-chem otherapy for glioblastoma developed an Epstein-Barr virus-positive primary d iffuse large B-cell CNS lymphoma. To our knowledge, this is the first such c ase reported in the literature showing that new tumefactions following aggre ssive treatment for glioblastomata might represent secondary malignancies.
Journal Title: British journal of neurosurgery

PUBMED ID: 23952800
DOI: doi.org/10.3171/2013.7.JNS13415
Titolo: Phase II clinical study on intraoperative photodynamic therapy with talaporfin sodium and semiconductor laser in patients with malignant brain t umors.
Autori: Muragaki Y., Akimoto J., Maruyama T., Iseki H., Ikuta S., Nitta M., Maebayashi K., Saito T., Okada Y., Kaneko S., Matsumura A., Kuroiwa T., Kara sawa K., Nakazato Y., Kayama T.
Data di Pubblicazione: 2013-08-20
Abstract: Intraoperative PDT using talaporfin sodium and a semiconductor las er may be considered as a potentially effective and sufficiently safe option for adjuvant management of primary malignant parenchymal brain tumors. The i nclusion of intraoperative PDT in a combined treatment strategy may have a p ositive impact on OS and local tumor control, particularly in patients with newly diagnosed GBMs. Clinical trial registration no.: JMA-IIA00026 (https:/ /dbcentre3.jmacct.med.or.jp/jmactr/App/JMACTRS06/JMACTRS06.aspx?seqno=862).
Journal Title: Journal of neurosurgery

PUBMED ID: 23927666
DOI: doi.org/10.1586/17512433.2013.811806

Titolo: An EGFRvIII-targeted bispecific T-cell engager overcomes limitations of the standard of care for glioblastoma.
Autori: Gedeon PC., Choi BD., Hodges TR., Mitchell DA., Bigner DD., Sampson JH.
Data di Pubblicazione: 2013-08-10
Abstract: While advanced surgical techniques, radiation therapy and chemothe rapeutic regimens provide a tangible benefit for patients with glioblastoma (GBM), the average survival from the time of diagnosis remains less than 15 months. Current therapy for GBM is limited by the nonspecific nature of trea tment, prohibiting therapy that is aggressive and prolonged enough to elimin ate all malignant cells. As an alternative, bispecific antibodies can redire ct the immune system to eliminate malignant cells with exquisite potency and specificity. We have recently developed an EGF receptor variant III (EGFRvII I)-targeted bispecific antibody that redirects T cells to eliminate EGFRvIII -expressing GBM. The absolute tumor specificity of EGFRvIII and the lack of immunologic crossreactivity with healthy cells allow this therapeutic to ove rcome limitations associated with the nonspecific nature of the current stan dard of care for GBM. Evidence indicates that the molecule can exert therape utically significant effects in the CNS following systemic administration. A dditional advantages in terms of ease-of-production and off-the-shelf availa bility further the clinical utility of this class of therapeutics.
Journal Title: Expert review of clinical pharmacology

PUBMED ID: 23909061
DOI: Mancante
Titolo: Tailored therapy in diffuse gliomas: using molecular classifiers to optimize clinical management.
Autori: Taylor JW., Chi AS., Cahill DP.
Data di Pubblicazione: 2013-08-06
Abstract: Diffuse gliomas are the most common primary malignant brain tumors in adults and continue to be almost universally fatal. Nevertheless, a strik ing variability in outcome has long been observed, with a subset of patients having prolonged survival. Recent molecular discoveries have provided new in sights into gliomagenesis and have enhanced clinical subclassification of gl iomas. Mutations in the isocitrate dehydrogenase (IDH) genes occur frequentl y in low-grade astrocytomas and oligodendrogliomas (World Health Organizatio n [WHO] grade II), and in higher-grade gliomas (WHO grades III and IV) that arise after malignant progression of low-grade tumors. IDH mutation has an e stablished role as a favorable prognostic marker; however, the utility of ID H mutation in guiding treatment is still under investigation. A subset of ID H-mutant tumors, predominantly oligodendrogliomas, also harbor codeletion of chromosomes 1 p and 19q, a feature that predicts responsiveness to chemother apy. Here, we review the current data regarding the prognostic and predictiv e value of IDH mutation and 1 p/19q codeletion in gliomas. We also discuss p ossible management algorithms using these biomarkers to tailor surgical and adjuvant therapy for specific diffuse gliomas. Ultimately, understanding the natural history of glioma subtypes and the predictive value of genetic marke rs may maximize survival and minimize treatment morbidity.
Journal Title: Oncology (Williston Park, N.Y.)

PUBMED ID: 23898108
DOI: Mancante
Titolo: Continuous tamoxifen and dose-dense temozolomide in recurrent gliobl astoma.
Autori: DI Cristofori A., Carrabba G., Lanfranchi G., Menghetti C., Rampini P., Caroli M.
Data di Pubblicazione: 2013-07-31

Abstract: The combinatorial administration of tamoxifen and TMZ appeared to be well-tolerated, and potentially effective in increasing the efficacy of d ose-dense TMZ schedule as a second-line therapeutic strategy.
Journal Title: Anticancer research

PUBMED ID: 23883555
DOI: doi.org/10.2176/nmc.53.447
Titolo: Updated therapeutic strategy for adult low-grade glioma stratified b y resection and tumor subtype.
Autori: Nitta M., Muragaki Y., Maruyama T., Iseki H., Ikuta S., Konishi Y., Saito T., Tamura M., Chernov M., Watanabe A., Okamoto S., Maebayashi K., Mit suhashi N., Okada Y.
Data di Pubblicazione: 2013-07-26
Abstract: The importance of surgical resection for patients with supratentor ial low-grade glioma (LGG) remains controversial. This retrospective study o f patients (n = 153) treated between 2000 to 2010 at a single institution as sessed whether increasing the extent of resection (EOR) was associated with improved progression-free survival (PFS) and overall survival (OS). Histolog ical subtypes of World Health Organization grade II tumors were as follows: diffuse astrocytoma in 49 patients (32.0%), oligoastrocytoma in 45 patients (29.4%), and oligodendroglioma in 59 patients (38.6%). Median pre- and posto perative tumor volumes and median EOR were 29.0 cm(3) (range 0.7-162 cm(3)) and 1.7 cm(3) (range 0-135.7 cm(3)) and 95%, respectively. Five- and 10-year OS for all LGG patients were 95.1% and 85.4%, respectively. Eight-year OS fo r diffuse astrocytoma, oligoastrocytoma, and oligodendroglioma were 70.7%, 9 1.2%, and 98.3%, respectively. Five-year PFS for diffuse astrocytoma, oligoa strocytoma, and oligodendroglioma were 42.6%, 71.3%, and 62.7%, respectively . Patients were divided into two groups by EOR ≥90% and <90%, and OS and PFS were analyzed. Both OS and PFS were significantly longer in patients with ≥9 0% EOR. Increased EOR resulted in better PFS for diffuse astrocytoma but not for oligodendroglioma. Multivariate analysis identified age and EOR as param eters significantly associated with OS. The only parameter associated with P FS was EOR. Based on these findings, we established updated therapeutic stra tegies for LGG. If surgery resulted in EOR <90%, patients with astrocytoma w ill require second-look surgery, whereas patients with oligodendroglioma or oligoastrocytoma, which are sensitive to chemotherapy, will be treated with chemotherapy.
Journal Title: Neurologia medico-chirurgica

PUBMED ID: 23883553
DOI: doi.org/10.2176/nmc.53.429
Titolo: Current knowledge and treatment strategies for grade II gliomas.
Autori: Narita Y.
Data di Pubblicazione: 2013-07-26
Abstract: World Health Organization grade II gliomas (GIIGs) include diffuse astrocytoma, oligodendroglioma, and oligoastrocytoma. GIIG is a malignant br ain tumor for which the treatment outcome can still be improved. Review of p revious clinical trials found the following: (1) GIIG increased in size by 3 -5 mm per year when observed or treated with surgery alone; (2) after pathol ogical diagnosis, the survival rate was increased by early aggressive tumor removal at an earlier stage compared to observation alone; (3) although the prognosis after total tumor removal was significantly better than that after partial tumor removal, half of the patients relapsed within 5 years; (4) com paring postoperative early radiotherapy (RT) and non-early RT after relapse, early RT prolonged progression-free survival (PFS) but did not affect overal l survival (OS); (5) local RT of 45 to 64.8 Gy did not impact PFS or OS; (6) in patients with residual tumors, RT combined with chemotherapy (procarbazin e plus lomustine plus vincristine) prolonged PFS compared with RT alone but

did not affect OS; and (7) poor prognostic factors included astrocytoma, non-total tumor removal, age ≥40 years, largest tumor diameter ≥4-6 cm, tumor crossing the midline, and neurological deficit. To improve treatment outcomes, surgery with functional brain mapping or intraoperative magnetic resonance imaging or chemoradiotherapy with temozolomide is important. In this review, current knowledge regarding GIIG is described and treatment strategies are explored.
Journal Title: Neurologia medico-chirurgica

PUBMED ID: 23721146
DOI: doi.org/10.1111/j.1754-9485.2012.02472.x
Titolo: MRI patterns of T1 enhancing radiation necrosis versus tumour recurrence in high-grade gliomas.
Autori: Reddy K., Westerly D., Chen C.
Data di Pubblicazione: 2013-06-01
Abstract: Identifying distinct patterns of contrast enhancement on MRI may help to differentiate between radiation necrosis and tumour recurrence in high-grade gliomas.
Journal Title: Journal of medical imaging and radiation oncology

PUBMED ID: 23670807
DOI: doi.org/10.1055/s-0033-1342938
Titolo: Cerebellar anaplastic astrocytoma in an adult with neurofibromatosis type 1: case report and review of literature.
Autori: Brokinkel B., Schober O., Ewelt C., Heindel W., Hargus G., Stummer W., Holling M., Wölfer J.
Data di Pubblicazione: 2013-05-15
Abstract: A literature search yielded only one previously published case of an AA in a 9-year-old girl with NF1. Tumor control after resection was achieved in both patients; however, the patient in the mentioned report received radiation instead of temozolomide. In spite of different adjuvant therapies, tumor control for at least 16 months was achieved in both published cases. Thus, even though the role of adjuvant treatment options remains to be further elucidated, surgery is the appropriate therapy in these uncommon tumors providing mass reduction and histological diagnosis as well as tumor control.
Journal Title: Journal of neurological surgery. Part A, Central European neurosurgery

PUBMED ID: 23634286
DOI: doi.org/10.1002/cam4.58
Titolo: Phase II trial of upfront bevacizumab and temozolomide for unresectable or multifocal glioblastoma.
Autori: Lou E., Peters KB., Sumrall AL., Desjardins A., Reardon DA., Lipp ES., Herndon JE., Coan A., Bailey L., Turner S., Friedman HS., Vredenburgh JJ.
Data di Pubblicazione: 2013-05-02
Abstract: Patients with unresectable glioblastomas have a poor prognosis, with median survival of 6-10 months. We conducted a phase II trial of upfront 5-day temozolomide (TMZ) and bevacizumab (BV) in patients with newly diagnosed unresectable or multifocal glioblastoma. Patients received up to four cycles of TMZ at 200 mg/m(2) on days 1-5, and BV at 10 mg/kg on days 1 and 15 of a 28-day cycle. Brain magnetic resonance imaging (MRI) was performed monthly. Therapy was continued as long as there was no tumor progression, grade 4 nonhematologic toxicity, or recurrent grade 4 hematologic toxicity after dose reduction. The primary end point was best tumor response as measured on MRI. Forty-one patients were accrued over 12 months; 39 had a full set of MRI scans available for evaluation. Assessment for best radiographic responses was as follows: partial responses in 24.4%, stable disease in 68.3%, and prog

ressive disease in 2.4%. Treatment-related toxicities included seven grade 4 toxicities and one grade 5 toxicity (myocardial infarction). From this study , it was concluded that an upfront regimen of TMZ and BV for unresectable gl ioblastoma was well tolerated and provided a significant level of disease st abilization. Therapeutic toxicities were consistent with those seen in the a djuvant setting using these agents. The upfront approach to treatment of gli oblastoma in the unresectable population warrants further investigation in r andomized controlled phase III trials.
Journal Title: Cancer medicine

PUBMED ID: 23630166
DOI: doi.org/10.1158/1078-0432.CCR-12-2119
Titolo: Prolonged inhibition of glioblastoma xenograft initiation and clonog enic growth following in vivo Notch blockade.
Autori: Chu Q., Orr BA., Semenkow S., Bar EE., Eberhart CG.
Data di Pubblicazione: 2013-05-01
Abstract: Weekly oral delivery of MRK003 results in significant in vivo inhi bition of Notch pathway activity, tumor growth, stem cell marker expression, and clonogenicity, providing preclinical support for the use of such compoun ds in patients with malignant brain tumors. Some of these effects can persis t for some time after in vivo therapy is complete.
Journal Title: Clinical cancer research : an official journal of the America n Association for Cancer Research

PUBMED ID: 23578667
DOI: doi.org/10.3174/ajnr.A3506
Titolo: Longitudinal restriction spectrum imaging is resistant to pseudoresp onse in patients with high-grade gliomas treated with bevacizumab.
Autori: Kothari P., White NS., Farid N., Chung R., Kuperman JM., Girard HM., Shankaranarayanan A., Kesari S., McDonald CR., Dale AM.
Data di Pubblicazione: 2013-04-13
Abstract: Restriction spectrum imaging is less influenced by reductions in F LAIR hyperintensity compared with ADC, which may confer an advantage of rest riction spectrum imaging over ADC for interpreting tumor response on imaging following antiangiogenic therapy.
Journal Title: AJNR. American journal of neuroradiology

PUBMED ID: 23570586
DOI: Mancante
Titolo: [Multicenter randomized controlled study of temozolomide versus semu stine in the treatment of recurrent malignant glioma].
Autori: Sun J., Yang XJ., Yang SY.
Data di Pubblicazione: 2013-04-11
Abstract: The efficacy of TMZ for patients with recurrent GBM or AA is bette r than that of Me-CCNU. And TMZ has an acceptable safety profile and its adv erse events are mostly mild.
Journal Title: Zhonghua yi xue za zhi

PUBMED ID: 23564811
DOI: Mancante
Titolo: Phase II study of bevacizumab and temsirolimus combination therapy f or recurrent glioblastoma multiforme.
Autori: Lassen U., Sorensen M., Gaziel TB., Hasselbalch B., Poulsen HS.
Data di Pubblicazione: 2013-04-09

Abstract: Temsirolimus can be safely administered in combination with bevaci zumab. This study failed to detect activity of such a combination in patient s with progressive GBM beyond bevacizumab therapy.
Journal Title: Anticancer research

PUBMED ID: 23549780
DOI: doi.org/10.1007/s00066-012-0296-8
Titolo: Quasi-VMAT in high-grade glioma radiation therapy.
Autori: Fadda G., Massazza G., Zucca S., Durzu S., Meleddu G., Possanzini M. , Farace P.
Data di Pubblicazione: 2013-04-04
Abstract: These findings suggest that qVMAT should be preferred to 3D-CRT fo r the treatment of high-grade gliomas. The qVMAT method could be applied in hospitals, for example, which have limited departmental resources and are no t equipped with systems capable of VMAT delivery.
Journal Title: Strahlentherapie und Onkologie : Organ der Deutschen Rontgeng esellschaft ... [et al]

PUBMED ID: 23496909
DOI: doi.org/10.1186/1471-2407-13-106
Titolo: The prospective application of a hypoxic radiosensitizer, doranidazo le to rat intracranial glioblastoma with blood brain barrier disruption.
Autori: Yasui H., Asanuma T., Kino J., Yamamori T., Meike S., Nagane M., Kub ota N., Kuwabara M., Inanami O.
Data di Pubblicazione: 2013-03-19
Abstract: Our results revealed that BBB disruption in glioma enables BBB-imp ermeable radiosensitizers to penetrate and distribute in the target region. This study is the first to propose that in malignant glioma the administrati on of hydrophilic hypoxic radiosensitizers could be a potent strategy for im proving the clinical outcome of radiotherapy without side effects.
Journal Title: BMC cancer

PUBMED ID: 23495876
DOI: doi.org/10.3171/2013.2.JNS121747
Titolo: Surgical management of multicentric diffuse low-grade gliomas: funct ional and oncological outcomes: clinical article.
Autori: Terakawa Y., Yordanova YN., Tate MC., Duffau H.
Data di Pubblicazione: 2013-03-19
Abstract: Multicentric DLGGs can be removed safely without inducing severe p ermanent neurological deficits. Interestingly, a single-stage resection of m ultiple lesions within different lobes may be performed if tumors are locate d in the same hemisphere. Therefore, the authors suggest considering surgery as the first therapeutic option for multicentric DLGGs, as in solitary DLGGs .
Journal Title: Journal of neurosurgery

PUBMED ID: 23486688
DOI: doi.org/10.1093/neuonc/not025
Titolo: STAT3 silencing inhibits glioma single cell infiltration and tumor g rowth.
Autori: Priester M., Copanaki E., Vafaizadeh V., Hensel S., Bernreuther C., Glatzel M., Seifert V., Groner B., Kögel D., Weissenberger J.
Data di Pubblicazione: 2013-03-15
Abstract: Our results show compelling evidence that STAT3 is a key driver of diffuse infiltration and glioma growth and might therefore represent a promi sing target for an anti-invasive therapy.

Journal Title: Neuro-oncology

PUBMED ID: 23453151
DOI: doi.org/10.1016/j.clineuro.2013.02.001
Titolo: Hypo-fractionated IMRT for patients with newly diagnosed glioblastoma multiforme: a 6 year single institutional experience.
Autori: Ciammella P., Galeandro M., D'Abbiero N., Podgornii A., Pisanello A., Botti A., Cagni E., Iori M., Iotti C.
Data di Pubblicazione: 2013-03-05
Abstract: The hypo-fractionated radiation therapy can be used for patients with GBM, resulting in favourable overall survival, low rates of toxicity and satisfying QoL. Future investigations are needed to determine the optimal fractionation for GBM.
Journal Title: Clinical neurology and neurosurgery

PUBMED ID: 23445331
DOI: doi.org/10.3109/02688697.2013.771136
Titolo: Diffusion tensor invasive phenotypes can predict progression-free survival in glioblastomas.
Autori: Mohsen LA., Shi V., Jena R., Gillard JH., Price SJ.
Data di Pubblicazione: 2013-03-01
Abstract: It is possible to identify three invasive phenotypes in GBMs using Diffusion tensor imaging , and these three phenotypes have different progression free survival. A minimal phenotype (20% of patients) predicts a greater delay to progression.
Journal Title: British journal of neurosurgery

PUBMED ID: 23427031
DOI: doi.org/10.1055/s-0032-1333417
Titolo: Bilateral ptosis as initial presentation of gliomatosis cerebri: case report.
Autori: Kovanda T., Braca J., Prabhu V.
Data di Pubblicazione: 2013-02-22
Abstract: Gliomatosis cerebri is a rare, diffuse glioma of neuroepithelial origin involving more than two cerebral lobes. Clinical presentation of gliomatosis cerebri is variable and depends on the degree, extent, and location of cortical involvement. Signs and symptoms related to supratentorial cortical involvement predominate and the diagnosis is reached through a combination of clinical, radiographic, and histopathological evaluations. This is a report of a young man who presented with visual problems and bilateral ptosis, which were eventually attributed to gliomatosis cerebri. Standard radiation and chemotherapy were administered but the patient eventually succumbed to the disease. The unique clinical presentation is discussed in light of this rare neoplasm of the central nervous system.
Journal Title: Journal of neurological surgery. Part A, Central European neurosurgery

PUBMED ID: 23422903
DOI: doi.org/10.1227/NEU.0b013e31827d102e
Titolo: Anaplastic ependymoma with holocordal and intracranial meningeal carcinomatosis and holospinal bone metastases.
Autori: Pérez-Bovet J., Rimbau-Muñoz J., Martín-Ferrer S.
Data di Pubblicazione: 2013-02-21
Abstract: To our knowledge, there are no previous descriptions of ependymomas with this extensive leptomeningeal, spinal, intracranial, and extraneural

dissemination at clinical onset. Bone metastases in spinal ependymoma have n
ot been previously reported.
Journal Title: Neurosurgery

PUBMED ID: 23422478
DOI: Mancante
Titolo: Clinical experience of treatment of metastatic melanoma and solid tu
mours adopting a derivative of diphtheria toxin: cross-reacting material 197
.
Autori: Fiorentini G., Banfi R., Dentico P., Moriconi S., Turrisi G., Pelago
tti F., Rossi S., Montagnani F.
Data di Pubblicazione: 2013-02-21
Abstract: CRM197, injected subcutaneously at 5 mg, elicited a generic inflam
matory response causing toxicity, and did not exert a significant degree of
antitumor activity in patients with advanced melanoma and solid tumour.
Journal Title: In vivo (Athens, Greece)

PUBMED ID: 23417358
DOI: doi.org/10.1007/s11060-013-1072-z
Titolo: Early response evaluation for recurrent high grade gliomas treated w
ith bevacizumab: a volumetric analysis using diffusion-weighted imaging.
Autori: Hwang EJ., Cha Y., Lee AL., Yun TJ., Kim TM., Park CK., Kim JH., Soh
n CH., Park SH., Kim IH., Heo DS., Lee SH., Choi SH.
Data di Pubblicazione: 2013-02-19
Abstract: Bevacizumab is a novel treatment for the recurrent high-grade glio
mas (rHGG). However, only a subset of the patients shows response to the bev
acizumab treatment and the response evaluation using conventional criteria i
s difficult. The purpose of our study was to evaluate the early response for
rHGG treated with bevacizumab using volumetric analysis of diffusion-weighte
d imaging (DWI). Twenty-nine patients who received bevacizumab therapy for r
HGG were included in our study. All patients received a conventional MRI sca
n with DWI before and after the initial bevacizumab dose. For each MRI, we m
easured the total volume of the T2 hyperintense lesion (HT2) of the rHGG, th
e volume of foci with a lower ADC value than that of the normal cortex (LADC
), and the proportion of LADC to HT2 (LADC/HT2). The Changes in the HT2, LAD
C and LADC/HT2 after bevacizumab treatment were also determined. Thereafter,
those volumetric data were compared to the progression free survival (PFS).
After the analyses, we found a significant negative correlation between the
PFS and the LADC for the post-bevacizumab ADC maps (r = -0.413, P = 0.026).
The patients with an LADC of <2.5 cm(3) showed a longer PFS than those with
an LADC of ≥2.5 cm(3) (median = 135 vs. 91 days, P = 0.002) on the post-beva
cizumab ADC maps. A multiple linear regression analysis revealed that only t
he post-bevacizumab LADC was a significant predictor of the PFS (P = 0.026).
In conclusion, the post-bevacizumab LADC can be used for an early response e
valuation and can predict the PFS for rHGG patients treated with bevacizumab
.
Journal Title: Journal of neuro-oncology

PUBMED ID: 23400732
DOI: doi.org/10.1007/s00432-013-1390-8
Titolo: Bevacizumab plus irinotecan in recurrent or progressive malign gliom
a: a multicenter study of the Anatolian Society of Medical Oncology (ASMO).
Autori: Demirci U., Tufan G., Aktas B., Balakan O., Alacacioglu A., Dane F.,
Engin H., Kaplan MA., Gunaydin Y., Ozdemir NY., Tugba Unek I., Karaca H., Ak
man T., Sonmez OU., Coskun U., Harputluoglu H., Sevinc A., Tonyali O., Buyuk
berber S., Benekli M.
Data di Pubblicazione: 2013-02-13

Abstract: Present study results were consistent with previous studies. In ad
dition, we detected similar outcomes in grade III and IV glial tumors.
Journal Title: Journal of cancer research and clinical oncology

PUBMED ID: 23399039
DOI: doi.org/10.1016/j.ejrad.2012.12.018
Titolo: MRI assessment of relapsed glioblastoma during treatment with bevaci
zumab: volumetric measurement of enhanced and FLAIR lesions for evaluation o
f response and progression--a pilot study.
Autori: Pichler J., Pachinger C., Pelz M., Kleiser R.
Data di Pubblicazione: 2013-02-13
Abstract: In this pilot study the applied imaging estimates objectively tumo
ur response and progression compared to the bi-dimensional measurement. The
quantitative parameters are reproducible and also applicable for the diffuse
infiltrating lesions.
Journal Title: European journal of radiology

PUBMED ID: 23373800
DOI: doi.org/10.3171/2013.1.JNS121323
Titolo: Brainstem gangliogliomas: a retrospective series.
Autori: Zhang S., Wang X., Liu X., Ju Y., Hui X.
Data di Pubblicazione: 2013-02-05
Abstract: The diagnosis of brainstem ganglioglioma is of great importance gi
ven its favorable prognosis. The authors recommend the maximal safe resectio
n followed by close observation without adjuvant therapy as the optimal trea
tment for this disease.
Journal Title: Journal of neurosurgery

PUBMED ID: 23363814
DOI: doi.org/10.1158/1078-0432.CCR-12-1707
Titolo: A phase I/II trial of pazopanib in combination with lapatinib in adu
lt patients with relapsed malignant glioma.
Autori: Reardon DA., Groves MD., Wen PY., Nabors L., Mikkelsen T., Rosenfeld
S., Raizer J., Barriuso J., McLendon RE., Suttle AB., Ma B., Curtis CM., Dar
MM., de Bono J.
Data di Pubblicazione: 2013-02-01
Abstract: The antitumor activity of this combination at the phase II dose te
sted was limited. Pharmacokinetic data indicated that exposure to lapatinib
was subtherapeutic in the phase II evaluation. Evaluation of intratumoral dr
ug delivery and activity may be essential for hypothesis-testing trials with
targeted agents in malignant glioma.
Journal Title: Clinical cancer research : an official journal of the America
n Association for Cancer Research

PUBMED ID: 23348245
DOI: doi.org/10.1097/CAD.0b013e32835c7a47
Titolo: Long-term response in high-grade optic glioma treated with medically
induced hypothyroidism and carboplatin: a case report and review of the lit
erature.
Autori: Ashur-Fabian O., Blumenthal DT., Bakon M., Nass D., Davis PJ., Hercb
ergs A.
Data di Pubblicazione: 2013-01-26
Abstract: Glioblastoma multiforme (GBM) is the most malignant and frequent b
rain tumor, with an aggressive growth pattern and poor prognosis despite bes
t treatment modalities. Long-term survival of patients with GBM is rare. Opt
ic glioma represents 0.6-1.2% of all brain tumors. Unlike low-grade optic gl

iomas in children, optic gliomas in adults are highly aggressive and death u
sually occurs in less than a year. Prolonged progression-free survival and s
urvival rates have been reported in association with induced hypothyroidism
in two clinical trials for recurrent GBM. We present the clinical, radiologi
cal, and pathological findings in a patient with inoperable GBM of the optic
chiasm. Following failure of initial, standard radiation and temozolomide th
erapy, chemical hypothyroidism was induced using the antithyroid thioamide,
propylthiouracil, followed by carboplatin chemotherapy. Initial thyroid stim
ulating hormone, free T4, and free T3 analysis was carried out and then mont
hly. This patient responded rapidly to treatment (clinically and with tumor
regression within 4 weeks) on two separate occasions with an extended remiss
ion period (2.5 years) and prolonged overall survival (4.5 years). We report
the successful long-term tumor response to medically induced chemical hypoth
yroidism in conjunction with carboplatinum chemotherapy of an adult patient
with grade IV GBM of the optic chiasm. These clinical observations find mech
anistic support from the recent identification of potent mitogenic actions o
f the thyroid hormone, L-thyroxine, in malignant glioma through binding to a
cognate thyroid hormone receptor on the αvβ3 integrin. Approaches to block i
ts activity are now explored in preclinical studies.
Journal Title: Anti-cancer drugs

PUBMED ID: 23344784
DOI: doi.org/10.1007/s11307-013-0613-3
Titolo: 2-Deoxy-2-[18F]fluoro-D-glucose positron emission tomography demonst
rates target inhibition with the potential to predict anti-tumour activity f
ollowing treatment with the AKT inhibitor AZD5363.
Autori: Maynard J., Ricketts SA., Gendrin C., Dudley P., Davies BR.
Data di Pubblicazione: 2013-01-25
Abstract: We conclude that 18F-FDG PET is a promising pharmacodynamic biomar
ker of AKT pathway inhibition, with potential to predict and demonstrate ant
i-tumour activity. It is a biomarker that may stop ineffective drug schedule
s, helping to make early stop decisions and identify responding subsets of p
atients, resulting in improved clinical decision making both during drug dev
elopment and patient management.
Journal Title: Molecular imaging and biology

PUBMED ID: 23341100
DOI: doi.org/10.1007/s11060-013-1058-x
Titolo: Gliomatosis cerebri: clinical characteristics, management, and outco
mes.
Autori: Chen S., Tanaka S., Giannini C., Morris J., Yan ES., Buckner J., Lac
hance DH., Parney IF.
Data di Pubblicazione: 2013-01-24
Abstract: Gliomatosis cerebri is a rare diffusely infiltrating primary neopl
astic glial process of the brain. Our objective is to review clinical presen
tation, management, and outcome in a large single institution series of glio
matosis cerebri patients. 54 consecutive gliomatosis cerebri cases presentin
g to Mayo Clinic Rochester between 1991 and 2008 were retrospectively review
ed. Inclusion criteria included involvement of at least three cerebral lobes
, lack of a single discrete mass and pathological confirmation of diffuse gl
ioma. Median overall survival (OS) was 18.5 months. Age, gender, presenting
symptoms, and contrast enhancement did not correlate significantly with surv
ival, though there was a trend toward decreased overall survival in patients
above the median age of 46 years. Karnofsky performance score <70 was associ
ated with poor OS (median 9.5 vs. 20.5 months, p = 0.02). Higher histologic
grade was associated with poor progression-free survival (PFS; median for WH
O grades II, III, and IV: 21.5, 6.5, and 4 months; p = 0.03) and OS (median
34, 15.5, and 8.5 months; p < 0.05). Radiation therapy was strongly associat

ed with better prognosis (PFS 16.5 vs. 4.5 months, p < 0.01; OS 27.5 vs. 6.5 , p < 0.01), but chemotherapy was not. Gliomatosis cerebri patients have a p oor prognosis. Lower KPS upon presentation and higher histologic grade predi ct decreased survival. Surgery's role is limited beyond biopsy for diagnosti c purposes. Radiotherapy appears beneficial, although selection bias could b e present in this retrospective study. Chemotherapy's value is not as clear but this must be interpreted with caution given variable treatment regimens in this series.
Journal Title: Journal of neuro-oncology

PUBMED ID: 23319493
DOI: doi.org/10.1530/ERC-12-0219
Titolo: Thyroid hormone, thyroid hormone receptors, and cancer: a clinical p erspective.
Autori: Moeller LC., Führer D.
Data di Pubblicazione: 2013-01-16
Abstract: Thyroid hormones (THs) may play a role in diseases other than hype r- and hypothyroidism. Several lines of evidence suggest tumor-promoting eff ects of TH and TH receptors. They are possibly mediated by phosphatidylinosi tol-3-kinase and MAPK and involve among others stimulation of angiogenesis v ia αvβ3. Thus, an increased risk for colon, lung, prostate, and breast cance r with lower TSH has been demonstrated in epidemiological studies, even sugg esting a TH dose effect on cancer occurrence. Furthermore, higher TH levels were associated with an advanced clinical stage of breast and prostate cance r. In rodent models, TH stimulated growth and metastasis of tumor transplant s, whereas hypothyroidism had opposite effects. In clinical studies of gliob lastoma and head and neck cancer, hypothyroid patients showed longer surviva l than euthyroid patients. Also, patients with renal cell cancer that were t reated with the tyrosine kinase inhibitor sunitinib and developed hypothyroi dism in due course showed significantly longer survival than patients that r emained euthyroid. Development of hypothyroidism was an independent predicto r for survival in two studies. Yet, it is still possible that hypothyroidism is only a surrogate marker for treatment efficacy and does not positively in fluence treatment outcome by itself. Future cancer treatment studies, especi ally with substances that can induce hypothyroidism, should therefore be des igned in a way that allows for an analysis of thyroid function status and it s contribution on treatment outcome.
Journal Title: Endocrine-related cancer

PUBMED ID: 23314822
DOI: doi.org/10.1007/s11060-013-1044-3
Titolo: Re-irradiation with and without bevacizumab as salvage therapy for r ecurrent or progressive high-grade gliomas.
Autori: Hundsberger T., Brügge D., Putora PM., Weder P., Weber J., Plasswilm L.
Data di Pubblicazione: 2013-01-15
Abstract: The optimal treatment for recurrent high-grade gliomas is unknown and a standard of care does not exist. Re-irradiation with concomitant bevac izumab represents an option. Retrospectively, we analyzed a cohort of heavil y pretreated patients (n = 14) with relapsing HGGs who underwent re-irradiat ion with conventional 3D-conformal or intensified modulated radiotherapy (IM RT). Ten of them received re-irradiation in combination with bevacizumab. Th e study population consisted of eight GBMs and six anaplastic gliomas. All p atients had previously undergone irradiation for first-line therapy, includi ng seven patients with radiochemotherapy with temozolomide. Patients without contraindications started with two infusions of bevacizumab (10 mg/kg of bod y weight every other week) prior to re-irradiation and continued through re- irradiation until progression. The median patient age was 45 years with a me

dian Karnofsky performance scale of 70. The median dose of re-irradiation was 41.6 Gy [39-55 Gy]. The median physical cumulative radiation dose was 101.6 Gy [65-110.4 Gy]. The median PFS from re-irradiation was 5.1 months [1.6-17.4] based on clinical and RANO criteria. Median OS from re-irradiation was 9.0 months [6.4-17.8]. We detected radionecrosis due to advanced imaging in one patient. Other toxicities were expected and attributable well known side effects of bevacizumab. This retrospective study provides additional feasibility and safety data of conventional 3D-conformal re-irradiation and IMRT in combination with bevacizumab in relapsing high-grade gliomas.
Journal Title: Journal of neuro-oncology

PUBMED ID: 23302906
DOI: doi.org/10.1177/107327481302000107
Titolo: Current status of immunotherapy and gene therapy for high-grade gliomas.
Autori: Marsh JC., Goldfarb J., Shafman TD., Diaz AZ.
Data di Pubblicazione: 2013-01-11
Abstract: Although phase III data are needed before immunologic therapies can be widely implemented into clinical practice, the existing phase I and phase II data suggest that these therapies can produce meaningful and sometimes durable responses in patients with glioblastoma multiforme with mild toxicity compared with other existing therapies.
Journal Title: Cancer control : journal of the Moffitt Cancer Center

PUBMED ID: 23299464
DOI: doi.org/10.1007/s11060-013-1048-z
Titolo: "One week on-one week off": efficacy and side effects of dose-intensified temozolomide chemotherapy: experiences of a single center.
Autori: Galldiks N., Berhorn T., Blau T., Dunkl V., Fink GR., Schroeter M.
Data di Pubblicazione: 2013-01-10
Abstract: To evaluate in a single center retrospectively the efficacy and tolerability of a weekly regimen, which alternates temozolomide (TMZ) in patients with recurrent or progressive high-grade glioma (HGG). From January 2005 until June 2011, 54 patients with recurrent or progressive HGG were treated with TMZ 150 mg/m²/day on days 1-7 and 15-21 of a 28-day cycle ("one week on-one week off" scheme; TMZ 7/14) with individual dose adjustment depending on toxicity. The majority of patients (n = 48, 89 %) was treated at first tumor recurrence or progression. All patients had received prior radiotherapy with or without concomitantly administered TMZ and, optionally, adjuvant chemotherapy. After initiation of TMZ 7/14, MRI was obtained every 8-12 weeks. Tumor response or progression was assessed according to Macdonald criteria. Blood examinations were performed weekly. Toxicity was evaluated according to Common Terminology Criteria for Adverse Events (CTCAE; version 3.0). A total of 434 treatment weeks with TMZ 7/14 were delivered. The median number of treatment weeks was 7 (range, 1-41 weeks). No grade 4 hematological toxicity and no opportunistic infections occurred. Patients with neutropenia were not observed. Two patients developed grade 3 and 4 patients grade 2 leukocytopenia. Thrombocytopenia grade 3 and grade 2 occurred in 4 patients and 6 patients, respectively. The progression-free survival (PFS) rate at 6 months was 43 %. Median PFS from treatment initiation was 18 weeks (95 % CI, 14-22 weeks) and median overall survival (OS) was 37 weeks (95 % CI, 31-42 weeks). The rates for PFS and OS at 1 year were 24 and 28 %, respectively. Our data suggest that treatment with TMZ 7/14 is safe and effective in patients with recurrent or progressive HGG.
Journal Title: Journal of neuro-oncology

PUBMED ID: 23292205

DOI: doi.org/10.1007/s00415-012-6812-z
Titolo: A phase I study of temozolomide and lapatinib combination in patient s with recurrent high-grade gliomas.
Autori: Karavasilis V., Kotoula V., Pentheroudakis G., Televantou D., Lambak i S., Chrisafi S., Bobos M., Fountzilas G.
Data di Pubblicazione: 2013-01-08
Abstract: We undertook this phase I study to investigate the feasibility of the combination of temozolomide (TMZ) and lapatinib (LP) and to define the m aximum tolerated dose (MTD) of LP in patients with relapsed high-grade gliom as. Eligible patients were enrolled in this dose escalation study of LP. TMZ was administered at a fixed dose of 200 mg/m2 d1-d5 every 28 days. Starting dose of LP was set at 1,000 mg daily continuously, escalated by 250 mg in co horts of minimum three patients. Translational research investigations were also undertaken in available biopsy material. Between January 2009 and Decem ber 2010, 16 patients were entered into the study at three LP levels: 1,000 mg sid (11 patients), 1,250 mg sid (4 patients) and 1,500 mg sid (1 patient) . A total of 55 cycles had been delivered. Fourteen patients had stopped tre atment because of disease progression, and two because of toxicity. Three pa tients received 10, 11 and 17 cycles of treatment. Dose-limiting hematologic al toxicity was observed in 2 patients at the second LP dose level of 1,250 mg sid. MTD was defined at LP 1,000 mg sid. Median progression-free survival (PFS) and survival were 2.4 and 5.9 months, respectively. EGFR amplification and EGFRvIII expression were not related to PFS. Combination of TMZ and LP i s feasible with manageable toxicity. The activity of this combination in pat ients with recurrent glioblastoma multiforme is further investigated in a re cently initiated phase II trial.
Journal Title: Journal of neurology

PUBMED ID: 23259383
DOI: Mancante
Titolo: [Personalized peptide vaccination].
Autori: Itoh K., Takahashi R., Yoshitomi M., Terasaki M., Noguchi M.
Data di Pubblicazione: 2012-12-25
Abstract: We conducted personalized peptide vaccination (PPV) for various ty pes of advanced cancers in the past 10 years. A maximum of four HLA-matched peptides, which were selected based on the pre-existing host immunity before vaccination, were subcutaneously administered at PPV trials. Randomized phas e II trial for patients with castration resistant prostate cancer showed the favorite clinical responses in the PPV group. PPV was also conducted for rec urrent or progressive glioblastoma multiforme patients with median overall s urvival of 10.6 months, resulting in the initiation of randomized phase III clinical trial. A randomized phase III trial is essential to prove clinical benefits of PPV.
Journal Title: Nihon rinsho. Japanese journal of clinical medicine

PUBMED ID: 23259381
DOI: Mancante
Titolo: [WT1-targeting cancer vaccine].
Autori: Sugiyama H.
Data di Pubblicazione: 2012-12-25
Abstract: Wilms' tumor gene WT1 encodes a transcription factor and functions as an oncogene. WT1 gene product WT1 protein is a promising par-tumor-associ ated antigen. WT1 peptide-based immunotherapy has been performing for more t han six hundred patients with leukemias and various types of solid tumors. T his immunotherapy is safe and has clinical benefit especially for leukemia, glioblastoma multiforme, advanced pancreatic cancer, and ovarian cancer. As a new strategy for cancer treatment, it should be recommended to initiate im

munotherapy that had a potential of eradication of cancer stem cells before surgery, chemo- and radio-therapy.
Journal Title: Nihon rinsho. Japanese journal of clinical medicine

PUBMED ID: 23216891
DOI: doi.org/10.1186/1471-2164-13-686
Titolo: A REST derived gene signature stratifies glioblastomas into chemothe rapy resistant and responsive disease.
Autori: Wagoner MP., Roopra A.
Data di Pubblicazione: 2012-12-11
Abstract: This report is the first to describe a REST gene signature that pr edicts response to multiple rounds of chemotherapy, the mainline therapy for this disease. The REST gene signature may have important clinical implicatio ns for the treatment of glioblastoma.
Journal Title: BMC genomics

PUBMED ID: 23204544
DOI: doi.org/10.1148/radiol.12111472
Titolo: Pseudoprogression of glioblastoma after chemo- and radiation therapy : diagnosis by using dynamic susceptibility-weighted contrast-enhanced perfu sion MR imaging with ferumoxytol versus gadoteridol and correlation with sur vival.
Autori: Gahramanov S., Muldoon LL., Varallyay CG., Li X., Kraemer DF., Fu R. , Hamilton BE., Rooney WD., Neuwelt EA.
Data di Pubblicazione: 2012-12-04
Abstract: Ferumoxytol as a blood pool agent facilitates differentiation betw een tumor progression and pseudoprogression, appears to be a good prognostic biomarker, and unlike gadoteridol, does not require contrast agent leakage c orrection.
Journal Title: Radiology

PUBMED ID: 23176331
DOI: doi.org/10.3171/2012.10.JNS112268
Titolo: Presentation, management, and outcome of newly diagnosed glioblastom a in elderly patients.
Autori: Tanaka S., Meyer FB., Buckner JC., Uhm JH., Yan ES., Parney IF.
Data di Pubblicazione: 2012-11-27
Abstract: The prognosis for GBM worsens with increasing age in elderly patie nts. With important risks, resection and adjuvant treatment are associated w ith prolonged survival. Although selection bias cannot be excluded in this r etrospective study, advanced age alone should not necessarily preclude optim al resection followed by adjuvant radiochemotherapy.
Journal Title: Journal of neurosurgery

PUBMED ID: 23140402
DOI: doi.org/10.1186/1748-717X-7-189
Titolo: First experiences in treatment of low-grade glioma grade I and II wi th proton therapy.
Autori: Hauswald H., Rieken S., Ecker S., Kessel KA., Herfarth K., Debus J., Combs SE.
Data di Pubblicazione: 2012-11-13
Abstract: Regarding early side effects, mild alopecia was the predominant fi nding. The rate of alopecia seems to be due to large treatment volumes as we ll as the anatomical locations of the target volumes and might be avoided by using multiple beams and the gantry in the future. Further evaluations inclu ding neuropsychological testing are in preparation.

Journal Title: Radiation oncology (London, England)

PUBMED ID: 23138021
DOI: doi.org/10.1258/ar.2012.120525
Titolo: Can MRI-derived factors predict the survival in glioblastoma patient s treated with postoperative chemoradiation therapy?
Autori: Nakamura H., Murakami R., Hirai T., Kitajima M., Yamashita Y.
Data di Pubblicazione: 2012-11-10
Abstract: The minimum ADC on pretreatment DW-MRI and gross residual tumor on early postoperative MRI can predict the survival in GBM patients treated wit h postoperative chemo-RT.
Journal Title: Acta radiologica (Stockholm, Sweden : 1987)

PUBMED ID: 23136223
DOI: doi.org/10.1093/neuonc/nos273
Titolo: Standards of care for treatment of recurrent glioblastoma--are we th ere yet?
Autori: Weller M., Cloughesy T., Perry JR., Wick W.
Data di Pubblicazione: 2012-11-09
Abstract: Newly diagnosed glioblastoma is now commonly treated with surgery, if feasible, or biopsy, followed by radiation plus concomitant and adjuvant temozolomide. The treatment of recurrent glioblastoma continues to be a movi ng target as new therapeutic principles enrich the standards of care for new ly diagnosed disease. We reviewed PubMed and American Society of Clinical On cology abstracts from January 2006 to January 2012 to identify clinical tria ls investigating the treatment of recurrent or progressive glioblastoma with nitrosoureas, temozolomide, bevacizumab, and/or combinations of these agents . At recurrence, a minority of patients are eligible for second surgery or r eirradiation, based on appropriate patient selection. In temozolomide-pretre ated patients, progression-free survival rates at 6 months of 20%-30% may be achieved either with nitrosoureas, temozolomide in various dosing regimens, or bevacizumab. Combination regimens among these agents or with other drugs have not produced evidence for superior activity but commonly produce more t oxicity. More research is needed to better define patient profiles that pred ict benefit from the limited therapeutic options available after the current standard of care has failed.
Journal Title: Neuro-oncology

PUBMED ID: 23134812
DOI: doi.org/10.1186/1471-2407-12-508
Titolo: Treatment of medulloblastoma using an oncolytic measles virus encodi ng the thyroidal sodium iodide symporter shows enhanced efficacy with radioi odine.
Autori: Hutzen B., Pierson CR., Russell SJ., Galanis E., Raffel C., Studebak er AW.
Data di Pubblicazione: 2012-11-09
Abstract: These data suggest MV-NIS plus radioiodine may be a potentially us eful therapy for the treatment of medulloblastoma.
Journal Title: BMC cancer

PUBMED ID: 23129347
DOI: doi.org/10.1007/s11060-012-0999-9
Titolo: Hypofractionated stereotactic radiotherapy and continuous low-dose t emozolomide in patients with recurrent or progressive malignant gliomas.
Autori: Minniti G., Scaringi C., De Sanctis V., Lanzetta G., Falco T., Di St efano D., Esposito V., Enrici RM.

Data di Pubblicazione: 2012-11-07
Abstract: To evaluate the efficacy of reirradiation and systemic chemotherap y as salvage treatment in patients with recurrent malignant glioma. Between May 2006 and December 2011, 54 patients with recurrent malignant glioma rece ived hypofractionated stereotactic radiotherapy (HSRT) plus systemic therapy at University of Rome Sapienza, Sant' Andrea Hospital. All patients had Karn ofsky performance score ≥60 and were previously treated with standard confor mal RT (60 Gy) with concomitant and adjuvant temozolomide (TMZ) up to 12 cyc les. Thirty-eight patients had a GBM and 16 patients had a grade 3 glioma. T he median time interval between primary RT and reirradiation was 15.5 months . At the time of recurrence all patients received HSRT (30 Gy in 6-Gy fracti ons) plus concomitant TMZ (75 mg/m(2)/day) followed by continuous TMZ at 50 mg/m(2) everyday up to 1 year or until progression. Median overall survival after HSRT was 12.4 months, and the 12- and 24-month survival rates were 53 and 16 %, respectively. The median progression-free survival (PFS) was 6 mon ths, and the 12- and 24-month PFS rates were 24 and 10 %, respectively. KPS >70 (P = 0.04) and grade 3 glioma were independent favourable prognostic fac tors for survival. In general chemoradiation regimen was well tolerated with relatively low treatment-related toxicity. HSRT plus concomitant TMZ followe d by continuous dose-intense TMZ is a feasible treatment option associated w ith survival benefits and low risk of complications in selected patients wit h recurrent malignant glioma. The potential advantages of combined chemoradi ation schedules in patients with recurrent malignant gliomas need to be expl ored in future studies.
Journal Title: Journal of neuro-oncology

PUBMED ID: 23118709
DOI: doi.org/10.2147/CE.S23244
Titolo: Polifeprosan 20, 3.85% carmustine slow-release wafer in malignant gl ioma: evidence for role in era of standard adjuvant temozolomide.
Autori: Kleinberg L.
Data di Pubblicazione: 2012-11-03
Abstract: The Polifeprosan 20 with carmustine (BCNU, bis-chloroethylnitrosou rea, Gliadel(®)) polymer implant wafer is a biodegradable compound containin g 3.85% carmustine which slowly degrades to release carmustine and protects it from exposure to water with resultant hydrolysis until the time of releas e. The carmustine implant wafer was demonstrated to improve survival in blin ded placebo-controlled trials in selected patients with newly diagnosed or r ecurrent malignant glioma, with little increased risk of adverse events. Bas ed on these trials and other supporting data, US and European regulatory aut horities granted approval for its use in recurrent and newly diagnosed malig nant glioma, and it remains the only approved local treatment. The preclinic al and clinical data suggest that it is optimally utilized primarily in the proportion of patients who may have total or near total removal of gross tum or. The aim of this work was to review the evidence for the use of carmustin e implants in the management of malignant astrocytoma (World Health Organiza tion grades III and IV), including newly diagnosed and recurrent disease, es pecially in the setting of a standard of care that has changed since the ran domized trials were completed. Therapy has evolved such that patients now ge nerally receive temozolomide chemotherapy during and after radiotherapy trea tment. For patients undergoing repeat resection for malignant glioma, a rand omized, blinded, placebo-controlled trial demonstrated a median survival for 110 patients who received carmustine polymers of 31 weeks compared with 23 w eeks for 122 patients who only received placebo polymers. The benefit achiev ed statistical significance only on analysis adjusting for prognostic factor s rather than for the randomized groups as a whole (hazard ratio = 0.67, P = 0.006). A blinded, placebo-controlled trial has also been performed for carm ustine implant placement in newly diagnosed patients prior to standard radio therapy. Median survival was improved from 11.6 to 13.9 months (P = 0.03), w

ith a 29% reduction in the risk of death. When patients with glioblastoma mu
ltiforme alone were analyzed, the median survival improved from 11.4 to 13.5
months, but this improvement was not statistically significant. When a Cox's
proportional hazard model was utilized to account for other potential progno
stic factors, there was a significant 31% reduction in the risk of death (P
= 0.04) in this subgroup. Data from other small reports support these result
s and confirm that the incidence of adverse events does not appear to be inc
reased meaningfully. Given the poor prognosis without possibility of cure, t
hese benefits from a treatment with a favorable safety profile were consider
ed meaningful. There is randomized evidence to support the use of carmustine
wafers placed during resection of recurrent disease. Therefore, although the
re is limited specific evidence, this treatment is likely to be efficacious
in an environment when nearly all patients receive temozolomide as part of i
nitial management. Given that half of the patients in the randomized trial a
ssessing the value of carmustine implants in recurrent disease had received
prior chemotherapy, it is likely that this remains a valuable treatment at t
he time of repeat resection, even after temozolomide. There are data from mu
ltiple reports to support safety. Although there is randomized evidence to s
upport the use of this therapy in newly diagnosed patients who will receive
radiotherapy alone, it is now standard to administer both adjuvant temozolom
ide and radiotherapy. There are survival outcome reports for small cohorts o
f patients receiving temozolomide with radiotherapy, but this information is
not sufficient to support firm recommendations. Based on the rationale and e
vidence of safety, this approach appears to be a reasonable option as more i
nformation is acquired. Available data support the safety of using carmustin
e wafers in this circumstance, although special attention to surgical guidel
ines for implanting the wafers is warranted.
Journal Title: Core evidence

PUBMED ID: 23095831
DOI: doi.org/10.1093/neuonc/nos199
Titolo: Seizures in low-grade gliomas: natural history, pathogenesis, and ou
tcome after treatments.
Autori: Rudà R., Bello L., Duffau H., Soffietti R.
Data di Pubblicazione: 2012-10-26
Abstract: Seizures represent a common symptom in low-grade gliomas; when unc
ontrolled, they significantly contribute to patient morbidity and negatively
impact quality of life. Tumor location and histology influence the risk for
epilepsy. The pathogenesis of tumor-related epilepsy is multifactorial and m
ay differ among tumor histologies (glioneuronal tumors vs diffuse grade II g
liomas). Gross total resection is the strongest predictor of seizure freedom
in addition to clinical factors, such as preoperative seizure duration, type
, and control with antiepileptic drugs (AEDs). Epilepsy surgery may improve
seizure control. Radiotherapy and chemotherapy with alkylating agents (proca
rbazine + CCNU+ vincristine, temozolomide) are effective in reducing the fre
quency of seizures in patients with pharmacoresistant epilepsy. Newer AEDs (
levetiracetam, topiramate, lacosamide) seem to be better tolerated than the
old AEDs (phenobarbital, phenytoin, carbamazepine), but there is lack of evi
dence regarding their superiority in terms of efficacy.
Journal Title: Neuro-oncology

PUBMED ID: 23092875
DOI: doi.org/10.1158/1078-0432.CCR-12-1501
Titolo: Do imaging biomarkers relate to outcome in patients treated with VEG
F inhibitors?
Autori: O'Connor JP., Jayson GC.
Data di Pubblicazione: 2012-10-25

Abstract: The management of solid tumors has been transformed by the advent of VEGF pathway inhibitors. Early clinical evaluation of these drugs has used pharmacodynamic biomarkers derived from advanced imaging such as dynamic MRI, computed tomography (CT), and ultrasound to establish proof of principle. We have reviewed published studies that used these imaging techniques to determine whether the same biomarkers relate to survival in renal, hepatocellular, and brain tumors in patients treated with VEGF inhibitors. Data show that in renal cancer, pretreatment measurements of K(trans) and early pharmacodynamic reduction in tumor enhancement and density have prognostic significance in patients treated with VEGF inhibitors. A weaker, but significant, relationship is seen with subtle early size change (10% in one dimension) and survival. Data from high-grade glioma suggest that pretreatment fractional blood volume and K(trans) were prognostic of overall survival. However, lack of control data with other therapies prevents assessment of the predictive nature of these biomarkers, and such studies are urgently required.
Journal Title: Clinical cancer research : an official journal of the American Association for Cancer Research

PUBMED ID: 23056240
DOI: doi.org/10.1371/journal.pone.0046104
Titolo: Tumor endothelial inflammation predicts clinical outcome in diverse human cancers.
Autori: Pitroda SP., Zhou T., Sweis RF., Filippo M., Labay E., Beckett MA., Mauceri HJ., Liang H., Darga TE., Perakis S., Khan SA., Sutton HG., Zhang W., Khodarev NN., Garcia JG., Weichselbaum RR.
Data di Pubblicazione: 2012-10-12
Abstract: This study provides the first prognostic cancer gene signature derived from an experimental model of tumor-associated endothelial inflammation. These findings support the notion that activation of inflammatory pathways in non-malignant tumor-infiltrating endothelial cells contributes to tumor growth and progression in multiple human cancers. Importantly, these results identify endothelial-derived factors that could serve as potential targets for therapy in diverse human cancers.
Journal Title: PloS one

PUBMED ID: 23056179
DOI: doi.org/10.1371/journal.pone.0044372
Titolo: Evaluation of tyrosine kinase inhibitor combinations for glioblastoma therapy.
Autori: Joshi AD., Loilome W., Siu IM., Tyler B., Gallia GL., Riggins GJ.
Data di Pubblicazione: 2012-10-12
Abstract: Glioblastoma multiforme (GBM) is the most common intracranial cancer but despite recent advances in therapy the overall survival remains about 20 months. Whole genome exon sequencing studies implicate mutations in the receptor tyrosine kinase pathways (RTK) for driving tumor growth in over 80% of GBMs. In spite of various RTKs being mutated or altered in the majority of GBMs, clinical studies have not been able to demonstrate efficacy of molecular targeted therapies using tyrosine kinase inhibitors in GBMs. Activation of multiple downstream signaling pathways has been implicated as a possible means by which inhibition of a single RTK has been ineffective in GBM. In this study, we sought a combination of approved drugs that would inhibit in vitro and in vivo growth of GBM oncospheres. A combination consisting of gefitinib and sunitinib acted synergistically in inhibiting growth of GBM oncospheres in vitro. Sunitinib was the only RTK inhibitor that could induce apoptosis in GBM cells. However, the in vivo efficacy testing of the gefitinib and sunitinib combination in an EGFR amplified/PTEN wild type GBM xenograft model revealed that gefitinib alone could significantly improve survival in animals whereas sunitinib did not show any survival benefit. Subsequent testing

of the same drug combination in a different syngeneic glioma model that lack ed EGFR amplification but was more susceptible to sunitinib in vitro demonst rated no survival benefit when treated with gefitinib or sunitinib or the ge fitinib and sunitinib combination. Although a modest survival benefit was ob tained in one of two animal models with EGFR amplification due to gefitinib alone, the addition of sunitinib, to test our best in vitro combination ther apy, did not translate to any additional in vivo benefit. Improved targeted therapies, with drug properties favorable to intracranial tumors, are likely required to form effective drug combinations for GBM.
Journal Title: PloS one

PUBMED ID: 23053494
DOI: doi.org/10.1007/s10014-012-0118-9
Titolo: Progressive adult primary glioblastoma in the medulla oblongata with an unmethylated MGMT promoter and without an IDH mutation.
Autori: Yoshikawa A., Nakada M., Watanabe T., Hayashi Y., Sabit H., Kato Y., Suzuki S., Ooi A., Sato H., Hamada J.
Data di Pubblicazione: 2012-10-12
Abstract: A 63-year-old woman presented with dizziness followed by gait dist urbance and loss of appetite. Magnetic resonance image (MRI) showed that a l esion located in the medulla oblongata, appearing as hyperintense on T2-weig hted image and with slight enhancement area, appeared in the ventral aspect of the mass on T1-weighted MR imaging with gadolinium. It was diagnosed as h igh-grade brain-stem glioma and the patient underwent chemoradiotherapy. How ever, she died 18 days after treatment, and autopsy was performed. The patho logical diagnosis was glioblastoma (GBM) with unmethylated O-6-methylguanine -DNA methyltransferase promoter and wild isocitrate dehydrogenase 1 gene. We report an extremely short clinical course of adult GBM in medulla oblongata with genetic analysis and present a review of the literature.
Journal Title: Brain tumor pathology

PUBMED ID: 23043578
DOI: doi.org/10.1111/j.1754-9485.2012.02414.x
Titolo: The addition of temozolomide does not change the pattern of progress ion of glioblastoma multiforme post-radiotherapy.
Autori: Gunjur A., Bressel M., Ryan G.
Data di Pubblicazione: 2012-10-10
Abstract: The pattern of progression in our GBM patients does not appear to have been altered by the addition of temozolomide. The overwhelming majority of first PD occurred within the original radiotherapy planning target volume , as is the case in patients treated with radiotherapy alone. Major changes to radiotherapy volumes are not indicated, with alternative strategies requi red to improve outcomes.
Journal Title: Journal of medical imaging and radiation oncology

PUBMED ID: 23039151
DOI: doi.org/10.3171/2012.9.JNS12504
Titolo: Impact of extent of resection for recurrent glioblastoma on overall survival: clinical article.
Autori: Bloch O., Han SJ., Cha S., Sun MZ., Aghi MK., McDermott MW., Berger MS., Parsa AT.
Data di Pubblicazione: 2012-10-09
Abstract: Extent of resection at recurrence is an important predictor of ove rall survival. If GTR is achieved at recurrence, overall survival is maximiz ed regardless of initial EOR, suggesting that patients with initial STR may benefit from surgery with a GTR at recurrence.
Journal Title: Journal of neurosurgery

PUBMED ID: 23017192
DOI: doi.org/10.1016/j.ejrad.2012.09.001
Titolo: Automatic multi-modal MR tissue classification for the assessment of response to bevacizumab in patients with glioblastoma.
Autori: Liberman G., Louzoun Y., Aizenstein O., Blumenthal DT., Bokstein F., Palmon M., Corn BW., Ben Bashat D.
Data di Pubblicazione: 2012-09-29
Abstract: This study emphasizes the important role of automatic tools based on a multi-modal view of the tissue in monitoring therapy response in patients with high grade gliomas specifically under anti-angiogenic therapy.
Journal Title: European journal of radiology

PUBMED ID: 22976140
DOI: doi.org/10.2176/nmc.52.570
Titolo: Effectiveness of maximal safe resection for glioblastoma including elderly and low Karnofsky performance status patients: retrospective review at a single institute.
Autori: Uzuka T., Aoki H., Natsumeda M., Takahashi H., Fujii Y.
Data di Pubblicazione: 2012-09-15
Abstract: Elderly and low Karnofsky performance status (KPS) patients have been excluded from most prospective trials. This retrospective study investigated glioblastoma treatment outcomes, including those of elderly and low KPS patients, and analyzed the prognostic factors using the medical records of 107 consecutive patients, 59 men and 48 women aged from 21 to 85 years (median 65 years), with newly diagnosed glioblastoma treated at our institute. There were 71 high-risk patients with age >70 years and/or KPS <70%. Based on the extent of resection, the patients were classified into 3 groups: more than subtotal resection (subtotal, n = 44), partial resection (partial, n = 29), and biopsy only (biopsy, n = 34). Median overall survival (OS) of all 107 patients was 13.5 months. Median OS was 13.2 months in the high-risk group. Median OSs were 15.8, 12.8, and 12.1 months in the subtotal, partial, and biopsy groups, respectively. Multivariate analysis of 73 patients in the subtotal and partial groups found age ≤65 years (p = 0.047), 60 Gy irradiation (p = 0.009), O(6)-methylguanine-deoxyribonucleic acid methyltransferase-negative (p = 0.027), and more than subtotal removal (p = 0.003) were significant prognostic factors. The median postoperative KPS score tended to be better than the preoperative score, even in the high-risk group. We recommend maximal safe resection for glioblastoma patients, even those with advanced age and/or with low KPS scores.
Journal Title: Neurologia medico-chirurgica

PUBMED ID: 22957524
DOI: doi.org/10.3171/2012.7.JNS111260
Titolo: Long-term outcomes for low-grade intracranial gangliоglioma: 30-year experience from the Mayo Clinic.
Autori: Compton JJ., Laack NN., Eckel LJ., Schomas DA., Giannini C., Meyer FB.
Data di Pubblicazione: 2012-09-11
Abstract: This single-institution retrospective series of patients with gangliogliomas is unique given its large cohort size with a long follow-up duration, and confirms the excellent long-term survival rate in this group. The study also shows the importance of resection extent on likelihood of recurrence. Patients with gangliogliomas who undergo STR or biopsy alone have poor PFS. Radiation therapy may delay time to progression in patients with unresectable disease.
Journal Title: Journal of neurosurgery

PUBMED ID: 22946346
DOI: Mancante
Titolo: Phase I/II study of oral erlotinib for treatment of relapsed/refractory glioblastoma multiforme and anaplastic astrocytoma.
Autori: Kesavabhotla K., Schlaff CD., Shin B., Mubita L., Kaplan R., Tsiouris AJ., Pannullo SC., Christos P., Lavi E., Scheff R., Boockvar JA.
Data di Pubblicazione: 2012-09-06
Abstract: We evaluated the safety and survival benefits of orally administered erlotinib monotherapy for patients with relapsed/refractory glioblastoma multiforme (GBM) or anaplastic astrocytoma (AA). A dose escalation schedule was administered with a starting dose of 150 mg/day for the first cycle (28 days), followed by 100 mg twice daily for 14 days, and 150 mg twice daily for another 14 days. Assuming no dose limiting toxicities were observed, dosage was maintained at 150 mg BID for 10 more cycles. Disease and tumor responses were assessed after every other cycle; toxicity assessments were conducted for a minimum of 10 weeks. Patients discontinued use of enzyme-inducing anticonvulsants (EIAED) and started non-EIAEDs. Patients with previous erlotinib exposure were ineligible. Eleven patients were enrolled: 8 (73%) GBM; 3 (27%) AA. Adverse events limited study accrual, originally intended to accrue 43 patients. Nine patients (90%) experienced rash within the first 2 cycles: 7 (64%) within cycle 1; 6 (60%) reported diarrhea within the first 2 cycles. Median progress-free survival (PFS) and overall survival (OS) was 1.9 months and 6.9 months. All patients showed disease progression while on the drug. Despite the sample size, the toxicity of erlotinib supersedes any marginal benefit it as a monotherapy for relapsed/refractory GBM/AA.
Journal Title: Journal of experimental therapeutics & oncology

PUBMED ID: 22932984
DOI: doi.org/10.1007/s11060-012-0964-7
Titolo: Phase I trial of verubulin (MPC-6827) plus carboplatin in patients with relapsed glioblastoma multiforme.
Autori: Grossmann KF., Colman H., Akerley WA., Glantz M., Matsuoko Y., Beelen AP., Yu M., De Groot JF., Aiken RD., Olson JJ., Olsen JJ., Evans BA., Jensen RL.
Data di Pubblicazione: 2012-08-31
Abstract: Verubulin (MPC-6827) is a microtubule-destabilizing agent that achieves high concentrations in the brain. Verubulin disrupts newly formed blood vessels in xenografts. We determined the safety and tolerability of verubulin administered in combination with carboplatin in patients with relapsed glioblastoma multiforme (GBM). Three pre-selected doses of verubulin were tested: 2.1, 2.7, and 3.3 mg/m(2) in a standard "3+3" design. Verubulin was given every second week of a 6-week cycle in the 2.1 mg/m(2) cohort or weekly for 3 weeks of a 4-week cycle in subsequent cohorts. Carboplatin was administered intravenously at an area under the curve (AUC) dosage 4 every 2 weeks for the 2.1 mg/m(2) cohort or on day 1 of each 4-week cycle in subsequent cohorts. Nineteen patients with GBM in first or second relapse were enrolled. Four patients (21 %) experienced a grade 3 or greater verubulin- or carboplatin-related adverse event, including hypesthesia, cerebral ischemia, anemia, and thrombocytopenia. The mean plasma half life of verubulin was 3.2 h (SD = 0.82). Two patients achieved at least a partial response by Macdonald criteria. One of these patients remains progression free and off treatment more than 24 months beyond his initiation of verubulin. Five patients had stable disease. Median progression-free survival (PFS) across all patients was 8 weeks, and the 6-month PFS rate was 21 %. The combination of verubulin at the previously determined single-agent maximum tolerated dose of 3.3 mg/m(2) with carboplatin in patients with recurrent/refractory GBM is safe and well toler

ated. In this patient population with a highly vascularized tumor, no cerebr al hemorrhage was observed.
Journal Title: Journal of neuro-oncology

PUBMED ID: 22913972
DOI: doi.org/10.1097/CCO.0b013e328357f503
Titolo: Chemotherapy in low-grade gliomas.
Autori: Viaccoz A., Lekoubou A., Ducray F.
Data di Pubblicazione: 2012-08-24
Abstract: It has now been widely accepted that chemotherapy is an interestin g treatment option in LGGs. However, several questions remain unanswered reg arding its optimal use. Ongoing phase III studies will allow a better deline ation of the role of chemotherapy in LGGs and will also help to better deter mine the potential predictive value of a 1p/19q codeletion, a MGMT promoter methylation and an IDH1 mutation.
Journal Title: Current opinion in oncology

PUBMED ID: 22877848
DOI: doi.org/10.1016/S1470-2045(12)70265-6
Titolo: Temozolomide versus standard 6-week radiotherapy versus hypofraction ated radiotherapy in patients older than 60 years with glioblastoma: the Nor dic randomised, phase 3 trial.
Autori: Malmström A., Grønberg BH., Marosi C., Stupp R., Frappaz D., Schultz H., Abacioglu U., Tavelin B., Lhermitte B., Hegi ME., Rosell J., Henriksson R., Henriksson R.
Data di Pubblicazione: 2012-08-11
Abstract: Merck, Lion's Cancer Research Foundation, University of Umeå, and the Swedish Cancer Society.
Journal Title: The Lancet. Oncology

PUBMED ID: 22825915
DOI: doi.org/10.3892/ijo.2012.1564
Titolo: IDH1/2 mutation is a prognostic marker for survival and predicts res ponse to chemotherapy for grade II gliomas concomitantly treated with radiat ion therapy.
Autori: Okita Y., Narita Y., Miyakita Y., Ohno M., Matsushita Y., Fukushima S., Sumi M., Ichimura K., Kayama T., Shibui S.
Data di Pubblicazione: 2012-07-25
Abstract: Reliable prognostic biomarkers of grade II gliomas remain unclear. This study aimed to examine the role of mutations of isocitrate dehydrogenas e (IDH1/2), 1p/19q co-deletion, and clinicopathological factors in patients with grade II glioma who were primarily treated with radiotherapy or chemora diotherapy after surgery. Seventy-two consecutive patients, including 49 cas es of diffuse astrocytomas (DA), 4 oligodendrogliomas (OL) and 19 oligoastro cytomas (OA), who underwent treatment from 1991 to 2010 at a single institut ion were examined. The overall survival (OS) of the DA patients (8.3 years) was significantly shorter than that of the OL and OA patients (11.7 years). IDH1/2 mutations were found in 46.9% of the DA patients and 82.6% of the OL and OA patients. The progression-free survival (PFS) and OS of the patients with IDH1/2 mutations (8.4 and 16.3 years) were significantly longer than th ose of the patients without IDH1/2 mutations (3.3 and 4.5 years). Among the patients with IDH1/2 mutations, those who were initially treated with chemor adiotherapy including nimustine hydrochloride (ACNU), had significantly long er PFS than those treated with radiotherapy alone, whereas no significant di fference in PFS was observed between the chemoradiotherapy and radiotherapy groups in the patients without IDH1/2 mutations. Oligodendroglial tumors, ag e <40 years, initial Karnofsky performance status (KPS) ≥80, and IDH1/2 muta

tions were favorable prognostic factors regarding PFS and OS. IDH1/2 mutatio n was a predictive factor of response to chemoradiotherapy in grade II gliom as. Patients with IDH1/2 mutations may benefit more from chemoraiotherapy th an those without IDH1/2 mutations.
Journal Title: International journal of oncology

PUBMED ID: 22809568
DOI: doi.org/10.1016/j.canlet.2012.07.012
Titolo: Increasing the efficacy of tumor cell vaccines by enhancing cross pr iming.
Autori: Andersen BM., Ohlfest JR.
Data di Pubblicazione: 2012-07-20
Abstract: Cancer immunotherapy has been attempted for more than a century, a nd investment has intensified in the last 20 years. The complexity of the im mune system is exemplified by the myriad of immunotherapeutic approaches und er investigation. While anti-tumor immunity has been achieved experimentally with multiple effector cells and molecules, particular promise is shown for harnessing the CD8 T cell response. Tumor cell-based vaccines have been empl oyed in hundreds of clinical trials to date and offer several advantages ove r subunit and peptide vaccines. However, tumor cell-based vaccines, often ai med at cross priming tumor-reactive CD8 T cells, have shown modest success i n clinical trials. Here we review the mechanisms of cross priming and discus s strategies to increase the efficacy of tumor cell-based vaccines. A synthe sis of recent findings on tissue culture conditions, cell death, and dendrit ic cell activation reveals promising new avenues for clinical investigation.
Journal Title: Cancer letters

PUBMED ID: 22744756
DOI: doi.org/10.1007/s11060-012-0913-5
Titolo: Procarbazine, carmustine, and vincristine (PBV) for chemotherapy pre -treated patients with recurrent glioblastoma: a single-institution analysis .
Autori: Kuhnhenn J., Kowalski T., Steenken S., Ostermann K., Schlegel U.
Data di Pubblicazione: 2012-06-30
Abstract: In newly diagnosed glioblastoma multiforme, surgery, combined radi o and chemotherapy, and adjuvant chemotherapy with temozolomide is the stand ard of care. Therapy for recurrent glioblastoma is less well established and comprises re-operation, re-irradiation, chemotherapy, targeted therapy, inhi bition of neoangiogenesis, and others. In this observational study we record ed the efficacy and toxicity of a combination of procarbazine, carmustine, a nd vincristine (PBV) for 69 patients with recurrent and/or progressive gliob lastoma after surgery, concomitant radio and/or chemotherapy, and adjuvant f irst-line temozolomide therapy. Of 41 patients evaluable for response by MRI , partial response was observed for one, minor response for three, stable di sease for at least 6 weeks for ten, and immediate progression for 27. Median PFS was 15 weeks, and PFS-6 was 21 % for 57 patients who could be followed; 12 other patients were lost to follow-up after application of the first PBV cycle. Grade III or IV leucopenia and/or grade III or IV thrombocytopenia we re seen in 26 % and 26 % of cycles, respectively. Haematological complicatio ns led to interruption of treatment for four (7 %) patients. Non-haematologi cal toxicity was moderate. Salvage PBV therapy in recurrent and/or progressi ve glioblastoma, pre-treated with temozolomide-based chemotherapy as first-l ine treatment, is of limited efficacy with a small number of long-term survi vors, but is hampered by relevant myelotoxicity.
Journal Title: Journal of neuro-oncology

PUBMED ID: 22740218

DOI: Mancante
Titolo: Long term experience in high grade glial tumors with temozolomide.
Autori: Demirci U., Buyukberber S., Coskun U., Akmansu M., Yaman E., Baykara M., Yamac D., Uner A., Benekli M.
Data di Pubblicazione: 2012-06-29
Abstract: Temozolomide is an effective agent in HGGs with favorable outcome and low toxicity profile even in advanced age.
Journal Title: Journal of B.U.ON. : official journal of the Balkan Union of Oncology

PUBMED ID: 22688802
DOI: doi.org/10.1007/s11060-012-0906-4
Titolo: Radiotherapy and concomitant temozolomide may improve survival of el derly patients with glioblastoma.
Autori: Barker CA., Chang M., Chou JF., Zhang Z., Beal K., Gutin PH., Iwamot o FM.
Data di Pubblicazione: 2012-06-13
Abstract: Survival of elderly patients with glioblastoma (GBM) is poor, but improves with tumor resection and radiotherapy (RT). Concurrent temozolomide (TMZ) chemotherapy during RT improves the survival of younger patients with GBM, but the benefit in elderly patients is unclear. Medical records of pati ents ≥65 years old with primary GBM, histologically confirmed at Memorial Sl oan-Kettering Cancer Center and treated with RT, were reviewed. Survival was associated with patient (age, performance status), tumor (single or multiple), and treatment (extent of surgery, RT field, technique, fractionation and use of concurrent TMZ) characteristics in a multivariable Cox regression mod el. Grade ≥3 hematologic toxicity rates were compared to reported rates in y ounger patients. Median age of the 291 patients studied was 71 years. Longer survival was associated with younger age, tumor resection, and concomitant T MZ and RT ($p < 0.01$). Concurrent TMZ and RT improved median survival of pati ents with favorable prognostic factors from 12 to 21 months and from 10 to 1 3 months in patients 65-70 and ≥71 years old, respectively. Concomitant TMZ and RT increased the 2 year OS rate from 14 to 41 % and from 5 to 24 % in pa tients 65-70 and ≥71 years old, respectively. Grade 3-4 thrombocytopenia was significantly more frequent in the present cohort. Survival of elderly patie nts with GBM may be prolonged with the use of concomitant TMZ during RT. An ongoing randomized study will determine the benefit of this approach in a pr ospective fashion.
Journal Title: Journal of neuro-oncology

PUBMED ID: 22688083
DOI: doi.org/10.1159/000339152
Titolo: Patupilone (epothilone B) for recurrent glioblastoma: clinical outco me and translational analysis of a single-institution phase I/II trial.
Autori: Oehler C., Frei K., Rushing EJ., McSheehy PM., Weber D., Allegrini P R., Weniger D., Lütolf UM., Knuth A., Yonekawa Y., Barath K., Broggini-Tenze r A., Pruschy M., Hofer S.
Data di Pubblicazione: 2012-06-13
Abstract: In recurrent GBM, patupilone can be given safely pre- and postoper atively. The drug accumulates in the tumor tissue. The treatment results in long-term PFS in some patients. Patupilone represents a valuable novel compo und which deserves further evaluation in combination with radiation therapy in patients with GBM.
Journal Title: Oncology

PUBMED ID: 22679179
DOI: doi.org/10.1158/1078-0432.CCR-12-0568

Titolo: Vismodegib.
Autori: Rudin CM.
Data di Pubblicazione: 2012-06-09
Abstract: Vismodegib (GDC-0449), an orally bioavailable small-molecule inhib itor of Hedgehog signaling, was recently approved by the U.S. Food and Drug Administration for the treatment of basal cell carcinoma that is either meta static or locally advanced in patients who are not candidates for surgical r esection or radiation. Given the absence of previously defined effective dru g therapy for this disease, approval was granted primarily on the basis of o utcome of a nonrandomized parallel cohort phase II study of 99 patients with advanced basal cell carcinoma, with a primary endpoint of objective response rate. Response rates of 30.3% and 42.9% were observed in metastatic and loca lly advanced cohorts in this study, respectively, associated with median pro gression-free survival in both cohorts of 9.5 months. Ongoing clinical inves tigations include evaluation of the potential efficacy of vismodegib in a va riety of diseases and in combination with other agents. The mechanism of act ion, preclinical and clinical data, and potential utility in other disease c ontexts are reviewed here.
Journal Title: Clinical cancer research : an official journal of the America n Association for Cancer Research

PUBMED ID: 22650980
DOI: doi.org/10.1517/17460441.2011.584530
Titolo: Advances in malignant glioma drug discovery.
Autori: Reardon DA., Perry JR., Brandes AA., Jalali R., Wick W.
Data di Pubblicazione: 2012-06-02
Abstract: Several factors limit the efficacy of therapeutics targeting GBM. However, significant advances from basic science laboratories have recently generated important insights into the pathophysiology and molecular genetic abnormalities of these tumors. Efforts to translate these findings into inno vative treatment strategies offer substantial promise to overcome therapeuti c hurdles and treat individual patients more effectively. Improved understan ding of malignant glioma biology and factors associated with treatment respo nse will probably lead to improved therapeutic options and a better patient outcome.
Journal Title: Expert opinion on drug discovery

PUBMED ID: 28519041
DOI: doi.org/10.1118/1.4735032
Titolo: SU-E-J-191: A Multivariate Framework for N-Tissue Classification in Treatment Assessment of Glioblastomas.
Autori: Schreibmann E., Crocker I., Shu H., Curran W., Fox T.
Data di Pubblicazione: 2017-05-19
Abstract: Usage of advanced classification techniques allows automated label ing of voxels into normal, pseudoprogression or tumoral tissue types. The te chnique allows for early detection of pseudo progression to spare patients f rom unnecessary surgery or toxic chemotherapy.
Journal Title: Medical physics

PUBMED ID: 22594978
DOI: doi.org/10.1016/j.pdpdt.2012.01.001
Titolo: Preliminary clinical report on safety and efficacy of photodynamic t herapy using talaporfin sodium for malignant gliomas.
Autori: Akimoto J., Haraoka J., Aizawa K.
Data di Pubblicazione: 2012-05-19
Abstract: We examined the safety and efficacy of PDT using talaporfin sodium as an additional intraoperative treatment for malignant glioma. PDT in addit

ion to surgical resection achieved better therapeutic results than conventio nal protocols, especially in patients with newly diagnosed malignant gliomas . However, the current methodology has some limitations with respect to pati ents with recurrent tumors. Larger-scale studies are required to confirm the clinical feasibility of PDT plus surgery.
Journal Title: Photodiagnosis and photodynamic therapy

PUBMED ID: 22580799
DOI: doi.org/10.1007/s11060-012-0889-1
Titolo: Stereotactic iodine-125 brachytherapy for treatment of inoperable fo cal brainstem gliomas of WHO grades I and II: feasibility and long-term outc ome.
Autori: Ruge MI., Kickingereder P., Simon T., Treuer H., Sturm V.
Data di Pubblicazione: 2012-05-15
Abstract: Microsurgical resection is the most frequently suggested treatment option for accessible focal brainstem gliomas (F-BSG) of World Health Organi zation (WHO) grades I and II. Because of their location in the highly eloque nt brain, however, resection is associated with permanent postoperative morb idity, ranging from 12 to 33 %. Only a few reports have suggested stereotact ic brachytherapy (SBT) with implantation of iodine-125 seeds as a local trea tment alternative. Between 1993 and 2010, 47 patients were treated with SBT (iodine-125 seeds; cumulative surface dose 50-65 Gy) for inoperable F-BSG, W HO grades I and II, in one of the largest reported patient series. We evalua ted procedure-related complications, clinical outcome, and progression-free and overall survival (PFS, OS). Median follow-up was 81.6 months. Procedure-related mortality was zero. Within 30 days of seed implantation six patients (12.8 %) had transient neurological deficits. Two patients (4.3 %) deteriora ted permanently. Space-occupying cysts occurred in six patients (12.8 %) aft er a median of 28.5 months, and required surgical intervention. Nine patient s (19.1 %) presented with tumor relapse after a median of 56.6 months (range 7.9-118.0 months). For the remaining 38 patients complete response was obser ved for 23.4 %, partial response for 29.8 %, and stable disease for 27.7 %. Actuarial PFS was 97.7 ± 2.2, 92.8 ± 4.0, 81.2 ± 6.5, and 62.0 ± 10.4 % afte r 1, 2, 5, and 10 years, respectively. Corresponding OS was 100 ± 0.0 % (1 a nd 2 years), 97.4 ± 2.6 % (5 years), and 87.6 ± 7.0 % (10 years). SBT is a c omparatively safe, minimally invasive, and highly effective local treatment option for patients with inoperable F-BSG WHO grades I and II; it merits fur ther evaluation in prospective randomized trials.
Journal Title: Journal of neuro-oncology

PUBMED ID: 22576886
DOI: doi.org/10.3174/ajnr.A3091
Titolo: Metabolic response of glioblastoma to superselective intra-arterial cerebral infusion of bevacizumab: a proton MR spectroscopic imaging study.
Autori: Jeon JY., Kovanlikaya I., Boockvar JA., Mao X., Shin B., K Burkhardt J., Kesavabhotla K., Christos P., Riina H., Shungu DC., Tsiouris AJ.
Data di Pubblicazione: 2012-05-12
Abstract: The results of this (1)H-MRS analysis suggest that GB treatment wi th SIACI of bevacizumab may be associated with a direct antiproliferative ef fect, as demonstrated by significant reductions of tCho/NAA after the interv ention.
Journal Title: AJNR. American journal of neuroradiology

PUBMED ID: 22555992
DOI: doi.org/10.1007/s11060-012-0887-3
Titolo: Can irradiation of potential cancer stem-cell niche in the subventri cular zone influence survival in patients with newly diagnosed glioblastoma?

Autori: Gupta T., Nair V., Paul SN., Kannan S., Moiyadi A., Epari S., Jalali R.
Data di Pubblicazione: 2012-05-05
Abstract: Glioblastoma progenitor or stem cells residing in the stem-cell niche in the subventricular zones (SVZ) can initiate or promote tumorigenesis. They can also migrate throughout the brain, resulting in disease progression. Irradiation of potential cancer stem-cell niche in the SVZ may influence survival. To analyze radiotherapy dose-volume parameters to the SVZ that correlate with survival in adequately treated patients with newly diagnosed glioblastoma, 40 adults with histopathologically proven supratentorial glioblastoma with available baseline imaging treated with postoperative conventionally fractionated focal conformal radiotherapy plus chemotherapy, available radiotherapy planning dataset, and documented event of progression or death or minimum 6-month follow-up were included in this retrospective study. Dose-volume parameters to the SVZ were extracted from treatment planning system and analyzed in relation to survival outcomes. Mean ipsilateral and contralateral SVZ volumes were 5.6 and 6.4 cc, respectively. With median follow-up of 15 months (interquartile range 12-18 months), median [95 % confidence interval (CI)] progression-free survival (PFS) and overall survival (OAS) was 11 months (95 % CI 8.9-13.0 months) and 17 months (95 % CI 11.6-22.4 months), respectively. Older age (>50 years), poor recursive partitioning analysis (RPA) class, and higher than median of mean contralateral SVZ dose were associated with significantly worse PFS and OAS. Multivariate analysis identified RPA class, Karnofsky performance status, and mean ipsilateral SVZ dose as independent predictors of survival. Increasing mean dose to the ipsilateral SVZ was associated with significantly improved OAS. Irradiation of potential cancer stem-cell niche influences survival outcomes in patients with newly diagnosed glioblastoma.
Journal Title: Journal of neuro-oncology

PUBMED ID: 22538078
DOI: doi.org/10.3174/ajnr.A3053
Titolo: Persistent diffusion-restricted lesions in bevacizumab-treated malignant gliomas are associated with improved survival compared with matched controls.
Autori: Mong S., Ellingson BM., Nghiemphu PL., Kim HJ., Mirsadraei L., Lai A., Yong W., Zaw TM., Cloughesy TF., Pope WB.
Data di Pubblicazione: 2012-04-28
Abstract: Restricted-diffusion lesions in malignant gliomas treated with bevacizumab are generally stable with time and are associated with improved outcomes. These results combined with physiologic imaging and histopathologic data suggest that these lesions are not consistent with aggressive tumor.
Journal Title: AJNR. American journal of neuroradiology

PUBMED ID: 22527250
DOI: doi.org/10.1007/s00262-012-1261-1
Titolo: Integration of autologous dendritic cell-based immunotherapy in the standard of care treatment for patients with newly diagnosed glioblastoma: results of the HGG-2006 phase I/II trial.
Autori: Ardon H., Van Gool SW., Verschuere T., Maes W., Fieuws S., Sciot R., Wilms G., Demaerel P., Goffin J., Van Calenbergh F., Menten J., Clement P., Debiec-Rychter M., De Vleeschouwer S.
Data di Pubblicazione: 2012-04-25
Abstract: Full integration of autologous DC-based tumor vaccination into standard postoperative radiochemotherapy for newly diagnosed glioblastoma seems safe and possibly beneficial. These results were used to power the currently running phase IIb randomized clinical trial.
Journal Title: Cancer immunology, immunotherapy : CII

PUBMED ID: 22464345
DOI: doi.org/10.1016/j.ejca.2012.02.004
Titolo: New prognostic factors and calculators for outcome prediction in pat ients with recurrent glioblastoma: a pooled analysis of EORTC Brain Tumour G roup phase I and II clinical trials.
Autori: Gorlia T., Stupp R., Brandes AA., Rampling RR., Fumoleau P., Dittric h C., Campone MM., Twelves CC., Raymond E., Hegi ME., Lacombe D., van den Be nt MJ.
Data di Pubblicazione: 2012-04-03
Abstract: This analysis confirms performance status but not age as a major p rognostic factor for PFS and OS in recurrent GBM. Patients with multiple and large lesions have an increased risk of death. With these data prognostic ca lculators with confidence intervals for both medians and fixed time probabil ities of survival were derived.
Journal Title: European journal of cancer (Oxford, England : 1990)

PUBMED ID: 24031101
DOI: doi.org/10.3109/01658107.2012.658594
Titolo: New prognostic factors and calculators for outcome prediction in pat ients with recurrent glioblastoma: a pooled analysis of EORTC Brain Tumour G roup phase I and II clinical trials.
Autori: Kang JJ., Hou JH., Bui KM., Michals E., Valyi-Nagy T., Koshy M., Mun son T., Charbel FT., Villano JL., Moss HE.
Data di Pubblicazione: 2013-09-14
Abstract: Malignant optic nerve glioma (MONG) is a rare but uniformly fatal disease that remains poorly understood. We describe a notable case of this r are disease occurring in the optic chiasm. Normal brain imaging and normal o phthalmic examination two years prior to diagnosis provide evidence for
Journal Title: Neuro-ophthalmology (Aeolus Press)

PUBMED ID: 22461640
DOI: doi.org/10.1126/scitranslmed.3003016
Titolo: Anti-invasive adjuvant therapy with imipramine blue enhances chemoth erapeutic efficacy against glioma.
Autori: Munson JM., Fried L., Rowson SA., Bonner MY., Karumbaiah L., Diaz B. , Courtneidge SA., Knaus UG., Brat DJ., Arbiser JL., Bellamkonda RV.
Data di Pubblicazione: 2012-03-31
Abstract: The invasive nature of glioblastoma (GBM) represents a major clini cal challenge contributing to poor outcomes. Invasion of GBM into healthy ti ssue restricts chemotherapeutic access and complicates surgical resection. H ere, we test the hypothesis that an effective anti-invasive agent can "conta in" GBM and increase the efficacy of chemotherapy. We report a new anti-inva sive small molecule, Imipramine Blue (IB), which inhibits invasion of glioma in vitro when tested against several models. IB inhibits NADPH (reduced form of nicotinamide adenine dinucleotide phosphate) oxidase-mediated reactive ox ygen species generation and alters expression of actin regulatory elements. In vivo, liposomal IB (nano-IB) halts invasion of glioma, leading to a more compact tumor in an aggressively invasive RT2 syngeneic astrocytoma rodent m odel. When nano-IB therapy was followed by liposomal doxorubicin (nano-DXR) chemotherapy, the combination therapy prolonged survival compared to nano-IB or nano-DXR alone. Our data demonstrate that nano-IB-mediated containment of diffuse glioma enhanced the efficacy of nano-DXR chemotherapy, demonstrating the promise of an anti-invasive compound as an adjuvant treatment for glioma .
Journal Title: Science translational medicine

PUBMED ID: 22440872
DOI: doi.org/10.1016/j.nec.2012.01.004
Titolo: The role of BCNU polymer wafers (Gliadel) in the treatment of malign ant glioma.
Autori: Nagpal S.
Data di Pubblicazione: 2012-03-24
Abstract: The 1,3-bis(2-chloroethyl)-1-nitrosourea (BCNU; carmustine) polyme r wafer (Gliadel) was developed for use in malignant glioma to deliver highe r doses of chemotherapy directly to tumor tissue while bypassing systemic si de effects. Phase III clinical trials for patients with newly diagnosed mali gnant gliomas demonstrated a small, but statistically significant, improveme nt in survival. However, the rate of complications, including an increase in cerebrospinal fluid leaks and intracranial hypertension, has limited their u se. This article reviews the current data for use of BCNU wafers in malignan t gliomas.
Journal Title: Neurosurgery clinics of North America

PUBMED ID: 22436661
DOI: doi.org/10.1186/1471-2407-12-99
Titolo: Phase I/IIa study of intratumoral/intracerebral or intravenous/intra cerebral administration of Parvovirus H-1 (ParvOryx) in patients with progre ssive primary or recurrent glioblastoma multiforme: ParvOryx01 protocol.
Autori: Geletneky K., Huesing J., Rommelaere J., Schlehofer JR., Leuchs B., Dahm M., Krebs O., von Knebel Doeberitz M., Huber B., Hajda J.
Data di Pubblicazione: 2012-03-23
Abstract: ClinicalTrials.gov Identifier: NCT01301430.
Journal Title: BMC cancer

PUBMED ID: 22416109
DOI: doi.org/10.1093/neuonc/nos069
Titolo: Dynamic imaging response following radiation therapy predicts long-t erm outcomes for diffuse low-grade gliomas.
Autori: Pallud J., Llitjos JF., Dhermain F., Varlet P., Dezamis E., Devaux B ., Souillard-Scémama R., Sanai N., Koziak M., Page P., Schlienger M., Daumas -Duport C., Meder JF., Oppenheim C., Roux FX.
Data di Pubblicazione: 2012-03-15
Abstract: Quantitative imaging assessment of radiation therapy (RT) for diff use low-grade gliomas (DLGG) by measuring the velocity of diametric expansio n (VDE) over time has never been studied. We assessed the VDE changes follow ing RT and determined whether this parameter can serve as a prognostic facto r. We reviewed a consecutive series of 33 adults with supratentorial DLGG tr eated with first-line RT with available imaging follow-up (median follow-up, 103 months). Before RT, all patients presented with a spontaneous tumor volu me increase (positive VDE, mean 5.9 mm/year). After RT, all patients demonst rated a tumor volume decrease (negative VDE, mean, -16.7 mm/year) during a m ean 49-month duration. In univariate analysis, initial tumor volume (>100 cm (3)), lack of IDH1 expression, p53 expression, high proliferation index, and fast post-RT tumor volume decrease (VDE at -10 mm/year or faster, fast respo nders) were associated with a significantly shorter overall survival (OS). T he median OS was significantly longer (120.8 months) for slow responders (po st-RT VDE slower than -10.0 mm/year) than for fast responders (47.9 months). In multivariate analysis, fast responders, larger initial tumor volume, lack of IDH1 expression, and p53 expression were independent poor prognostic fact ors for OS. A high proliferation index was significantly more frequent in th e fast responder subgroup than in the slow responder subgroup. We conclude t hat the pattern of post-RT VDE changes is an independent prognostic factor f or DLGG and offers a quantitative parameter to predict long-term outcomes. W

e propose to monitor individually the post-RT VDE changes using MRI follow-up, with particular attention to fast responders.
Journal Title: Neuro-oncology

PUBMED ID: 22396071
DOI: doi.org/10.1007/s11060-012-0832-5
Titolo: Dose dense 1 week on/1 week off temozolomide in recurrent glioma: a retrospective study.
Autori: Taal W., Segers-van Rijn JM., Kros JM., van Heuvel I., van der Rijt CC., Bromberg JE., Sillevis Smitt PA., van den Bent MJ.
Data di Pubblicazione: 2012-03-08
Abstract: Alternative temozolomide regimens have been proposed to overcome O(6)-methylguanine-DNA methyltransferase mediated resistance. We investigated the efficacy and tolerability of 1 week on/1 week off temozolomide (ddTMZ) regimen in a cohort of patients treated with ddTMZ between 2005 and 2011 for the progression of a glioblastoma during or after chemo-radiation with temozolomide or a recurrence of another type of glioma after radiotherapy and at least one line of chemotherapy. Patients received ddTMZ at 100-150 mg/m(2)/d (days 1-7 and 15-21 in cycles of 28-days). All patients had a contrast enhancing lesion on MRI and the response was assessed by MRI using the RANO criteria; complete and partial responses were considered objective responses. Fifty-three patients were included. The median number of cycles of ddTMZ was 4 (range 1-12). Eight patients discontinued chemotherapy because of toxicity. Two of 24 patients with a progressive glioblastoma had an objective response; progression free survival at 6 months (PFS-6) in glioblastoma was 29%. Three of the 16 patients with a recurrent WHO grade 2 or 3 astrocytoma or oligodendroglioma or oligo-astrocytoma without combined 1p and 19q loss had an objective response and PFS-6 in these patients was 38%. Four out of the 12 evaluable patients with a recurrent WHO grade 2 or 3 oligodendroglioma or oligo-astrocytoma with combined 1p and 19q loss had an objective response; PFS-6 in these patients was 62%. This study indicates that ddTMZ is safe and effective in recurrent glioma, despite previous temozolomide and/or nitrosourea chemotherapy. Our data do not suggest superior efficacy of this schedule as compared to the standard day 1-5 every 4 weeks schedule.
Journal Title: Journal of neuro-oncology

PUBMED ID: 22371319
DOI: doi.org/10.1002/cncr.26541
Titolo: Phase II study of Gleevec plus hydroxyurea in adults with progressive or recurrent low-grade glioma.
Autori: Reardon DA., Desjardins A., Vredenburgh JJ., Herndon JE., Coan A., Gururangan S., Peters KB., McLendon R., Sathornsumetee S., Rich JN., Lipp ES., Janney D., Friedman HS.
Data di Pubblicazione: 2012-02-29
Abstract: Imatinib plus hydroxyurea was well tolerated among recurrent/progressive LGG patients but this regimen demonstrated negligible antitumor activity.
Journal Title: Cancer

PUBMED ID: 22364864
DOI: doi.org/10.1016/j.ophtha.2011.12.035
Titolo: Longitudinal measures of visual function, tumor volume, and prediction of visual outcomes after treatment of optic pathway gliomas.
Autori: Kelly JP., Leary S., Khanna P., Weiss AH.
Data di Pubblicazione: 2012-02-28
Abstract: The author(s) have no proprietary or commercial interest in any materials discussed in this article.

Journal Title: Ophthalmology

PUBMED ID: 22341931
DOI: doi.org/10.1016/j.clineuro.2012.01.030
Titolo: Marked response of gliomatosis cerebri to temozolomide and whole bra in radiotherapy.
Autori: Mattox AK., Lark AL., Adamson DC.
Data di Pubblicazione: 2012-02-21
Abstract: Gliomatosis cerebri (GC) represents an unfortunate, rare variant o f glioma with a very poor prognosis. Given this lesion's rarity, little info rmation exists on appropriate treatment options. The diffuse, infiltrative n ature of GC precludes any surgical resection and limits therapy. Because of the improved survival seen with the use of temozolomide (TMZ) in malignant g lioma, a rigorous systematic review of the published literature was performe d to ascertain the benefit of TMZ in GC. We identified all GC cases in the l iterature where there was enough information to ascertain a clear response t o a specific chemoradiotherapeutic treatment. In addition to our experience with a recent case, we have identified 61 patients with GC in the published literature who demonstrated a positive radiographic or clinic response after treatment. Statistical analysis of survival was performed by Kaplan-Meier an alysis. A positive radiographic and clinical response was seen in patients r anging in age from 4 to 84 years. Overall median survival in patients diagno sed with GC who demonstrated a response after treatment was 25 months, with 1- and 2-year survival rates of 89% and 55%, respectively. The most common t reatment regimens for responders included TMZ alone (26.2%), external whole- brain radiotherapy (WBRT) (26.2%), and concomitant TMZ and WBRT (20%). Our p atient was treated with concomitant TMZ (150 mg/m(2)/day over 5 days) and WB RT (50 Gy) and has remained with a complete radiographic response after 36 m onths. In conclusion, patients with GC confirmed by surgical biopsy should b e aggressively treated with concomitant TMZ and WBRT, as marked responses ha ve been seen, and this appears to offer overall survival benefit.
Journal Title: Clinical neurology and neurosurgery

PUBMED ID: 22322851
DOI: doi.org/10.1700/1018.11101
Titolo: Bone marrow metastases from anaplastic oligodendroglioma presenting with pancytopenia and hypogammaglobulinemia: a case report.
Autori: Cordiano V., Miserocchi F., Storti M.
Data di Pubblicazione: 2012-02-11
Abstract: We report the case of a 40-year-old man whose bone marrow metastas es occurred 57 months after the initial diagnosis and 9 months after complet ing radiotherapy for an anaplastic oligodendroglioma. Four months before the demonstration of visceral metastases was obtained by bone marrow biopsy, the patient developed diffuse bone pain, pancytopenia, hypercalcemia, and panhyp ogammaglobulinemia. These abnormalities and other clinical signs of extracra nial dissemination of the primary brain tumor were initially unrecognized un til the patient was admitted with the suspicion of a nonsecretory multiple m yeloma. We also briefly review the factors predisposing these tumors to spre ad outside the CNS, albeit rarely, and discuss the clinical implications of a misdiagnosis of extracranial invasion by anaplastic oligodendroglioma, who se chemosensitivity has been definitively demonstrated.
Journal Title: Tumori

PUBMED ID: 22268382
DOI: doi.org/10.2174/156800912799277557
Titolo: Targeting EGFR for treatment of glioblastoma: molecular basis to ove rcome resistance.

Autori: Taylor TE., Furnari FB., Cavenee WK.
Data di Pubblicazione: 2012-01-25
Abstract: Glioblastoma (glioblastoma multiforme; GBM; WHO Grade IV) accounts for the majority of primary malignant brain tumors in adults. Amplification and mutation of the epidermal growth factor receptor (EGFR) gene represent s ignature genetic abnormalities encountered in GBM. A range of potential ther apies that target EGFR or its mutant constitutively active form, ΔEGFR, incl uding tyrosine kinase inhibitors (TKIs), monoclonal antibodies, vaccines, an d RNA-based agents, are currently in development or in clinical trials for t he treatment of GBM. Data from experimental studies evaluating these therapi es have been very promising; however, their efficacy in the clinic has so fa r been limited by both upfront and acquired drug resistance. This review dis cusses the current status of anti-EGFR agents and the recurrent problem of r esistance to these agents that strongly indicates that a multiple target app roach will provide a more favorable future for these types of targeted thera pies in GBM.
Journal Title: Current cancer drug targets

PUBMED ID: 22214463
DOI: doi.org/10.2174/092986712799320646
Titolo: Efficacy and safety of bevacizumab in glioblastomas.
Autori: De Fazio S., Russo E., Ammendola M., Donato Di Paola E., De Sarro G.
Data di Pubblicazione: 2012-01-05
Abstract: Glioblastoma multiforme (GBM) is a common and malignant primary br ain tumor arising from glial precursors the survival of which is estimated t o be about 14 months after diagnosis despite current standard care with radi otherapy, surgery, and chemotherapies. Therapeutic approaches were greatly i mproved in the last years; however, GBM still represents the most lethal sub type of glioma. Actually, it has been estimated that only about 3.4% of pati ents will survive at the most five years when obtaining the best outcome fro m treatment; however, this depends on tumor resistance, which is generally r elated to repairing radiation injury, and self- improving cell growth repair and survival. All GBMs recur after initial therapy, limiting patients sur vival at 20-25% within 1 year after diagnosis of recurrent disease. Moreover , for recurrent GBM response rates are less than 10% (ranging from 5% to 9%) , and progression free survival at 6-month (PFS-6) rates ranges between 9% a nd 28% (median 15%). The development of targeted therapy based on tumor vasc ular blockade led to the approval of bevacizumab for recurrent or progressiv e glioblastoma, since it was proven that this offers a new opportunity for p atients suffering from this malignancy. Bevacizumab is a recombinant antivas cular monoclonal antibody binding to circulating Vascular Endothelial Growth Factor (VEGF) preventing this cytokine from reaching its receptors (VEGFR1 a nd VEGFR2) on endothelium, resulting in an inhibition of cells proliferation and vessels sprouting. The aim of this review is to address bevacizumab mode of action in malignant gliomas and provide a summary on currently available data on efficacy and safety.
Journal Title: Current medicinal chemistry

PUBMED ID: 22159180
DOI: doi.org/10.2967/jnumed.111.092387
Titolo: 3'-deoxy-3'-18F-fluorothymidine PET and MRI for early survival predi ctions in patients with recurrent malignant glioma treated with bevacizumab.
Autori: Schwarzenberg J., Czernin J., Cloughesy TF., Ellingson BM., Pope WB. , Geist C., Dahlbom M., Silverman DH., Satyamurthy N., Phelps ME., Chen W.
Data di Pubblicazione: 2011-12-14
Abstract: Changes in tumor (18)F-FLT uptake were highly predictive of progre ssion-free and overall survival in patients with recurrent malignant glioma

on bevacizumab therapy. (18)F-FLT PET seems to be more predictive than MRI f
or early treatment response.
Journal Title: Journal of nuclear medicine : official publication, Society o
f Nuclear Medicine

PUBMED ID: 22158493
DOI: doi.org/10.1700/989.10721
Titolo: Treatment of recurrent high-grade gliomas with GliaSite brachythera
py: a prospective mono-institutional Italian experience.
Autori: Gobitti C., Borsatti E., Arcicasa M., Roncadin M., Franchin G., Mina
tel E., Skrap M., Zanotti B., Tuniz F., Cimitan M., Capra E., Drigo A., Trov
ò MG.
Data di Pubblicazione: 2011-12-14
Abstract: Patients with recurrent high-grade glioma can be treated with addi
tional surgery and GliaSite brachytherapy, delivering 4500 cGy at 1 cm depth
without significant acute side effects but with a significant rate (20%) of
late radiation necrosis, resulting in 13% of treatment-related deaths. Compa
red with the literature, survival results in our study appear to be satisfac
tory, but they may be related to patient selection criteria. Re-intervention
followed by GliaSite brachytherapy should not be offered as a standard treat
ment for recurrent high-grade glioma, because of the high rate of late compl
ications, treatment-related deaths, and high treatment costs.
Journal Title: Tumori

PUBMED ID: 22145948
DOI: doi.org/10.1186/1746-1596-6-119
Titolo: Intraventricular glioneuronal tumor with disseminated lesions at dia
gnosis--a case report.
Autori: Yano H., Nakayama N., Hirose Y., Ohe N., Shinoda J., Yoshimura S., I
wama T.
Data di Pubblicazione: 2011-12-08
Abstract: A 55-year-old man presented with a large tumor in his lateral vent
ricles. Magnetic resonance imaging revealed disseminated lesions in the thir
d and fourth ventricles at the time of diagnosis. The patient underwent a pa
rtial removal of the tumor in the lateral ventricles. Histologically, the su
rgical specimens showed glioneuronal differentiation with ganglion or gangli
oid cells, Rosenthal fibers, oligodendroglia-like honeycomb appearances, a s
pongy pattern, perivascular pseudorosettes, and many hyalinized blood vessel
s. Papillary structure was not observed. The neuronal component showed a mod
erately high labeling index of Ki-67/MIB-1. We diagnosed this tumor as atypi
cal intraventricular glioneuronal tumor. The disseminated lesions disappeare
d after chemoradiation therapy with temozolomide, and the residual tumors in
the lateral ventricles remained stable for 3 years after the surgery. We dis
cuss the pathological diagnosis, therapy and clinical course with review of
the literatures.
Journal Title: Diagnostic pathology

PUBMED ID: 22117160
DOI: doi.org/10.1586/era.11.103
Titolo: Towards personalized therapy for patients with glioblastoma.
Autori: Shirai K., Chakravarti A.
Data di Pubblicazione: 2011-11-26
Abstract: Combined therapy with temozolomide and radiotherapy is a standard
treatment and improves the survival for patients with newly diagnosed gliobl
astoma. However, the prognosis remains poor, with a median survival time of
12-15 months. Currently, several clinical trials of dose-dense temozolomide
regimen or molecular-targeting therapies have been performed to overcome the

resistance of glioblastoma. In these therapies, rational prognostic biomarke rs have also been investigated to predict their outcome and response to trea tment. This advanced understanding of the biological markers can help to dev elop personalized therapies for glioblastoma patients. Generally, due to a r educed tolerance, elderly patients do not seem to benefit from intensive tre atment. This population needs individual treatments depended on their age or performance status. In this article, we review the recent studies that can p rovide personalized therapy for glioblastoma, based on molecular tumor profi ling or patients' physical status.
Journal Title: Expert review of anticancer therapy

PUBMED ID: 22104357
DOI: doi.org/10.1016/j.ijrobp.2011.06.1952
Titolo: Experience with carbon ion radiotherapy for WHO Grade 2 diffuse astr ocytomas.
Autori: Hasegawa A., Mizoe JE., Tsujii H., Kamada T., Jingu K., Iwadate Y., Nakazato Y., Matsutani M., Takakura K., Takakura K.
Data di Pubblicazione: 2011-11-23
Abstract: High-dose group patients showed significant improvement in PFS and OS rates compared to those in the low-dose group, and both dose groups showe d acceptable toxicity.
Journal Title: International journal of radiation oncology, biology, physics

PUBMED ID: 22101221
DOI: doi.org/10.1016/j.cct.2011.10.010
Titolo: A phase I trial of carboplatin administered by convection-enhanced d elivery to patients with recurrent/progressive glioblastoma multiforme.
Autori: White E., Bienemann A., Taylor H., Hopkins K., Cameron A., Gill S.
Data di Pubblicazione: 2011-11-22
Abstract: Glioblastoma multiforme (GBM) is the commonest primary malignant b rain tumour in adults. Standard treatment comprises surgery, radiotherapy an d chemotherapy; however this condition remains incurable as these tumours ar e highly invasive and involve critical areas of the brain making it impossib le to remove them surgically or cure them with radiotherapy. In the majority of cases the tumour recurs within 2 to 3 cm of the original site of tumour r esection. Furthermore, the blood-brain barrier profoundly limits the access of many systemically administered chemotherapeutics to the tumour. Convectio n-enhanced delivery (CED) is a promising technique of direct intracranial dr ug delivery involving the implantation of microcatheters into the brain. Car boplatin represents an ideal chemotherapy to administer using this technique as glioblastoma cells are highly sensitive to carboplatin in vitro at concen trations that are not toxic to normal brain in vivo. This protocol describes a single-centre phase I dose-escalation study of carboplatin administered by CED to patients with recurrent or progressive GBM despite full standard trea tment. This trial will incorporate 6 cohorts of 3 patients each. Cohorts wil l be treated in a sequential manner with increasing doses of carboplatin, su bject to dose-limiting toxicity not being observed. This protocol should fac ilitate the identification of the maximum-tolerated infused concentration of carboplatin by CED into the supratentorial brain. This should facilitate the safe application of this technique in a phase II trial, treating patients wi th GBM, as well as for the treatment of other forms of malignant brain tumou rs, including metastases.
Journal Title: Contemporary clinical trials

PUBMED ID: 22076316
DOI: doi.org/10.1007/s10014-011-0070-0

Titolo: Adult cerebellar glioblastoma cases have different characteristics f rom supratentorial glioblastoma.
Autori: Utsuki S., Oka H., Miyajima Y., Kijima C., Yasui Y., Fujii K.
Data di Pubblicazione: 2011-11-15
Abstract: This study is a histological and clinical investigation of four ca ses of cerebellar glioblastoma, a rare tumor. The cases included three males and one female, from 33 to 67 years in age (mean 49 years). Tumor resection, postoperative irradiation and chemotherapy were performed in all cases. Two patients died of local tumor recurrence after 14 and 27 months. Another pati ent relapsed after 10 months; however, after additional tumor resection and second line chemotherapy, she remains disease-free 41 months after the initi al treatment. The fourth patient has not relapsed in the 6 months since init ial treatment. The histopathology of all cases was glioblastoma with pseudop alisading necrosis. However, low-grade glioma histopathology was found in th ree patients. All glioblastomas were immunopositive for p53 and immunonegati ve for epidermal growth factor receptor (EGFR) and isocitrate dehydrogenase 1 (IDH1). These adult cerebellar glioblastoma cases had similar clinical and pathological characteristics, and had different characteristics compared wit h supratentorial glioblastomas.
Journal Title: Brain tumor pathology

PUBMED ID: 22059142
DOI: doi.org/10.4103/2152-7806.86226
Titolo: Rare case of intracranial Salmonella enteritidis abscess following g lioblastoma resection: Case report and review of the literature.
Autori: Sait M., Rahmathulla G., Chen TL., Barnett GH.
Data di Pubblicazione: 2011-11-08
Abstract: Re-operative tumor surgery has a higher incidence of post-operativ e infections, with Gram positive cocci being the most common pathogens. Pred isposing factors reported for intracranial salmonellosis include compromised immunity, diabetes, HIV, and recent travel. Chronic corticosteroid use, mult iple regimens of chemotherapy, and regions of tumor necrosis likely potentia te this rare infection in GBM patients.
Journal Title: Surgical neurology international

PUBMED ID: 22057917
DOI: doi.org/10.1007/s11060-011-0744-9
Titolo: Salvage gamma knife stereotactic radiosurgery followed by bevacizuma b for recurrent glioblastoma multiforme: a case-control study.
Autori: Park KJ., Kano H., Iyer A., Liu X., Niranjan A., Flickinger JC., Lie berman FS., Lunsford LD., Kondziolka D.
Data di Pubblicazione: 2011-11-08
Abstract: We evaluated the efficacy and safety of gamma knife stereotactic r adiosurgery (GKSR) followed by bevacizumab combined with chemotherapy in 11 patients with recurrent glioblastoma multiforme who experienced tumor progre ssion despite aggressive initial multi-modality treatment. Our experience in cluded eight male and three female patients. The median patient age at GKSR was 62 years (range 46-72 years). At the time of GKSR, seven patients had a first recurrence and four had two or more recurrences. The median interval f rom the initial diagnosis until GKSR was 17 months (range 5-34.5 months). Th e median tumor volume was 13.6 cm(3) (range 1.2-45.1 cm(3)) and the median m argin dose of GKSR was 16 Gy (range 13-18 Gy). Following GKSR, bevacizumab w as administrated with irinotecan in nine patients and with temozolomide in o ne patient. One patient was treated with bevacizumab monotherapy. The treatm ent outcomes were compared to 44 case-matched controls who underwent GKSR wi thout additional bevacizumab. At a median of 13.7 months (range 4.6-28.3 mon ths) after radiosurgery, tumor progression was evident in seven patients. Th e median progression-free survival (PFS) was 15 months (95% confidential int

erval (CI), 6.5-23.3 months). Six-month and 1-year PFS rates were 73 and 55% , respectively. The median overall survival (OS) from GKSR was 18 months (95 % CI, 10.1-25.7 months) and 1-year OS rate was 73%. One patient (9%) experie nced grade III toxicity and one patient (9%) had major adverse radiation eff ects. Compared with patients who did not receive bevacizumab, the patients w ho received bevacizumab had significantly prolonged PFS (15 months vs. 7 mon ths, P = 0.035) and OS (18 months vs. 12 months, P = 0.005), and were less l ikely to develop an adverse radiation effect (9 vs. 46%, P = 0.037). The com bination of salvage GKSR followed by bevacizumab added potential benefit and little additional risk in a small group of patients with progressive gliobla stoma. Further experience is needed to define the efficacy and long-term tox icity with this strategy.
Journal Title: Journal of neuro-oncology

PUBMED ID: 22044816
DOI: doi.org/10.4103/0973-1482.87039
Titolo: Invasion is not an independent prognostic factor in high-grade gliom a.
Autori: Narayana A., Perretta D., Kunnakkat S., Gruber D., Golfinos J., Park er E., Medabalmi P., Zagzag D., Pat Eagan RN., Gruber M.
Data di Pubblicazione: 2011-11-03
Abstract: Presence of diffuse invasive disease not accompanied by angiogenes is either prior to therapy or subsequent to anti-angiogenic therapy does not seem to have prognostic significance. However, invasion accompanied by angio genesis in newly diagnosed HGG may confer a poor prognosis.
Journal Title: Journal of cancer research and therapeutics

PUBMED ID: 22035272
DOI: doi.org/10.3171/2011.9.JNS11656
Titolo: A clinical trial of bevacizumab, temozolomide, and radiation for new ly diagnosed glioblastoma.
Autori: Narayana A., Gruber D., Kunnakkat S., Golfinos JG., Parker E., Raza S., Zagzag D., Eagan P., Gruber ML.
Data di Pubblicazione: 2011-11-01
Abstract: The addition of bevacizumab to conventional therapy in newly diagn osed GBM appears to improve both PFS and OS in patients with newly diagnosed GBM, with acceptable morbidity. A shift toward diffuse relapse was noted in a significant number of patients. Ongoing Phase III clinical trials will sho w the true benefit of this antiangiogenic approach.
Journal Title: Journal of neurosurgery

PUBMED ID: 21993440
DOI: doi.org/10.1093/neuonc/nor173
Titolo: Low-dose fractionated radiotherapy and concomitant chemotherapy in g lioblastoma multiforme with poor prognosis: a feasibility study.
Autori: Balducci M., Chiesa S., Diletto B., D'Agostino GR., Mangiola A., Man frida S., Mantini G., Albanese A., Fiorentino A., Frascino V., De Bari B., M icciche' F., De Rose F., Morganti AG., Anile C., Valentini V.
Data di Pubblicazione: 2011-10-14
Abstract: We explored the feasibility of concurrent palliative chemotherapy and low-dose fractionated radiotherapy (LD-FRT) in glioblastoma multiforme (GBM). Patients with recurrent/progressive GBM at least 3 months after the en d of primary radiotherapy received 0.3 Gy twice daily with cisplatin and fot emustine if progressing on temozolomide, or 0.4 Gy twice daily with temozolo mide if recurrent 4-6 months later (retreatment group). Newly diagnosed GBM with gross residual mass received 30 Gy with concomitant and adjuvant temozo lomide and 0.4 Gy twice daily from the second adjuvant cycle (naive group) f

or 2-4 cycles. Twenty-six patients were enrolled. In the retreatment group (n = 17; median LD-FRT total dose 7.2 Gy [range 2.4-11.6]), grade 3 or 4 hema tological toxicity was observed in 5.9% of patients. Median follow-up time w as 20 months (range 4-35). Median progression-free survival (PFS) and overal l survival (OS) from the time of recurrence or progression were 4 and 8 mont hs, respectively (OS at 6 months, 69%; at 12 months, 16.7%). In the naive gr oup (n = 9; median LD-FRT total dose 8 Gy [range 3.2-16]), grade 3 or 4 hema tological toxicity was observed in 11.1% of patients. Median follow-up time was 17 months (range 8-20)-median PFS was 9 months, with PFS at 6 months and at 1 year of 66.7% and 26.7%, respectively; and median OS was 12 months, wit h OS at 6 months and at 1 year of 77.8% and 34.6%, respectively. LD-FRT with concurrent chemotherapy was well tolerated.
Journal Title: Neuro-oncology

PUBMED ID: 21986722
DOI: doi.org/10.1007/s11060-011-0722-2
Titolo: Phase II study of carboplatin, irinotecan, and bevacizumab for bevac izumab naïve, recurrent glioblastoma.
Autori: Reardon DA., Desjardins A., Peters KB., Gururangan S., Sampson JH., McLendon RE., Herndon JE., Bulusu A., Threatt S., Friedman AH., Vredenburgh JJ., Friedman HS.
Data di Pubblicazione: 2011-10-12
Abstract: We evaluated the efficacy of carboplatin, irinotecan, and bevacizu mab among bevacizumab-naïve, recurrent glioblastoma (GBM) patients in a phas e 2, open-label, single arm trial. Forty eligible patients received carbopla tin (area under the plasma curve [AUC] 4 mg/ml-min) on day one, while bevaci zumab (10 mg/kg) and irinotecan (340 mg/m(2) for patients on CYP3A-enzyme-in ducing anti-epileptics [EIAEDs] and 125 mg/m(2) for patients not on EIAEDs) were administered on days 1 and 14 of every 28-day cycle. Patients were eval uated after each of the first two cycles and then after every other cycle. T reatment continued until progressive disease, unacceptable toxicity, non-com pliance, or voluntary withdrawal. The primary endpoint was progression-free survival at 6 months (PFS-6) and secondary endpoints included safety and med ian overall survival (OS). All patients had progression after standard thera py. The median age was 51 years. Sixteen patients (40%) had a KPS of 90-100, while 27 (68%) were at first progression. The median time from original diag nosis was 11.4 months. The PFS-6 rate was 46.5% (95% CI: 30.4, 61.0%) and th e median OS was 8.3 months [95% confidence interval (CI): 5.9, and 10.7 mont hs]. Grade 4 events were primarily hematologic and included neutropenia and thrombocytopenia in 20 and 10%, respectively. The most common grade 3 events were neutropenia, thrombocytopenia, fatigue, and infection in 25, 20, 13, an d 10%, respectively. Eleven patients (28%) discontinued study therapy due to toxicity and 17 patients (43%) required dose modification. One patient died due to treatment-related intestinal perforation. The addition of carboplatin and irinotecan to bevacizumab significantly increases toxicity but does not improve anti-tumor activity to that achieved historically with single-agent bevacizumab among bevacizumab-naïve, recurrent GBM patients. (ClinicalTrials .gov number NCT00953121).
Journal Title: Journal of neuro-oncology

PUBMED ID: 21984222
DOI: doi.org/10.1007/s00280-011-1754-1
Titolo: Pharmacokinetic drug interaction between AEE788 and RAD001 causing t hrombocytopenia in patients with glioblastoma.
Autori: Reardon DA., Cloughesy T., Rich J., Alfred Yung WK., Yung L., DiLea C., Huang J., Dugan M., Mietlowski W., Maes A., Conrad C.
Data di Pubblicazione: 2011-10-11

Abstract: The coadministration of AEE788 and RAD001 in glioblastoma patients caused a clinically significant thrombocytopenia and a higher-than-expected RAD001 area under the curve concentration when dosed at 200 and 5 mg/day, respectively. After a dose reduction to AEE788 (150 mg/day) and RAD001 (5 mg qod), the combination appeared to be better tolerated.
Journal Title: Cancer chemotherapy and pharmacology

PUBMED ID: 21982454
DOI: doi.org/10.1186/1471-2407-11-432
Titolo: A phase I trial of PR-104, a pre-prodrug of the bioreductive prodrug PR-104A, given weekly to solid tumour patients.
Autori: McKeage MJ., Gu Y., Wilson WR., Hill A., Amies K., Melink TJ., Jameson MB.
Data di Pubblicazione: 2011-10-11
Abstract: Thrombocytopenia, and to a lesser extent neutropenia, was the DLT of weekly PR-104. The MTD was 675 mg/m2/week. PR-104 given weekly may be a suitable protocol for further clinical evaluation as a short course of treatment with fractionated radiotherapy or haematopoietic stem cell support, as its duration of dosing is restricted by delayed-onset and protracted thrombocytopenia.
Journal Title: BMC cancer

PUBMED ID: 21975337
DOI: doi.org/10.1007/s12094-011-0726-6
Titolo: A safety and toxicity assessment of the administration of multiple intracerebral injections of irinotecan or doxorubicin drug-eluting beads.
Autori: Held N., Lewis AL., Hedrich HJ., Brinker T., Glage S.
Data di Pubblicazione: 2011-10-07
Abstract: OBJECTIVE Previous research in a rat glioma model has shown that the local intratumoral application of polymerbased drug-eluting beads (DEBs) loaded with doxorubicin or irinotecan suppress tumour growth and prolong survival. For translation into a clinical setting, the present experiment investigates in the healthy cat brain the local and systemic toxicity of a multiple injection shot technique. METHODS Three injection shots were placed, each at a 1 cm distance in the frontal lobe. The DEBs were suspended in an aqueous alginate excipient solution, which becomes subject to a sol-gel transition when injected into the Ca(2+)- rich brain tissue environment. Systemic and local side effects were monitored over a period of two weeks. Injection sites were histologically investigated. RESULTS Gelling of the alginate results in the permanent immobilisation of the microspheres at the implantation site. A distinct local cytotoxic effect of doxorubicin was found with intracerebral and intraventricular haemorrhages, and signs of brain tissue necrosis. In cats injected with irinotecan DEBs, such local adverse side effects did not occur. No signs of systemic toxicity were found with both chemotherapeutics. DISCUSSION We conclude that the multiple injection shot technique with irinotecan DEBs meets feasibility criteria and safety requirements for a clinical application.
Journal Title: Clinical & translational oncology : official publication of the Federation of Spanish Oncology Societies and of the National Cancer Institute of Mexico

PUBMED ID: 21968944
DOI: doi.org/10.1007/s11060-011-0721-3
Titolo: O^6-methylguanine-DNA methyltransferase promoter methylation in 45 primary central nervous system lymphomas: quantitative assessment of methylation and response to temozolomide treatment.

Autori: Adachi J., Mishima K., Wakiya K., Suzuki T., Fukuoka K., Yanagisawa T., Matsutani M., Sasaki A., Nishikawa R.
Data di Pubblicazione: 2011-10-05
Abstract: Favorable responses to temozolomide chemotherapy have recently bee n reported in primary central nervous system lymphoma (PCNSL) patients who a re refractory to high-dose methotrexate therapy. The gene encoding the DNA r epair enzyme O (6)-methylguanine-DNA methyltransferase (MGMT) is transcripti onally silenced by promoter methylation in several human tumors, including g liomas and systemic lymphomas. MGMT promoter methylation is also a prognosti c marker in glioblastoma patients treated with temozolomide. To validate tem ozolomide treatment in PCNSL, we applied methylation-sensitive high resoluti on melting (MS-HRM) analysis to quantitate MGMT methylation in PCNSL. MGMT p romoter methylation was detected in tumors from 23 (51%) of 45 PCNSL patient s, 11 of which were considered to have high (more than 70.0%) methylation st atus. Of the five recurrent PCNSLs treated with temozolomide, four cases res ponded, with three achieving complete response and one, a partial response. All four responsive PCNSLs had methylated MGMT promoters, whereas the non-re sponsive recurrent PCNSL did not. Thus, the use of quantitative MS-HRM analy sis for the detection of MGMT promoter methylation has been suggested in PCN SL for the first time. The assay allows rapid and high-throughput evaluation of the MGMT methylation status, and seems to be promising in clinical settin gs. MGMT promoter methylation may become a useful marker for predicting the response of PCNSLs to temozolomide.
Journal Title: Journal of neuro-oncology

PUBMED ID: 21961538
DOI: doi.org/10.3171/2011.7.PEDS11179
Titolo: Concomitant intraventricular colloid cyst and low-grade astrocytoma of the brainstem in a 16-year-old boy.
Autori: Amirjamshidi A., Amiri RS., Alimohamadi M., Abbassioun K.
Data di Pubblicazione: 2011-10-04
Abstract: Multiple primary brain tumors are commonly observed in patients wi th a history of brain radiation therapy or neurofibromatosis. The concomitan t presence of 2 different types of brain tumors in a single location or cham ber is a very rare clinical presentation in the absence of such a predisposi ng factor. The authors report on the case of a 16-year-old boy presenting wi th different types of brain tumors in 2 ventricular chambers concomitantly. This boy had a medium-sized colloid cyst of the third ventricle and a large fibrillary astrocytoma fungating from the brainstem into the floor of the fo urth ventricle. The lesions were successfully excised in 2 separate surgerie s. Radiotherapy was used as the adjuvant mode of therapy. There has been no sign of tumor recurrence after 16 months of follow-up. Clinical awareness an d recognition of such a combination of tumors is important because they will dictate special treatment strategies depending on the individual biological aggressiveness of each tumor.
Journal Title: Journal of neurosurgery. Pediatrics

PUBMED ID: 21954442
DOI: doi.org/10.1093/neuonc/nor145
Titolo: Phase I trial of sorafenib in patients with recurrent or progressive malignant glioma.
Autori: Nabors LB., Supko JG., Rosenfeld M., Chamberlain M., Phuphanich S., Batchelor T., Desideri S., Ye X., Wright J., Gujar S., Grossman SA., Grossma n SA.
Data di Pubblicazione: 2011-09-29
Abstract: Sorafenib is an inhibitor of multiple kinases that has demonstrate d antiproliferative and antiangiogenic activity in a number of in vitro and in vivo model systems. A phase I study was conducted to determine the maximu

m tolerated dose (MTD) of sorafenib in patients with recurrent malignant gli oma. Sorafenib was given orally, twice a day (BID), continuously in 28-day c ycles. The dose was escalated in 2 groups of patients stratified by use of e nzyme-inducing antiseizure drugs (± EIASDs). Dose-limiting toxicity (DLT) wa s defined as any grades 3-4 nonhematological toxicity, grade 4 hematological toxicity, and febrile neutropenia. The number of evaluable patients enrolled in the +EIASD and -EIASD arms were 23 and 24, respectively. DLTs were predom inantly dermatological and gastrointestinal effects, as observed in previous clinical trials of sorafenib. The MTD was 600 mg BID for patients receiving EIASDs and 800 mg BID for those who were not. The plasma pharmacokinetics of sorafenib were not significantly affected by the concurrent administration o f EIASDs. The MTD of sorafenib given orally BID on a continuous basis was es tablished as 600 mg BID in patients with malignant glioma who were concurren tly receiving EIASDs and 800 mg BID in those who were not. Further evaluatio n is warranted of sorafenib at the recommended MTD against recurrent or prog ressive malignant glioma in combination with other molecularly targeted drug s or in the newly diagnosed setting concurrent with chemoradiation.
Journal Title: Neuro-oncology

PUBMED ID: 21943399
DOI: doi.org/10.1186/1748-717X-6-121
Titolo: Evaluation of early imaging response criteria in glioblastoma multif orme.
Autori: Gladwish A., Koh ES., Hoisak J., Lockwood G., Millar BA., Mason W., Yu E., Laperriere NJ., Ménard C.
Data di Pubblicazione: 2011-09-28
Abstract: We show that while a subjective interpretation of early radiologic al progression from baseline is generally associated with poor outcome, true progressors cannot be distinguished from pseudoprogressors. In contrast, the magnitude of early imaging volumetric response may be a predictive and quant itative metric of favorable outcome.
Journal Title: Radiation oncology (London, England)

PUBMED ID: 23905037
DOI: Mancante
Titolo: Potential clinical role of telomere length in human glioblastoma.
Autori: La Torre D., Aguennouz M., Conti A., Giusa M., Raffa G., Abbritti RV ., Germano' A., Angileri FF.
Data di Pubblicazione: 2013-08-02
Abstract: Glioblastoma Multiforme (GBM) is the most common and lethal of hum an primary central nervous system (CNS) tumors. Due to the tumour's intrinsi c clinical and molecular heterogeneity, choice of initial treatment, predict ion of survival, stratification of patients, prediction and monitoring of re sponse to therapy, represent some of the greatest challenges in the manageme nt of GBM patients. Patients, despite optimal surgery, radiation and chemoth erapy, still have a median survival of 14-16 months. A reason for this disma l prognosis is because of the relative inaccuracy of current prognostic mark ers, so far based on clinical or pathological variables. Molecular markers t hat effectively predict response to therapy and survival outcomes are limite d. Consequently, there is a strong need to develop novel and independent mar kers of prognosis. Ideal biomarkers for solid tumors would serve one or more important functions. Telomeres, guanine-rich tandem DNA repeats of the chrom osomal end, provide chromosomal stability, regulates important cellular proc esses, and seem to be implicated in human carcinogenesis. Recently, telomere s have been shown either to be associated with clinical markers of disease p rogression or to be independent markers of cancer prognosis in solid tumours , including GBM. Nevertheless, a corresponding comprehensive discussion of t hese promising developments in brain tumours has not yet been available in t

he literature. Therefore, here we reviewed studies focused on the assessment of telomeric length in brain tumours with the aim to emphasized those findin gs indicating a potential clinical role of telomeres in GBM. With the aim to enhance the awareness of the potential clinical role of telomeres' length in formation in GBM, using a southern blot analysis, telomeric length in excise d tumour samples was analyzed. Moreover, an attempt to correlated telomere l ength with patients' overall survival, was also performed. The findings here reviewed shows some contradictory results, due to different tissues used as controls, but mainly to cellular and molecular heterogeneity in GBMs that dr ive molecular mechanisms controlling telomere length, included telomerase an d Alternative Lengthening of Telomeres (ALT), through multiple mechanisms. H owever, overall these studies, including our own, are consistent with the hy pothesis that GBMs' telomeres were always shorter when compared with Normal Brain Tissue (NBT), and together with higher telomerase activity seem to be associated with malignancy and poor outcome; while tumours with ALT phenotyp e have longer telomeres, "less malignant" behaviour and better prognosis. We conclude that, although not entirely consistent in the type of telomere alte ration, i.e., attrition vs. elongation, and unclear on the underlying mechan isms, multiple studies in brain tumours have shown that telomere dysfunction s are associated with parameters of clinical outcome in patients with GBMs a nd therefore will be part of novel risk assessment and prognostic modalities for patients with these still dismal disease.
Journal Title: Translational medicine @ UniSa

PUBMED ID: 21870118
DOI: doi.org/10.1007/s11060-011-0698-y
Titolo: A phase II trial of thalidomide and procarbazine in adult patients w ith recurrent or progressive malignant gliomas.
Autori: Ruiz J., Case D., Enevold G., Rosdhal R., Tatter SB., Ellis TL., McQ uellon RP., McMullen KP., Stieber VW., Shaw EG., Lesser GJ.
Data di Pubblicazione: 2011-08-27
Abstract: Thalidomide and procarbazine have demonstrated single agent activi ty against malignant gliomas (MG). We evaluated the combination of thalidomi de and procarbazine with a single arm phase II trial in adults with recurren t or progressive MG. Procarbazine was given at a dose of 250 mg/m(2)/d × 5da y q 28 days. Thalidomide was administered at a dose of 200 mg/day continuous ly. Intrapatient dose escalation of thalidomide was attempted (increase by 1 00 mg/day weekly as tolerated) to a maximum of 800 mg/day. The primary outco me was tumor response, assessed by MRI and CT. Secondary outcomes were progr ession free survival (PFS), overall survival (OS) and toxicity. In addition, quality of life questionnaires were performed at baseline and prior to each odd cycle in all treated patients. Eighteen patients (median age of 50) were accrued and received a total of 36 cycles (median 2) of therapy. The median maximum thalidomide dose achieved was 400 mg (range 0-800). No complete or p artial responses were seen. One patient (6%) experienced stable disease, fou rteen (78%) progressed as best response and three (17%) were not evaluable f or response. Median time to progression was 2.1 months (95% CI, 1.5-2.5). Se venteen patients have died (one patient lost to follow-up after progression) ; median survival from enrollment was 7.6 months (95% CI, 3.5-9.4). Grade 3/ 4 drug related toxicity was minimal. Quality of life diminished over time. T he combination of thalidomide and procarbazine demonstrated no efficacy in t his trial.
Journal Title: Journal of neuro-oncology

PUBMED ID: 21868412
DOI: doi.org/10.1093/neuonc/nor100
Titolo: Stereotactic brachytherapy of low-grade cerebral glioma after tumor resection.

Autori: Suchorska B., Ruge M., Treuer H., Sturm V., Voges J.
Data di Pubblicazione: 2011-08-27
Abstract: The purpose of this study was to assess the impact of stereotactic brachytherapy (SBT) on survival time and outcome when applied after resectio n of low-grade glioma (LGG) of World Health Organization grade II. From Janu ary 1982 through December 2006 we treated 1024 patients who had glioma with stereotactic implantation of iodine-125 seeds and SBT in accordance with a p rospective protocol. For the present analysis, we selected 95 of 277 patient s with LGG, in whom SBT was applied to treat progressive (43 patients) or re current (52 patients) tumor after resection. At 24 months after seed implant ation, the tumor response rate was 35.9%, and the tumor control rate was 97. 3%. The median progression-free-survival (PFS) duration after SBT was 52.7 ± 7.1 months. Five-year and 10-year PFS probabilities were 43.4% and 10.7%, re spectively. Malignant tumor transformation, the diagnosis "astrocytoma," and tumor volume >20 mL were significantly associated with reduced PFS. Tumor pr ogression or relapse after SBT (53 of 95 patients) was treated with tumor re section, a second SBT, chemotherapy, and/or radiotherapy. The median overall survival duration (from the first diagnosis of LGG until the patient's last contact) was 245.0 ± 4.9 months. Patients still under observation after seed implantation had a median follow-up time of 156.4 ± 55.7 months. Perioperati ve transient morbidity was 1.1%, and the frequency of permanent morbidity ca used by SBT was 3.3%. In conclusion, SBT of recurrent or progressive LGG aft er resection located in functionally critical brain areas has high local eff icacy and comparably low morbidity. Referred to individually adopted glioma treatment concepts SBT provides a reasonably long PFS, thus improving overal l survival. In selected patients, SBT can lead to delays in the application of chemotherapy and/or radiotherapy.
Journal Title: Neuro-oncology

PUBMED ID: 21865400
DOI: doi.org/10.1093/neuonc/nor091
Titolo: A phase II trial of single-agent bevacizumab in patients with recurr ent anaplastic glioma.
Autori: Kreisl TN., Zhang W., Odia Y., Shih JH., Butman JA., Hammoud D., Iwa moto FM., Sul J., Fine HA.
Data di Pubblicazione: 2011-08-26
Abstract: The purpose of this study was to evaluate the activity of single-a gent bevacizumab in patients with recurrent anaplastic glioma and assess cor relative advanced imaging parameters. Patients with recurrent anaplastic gli oma were treated with bevacizumab 10 mg/kg every 2 weeks. Complete patient e valuations were repeated every 4 weeks. Correlative dynamic contrast-enhance d MR and (18)fluorodeoxyglucose PET imaging studies were obtained to evaluat e physiologic changes in tumor and tumor vasculature at time points includin g baseline, 96 h after the first dose, and after the first 4 weeks of therap y. Median overall survival was 12 months (95% confidence interval [CI]: 6.08 -22.8). Median progression-free survival was 2.93 months (95% CI: 2.01-4.93) , and 6-month progression-free survival was 20.9% (95% CI: 10.3%-42.5%). Thi rteen (43%) patients achieved a partial response. The most common grade ≥ 3 treatment-related toxicities were hypertension, hypophosphatemia, and thromb oembolism. Single-agent bevacizumab produces significant radiographic respon se in patients with recurrent anaplastic glioma but did not meet the 6-month progression-free survival endpoint. Early change in enhancing tumor volume a t 4 days after start of therapy was the most significant prognostic factor f or overall and progression-free survival.
Journal Title: Neuro-oncology

PUBMED ID: 21859839
DOI: doi.org/10.1158/1535-7163.MCT-11-0268

Titolo: A molecular screening approach to identify and characterize inhibito rs of glioblastoma stem cells.
Autori: Visnyei K., Onodera H., Damoiseaux R., Saigusa K., Petrosyan S., De Vries D., Ferrari D., Saxe J., Panosyan EH., Masterman-Smith M., Mottahedeh J., Bradley KA., Huang J., Sabatti C., Nakano I., Kornblum HI.
Data di Pubblicazione: 2011-08-24
Abstract: Glioblastoma (GBM) is among the most lethal of all cancers. GBM co nsist of a heterogeneous population of tumor cells among which a tumor-initi ating and treatment-resistant subpopulation, here termed GBM stem cells, hav e been identified as primary therapeutic targets. Here, we describe a high-t hroughput small molecule screening approach that enables the identification and characterization of chemical compounds that are effective against GBM st em cells. The paradigm uses a tissue culture model to enrich for GBM stem ce lls derived from human GBM resections and combines a phenotype-based screen with gene target-specific screens for compound identification. We used 31,62 4 small molecules from 7 chemical libraries that we characterized and ranked based on their effect on a panel of GBM stem cell-enriched cultures and thei r effect on the expression of a module of genes whose expression negatively correlates with clinical outcome: MELK, ASPM, TOP2A, and FOXM1b. Of the 11 c ompounds meeting criteria for exerting differential effects across cell type s used, 4 compounds showed selectivity by inhibiting multiple GBM stem cells -enriched cultures compared with nonenriched cultures: emetine, n-arachidono yl dopamine, n-oleoyldopamine (OLDA), and n-palmitoyl dopamine. ChemBridge c ompounds #5560509 and #5256360 inhibited the expression of the 4 mitotic mod ule genes. OLDA, emetine, and compounds #5560509 and #5256360 were chosen fo r more detailed study and inhibited GBM stem cells in self-renewal assays in vitro and in a xenograft model in vivo. These studies show that our screenin g strategy provides potential candidates and a blueprint for lead compound i dentification in larger scale screens or screens involving other cancer type s.
Journal Title: Molecular cancer therapeutics

PUBMED ID: 21858608
DOI: doi.org/10.1007/s11060-011-0677-3
Titolo: Treatment of recurrent diffuse intrinsic pontine glioma: the MD Ande rson Cancer Center experience.
Autori: Wolff JE., Rytting ME., Vats TS., Zage PE., Ater JL., Woo S., Kuttes ch J., Ketonen L., Mahajan A.
Data di Pubblicazione: 2011-08-23
Abstract: Recurrent diffuse intrinsic pontine gliomas (DIPG) are traditional ly treated with palliative care since no effective treatments have been desc ribed for these tumors. Recently, clinical studies have been emerging, and i ndividualized treatment is attempted more frequently. However, an informativ e way to compare the treatment outcomes has not been established, and histor ical control data are missing for recurrent disease. We conducted a retrospe ctive chart review of patients with recurrent DIPG treated between 1998 and 2010. Response progression-free survival and possible influencing factors we re evaluated. Thirty-one patients were identified who were treated in 61 tre atment attempts using 26 treatment elements in 31 different regimens. The mo st frequently used drugs were etoposide (14), bevacizumab (13), irinotecan (13), nimotuzumab (13), and valproic acid (13). Seven patients had repeat rad iation therapy to the primary tumor. Response was recorded after 58 treatmen t attempts and was comprised of 0 treatment attempts with complete responses , 7 with partial responses, 20 with stable diseases, and 31 with progressive diseases The median progression-free survival after treatment start was 0.16 years (2 months) and was found to be correlated to the prior time to progres sion but not to the number of previous treatment attempts. Repeat radiation resulted in the highest response rates (4/7), and the longest progression-fr ee survival. These data provide a basis to plan future clinical trials for r

ecurrent DIPG. Repeat radiation therapy should be tested in a prospective cl inical study.
Journal Title: Journal of neuro-oncology

PUBMED ID: 21845585
DOI: doi.org/10.5137/1019-5149.JTN.2947-10.0
Titolo: Cerebral tuberculoma mimicking high grade glial tumor.
Autori: Suslu HT., Bozbuga M., Bayindir C.
Data di Pubblicazione: 2011-08-17
Abstract: Tuberculosis has been an important public health problem in both d eveloping and develop nations. Tuberculosis of the central nervous system is rare. Tuberculosis meningitis and tuberculoma are the two most important man ifestations of tuberculosis of the CNS. Intracranial tuberculomas may be sol itary or multiple. Solitary tuberculomas may be indistinguishable from crani al abscess or primary brain tumor. It is necessary to rule out tuberculoma i n patients with intracranial mass lesions. We present a case of tuberculoma mimicking a high grade glial tumor on magnetic resonance imaging and clinica l presentation. A 30-year-old woman presented with one-month history of epil epsy. Cranial magnetic resonance imaging showed a left occipital peripheral ring-enhanced lesion with central necrosis. There was a strong suspicion of glial tumor. The lesion was totally excised with left occipital craniotomy. Histological examination of mass revealed a tuberculoma. The patient was tre ated with antituberculous chemotherapy.
Journal Title: Turkish neurosurgery

PUBMED ID: 21827415
DOI: doi.org/10.2174/138161211797249189
Titolo: The role of integrins in glioma biology and anti-glioma therapies.
Autori: Tabatabai G., Tonn JC., Stupp R., Weller M.
Data di Pubblicazione: 2011-08-11
Abstract: The tumor environment is critical for tumor maintenance and progre ssion. Integrins are a large family of cell surface receptors mediating the interaction of tumor cells with their microenvironment and play important ro les in glioma biology, including migration, invasion, angiogenesis and tumor stem cell anchorage. Here, we review preclinical and clinical data on integr in inhibition in malignant gliomas. Various pharmacological approaches to th e modulation of integrin signaling have been explored including antibodies a nd peptide-based agents. Cilengitide, a cyclic RGD-mimetic peptide of αvβ3 a nd αvβ5 integrins is in advanced clinical development in glioblastoma. Cilen gitide had only limited activity as a single agent in glioblastoma, but, whe n added to standard radiochemotherapy, appeared to prolong progression-free and overall survival in patients with newly diagnosed glioblastomas and meth ylation of the promoter of the O^6 methylguanine methyltransferase (MGMT) gen e. MGMT gene promoter methylation in turn predicts benefit from alkylating c hemotherapy. A phase III randomized clinical trial in conjunction with stand ard radiochemotherapy in newly diagnosed glioblastoma patients with MGMT gen e promoter methylation has recently completed accrual (EORTC 26071-22072). A companion trial explores a dose-escalated regimen of cilengitide added to ra diotherapy plus temozolomide in patients without MGMT gene promoter methylat ion. Promising results in these trials would probably result in a broader in terest in integrins as targets for glioma therapy and hopefully the developm ent of a broader panel of anti-integrin agents.
Journal Title: Current pharmaceutical design

PUBMED ID: 21813279
DOI: doi.org/10.1016/j.jocn.2011.02.026

Titolo: Phase 2 trial of temozolomide and pegylated liposomal doxorubicin in the treatment of patients with glioblastoma multiforme following concurrent radiotherapy and chemotherapy.
Autori: Ananda S., Nowak AK., Cher L., Dowling A., Brown C., Simes J., Rosenthal MA., Rosenthal MA.
Data di Pubblicazione: 2011-08-05
Abstract: Concurrent and post-radiotherapy temozolomide (T) significantly improves survival in patient with newly diagnosed glioblastoma multiforme. We aimed to assess the activity of the combination of T and pegylated liposomal doxorubicin (PLD) in this population. A combination of T (days 1-5, 200mg/m(2) orally) and PLD (day 1, 40 mg/m(2) intravenous) was given every 4 weeks for six cycles following chemo-radiotherapy as a post-operative treatment. The primary endpoint was 6-month progression free survival (6PFS). Of the 40 patients who enrolled (53 years median age, 73% male), the 6PFS was 58% (95% confidence interval [CI], 41-72%). The median time to progression was 6.2 months (95% CI, 5.6-8.0 months) and overall survival (OS) was 13.4 months (95% CI, 12.7-15.8 months). Thirty-four patients had measurable disease: one had a complete response (3%), 28 had stable disease (82%), and five had progressive disease (15%). Treatment was well tolerated: hematological toxicity included grade 3 neutropenia (8%). Grade 3 non-hematologic toxicity included nausea and vomiting (8%) and palmar-plantar toxicity (5%). We concluded that combination T and PLD is well tolerated but does not add significant clinical benefit regarding 6PFS and OS.
Journal Title: Journal of clinical neuroscience : official journal of the Neurosurgical Society of Australasia

PUBMED ID: 21807073
DOI: doi.org/10.1016/j.brainresbull.2011.07.010
Titolo: Candidate genes influencing sensitivity and resistance of human glioblastoma to Semustine.
Autori: Zhao Z., Liu Y., He H., Chen X., Chen J., Lu YC.
Data di Pubblicazione: 2011-08-03
Abstract: Bioinformatics may help excavate and analyze large amounts of data in microarrays by means of rigorous experimental planning, scientific statistical analysis and collection of complete data about survival of GBM patients. In the present study, a novel differential gene expression pattern was constructed and advanced study will provide new targets for chemosensitivity of GBM.
Journal Title: Brain research bulletin

PUBMED ID: 21792866
DOI: doi.org/10.1002/cncr.26381
Titolo: Bevacizumab and daily temozolomide for recurrent glioblastoma.
Autori: Desjardins A., Reardon DA., Coan A., Marcello J., Herndon JE., Bailey L., Peters KB., Friedman HS., Vredenburgh JJ.
Data di Pubblicazione: 2011-07-28
Abstract: The current study demonstrated that a regimen of combined daily temozolomide and biweekly bevacizumab had some activity and was well tolerated. However, the results obtained in this study were inferior to those observed in studies of bevacizumab monotherapy and of combined irinotecan and bevacizumab therapy. The current patient population was more heterogeneous and was pretreated more heavily than patients in previous studies.
Journal Title: Cancer

PUBMED ID: 21748491
DOI: doi.org/10.1007/s11060-011-0657-7

Titolo: Using different schedules of Temozolomide to treat low grade gliomas : systematic review of their efficacy and toxicity.
Autori: Lashkari HP., Saso S., Moreno L., Athanasiou T., Zacharoulis S.
Data di Pubblicazione: 2011-07-13
Abstract: Low grade gliomas (LGG) contribute to 50% of all central nervous t umors in children and 15% of all gliomas in adults. Temozolomide (TMZ) is an oral alkylating agent with activity in high and LGG. Various regimens of TMZ are currently in use. We attempted to assess the impact of different TMZ reg imens on the treatment of LGG. A systematic review of the literature identif ied all the studies published in Pubmed, EMBASE and Cochrane databases which met the inclusion criteria. The primary outcome measure was the impact of di fferent TMZ regimens on the 12 month progression-free survival (PFS) rates o f patients diagnosed with progressive LGG. Secondary outcome measures looked at the ability of the three regimens to elicit an objective response and the associated toxicity. Statistical pooling and calculation of weighted mean av erage of each proportion (WMAP) was conducted using a random-effects model. 18 studies (736 patients) were analyzed. PFS at 12 months revealed a WMAP of 0.61 (95% CI 0.44-0.78) for regimen A, 0.59 (0.28-0.89) for regimen B, and 0 .91 (95% CI 0.83-0.99) for regimen C (Regimen A--200 mg/m(2)/day for 5 days, repeated every 4 weeks; B--75 mg/m(2)/day for 21 days repeated every 4 weeks ; C--75 mg/m(2)/day for 7 weeks with 4 weeks of every 11 weeks). In terms of objective response, WMAP were 0.19 (95% 0.13-0.25), 0.27 (95% CI 0.15-0.39) and 0.21 (95% CI 0.10-0.32) for regimen A, B, C respectively. When analyzing hematological toxicity, WMAPs were 0.14 (95% 0.11-0.18), 0.35 (0.14-0.56) an d 0.23 (95% CI 0.03-0.43). The bulk of evidence originates from the standard 5 day/month regimen A but with a lack of comparative studies. Analysis revea led significant heterogeneity. Although there is possibly an indication that metronomic regimens of TMZ result in better PFS and response rate when compa red to the conventional standard 5 day regimen, insufficient available data and study heterogeneity preclude any safe conclusions. Well designed randomi zed controlled clinical trials are needed to establish the efficacy of metro nomic regimens of TMZ in LGGs.
Journal Title: Journal of neuro-oncology

PUBMED ID: 21740923
DOI: doi.org/10.1016/j.pbiomolbio.2011.06.007
Titolo: Coupling biomechanics to a cellular level model: an approach to pati ent-specific image driven multi-scale and multi-physics tumor simulation.
Autori: May CP., Kolokotroni E., Stamatakos GS., Büchler P.
Data di Pubblicazione: 2011-07-12
Abstract: Modeling of tumor growth has been performed according to various a pproaches addressing different biocomplexity levels and spatiotemporal scale s. Mathematical treatments range from partial differential equation based di ffusion models to rule-based cellular level simulators, aiming at both impro ving our quantitative understanding of the underlying biological processes a nd, in the mid- and long term, constructing reliable multi-scale predictive platforms to support patient-individualized treatment planning and optimizat ion. The aim of this paper is to establish a multi-scale and multi-physics a pproach to tumor modeling taking into account both the cellular and the macr oscopic mechanical level. Therefore, an already developed biomodel of clinic al tumor growth and response to treatment is self-consistently coupled with a biomechanical model. Results are presented for the free growth case of the imageable component of an initially point-like glioblastoma multiforme tumor . The composite model leads to significant tumor shape corrections that are achieved through the utilization of environmental pressure information and t he application of biomechanical principles. Using the ratio of smallest to l argest moment of inertia of the tumor material to quantify the effect of our coupled approach, we have found a tumor shape correction of 20% by coupling biomechanics to the cellular simulator as compared to a cellular simulation

without preferred growth directions. We conclude that the integration of the two models provides additional morphological insight into realistic tumor gr owth behavior. Therefore, it might be used for the development of an advance d oncosimulator focusing on tumor types for which morphology plays an import ant role in surgical and/or radio-therapeutic treatment planning.
Journal Title: Progress in biophysics and molecular biology

PUBMED ID: 21715567
DOI: doi.org/10.1158/1078-0432.CCR-10-3124
Titolo: Regression of glioma in rat models by intranasal application of parv ovirus h-1.
Autori: Kiprianova I., Thomas N., Ayache A., Fischer M., Leuchs B., Klein M. , Rommelaere J., Schlehofer JR.
Data di Pubblicazione: 2011-07-01
Abstract: In view of an ongoing clinical trial on the use of H-1PV for oncol ytic virotherapy of glioma, the option of applying the virus intranasally ma y be a valuable alternative to invasive routes of infection.
Journal Title: Clinical cancer research : an official journal of the America n Association for Cancer Research

PUBMED ID: 21715171
DOI: doi.org/10.1016/j.jocn.2010.11.034
Titolo: A phase I/II clinical trial investigating the adverse and therapeuti c effects of a postoperative autologous dendritic cell tumor vaccine in pati ents with malignant glioma.
Autori: Chang CN., Huang YC., Yang DM., Kikuta K., Wei KJ., Kubota T., Yang WK.
Data di Pubblicazione: 2011-07-01
Abstract: Previous clinical trials of dendritic cell (DC)-based immunotherap y in patients with glioblastoma multiforme (GBM) have reported induction of systemic immune responses and prolonged survival. From 2003 to 2005, we perf ormed a clinical trial in which patients with malignant glioma underwent sur gery for maximal cytoreduction followed by a 6-month 10-injection course of autologous DC-tumor vaccine therapy, each injection containing 1-6×10(7) DC. Of the 17 treated patients (16 with World Health Organization grade IV and o ne with grade III glioma), eight (47.1%) had an initial transient elevation in aspartate aminotransferase (AST)/alanine aminotransferase (ALT). Vaccinat ion caused some tumor shrinkage and increased concentration of tumor-infiltr ating CD8(+) lymphocytes. Median survival and 5-year survival were 525 days and 18.8%, respectively, for 16 patients with grade IV glioma (381 days and 12.5% for eight newly diagnosed; 966 days and 25% for eight relapsed patient s) compared to 380 days and 0% for 63 historical control patients. We conclu ded that autologous DC-tumor immunotherapy benefits patients with malignant glioma but may cause transient but reversible elevation of serum AST/ALT lev els.
Journal Title: Journal of clinical neuroscience : official journal of the Ne urosurgical Society of Australasia

PUBMED ID: 21712019
DOI: Mancante
Titolo: Stem cell-mediated gene therapies for malignant gliomas: a promising targeted therapeutic approach?
Autori: Tabatabai G., Wick W., Weller M.
Data di Pubblicazione: 2011-06-30
Abstract: Glioblastomas are aggressive intrinsic brain tumors. The median ov erall survival does not exceed 15 months despite surgical resection, radioth erapy, and chemotherapy even in selected clinical trial populations. One rea

son for this poor outcome is the characteristic infiltrative growth pattern of glioblastomas with tumor cells deeply infiltrating into the normal brain parenchyma and thereby escaping surgical debulking and involved-field radiation therapy. Novel therapeutic strategies are urgently needed including those that target disseminated tumor cells, too. In this regard, the application of adult stem cells as cellular vehicles for the delivery of therapeutic molecules has emerged during the last decade as an experimental approach. Adult stem cells with a tropism for gliomas include neural stem and progenitor cells, mesenchymal stem cells, hematopoietic progenitor cells, and endothelial progenitor cells. Importantly, these candidate cellular carriers also localize to sites of hypoxia and invasive tumor borders which are usually not targeted by currently available therapeutic approaches. Stem cell-based therapeutic approaches could therefore help to overcome some of the current limitations of radio- and chemotherapy and may circumvent toxicity to normal resident cells of the central nervous system. The development of neural stem- and progenitor-based therapies is advanced with a currently ongoing phase I clinical study. We review rationale, achievements, and future challenges in this field.
Journal Title: Discovery medicine

PUBMED ID: 21707241
DOI: doi.org/10.3109/02688697.2011.583365
Titolo: Differential expression of a novel voltage gated potassium channel--Kv 1.5 in astrocytomas and its impact on prognosis in glioblastoma.
Autori: Arvind S., Arivazhagan A., Santosh V., Chandramouli BA.
Data di Pubblicazione: 2011-06-29
Abstract: Kv1.5 expression occurs more in DA, when compared to high grade astrocytoma. GBM patients with higher Kv1.5 expression had better survival, though not reaching statistical significance.
Journal Title: British journal of neurosurgery

PUBMED ID: 21610707
DOI: doi.org/10.1038/bjc.2011.174
Titolo: Predicting the outcome of grade II glioma treated with temozolomide using proton magnetic resonance spectroscopy.
Autori: Guillevin R., Menuel C., Taillibert S., Capelle L., Costalat R., Abud L., Habas C., De Marco G., Hoang-Xuan K., Chiras J., Vallée JN.
Data di Pubblicazione: 2011-05-26
Abstract: The (1)H-MRS profile changes more widely and rapidly than tumour volume during the response and relapse phases, and represents an early predictive factor of outcome over 14 months of follow-up. Thus, (1)H-MRS may be a promising, non-invasive tool for predicting and monitoring the clinical response to TMZ.
Journal Title: British journal of cancer

PUBMED ID: 21590996
DOI: doi.org/10.1002/jmri.22563
Titolo: Detection of early response to temozolomide treatment in brain tumors using hyperpolarized 13C MR metabolic imaging.
Autori: Park I., Bok R., Ozawa T., Phillips JJ., James CD., Vigneron DB., Ronen SM., Nelson SJ.
Data di Pubblicazione: 2011-05-19
Abstract: The results from this study suggest that metabolic imaging with hyperpolarized [1-(13)C]-pyruvate may provide a unique tool that clinical neuro-oncologists can use in the future to monitor tumor response to therapy for patients with brain tumors.
Journal Title: Journal of magnetic resonance imaging : JMRI

PUBMED ID: 21590689
DOI: doi.org/10.1002/cncr.26188
Titolo: Phase 2 study of carboplatin, irinotecan, and bevacizumab for recurrent glioblastoma after progression on bevacizumab therapy.
Autori: Reardon DA., Desjardins A., Peters KB., Vredenburgh JJ., Gururangan S., Sampson JH., McLendon RE., Herndon JE., Coan A., Threatt S., Friedman AH., Friedman HS.
Data di Pubblicazione: 2011-05-19
Abstract: Carboplatin, irinotecan, and bevacizumab was associated with modest activity and adequate safety among recurrent GBM patients who progressed on bevacizumab previously.
Journal Title: Cancer

PUBMED ID: 21558404
DOI: doi.org/10.1158/1078-0432.CCR-10-3194
Titolo: Molecular markers in low-grade gliomas: predictive or prognostic?
Autori: Hartmann C., Hentschel B., Tatagiba M., Schramm J., Schnell O., Seidel C., Stein R., Reifenberger G., Pietsch T., von Deimling A., Loeffler M., Weller M., Weller M.
Data di Pubblicazione: 2011-05-12
Abstract: None of the parameters are sensitive prognostic biomarkers in WHO grade II glioma patients who do not receive radiotherapy or chemotherapy after surgery. Limitations of this study include the selection of patients with favorable outcome, the nonrandomized allocation of treatment, and the insufficient sample size to distinguish between effects of radiotherapy versus chemotherapy. Regardless of histology, IDH1 mutation status is the strongest prognostic marker for OS.
Journal Title: Clinical cancer research : an official journal of the American Association for Cancer Research

PUBMED ID: 21558074
DOI: doi.org/10.1093/neuonc/nor024
Titolo: Neurocognitive function in patients with recurrent glioblastoma treated with bevacizumab.
Autori: Wefel JS., Cloughesy T., Zazzali JL., Zheng M., Prados M., Wen PY., Mikkelsen T., Schiff D., Abrey LE., Yung WK., Paleologos N., Nicholas MK., Jensen R., Vredenburgh J., Das A., Friedman HS.
Data di Pubblicazione: 2011-05-12
Abstract: Neurocognitive decline is a frequent adverse effect of glioblastoma. Antitumor therapies that are efficacious, as measured by traditional endpoints such as objective response (OR) and progression-free survival (PFS), and have beneficial effects on neurocognitive function (NCF) are of clinical benefit to these patients. We evaluated neurocognitive changes across time in 167 patients with recurrent glioblastoma treated with bevacizumab-based therapy in BRAIN, a phase II, randomized, multicenter trial. All patients underwent MRI and neurocognitive testing at baseline and every 6 weeks thereafter. Memory, visuomotor scanning speed, and executive function were evaluated using the Hopkins Verbal Learning Test-Revised, the Trail Making Test, and the Controlled Oral Word Association test, respectively. NCF relative to baseline for patients with an OR, PFS >6 months, or disease progression was evaluated at time of OR, 24 weeks, and time of progression, respectively. For patients with an OR or PFS >6 months, median standardized test scores were examined from baseline to week 24. Most patients with an OR or PFS >6 months had poorer NCF performance compared to the general population at baseline and had improved or stable NCF at the time of response or at the 24-week assessment, respectively; most patients with progressive disease had neurocognitive

decline at the time of progression. For patients with an OR or PFS >6 months , median standardized test scores were largely stable across the first 24 we eks on study. Neurocognitive testing was an objective, valid, and feasible m ethod of monitoring NCF in patients with recurrent glioblastoma.
Journal Title: Neuro-oncology

PUBMED ID: 21538632
DOI: doi.org/10.1002/nbm.1669
Titolo: Assessment of therapeutic response and treatment planning for brain tumors using metabolic and physiological MRI.
Autori: Nelson SJ.
Data di Pubblicazione: 2011-05-04
Abstract: MRI is routinely used for diagnosis, treatment planning and assess ment of response to therapy for patients with glioma. Gliomas are spatially heterogeneous and infiltrative lesions that are quite variable in terms of t heir response to therapy. Patients classified as having low-grade histology have a median overall survival of 7 years or more, but need to be monitored carefully to make sure that their tumor does not upgrade to a more malignant phenotype. Patients with the most aggressive grade IV histology have a media n overall survival of 12-15 months and often undergo multiple surgeries and adjuvant therapies in an attempt to control their disease. Despite improveme nts in the spatial resolution and sensitivity of anatomic images, there rema in considerable ambiguities in the interpretation of changes in the size of the gadolinium-enhancing lesion on T(1) -weighted images as a measure of tre atment response, and in differentiating between treatment effects and infilt rating tumor within the larger T(2) lesion. The planning of focal therapies, such as surgery, radiation and targeted drug delivery, as well as a more rel iable assessment of the response to therapy, would benefit considerably from the integration of metabolic and physiological imaging techniques into routi ne clinical MR examinations. Advanced methods that have been shown to provid e valuable data for patients with glioma are diffusion, perfusion and spectr oscopic imaging. Multiparametric examinations that include the acquisition o f such data are able to assess tumor cellularity, hypoxia, disruption of nor mal tissue architecture, changes in vascular density and vessel permeability , in addition to the standard measures of changes in the volume of enhancing and nonenhancing anatomic lesions. This is particularly critical for the int erpretation of the results of Phase I and Phase II clinical trials of novel therapies, which are increasingly including agents that are designed to have anti-angiogenic and anti-proliferative properties as opposed to having a dir ect effect on tumor cell viability.
Journal Title: NMR in biomedicine

PUBMED ID: 21531084
DOI: doi.org/10.1016/j.prp.2011.03.002
Titolo: Epidermal growth factor receptor (EGFR) and squamous cell carcinoma of the skin: molecular bases for EGFR-targeted therapy.
Autori: Uribe P., Gonzalez S.
Data di Pubblicazione: 2011-05-03
Abstract: Cutaneous squamous cell carcinoma (SCC) ranks second in the freque ncy of all skin tumors. Its incidence has risen significantly due to an incr eased sun exposure and the number of immunocompromised patients. It has a we ll-defined progression with known precursor lesions called actinic keratosis . The degree of cellular differentiation, tumor thickness, location, and oth er features has prognostic value. It has a better prognosis than mucosal SCC of the head and neck, also called head and neck squamous cell carcinoma (HNS CC). Ultraviolet light plays a fundamental role as an initiator and promoter of carcinogenesis of SCC, allowing the accumulation of genetic alterations t hat allows a selective growth advantage. The TP53 (p53) gene often mutates a

nd Ras is frequently activated, but with low frequency of mutations. Normall y, the extracellular signals determine whether the cells move from a quiesce nt state into an active proliferative state. In tumor cells an increase in t he production of growth factors and its receptors can be often seen that giv es rise to such an autocrine circuit facilitating cellular division. Recentl y, frequent mutations in the epidermal growth factor receptor (EGFR) have be en detected in lung cancer, mainly deletions in exon 19 and L858R mutation i n exon 21. These are located at the EGFR tyrosine kinase domain (TK). EGFR T K mutations produce activation of the signaling pathways downstream and pref erentially activated antiapoptotic pathways (PI3K/AKT, JAK-STAT and ERK/MAPK). These mutations are correlated with the clinical response of patients to tyrosine kinase inhibitors (gefinitib and erlotinib), because the tumor cell s are addicted to the constant activation of specific signaling pathways. Gl ioblastoma shows another EGFR mutation (EGFRvIII), corresponding to a deleti on of the extracellular domain, and it is present in 24-67% of these tumors. This variant has been found in 42% of HNSCC, related to the poor response to monoclonal antibody cetuximab. Many observations show that there are abnorma lities in the expression of epidermal growth factor receptor (EGFR) and/or i ts ligands in HNSCC with frequent activation of multiple pathways downstream EGFR, and unrelated to RAS mutation. This suggests the possibility of activa tion by mutation or overexpression of a component of the pathway located ups tream-Ras. While in other tumors, especially lung cancer and glioblastoma, t he EGFR mutations are frequent genetic events, it is unknown whether EGFR is mutated or amplified in SCC of the skin and what would be its pathogenic rol e in this malignancy and its precursors.
Journal Title: Pathology, research and practice

PUBMED ID: 21515959
DOI: doi.org/10.2176/nmc.51.319
Titolo: Pathological changes after autologous formalin-fixed tumor vaccine t herapy combined with temozolomide for glioblastoma - three case reports - .
Autori: Sakamoto N., Ishikawa E., Yamamoto T., Satomi K., Nakai K., Sato M., Enomoto T., Morishita Y., Takano S., Ohno T., Tsuboi K., Matsumura A.
Data di Pubblicazione: 2011-04-26
Abstract: Temozolomide (TMZ), an alkylating agent widely used for patients w ith glioblastoma multiforme (GBM), has the potential to enhance the acquired immune response to GBM. Here, we describe 3 cases of GBM patients treated wi th autologous formalin-fixed tumor vaccine (AFTV) combined with TMZ. All cas es demonstrated pathological changes associated with the therapy. After a 4- week break from the standard initial treatments, 1 patient with primary GBM and 2 patients with secondary GBM received adjuvant TMZ for 5 days combined with AFTV injection and were subsequently treated with multiple cycles of ad juvant TMZ for 5 days every 28 days (AFTV/TMZ therapy). Adverse effects rela ted to AFTV plus TMZ were very minor in all patients. Magnetic resonance ima ging revealed partial response in 2 patients. CD3(+)CD8(+) lymphocytes were frequently detected in surgical specimens and MIB-1 labeling index in 2 case s decreased after AFTV/TMZ therapy. AFTV/TMZ therapy is suitable for larger scale clinical trials.
Journal Title: Neurologia medico-chirurgica

PUBMED ID: 21515957
DOI: doi.org/10.2176/nmc.51.310
Titolo: Pleomorphic xanthoastrocytoma and moyamoya disease in a patient with neurofibromatosis type 1 - case report - .
Autori: Horiguchi S., Mitsuya K., Watanabe R., Yagishita S., Nakasu Y.
Data di Pubblicazione: 2011-04-26
Abstract: A 32-year-old man with familial neurofibromatosis type 1 presented with a rare case of coexisting pleomorphic xanthoastrocytoma (PXA) and moyam

oya disease manifesting as progressive right hemiparesis. Magnetic resonance (MR) imaging with gadolinium showed an enhanced mass lesion in the left basa l ganglia extending to the left parietal lobe. Preoperative angiography show ed severe stenosis of the bilateral internal carotid arteries, and moyamoya vessels. The patient underwent open biopsy. Histological examination showed the characteristic findings of PXA. After radiation therapy and chemotherapy , MR imaging showed decreased size and enhancement of the tumor, but his cli nical condition worsened with generalized convulsions and consciousness dist urbance. He died 1 year and 6 months after the first presentation. Autopsy f indings demonstrated necrosis in the main mass and tumor cell dissemination without anaplastic change. The rare combination of PXA and moyamoya disease in the basal ganglia limited treatment options. Injured moyamoya vessels and ischemic condition might have caused tumor progression and dissemination. Ra diation therapy, in combination with moyamoya disease, induced decreased cer ebral blood flow (CBF) in the left frontal lobe. Tumor dissemination, CBF de crease, and hydrocephalus led to the clinical deterioration of this patient.
Journal Title: Neurologia medico-chirurgica

PUBMED ID: 21499132
DOI: doi.org/10.1097/CJI.0b013e318215e300
Titolo: Immune response in patients with newly diagnosed glioblastoma multif orme treated with intranodal autologous tumor lysate-dendritic cell vaccinat ion after radiation chemotherapy.
Autori: Fadul CE., Fisher JL., Hampton TH., Lallana EC., Li Z., Gui J., Szcz epiorkowski ZM., Tosteson TD., Rhodes CH., Wishart HA., Lewis LD., Ernstoff MS.
Data di Pubblicazione: 2011-04-19
Abstract: Patients with glioblastoma multiforme (GBM) are profoundly immunos uppressed and may benefit from restoration of an antitumor immune response i n combination with conventional radiation therapy and temozolomide (TMZ). Th e optimal strategies to evaluate clinically relevant immune responses to tre atment have yet to be determined. The primary objective of our study was to determine immunologic response to cervical intranodal vaccination with autol ogous tumor lysate-loaded dendritic cells (DCs) in patients with GBM after r adiation therapy and TMZ. We used a novel hierarchical clustering analysis o f immune parameters measured before and after vaccination. Secondary objecti ves were to assess treatment feasibility and to correlate immune response wi th progression-free survival (PFS) and overall survival. Ten eligible patien ts received vaccination. Tumor-specific cytotoxic T-cell response measured a fter vaccination was enhanced for the precursor frequency of CD4+ T and CD4+ interferon γ-producing cells. Hierarchical clustering analysis of multiple f unctional outcomes discerned 2 groups of patients according to their immune response, and additionally showed that patients in the top quintile for at l east one immune function parameter had improved survival. There were no seri ous adverse events related to DC vaccination. All patients were alive at 6 m onths after diagnosis and the 6-month PFS was 90%. The median PFS was 9.5 mo nths and overall survival was 28 months. In patients with GBM, immune therap y with DC vaccination after radiation and TMZ resulted in tumor-specific imm une responses that were associated with prolonged survival. Our data suggest that DC vaccination in combination with radiation and chemotherapy in patien ts with GBM is feasible, safe, and may induce tumor-specific immune response s.
Journal Title: Journal of immunotherapy (Hagerstown, Md. : 1997)

PUBMED ID: 21489708
DOI: doi.org/10.1016/j.ijrobp.2010.12.074
Titolo: Safety and efficacy of stereotactic radiosurgery and adjuvant bevaci zumab in patients with recurrent malignant gliomas.

Autori: Cuneo KC., Vredenburgh JJ., Sampson JH., Reardon DA., Desjardins A., Peters KB., Friedman HS., Willett CG., Kirkpatrick JP.
Data di Pubblicazione: 2011-04-15
Abstract: The combination of salvage radiosurgery and bevacizumab to treat recurrent malignant gliomas is well tolerated and seems to be associated with improved outcomes. Prospective multiinstitutional studies are required to determine efficacy and long-term toxicity with this approach.
Journal Title: International journal of radiation oncology, biology, physics

PUBMED ID: 21432029
DOI: doi.org/10.1007/s12325-011-0007-3
Titolo: AVAglio: Phase 3 trial of bevacizumab plus temozolomide and radiotherapy in newly diagnosed glioblastoma multiforme.
Autori: Chinot OL., de La Motte Rouge T., Moore N., Zeaiter A., Das A., Phillips H., Modrusan Z., Cloughesy T.
Data di Pubblicazione: 2011-03-25
Abstract: Despite treatment with the current standard-of-care therapies, patients with newly diagnosed glioblastoma multiforme (GBM) exhibit dismal prognoses. Bevacizumab has demonstrated activity in patients with recurrent GBM and phase 2 trials indicate that the combination of bevacizumab with standard-of-care therapy is feasible and active for patients with newly diagnosed GBM. Bevacizumab has been granted US approval for use as single-agent therapy for patients with progressive GBM following prior therapy, although it has not received approval for use in patients with GBM in Europe. Phase 3 studies have been initiated in patients with newly diagnosed GBM and are currently recruiting patients. We describe the protocol for the AVAglio phase 3 registration trial, which is designed to evaluate the efficacy and safety of combining bevacizumab with standard-of-care therapy in patients with newly diagnosed GBM.
Journal Title: Advances in therapy

PUBMED ID: 21427185
DOI: doi.org/10.1259/bjr/29022270
Titolo: Prognostic factors in glioblastoma multiforme patients receiving high-dose particle radiotherapy or conventional radiotherapy.
Autori: Matsuda M., Yamamoto T., Ishikawa E., Nakai K., Zaboronok A., Takano S., Matsumura A.
Data di Pubblicazione: 2011-03-24
Abstract: The aim of this study was to evaluate the influence of prognostic factors related to patient selection on survival outcomes. Survival outcomes were retrospectively analysed in a consecutive series of 67 newly diagnosed glioblastoma multiforme (GBM) patients who had received either conventional fractionated photon radiotherapy (CRT) or high-dose particle radiotherapy (HDT). In the CRT protocol, a total dose of 60.0-61.2 Gy was administered. In the HDT protocol, an average dose of approximately 30 GyE in a single session and additional fractionated photon irradiation of total dose 30 Gy were administered to patients receiving boron neutron capture therapy; and a total dose of 96.6 GyE was administered to patients receiving proton therapy. Most of the patients had received chemotherapy with nimustine hydrochloride (ACNU) alone or with ACNU, procarbazine and vincristine. The median overall survival (OS) and progression-free survival times for all patients were 17.7 months [95% confidence interval (CI), 14.6-20.9 months] and 7.8 months (95% CI, 5.7-9.9 months), respectively. The 1- and 2-year survival rates were 67.2% and 33.7%, respectively. For patients treated with HDT, the median OS was 24.4 months (95% CI, 18.2-30.5 months), compared with 14.2 months (95% CI, 10.0-18.3 months) for those treated with CRT. The Cox proportional hazards model revealed radiation modality (HDT vs CRT) and European Organisation for Research and Treatment of Cancer recursive partitioning analysis class to be the

significant prognostic factors. Age, sex, pre-operative performance status, treatment with or without advanced neuroimaging, extent of surgery and regimen of chemotherapy were not statistically significant factors in predicting prognosis. The median OS was 18.5 months (95% CI, 9.9-27.1 months) in patients of 65 years and older, compared with 16.8 months (95% CI, 13.6-20.1 months) in those 64 years and younger (p=0.871). The positive effect of HDT treatment is unlikely to reflect patient selection alone. Randomised trials with strictly controlled inclusion criteria to ensure the comparable selection of patients are required to demonstrate conclusively that prolonged survival can be attributed to high-dose particle radiotherapies.
Journal Title: The British journal of radiology

PUBMED ID: 21421463
DOI: doi.org/10.1007/s12094-011-0638-5
Titolo: Spinal cord astrocytoma: multidisciplinary experience.
Autori: Tovar Martín MI., López Ramírez E., Saura Rojas E., Arregui Castillo G., Zurita Herrera M.
Data di Pubblicazione: 2011-03-23
Abstract: The optimal treatment remains controversial. Radiotherapy should be considered for tumors with high-grade histopathology, clinically progressive and when a substantial resection cannot be achieved. New therapeutic strategies need to be studied to improve survival.
Journal Title: Clinical & translational oncology : official publication of the Federation of Spanish Oncology Societies and of the National Cancer Institute of Mexico

PUBMED ID: 21342033
DOI: doi.org/10.1586/era.10.227
Titolo: 2010 Society for Neuro-Oncology Annual Meeting: a report of selected studies.
Autori: Ahluwalia MS.
Data di Pubblicazione: 2011-02-24
Abstract: A number of important studies were presented at the Society for Neuro-Oncology annual meeting in Montréal, Canada, on 18-21 November 2010. Cediranib as monotherapy or in combination with lomustine did not show increased efficacy when compared with lomustine alone in patients with recurrent glioblastoma (GBM). Addition of temozolomide (TMZ) or irinotecan (CPT) to bevacizumab (BEV) in patients with recurrent GBM was well tolerated, with similar efficacy to BEV alone. The addition of BEV to radiation and TMZ in newly diagnosed GBM improved progression-free survival but did not improve overall survival. TMZ alone may be a reasonable approach in elderly GBM patients with poor performance status. Two Phase II trials with sunitinib and vatalanib showed a hint of activity in patients with recurrent or progressive meningiomas.
Journal Title: Expert review of anticancer therapy

PUBMED ID: 21339260
DOI: doi.org/10.1634/theoncologist.2010-0335
Titolo: Controversies in the adjuvant therapy of high-grade gliomas.
Autori: Holdhoff M., Grossman SA.
Data di Pubblicazione: 2011-02-23
Abstract: The 2-year survival rate of patients with glioblastoma accrued to research studies increased from 10% to nearly 40% from 2000 to 2010. These improvements began with the demonstration of a survival benefit when daily temozolomide was administered with 6 weeks of standard radiation and for 6 months thereafter. This treatment regimen is often associated with significant lymphopenia, thrombocytopenia, and progressive blood-brain barrier dysfuncti

on that can result in clinical and radiologic deterioration without true tum or progression ("pseudoprogression"). With new evidence that combining this cytotoxic agent with radiation improves survival in this malignancy, many in vestigators have modified the regimen to further improve patient outcomes. T hese largely uncontrolled studies highlight controversies regarding the opti mal therapy of this disease. This review focuses on the following selected c ontroversies: (a) What is the appropriate temozolomide dose, schedule, and d uration in the postradiation period? (b) How should other U.S. Food and Drug Administration-approved therapies (such as carmustine wafers and bevacizumab) be incorporated into this treatment regimen? (c) Should the results in gli oblastoma be extrapolated to patients aged >70 and to patients with lower gr ade gliomas? and (d) How should novel therapeutic approaches be added to rad iation and temozolomide in clinical trials for patients with newly diagnosed glioblastoma?
Journal Title: The oncologist

PUBMED ID: 21310734
DOI: doi.org/10.1093/neuonc/noq203
Titolo: Clinical trial end points for high-grade glioma: the evolving landsc ape.
Autori: Reardon DA., Galanis E., DeGroot JF., Cloughesy TF., Wefel JS., Lamb orn KR., Lassman AB., Gilbert MR., Sampson JH., Wick W., Chamberlain MC., Ma cdonald DR., Mehta MP., Vogelbaum MA., Chang SM., Van den Bent MJ., Wen PY.
Data di Pubblicazione: 2011-02-12
Abstract: To review the strengths and weaknesses of primary and auxiliary en d points for clinical trials among patients with high-grade glioma (HGG). Re cent advances in outcome for patients with newly diagnosed and recurrent HGG , coupled with the development of multiple promising therapeutics with myria d antitumor actions, have led to significant growth in the number of clinica l trials for patients with HGG. Appropriate clinical trial design and the in corporation of optimal end points are imperative to efficiently and effectiv ely evaluate such agents and continue to advance outcome. Growing recognitio n of limitations weakening the reliability of traditional clinical trial pri mary end points has generated increasing uncertainty of how best to evaluate promising therapeutics for patients with HGG. The phenomena of pseudoprogres sion and pseudoresponse have made imaging-based end points, including overal l radiographic response and progression-free survival, problematic. Although overall survival is considered the "gold-standard" end point, recently ident ified active salvage therapies such as bevacizumab may diminish the associat ion between presalvage therapy and overall survival. Finally, advances in im aging as well as the assessment of patient function and well being have stre ngthened interest in auxiliary end points assessing these aspects of patient care and outcome. Better appreciation of the strengths and limitations of pr imary end points will lead to more effective clinical trial strategies. Tech nical advances in imaging as well as improved survival for patients with HGG support the further development of auxiliary end points evaluating novel ima ging approaches as well as measures of patient function and well being.
Journal Title: Neuro-oncology

PUBMED ID: 21297433
DOI: doi.org/10.1097/COC.0b013e318201a2b7
Titolo: Palliative reirradiation for progressive diffuse intrinsic pontine g lioma.
Autori: Fontanilla HP., Pinnix CC., Ketonen LM., Woo SY., Vats TS., Rytting ME., Wolff JE., Mahajan A.
Data di Pubblicazione: 2011-02-08
Abstract: Reirradiation with chemotherapy may be feasible to improve symptom s and delay progression with minimal toxicity. Patients who are most likely

to benefit may be those with prolonged response to initial therapy and a lon g interval since initial radiation.
Journal Title: American journal of clinical oncology

PUBMED ID: 21282590
DOI: doi.org/10.1212/WNL.0b013e31820a0a8a
Titolo: Patterns of progression in patients with recurrent glioblastoma trea ted with bevacizumab.
Autori: Pope WB., Xia Q., Paton VE., Das A., Hambleton J., Kim HJ., Huo J., Brown MS., Goldin J., Cloughesy T.
Data di Pubblicazione: 2011-02-02
Abstract: Most patients treated with BEV or BEV+CPT-11 on BRAIN did not expe rience a change from baseline in radiographic characteristics of disease at the time of progression.
Journal Title: Neurology

PUBMED ID: 21240059
DOI: doi.org/10.1097/PAT.0b013e328340bb98
Titolo: The evolution of the histology in pleomorphic xanthoastrocytomas in children: a study of 15 cases.
Autori: Wu X., Bandopadhayay P., Ng J., Ashley D., Chow CW.
Data di Pubblicazione: 2011-01-18
Abstract: PXA should be considered in superficial cerebral tumours composed only of compact bundles of glial fibrillary acidic protein positive spindle cells with inconspicuous mitosis, even when the highly characteristic featur es of this tumour are not seen. The prominent variation in histology makes s mall biopsies difficult for diagnosis and assessing anaplasia. Patients with non-anaplastic tumours can often be salvaged by more treatment for tumour pr ogression.
Journal Title: Pathology

PUBMED ID: 21235315
DOI: doi.org/10.3171/2010.12.JNS10846
Titolo: Cortical ependymoma: an unusual epileptogenic lesion.
Autori: Van Gompel JJ., Koeller KK., Meyer FB., Marsh WR., Burger PC., Ronca roli F., Worrell GA., Giannini C.
Data di Pubblicazione: 2011-01-18
Abstract: Cortical ependymomas represent a rare type of ependymoma occurring superficially in the cortex. Morphologically, these tumors are protean, vary ing from classic to epithelioid, clear cell, and tanycytic. Some also exhibi ted features typical of AG. Most tumors were low grade and cured with resect ion. Anaplastic tumors occur and may recur locally despite provision of radi ation therapy. Cortical ependymomas frequently, but not always, present with seizures, but despite their high association with epilepsy, none occurred in the temporal lobe in any of the authors' 9 patients. Overall, CEs appear to have a relatively favorable prognosis compared with other supratentorial epe ndymomas.
Journal Title: Journal of neurosurgery

PUBMED ID: 24213125
DOI: doi.org/10.3390/cancers3044061
Titolo: A Review of the Role of Re-Irradiation in Recurrent High-Grade Gliom a (HGG).
Autori: Amichetti M., Amelio D.
Data di Pubblicazione: 2013-11-12

Abstract: Despite the use of more effective multimodal treatments in high-gr ade glioma (HGG), the outcome of patients affected by this disease is still dismal and recurrence is a very common event. Many therapeutic approaches, a lone or combined (surgery, drugs, targeted agents, immunotherapy, radiothera py, supportive therapy), are available in the clinical armamentarium so far. The attitude of physicians is increasingly interventionist, but recurrent HG G still remains a very difficult scenario to be treated. Radiotherapy with d ifferent re-irradiation techniques is increasingly proposed as a therapeutic option with interesting results, even though the resulting duration of respo nse is usually quite short. Most lesions re-recur locally, with inadequate i dentification and targeting of viable tumor being the most important cause o f failure. Prognosis is affected by many patient-, tumor-, and treatment-ass ociated prognostic factors. Radiotherapy is delivered with many advanced mod alities: 3D-CRT, intensity-modulated radiation therapy, stereotactic fractio nated radiotherapy, radiosurgery, and brachitherapy with or without chemothe rapy administration. In order to evaluate the feasibility and efficacy of re -irradiation in this setting, we reviewed the PubMed and MEDLINE databases r estricting the search to original reports published from January 1990 to Jun e 2011. The search resulted in a total of 155 reports: 78 of them covering 2 ,688 patients treated with different irradiation modalities overall fulfille d the entry criteria. Radiation therapy demonstrated to be an acceptable opt ion in recurrent HGG with good response rates and acceptable toxicity.
Journal Title: Cancers

PUBMED ID: 21187515
DOI: Mancante
Titolo: Bevacizumab and glioblastomas, a single-centre experience: how disea se history and characteristics may affect clinical outcome.
Autori: Zustovich F., Lombardi G., Pastorelli D., Farina P., Furini L., Mana ra R., Dalla Palma M., Rotilio A., Nicoletto O., Zagonel V.
Data di Pubblicazione: 2010-12-29
Abstract: Although well-tolerated, the efficacy of bevacizumab was somewhat disappointing, possibly due to the high rate of secondary high-grade gliomas in the studied patient cohort and the late use of bevacizumab in the course of the disease.
Journal Title: Anticancer research

PUBMED ID: 21181283
DOI: doi.org/10.1007/s10354-010-0863-5
Titolo: [Drug therapy of patients with recurrent glioblastoma: is there any evidence?].
Autori: Pichler J., Marosi C.
Data di Pubblicazione: 2010-12-25
Abstract: Thorough consideration of the individual patient's characteristics to evaluate the best fitted treatment is warranted, preferentially in the co ntext of an interdisciplinary tumour board.
Journal Title: Wiener medizinische Wochenschrift (1946)

PUBMED ID: 21177338
DOI: doi.org/10.1093/neuonc/noq177
Titolo: First-line temozolomide chemotherapy in progressive low-grade astroc ytomas after radiotherapy: molecular characteristics in relation to response .
Autori: Taal W., Dubbink HJ., Zonnenberg CB., Zonnenberg BA., Postma TJ., Gi jtenbeek JM., Boogerd W., Groenendijk FH., Kros JM., Kouwenhoven MC., van Ma rion R., van Heuvel I., van der Holt B., Bromberg JE., Sillevis Smitt PA., D injens WN., van den Bent MJ., van den Bent MJ.

Data di Pubblicazione: 2010-12-24
Abstract: Only a few studies examined the effect of temozolomide (TMZ) in recurrent low-grade astrocytoma (LGA) after surgery, none of which included a homogeneous and sufficiently sized group of patients with progression after radiotherapy (RT). We evaluated a cohort of 58 patients treated with TMZ for progression after RT of a previous LGA and investigated the relation between outcome and mutations in the IDH1, IDH2, and TP53 genes, O^6-methylguanine-methyltransferase (MGMT) promoter methylation, trisomy of chromosome 7, and loss of chromosomes 1p and 19q. All patients received first-line TMZ 200 mg/m² /day on days 1-5 every 4 weeks for a progressive LGA with a contrast-enhancing lesion on MRI after RT. Six months progression-free survival (PFS) was 67 %, and the median overall survival was 14 months. An objective response was obtained in 54%. TP53 mutations and loss of chromosome 19q showed a borderline association with PFS, but none of the other molecular characteristics were correlated with the outcome to TMZ. Both a methylated MGMT promoter gene and IDH1 mutations were found in 86% of the tumor samples. A correlation was found between IDH1 mutations and MGMT promoter methylation ($P < .001$). Neither MGMT promoter methylation nor IDH1 mutations correlated with PFS, but the interval between the very first symptom of the LGA and the start of the TMZ was significantly longer in the patients with IDH1 mutations ($P = .01$) and a methylated MGMT promoter ($P = .02$). We conclude that MGMT promoter methylation and IDH1 mutations seem to predict survival from the time of diagnosis, but not PFS to TMZ.
Journal Title: Neuro-oncology

PUBMED ID: 21158519
DOI: doi.org/10.3109/02688697.2010.528473
Titolo: Case report: extracranial metastasis from gliosarcoma--the influence of immune system.
Autori: Rapp M., Felsberg J., Sorg RV., Gerharz CD., Sabel M.
Data di Pubblicazione: 2010-12-17
Abstract: Extracranial metastasis of malignant glioma is an extremely rare event. We report on a 67-year-old patient with a primary gliosarcoma that was treated by open resection. The concomitant radio-chemotherapy which followed induced an unusually severe and early leucocytopenia. Ten months after diagnosis, the patient presented with multiple metastases in the lung and the skeletal system. The clinical, radiological and neuropathological findings are described. In addition, we discuss the possible role of a compromised immune system in the development of extracranial glioma metastasis.
Journal Title: British journal of neurosurgery

PUBMED ID: 21148162
DOI: doi.org/10.1093/jjco/hyq224
Titolo: The correlation between promoter methylation status and the expression level of O6-methylguanine-DNA methyltransferase in recurrent glioma.
Autori: Suzuki T., Nakada M., Yoshida Y., Nambu E., Furuyama N., Kita D., Hayashi Y., Hayashi Y., Hamada J.
Data di Pubblicazione: 2010-12-15
Abstract: Our results give the evidence that the increase of O(6)-methylguanine-DNA methyltransferase mRNA expression caused by methylation changes in recurrence may be associated with chemoresistance in the recurrent glioma.
Journal Title: Japanese journal of clinical oncology

PUBMED ID: 21107549
DOI: doi.org/10.1007/s00234-010-0802-6

Titolo: MR perfusion and diffusion imaging in the follow-up of recurrent gli oblastoma treated with dendritic cell immunotherapy: a pilot study.
Autori: Vrabec M., Van Cauter S., Himmelreich U., Van Gool SW., Sunaert S., De Vleeschouwer S., Suput D., Demaerel P.
Data di Pubblicazione: 2010-11-26
Abstract: The maximum lesional rCBV ratios and minimum ADC values in the con trast-enhancing area are potential radiological markers to differentiate bet ween immune therapy-induced inflammatory response and recurrent glioblastoma tumour growth in glioblastoma patients treated with immune therapy.
Journal Title: Neuroradiology

PUBMED ID: 20952169
DOI: doi.org/10.1016/j.clon.2010.09.007
Titolo: Carboplatin chemotherapy in patients with recurrent high-grade gliom a.
Autori: Murray LJ., Bridgewater CH., Levy D.
Data di Pubblicazione: 2010-10-19
Abstract: Single-agent carboplatin has modest activity in patients with recu rrent HGG who have received at least two lines of chemotherapy. The overall time to progression is short and over two-thirds of patients had to disconti nue treatment due to progressive disease. Among the small proportion of pati ents achieving stable disease or a partial response to treatment, the median survival is improved. More effective but well tolerated regimens are require d for this patient population.
Journal Title: Clinical oncology (Royal College of Radiologists (Great Brita in))

PUBMED ID: 20925951
DOI: doi.org/10.1186/1471-2407-10-533
Titolo: Randomised phase I/II study to evaluate carbon ion radiotherapy vers us fractionated stereotactic radiotherapy in patients with recurrent or prog ressive gliomas: the CINDERELLA trial.
Autori: Combs SE., Burkholder I., Edler L., Rieken S., Habermehl D., Jäkel O ., Haberer T., Haselmann R., Unterberg A., Wick W., Debus J.
Data di Pubblicazione: 2010-10-08
Abstract: NCT01166308.
Journal Title: BMC cancer

PUBMED ID: 20809868
DOI: doi.org/10.1517/14728222.2010.515980
Titolo: Taking aim at Mer and Axl receptor tyrosine kinases as novel therape utic targets in solid tumors.
Autori: Linger RM., Keating AK., Earp HS., Graham DK.
Data di Pubblicazione: 2010-09-03
Abstract: Axl and Mer mediate multiple oncogenic phenotypes and activation o f these RTKs constitutes a mechanism of chemoresistance in a variety of soli d tumors. Targeted inhibition of these RTKs may be effective as anti-tumor a nd/or anti-metastatic therapy, particularly if combined with standard cytoto xic therapies.
Journal Title: Expert opinion on therapeutic targets

PUBMED ID: 20736948
DOI: doi.org/10.1038/sj.bjc.6605796
Titolo: MGMT gene promoter methylation correlates with tolerance of temozolo mide treatment in melanoma but not with clinical outcome.

Autori: Hassel JC., Sucker A., Edler L., Kurzen H., Moll I., Stresemann C., Spieth K., Mauch C., Rass K., Dummer R., Schadendorf D.
Data di Pubblicazione: 2010-08-26
Abstract: In advanced melanoma MGMT promoter, methylation correlates with to lerance of therapy, but not with clinical outcome.
Journal Title: British journal of cancer

PUBMED ID: 20730617
DOI: doi.org/10.1007/s11060-010-0354-y
Titolo: Hepatic encephalopathy after treatment with temozolomide.
Autori: Goldbecker A., Tryc AB., Raab P., Worthmann H., Herrmann J., Weissen born K.
Data di Pubblicazione: 2010-08-24
Abstract: Temozolomide in combination with radiation has been in use for mor e than 5 years for the therapy of glioblastoma. Known adverse effects concer ning the gastrointestinal system are elevation of liver enzymes. We present the case of a patient treated with temozolomide who developed severe cholest atic liver damage and consecutive hepatic encephalopathy. Neurological sympt oms were mistaken as being caused by focal brain damage for more than 9 mont hs. After the correct diagnosis had been made and the treatment had been sta rted, the patient's condition ameliorated. In conclusion, neurological defic its in patients with known brain lesion should not be attributed automatical ly to the pre-existing damage even if it is progressive but should be examin ed carefully, also including toxic and metabolic encephalopathies into the d ifferential diagnosis. Furthermore, new side effects of drugs have to be con sidered. At least this case might lead to a closer monitoring of liver enzym es during temozolomide therapy.
Journal Title: Journal of neuro-oncology

PUBMED ID: 20724193
DOI: doi.org/10.1016/j.canrad.2010.03.021
Titolo: [Systematic review of stereotactic radiotherapy for high-grade gliom as].
Autori: Clavier JB., Voirin J., Kehrli P., Noël G.
Data di Pubblicazione: 2010-08-21
Abstract: The purpose of this literature systematic review was the use of st ereotactic radiotherapy in glioma. Research was performed in Medline/PubMed and associated references found in published articles without publication da te limit. The quality of series is variable and many biases can be evidenced . Only two randomized trials have been published using stereotactic radiothe rapy for up-front treatment. There is a lack of evidence of survival advanta ges to use this treatment at the time of diagnosis or relapse. There is also insufficient evidence regarding the benefice/harms in the use of stereotacti c fractionated radiation therapy for patients with glioma. No recommendation s can be enounced. Stereotactic irradiation as boost in primary diagnosed gl ioma or relapsed tumour is not associated with survival improvement. For rel apsed patients, treatment needs to be discussed according to the other treat ment options.
Journal Title: Cancer radiotherapie : journal de la Societe francaise de rad iotherapie oncologique

PUBMED ID: 20683757
DOI: doi.org/10.1007/s11060-010-0325-3
Titolo: Phase II trial of ritonavir/lopinavir in patients with progressive o r recurrent high-grade gliomas.
Autori: Ahluwalia MS., Patton C., Stevens G., Tekautz T., Angelov L., Vogelb aum MA., Weil RJ., Chao S., Elson P., Suh JH., Barnett GH., Peereboom DM.

Data di Pubblicazione: 2010-08-05
Abstract: Current therapies for recurrent or progressive high-grade gliomas (HGG, WHO grade 3-4) produce a 6-month progression-free survival of only 10-25%. Migration and invasion by HGG is mediated in part by matrix metalloproteases (MMPs) which promote remodeling of the extracellular matrix. Several HIV protease inhibitors (HIVPI) decrease the expression of MMPs in astrocytes and microglia. Given these mechanisms of antitumor activity of HIVPI, we evaluated the efficacy of ritonavir/lopinavir, a combination HIVPI, in patients with progressive or recurrent HGG in an open label phase II trial. Nineteen patients were treated in this study. Patients received ritonavir/lopinavir (400 mg/100 mg) orally twice daily. All patients were treated until progression of disease or unacceptable toxicity. A complete response was seen in one patient (5%). Three patients (16%) had stable disease as the best response. Fifteen patients (79%) had progressive disease. The 6-month progression free survival (PFS(6)) was 11% (2 of 19 patients). Ritonavir/lopinavir was well tolerated in patients with heavily pretreated refractory HGG, and no grade 3 or 4 toxicity was seen. The activity at the dose and schedule used in this study, however, was modest and the study did not meet its efficacy endpoint.
Journal Title: Journal of neuro-oncology

PUBMED ID: 20632556
DOI: doi.org/10.1118/1.3425792
Titolo: Significant dose can be lost by extended delivery times in IMRT with x rays but not high-LET radiations.
Autori: Joiner MC., Mogili N., Marples B., Burmeister J.
Data di Pubblicazione: 2010-07-17
Abstract: Prolonged delivery times of photon fractions could have a significant impact on treatment outcome especially for tumors with a low alpha/beta ratio and short repair halftime. These effects are significant at delivery times commonly associated with IMRT and are variable with cell type. X-ray IMRT should therefore always be planned to minimize dose-fraction delivery time. However, if IMRT treatments are delivered with high-LET radiation, this considerably reduces the dependence of the biological effect on fraction delivery time even out to 2 h.
Journal Title: Medical physics

PUBMED ID: 20586629
DOI: doi.org/10.1043/2009-0015-OA.1
Titolo: Myelodysplastic syndromes arising in patients with germline TP53 mutation and Li-Fraumeni syndrome.
Autori: Talwalkar SS., Yin CC., Naeem RC., Hicks MJ., Strong LC., Abruzzo LV.
Data di Pubblicazione: 2010-07-01
Abstract: Patients with LFS may develop MDS, which is most likely therapy-related and is associated with cytogenetic markers of poor prognosis.
Journal Title: Archives of pathology & laboratory medicine

PUBMED ID: 20564393
DOI: doi.org/10.1002/cncr.25035
Titolo: Dose-dense temozolomide regimens: antitumor activity, toxicity, and immunomodulatory effects.
Autori: Neyns B., Tosoni A., Hwu WJ., Reardon DA.
Data di Pubblicazione: 2010-06-22
Abstract: Temozolomide is an oral alkylating agent with established antitumor activity in patients with primary brain tumors and melanoma. The originally approved temozolomide dosing regimen is 150 to 200 mg/m(2) per day (Days 1 to 5 every 28-day cycle [5 of 28 days]). However, extended dosing regimens (

eg, 7 of 14 days, 21 of 28 days, 6 of 8 weeks, or continuously daily) allow for administration of a higher cumulative dose per cycle and have been shown to deplete O(6)-methylguanine-DNA methyltransferase, which may enhance cytotoxic activity. This article reviews efficacy and safety data from studies that investigated dose-dense temozolomide regimens in patients with recurrent glioma and advanced metastatic melanoma. The clinical benefits of these dose-dense regimens compared with the standard 5 of 28-day regimen have yet to be established. Although the toxicity profile of dose-dense temozolomide is generally similar to that of the standard 5 of 28-day regimen, it is associated with an increased incidence and severity of lymphocytopenia. The clinical management of temozolomide-associated lymphodepletion and the potential risks and benefits of extended dosing with temozolomide are discussed. Preclinical and clinical evidence suggests that temozolomide-associated lymphodepletion may enhance the host immune response to tumor-associated antigens and/or immunotherapy and may overcome tumor-mediated immunosuppression. Further studies exploring the clinical implications of lymphodepletion are warranted.
Journal Title: Cancer

PUBMED ID: 20440540
DOI: doi.org/10.1007/s11060-010-0200-2
Titolo: Efficacy and safety of bevacizumab in active brain metastases from non-small cell lung cancer.
Autori: De Braganca KC., Janjigian YY., Azzoli CG., Kris MG., Pietanza MC., Nolan CP., Omuro AM., Holodny AI., Lassman AB.
Data di Pubblicazione: 2010-05-05
Abstract: Bevacizumab is effective for the treatment of non-small cell lung cancer (NSCLC). Ongoing trials are exploring the safety of bevacizumab in patients with inactive, previously treated brain metastases. However, bevacizumab safety and efficacy in the treatment of active brain metastases is unknown. Bevacizumab received accelerated FDA approval for progressive glioblastoma, a primary brain tumor, because of high response rates and low incidence of intracranial hemorrhage. We retrospectively identified patients treated with bevacizumab for active (treatment naïve or progressive) central nervous system (CNS) metastases from NSCLC. MRI scans performed at least 6 weeks after initiating bevacizumab were assessed for response. There were six patients, four women and two men with a median age of 60 years (range 59-77) at initiation of bevacizumab. Five patients had progressive CNS metastases despite prior treatment including surgery, radiotherapy, and/or chemotherapy; one patient had treatment-naïve brain metastases. Two patients had leptomeningeal metastases, isolated or coexistent with parenchymal brain metastases in one patient each. Bevacizumab was administered alone to one patient and in combination with various cytotoxic chemotherapies in the others. Toxicity included an asymptomatic (Grade 1) intra-tumoral hemorrhage which occurred in one of three patients receiving concurrent anticoagulation with bevacizumab. There was no recurrent CNS bleeding in two patients with a prior history of such hemorrhage. Best CNS response (RECIST) was partial in two, stable disease in three, and progression in one. Median progression-free survival (PFS) was 7.8 months and median overall survival (OS) was 14.1 months following initiation of bevacizumab. Clinical benefit was also observed in the form of improved symptoms and reduced corticosteroid requirements. Bevacizumab should be used with caution in patients with active CNS metastases pending additional safety data. This series suggests bevacizumab may be safe and effective for progressive brain metastases from NSCLC and deserves further study.
Journal Title: Journal of neuro-oncology

PUBMED ID: 20425045
DOI: doi.org/10.1007/s10014-010-0265-9

Titolo: Prognostic value of WT1 protein expression level and MIB-1 staining index as predictor of response to WT1 immunotherapy in glioblastoma patients .
Autori: Chiba Y., Hashimoto N., Tsuboi A., Rabo C., Oka Y., Kinoshita M., Kagawa N., Oji Y., Sugiyama H., Yoshimine T.
Data di Pubblicazione: 2010-04-29
Abstract: The use of Wilms' tumor 1 (WT1) immunotherapy is considered to be an innovative approach for the treatment of malignant gliomas. Because of its novelty, tools that can accurately predict response to this therapy are still lacking. In this article, we investigated the role of WT1 protein expression level (score 1-4) and MIB-1 staining index in predicting survival outcome after therapy in patients with recurrent or progressive glioblastoma multiforme. Tumor samples from 37 patients enrolled in a phase II clinical trial on WT1 immunotherapy were immunohistochemically analyzed for WT1 levels and MIB-1 index. Results showed that median progression-free survival (PFS) was longer in the WT1 high expression group (score 3 and 4) compared with that of the low expression group (score 1 and 2) (20.0 weeks vs. 8.0 weeks; P = 0.022), and that the median overall survival (OS) was likewise longer in the former compared to the latter group (54.4 weeks vs. 28.4 weeks; P = 0.035). Furthermore, within the WT1 high expression group, tumors with intermediate staining intensity (WT1 score 3) have both the longest median PFS and OS, 24.4 weeks and 69.4 weeks, respectively. On the other hand, no significant correlation was noted between MIB-1 staining index and survival. In conclusion, our study has shown that WT1 protein expression level, not MIB-1 staining index, can be used as a prognostic marker to foretell outcome after immunotherapy, and that patients whose tumors have intermediate WT1 expression have the best survival outcome.
Journal Title: Brain tumor pathology

PUBMED ID: 20368564
DOI: doi.org/10.1200/JCO.2009.25.3971
Titolo: Parametric response map as an imaging biomarker to distinguish progression from pseudoprogression in high-grade glioma.
Autori: Tsien C., Galbán CJ., Chenevert TL., Johnson TD., Hamstra DA., Sundgren PC., Junck L., Meyer CR., Rehemtulla A., Lawrence T., Ross BD.
Data di Pubblicazione: 2010-04-07
Abstract: PRM(rCBV) at week 3 during chemoradiotherapy is a potential early imaging biomarker of response that may be helpful in distinguishing pseudoprogression from true progression in patients with high-grade glioma.
Journal Title: Journal of clinical oncology : official journal of the American Society of Clinical Oncology

PUBMED ID: 20339274
DOI: doi.org/10.2176/nmc.50.228
Titolo: Anaplastic ganglioglioma with malignant features in both neuronal and glial components--case report.
Autori: Kawataki T., Sato E., Sato T., Kinouchi H.
Data di Pubblicazione: 2010-03-27
Abstract: A 34-year-old man presented with a case of anaplastic gangliogliomа with malignant features in both neuronal and glial components manifesting as seizure episodes over 11 months. The tumor was subtotally removed, followed by irradiation and chemotherapy. The histological diagnosis was anaplastic ganglioglioma. Atypical cells were morphologically estimated as glial and neuronal cells. Though these cells were weakly positive for synaptophysin and glial fibrillary acidic protein, the neural stem cell marker nestin was extremely expressed in both these cells. The MIB-1 index was 15%. Two months later, the tumor recurred with more pleomorphic appearance and higher cellularity with increased nestin expression level. Mitotic cells and multinucleate

d cells were found in the neuronal components. Cytological examination found dissemination to the leptomeningeal space. The patient died 6 months after t he first surgery. This rare case of anaplastic ganglioglioma with both neuro nal and glial components, which were extremely positive for nestin, showed p rogressive worsening of the clinical course. The expression of nestin may su ggest that the origin or malignant transformation in anaplastic gangliogliom as is related to the undifferentiated neural stem cells.
Journal Title: Neurologia medico-chirurgica

PUBMED ID: 20238235
DOI: doi.org/10.1007/s11060-010-0141-9
Titolo: The addition of high-dose tamoxifen to standard radiotherapy does no t improve the survival of patients with diffuse intrinsic pontine glioma.
Autori: Michalski A., Bouffet E., Taylor RE., Hargrave D., Walker D., Picton S., Robinson K., Pizer B., Bujkiewicz S.
Data di Pubblicazione: 2010-03-19
Abstract: The study aimed to examine the tolerability of the combination of radiotherapy and tamoxifen and the effect on median and event free survival as well as collecting data on the use of steroids in this population. 31 pat ients with diffuse intrinsic pontine glioma, diagnosed on clinical and radio logical criteria, were treated with high-dose oral tamoxifen (120 mg/m(2)/da y) given concomitantly with standard dose radiotherapy (54 Gy in 1.8 Gy frac tions over 6 weeks). Results Tamoxifen was well tolerated with no grade 3 or 4 CTC toxicity reported. At 1 year, the progression free and event free surv ival were 3.2% (95% CI: 0.2-14.1%), and at 6 months 19.4% (CI: 7.9% to 34.6%). The overall survival at 1 year was 16.1% (CI: 5.9-30.9%) with median surv ival 6.32 months. In this study, in which tamoxifen was used in conjunction with radiotherapy, progression free survival was shown to be less good when compared with historical data HR = 3.1 (CI: 1.7-5.7). There was no significa nt reduction in overall survival. The addition of high-dose tamoxifen, altho ugh well tolerated, confers no clinical benefit to patients treated with dif fuse intrinsic pontine glioma treated with standard radiotherapy.
Journal Title: Journal of neuro-oncology

PUBMED ID: 20177703
DOI: doi.org/10.1007/s00432-010-0827-6
Titolo: Long-term adjuvant administration of temozolomide in patients with g lioblastoma multiforme: experience of a single institution.
Autori: Seiz M., Krafft U., Freyschlag CF., Weiss C., Schmieder K., Lohr F., Wenz F., Thomé C., Tuettenberg J.
Data di Pubblicazione: 2010-02-24
Abstract: This data set suggests that long-term administration of temozolomi de is safe and efficacious. Side effects occur more frequently in the early phase of drug administration (<6 cycles). There is a strong correlation of l ong-term temozolomide on PFS and OS regardless of the extent of surgery and other factors.
Journal Title: Journal of cancer research and clinical oncology

PUBMED ID: 20158881
DOI: doi.org/10.1186/bcr2479
Titolo: Survival and self-renewing capacity of breast cancer initiating cell s during fractionated radiation treatment.
Autori: Lagadec C., Vlashi E., Della Donna L., Meng Y., Dekmezian C., Kim K. , Pajonk F.
Data di Pubblicazione: 2010-02-18
Abstract: The breast CIC population retains increased self-renewal capacity over several generations and therefore, we conclude that increases in the nu

mber of CICs after sublethal doses of radiation have potential clinical impo rtance. Prevention of this process may lead to improved clinical outcome.
Journal Title: Breast cancer research : BCR

PUBMED ID: 20122270
DOI: doi.org/10.1186/1471-2407-10-30
Titolo: BCNU for recurrent glioblastoma multiforme: efficacy, toxicity and p rognostic factors.
Autori: Reithmeier T., Graf E., Piroth T., Trippel M., Pinsker MO., Nikkhah G.
Data di Pubblicazione: 2010-02-04
Abstract: In summary, BCNU treatment appears to be a valuable therapeutic op tion for recurrent glioblastomas, where no other validated radio- and/or che motherapy are available.
Journal Title: BMC cancer

PUBMED ID: 20063115
DOI: doi.org/10.1007/s11060-009-0103-2
Titolo: Phase II NCCTG trial of RT + irinotecan and adjuvant BCNU plus irino tecan for newly diagnosed GBM.
Autori: Jaeckle KA., Ballman KV., Giannini C., Schomberg PJ., Ames MM., Reid JM., McGovern RM., Safgren SL., Galanis E., Uhm JH., Brown PD., Hammack JE., Arusell R., Nikcevich DA., Morton RF., Wender DB., Buckner JC.
Data di Pubblicazione: 2010-01-12
Abstract: Irinotecan has radiosensitizing effects and shows synergism with n itrosoureas. We performed a Phase II study of RT and irinotecan, followed by BCNU plus irinotecan in newly-diagnosed GBM. The MTD for patients receiving enzyme-inducing anticonvulsants (EIAC) was as follows: irinotecan 400 mg/m(2)/week on Days 1, 8, 22 and 29 during RT, followed by BCNU 100 mg/m(2) Day 1 , and irinotecan, 400 mg/m(2) on Days 1, 8, 22 and 29, every 6 weeks. The MT D for non-EIAC patients was as follows: irinotecan 125 mg/m(2)/week on Days 1, 8, 22 and 29 during RT, followed by BCNU 100 mg/m(2) Day 1 and irinotecan 75 mg/m(2) Days 1, 8, 22 and 29, every 6 weeks. Median OS was 10.8 mos. (95% CI: 7.7-14.9); OS at 12 months was 44.6% (95% CI: 33.3-59.8) and PFS 6 was 2 8.6% (95% CI: 18.9-43.2). Patients went off treatment due to adverse events (7%), refusal (11%), progressive disease (48%), death (9%), and other (9%); 16% completed protocol treatment. Survival was similar in patients with vari ant (6/7 or 7/7) and wild-type (6/6) UGT1A1*28 genotypic alleles. Grade 3-4 toxicity was more common in non-EIAC patients with variant alleles. SN-38 C(max) and AUC in EIAC patients receiving 400 mg/m(2) irinotecan were 20.9 ng/ ml and 212 ng/ml h, and in non-EIAC patients receiving 125 mg/m(2), 15.5 ng/ ml and 207 ng/ml h. SN-38 AUC varied by UGT1A1*28 status in non-EIAC patient s. This regimen was not significantly active and radiosensitization was not observed. Non-EIAC patients with UGT1A1*28 variant alleles appear particular ly sensitive to toxicity from irinotecan.
Journal Title: Journal of neuro-oncology

PUBMED ID: 23226044
DOI: doi.org/10.2147/pgpm.s7940
Titolo: Update and developments in the treatment of glioblastoma multiforme - focus on bevacizumab.
Autori: Wagle N., Nghiemphu L., Lai A., Pope W., Mischel PS., Cloughesy T.
Data di Pubblicazione: 2012-12-11
Abstract: Glioblastoma is the most common primary brain tumor with a relativ ely poor prognosis. This article reviews the current standard therapy and di scusses new developments in treatment of this disease. Surgical resection fo llowed by radiation and chemotherapy has proven to be the most effective ini

tial therapy. Recent advancement in molecular targeted therapies has led to the Food and Drug Administration (FDA) approval of bevacizumab in the settin g of recurrent glioblastoma. The molecular pathways of glioblastoma growth a re highlighted in this review. While numerous molecular targets are currentl y being intensely investigated, vascular endothelial growth factor (VEGF) re ceptor targeted therapy has been the only one to have shown clinical effect. The role of bevacizumab in this context provides a dynamic breakthrough in c ancer therapy. Clinical trials have demonstrated significantly increased ove rall survival and six month progression free survival (PFS) in recurrent gli oblastoma treated with bevacizumab alone or in combination with irinotecan. The use of this agent has also dramatically changed the imaging characterist ics of glioblastoma. The anti-angiogenesis effects of bevacizumab have compl icated the criterion for determining tumor growth. This may lead to redefini tion of progressive disease based on non-invasive monitoring.
Journal Title: Pharmacogenomics and personalized medicine

PUBMED ID: 20033471
DOI: doi.org/10.1007/s11060-009-0093-0
Titolo: Transcranial electro-hyperthermia combined with alkylating chemother apy in patients with relapsed high-grade gliomas: phase I clinical results.
Autori: Wismeth C., Dudel C., Pascher C., Ramm P., Pietsch T., Hirschmann B. , Reinert C., Proescholdt M., Rümmele P., Schuierer G., Bogdahn U., Hau P.
Data di Pubblicazione: 2009-12-25
Abstract: Non-invasive loco-regional electro-hyperthermia (EHT) plus alkylat ing chemotherapy is occasionally used as salvage treatment in the relapse of patients with high-grade gliomas. Experimental data and retrospective studie s suggest potential effects. However, no prospective clinical results are av ailable. We performed a single-center prospective non-controlled single-arm Phase I trial. Main inclusion criteria were recurrent high-grade glioma WHO Grade III or IV, age 18-70, and Karnofsky performance score > or = 70. Prima ry endpoints were dose-limiting toxicities (DLT) and maximum tolerated dose (MTD) with the combined regimen. Groups of 3 or 4 patients were treated 2-5 times a week in a dose-escalation scheme with EHT. Alkylating chemotherapy (ACNU, nimustin) was administered at a dose of 90 mg/m(2) on day 1 of 42 days for up to six cycles or until tumor progression (PD) or DLT occurred. Fiftee n patients with high-grade gliomas were included. Relevant toxicities were l ocal pain and increased focal neurological signs or intracranial pressure. N o DLT occurred. In some patients, the administration of mannitol during EHT or long-term use of corticosteroids was necessary to resolve symptoms. Altho ugh some patients showed responses in their primarily treated sites, the pat tern of response was not well defined. EHT plus alkylating chemotherapy is t olerable in patients with relapse of high-grade gliomas. Episodes of intracr anial pressure were, at least, possibly attributed to EHT but did not cause DLTs. A Phase II trial targeting treatment effects is warranted on the basis of the results raised in this trial.
Journal Title: Journal of neuro-oncology

PUBMED ID: 19956971
DOI: doi.org/10.1007/s00432-009-0741-y
Titolo: Controversies concerning the application of brachytherapy in central nervous system tumors.
Autori: Liu BL., Cheng JX., Zhang X., Zhang W.
Data di Pubblicazione: 2009-12-04
Abstract: Though it is inconvincible to argue for the routine use of BRT, BR T may provide a choice for patients with large recurrent or inoperable deep-seated tumors, especially with the Glia-site technique. Radiotherapies inclu ding BRT may hold more promise if biologic mechanisms of radiation could be

better understand and biologic modifications could be added in clinical tria ls.
Journal Title: Journal of cancer research and clinical oncology

PUBMED ID: 19951140
DOI: doi.org/10.1586/ern.09.116
Titolo: Molecularly targeted therapies for malignant glioma: rationale for c ombinatorial strategies.
Autori: Thaker NG., Pollack IF.
Data di Pubblicazione: 2009-12-03
Abstract: Median survival of patients with malignant glioma (MG) from time o f diagnosis is approximately 1 year, despite surgery, irradiation and conven tional chemotherapy. Improving patient outcome relies on our ability to deve lop more effective therapies that are directed against the unique molecular aberrations within a patient's tumor. Such molecularly targeted therapies ma y provide novel treatments that are more effective than conventional chemoth erapeutics. Recently developed therapeutic strategies have focused on target ing several core glioma signaling pathways, including pathways mediated by g rowth-factors, PI3K/Akt/PTEN/mTOR, Ras/Raf/MEK/MAPK and other vital pathways . However, given the molecular diversity, heterogeneity and diverging and co nverging signaling pathways associated with MG, it is unlikely that any sing le agent will have efficacy in more than a subset of tumors. Overcoming thes e therapeutic barriers will require multiple agents that can simultaneously inhibit these processes, providing a rationale for combination therapies. Th is review summarizes the currently implemented single-agent and combination molecularly targeted therapies for MG.
Journal Title: Expert review of neurotherapeutics

PUBMED ID: 19951061
DOI: doi.org/10.3171/2009.9.FOCUS09187
Titolo: Role of stereotactic radiosurgery and fractionated stereotactic radi otherapy for the treatment of recurrent glioblastoma multiforme.
Autori: Romanelli P., Conti A., Pontoriero A., Ricciardi GK., Tomasello F., De Renzis C., Innocenzi G., Esposito V., Cantore G.
Data di Pubblicazione: 2009-12-03
Abstract: Glioblastoma multiforme (GBM) is a devastating malignant brain tum or characterized by resistance to available therapeutic approaches and relen tless malignant progression that includes widespread intracranial invasion, destruction of normal brain tissue, progressive disability, and death. Stere otactic radiosurgery (SRS) and fractionated stereotactic radiotherapy (fSRT) are increasingly used in patients with recurrent GBM to complement tradition al treatments such as resection, conventional external beam radiotherapy, an d chemotherapy. Both SRS and fSRT are powerful noninvasive therapeutic modal ities well suited to treat focal neoplastic lesions through the delivery of precise, highdose radiation. Although no randomized clinical trials have bee n performed, a variety of retrospective studies have been focused on the use of SRS and fSRT for recurrent GBMs. In addition, state-of-the-art neuroimagi ng techniques, such as MR spectroscopic imaging, diffusion tensor tractograp hy, and nuclear medicine imaging, have enhanced treatment planning methods l eading to potentially improved clinical outcomes. In this paper the authors reviewed the current applications and efficacy of SRS and fSRT in the treatm ent of GBM, highlighting the value of these therapies for recurrent focal di sease.
Journal Title: Neurosurgical focus

PUBMED ID: 19945857
DOI: doi.org/10.1016/j.ejca.2009.10.029

Titolo: EORTC study 26041-22041: phase I/II study on concomitant and adjuvan t temozolomide (TMZ) and radiotherapy (RT) with PTK787/ZK222584 (PTK/ZK) in newly diagnosed glioblastoma.
Autori: Brandes AA., Stupp R., Hau P., Lacombe D., Gorlia T., Tosoni A., Mir imanoff RO., Kros JM., van den Bent MJ.
Data di Pubblicazione: 2009-12-01
Abstract: In our phase I study once daily administration of up to 1000 mg of PTK/ZK in conjunction with concomitant temozolomide and radiotherapy was fea sible and safe. Prolonged administration of this oral agent is manageable. T he planned randomised phase II trial was discontinued right at its onset due to industry decision not to further develop this agent.
Journal Title: European journal of cancer (Oxford, England : 1990)

PUBMED ID: 19944967
DOI: doi.org/10.1016/j.nec.2009.08.010
Titolo: Passive antibody-mediated immunotherapy for the treatment of maligna nt gliomas.
Autori: Mitra S., Li G., Harsh GR.
Data di Pubblicazione: 2009-12-01
Abstract: Despite advances in understanding the molecular mechanisms of brai n cancer, the outcome of patients with malignant gliomas treated according t o the current standard of care remains poor. Novel therapies are needed, and immunotherapy has emerged with great promise. The diffuse infiltration of ma lignant gliomas is a major challenge to effective treatment; immunotherapy h as the advantage of accessing the entire brain with specificity for tumor ce lls. Therapeutic immune approaches include cytokine therapy, passive immunot herapy, and active immunotherapy. Cytokine therapy involves the administrati on of immunomodulatory cytokines to activate the immune system. Active immun otherapy is the generation or augmentation of an immune response, typically by vaccination against tumor antigens. Passive immunotherapy connotes either adoptive therapy, in which tumor-specific immune cells are expanded ex vivo and reintroduced into the patient, or passive antibody-mediated therapy. In this article, the authors discuss the preclinical and clinical studies that have used passive antibody-mediated immunotherapy, otherwise known as seroth erapy, for the treatment of malignant gliomas.
Journal Title: Neurosurgery clinics of North America

PUBMED ID: 19940404
DOI: doi.org/10.2176/nmc.49.532
Titolo: Glioblastoma multiforme associated with klinefelter syndrome.
Autori: Sasayama T., Mizukawa K., Sakagami Y., Mizowaki T., Tanaka K., Ohbay ashi C., Mori K., Kitazawa S., Kohmura E.
Data di Pubblicazione: 2009-11-27
Abstract: A 54-year-old man with Klinefelter syndrome presented with gliobla stoma multiforme manifesting as a 2-week history of motor weakness of the bi lateral extremities. Magnetic resonance imaging showed multiple heterogeneou sly enhanced tumors in the bilateral frontal lobes. Angiography showed no tu mor stain or arteriovenous shunt. The tumor was partially removed through a right craniotomy. The histological diagnosis was glioblastoma. Immunohistoch emical examination showed no O(6)-methylguanine-deoxyribonucleic acid methyl transferase protein expression. Postoperative local radiotherapy (60 Gy/30 f ractions) combined with temozolomide (75 mg/m(2) x 42 days) and interferon-b eta (3,000,000 U, 3 times/week) was performed. The patient's clinical status rapidly deteriorated during chemoradiotherapy, and he died of tumor progress ion 3.5 months after the surgery. Postmortem examination revealed widespread glioblastoma infiltrating the basal ganglia and thalamus. Klinefelter syndro me is associated with increased cancer predisposition, especially for male b reast cancer and germ cell tumors, but glioma is extremely rare. The abnorma

l genetic constitution of this patient may have been directly responsible fo
r the poor outcome.
Journal Title: Neurologia medico-chirurgica

PUBMED ID: 19933982
DOI: doi.org/10.1212/WNL.0b013e3181c34ace
Titolo: IDH1 mutations in low-grade astrocytomas predict survival but not re
sponse to temozolomide.
Autori: Dubbink HJ., Taal W., van Marion R., Kros JM., van Heuvel I., Brombe
rg JE., Zonnenberg BA., Zonnenberg CB., Postma TJ., Gijtenbeek JM., Boogerd
W., Groenendijk FH., Smitt PA., Dinjens WN., van den Bent MJ.
Data di Pubblicazione: 2009-11-26
Abstract: These results indicate that IDH1 mutations identify a subgroup of
gliomas with an improved survival, but are unrelated to the temozolomide res
ponse.
Journal Title: Neurology

PUBMED ID: 19829279
DOI: doi.org/10.1097/BRS.0b013e3181b95c6f
Titolo: Primary intramedullary tumors of the spinal cord.
Autori: Harrop JS., Ganju A., Groff M., Bilsky M.
Data di Pubblicazione: 2009-10-16
Abstract: The most important factor in determining the IMSCT patient's long-
term neurologic and functional outcome after surgery is the patient's preope
rative neurologic status. However, this must be taken in the context of the
underlying tumor histology. Therefore, resection is reserved for progressive
neurologic decline and serial monitoring for asymptomatic individuals. Adjuv
ant therapy is an option for high grade astrocytomas (WHO grades 3-4).
Journal Title: Spine

PUBMED ID: 19904263
DOI: doi.org/10.1038/sj.bjc.6605411
Titolo: Multicentre phase II studies evaluating imatinib plus hydroxyurea in
patients with progressive glioblastoma.
Autori: Reardon DA., Dresemann G., Taillibert S., Campone M., van den Bent M
., Clement P., Blomquist E., Gordower L., Schultz H., Raizer J., Hau P., Eas
aw J., Gil M., Tonn J., Gijtenbeek A., Schlegel U., Bergstrom P., Green S.,
Weir A., Nikolova Z.
Data di Pubblicazione: 2009-11-12
Abstract: Imatinib in addition to hydroxyurea was well tolerated among patie
nts with recurrent GBM but did not show clinically meaningful anti-tumour ac
tivity.
Journal Title: British journal of cancer

PUBMED ID: 19859666
DOI: doi.org/10.1007/s11060-009-9981-6
Titolo: Imaging response criteria for recurrent gliomas treated with bevaciz
umab: role of diffusion weighted imaging as an imaging biomarker.
Autori: Jain R., Scarpace LM., Ellika S., Torcuator R., Schultz LR., Hearshe
n D., Mikkelsen T.
Data di Pubblicazione: 2009-10-28
Abstract: The purpose of this study was to assess the usefulness of diffusio
n weighted imaging as an additional imaging biomarker for treatment response
in recurrent/progressive malignant gliomas treated with bevacizumab alone or
in combination with other chemotherapeutic agents. Twenty patients treated w
ith bevacizumab alone or concurrent chemotherapy were followed up with seria

l MR imaging. Volume and ADC values of contrast enhancing lesion (CEL(vol), CEL(ADC)) and also of non-enhancing lesion (NEL(vol), NEL(ADC)) were obtaine d. CEL(vol) showed a progressive decrease in non-progressors with a median p ercentage change of -73.2% (P = 0.001) as compared to -33.4% for progressors by 1 year/last imaging (P = 0.382). NEL(vol) also showed a decrease in non-p rogressors on follow up imaging though only significant for 3 months follow up (P = 0.042). In progressors, CEL(vol) and NEL(vol) showed initial decreas e followed by slight increase by 1 year/last imaging though not significant (P value of 0.382 and 0.46, respectively). CEL(ADC) and NEL(ADC) in non-prog ressors did not show any statistically significant change though there was s light trend for positive percent change especially for CEL(ADC) by 1 year/la st imaging follow up study (P value of 0.077 and 0.339, respectively). Progr essors showed a progressive negative percent change of CEL(ADC) and NEL(ADC) . In progressors, NEL(ADC) decreased at 6 weeks (P = 0.054), 3 months (P = 0 .023) and 1 year/last (P = 0.078) as compared to baseline study and was also statistically significant as compared to non-progressors at 6 weeks (P = 0.0 47) and 3 months (P = 0.025). CEL(ADC) and NEL(ADC) appear to follow differe nt trends over time for non-progressors and progressors with a stable to sli ghtly progressive increase in non-progressors and a progressive decrease in progressors, especially early on. These findings suggest that DWI may be use d as an additional imaging biomarker for early treatment response.
Journal Title: Journal of neuro-oncology

PUBMED ID: 19847765
DOI: Mancante
Titolo: Gliosarcoma with chondroblastic osteosarcomatous differentation: rep ort of two case with clinicopathologic and immunohistochemical features.
Autori: Barut F., Kandemir NO., Ozdamar SO., Gul S., Bektas S., Gun BD., Bah adir B.
Data di Pubblicazione: 2009-10-23
Abstract: Gliosarcoma is a rare tumor of the central nervous system characte rized by a biphasic histological pattern. Our objective is to describe clini cal, morphological and immunohistochemical features of two cases of gliosarc oma with chondroblastic osteosarcomatous differentiation and to discuss its pathogenetic mechanisms. CASE 1: A 52- year-old male patient underwent parie tal craniotomy due to anaplastic ependymoma. The case had radiotherapy and c hemotherapy postoperatively. After the first operation, additional resection s were performed for tumor because of recurrences at the fourth, seventh and tenth months. The patient died after the last tumor resection. Histopatholog ic examination of the postmortem biopsy revealed neoplasm displaying a bipha sic morphologic pattern including both gliomatous and sarcomatous components . CASE 2: The case was a 69-year-old male patient with a right frontal lobe mass histologically diagnosed as gliosarcoma displaying sarcomatous and glia l components. Immunohistochemical features were similar to those of the firs t case in general, but diffuse nuclear reaction with p53 protein was detecte d in both components. We report two cases with an extremely rare histopathol ogical diagnosis of "gliosarcoma with features of chondroblastic osteosarcom a".
Journal Title: Turkish neurosurgery

PUBMED ID: 19840379
DOI: doi.org/10.1186/1471-2407-9-372
Titolo: Early termination of ISRCTN45828668, a phase 1/2 prospective, random ized study of sulfasalazine for the treatment of progressing malignant gliom as in adults.
Autori: Robe PA., Martin DH., Nguyen-Khac MT., Artesi M., Deprez M., Albert A., Vanbelle S., Califice S., Bredel M., Bours V.
Data di Pubblicazione: 2009-10-21

Abstract: Current Controlled Trials ISRCTN45828668.
Journal Title: BMC cancer

PUBMED ID: 19836372
DOI: doi.org/10.1016/j.ejphar.2009.10.010
Titolo: EGF receptor inhibitors in the treatment of glioblastoma multiform: old clinical allies and newly emerging therapeutic concepts.
Autori: Gadji M., Crous AM., Fortin D., Krcek J., Torchia M., Mai S., Drouin R., Klonisch T.
Data di Pubblicazione: 2009-10-20
Abstract: Glioblastoma multiform (GBM) is the most common malignant brain tumour in adults. Despite decades of experimentation to improve the outcome of patients with GBM this highly aggressive tumour remains fatal. Primary GBM are often characterized by the over-expression of epidermal growth factor (EGF) receptor/HER1 and/or its mutational variants, with ligand-independent, constitutively active EGF receptor vIII variant most frequently observed in GBM. EGF receptor signalling can promote tumorigenesis by increasing cell proliferation, tissue invasion, neoangiogenesis, tumour cell chemoresistance, and by inhibiting apoptosis of cancer cells. EGF receptor was the first receptor to serve as target for cancer therapy of many solid tumours. After 2 decades of intensive targeting of EGF receptor for molecular therapy, several anti-EGF receptor inhibitors are now available in the clinic. Therapeutic strategies to target EGF receptor and EGF receptor mutant forms in GBM include humanized monoclonal antibodies, tyrosine kinase inhibitors, and RNAi compounds. However, despite the fact that most EGF receptor-directed glioma therapies to date have focused on single therapeutic agents, a multi-directional approach involving targeted inhibition of multiple signalling pathways has emerged as a more robust therapeutical approach. Furthermore, the emergence of the hypothesis of "brain cancer stem cells" in the bulb of GBM identifies this population of cells with self-renewal capacity as novel obligatory targets for efficient cure of GBM. Here we summarize current findings on the clinical role of these EGF receptor inhibitory therapeutic agents in the treatment of GBM.
Journal Title: European journal of pharmacology

PUBMED ID: 19822869
DOI: doi.org/10.1212/WNL.0b013e3181bc0184
Titolo: Patterns of relapse and prognosis after bevacizumab failure in recurrent glioblastoma.
Autori: Iwamoto FM., Abrey LE., Beal K., Gutin PH., Rosenblum MK., Reuter VE., DeAngelis LM., Lassman AB.
Data di Pubblicazione: 2009-10-14
Abstract: Contrast enhanced MRI does not adequately assess disease status during bevacizumab therapy for recurrent glioblastoma (GBM). A nonenhancing tumor pattern of progression is common after treatment with bevacizumab for GBM and is correlated with worse survival. Treatments after bevacizumab failure provide only transient tumor control.
Journal Title: Neurology

PUBMED ID: 19751941
DOI: doi.org/10.1016/j.jns.2009.08.047
Titolo: Primary leptomeningeal anaplastic oligodendroglioma with a 1p36-19q13 deletion: report of a unique case successfully treated with Temozolomide.
Autori: Michotte A., Chaskis C., Sadones J., Veld PI., Neyns B.
Data di Pubblicazione: 2009-09-16
Abstract: Primary leptomeningeal oligodendroglioma occurs very rarely and in only one patient a deletion of chromosome 1p has been reported. We describe

a 60-year-old man with a prior history of an epileptic seizure three years e arlier, who was referred because of depression and a rapid evolving cognitiv e impairment. Brain MRI showed a diffuse right parieto-occipital subarachnoi d enhancing lesion without intra-axial extension. The diagnosis of an anapla stic oligodendroglioma (WHO grade 3) was made on pathological examination. M olecular analysis using the FISH technique revealed a combined deletion of c hromosomes 1p36 and 19q13. A rapid progression of the lesion was shown on MR I with leptomeningeal spinal metastases. The patient was treated with Temozo lomide (TMZ) 150 mg/m(2) for 5 days every 4 weeks and showed a marked clinic al recovery. Serial MRI disclosed a near complete regression of the lesions with no residual enhancement left after 6 cycles of chemotherapy. At progres sion following 8 cycles of TMZ the patient underwent craniospinal radiothera py with complete response of his disease. To our knowledge this is the first report of a patient with a primary leptomeningeal anaplastic oligodendroglio ma with diffuse spinal seeding bearing a 1p36/19q13 deletion. Our patient ac hieved a durable clinical and radiological remission following TMZ treatment . Molecular analysis with determination of chromosome 1p/19q deletions shoul d be performed in all cases of leptomeningeal gliomas to select those patien ts who might benefit from TMZ chemotherapy.
Journal Title: Journal of the neurological sciences

PUBMED ID: 19737359
DOI: doi.org/10.1111/j.1440-1789.2009.01051.x
Titolo: B-cell dominant lymphocytic primary angiitis of the central nervous system: four biopsy-proven cases.
Autori: Myung J., Kim B., Yoon BW., Lee SK., Sung JJ., Chung CK., Chang KH., Park SH.
Data di Pubblicazione: 2009-09-10
Abstract: We report four cases of biopsy-proven B-cell-rich primary angiitis of the central nervous system (PACNS). The mean age of the patients was 29 y ears (range, 23-37 years). The patients suffered from unilateral weakness (n = 2), seizure (n = 1), and hypersomnia, anorexia and confusion (n = 1). The vital signs and the results of laboratory tests were within normal limits in all the four cases except erythrocyte sedimentation rate (ESR) and C-reactiv e protein (CRP). ESR was elevated in one patient and CRP was elevated in two patients. The magnetic resonance imaging (MRI) scans revealed single (n = 2) or multiple (n = 2) irregularly enhancing lesions. Radiological studies init ially indicated tumors such as glioma (n = 2) or lymphoma (n = 1), except in one case, in which the radiological analysis indicated vasculitis or demyeli nating disease. All the cases involved both medium-sized (50-250 microm in d iameter) and small-sized vessels (20-49 microm in diameter). The vascular, p erivascular and parenchymal lymphocytes were polymorphous; however, CD20-pos itive B-cells were predominated in blood vessels while the CD8-positive T-ce lls infiltrated predominantly in brain parenchyma. Therefore, our patients r evealed B-cell dominant lymphocytic vasculitis. Two patients who underwent a ctive treatment (corticosteroid alone or with cyclophosphamide) showed remar kable clinical and radiological improvement but two patients still have init ial neurological symptoms, namely, confusion and newly developed seizures, r espectively, during the 19-101-month follow-up periods; this effect can be a ttributed to irreversible brain damage. Therefore, although early brain biop sy may be associated with histopathologic diagnostic pitfalls, it is a manda tory procedure for obtaining a confirmative diagnosis as well initiating ear ly therapy, thereby reducing brain damage.
Journal Title: Neuropathology : official journal of the Japanese Society of Neuropathology

PUBMED ID: 19717889
DOI: doi.org/10.1088/0031-9155/54/18/012

Titolo: The quantification of dynamic FET PET imaging and correlation with t
he clinical outcome in patients with glioblastoma.
Autori: Thiele F., Ehmer J., Piroth MD., Eble MJ., Coenen HH., Kaiser HJ., S
chaefer WM., Buell U., Boy C.
Data di Pubblicazione: 2009-09-01
Abstract: The PET tracer O-(2-[18F]Fluoroethyl)-l-tyrosine (FET) has been sh
own to be valuable for different roles in the management of brain tumours. T
he aim of this study was to evaluate several quantitative measures of dynami
c FET PET imaging in patients with resected glioblastoma. We evaluated dynam
ic FET PET in nine patients with histologically confirmed glioblastoma. Foll
owing FET PET, all subjects had radiation and chemotherapy. Tumour ROIs were
defined by a threshold-based region-growing algorithm. We compared several s
tandard measures of tumour uptake and uptake kinetics: SUV, SUV/background,
distribution volume ratio (DVR), weighted frame differences and compartment
model parameters. These measures were correlated with disease-free and overa
ll survival, and analysed for statistical significance. We found that severa
l measures allowed robust quantification. SUV and distribution volume did no
t correlate with clinical outcome. Measures that are based on a background r
egion (SUV/BG, Logan-DVR) highly correlated with disease-free survival (r =
-0.95, p < 0.0001), but not overall survival. Some advanced measures also sh
owed a prognostic value but no improvement over the simpler methods. We conc
lude that FET PET probably has a prognostic value in patients with resected
glioblastoma. The ratio of SUV to background may provide a simple and valuab
le predictive measure of the clinical outcome. Further studies are needed to
confirm these explorative results.
Journal Title: Physics in medicine and biology

PUBMED ID: 19688297
DOI: doi.org/10.1007/s11060-009-9976-3
Titolo: Imatinib in combination with hydroxyurea versus hydroxyurea alone as
oral therapy in patients with progressive pretreated glioblastoma resistant
to standard dose temozolomide.
Autori: Dresemann G., Weller M., Rosenthal MA., Wedding U., Wagner W., Engel
E., Heinrich B., Mayer-Steinacker R., Karup-Hansen A., Fluge O., Nowak A., M
ehdorn M., Schleyer E., Krex D., Olver IN., Steinbach JP., Hosius C., Sieder
C., Sorenson G., Parker R., Nikolova Z.
Data di Pubblicazione: 2009-08-19
Abstract: A randomized, multicenter, open-label, phase 3 study of patients w
ith progressive, recurrent glioblastoma multiforme (GBM) for whom front-line
therapy had failed was conducted. This study was designed to determine wheth
er combination therapy with imatinib and hydroxyurea (HU) has superior antit
umor activity compared with HU monotherapy in the treatment of recurrent GBM
. The target population consisted of patients with confirmed recurrent GBM a
nd an Eastern Cooperative Oncology Group performance status of 0-2 who had c
ompleted previous treatment comprising surgical resection, irradiation thera
py, and first-line chemotherapy (preferably temozolomide (TMZ) containing re
gimen) and who have progressed despite treatment. If first-line chemotherapy
did not contain TMZ, a second completed chemotherapy was acceptable. The pri
mary efficacy parameter was progression-free survival (PFS). The primary com
parison of combination therapy versus monotherapy for PFS was not significan
t (adjusted P = 0.56). The hazard ratio (HR) (adjusted HR = 0.93) was not cl
inically relevant. The median PFS for the combination arm was low at 6 weeks
and similar to the median PFS in the monotherapy arm (6 weeks). The 6-month
PFS for the two treatment groups was very similar (5% in the combination arm
vs. 7% in the monotherapy arm). No clinically meaningful differences were fo
und between the two treatment arms, and the primary study end point was not
met. Among the patients receiving imatinib, no adverse events were reported
that were either previously unknown or unexpected as a consequence of the di
sease.

Journal Title: Journal of neuro-oncology

PUBMED ID: 19669096
DOI: doi.org/10.1007/s11060-009-9980-7
Titolo: Extended-schedule dose-dense temozolomide in refractory gliomas.
Autori: Berrocal A., Perez Segura P., Gil M., Balaña C., Garcia Lopez J., Ya ya R., Rodríguez J., Reynes G., Gallego O., Iglesias L., Iglesias L.
Data di Pubblicazione: 2009-08-12
Abstract: This multicenter phase II study conducted by the Spanish Neuro-Onc ology Group evaluated the activity of an extended, dose-dense temozolomide r egimen in patients with temozolomide-refractory malignant glioma. Adult pati ents (at least 18 years of age) with WHO grade III or IV glioma and a Karnof sky Performance Status of 60 or higher were treated with temozolomide (85 mg /m(2)/day) for 21 consecutive days every 28-day cycle until disease progress ion or unacceptable toxicity. All patients had developed progressive disease either during or less than 3 months after completing previous temozolomide t reatment. Forty-seven patients were treated with a median of 2 (range, 1-13) cycles of temozolomide. Before study entry, patients had received a median o f 6 cycles of temozolomide: 39 (83%) as part of initial therapy and 23 (49%) as second-line therapy. Three patients (6.4%) had a partial response with du rations of 8.0, 3.5, and 3.2 months; 15 patients (31.9%) had stable disease with a median duration of 2.1 months, including 2 patients with stable disea se (SD) for greater than 6 months (14 and 16 months). Median time to progres sion was 2 months, and median overall survival from study entry was 5.1 mont hs. The 6-month progression-free survival rate was 16.7%. The most common he matologic toxicities were lymphopenia, thrombocytopenia, and leukopenia. Lym phopenia occurred in 83% of patients and was grade 3 in 28%, but no opportun istic infections occurred. In conclusion, this extended dose-dense schedule of temozolomide appears to have modest activity in patients refractory to pr evious treatment with temozolomide and is associated with manageable toxicit y.
Journal Title: Journal of neuro-oncology

PUBMED ID: 19618121
DOI: doi.org/10.1007/s11060-009-9960-y
Titolo: Comparing neuropsychological tasks to optimize brief cognitive batte ries for brain tumor clinical trials.
Autori: Lageman SK., Cerhan JH., Locke DE., Anderson SK., Wu W., Brown PD.
Data di Pubblicazione: 2009-07-21
Abstract: Neuropsychological tests are increasingly being used as outcome me asures in clinical trials of brain tumor therapies. This study informs devel opment of brief neurocognitive batteries for clinical trials by identifying cognitive tasks that detect effects on a group level in a mixed brain tumor population. This is a retrospective study of brain tumor patients who comple ted a standardized battery sampling multiple cognitive domains using twelve subtests with widely-used task formats (the Repeatable Battery for the Asses sment of Neuropsychological Status). Sixty-eight patients with brain tumors were studied (60% high-grade glioma). Forty patients (58.8%) were impaired (>2 standard deviations below published means) on at least one subtest. A com bination of four subtests (Figure Copy, Coding, List Recognition, and Story Recall) captured 90% of the impaired subgroup. These results suggest visuoco nstruction, processing speed, and verbal memory measures may be the most imp ortant domains to assess when evaluating cognitive change in brain tumor cli nical trials.
Journal Title: Journal of neuro-oncology

PUBMED ID: 19593660

DOI: doi.org/10.1007/s11060-009-9957-6
Titolo: Salvage therapy with single agent bevacizumab for recurrent glioblastoma.
Autori: Chamberlain MC., Johnston SK.
Data di Pubblicazione: 2009-07-14
Abstract: A retrospective evaluation of single agent bevacizumab in adults with recurrent glioblastoma (GBM) with an objective of determining progression free survival (PFS). There is no standard therapy for recurrent GBM after failure of alkylator-based chemotherapy. A total of 50 adults, ages 36-70 years (median 64), with recurrent GBM were treated. All patients had previously been treated with surgery, concurrent radiotherapy and temozolomide, post-radiotherapy temozolomide and in 34 patients, one salvage regimen (PCV: 21, cyclophosphamide: 13). A total of 13 patients underwent repeat surgery. Patients were treated at first or second recurrence with bevacizumab, once every 2 weeks, defined as a single cycle. Neurological evaluation was performed every 2 weeks and neuroradiographic assessment following the initial 2 cycles of bevacizumab and subsequently after every 4 cycles of bevacizumab. A total of 468 cycles of bevacizumab (median 2 cycles; range 1-30) was administered. Bevacizumab-related toxicity included fatigue (16 patients; 4 grade 3), leukopenia (9; 1 grade 3), anemia (5; 0 grade 3), hypertension (7; 1 grade 3), deep vein thrombosis (4; 1 grade 3) and wound dehiscence (2; 1 grade 3). 21 patients (42%) demonstrated a partial radiographic response and 29 (58%) progressive disease following 1-2 cycles of bevacizumab. Time to tumor progression ranged from 0.5 to 15 months (median: 1.0 months). Survival ranged from 2 to 17 months (median: 8.5 months). 6-month and 12-month PFS were 42% and 22% respectively. Single agent bevacizumab demonstrated efficacy and acceptable toxicity in this cohort of adults with recurrent alkylator-refractory GBM.
Journal Title: Journal of neuro-oncology

PUBMED ID: 19584260
DOI: doi.org/10.1158/1541-7786.MCR-08-0479
Titolo: Therapeutic inhibition of the epidermal growth factor receptor in high-grade gliomas: where do we stand?
Autori: Karpel-Massler G., Schmidt U., Unterberg A., Halatsch ME.
Data di Pubblicazione: 2009-07-09
Abstract: High-grade gliomas account for the majority of intra-axial brain tumors. Despite abundant therapeutic efforts, clinical outcome is still poor. Thus, new therapeutic approaches are intensely being investigated. Overexpression of the epidermal growth factor receptor (HER1/EGFR) is found in various epithelial tumors and represents one of the most common molecular abnormalities seen in high-grade gliomas. Dysregulated HER1/EGFR is found in 40% to 50% of glioblastoma, the most malignant subtype of glioma. Several agents such as tyrosine kinase (TK) inhibitors, antibodies, radio-immuno conjugates, ligand-toxin conjugates, or RNA-based agents have been developed to target HER1/EGFR or its mutant form, EGFRvIII. To date, most agents are in various stages of clinical development. Clinical data are sparse but most advanced for TK inhibitors. Although data from experimental studies seem promising, proof of a significant clinical benefit is still missing. Among the problems that have to be further addressed is the prediction of the individual patient's response to HER1/EGFR-targeted therapeutics based on molecular determinants. It is quite possible that blocking HER1/EGFR alone will not sufficiently translate into a clinical benefit. Therefore, a multiple target approach concomitantly aimed at different molecular sites might be a favorable concept. This review focuses on current HER1/EGFR-targeted therapeutics and their development for high-grade gliomas.
Journal Title: Molecular cancer research : MCR

PUBMED ID: 19569246

DOI: doi.org/10.1002/cncr.24524
Titolo: Temozolomide for recurrent intracranial supratentorial platinum-refr actory ependymoma.
Autori: Chamberlain MC., Johnston SK.
Data di Pubblicazione: 2009-07-02
Abstract: TMZ in this dose schedule demonstrated little efficacy in a cohort of adults with recurrent, intracranial, platinum-refractory ependymoma.
Journal Title: Cancer

PUBMED ID: 19567132
DOI: Mancante
Titolo: Antiangiogenic therapy with bevacizumab in recurrent malignant gliom as: analysis of the response and core pathway aberrations.
Autori: Zhang W., Qiu XG., Chen BS., Li SW., Cui Y., Ren H., Jiang T.
Data di Pubblicazione: 2009-07-02
Abstract: Bevacizumab in combination with chemotherapeutic agents may be an effective strategy for patients with recurrent malignant glioma. Activated M APK and AKT might be possible biomarkers for selecting suitable patients for this targeted therapy.
Journal Title: Chinese medical journal

PUBMED ID: 19557499
DOI: doi.org/10.1007/s11060-009-9946-9
Titolo: Neurological outcome of long-term glioblastoma survivors.
Autori: Hottinger AF., Yoon H., DeAngelis LM., Abrey LE.
Data di Pubblicazione: 2009-06-27
Abstract: Extended survival of 3 or more years is rare in patients with glio blastoma (GBM) but is becoming more common. Clinical outcome has not been we ll studied. We reviewed GBM patients at Memorial Sloan-Kettering Cancer Cent er between 2001 and 2003 who were seen for two or more visits. Patient chara cteristics and long-term clinical outcomes were reviewed for patients who ha d survived 3 or more years following diagnosis. Thirty-nine (11%) of 352 GBM patients were identified as long-term survivors. Median survival was 9.15 ye ars (range: 3-18 years). Median age was 47 years (range: 16-69); 13% were 65 years or older. Median KPS was 90 (range: 50-100). One long-term survivor un derwent biopsy alone; 19 patients each had either complete or subtotal resec tion. All received focal radiotherapy (RT) with a median dose of 5940 cGy; 1 8% received concurrent temozolomide. Adjuvant chemotherapy was administered to 35 (90%). Twelve patients (31%) remained in continuous remission. Twenty-seven had tumor progression a median of 29.2 months after diagnosis (range: 1.2-167 months); 18 had multiple relapses. Median KPS at last follow-up was 70 (range: 40-100); 85% of long-term survivors had at least one significant neurologic deficit. Eleven (28%) had clinically significant RT-induced leuko encephalopathy, 9 (23%) developed RT necrosis and 9 (23%) treatment-related strokes. Treatment-related complications occurred a median of 2.7 years from diagnosis (range: 0.9-11.5 years). Long-term survivors remain rare, but are found across all age groups despite multiple recurrences; clinically signifi cant delayed complications of treatment are common.
Journal Title: Journal of neuro-oncology

PUBMED ID: 19549889
DOI: doi.org/10.1158/0008-5472.CAN-09-0814
Titolo: A "vascular normalization index" as potential mechanistic biomarker to predict survival after a single dose of cediranib in recurrent glioblasto ma patients.

Autori: Sorensen AG., Batchelor TT., Zhang WT., Chen PJ., Yeo P., Wang M., J ennings D., Wen PY., Lahdenranta J., Ancukiewicz M., di Tomaso E., Duda DG., Jain RK.
Data di Pubblicazione: 2009-06-25
Abstract: Early imaging or blood biomarkers of tumor response are desperatel y needed to customize antiangiogenic therapy for cancer patients. Anti-vascu lar endothelial growth factor (VEGF) therapy can "normalize" brain tumor vas culature by decreasing vessel diameter and permeability, and thinning the ab normally thick basement membrane. We hypothesized that the extent of vascula r normalization will be predictive of outcome of anti-VEGF therapy in gliobl astoma. We used advanced magnetic resonance imaging methods to monitor vascu lar parameters and treatment response in 31 recurrent glioblastoma patients enrolled in a phase II trial of cediranib, an oral pan-VEGF receptor tyrosin e kinase inhibitor. We evaluated the correlation between clinical outcome an d magnetic resonance imaging-measured changes in vascular permeability/flow (i.e., K(trans)) and in microvessel volume, and the change of circulating co llagen IV levels, all after a single dose of cediranib. Here, we show that e valuation of biomarkers as early as after one day of anti-VEGF therapy with cediranib is predictive of response in patients with recurrent glioblastoma. Changes in K(trans), microvessel volume, and circulating collagen IV correla ted with duration of overall survival and/or progression-free survival ($P < 0.05$). When we combined these three parameters into a "vascular normalizatio n index," we found that it closely associated with overall survival ($rho = 0 .54$; $P = 0.004$) and progression-free survival ($rho = 0.6$; $P = 0.001$). The va scular normalization index described here should be validated in randomized clinical trials.
Journal Title: Cancer research

PUBMED ID: 19536096
DOI: doi.org/10.1038/sj.bjc.6605127
Titolo: Extent of MGMT promoter methylation correlates with outcome in gliob lastomas given temozolomide and radiotherapy.
Autori: Dunn J., Baborie A., Alam F., Joyce K., Moxham M., Sibson R., Crooks D., Husband D., Shenoy A., Brodbelt A., Wong H., Liloglou T., Haylock B., Wa lker C.
Data di Pubblicazione: 2009-06-19
Abstract: These data indicate that MGMT methylation is prognostically signif icant in glioblastomas given chemoradiotherapy in the routine clinic; furthe rmore, the extent of methylation may be used to provide additional prognosti c stratification.
Journal Title: British journal of cancer

PUBMED ID: 19506143
DOI: doi.org/10.1001/archneurol.2009.74
Titolo: Occurrence of basal ganglia germ cell tumors without a mass.
Autori: Almubarak S., Gan YC., Steinbok P., Hendson G., Poskitt K., Nadel H. , Goddard K., Hukin J.
Data di Pubblicazione: 2009-06-10
Abstract: Germ cell tumor should be considered in patients with an indolentl y progressive neurological course, particularly if basal ganglia calcificati on is present with or without enhancement, asymmetric brain atrophy, or a ma ss.
Journal Title: Archives of neurology

PUBMED ID: 19491283
DOI: doi.org/10.1093/annonc/mdp032

Titolo: Stratified phase II trial of cetuximab in patients with recurrent hi gh-grade glioma.
Autori: Neyns B., Sadones J., Joosens E., Bouttens F., Verbeke L., Baurain J F., D'Hondt L., Strauven T., Chaskis C., In't Veld P., Michotte A., De Greve J.
Data di Pubblicazione: 2009-06-04
Abstract: Cetuximab was well tolerated but had limited activity in this pati ent population with progressive HGG. A minority of patients may derive a mor e durable benefit but were not prospectively identified by EGFR gene copy nu mber.
Journal Title: Annals of oncology : official journal of the European Society for Medical Oncology

PUBMED ID: 19485728
DOI: doi.org/10.3171/2009.2.PEDS0861
Titolo: Predictors of tumor progression among children with gangliogliomas. Clinical article.
Autori: El Khashab M., Gargan L., Margraf L., Koral K., Nejat F., Swift D., Weprin B., Bowers DC.
Data di Pubblicazione: 2009-06-03
Abstract: The PFS and overall survival of children with gangliogliomas are g ood. Tumors located in the cerebral hemispheres, the achievement of total re section, and seizures at presentation were associated with prolonged PFS. Co x regression analysis identified presenting symptoms including seizures as s ignificant predictive factors of PFS. Prospective studies with larger number s of children are needed to define the significant factors of tumor progress ion.
Journal Title: Journal of neurosurgery. Pediatrics

PUBMED ID: 19484244
DOI: doi.org/10.1007/s00347-009-1927-z
Titolo: [Clinical course of a solitary retinal astrocytoma].
Autori: Töteberg-Harms M., Paulsen F., Duncker GI., Sel S.
Data di Pubblicazione: 2009-06-02
Abstract: Retinal astrocytomas are benign tumors of the retina. Their locali zation can be solitary, multiple, or bilateral in both eyes. It is also know n that they can be part of a phakomatosis syndrome (i.e., tuberous sclerosis or neurofibromatosis). Because retinal astrocytomas have a slow growth rate, yearly controls by an ophthalmologist with interdisciplinary consultation ar e adequate. Some uncommon cases have been reported in which the tumor has gr own more aggressively. These tumors may require therapeutic interventions (e .g., vitreoretinal surgery, brachytherapy, photodynamic therapy, or cryother apy).
Journal Title: Der Ophthalmologe : Zeitschrift der Deutschen Ophthalmologisc hen Gesellschaft

PUBMED ID: 19476269
DOI: Mancante
Titolo: Current status and future potential of advanced technologies in radi ation oncology. Part 2. State of the science by anatomic site.
Autori: Vikram B., Coleman CN., Deye JA.
Data di Pubblicazione: 2009-05-30
Abstract: In December 2006, the Radiation Research Program of the Division o f Cancer Treatment and Diagnosis of the National Cancer Institute hosted a w orkshop intended to address current issues related to advanced radiation the rapy technologies, with an eye toward (1) defining the specific toxicities t hat have limited the success of "conventional" radiation therapy, (2) examin

ing the evidence from phase III studies for the improvements attributed to t
he advanced technologies in the treatment of several cancers commonly treate
d with radiation therapy, and (3) determining the opportunities and prioriti
es for further technologic development and clinical trials. The new technolo
gies offer substantial theoretical advantage in radiation dose distributions
that, if realized in clinical practice, may help many cancer patients live l
onger and/or better. The precision of the advanced technologies may allow us
to reduce the volume of normal tissue irradiated in the vicinity of the clin
ical target volume. Part 1 of this two-part article, which appeared in the M
arch issue of ONCOLOGY, provided a general overview of the workshop discussi
on, focusing on the challenges posed by the new technologies and resources a
vailable or in development for meeting those challenges. This month, part 2
will outline the state of the science for each disease site.
Journal Title: Oncology (Williston Park, N.Y.)

PUBMED ID: 19465788
DOI: doi.org/10.2176/nmc.49.193
Titolo: Pharmacokinetic investigation of increased efficacy against malignan
t gliomas of carboplatin combined with hyperbaric oxygenation.
Autori: Suzuki Y., Tanaka K., Negishi D., Shimizu M., Yoshida Y., Hashimoto
T., Yamazaki H.
Data di Pubblicazione: 2009-05-26
Abstract: The efficacy of intravenous administration of 400 mg carboplatin/m
(2) body surface area over 60 minutes combined with hyperbaric oxygenation (
HBO) therapy (0.2 MPa for 60 min) was investigated in 6 Japanese patients (a
ged 36-67 years) with malignant or brainstem gliomas. Plasma ultra-filtrate
samples were analyzed by high-performance liquid chromatography to evaluate
the relationship between efficacy and pharmacokinetics. Brain tumor response
was evaluated by magnetic resonance imaging as a function of maximum plasma
concentration, area under the curve, or mean residence time (MRT) for carbop
latin. The MRT for carboplatin in the complete or partial response group (me
an +/- standard deviation 4.3 +/- 1.7 hrs; 6 courses in 3 patients) was sign
ificantly longer ($p < 0.05$) than that in the progressive disease group (2.4
+/- 0.1 hrs; 3 courses in 3 patients), but maximum plasma concentration and
area under the curve showed no differences. These results suggest that HBO t
herapy prolongs the biological residence time of carboplatin. MRT for carbop
latin may be useful for predicting continuation or modification of chemother
apy and/or clinical antitumor effects in patients with malignant gliomas.
Journal Title: Neurologia medico-chirurgica

PUBMED ID: 19464817
DOI: doi.org/10.1016/j.ijrobp.2009.01.079
Titolo: Factors associated with neurological recovery of brainstem function
following postoperative conformal radiation therapy for infratentorial epend
ymoma.
Autori: Merchant TE., Chitti RM., Li C., Xiong X., Sanford RA., Khan RB.
Data di Pubblicazione: 2009-05-26
Abstract: Incomplete recovery of brainstem function after CRT for infratento
rial ependymoma is related to surgical morbidity and the volume and the exte
nt of tumor.
Journal Title: International journal of radiation oncology, biology, physics

PUBMED ID: 19415180
DOI: doi.org/10.1007/s00701-009-0306-5
Titolo: Combined multiple surgical intervention and chemotherapy for multice
ntric WHO grade II glioma : a long-term follow-up study.
Autori: Vergani F., Sanson M., Duffau H.

Data di Pubblicazione: 2009-05-06
Abstract: The problems concerning the pathophysiology, diagnosis and treatme nt of this condition are discussed. On the basis of our results, we suggest that an active therapeutic strategy, by combining multiple surgical procedur es and complementary treatment, should be systematically considered in multi centric WHO grade II gliomas, as in similar unifocal neoplasms.
Journal Title: Acta neurochirurgica

PUBMED ID: 19414327
DOI: Mancante
Titolo: Efficacy of temozolomide treatment in patients with high-grade gliom a.
Autori: Oshiro S., Tsugu H., Komatsu F., Ohmura T., Ohta M., Sakamoto S., Fu kushima T., Inoue T.
Data di Pubblicazione: 2009-05-06
Abstract: TMZ chemotherapy is effective for the treatment of high-grade glio ma in some patients without serious toxicity. Assessing the true efficacy of TMZ will require a larger study with comparison of long-term outcomes betwee n other agents or combined therapeutic modalities.
Journal Title: Anticancer research

PUBMED ID: 21475844
DOI: doi.org/10.3892/mmr_00000115
Titolo: Salvage therapy with temozolomide for recurrent or progressive high-grade gliomas refractory to ACNU [1-(4-amino-2-methyl-5-pyrimidynyl) methyl-3-(2-chloroethyl)-3-nitrosourea hydrochloride].
Autori: Terasaki M., Tokutomi T., Shigemori M.
Data di Pubblicazione: 2011-04-09
Abstract: This study aimed to determine safety, response rate, toxicity and 6-month progression-free survival (PFS) by using temozolomide (TMZ) as salva ge chemotherapy for 25 adults with recurrent or progressive high-grade gliom as (HGGs) who failed 1-(4-amino-2-methyl-5-pyrimidynyl) methyl-3-(2-chloroet hyl)-3-nitrosourea hydrochloride (ACNU) therapy. Twenty-six patients with re current or progressive ACNU refractory HGG, including 12 with glioblastoma (GBM) and 13 with anaplastic astrocytoma (AA) were evaluated in a prospective study of temozolomide salvage chemotherapy. Following maximal surgical resec tion, the patients received 2-4 cycles of procarbazine (100 mg/m2, days 1-5) , ACNU (80 mg/m2/d1, day 5) and, on days 5 and 12, cepharantine (70 mg) and vincristine (1.4 mg/m2). TMZ (150-200 mg/m2/d, days 1-5) was also administer ed every 28 days for ≤24 cycles. The six-month PFS was 50% (mean 10 months; 95% CI, 7-14 months) in 12 GBM patients and 39% (mean 17 months; 95% CI, 7-2 8 months) in 13 patients with AA. The best response to chemotherapy had no i mpact on the duration of disease control. Treatment-related toxicities inclu ded infections, while two (8%) patients developed neutropenia. In conclusion , TMZ can benefit patients with ACNU refractory HGG.
Journal Title: Molecular medicine reports

PUBMED ID: 19335893
DOI: doi.org/10.1186/1471-2407-9-101
Titolo: Treatment of recurrent malignant gliomas with fotemustine monotherap y: impact of dose and correlation with MGMT promoter methylation.
Autori: Fabi A., Metro G., Russillo M., Vidiri A., Carapella CM., Maschio M. , Cognetti F., Jandolo B., Mirri MA., Sperduti I., Telera S., Carosi M., Pac e A.
Data di Pubblicazione: 2009-04-02
Abstract: Low-dose fotemustine at 65-75 mg/m(2) (induction phase) followed b y 75-85 mg/m(2) (maintenance phase) has an activity comparable to that of th

e conventional schedule. By determination of the MGMT promoter methylation s tatus patients might be identified who are more likely to benefit from fotem ustine chemotherapy.
Journal Title: BMC cancer

PUBMED ID: 19307505
DOI: doi.org/10.1200/JCO.2008.19.0694
Titolo: Phase II trial of vorinostat in recurrent glioblastoma multiforme: a north central cancer treatment group study.
Autori: Galanis E., Jaeckle KA., Maurer MJ., Reid JM., Ames MM., Hardwick JS ., Reilly JF., Loboda A., Nebozhyn M., Fantin VR., Richon VM., Scheithauer B ., Giannini C., Flynn PJ., Moore DF., Zwiebel J., Buckner JC.
Data di Pubblicazione: 2009-03-25
Abstract: Vorinostat monotherapy is well tolerated in patients with recurren t GBM and has modest single-agent activity. Histone acetylation analysis and RNA expression profiling indicate that vorinostat in this dose and schedule affects target pathways in GBM. Additional testing of vorinostat in combinat ion regimens is warranted.
Journal Title: Journal of clinical oncology : official journal of the Americ an Society of Clinical Oncology

PUBMED ID: 19289491
DOI: doi.org/10.1215/15228517-2009-007
Titolo: Phase I trial of temozolomide plus O6-benzylguanine 5-day regimen wi th recurrent malignant glioma.
Autori: Quinn JA., Jiang SX., Reardon DA., Desjardins A., Vredenburgh JJ., R ich JN., Gururangan S., Friedman AH., Bigner DD., Sampson JH., McLendon RE., Herndon JE., Walker A., Friedman HS.
Data di Pubblicazione: 2009-03-18
Abstract: This phase I clinical trial conducted with patients who had recurr ent or progressive malignant glioma (MG) was designed to determine the maxim um tolerated dose (MTD) and toxicity of three different 5-day dosing regimen s of temozolomide (TMZ) in combination with O(6)-benzylguanine (O(6)-BG). Bo th TMZ and O(6)-BG were administered on days 1-5 of a 28-day treatment cycle . A bolus infusion of O(6)-BG was administered at 120 mg/m(2) over 1 h on da ys 1, 3, and 5, along with a continuous infusion of O(6)-BG at 30 mg/m(2)/da y. TMZ was administered at the end of the first bolus infusion of O(6)-BG an d then every 24 h for 5 days during the continuous infusion of O(6)-BG. Pati ents were accrued to one of three 5-day dosing regimens of TMZ. Twenty-nine patients were enrolled into this study. The dose-limiting toxicities (DLTs) were grade 4 neutropenia, leukopenia, and thrombocytopenia. The MTD for TMZ for the three different 5-day dosing schedules was determined as follows: sc hedule 1, 200 mg/m(2) on day 1 and 50 mg/m(2)/day on days 2-5; schedule 2, 5 0 mg/m(2)/day on days 1-5; and schedule 3, 50 mg/m(2)/day on days 1-5 while receiving pegfilgrastim. Thus, the 5-day TMZ dosing schedule that maximized the total dose of TMZ when combined with O(6)-BG was schedule 1. This study provides the foundation for a phase II trial of O(6)-BG in combination with a 5-day dosing schedule of TMZ in TMZ-resistant MG.
Journal Title: Neuro-oncology

PUBMED ID: 19252415
DOI: doi.org/10.4161/cbt.8.8.7927
Titolo: Pro-survival AKT and ERK signaling from EGFR and mutant EGFRvIII enh ances DNA double-strand break repair in human glioma cells.
Autori: Golding SE., Morgan RN., Adams BR., Hawkins AJ., Povirk LF., Valerie K.
Data di Pubblicazione: 2009-03-03

Abstract: The epidermal growth factor receptor (EGFR) is frequently dysregul
ated in malignant glioma that leads to increased resistance to cancer therap
y. Upregulation of wild type or expression of mutant EGFR is associated with
tumor radioresistance and poor clinical outcome. EGFR variant III (EGFRvIII)
is the most common EGFR mutation in malignant glioma. Radioresistance is tho
ught to be, at least in part, the result of a strong cytoprotective response
fueled by signaling via AKT and ERK that is heightened by radiation in the c
linical dose range. Several groups including ours have shown that this respo
nse may modulate DNA repair. Herein, we show that expression of EGFRvIII pro
moted gamma-H2AX foci resolution, a surrogate for double-strand break (DSB)
repair, and thus enhanced DNA repair. Conversely, small molecule inhibitors
targeting EGFR, MEK, and the expression of dominant-negative EGFR (EGFR-CD53
3) significantly reduced the resolution of gamma-H2AX foci. When homologous
recombination repair (HRR) and non-homologous end joining (NHEJ) were specif
ically examined, we found that EGFRvIII stimulated and CD533 compromised HRR
and NHEJ, respectively. Furthermore, NHEJ was blocked by inhibitors of AKT a
nd ERK signaling pathways. Moreover, expression of EGFRvIII and CD533 increa
sed and reduced, respectively, the formation of phospho-DNA-PKcs and -ATM re
pair foci, and RAD51 foci and expression levels, indicating that DSB repair
is regulated at multiple levels. Altogether, signaling from EGFR and EGFRvII
I promotes both HRR and NHEJ that is likely a contributing factor towards th
e radioresistance of malignant gliomas.
Journal Title: Cancer biology & therapy

PUBMED ID: 19250783
DOI: doi.org/10.1016/j.ejrad.2009.01.013
Titolo: Glioblastoma treated with postoperative radio-chemotherapy: prognost
ic value of apparent diffusion coefficient at MR imaging.
Autori: Yamasaki F., Sugiyama K., Ohtaki M., Takeshima Y., Abe N., Akiyama Y
., Takaba J., Amatya VJ., Saito T., Kajiwara Y., Hanaya R., Kurisu K.
Data di Pubblicazione: 2009-03-03
Abstract: The ADC(MIN) value obtained from pretreatment MR images is a usefu
l clinical prognostic biomarker in patients with glioblastoma.
Journal Title: European journal of radiology

PUBMED ID: 19240962
DOI: doi.org/10.1007/s00415-009-5006-9
Titolo: Rechallenge with temozolomide in patients with recurrent gliomas.
Autori: Wick A., Pascher C., Wick W., Jauch T., Weller M., Bogdahn U., Hau P
.
Data di Pubblicazione: 2009-02-26
Abstract: Temozolomide (TMZ) is the standard of care for patients with newly
diagnosed glioblastoma (GBM) as well as those with recurrent anaplastic glio
ma (AG) and GBM. It has become common practice to re-expose patients to TMZ
who had been previously treated with TMZ, or to switch patients to alternati
ve dosing regimens of TMZ when there are signs of relapse or progress on sta
ndard TMZ therapeutic regimens. To date, however, there is a scarcity of dat
a on the efficacy of this therapeutic strategy, currently referred to as TMZ
rechallenge. We have conducted a retrospective review of patients with recur
rent glioma rechallenged with TMZ. Patients experiencing progressive disease
(PD) during TMZ therapy who were rechallenged with alternative TMZ regimens
and patients rechallenged after stable disease in a TMZ-free interval were e
valuated separately. A total of 90 rechallenges were identified in 80 patien
ts. The progression-free survival at 6 months (PFS-6) was 48% in patients wi
th AG (12/25) and 27.7% in those with GBM (14/47). The PFS-6 was 16.7% in AG
and 26.3% in GBM for patients switched during TMZ and 57.9 and 28.6% in pati
ents rechallenged after a TMZ-free interval of at least 8 weeks. Relevant he
matological toxicity (NCI-CTC grade 3-5) was observed in 22 of 90 rechalleng

es, and relevant non-hematological in ten of 90 rechallenges. Temozolomide w as well tolerated and generated promising PFS-6 in patients who had previous ly failed TMZ, regardless if they progressed during TMZ treatment, or if the y were rechallenged after a TMZ-free interval. These results suggest that th e TMZ rechallenge strategy warrants further investigation in a prospective r andomized trial.
Journal Title: Journal of neurology

PUBMED ID: 19221865
DOI: doi.org/10.1007/s11060-009-9809-4
Titolo: Effect of adding temozolomide to radiation therapy on the incidence of pseudo-progression.
Autori: Gerstner ER., McNamara MB., Norden AD., Lafrankie D., Wen PY.
Data di Pubblicazione: 2009-02-18
Abstract: Recently, there has been greater awareness that combination radiat ion and temozolomide used to treat glioblastomas may cause increased contras t enhancement on the first post radiation MRI scan. However, this increased enhancement may stabilize or decrease over time and represent pseudo-progres sion (psPD) rather than true progressive disease. It has never been shown th at this phenomenon is greater with combination therapy than radiation alone. To address this question, we reviewed MRI scans in glioblastoma patients tre ated with radiation alone versus patients treated with radiation and concomi tant temozolomide and compared the frequency of psPD in the two groups. Eigh teen of 47 patients (38%) treated with radiation alone demonstrated enlargem ent on their first post-radiation MRI scan and 11 of these 18 (61%) proved t o have psPD as defined by no further enlargement on stable therapy for 3 mon ths following radiation. Twenty-four of 45 patients (53%) treated with radia tion and temozolomide had enlargement on their first post-radiation MRI scan and 13 of these 24 (54%) had psPD. Median overall survival (OS) in patients with psPD treated with radiation alone was 15.6 versus 12.8 months in those without psPD. Median OS in patients treated with radiation and concomitant t emozolomide who had psPD was 24.4 versus 15.9 months in those who did not ha ve psPD. We were unable to detect a difference in OS between the four groups . Presence of psPD, independent of treatment, was associated with prolonged progression-free survival (P = 0.05) but not OS. psPD may be more common in combination therapy but most likely by a small margin.
Journal Title: Journal of neuro-oncology

PUBMED ID: 19204207
DOI: doi.org/10.1200/JCO.2008.17.5984
Titolo: Randomized phase II trial of erlotinib versus temozolomide or carmus tine in recurrent glioblastoma: EORTC brain tumor group study 26034.
Autori: van den Bent MJ., Brandes AA., Rampling R., Kouwenhoven MC., Kros JM ., Carpentier AF., Clement PM., Frenay M., Campone M., Baurain JF., Armand J P., Taphoorn MJ., Tosoni A., Kletzl H., Klughammer B., Lacombe D., Gorlia T.
Data di Pubblicazione: 2009-02-11
Abstract: Erlotinib has insufficient single-agent activity in unselected GBM . No clear biomarker associated with improved outcome to erlotinib was ident ified.
Journal Title: Journal of clinical oncology : official journal of the Americ an Society of Clinical Oncology

PUBMED ID: 19197992
DOI: doi.org/10.1002/cncr.24179
Titolo: Bevacizumab for recurrent alkylator-refractory anaplastic oligodendr oglioma.
Autori: Chamberlain MC., Johnston S.

Data di Pubblicazione: 2009-02-07
Abstract: Bevacizumab demonstrated efficacy and acceptable toxicity in this cohort of adults with recurrent 1p19q codeleted alkylator-refractory AO.
Journal Title: Cancer

PUBMED ID: 19192961
DOI: doi.org/10.1586/14737140.9.2.235
Titolo: Interactions between PTEN and receptor tyrosine kinase pathways and their implications for glioma therapy.
Autori: Abounader R.
Data di Pubblicazione: 2009-02-06
Abstract: Gliomas are the most common and deadly form of malignant primary b rain tumors. Loss of the tumor-suppressor PTEN and activation of the recepto r tyrosine kinases (RTKs) EGF receptor, c-Met, PDGF receptor and VEGF recept or are among the most common molecular dysfunctions associated with glioma m alignancy. PTEN interacts with RTK-dependent signaling at multiple levels. T hese include the ability of PTEN to counteract PI3K activation by RTKs, as w ell as possible effects of PTEN on RTK activation of the MAPK pathway and RT K-dependent gene-expression regulation. Consequently, PTEN expression affect s RTK-induced malignancy. Importantly, the PTEN status was recently found to be critical for the outcome of RTK-targeted clinical therapies that have bee n developed recently. Combining RTK-targeted therapies with therapies aimed at counteracting the effects of PTEN loss, such as mTOR inhibition, might al so have therapeutic advantage. This article reviews the known molecular and functional interactions between PTEN and RTK pathways and their implications for glioma therapy.
Journal Title: Expert review of anticancer therapy

PUBMED ID: 19190249
DOI: doi.org/10.1182/blood-2008-07-171389
Titolo: Green tea polyphenols block the anticancer effects of bortezomib and other boronic acid-based proteasome inhibitors.
Autori: Golden EB., Lam PY., Kardosh A., Gaffney KJ., Cadenas E., Louie SG., Petasis NA., Chen TC., Schönthal AH.
Data di Pubblicazione: 2009-02-05
Abstract: The anticancer potency of green tea and its individual components is being intensely investigated, and some cancer patients already self-medic ate with this "miracle herb" in hopes of augmenting the anticancer outcome o f their chemotherapy. Bortezomib (BZM) is a proteasome inhibitor in clinical use for multiple myeloma. Here, we investigated whether the combination of t hese compounds would yield increased antitumor efficacy in multiple myeloma and glioblastoma cell lines in vitro and in vivo. Unexpectedly, we discovere d that various green tea constituents, in particular (-)-epigallocatechin ga llate (EGCG) and other polyphenols with 1,2-benzenediol moieties, effectivel y prevented tumor cell death induced by BZM in vitro and in vivo. This prono unced antagonistic function of EGCG was evident only with boronic acid-based proteasome inhibitors (BZM, MG-262, PS-IX), but not with several non-boronic acid proteasome inhibitors (MG-132, PS-I, nelfinavir). EGCG directly reacted with BZM and blocked its proteasome inhibitory function; as a consequence, B ZM could not trigger endoplasmic reticulum stress or caspase-7 activation, a nd did not induce tumor cell death. Taken together, our results indicate tha t green tea polyphenols may have the potential to negate the therapeutic eff icacy of BZM and suggest that consumption of green tea products may be contr aindicated during cancer therapy with BZM.
Journal Title: Blood

PUBMED ID: 19169684

DOI: doi.org/10.1007/s00280-009-0926-8
Titolo: Fotemustine as second-line treatment for recurrent or progressive gl
ioblastoma after concomitant and/or adjuvant temozolomide: a phase II trial
of Gruppo Italiano Cooperativo di Neuro-Oncologia (GICNO).
Autori: Brandes AA., Tosoni A., Franceschi E., Blatt V., Santoro A., Faedi M
., Amistà P., Gardiman M., Labianca R., Bianchini C., Ermani M., Reni M.
Data di Pubblicazione: 2009-01-27
Abstract: The findings of the present trial, that evaluate fotemustine in a
homogeneous population, may represent a new benchmark for nitrosourea activi
ty. Moreover, this is the first study to evaluate correlation between MGMT p
romoter status and outcome of fotemustine for relapsing GBM previously treat
ed with radiotherapy and temozolomide.
Journal Title: Cancer chemotherapy and pharmacology

PUBMED ID: 19164435
DOI: doi.org/10.1215/15228517-2008-114
Titolo: Plasma IGFBP-2 levels predict clinical outcomes of patients with hig
h-grade gliomas.
Autori: Lin Y., Jiang T., Zhou K., Xu L., Chen B., Li G., Qiu X., Jiang T.,
Zhang W., Song SW.
Data di Pubblicazione: 2009-01-24
Abstract: Insulin-like growth factor binding protein 2 (IGFBP-2) is a malign
ancy-associated protein measurable in tumors and blood. Increased IGFBP-2 is
associated with shortened survival of advanced glioma patients. Thus, we exa
mined plasma IGFBP-2 levels in glioma patients and healthy controls to evalu
ate its value as a plasma biomarker for glioma. Plasma IGFBP-2 levels in 196
patients with newly diagnosed glioma and 55 healthy controls were analyzed u
sing an IGFBP-2 ELISA kit. Blood was collected before surgery, after two-cyc
le adjuvant chemotherapy, and at recurrence. Plasma IGFBP-2 levels were corr
elated with disease-free survival (DFS) using Cox regression analyses. We fo
und that preoperative plasma IGFBP-2 levels were significantly higher in hig
h-grade glioma patients (n = 43 for grade III glioma; n = 72 for glioblastom
a multiforme [GBM]) than in healthy controls (n = 55; p < 0.001) and low-gra
de (grade II) glioma patients (n = 81; p < 0.001). No significant difference
s in preoperative plasma IGFBP-2 levels were observed between grade III glio
ma and GBM patients or between grade II glioma patients and healthy controls
. After recurrence, plasma IGFBP-2 levels were significantly increased in GB
M patients (n = 26; p < 0.001). Preoperative plasma IGFBP-2 levels were sign
ificantly correlated with DFS in GBM patients (hazard ratio, 1.404; 95% conf
idence interval, 1.078-1.828; p = 0.012). We conclude that preoperative plas
ma IGFBP-2 levels are significantly higher in high-grade glioma patients tha
n in low-grade glioma patients and healthy subjects, and are significantly c
orrelated with recurrence and DFS in patients with GBM. Longitudinal studies
with a larger study population are needed to confirm these findings.
Journal Title: Neuro-oncology

PUBMED ID: 19139825
DOI: doi.org/10.1007/s11060-008-9774-3
Titolo: Topotecan in combination with radiotherapy in unresectable glioblast
oma: a phase 2 study.
Autori: Lesimple T., Riffaud L., Frappaz D., Ben Hassel M., Gédouin D., Bay
JO., Linassier C., Hamlat A., Piot G., Fabbro M., Saïkali S., Carsin B., Gué
gan Y.
Data di Pubblicazione: 2009-01-14
Abstract: Improving glioblastoma multiforme (GBM) treatment with radio-chemo
therapy remains a challenge. Topotecan is an attractive option as it exhibit
s growth inhibition of human glioma as well as brain penetration. The presen
t study assessed the combination of radiotherapy (60 Gy/30 fractions/40 days

) and topotecan (0.9 mg/m(2)/day on days 1-5 on weeks 1, 3 and 5) in 50 adul ts with histologically proven and untreated GBM. The incidence of non-hemato logical toxicities was low and grade 3-4 hematological toxicities were repor ted in 20 patients (mainly lymphopenia and neutropenia). Partial response an d stabilization rates were 2% and 32%, respectively, with an overall time to progression of 12 weeks. One-year overall survival (OS) rate was 42%, with a median OS of 40 weeks. Topotecan in combination with radiotherapy was well t olerated. However, while response and stabilization concerned one-third of t he patients, the study did not show increased benefits in terms of survival in patients with unresectable GBM.
Journal Title: Journal of neuro-oncology

PUBMED ID: 19118062
DOI: doi.org/10.1158/1078-0432.CCR-08-0888
Titolo: Phase II study of protracted daily temozolomide for low-grade glioma s in adults.
Autori: Kesari S., Schiff D., Drappatz J., LaFrankie D., Doherty L., Macklin EA., Muzikansky A., Santagata S., Ligon KL., Norden AD., Ciampa A., Bradshaw J., Levy B., Radakovic G., Ramakrishna N., Black PM., Wen PY.
Data di Pubblicazione: 2009-01-02
Abstract: A protracted course of daily temozolomide is a well-tolerated regi men and seems to produce effective tumor control. This compares favorably wi th historical data on the standard 5-day temozolomide regimen.
Journal Title: Clinical cancer research : an official journal of the America n Association for Cancer Research

PUBMED ID: 19116635
DOI: doi.org/10.1038/mt.2008.275
Titolo: Phase ib trial of oncolytic herpes virus G207 shows safety of multip le injections and documents viral replication.
Autori: Aghi MK., Chiocca EA.
Data di Pubblicazione: 2009-01-01
Abstract:
Journal Title: Molecular therapy : the journal of the American Society of Ge ne Therapy

PUBMED ID: 19062723
DOI: Mancante
Titolo: [Multicenter phase II clinical trial of uroacitides injection in the treatment for advanced malignant tumors].
Autori: Li Q., Feng FY., Chen Q., Jiao SC., Li F., Wang HQ., Huang WX., Ling CQ., Li MZ., Ren J., Zhang Y., Qin FZ., Zhou MZ., Zhu RZ.
Data di Pubblicazione: 2008-12-10
Abstract: Uroacitides injection is effective in the control for various kind s of advanced cancers with mild, reversible and tolerable adverse effects, a nd can also improve the patient's quality of life. It is worth being studied further.
Journal Title: Zhonghua zhong liu za zhi [Chinese journal of oncology]

PUBMED ID: 19057330
DOI: doi.org/10.1227/01.NEU.0000334052.60634.84
Titolo: Intraparenchymal and intratumoral interstitial infusion of anti-glio ma monoclonal antibody 8H9.
Autori: Luther N., Cheung NK., Dunkel IJ., Fraser JF., Edgar MA., Gutin PH., Souweidane MM.
Data di Pubblicazione: 2008-12-06

Abstract: Finally, intratumoral interstitial infusion of a reactive MAb has been performed similarly to delivery to a normal brain. This finding is encouraging from a therapeutic standpoint, given the clinical need to affect large domains of these infiltrative tumors.
Journal Title: Neurosurgery

PUBMED ID: 19031176
DOI: doi.org/10.1080/02841860802537924
Titolo: Bevacizumab plus irinotecan in the treatment patients with progressive recurrent malignant brain tumours.
Autori: Poulsen HS., Grunnet K., Sorensen M., Olsen P., Hasselbalch B., Nelausen K., Kosteljanetz M., Lassen U.
Data di Pubblicazione: 2008-11-26
Abstract: We conclude that the combination of bevacizumab and irinotecan shows acceptable safety and is a clinically relevant choice of therapy in heavily pre-treated patients with recurrent high-grade brain tumours.
Journal Title: Acta oncologica (Stockholm, Sweden)

PUBMED ID: 19025795
DOI: doi.org/10.1002/gcc.20635
Titolo: Stepwise accumulation of distinct genomic aberrations in a patient with progressively metastasizing ependymoma.
Autori: Milde T., Pfister S., Korshunov A., Deubzer HE., Oehme I., Ernst A., Starzinski-Powitz A., Seitz A., Lichter P., von Deimling A., Witt O.
Data di Pubblicazione: 2008-11-26
Abstract: Nonresectable ependymomas are associated with poor prognosis despite intensive radiochemotherapy and radiation. The molecular pathogenesis of ependymoma initiation and progression is largely unknown. We here present a case of therapy-refractory, progressive ependymoma with cerebrospinal as well as extraneural metastases, which allowed us for the first time to follow the stepwise accumulation of chromosome aberrations during disease progression. Genome-wide DNA copy-number analysis showed sequential deletions on chromosomes 1, 9, and 14 as well as a homozygous deletion of the CDKN2A locus, underscoring its role in tumor progression. Gradual loss at 1p36 was associated with loss of protein expression of the putative tumor suppressor gene AJAP1/SHREW1. In summary, this is the first report on acquired genomic aberrations in ependymoma over time pointing to novel candidate tumor suppressor genes. This analysis provides molecular insights into the chronology of genetic events in this case from initial localized tumor to widespread metastasized disease.
Journal Title: Genes, chromosomes & cancer

PUBMED ID: 19018476
DOI: doi.org/10.1007/s11060-008-9739-6
Titolo: A multi-institutional phase II study on second-line Fotemustine chemotherapy in recurrent glioblastoma.
Autori: Fabrini MG., Silvano G., Lolli I., Perrone F., Marsella A., Scotti V., Cionini L.
Data di Pubblicazione: 2008-11-20
Abstract: The present study aims to assess the feasibility and the effectiveness of a second-line Fotemustine chemotherapy in patients with recurrent Glioblastoma after standard primary treatment. Between 2005 and 2007, 50 patients with relapsed malignant glioma (median age=56.8 years; median KPS=90) underwent a second-line chemotherapy with Fotemustine. Selected patients were previously treated with a standard 60 Gy Radiotherapy course and Temozolomide Chemotherapy. Patients were stratified into classes according to the prognostic Recursive Partition Analysis. Endpoints of the study were Progression

Free Survival at 6 months, duration of Objective Response and Stabilization, Overall Survival and toxicity. At analysis, 36 patients were dead and 14 wer e alive. Median follow-up from primary diagnosis was 26.6 months. The Effica cy control of the disease was 62%. PFS was 6.1 months; PFS-6 was 52% and med ian overall survival from primary diagnosis was 24.5 months, with few manage able haematological toxicities. Fotemustine was safe and effective as second -line chemotherapy in recurrent glioblastoma.
Journal Title: Journal of neuro-oncology

PUBMED ID: 18987781
DOI: doi.org/10.1007/s11060-008-9728-9
Titolo: ACNU-based chemotherapy for recurrent glioma in the temozolomide era .
Autori: Happold C., Roth P., Wick W., Steinbach JP., Linnebank M., Weller M. , Eisele G.
Data di Pubblicazione: 2008-11-07
Abstract: No standard of care for patients with recurrent glioblastoma has b een defined since temozolomide has become the treatment of choice for patien ts with newly diagnosed glioblastoma. This has renewed interest in the use o f nitrosourea-based regimens for patients with progressive or recurrent dise ase. The most commonly used regimens are carmustine (BCNU) monotherapy or lo mustine (CCNU) combined with procarbazine and vincristine (PCV). Here we rep ort our institutional experience with nimustine (ACNU) alone (n=14) or in co mbination with other agents (n=18) in 32 patients with glioblastoma treated previously with temozolomide. There were no complete and two partial respons es. The progression-free survival (PFS) rate at 6 months was 20% and the sur vival rate at 12 months 26%. Grade III or IV hematological toxicity was obse rved in 50% of all patients and led to interruption of treatment in 13% of p atients. Non-hematological toxicity was moderate to severe and led to interr uption of treatment in 9% of patients. Thus, in this cohort of patients pret reated with temozolomide, ACNU failed to induce a substantial stabilization of disease in recurrent glioblastoma, but caused a notable hematotoxicity. T his study does not commend ACNU as a therapy of first choice for patients wi th recurrent glioblastomas pretreated with temozolomide.
Journal Title: Journal of neuro-oncology

PUBMED ID: 21479498
DOI: doi.org/10.3892/mmr_00000042
Titolo: Rechallenge with temozolomide with different scheduling is effective in recurrent malignant gliomas.
Autori: Strik HM., Buhk JH., Wrede A., Hoffmann AL., Bock HC., Christmann M. , Kaina B.
Data di Pubblicazione: 2011-04-12
Abstract: Treatment of recurrent malignant glioma, which has a poor patient prognosis, has not been standardised. Moreover, it is unclear whether repeat ed treatment with temozolomide is effective in patients who received previou s temozolomide treatment before developing a recurrence. Here, we present th e results of a high-dose individually adapted 21-day regimen demonstrating t hat rechallenge is effective even in patients expressing O6-methylguanine-DN A methyltransferase (MGMT) in the tumor. Twenty-one patients with recurrent malignant gliomas pre-treated with temozolomide, 18 WHO IV glioblastoma (GBM) and 3 WHO III patients, received 100 mg/m2 temozolomide on days 1-21/28. T he GBM patients had a median Karnofsky performance status of 60% and a media n age of 54.8 years. Blood counts decreased continuously, enabling a gradual dose adaptation. When blood counts dropped below normal values, temozolomide was applied on days 1-5/7. Dosage was reduced to 50-75 mg/m2 in 11 patients and gradually increased up to 130 mg/m2 in 3 patients. WHO grade 3/4 toxicit y was hematological in 3 patients and non-hematological in 3 patients. In GB

M patients (n=18), response after >3 months was complete in 3 patients, part ial in 1 (22%), stable disease in 7 (39%) and progressive disease in 7 (39%) . Progression-free survival at 6 months (PFS-6M) was 39%. Median survival wa s 9.1 months from relapse and 17.9 months overall. Of the patients with unme thylated MGMT promoter, 2/7 were progression-free for >6 (15 and 19) months. The data indicate that rechallenge with near-continuous, higher-dose temozol omide (100 mg/m2 on days 1-21/28 or days 1-5/7 with individual dose adaptati on) is also feasible in patients with critical blood counts. Objective respo nses can be achieved even after relapse during a conventional 5/28-day regim en. The resistance of tumors characterized by unmethylated MGMT promoter may be overcome by near continuous temozolomide administration, which is probabl y most effective with a 5/7-day schedule. In spite of the relatively poor cl inical prognosis, the data indicate that rechallenge with temozolomide with a dose-dense and long-lasting administration protocol is tolerable and compa rable with other reported treatment protocols involving temozolomide.
Journal Title: Molecular medicine reports

PUBMED ID: 18957964
DOI: doi.org/10.1038/mt.2008.228
Titolo: Phase Ib trial of mutant herpes simplex virus G207 inoculated pre-an d post-tumor resection for recurrent GBM.
Autori: Markert JM., Liechty PG., Wang W., Gaston S., Braz E., Karrasch M., Nabors LB., Markiewicz M., Lakeman AD., Palmer CA., Parker JN., Whitley RJ., Gillespie GY.
Data di Pubblicazione: 2008-10-30
Abstract: We have previously demonstrated safety of G207, a doubly mutated (deletion of both gamma(1)34.5 loci, insertional inactivation of U(L)39) herp es simplex virus (HSV) for patients stereotactically inoculated in enhancing portions of recurrent malignant gliomas. We have now determined safety of tw o inoculations of G207, before and after tumor resection. Inclusion criteria were histologically proven recurrent malignant glioma, Karnofsky score >or=7 0, and ability to resect the tumor without ventricular system breach. Patien ts received two doses of G207 totaling 1.15 x 10(9) plaque-forming units wit h 13% of this total injected via a catheter placed stereotactically in the t umor. Two or five days later, tumor was resected en bloc with catheter in pl ace. The balance of G207 dose was injected into brain surrounding the resect ion cavity. Six patients with recurrent glioblastoma multiforme were enrolle d. Two days after the second G207 inoculation, one patient experienced trans ient fever, delirium, and hemiparesis, which entirely resolved on high-dose dexamethasone. No patient developed HSV encephalitis or required treatment w ith acyclovir. Radiographic and neuropathologic evidence suggestive of antit umor activity is reported. Evidence of viral replication was demonstrated. G 207 appears safe for multiple dose delivery, including direct inoculation in to the brain surrounding tumor resection cavity.
Journal Title: Molecular therapy : the journal of the American Society of Ge ne Therapy

PUBMED ID: 18953491
DOI: doi.org/10.1007/s11060-008-9722-2
Titolo: Salvage chemotherapy with bevacizumab for recurrent alkylator-refrac tory anaplastic astrocytoma.
Autori: Chamberlain MC., Johnston S.
Data di Pubblicazione: 2008-10-28
Abstract: A retrospective study of bevacizumab only in adults with recurrent temozolomide (TMZ)-refractory anaplastic astrocytoma (AA) with a primary obj ective of determining progression free survival (PFS). There is no standard therapy for alkylator-resistant AA and hence a need exists for new therapies . Twenty-five patients (15 men; 10 women) ages 26-63 (median 50), with radio

graphically recurrent AA were treated. All patients had previously been trea ted with surgery, involved-field radiotherapy, and alkylator-based chemother apy. Fourteen patients underwent repeat surgery. Patients were treated at se cond recurrence with bevacizumab (10 mg/kg), once every 2 weeks (defined as a single cycle). Neurological evaluation was performed every 2 weeks and neu roradiographic assessment following the initial two cycles of bevacizumab an d subsequently after every four cycles of bevacizumab. All patients were eva luable for toxicity and response. A total of 360 cycles of bevacizumab (medi an 14 cycles; range 2-40) was administered. Bevacizumab-related toxicity inc luded fatigue (14 patients; 2 grade 3), leukopenia (7; 1 grade 3), deep vein thrombosis (5; 2 grade 3), hypertension (5; 1 grade 3), anemia (4; 0 grade 3) and wound dehiscence (1; 1 grade 3). Sixteen patients (64%) demonstrated a partial radiographic response, 2 (8.0%) stable disease and 7 (28%) progressi ve disease following two cycles of bevacizumab. Time to tumor progression ra nged from 1 to 20 months (median: 7). Survival ranged from 2 to 23 months (m edian: 9.0). 6-month and 12-month PFS were 60 and 20%, respectively. Bevaciz umab demonstrated efficacy and acceptable toxicity in this cohort of adults with recurrent alkylator refractory AA.
Journal Title: Journal of neuro-oncology

PUBMED ID: 18928344
DOI: doi.org/10.1586/14737175.8.10.1507
Titolo: MRI for identification of progression in brain tumors: from morpholo gy to function.
Autori: Weber MA., Giesel FL., Stieltjes B.
Data di Pubblicazione: 2008-10-22
Abstract: For monitoring of brain tumors, it is crucial to identify progress ion or treatment failure early during follow-up to change treatment schemes and, thereby, optimize patient outcome. In the past years, several areas wit hin the field of magnetic resonance (MR) have seen considerable advances: mo dern contrast media, advanced morphologic approaches and several functional techniques, for example, in the visualization of tumor perfusion or tumor ce ll metabolism. This review presents these recent advances by introducing the different techniques and outlining their benefit for identification of progr ession in brain tumors, with a focus on gliomas, metastases and meningiomas. After radiotherapy, MR spectroscopy helps to more accurately discriminate be tween radiation necrosis and glioma progression. In low-grade gliomas, perfu sion MR techniques enable a more sensitive detection of anaplastic transform ation than conventional MRI. Modern contrast media, as well as diffusion ten sor imaging, allow for an improved tumor delineation and assessment of tumor extension. We will also highlight the biological background of these techniq ues, their applicability and current limitations. In conclusion, modern MRI techniques have been developed that are on the doorstep to be integrated in clinical routine.
Journal Title: Expert review of neurotherapeutics

PUBMED ID: 18834263
DOI: doi.org/10.3171/2008.4.17492
Titolo: Antiangiogenic therapy using bevacizumab in recurrent high-grade gli oma: impact on local control and patient survival.
Autori: Narayana A., Kelly P., Golfinos J., Parker E., Johnson G., Knopp E., Zagzag D., Fischer I., Raza S., Medabalmi P., Eagan P., Gruber ML.
Data di Pubblicazione: 2008-10-07
Abstract: Antiangiogenic therapy using bevacizumab appears to improve surviv al in patients with recurrent high-grade glioma. A possible change in the in vasiveness of the tumor following therapy is worrisome and must be closely m onitored.
Journal Title: Journal of neurosurgery

PUBMED ID: 18797358
DOI: doi.org/10.1227/01.NEU.0000315282.61035.48
Titolo: Persistent outpatient hyperglycemia is independently associated with decreased survival after primary resection of malignant brain astrocytomas.
Autori: McGirt MJ., Chaichana KL., Gathinji M., Attenello F., Than K., Jimenez Ruiz A., Olivi A., Quiñones-Hinojosa A.
Data di Pubblicazione: 2008-09-18
Abstract: In our experience, persistent outpatient hyperglycemia was associated with decreased survival in patients undergoing surgical resection for malignant astro- cytomas and was independent of the degree of disability, tumor grade, diabetes, prolonged dexamethasone use, or subsequent treatment modalities. Increased glucose control is warranted in this patient population and may contribute to improved outcomes in the treatment of malignant brain astrocytomas.
Journal Title: Neurosurgery

PUBMED ID: 18726148
DOI: doi.org/10.1007/s00005-008-0027-0
Titolo: Ras pathway activation in gliomas: a strategic target for intranasal administration of perillyl alcohol.
Autori: da Fonseca CO., Linden R., Futuro D., Gattass CR., Quirico-Santos T.
Data di Pubblicazione: 2008-08-30
Abstract: The preliminary results indicate that intranasal administration of the signal transduction inhibitor POH is a safe, noninvasive, and low-cost method. There were no toxicity events and the regression of tumor size in some patients is suggestive of antitumor activity.
Journal Title: Archivum immunologiae et therapiae experimentalis

PUBMED ID: 18711186
DOI: doi.org/10.1200/JCO.2007.15.9970
Titolo: Predicting change in academic abilities after conformal radiation therapy for localized ependymoma.
Autori: Conklin HM., Li C., Xiong X., Ogg RJ., Merchant TE.
Data di Pubblicazione: 2008-08-20
Abstract: CRT may result in better long-term cognitive outcomes when compared to conventional radiation therapy approaches. Reading appears more vulnerable than other academic skills and may decline over time despite stable intellectual functioning.
Journal Title: Journal of clinical oncology : official journal of the American Society of Clinical Oncology

PUBMED ID: 18676355
DOI: doi.org/10.1215/15228517-2008-058
Titolo: A novel tool to analyze MRI recurrence patterns in glioblastoma.
Autori: Wick W., Stupp R., Beule AC., Bromberg J., Wick A., Ernemann U., Platten M., Marosi C., Mason WP., van den Bent M., Weller M., Rorden C., Karnath HO., Karnath HO.
Data di Pubblicazione: 2008-08-05
Abstract: At least 10% of glioblastoma relapses occur at distant and even contralateral locations. This disseminated growth limits surgical intervention and contributes to neurological morbidity. Preclinical data pointed toward a role for temozolomide (TMZ) in reducing radiotherapy-induced glioma cell invasiveness. Our objective was to develop and validate a new analysis tool of MRI data to examine the clinical recurrence pattern of glioblastomas. MRIcro software was used to map the location and extent of initial preoperative and

recurrent tumors on MRI of 63 patients in the European Organisation for Rese arch and Treatment of Cancer (EORTC) 26981/22981/National Cancer Institute o f Canada (NCIC) CE.3 study into the same stereotaxic space. This allowed us to examine changes of site and distance between the initial and the recurren t tumor on the group level. Thirty of the 63 patients were treated using rad iotherapy, while the other patients completed a radiotherapy-plus-TMZ treatm ent. Baseline characteristics (median age, KPS) and outcome data (progressio n-free survival, overall survival) of the patients included in this analysis resemble those of the general study cohort. The patient groups did not diffe r in the promoter methylation status of methyl guanine methyltransferase (MG MT). Overall frequency of distant recurrences was 20%. Analysis of recurrenc e patterns revealed no difference between the groups in the size of the recu rrent tumor or in the differential effect on the distance of the recurrences from the preoperative tumor location. The data show the feasibility of group wise recurrence pattern analysis. An effect of TMZ treatment on the recurren ce pattern in the EORTC 26981/22981/NCIC CE.3 study could not be demonstrate d.
Journal Title: Neuro-oncology

PUBMED ID: 18671639
DOI: doi.org/10.3171/JNS/2008/109/8/0268
Titolo: Bevacizumab and irinotecan therapy in glioblastoma multiforme: a ser ies of 13 cases.
Autori: Ali SA., McHayleh WM., Ahmad A., Sehgal R., Braffet M., Rahman M., B ejjani G., Friedland DM.
Data di Pubblicazione: 2008-08-02
Abstract: The combination of bevacizumab and irinotecan is safe and has exce llent activity even in this relapsed, heavily pretreated population of patie nts with high-grade malignant glioma, most of whom would not be candidates f or clinical trials.
Journal Title: Journal of neurosurgery

PUBMED ID: 18632651
DOI: doi.org/10.1158/0008-5472.CAN-07-5973
Titolo: Vaccination elicits correlated immune and clinical responses in glio blastoma multiforme patients.
Autori: Wheeler CJ., Black KL., Liu G., Mazer M., Zhang XX., Pepkowitz S., G oldfinger D., Ng H., Irvin D., Yu JS.
Data di Pubblicazione: 2008-07-18
Abstract: Cancer vaccine trials have failed to yield robust immune-correlate d clinical improvements as observed in animal models, fueling controversy ov er the utility of human cancer vaccines. Therapeutic vaccination represents an intriguing additional therapy for glioblastoma multiforme (GBM; grade 4 g lioma), which has a dismal prognosis and treatment response, but only early phase I vaccine trial results have been reported. Immune and clinical respon ses from a phase II GBM vaccine trial are reported here. IFN-gamma responsiv eness was quantified in peripheral blood of 32 GBM patients given therapeuti c dendritic cell vaccines. Posttreatment times to tumor progression (TTP) an d survival (TTS) were compared in vaccine responders and nonresponders and w ere correlated with immune response magnitudes. GBM patients (53%) exhibited >or=1.5-fold vaccine-enhanced cytokine responses. Endogenous antitumor respo nses of similar magnitude occurred in 22% of GBM patients before vaccination . Vaccine responders exhibited significantly longer TTS and TTP relative to nonresponders. Immune enhancement in vaccine responders correlated logarithm ically with TTS and TTP spanning postvaccine chemotherapy, but not with init ial TTP spanning vaccination alone. This is the first report of a progressiv e correlation between cancer clinical outcome and T-cell responsiveness afte r therapeutic vaccination in humans and the first tracing of such correlatio

n to therapeutically exploitable tumor alteration. As such, our findings off
er unique opportunities to identify cellular and molecular components of cli
nically meaningful antitumor immunity in humans.
Journal Title: Cancer research

PUBMED ID: 18615600
DOI: doi.org/10.1002/cncr.23677
Titolo: Temozolomide for recurrent low-grade spinal cord gliomas in adults.
Autori: Chamberlain MC.
Data di Pubblicazione: 2008-07-11
Abstract: TMZ demonstrated modest efficacy with acceptable toxicity in this
cohort of adult patients with recurrent low-grade spinal cord gliomas.
Journal Title: Cancer

PUBMED ID: 18602834
DOI: doi.org/10.1016/j.critrevonc.2008.05.005
Titolo: Treatment options for malignant gliomas, emphasizing towards new mol
ecularly targeted therapies.
Autori: Argyriou AA., Antonacopoulou A., Iconomou G., Kalofonos HP.
Data di Pubblicazione: 2008-07-08
Abstract: Malignant gliomas (MGs), including glioblastomas and anaplastic as
trocytomas are the most common primary brain tumors. Despite treatment advan
ces, the outcome of patients diagnosed with MGs is poor. The current standar
d treatment protocols for managing these tumors include maximally safe surgi
cal resection, followed by fractioned radiation therapy of the tumor and sur
rounding brain parenchyma. Until recently, the use of systemic chemotherapy
was restricted and ineffective, due to the fact that the blood brain barrier
inhibits the adequate therapeutic concentrations of most chemotherapeutic ag
ents into the tumor and peritumoral area. Genetic transformation, like the e
xpression of the DNA repair enzyme methylguanine methyltransferase (MGMT) an
d specific characteristics of these neoplasms are also causal factors, accou
nting for the development of treatment resistance to standard chemotherapy o
ptions with alkylating compounds. Recent advances, mostly, in thorough under
standing of the complex molecular pathogenesis of MGs have led to arousal of
rational development of new molecularly targeted treatment options that simu
ltaneously affect multiple signalling pathways. Currently, several molecular
ly targeted agents, like tyrosine kinase and growth factor inhibitors have b
een tested in clinical trials to establish future directions in the therapy
of MGs. A number of novel targeted strategies, including among others radio-
immuno and ligand-toxin conjugates and RNA-based therapies, are also under i
nvestigation. We herein review and discuss the standard treatment options an
d recent advances in the therapy of MGs, with emphasis on the current knowle
dge towards the molecular pathogenesis of MGs as well as molecularly targete
d therapies. We also highlight areas of future research.
Journal Title: Critical reviews in oncology/hematology

PUBMED ID: 18576918
DOI: doi.org/10.1089/hum.2008.035
Titolo: Toxicology study of repeat intracerebral administration of a measles
virus derivative producing carcinoembryonic antigen in rhesus macaques in su
pport of a phase I/II clinical trial for patients with recurrent gliomas.
Autori: Myers R., Harvey M., Kaufmann TJ., Greiner SM., Krempski JW., Raffel
C., Shelton SE., Soeffker D., Zollman P., Federspiel MJ., Blanco M., Galanis
E.
Data di Pubblicazione: 2008-06-26
Abstract: Gliomas have a dismal prognosis, with the median survival of patie
nts with the most common histology, glioblastoma multiforme, being only 12-1

5 months. Development of novel therapeutic agents is urgently needed. We hav e previously demonstrated that oncolytic measles virus strains derived from the Edmonston vaccine lineage have significant antitumor activity against gl iomas [Phuong, L.K., Allen, C., Peng, K.W., Giannini, C., Greiner, S., Teney ck, C.J., Mishra, P.K., Macura, S.I., Russell, S.J., Galanis, E.C. (2003). C ancer. Res. 63, 2462-2469]. MV-CEA is an Edmonston vaccine lineage measles v irus strain engineered to express the marker peptide carcinoembryonic antige n (CEA): CEA levels can serve as a correlate of viral gene expression. In su pport of a phase I clinical trial of intratumoral and resection cavity admin istration of MV-CEA to patients with recurrent gliomas, we assessed the neur otoxicity of MV-CEA in adult immune male rhesus macaques (Macaca mulatta). T he animals ' immune status and administration schedule mimicked the trial po pulation and proposed administration schema. Macaca mulatta represents the p rototype animal species for assessment of measles neurotoxicity. The animals were stereotactically administered either vehicle (n = 1) or MV-CEA at 2 x 1 0(5)or 2 x 10(6) TCID(50) (each, n = 2) in the right frontal lobe in two inj ections on days 1 and 5. Macaques were closely monitored clinically for neur otoxicity. Body weight, temperature, complete blood count, CEA, clinical che mistries, coagulation, complement levels, immunoglobulin, measles antibody t iters, viremia, and shedding (buccal swabs) were tested at multiple time poi nts. Furthermore, cisterna magna spinal taps were performed on day 9 and 1 y ear after the first viral dose administration, and samples were analyzed for protein, glucose, cell differential, and presence of MV-CEA. Magnetic resona nce imaging (MRI) was performed between 4 and 5 months after article adminis tration to assess for subclinical neurotoxicity. To date, 36+ months from st udy initiation there has been no clinical or biochemical evidence of toxicit y, including lack of neurological symptoms, fever, or other systemic symptom s and lack of immunosuppression. Quantitative RT-PCR analysis of blood, bucc al swabs, and cerebrospinal fluid (CSF) was negative for MV-CEA at all time points, with the exception of viral genome deletion in the blood of one asym ptomatic animal at the 2 x 10(6) TCID(50) dose level on day 85. Vero cell ov erlays of CSF cells and supernatant were negative for viral recovery. There was no detection of CEA in serum or CSF at any time point. MRI scans were ne gative for imaging abnormalities and showed no evidence of encephalitis. Our results support the safety of CNS administration of MV-CEA in glioma patient s. A clinical trial of intratumoral and resection cavity administration of M V-CEA in patients with recurrent glioblastoma multiforme is currently ongoin g.
Journal Title: Human gene therapy

PUBMED ID: 18521920
DOI: doi.org/10.1002/cncr.23585
Titolo: External beam irradiation and the combination of cisplatin and carmu stine followed by carmustine alone for the treatment of high-grade glioma: a phase 2 Southwest Oncology Group trial.
Autori: Blumenthal DT., Rankin C., Eyre HJ., Livingston RB., Spence AM., Ste lzer KJ., Rushing EJ., Berger MS., Rivkin SE., Cohn AL., Petersdorf SH.
Data di Pubblicazione: 2008-06-04
Abstract: Despite the presence of a cohort of long-term survivors, the resul ts of the current study do not appear to support the additional study or rou tine use of concurrent cisplatin and carmustine.
Journal Title: Cancer

PUBMED ID: 18484594
DOI: doi.org/10.1002/cncr.23562
Titolo: Incidence of early pseudo-progression in a cohort of malignant gliom a patients treated with chemoirradiation with temozolomide.

Autori: Taal W., Brandsma D., de Bruin HG., Bromberg JE., Swaak-Kragten AT., Smitt PA., van Es CA., van den Bent MJ.
Data di Pubblicazione: 2008-05-20
Abstract: Up to 50% of malignant glioma patients treated with RT/TMZ and progression immediately after RT develop pseudo-progression. The current study data support the idea to continue TMZ in the case of progressive lesions immediately after RT/TMZ. Surgery should be considered in symptomatic cases. The inclusion of patients with progressive lesions developing directly after chemoradiation in studies regarding recurrent gliomas will lead to an overestimation of the results.
Journal Title: Cancer

PUBMED ID: 18483377
DOI: doi.org/10.1158/1078-0432.CCR-07-4875
Titolo: Postoperative adjuvant dendritic cell-based immunotherapy in patients with relapsed glioblastoma multiforme.
Autori: De Vleeschouwer S., Fieuws S., Rutkowski S., Van Calenbergh F., Van Loon J., Goffin J., Sciot R., Wilms G., Demaerel P., Warmuth-Metz M., Soerensen N., Wolff JE., Wagner S., Kaempgen E., Van Gool SW.
Data di Pubblicazione: 2008-05-17
Abstract: Adjuvant DC-based immunotherapy for patients with relapsed GBM is safe and can induce long-term survival. A trend to PFS improvement was shown in the faster vaccination schedule. The importance of age and a minimal residual disease status at the start of the vaccination is underscored.
Journal Title: Clinical cancer research : an official journal of the American Association for Cancer Research

PUBMED ID: 18480965
DOI: doi.org/10.1007/s11060-008-9613-6
Titolo: CPT-11 for recurrent temozolomide-refractory 1p19q co-deleted anaplastic oligodendroglioma.
Autori: Chamberlain MC., Glantz MJ.
Data di Pubblicazione: 2008-05-16
Abstract: CPT-11 demonstrated modest efficacy (similar to other salvage glioma regimens) with acceptable toxicity in this cohort of adults with recurrent, 1p19q co-deleted AO all of whom had failed prior TMZ chemotherapy.
Journal Title: Journal of neuro-oncology

PUBMED ID: 18461281
DOI: doi.org/10.1007/s11060-008-9607-4
Titolo: Radiochemotherapy with temozolomide as re-irradiation using high precision fractionated stereotactic radiotherapy (FSRT) in patients with recurrent gliomas.
Autori: Combs SE., Bischof M., Welzel T., Hof H., Oertel S., Debus J., Schulz-Ertner D.
Data di Pubblicazione: 2008-05-08
Abstract: Re-irradiation and TMZ is safe and effective in a subgroup of patients with recurrent gliomas. Further evaluation of radiochemotherapy regimens for recurrent or progressive gliomas is warranted.
Journal Title: Journal of neuro-oncology

PUBMED ID: 18452856
DOI: doi.org/10.1016/S1470-2045(08)70125-6
Titolo: Clinical features, mechanisms, and management of pseudoprogression in malignant gliomas.
Autori: Brandsma D., Stalpers L., Taal W., Sminia P., van den Bent MJ.

Data di Pubblicazione: 2008-05-03
Abstract: Since the introduction of chemoradiotherapy with temozolomide as t he new standard of care for patients with glioblastoma, there has been an in creasing awareness of progressive and enhancing lesions on MRI, noted immedi ately after the end of treatment, which are not related to tumour progressio n, but which are a treatment effect. This so-called pseudoprogression can oc cur in up to 20% of patients who have been treated with temozolomide chemora diotherapy, and can explain about half of all cases of increasing lesions af ter the end of this treatment. These lesions decrease in size or stabilise w ithout additional treatments and often remain clinically asymptomatic. Addit ionally, there is evidence that treatment-related necrosis occurs more frequ ently and earlier after temozolomide chemotherapy than after radiotherapy al one. The mechanisms behind these events have not yet been fully elucidated, but the likelihood is that chemoradiotherapy causes a higher degree of (desi red) tumour-cell and endothelial-cell killing. This increased cell kill migh t lead to secondary reactions, such as oedema and abnormal vessel permeabili ty in the tumour area, mimicking tumour progression, in addition to subseque nt early treatment-related necrosis in some patients and milder subacute rad iotherapy reactions in others. In patients managed with temozolomide chemora diotherapy who have clinically asymptomatic progressive lesions at the end o f treatment, adjuvant temozolomide should be continued; in clinically sympto matic patients, surgery should be considered. If mainly necrosis is noted du ring surgery, continuation of adjuvant temozolomide is logical. Trials on th e treatment of recurrent malignant glioma should exclude patients with progr ession within the first 3 months after temozolomide chemoradiotherapy unless histological confirmation of tumour recurrence is available. Further researc h is needed to establish reliable imaging parameters that distinguish betwee n true tumour progression and pseudoprogression or treatment-related necrosi s.
Journal Title: The Lancet. Oncology

PUBMED ID: 18447714
DOI: doi.org/10.3171/JNS/2008/108/5/0963
Titolo: Phase II clinical trial of Wilms tumor 1 peptide vaccination for pat ients with recurrent glioblastoma multiforme.
Autori: Izumoto S., Tsuboi A., Oka Y., Suzuki T., Hashiba T., Kagawa N., Has himoto N., Maruno M., Elisseeva OA., Shirakata T., Kawakami M., Oji Y., Nish ida S., Ohno S., Kawase I., Hatazawa J., Nakatsuka S., Aozasa K., Morita S., Sakamoto J., Sugiyama H., Yoshimine T.
Data di Pubblicazione: 2008-05-02
Abstract: Although a small uncontrolled nonrandomized trial, this study show ed that WT1 vaccine therapy for patients with WT1/HLA-A*2402-positive recurr ent GBM was safe and produced a clinical response. Based on these results, f urther clinical studies of WT1 vaccine therapy in patients with malignant gl ioma are warranted.
Journal Title: Journal of neurosurgery

PUBMED ID: 18403492
DOI: doi.org/10.1215/15228517-2008-005
Titolo: Phase II study of temozolomide, thalidomide, and celecoxib for newly diagnosed glioblastoma in adults.
Autori: Kesari S., Schiff D., Henson JW., Muzikansky A., Gigas DC., Doherty L., Batchelor TT., Longtine JA., Ligon KL., Weaver S., Laforme A., Ramakrish na N., Black PM., Drappatz J., Ciampa A., Folkman J., Kieran M., Wen PY.
Data di Pubblicazione: 2008-04-12
Abstract: We conducted a phase II study of the combination of temozolomide a nd angiogenesis inhibitors for treating adult patients with newly diagnosed glioblastoma. Patients who had stable disease following standard radiation t

herapy received temozolomide for 5 days in 28-day cycles, in combination wit h daily thalidomide and celecoxib. Patients were treated until tumor progres sion or development of unacceptable toxicity. Four-month progression-free su rvival (PFS) from study enrollment was the primary end point, and overall su rvival (OS) was the secondary end point. In addition, we sought to correlate response with O(6)-methylguanine-DNA methyltransferase promoter methylation status and serum levels of angiogenic peptides. Fifty patients with glioblas toma were enrolled (18 women, 32 men). Median age was 54 years (range, 29-78) and median KPS score was 90 (range, 70-100). From study enrollment, median PFS was 5.9 months (95% confidence interval [CI]: 4.2-8.0) and 4-month PFS w as 63% (95% CI: 46%-75%). Median OS was 12.6 months (95% CI: 8.5-16.4) and 1 -year OS was 47%. Of the 47 patients evaluable for best response, none had a complete response, five (11%) had partial response, four (9%) had minor resp onse, 22 (47%) had stable disease, and 16 (34%) had progressive disease. Ana lysis of serial serum samples obtained from 47 patients for four angiogenic peptides failed to show a significant correlation with response or survival for three of the peptides; higher vascular endothelial growth factor levels showed a trend toward correlation with decreased OS (p=0.07) and PFS (p=0.09). The addition of celecoxib and thalidomide to adjuvant temozolomide was we ll tolerated but did not meet the primary end point of improvement of 4-mont h PFS from study enrollment.
Journal Title: Neuro-oncology

PUBMED ID: 18362333
DOI: doi.org/10.1073/pnas.0801279105
Titolo: Identification of noninvasive imaging surrogates for brain tumor gen e-expression modules.
Autori: Diehn M., Nardini C., Wang DS., McGovern S., Jayaraman M., Liang Y., Aldape K., Cha S., Kuo MD.
Data di Pubblicazione: 2008-03-26
Abstract: Glioblastoma multiforme (GBM) is the most common and lethal primar y brain tumor in adults. We combined neuroimaging and DNA microarray analysi s to create a multidimensional map of gene-expression patterns in GBM that p rovided clinically relevant insights into tumor biology. Tumor contrast enha ncement and mass effect predicted activation of specific hypoxia and prolife ration gene-expression programs, respectively. Overexpression of EGFR, a rec eptor tyrosine kinase and potential therapeutic target, was also directly in ferred by neuroimaging and was validated in an independent set of tumors by immunohistochemistry. Furthermore, imaging provided insights into the intrat umoral distribution of gene-expression patterns within GBM. Most notably, an "infiltrative" imaging phenotype was identified that predicted patient outco me. Patients with this imaging phenotype had a greater tendency toward havin g multiple tumor foci and demonstrated significantly shorter survival than t heir counterparts. Our findings provide an in vivo portrait of genome-wide g ene expression in GBM and offer a potential strategy for noninvasively selec ting patients who may be candidates for individualized therapies.
Journal Title: Proceedings of the National Academy of Sciences of the United States of America

PUBMED ID: 18361434
DOI: doi.org/10.1002/cncr.23404
Titolo: Salvage chemotherapy with CPT-11 for recurrent temozolomide-refracto ry anaplastic astrocytoma.
Autori: Chamberlain MC., Wei-Tsao DD., Blumenthal DT., Glantz MJ.
Data di Pubblicazione: 2008-03-26
Abstract: CPT-11 demonstrated modest efficacy with acceptable toxicity in th is cohort of adult patients with recurrent AA, all of whom had failed on pri or temozolomide chemotherapy.

Journal Title: Cancer

PUBMED ID: 18336940
DOI: doi.org/10.1016/j.radonc.2006.04.015
Titolo: Boron neutron capture therapy (BNCT) for glioblastoma multiforme: a phase II study evaluating a prolonged high-dose of boronophenylalanine (BPA).
Autori: Henriksson R., Capala J., Michanek A., Lindahl SA., Salford LG., Franzén L., Blomquist E., Westlin JE., Bergenheim AT., Bergenheim AT.
Data di Pubblicazione: 2008-03-14
Abstract: Although, the efficacy of BNCT in the present protocol seems to be comparable with conventional radiotherapy and the treatment time is shorter, the observed side effects and the requirement of complex infrastructure and higher resources emphasize the need of further phase I and II studies, especially directed to improve the accumulation of (10)B in tumour cells.
Journal Title: Radiotherapy and oncology : journal of the European Society for Therapeutic Radiology and Oncology

PUBMED ID: 18295834
DOI: doi.org/10.1016/j.surneu.2007.07.040
Titolo: Preliminary results from a phase I/II study of perillyl alcohol intranasal administration in adults with recurrent malignant gliomas.
Autori: da Fonseca CO., Schwartsmann G., Fischer J., Nagel J., Futuro D., Quirico-Santos T., Gattass CR.
Data di Pubblicazione: 2008-02-26
Abstract: There were no toxicity events. Perillyl alcohol is well tolerated and regression of tumor size in some patients is suggestive of antitumor activity. This work discusses POH intranasal delivery as a potential adjuvant therapeutic strategy for patients with malignant gliomas.
Journal Title: Surgical neurology

PUBMED ID: 21892317
DOI: doi.org/10.4137/cmo.s827
Titolo: A Single Institution's Experience with Bevacizumab in Combination with Cytotoxic Chemotherapy in Progressive Malignant Glioma.
Autori: Mayer T., Lacy J., Baehring J.
Data di Pubblicazione: 2011-09-06
Abstract: Overall, our results confirm the efficacy and safety of bevacizumab in combination with chemotherapy in patients with progressive malignant glioma. Although the TTF and OS were less than previously reported with the combination of bevacizumab and irinotecan, this was an unselected patient population with 50% of patients having received >1 prior chemotherapy regimen.
Journal Title: Clinical medicine. Oncology

PUBMED ID: 18079578
DOI: doi.org/10.4103/0973-1482.37408
Titolo: Synchronous dual malignancy: successfully treated cases.
Autori: Agrawal R.
Data di Pubblicazione: 2007-12-15
Abstract: The occurrence of a second malignancy in a patient with a known malignant tumour is not uncommon. Synchronous primary malignancies are still unusual We are presenting two cases treated successfully at our centre. Case report 1-A 70 year old female presented to us with lump in right breast for two years and bleeding per vaginum for two years. Histopathology of cervix showed squamous cell carcinoma (large cell non keratinizing) and clinical stage was IIIB. HPE mastectomy specimen showed infiltrating duct carcinoma and

stage II. Patient was treated with external beam radiotherapy for carcinoma cervix and breast simultaneously and chemotherapy as required. Patient is on regular follow up and clinically no evidence of disease. Case Report 2 -A 40 year old female presented with mild headache off and on for one year, projec tile vomiting for three months and right side facial swelling for three mont hs. HPE brain tissue showed astrocytoma grade II and HPE parotid tumour show ed low grade muco-epidermoid carcinoma. Patient was treated with surgery fir st then radiotherapy. Patient is in regular follow up,having no complain,cli nically no neurological dysfunction and no evidence of disease at right paro tid and neck region. Thus it was concluded that patients responded well to t reatment. Treatment strategies in case of synchronous double malignancy depe nd on treating the malignancy that is more advanced first or sometimes both could be treated simultaneously. In our case we concluded that synchronous d ouble malignancy may be treated successfully. Both sites should be treated f ully as if they were occurring separately considering toxicities.
Journal Title: Journal of cancer research and therapeutics

PUBMED ID: 17679463
DOI: Mancante
Titolo: Epidermal growth factor receptor serum levels and prognostic value i n malignant gliomas.
Autori: Quaranta M., Divella R., Daniele A., Di Tardo S., Venneri MT., Lolli I., Troccoli G.
Data di Pubblicazione: 2007-08-08
Abstract: Although a prospective study with large sample size is warranted, serum EGFR extracellular domain may be potentially useful as a biological ma rker of gliomas for prediction of prognosis and follow-up after treatment.
Journal Title: Tumori

PUBMED ID: 17628746
DOI: doi.org/10.1007/s11060-007-9459-3
Titolo: Primary diffuse leptomeningeal gliosarcomatosis.
Autori: Watanabe Y., Hotta T., Yoshioka H., Itou Y., Taniyama K., Sugiyama K .
Data di Pubblicazione: 2007-07-14
Abstract: We report a 48-year-old woman with primary diffuse leptomeningeal gliomatosis (PDLG) histologically diagnosed as gliosarcoma. She was admitted complaining of headache, numbness of the right arm, double vision, and visua l field defects. Computerized tomography (CT) scans showed ventricular dilat ation consistent with communicating hydrocephalus. Magnetic resonance imagin g (MRI) revealed diffuse meningeal thickening and gadolinium enhancement wit hout a definite intraparenchymal lesion. Whole-spine MRI demonstrated across -the-board dural thickening and gadolinium enhancement. Cytological examinat ion showed atypical anaplastic cells. As no diagnosis could be made she unde rwent biopsy of the leptomeninges. Histological examination of the specimen returned a diagnosis of gliosarcoma. Despite chemotherapy and radiotherapy s he died 11 months after admission. Autopsy findings included gliosarcoma in the leptomeninges and spinal cord without an underlying parenchymal tumor. T o our knowledge, this is the first report of primary diffuse leptomeningeal gliosarcomatosis.
Journal Title: Journal of neuro-oncology

PUBMED ID: 17594055
DOI: doi.org/10.1007/s11060-007-9408-1
Titolo: Myelosuppression in patients benefiting from imatinib with hydroxyur ea for recurrent malignant gliomas.

Autori: Shah GD., Silver JS., Rosenfeld SS., Gavrilovic IT., Abrey LE., Lassman AB.
Data di Pubblicazione: 2007-06-28
Abstract: Reports suggest reasonable efficacy and minimal myelosuppression from combination imatinib and hydroxyurea for recurrent malignant glioma. We retrospectively reviewed 16 patients treated with this regimen who were evaluable for toxicity; 14 were also evaluable for response. The incidence of grade 3-4 hematologic toxicity was 25%. The best radiographic response, by Macdonald criteria, was partial response (PR) in three patients (21%), stable disease (SD) in four (29%), and progressive disease (PD) in seven (50%). One patient with a PR developed therapy-limiting hematologic toxicity on day 19 of treatment, progressing to grade 4 on day 64, and persisting until death on day 127 despite discontinuing both drugs. Another patient with PR and two of four patients with SD also developed grade 3 hematologic toxicity. All patients with grade 3-4 hematologic toxicity had disease control (PR or SD) as best radiographic response, whereas none with PD suffered grade 3-4 hematologic toxicity. Combining imatinib with hydroxyurea is effective in some patients with malignant glioma. However, myelosuppression can persist for months after discontinuing the regimen, precluding further chemotherapy. Disease control may also correlate with hematologic toxicity (p = 0.08), suggesting that glioma and marrow stem cells may share a common sensitivity to this chemotherapy regimen.
Journal Title: Journal of neuro-oncology

PUBMED ID: 17576523
DOI: doi.org/10.1007/s11060-007-9427-y
Titolo: Salvage chemotherapy with procarbazine and fotemustine combination in the treatment of temozolomide treated recurrent glioblastoma patients.
Autori: Silvani A., Lamperti E., Gaviani P., Eoli M., Fiumani A., Salmaggi A., Falcone C., Filippini G., Botturi A., Boiardi A.
Data di Pubblicazione: 2007-06-20
Abstract: The purpose of this study was to evaluate safety and efficacy of Procarbazine (PCB) and fotemustine (FTM) combination in the treatment of pre-temozolomide treated, recurrent GBM patients. The primary end-point was progression free survival at 6 months (PFS-6). Secondary end-points were overall survival, response rates (CR + PR) and toxicity. About 54 patients (41 men and 13 women) aged 26-68 years (median age, 53.5 years) with recurrent GBM were treated. PCB was administered as an oral dosage of 450 mg on days 1-2 and a total dose of 300 mg on day 3. FTM was administered on day 3, 3 h after the last PCB intake at a dose of 110 mg/mq/BSA. The treatment was repeated every 5 weeks. Treatment was continued for a maximum of six cycles or until disease progression. After two cycles of chemotherapy: 6 patients (11.2%) experienced a neuroradiographic partial response (PR), 29 patients (53.7%) had stable disease (SD), and 19 patients (35.1%) had progressive disease (PD). For the whole group of patients, the median PFS was 19.3 weeks (95% CI, 14.1-24.4 weeks), and PFS-6 was 26.7% (95% CI, 10.6-42.8%). Overall MST from the beginning of PCB + FTM chemotherapy was 28.7 weeks (95% CI, 24.8-32.7 weeks). At 6 and 12 months, 64.4% (95% CI, 51.5-77.3%) and 23.6% (95% CI, 10.1-37.1%) of patients were alive. The median survival time calculated from the first diagnosis was 20.8 months (95% CI, 16.7-24.8). We concluded that the PCB + FTM combination as done in the current trial for patients with recurrent GBM after treatment with TMZ showed some benefit with regards to increased survival and that a Phase III trial is warranted.
Journal Title: Journal of neuro-oncology

PUBMED ID: 17553214
DOI: doi.org/10.1179/016164107X208068

Titolo: Loss of heterozygosity analysis in an anaplastic oligodendroglioma a rising after radiation therapy.
Autori: Hata N., Shono T., Mizoguchi M., Matsumoto K., Guan Y., Nagata S., H ayashi K., Iwaki T., Sasaki T.
Data di Pubblicazione: 2007-06-08
Abstract: The anaplastic oligodendroglioma presented in this report showed a more aggressive clinical course than was expected from the genetic analysis. The significance of 1p and 19q LOH in radiation-induced oligodendroglial tum ors might differ from that in spontaneous counterparts.
Journal Title: Neurological research

PUBMED ID: 17551011
DOI: doi.org/10.1073/pnas.0702916104
Titolo: Alternating electric fields arrest cell proliferation in animal tumo r models and human brain tumors.
Autori: Kirson ED., Dbalý V., Tovarys F., Vymazal J., Soustiel JF., Itzhaki A., Mordechovich D., Steinberg-Shapira S., Gurvich Z., Schneiderman R., Wass erman Y., Salzberg M., Ryffel B., Goldsher D., Dekel E., Palti Y.
Data di Pubblicazione: 2007-06-07
Abstract: We have recently shown that low intensity, intermediate frequency, electric fields inhibit by an anti-microtubule mechanism of action, cancerou s cell growth in vitro. Using implanted electrodes, these fields were also s hown to inhibit the growth of dermal tumors in mice. The present study exten ds these findings to additional cell lines [human breast carcinoma; MDA-MB-2 31, and human non-small-cell lung carcinoma (H1299)] and to animal tumor mod els (intradermal B16F1 melanoma and intracranial F-98 glioma) using external insulated electrodes. These findings led to the initiation of a pilot clinic al trial of the effects of TTFields in 10 patients with recurrent glioblasto ma (GBM). Median time to disease progression in these patients was 26.1 week s and median overall survival was 62.2 weeks. These time to disease progress ion and OS values are more than double the reported medians of historical co ntrol patients. No device-related serious adverse events were seen after >70 months of cumulative treatment in all of the patients. The only device-relat ed side effect seen was a mild to moderate contact dermatitis beneath the fi eld delivering electrodes. We conclude that TTFields are a safe and effectiv e new treatment modality which effectively slows down tumor growth in vitro, in vivo and, as demonstrated here, in human cancer patients.
Journal Title: Proceedings of the National Academy of Sciences of the United States of America

PUBMED ID: 17517052
DOI: doi.org/10.1111/j.1349-7006.2007.00518.x
Titolo: Clinical trial of autologous formalin-fixed tumor vaccine for gliobl astoma multiforme patients.
Autori: Ishikawa E., Tsuboi K., Yamamoto T., Muroi A., Takano S., Enomoto T. , Matsumura A., Ohno T.
Data di Pubblicazione: 2007-05-23
Abstract: A pilot study was performed to investigate the safety and feasibil ity of autologous formalin-fixed tumor vaccines (AFTV) and the clinical resp onses to these vaccines by glioblastoma multiforme (GBM) patients. Twelve pr imary GBM patients were recruited. Eight had recurrent disease while four ha d been treated for primary disease but retained a visible tumor mass. AFTV w ere prepared from formalin-fixed and/or paraffin-embedded tumor tissue obtai ned upon surgery and premixed with original adjuvant materials. The patients were given three five-site intradermal inoculations at weekly intervals. A d elayed-type hypersensitivity test was performed before and after each vaccin ation. In addition, the tumor tissues were subjected to immunohistochemical analysis to determine whether MIB-1, p53, and major histocompatibility compl

ex (MHC) class-I complex expression could predict the response to the treatm ent. The treatment was well tolerated, with only local erythema, induration, and low-grade fever being reported. Of the 12 patients, one showed a complet e response, one showed a partial response, two showed minor responses, one h ad stable disease, and seven exhibited progressive disease. The median survi val period was 10.7 months from the initiation of the AFTV treatment but thr ee of the five responders survived for 20 months or more after AFTV inoculat ion. Low p53 and high MHC class-I expression by the tumor may help predict t he efficacy of this therapy. Thus, the AFTV is safe and feasible, and could significantly improve the outcome of GBM. Further clinical investigations to confirm this are highly desirable.
Journal Title: Cancer science

PUBMED ID: 17515545
DOI: doi.org/10.1212/01.wnl.0000262034.26310.a2
Titolo: Temozolomide for low-grade gliomas: predictive impact of 1p/19q loss on response and outcome.
Autori: Kaloshi G., Benouaich-Amiel A., Diakite F., Taillibert S., Lejeune J ., Laigle-Donadey F., Renard MA., Iraqi W., Idbaih A., Paris S., Capelle L., Duffau H., Cornu P., Simon JM., Mokhtari K., Polivka M., Omuro A., Carpentie r A., Sanson M., Delattre JY., Hoang-Xuan K.
Data di Pubblicazione: 2007-05-23
Abstract: Low-grade gliomas respond to temozolomide and loss of chromosome 1 p/19q predicts both a durable chemosensitivity and a favorable outcome.
Journal Title: Neurology

PUBMED ID: 17452651
DOI: doi.org/10.1215/15228517-2007-006
Titolo: Phase II study of metronomic chemotherapy for recurrent malignant gl iomas in adults.
Autori: Kesari S., Schiff D., Doherty L., Gigas DC., Batchelor TT., Muzikans ky A., O'Neill A., Drappatz J., Chen-Plotkin AS., Ramakrishna N., Weiss SE., Levy B., Bradshaw J., Kracher J., Laforme A., Black PM., Folkman J., Kieran M., Wen PY.
Data di Pubblicazione: 2007-04-25
Abstract: Preclinical evidence suggests that continuous low-dose daily (metr onomic) chemotherapy may inhibit tumor endothelial cell proliferation (angio genesis) and prevent tumor growth. This phase II study evaluated the feasibi lity of this antiangiogenic chemotherapy regimen in adults with recurrent ma lignant gliomas. The regimen consisted of low-dose etoposide (35 mg/m2 [maxi mum, 100 mg/day] daily for 21 days), alternating every 21 days with cyclopho sphamide (2 mg/kg [maximum, 100 mg/day] daily for 21 days), in combination w ith daily thalidomide and celecoxib, in adult patients with recurrent malign ant gliomas. Serum and urine samples were collected for measurement of angio genic peptides. Forty-eight patients were enrolled (15 female, 33 male). Twe nty-eight patients had glioblastoma multiforme (GBMs), and 20 had anaplastic gliomas (AGs). Median age was 53 years (range, 33-74 years), and median KPS was 70 (range, 60-100). Therapy was reasonably well tolerated in this heavil y pretreated population. Two percent of patients had partial response, 9% ha d a minor response, 59% had stable disease, and 30% had progressive disease. For GBM patients, median progression-free survival (PFS) was 11 weeks, six-m onth PFS (6M-PFS) was 9%, and median overall survival (OS) was 21 weeks. For AG patients, median PFS was 14 weeks, 6M-PFS was 26%, and median OS was 41.5 weeks. In a limited subset of patients, serum and urine angiogenic peptides did not correlate with response or survival ($p > 0.05$). Although there were some responders, this four-drug, oral metronomic regimen did not significant ly improve OS in this heavily pretreated group of patients who were generall y not eligible for conventional protocols. While metronomic chemotherapy may

not be useful in patients with advanced disease, further studies using metro nomic chemotherapy combined with more potent antiangiogenic agents in patien ts with less advanced disease may be warranted.
Journal Title: Neuro-oncology

PUBMED ID: 17442989
DOI: doi.org/10.1200/JCO.2006.07.4807
Titolo: Correlation between O6-methylguanine-DNA methyltransferase and survi val in inoperable newly diagnosed glioblastoma patients treated with neoadju vant temozolomide.
Autori: Chinot OL., Barrié M., Fuentes S., Eudes N., Lancelot S., Metellus P ., Muracciole X., Braguer D., Ouafik L., Martin PM., Dufour H., Figarella-Br anger D.
Data di Pubblicazione: 2007-04-20
Abstract: This dose-dense temozolomide regimen resulted in modest antitumor activity with an acceptable safety profile in the neoadjuvant setting, and e xpression of MGMT correlated with response to temozolomide. However, this tr eatment approach seems to be inferior to standard concomitant RT plus temozo lomide.
Journal Title: Journal of clinical oncology : official journal of the Americ an Society of Clinical Oncology

PUBMED ID: 17431544
DOI: doi.org/10.1007/s11060-007-9370-y
Titolo: Prognosis in patients with anaplastic oligoastrocytoma is associated with histologic grade.
Autori: Buckner JC., O'Fallon JR., Dinapoli RP., Schomberg PJ., Farr G., Sch aefer P., Giannini C., Scheithauer BW., Ballman KV.
Data di Pubblicazione: 2007-04-14
Abstract: Patients with anaplastic oligoastrocytoma have distinct outcomes b ased upon grade (OA3 vs. OA4) and in comparison with pure astrocytoma (AA or GBM). Future trials which include more than one histologic entity need to re port results by cell type and grade and account for the varying prognoses in interpreting treatment outcomes.
Journal Title: Journal of neuro-oncology

PUBMED ID: 17401087
DOI: doi.org/10.2967/jnumed.106.037895
Titolo: Prognostic value of O-(2-18F-fluoroethyl)-L-tyrosine PET and MRI in low-grade glioma.
Autori: Floeth FW., Pauleit D., Sabel M., Stoffels G., Reifenberger G., Riem enschneider MJ., Jansen P., Coenen HH., Steiger HJ., Langen KJ.
Data di Pubblicazione: 2007-04-03
Abstract: We conclude that baseline amino acid uptake on (18)F-FET PET and a diffuse versus circumscribed tumor pattern on MRI are strong predictors for the outcome of patients with low-grade glioma.
Journal Title: Journal of nuclear medicine : official publication, Society o f Nuclear Medicine

PUBMED ID: 17393043
DOI: doi.org/10.1016/s1130-1473(07)70305-6
Titolo: Cerebral blood flow increase in cancer patients by applying cervical spinal cord stimulation.
Autori: Clavo B., Robaina F., Catalá L., Lloret M., Pinar B., Caramés MA., R uiz A., Cabezón A., González G., Lara P., Ruiz-Egea E., Hernández MA.
Data di Pubblicazione: 2007-03-30

Abstract: The results suggest that neuro-stimulation spinal cord electrical stimulation can increase cerebral blood flow in cancer patients. The implication is that this technique could be useful in modifying locoregional ischemia in brain tumors thus improving the outcomes of after radio-chemotherapy. Further research is in progress to confirm the advantages of the technique.
Journal Title: Neurocirugia (Asturias, Spain)

PUBMED ID: 17388696
DOI: doi.org/10.1667/RR0725.1
Titolo: Image fusion analysis of volumetric changes after interstitial low-dose-rate iodine-125 irradiation of supratentorial low-grade gliomas.
Autori: Julow J., Major T., Mangel L., Bajzik G., Viola A.
Data di Pubblicazione: 2007-03-29
Abstract: The aim of this study was to compare the volumes of tumor necrosis, reactive zone and edema with the three-dimensional dose distributions after brachytherapy treatments of gliomas. The investigation was performed an average of 14.2 months after low-dose-rate (125)I interstitial irradiation of 25 inoperable low-grade gliomas. The prescribed dose was 50-60 Gy to the tumor surface. Dose planning and image fusion were performed with the BrainLab-Target 1.19 software. In the CT/ MRI images, the "triple ring" (tumor necrosis, reactive ring and edema) developing after the interstitial irradiation of the brain tumors was examined. The images with the triple ring were fused with the planning images, and the isodose curves were superimposed on them. The volumes of the three regions were measured. The average dose at the necrosis border was determined from the isodose distribution. For quantitative assessment of the dose distributions, the dose nonuniformity ratio (DNR), homogeneity index (HI), coverage index (CI) and conformal index (COIN) were calculated. The relative volumes of the different parts of the triple ring after the interstitial irradiation compared to the reference dose volume were the following: necrosis, 40.9%, reactive zone, 47.1%, and edema, 367%. The tumor necrosis developed at 79.1 Gy on average. The average DNR, HI, CI and COIN were 0.45, 0.24, 0.94 and 0.57, respectively. The image fusion analysis of the volume of tumor necrosis, reactive ring and edema caused by interstitial irradiation and their correlation with the dose distribution provide valuable information for patient follow-up, treatment options, and effects and side effects of radio therapy.
Journal Title: Radiation research

PUBMED ID: 17353924
DOI: doi.org/10.1038/sj.bjc.6603669
Titolo: Gefitinib in patients with progressive high-grade gliomas: a multicentre phase II study by Gruppo Italiano Cooperativo di Neuro-Oncologia (GICNO).
Autori: Franceschi E., Cavallo G., Lonardi S., Magrini E., Tosoni A., Grosso D., Scopece L., Blatt V., Urbini B., Pession A., Tallini G., Crinò L., Brandes AA.
Data di Pubblicazione: 2007-03-14
Abstract: To investigate the role of gefitinib in patients with high-grade gliomas (HGGs), a phase II trial (1839IL/0116) was conducted in patients with disease recurrence following surgery plus radiotherapy and first-line chemotherapy. Adult patients with histologically confirmed recurrent HGGs following surgery, radiotherapy and first-line chemotherapy, were considered eligible. Patients were treated with gefitinib (250 mg day(-1)) continuously until disease progression. The primary end point was progression-free survival at 6 months progression-free survival at 6 months (PFS-6). Tissue biomarkers (epidermal growth factor receptor (EGFR) gene status and expression, phosphorylated Akt (p-Akt) expression) were assessed. Twenty-eight patients (median age, 55 years; median ECOG performance status, 1) were enrolled; all were eva

luable for drug activity and safety. Sixteen patients had glioblastoma, thre e patients had anaplastic oligodendrogliomas and nine patients had anaplasti c astrocytoma. Five patients (17.9%, 95% CI 6.1-36.9%) showed disease stabil isation. The overall median time to progression was 8.4 (range 2-104+) weeks and PFS-6 was 14.3% (95% CI 4.0-32.7%). The median overall survival was 24.6 weeks (range 4-104+). No grade 3-4 gefitinib-related toxicity was found. Gef itinib showed limited activity in patients affected by HGGs. Epidermal growt h factor receptor expression or gene status, and p-Akt expression do not see m to predict activity of this drug.
Journal Title: British journal of cancer

PUBMED ID: 17245623
DOI: doi.org/10.1007/s11060-006-9302-2
Titolo: Phase II study of imatinib mesylate and hydroxyurea for recurrent gr ade III malignant gliomas.
Autori: Desjardins A., Quinn JA., Vredenburgh JJ., Sathornsumetee S., Friedm an AH., Herndon JE., McLendon RE., Provenzale JM., Rich JN., Sampson JH., Gu rurangan S., Dowell JM., Salvado A., Friedman HS., Reardon DA.
Data di Pubblicazione: 2007-01-25
Abstract: Imatinib mesylate plus hydroxyurea, is well tolerated and associat ed with anti-tumor activity in some patients with recurrent grade 3 MG.
Journal Title: Journal of neuro-oncology

PUBMED ID: 17228264
DOI: doi.org/10.1227/01.NEU.0000249203.73849.5D
Titolo: Genetic aberrations in gliomatosis cerebri.
Autori: Ware ML., Hirose Y., Scheithauer BW., Yeh RF., Mayo MC., Smith JS., Chang S., Cha S., Tihan T., Feuerstein BG.
Data di Pubblicazione: 2007-01-18
Abstract: Chromosomal aberrations associated with aggressive astrocytomas ar e predictors of poor outcome in patients with GC. This suggests that GC may be an architectural variant of diffuse astrocytomas. The presence of these a berrations and the presence of any contrast enhancement on magnetic resonanc e imaging scans are possible stratifiers for patients with GC. Stratificatio n of GC into higher- and lower-grade forms may be useful in tailoring treatm ents to patients with this disease.
Journal Title: Neurosurgery

PUBMED ID: 17171442
DOI: doi.org/10.1007/s11060-006-9295-x
Titolo: Gliosarcoma with multiple extracranial metastases: case report and r eview of the literature.
Autori: Beaumont TL., Kupsky WJ., Barger GR., Sloan AE.
Data di Pubblicazione: 2006-12-16
Abstract: Gliosarcoma is a rare malignant neoplasm of the central nervous sy stem with a propensity for metastasis. There are fewer than 20 reported case s of extracranial metastases of gliosarcoma with the majority of cases refle cting a tendency for hematogenous dissemination. Here we describe the case o f a 47-year-old man who developed pervasive extracranial metastases from a t emporal gliosarcoma following radio- and chemotherapy for a primary glioblas toma. The patient initially presented with progressively worsening headaches , left-sided weakness and numbness associated with right temporo-parietal ma ss for which he underwent craniotomy with stereotactic gross-total excision. Two months postoperatively, interstitial brachytherapy and external beam rad iotherapy were initiated. The patient initially declined chemotherapy. The t umor recurred twice and the patient underwent re-operation and multiple cour ses of chemotherapy; histopathological diagnosis remained glioblastoma multi

forme. Nineteen months following initial resection the patient's clinical st atus deteriorated and CT scan demonstrated multiple intrathoracic, hepatic a nd splenic lesions. Postmortem examination revealed widespread, infiltrating gliosarcoma with intravascular gliomatosis and extensive visceral metastases . This is the first report of pervasive extracranial metastases to numerous sites, several of which have not been previously reported. The histogenesis and the potential role of therapeutic irradiation in the development of glio sarcoma are briefly reviewed.
Journal Title: Journal of neuro-oncology

PUBMED ID: 17145324
DOI: doi.org/10.1016/j.surneu.2006.02.034
Titolo: Anaplastic oligodendroglioma responding favorably to intranasal deli very of perillyl alcohol: a case report and literature review.
Autori: Da Fonseca CO., Masini M., Futuro D., Caetano R., Gattass CR., Quiri co-Santos T.
Data di Pubblicazione: 2006-12-06
Abstract: Whereas surgery continues to be the primary treatment for oligoden droglioma, the scheme for postoperative therapy has shifted primarily becaus e of the lesion's relative chemosensitivity. This article evaluates the effe cts of intranasal delivery of POH in a case of regression of anaplastic olig odendroglioma.
Journal Title: Surgical neurology

PUBMED ID: 17082887
DOI: doi.org/10.1007/s11060-006-9280-4
Titolo: Toxicity and efficacy of protracted low dose temozolomide for the tr eatment of low grade gliomas.
Autori: Pouratian N., Gasco J., Sherman JH., Shaffrey ME., Schiff D.
Data di Pubblicazione: 2006-11-04
Abstract: Protracted low dose temozolomide (75 mg/m(2)/day on days 1-21 of 2 8 days) offers potential advantages over standard temozolomide schedules (20 0 mg/m(2)/day on days 1-5 of 28 days) including greater cumulative drug expo sure and depletion of O(6)-alkylguanine DNA alkyltransferase levels, theoret ically overcoming intrinsic chemoresistance. We retrospectively review our e xperience in 25 patients with pathologically proven low grade gliomas (LGG) treated with protracted low dose temozolomide to primarily quantify its toxi city and secondarily to assess efficacy. None had previously received radiat ion. Tumor response was graded based on changes in tumor size, steroid requi rements, and clinical exam. About 243 cycles of protracted low dose temozolo mide were administered. Three patients (12%) were changed to standard temozo lomide dosing due to side effects, including intractable nausea (n = 2) and multiple cytopenias (n = 1). The most frequent toxicities were fatigue (76%) , lymphopenia (72% [48% high grade]), constipation (56%), and nausea (52%). High grade toxicities (other than lymphopenia) included secondary malignancy , pruritus, hyponatremia, neutropenia, leukopenia, and cognitive decline (n = 1 for each). Tumor response rate was 52% and and disease control rate was 84%. Six month PFS was 92% and 12 month PFS was 72%. Response rates and PFS were independent of pathological subtype, deletion status, and indication fo r chemotherapy. Protracted low dose temozolomide has a distinct spectrum of toxicities compared to standard dosing but is well tolerated in most patient s and may provide improved response rates compared to standard dosing. The r esults of larger randomized trials are needed to assess its potential advant ages over other management schemes.
Journal Title: Journal of neuro-oncology

PUBMED ID: 17053987

DOI: doi.org/10.1007/s10637-006-9017-4
Titolo: Phase I dose escalation clinical trial of phenylbutyrate sodium administered twice daily to patients with advanced solid tumors.
Autori: Camacho LH., Olson J., Tong WP., Young CW., Spriggs DR., Malkin MG.
Data di Pubblicazione: 2006-10-21
Abstract: Administration of PBA in a twice-daily infusion schedule is safe. The maximum tolerated dose is 300 mg/kg/day. Study designs with more convenient treatment schedules and specific molecular correlates may help to further delineate the mechanism of action of this compound. Future studies evaluating PBA's ability to induce histone acetylation and cell differentiation alone or in combination with other anti-neoplastics are recommended.
Journal Title: Investigational new drugs

PUBMED ID: 17032910
DOI: doi.org/10.1148/radiol.2413051276
Titolo: Malignant astrocytic tumors: clinical importance of apparent diffusion coefficient in prediction of grade and prognosis.
Autori: Higano S., Yun X., Kumabe T., Watanabe M., Mugikura S., Umetsu A., Sato A., Yamada T., Takahashi S.
Data di Pubblicazione: 2006-10-13
Abstract: The minimum ADC of malignant astrocytomas can provide additional information about their clinical malignancy related to posttreatment prognosis.
Journal Title: Radiology

PUBMED ID: 17031563
DOI: doi.org/10.1007/s11060-006-9219-9
Titolo: A case report and review of the literature.
Autori: Yomo S., Tada T., Hirayama S., Tachibana N., Otani M., Tanaka Y., Hongo K.
Data di Pubblicazione: 2006-10-13
Abstract: Primary diffuse leptomeningeal gliomatosis (PDLG) is a rare central nervous system neoplasm in which gliomatous tissue is diffusely identified in the subarachnoid space with no evidence of a primary intraparenchymal tumor. A 52-year-old man presented low back pain followed by sudden unconsciousness and had also cognitive dysfunction and meningeal sign. Examinations of cerebrospinal fluid (CSF) did not show malignant cells but increased protein and pleocytosis. Magnetic resonance (MR) imaging demonstrated diffuse leptomeningeal enhancement without any source of intraparenchymal lesion. Fluid-attenuated inversion recovery (FLAIR) also demonstrated individual diffuse high intensity area in the subarachnoid space. A biopsy disclosed wide spreading of anaplastic glial cells within the leptomeninges. He died 3 months later because of disease progression despite both radiotherapy and chemotherapy. Post-mortem examination identified PDLG and several neuropathological features of glioblastoma as well. Reviewing previous cases of PDLG instructs that this entity is rare, resembles meningitis in clinical pictures, usually occurs in a relatively younger population and has more progressive clinical course than the ordinary form of malignant gliomas.
Journal Title: Journal of neuro-oncology

PUBMED ID: 16984371
DOI: doi.org/10.1111/j.1349-7006.2006.00272.x
Titolo: Personalized peptide vaccines: a new therapeutic modality for cancer.
Autori: Itoh K., Yamada A.
Data di Pubblicazione: 2006-09-21

Abstract: Therapeutic cancer vaccines have enjoyed little success so far, al
though many clinical trials have been conducted. Therefore, the creation of
new protocols capable of inducing an objective response is required. We exam
ined two of these protocols in the present review. The first is a personaliz
ed protocol to take into account the immunological diversity of cytotoxic T
lymphocyte responses among patients. The second is a combination therapy des
igned to adapt to the presence of major histocompatibility complex (MHC)-los
s cancer cells. The objective response rates of our classical (non-personali
zed) peptide vaccines were 0%, whereas that of personalized vaccines was 11.
1% in the total advanced cancers and > or = 20% in malignant glioma and cerv
ical cancers, respectively. A > or = 50% decrease in serum prostate-specific
antigen (PSA) was seen in 8.7% of advanced hormone refractory prostate cance
r patients by personalized vaccination alone, whereas such a decrease was se
en in 54% of patients when the personalized vaccination was combined with a
low dose of estramustine. Based on these experiences, we propose a personali
zed peptide vaccine combined with chemotherapy as a new treatment modality f
or cancers.
Journal Title: Cancer science

PUBMED ID: 16944367
DOI: doi.org/10.1007/s10354-006-0308-3
Titolo: Molecular therapies for malignant glioma.
Autori: Hutterer M., Gunsilius E., Stockhammer G.
Data di Pubblicazione: 2006-09-01
Abstract: Due to the dismal prognosis of malignant glioma with currently ava
ilable therapies there is an urgent need for new treatments based on a bette
r molecular understanding of gliomagenesis. Several concepts of molecular th
erapies for malignant glioma are currently being studied in preclinical and
clinical settings, including small molecules targeting specific receptor-med
iated signaling pathways and gene therapy. Many growth factors, growth facto
r receptors--usually receptor tyrosine kinases--and receptor-associated sign
aling pathways are critically involved in gliomagenesis. Numerous selective
inhibitors, which specifically block such molecules, are currently evaluated
for clinical applicability. Several gene therapy approaches have shown antit
umor efficacy in experimental studies, and the first clinical trials for the
treatment of malignant glioma were conducted in the 1990s. In clinical trial
s, retroviral herpes-simplex-thymidinkinase- (HSV-Tk-) gene therapy has been
the pioneering and most commonly used approach. However, efficient gene deli
very into the tumor cells still remains the crucial obstacle for successful
clinical gene therapy. During the past few years a number of new gene transf
er vectors based on adeno-, adeno-associated-, herpes- and lentiviruses as w
ell as new carrier cell systems, including neural and endothelial progenitor
cells, have been developed. In addition, antisense technologies have advance
d in recent years and entered clinical testing utilizing intratumoral admini
stration by convection-enhanced delivery, exemplified by ongoing clinical tr
ials of intratumoral administration of antisense TGF-beta. This paper summar
izes some of these recent developments in molecular therapies for malignant
glioma, focusing on targeted therapies using selective small molecules and g
ene therapy concepts.
Journal Title: Wiener medizinische Wochenschrift (1946)

PUBMED ID: 16944363
DOI: doi.org/10.1007/s10354-006-0304-7
Titolo: Malignant glioma: neuropathology and neurobiology.
Autori: Preusser M., Haberler C., Hainfellner JA.
Data di Pubblicazione: 2006-09-01
Abstract: Malignant gliomas may manifest at any age including congenital and
childhood cases. Peak incidence is, however, in adults older than 40 years.

Males are more frequently affected than females. The sole unequivocal risk f
actor is therapeutic ionizing irradiation. Malignant gliomas comprise a spec
trum of different tumor subtypes. Within this spectrum, glioblastoma, anapla
stic astrocytoma and anaplastic oligodendroglioma share as basic features pr
eferential location in cerebral hemispheres, diffuse infiltration of brain t
issue, fast tumor growth with fatal outcome within months or years. Invasion
is regarded as one of the main reasons for poor therapeutic success, because
it makes complete surgical removal of gliomas impossible. Invasion of glioma
cells requires interaction with the extracellular matrix and with surroundin
g cells of the healthy brain tissue. Vascular proliferates and tissue necros
is are characteristic features of malignant gliomas, in particular glioblast
oma. These features are most likely the consequence of rapidly increasing tu
mor mass that is inadequately oxygenized by the preexisting vasculature. In
malignant glioma, distinct molecular pathways including the p53 pathway, the
RB pathway and the EGFR pathway show frequent alterations that seem to be pa
thogenetically relevant. Methylguanine-methyltransferase (MGMT) promoter met
hylation status in glioblastoma and 1p19q deletion status in anaplastic olig
odendroglioma are associated with response to chemotherapy. The role of neur
opathology and neurobiology in neurooncology is 1. to provide a clinically m
eaningful classification of brain tumors on basis of pathobiological factors
, 2. to clarify etiology and pathogenesis of brain tumors as rational basis
for development of new diagnostic tests and therapies, and 3. to translate t
esting for new clinically relevant molecular parameters into clinical applic
ation.
Journal Title: Wiener medizinische Wochenschrift (1946)

PUBMED ID: 16914310
DOI: doi.org/10.1016/j.ejca.2006.05.021
Titolo: 1p/19q loss within oligodendroglioma is predictive for response to f
irst line temozolomide but not to salvage treatment.
Autori: Kouwenhoven MC., Kros JM., French PJ., Biemond-ter Stege EM., Gravel
and WJ., Taphoorn MJ., Brandes AA., van den Bent MJ.
Data di Pubblicazione: 2006-08-18
Abstract: Combined 1p/19q loss is mainly observed in classical OD. Responses
to first line temozolomide are strongly correlated to loss of 1p. Response t
o second line alkylating treatment is modest even in tumours with 1p/19q los
s. For further improvement of outcome in OD novel treatments are needed.
Journal Title: European journal of cancer (Oxford, England : 1990)

PUBMED ID: 16891823
DOI: doi.org/10.3346/jkms.2006.21.4.739
Titolo: Temozolomide chemotherapy in patients with recurrent malignant gliom
as.
Autori: Yang SH., Kim MK., Lee TK., Lee KS., Jeun SS., Park CK., Kang JK., K
im MC., Hong YK.
Data di Pubblicazione: 2006-08-08
Abstract: Numerous studies have demonstrated the clinical activity of temozo
lomide, a second-generation alkylating agent, against malignant brain tumors
, however, its activity has not been reported in an Asian population. This s
tudy analyzed the efficacy and toxicity of temozolomide in 25 adult patients
with recurrent or progressive malignant gliomas after surgery and standard r
adiation therapy with or without chemotherapy, enrolled in our institution s
ince July 2000. Sixteen patients had glioblastoma multiforme (GBM), six with
anaplastic astrocytoma, and three with anaplastic oligodendroglioma. Of the
25 patients, 3 (12%) achieved a complete response (CR), 8 (32%) achieved a p
artial response (PR), 6 (24%) had stable disease (SD), and 8 (32%) had progr
essive disease (PD). Two patients achieved a CR, 4 patients achieved a PR, 3
patients had SD and 7 patients had PD in GBM, and 1 patient achieved a CR, 4

patients achieved a PR, 3 patients had SD, 1 patient had PD in the non-GBM p
atients. Median progression free survival was 8 weeks in GBM and 22 weeks in
the non-GBM patients. The median overall survival of each group was 17 weeks
and 28 weeks. Temozolomide demonstrated moderate activity in recurrent and p
rogressive malignant gliomas without serious toxicity.
Journal Title: Journal of Korean medical science

PUBMED ID: 16873085
DOI: Mancante
Titolo: Primary and metastatic brain tumors.
Autori: Franceschi E., Scopece L., Gori S., Chiari R., Crino L.
Data di Pubblicazione: 2006-07-29
Abstract: High-grade malignant gliomas (HGG) are the most common and maligna
nt primary central nervous system tumors. Despite therapeutic efforts and ad
vances in biologic knowledge, these diseases remain lethal. Standard treatme
nt of HGG is based on surgery and radiotherapy, usually followed by adjuvant
chemotherapy. Many randomized trials addressing the role of post-radiation o
r "adjuvant" chemotherapy have been conducted in the last three decades, yie
lding inconclusive results. However, a statistically significant survival be
nefit with adjuvant chemotherapy has been demonstrated in two meta-analyses
with nitrosourea-based adjuvant chemotherapy and a recent phase III trial ha
s demonstrated a survival advantage for radiotherapy with concomitant and ad
juvant temozolomide (TMZ) in patients with newly diagnosed glioblastoma. Sin
ce high-grade malignant gliomas can seldom be cured, the primary aim of trea
tments for recurrent disease is to improve progression-free survival (PFS),
and to improve or preserve neurological functions. TMZ showed activity even
in the treatment of recurrent HGG with a good toxicity profile, whether few
data are available for effective treatments in patients treated with adjuvan
t TMZ. As a result, new agents and novel approaches are required. Furthermor
e, molecular studies to evaluate chemosensitivity predictors are necessary f
or patients' selection. Brain metastases are estimated to occur in 20% to 40
% of cancer patients, with a higher risk in lung cancer, breast cancer and m
elanoma. The incidence of brain metastases is rising as results of better im
aging procedures and improvements in treatments which leave more cancer pati
ents at risk as survival increases. The prognosis is dependent on a number o
f factors such as histology of primary tumor, performance status, localizati
on number and size of brain metastases and status of extra cranial disease.
Surgery and radiotherapy are indicated in controlled disease with isolated b
rain metastases. Systemic chemotherapy represents he optimal treatment in ch
emosensitive tumors with multiple or isolated brain metastases.
Journal Title: Forum (Genoa, Italy)

PUBMED ID: 16826191
DOI: doi.org/10.1038/sj.cgt.7700975
Titolo: Phase I clinical trial of a TGF-beta antisense-modified tumor cell v
accine in patients with advanced glioma.
Autori: Fakhrai H., Mantil JC., Liu L., Nicholson GL., Murphy-Satter CS., Ru
ppert J., Shawler DL.
Data di Pubblicazione: 2006-07-11
Abstract: We performed a phase I clinical trial in grade IV astrocytoma to a
ssess the safety of a whole-cell vaccine comprising autologous tumor cells g
enetically modified by a transforming growth factor-beta2 (TGF-beta2) antise
nse vector. Blocking secretion of the immunosuppressive molecule TGF-beta in
this manner should inhibit one of the major mechanisms by which tumor cells
evade immune surveillance and should lead to clinically effective antitumor
immunity. Six patients with progressive WHO grade IV astrocytoma were enroll
ed in the trial. Patients received 2-7 subcutaneous injections of 5 x 10(6)-
2 x 10(7) autologous tumor cells per injection. TGF-beta2 secretion by the t

umor cells used to vaccinate patients was inhibited by 53-98%. Treatment was well tolerated with only low-grade, transient treatment-related toxicities r eported. Two patients had partial regressions and two had stable disease fol lowing therapy. The overall median survival was 68 weeks. Median survival of the responding patients was 78 weeks, compared to a historic value of 47 wee ks for glioma patients treated conventionally. There were indications of hum oral and cellular immunity induced by the vaccine. These findings support fu rther clinical evaluation of vaccines comprised of TGF-beta antisense-modifi ed tumor cells.
Journal Title: Cancer gene therapy

PUBMED ID: 16817692
DOI: doi.org/10.3171/foc.2000.9.6.10
Titolo: Adoptive immunotherapy in patients with recurrent malignant glioma: preliminary results of using autologous whole-tumor vaccine plus granulocyte -macrophage colony-stimulating factor and adoptive transfer of anti-CD3-acti vated lymphocytes.
Autori: Sloan AE., Dansey R., Zamorano L., Barger G., Hamm C., Diaz F., Bayn es R., Wood G.
Data di Pubblicazione: 2006-07-05
Abstract: These preliminary results suggest that autologous whole-tumor cell vaccines induce a cell-mediated immune response, which appears to be tumor s pecific in most patients. Furthermore, vaccination combined with adoptive im munotherapy with in vitro activated cells may induce a radiologically demons trated tumor response and improved survival despite a condition of advanced disease and immunosuppression resulting from previous treatment or tumor bur den. Further studies of immunotherapy are warranted.
Journal Title: Neurosurgical focus

PUBMED ID: 16794761
DOI: doi.org/10.1007/s00508-006-0576-3
Titolo: Temozolomide for recurrent or progressive high-grade malignant gliom a: results of an Austrian multicenter observational study.
Autori: Hassler M., Micksche M., Stockhammer G., Pichler J., Payer F., Abuja B., Deinsberger R., Marosi C.
Data di Pubblicazione: 2006-06-24
Abstract: The study data confirm the feasibility and efficacy of chemotherap y with temozolomide in patients with relapsed/progressive HGG.
Journal Title: Wiener klinische Wochenschrift

PUBMED ID: 16741299
DOI: Mancante
Titolo: Novel human IgG2b/murine chimeric antitenascin monoclonal antibody c onstruct radiolabeled with 131I and administered into the surgically created resection cavity of patients with malignant glioma: phase I trial results.
Autori: Reardon DA., Quinn JA., Akabani G., Coleman RE., Friedman AH., Fried man HS., Herndon JE., McLendon RE., Pegram CN., Provenzale JM., Dowell JM., Rich JN., Vredenburgh JJ., Desjardins A., Sampson JH., Gururangan S., Wong T Z., Badruddoja MA., Zhao XG., Bigner DD., Zalutsky MR.
Data di Pubblicazione: 2006-06-03
Abstract: The MTD of (131)I-ch81C6 is 2.96 GBq (80 mCi) because of dose-limi ting hematologic toxicity. Although encouraging survival was observed, (131) I-ch81C6 was associated with greater hematologic toxicity, probably due to t he enhanced stability of the IgG2 construct, than previously observed with (131)I-murine 81C6.
Journal Title: Journal of nuclear medicine : official publication, Society o f Nuclear Medicine

PUBMED ID: 16645720
DOI: doi.org/10.1007/s11060-006-9144-y
Titolo: Carboplatin and etoposide (CE) chemotherapy in patients with recurrent or progressive oligodendroglial tumors.
Autori: Scopece L., Franceschi E., Cavallo G., Paioli A., Paioli G., Conforti R., Palmerini E., Berzioli C., Spagnolli F., Esposti RD., Crinò L.
Data di Pubblicazione: 2006-04-29
Abstract: In this trial CE regimen has shown relevant activity with a favourable safety profile.
Journal Title: Journal of neuro-oncology

PUBMED ID: 16632619
DOI: doi.org/10.1259/bjr/30604050
Titolo: A four-dimensional computer simulation model of the in vivo response to radiotherapy of glioblastoma multiforme: studies on the effect of clonogenic cell density.
Autori: Stamatakos GS., Antipas VP., Uzunoglu NK., Dale RG.
Data di Pubblicazione: 2006-04-25
Abstract: Tumours behave as complex, self-organizing, opportunistic dynamic systems. In an attempt to better understand and describe the highly complicated tumour behaviour, a novel four-dimensional simulation model of in vivo tumour growth and response to radiotherapy has been developed. This paper presents the latest improvements to the model as well as a parametric validation of it. Improvements include an advanced algorithm leading to conformal tumour shrinkage, a quantitative consideration of the influence of oxygenation on radiosensitivity and a more realistic, imaging based description of the neovasculature distribution. The tumours selected for the validation of the model are a wild type and a mutated p53 gene glioblastomas multiforme. According to the model predictions, a whole tumour with larger cell cycle duration tends to repopulate more slowly. A lower oxygen enhancement ratio value leads to a more radiosensitive whole tumour. Higher clonogenic cell density (CCD) produces a higher number of proliferating tumour cells and, therefore, a more difficult tumour to treat. Simulation predictions agree at least semi-quantitatively with clinical experience, and particularly with the outcome of the Radiation Therapy Oncology Group (RTOG) Study 83-02. It is stressed that the model allows a quantitative study of the interrelationship between the competing influences in a complex, dynamic tumour environment. Therefore, the model can already be useful as an educational tool with which to study, understand and demonstrate the role of various parameters in tumour growth and response to irradiation. A long term quantitative clinical adaptation and validation of the model aiming at its integration into the treatment planning procedure is in progress.
Journal Title: The British journal of radiology

PUBMED ID: 16613322
DOI: doi.org/10.1016/j.humpath.2005.11.010
Titolo: Prognostic value of detecting recurrent glioblastoma multiforme in surgical specimens from patients after radiotherapy: should pathology evaluation alter treatment decisions?
Autori: Tihan T., Barletta J., Parney I., Lamborn K., Sneed PK., Chang S.
Data di Pubblicazione: 2006-04-15
Abstract: The prognostic significance of the histologic type and grade of gliomas at initial surgery is well established, but the value of histologic findings in resections after radiotherapy is unclear. Despite this uncertainty, pathologic interpretation of specimens after radiotherapy influences immediate treatment decisions. It is important to determine if, and to what exten

t, treatment decisions should be based on this information. We aimed to dete rmine the prognostic value of pathologic evaluation in postradiation specime ns from 54 patients with similar clinical features who underwent a second su rgery for the treatment of radiologic worsening after external beam radiothe rapy. We categorized the specimens from the second surgery as either recurre nt tumor (category 1) or radionecrosis (category 2). Patients in category 1 had actively proliferating neoplasms with classical features of glioblastoma , whereas patients in category 2 had no evidence of tumor in their surgical specimens. Cases in which a clear-cut definition could not be made were labe led indeterminate (category 3). Despite the morphological evidence of tumor, there were no significant differences between categories 1 and 2 in any of t he survival parameters tested. The only difference between groups was higher frequency of iodine 125 (125I) placement at second surgery in category 1 pat ients (P <.028). Patients in category 1 with or without 125I treatment had s imilar survival characteristics. We conclude that histopathologic evaluation of postradiotherapy specimens was not helpful in predicting outcome or dicta ting further management. A comprehensive prospective study with advanced rad iologic, pathologic, and molecular analyses may be more useful to determine prognostically valuable parameters.
Journal Title: Human pathology

PUBMED ID: 16598430
DOI: doi.org/10.1007/s11060-005-9087-8
Titolo: Extraneural metastatic medulloblastoma in an adult.
Autori: Wendland MM., Shrieve DC., Watson GA., Chin SS., Blumenthal DT.
Data di Pubblicazione: 2006-04-07
Abstract: Medulloblastoma is a rare malignancy in adults, accounting for app roximately 1% of all primary brain tumors. Extraneural metastases have been reported in 10-30% of cases and most commonly involve bone; rarely lymph nod es, visceral organs and bone marrow may be involved with disease. We report here our experience with a 26 year-old woman with medulloblastoma treated wi th gross total resection followed by radiation therapy to her craniospinal a xis. She subsequently developed widespread metastatic disease involving bone exclusive of the calvarium and spine for which multi-agent salvage chemother apy was utilized with initial good clinical response. She later relapsed wit hin the lymph nodes and soft tissues of the pelvis and eventually suffered a local recurrence within the posterior fossa. The treatment of medulloblastom a, particularly salvage therapy following disease recurrence, is reviewed.
Journal Title: Journal of neuro-oncology

PUBMED ID: 16533878
DOI: doi.org/10.1215/15228517-2005-010
Titolo: A phase 2 trial of irinotecan (CPT-11) in patients with recurrent ma lignant glioma: a North American Brain Tumor Consortium study.
Autori: Prados MD., Lamborn K., Yung WK., Jaeckle K., Robins HI., Mehta M., Fine HA., Wen PY., Cloughesy T., Chang S., Nicholas MK., Schiff D., Greenber g H., Junck L., Fink K., Hess K., Kuhn J., Kuhn J.
Data di Pubblicazione: 2006-03-15
Abstract: The purpose of this study was to determine the response to CPT-11 administered every three weeks to adults with progressive malignant glioma, treated with or without enzyme-inducing antiepileptic drug (EIAED) therapy, at the recommended phase 2 dose determined from a previous phase 1 study. Ad ult patients age 18 or older with a KPS of 60 or higher who had measurable r ecurrent grade III anaplastic glioma (AG) or grade IV glioblastoma multiform e (GBM) were eligible. No more than one prior chemotherapy was allowed, eith er as adjuvant therapy or for recurrent disease. The CPT-11 dose was 350 mg/ m(2) i.v. every three weeks in patients not on EIAED and 750 mg/m(2) in pati ents on EIAED therapy. Patients with stable or responding disease could be t

reated until tumor progression or a total of 12 months of therapy. The prima ry end point of the study was to determine whether CPT-11 could significantl y delay tumor progression, using the rate of six-month progression-free surv ival (PFS-6). The trial was sized to be able to discriminate between a 15% a nd 35% rate for the GBM group alone and between a 20% and 40% rate for the e ntire cohort. There were 51 eligible patients, including 38 GBM and 13 AG pa tients, enrolled. The median age was 52 and 42 years, respectively. PFS-6 fo r the entire cohort was 17.6%. PFS-6 was 15.7% (95% confidence interval [CI] , 0.07-0.31) for the GBM patients and 23% (95% CI, 0.07-0.52) for AG patient s. Toxicity for the group included diarrhea and myelosuppression. We conclud e that the recommended phase 2 dose of CPT-11 for patients with or without E IAED was ineffective on this schedule, in this patient population.
Journal Title: Neuro-oncology

PUBMED ID: 16525180
DOI: doi.org/10.1200/JCO.2005.04.5302
Titolo: Recent advances in the treatment of malignant astrocytoma.
Autori: Reardon DA., Rich JN., Friedman HS., Bigner DD.
Data di Pubblicazione: 2006-03-10
Abstract: Malignant gliomas, including the most common subtype, glioblastoma multiforme (GBM), are among the most devastating of neoplasms. Their aggress ive infiltration in the CNS typically produces progressive and profound disa bility--ultimately leading to death in nearly all cases. Improvement in outc ome has been elusive despite decades of intensive clinical and laboratory re search. Surgery and radiotherapy, the traditional cornerstones of therapy, p rovide palliative benefit, while the value of chemotherapy has been marginal and controversial. Limited delivery and tumor heterogeneity are two fundamen tal factors that have critically hindered therapeutic progress. A novel chem oradiotherapy approach, consisting of temozolomide administered concurrently during radiotherapy followed by adjuvant systemic temozolomide, has recently demonstrated a meaningful, albeit modest, improvement in overall survival fo r newly diagnosed GBM patients. As cell-signaling alterations linked to the development and progression of gliomas are being increasingly elucidated, ta rgeted therapies have rapidly entered preclinical and clinical evaluation. R esponses to therapies that function via DNA damage have been associated with specific mediators of resistance that may also be subject to targeted therap ies. Other approaches include novel locoregional delivery techniques to over come barriers of delivery. The simultaneous development of multiple advanced therapies based on specific tumor biology may finally offer glioma patients improved survival.
Journal Title: Journal of clinical oncology : official journal of the Americ an Society of Clinical Oncology

PUBMED ID: 16524945
DOI: doi.org/10.1215/15228517-2005-009
Titolo: High-dose chemotherapy with stem cell rescue as initial therapy for anaplastic oligodendroglioma: long-term follow-up.
Autori: Abrey LE., Childs BH., Paleologos N., Kaminer L., Rosenfeld S., Salz man D., Finlay JL., Gardner S., Peterson K., Hu W., Swinnen L., Bayer R., Fo rsyth P., Stewart D., Smith AM., Macdonald DR., Weaver S., Ramsay DA., Nimer SD., DeAngelis LM., Cairncross JG.
Data di Pubblicazione: 2006-03-10
Abstract: We previously reported a phase 2 trial of 69 patients with newly d iagnosed anaplastic or aggressive oligodendroglioma who were treated with in tensive procarbazine, CCNU (lomustine), and vincristine (PCV) followed by hi gh-dose thiotepa with autologous stem cell rescue. This report summarizes th e long-term follow-up of the cohort of 39 patients who received high-dose th iotepa with autologous stem cell support. Thirty-nine patients with a median

age of 43 (range, 18-67) and a median KPS of 100 (range, 70-100) were treate d. Surviving patients now have a median follow-up of 80.5 months (range, 44- 142). The median progression-free survival is 78 months, and median overall survival has not been reached. Eighteen patients (46%) have relapsed. Neithe r histology nor prior low-grade oligodendroglioma correlated with risk of re lapse. Persistent nonenhancing tumor at transplant was identified in our ini tial report as a significant risk factor for relapse; however, long-term fol low-up has not confirmed this finding. Long-term neurotoxicity has developed only in those patients whose disease relapsed and required additional therap y; no patient in continuous remission has developed a delayed neurologic inj ury. This treatment strategy affords long-term disease control to a subset o f patients with newly diagnosed anaplastic oligodendroglioma without evidenc e of delayed neurotoxicity or myelodysplasia.
Journal Title: Neuro-oncology

PUBMED ID: 16523808
DOI: doi.org/10.1016/j.clon.2005.08.017
Titolo: Mathematical modelling of survival of glioblastoma patients suggests a role for radiotherapy dose escalation and predicts poorer outcome after de lay to start treatment.
Autori: Burnet NG., Jena R., Jefferies SJ., Stenning SP., Kirkby NF.
Data di Pubblicazione: 2006-03-10
Abstract: Using the model, we have extracted biological information from cli nical data. The model could be used to assess the potential benefit, or lack of benefit, from a proposed radiotherapy trial, and to estimate the necessar y size. It shows that a single modality is unlikely to achieve a major impro vement in long-term survival, although radiotherapy dose escalation should h ave a role, provided it can be given safely. The model could be extended to include chemotherapy, bio-reductive drugs, or gene therapy.
Journal Title: Clinical oncology (Royal College of Radiologists (Great Brita in))

PUBMED ID: 16484713
DOI: doi.org/10.1177/1534735405285380
Titolo: Targeted therapy with antineoplastons A10 and AS2-1 of high-grade, r ecurrent, and progressive brainstem glioma.
Autori: Burzynski SR., Janicki TJ., Weaver RA., Burzynski B.
Data di Pubblicazione: 2006-02-18
Abstract: Antineoplastons contributed to more than a 5-year survival in recu rrent diffuse intrinsic glioblastomas and anaplastic astrocytomas of the bra instem in a small group of patients.
Journal Title: Integrative cancer therapies

PUBMED ID: 16467100
DOI: doi.org/10.1158/1078-0432.CCR-05-2215
Titolo: Phase 1 trial of gefitinib plus sirolimus in adults with recurrent m alignant glioma.
Autori: Reardon DA., Quinn JA., Vredenburgh JJ., Gururangan S., Friedman AH. , Desjardins A., Sathornsumetee S., Herndon JE., Dowell JM., McLendon RE., P rovenzale JM., Sampson JH., Smith RP., Swaisland AJ., Ochs JS., Lyons P., To urt-Uhlig S., Bigner DD., Friedman HS., Rich JN.
Data di Pubblicazione: 2006-02-10
Abstract: We show that gefitinib plus sirolimus can be safely coadministered on a continuous, daily dosing schedule, and established the recommended dose level of these agents in combination for future phase 2 clinical trials.
Journal Title: Clinical cancer research : an official journal of the America n Association for Cancer Research

PUBMED ID: 16448552
DOI: doi.org/10.1186/1471-2407-6-29
Titolo: A phase 1-2, prospective, double blind, randomized study of the safe ty and efficacy of Sulfasalazine for the treatment of progressing malignant gliomas: study protocol of [ISRCTN45828668].
Autori: Robe PA., Martin D., Albert A., Deprez M., Chariot A., Bours V.
Data di Pubblicazione: 2006-02-02
Abstract: The aim of this study is to evaluate the safety and efficacy of Su lfasalazine as a treatment for recurring malignant gliomas. The safety and e fficacy of this drug are analyzed as primary endpoints. Overall survival and progression-free survival are secondary endpoint.
Journal Title: BMC cancer

PUBMED ID: 16443950
DOI: doi.org/10.1215/S1522851705000451
Titolo: Phase 1 study of erlotinib HCl alone and combined with temozolomide in patients with stable or recurrent malignant glioma.
Autori: Prados MD., Lamborn KR., Chang S., Burton E., Butowski N., Malec M., Kapadia A., Rabbitt J., Page MS., Fedoroff A., Xie D., Kelley SK.
Data di Pubblicazione: 2006-01-31
Abstract: The purpose of this study was to define the maximum tolerated dose of erlotinib and characterize its pharmaco-kinetics and safety profile, alon e and with temozolomide, with and without enzyme-inducing antiepileptic drug s (EIAEDs), in patients with malignant gliomas. Patients with stable or prog ressive malignant primary glioma received erlotinib alone or combined with t emozolomide in this dose-escalation study. In each treatment group, patients were stratified by coadministration of EIAEDs. Erlotinib was started at 100 mg orally once daily as a 28-day treatment cycle, with dose escalation by 50 mg/day up to 500 mg/day. Temozolomide was administered at 150 mg/m2 for five consecutive days every 28 days, with dose escalation up to 200 mg/m2 at the second cycle. Eightythree patients were evaluated. Rash, fatigue, and diarrh ea were the most common adverse events and were generally mild to moderate. The recommended phase 2 dose of erlotinib is 200 mg/day for patients with gl ioblastoma multiforme who are not receiving an EIAED, 450 mg/day for those r eceiving temozolomide plus erlotinib with an EIAED, and at least 500 mg/day for those receiving erlotinib alone with an EIAED. Of the 57 patients evalua ble for response, eight had a partial response (PR). Six of the 57 patients had a progression-free survival of longer than six months, including four pa tients with a PR. Coadministration of EIAEDs reduced exposure to erlotinib a s compared with administration of erlotinib alone (33%-71% reduction). There was a modest pharmacokinetic interaction between erlotinib and temozolomide. The favorable tolerability profile and evidence of antitumor activity indica te that further investigation of erlotinib is warranted.
Journal Title: Neuro-oncology

PUBMED ID: 16391896
DOI: doi.org/10.1007/s11060-005-9062-4
Titolo: Combination chemotherapy with 13-cis-retinoic acid and celecoxib in the treatment of glioblastoma multiforme.
Autori: Levin VA., Giglio P., Puduvalli VK., Jochec J., Groves MD., Yung WK. , Hess K.
Data di Pubblicazione: 2006-01-05
Abstract: In a phase II clinical trial, we sought to determine if combining celecoxib with 13-cis-retinoic acid (13-cRA, Accutane) was efficacious in th e treatment of recurrent (progressive) glioblastoma multiforme (GBM). In par allel, we also sought to determine to what extent the outcomes from this cli

nical trial correlated with the findings from studies utilizing two murine i ntracerebral GBM models, U87MG and U251HF, to determine the predictive value of these murine models. In the clinical trial, 25 patients were studied at r ecurrence. Stable disease, which occurred in 44% of the patients, was the be st response. The median progression-free survival (PFS) was 8 weeks, with a PFS at 6 months of only 19%. For the patients with stable disease, the media n PFS was 24 weeks. The toxicity profile was unremarkable. The modest effect on PFS seen in this study agreed with the recent findings of another study, which showed a 19% PFS at 6 months in patients treated with 13-cRA alone. Th us, the combination of 13-cRA with celecoxib is not more effective than 13-c RA in the treatment of progressive GBM. In the murine model study, we found that long-term dosing with 13-cRA or celecoxib alone or in combination did n ot increase survival in animals with U87MG tumors but modestly increased sur vival in animals with U251HF tumors. There was no evidence of synergism betw een the two drugs. From this, we concluded that the animal studies generally predicted that the two agents would have only a modest effect alone and no a dditive effect when given in combination to patients.
Journal Title: Journal of neuro-oncology

PUBMED ID: 16378678
DOI: doi.org/10.1016/j.clineuro.2005.11.015
Titolo: Anaplastic oligodendroglioma and gliomatosis type 2 in interferon-be ta treated multiple sclerosis patients. Report of two cases.
Autori: Sega S., Horvat A., Popovic M.
Data di Pubblicazione: 2005-12-28
Abstract: The concurrence of multiple sclerosis (MS) and brain tumors has be en reported, but it is not known whether MS patients are at greater risk of harbouring the latter. The most common cerebral neoplasms reported in MS pat ients were oligodendroglioma, astrocytoma, glioblastoma and gliomatosis. MS can also present as a mass lesion that mimics a brain tumor. To establish th e correct diagnosis radiological follow-up and/or histological confirmation is needed. Two cases of coincidental MS and brain tumors are reviewed. One i s a 26-year-old woman with relapsing-remitting MS and an anaplastic oligoden droglioma, the other a 49-year-old woman patient with relapsing-remitting MS and gliomatosis type 2. Both patients were treated with interferon-beta1b an d both died from the tumor. The concurrence of MS and brain tumors could be purely coincidental, or the result of neoplastic transformation of reactive glial cells in the areas of demyelination. The combination of a brain tumor and MS, and interferon-beta treatment could also be pure coincidence or an u nknown side effect of treatment. Although interferon-beta has been said to f unction as a tumor-suppressor protein, the influence of long-term treatment of MS patients on cancer development is not known.
Journal Title: Clinical neurology and neurosurgery

PUBMED ID: 16361636
DOI: doi.org/10.1200/JCO.2005.03.2185
Titolo: Phase II study of imatinib mesylate plus hydroxyurea in adults with recurrent glioblastoma multiforme.
Autori: Reardon DA., Egorin MJ., Quinn JA., Rich JN., Rich JN., Gururangan S ., Gururangan I., Vredenburgh JJ., Desjardins A., Sathornsumetee S., Provenz ale JM., Herndon JE., Dowell JM., Badruddoja MA., McLendon RE., Lagattuta TF ., Kicielinski KP., Dresemann G., Sampson JH., Friedman AH., Salvado AJ., Fr iedman HS.
Data di Pubblicazione: 2005-12-20
Abstract: Imatinib mesylate plus hydroxyurea is well tolerated and associate d with durable antitumor activity in some patients with recurrent GBM.
Journal Title: Journal of clinical oncology : official journal of the Americ an Society of Clinical Oncology

PUBMED ID: 16334150
DOI: Mancante
Titolo: Treatment of unresectable glioblastoma multiforme.
Autori: Nieder C., Grosu AL., Astner S., Molls M.
Data di Pubblicazione: 2005-12-13
Abstract: Uncertainty exists about the adequate treatment of adult patients with unresectable, primary, biopsy-proven glioblastoma multiforme (GBM), bec ause the different options for this group of patients have not been evaluate d in randomized clinical trials to date. Usually, these patients are lumped together in studies of radiotherapy or combined modality treatment with pati ents who have undergone extensive surgical resection, although they represen t an unfavorable subgroup. This fact led us to review the recently published results for combined radio- and chemotherapy and to compare them with histor ical data. Management with best supportive care after biopsy resulted in a m edian survival time of 3 months. Median survival in a historical series of r adiotherapy was of the order of 6-7 months and 2-year survival was less than 10%. Combined treatment consistently resulted in a 2-year survival rate of 1 0-18%. However, the median survival in contemporary series is highly variabl e, still ranging from 5 to 13 months. Even with the same regimen, large diff erences in outcome were observed (median survival 5 vs. 9.4 months). In a la rge randomized trial of radiotherapy vs. radiotherapy plus temozolomide, the subgroup with biopsy only did not benefit significantly from combined treatm ent. With different radiochemotherapy approaches, the median survival was ap proximately 5 months in recursive partitioning analysis (RPA) class VI, but 8-14 months in classes IV and V Thus, careful patient selection is necessary to avoid overtreatment in prognostically unfavorable groups with unresectabl e GBM. In patients qualifying for lengthy regimens of radio-chemotherapy, pr ospective randomized trials should study whether simultaneous radio- and che motherapy is superior to radiotherapy alone and, if so, what are the effects of addition of either upfront chemotherapy orpostradiation chemotherapy. Rec ent data suggest that class prediction models, based on defined molecular pr ofiles, and assessment of MGMT promoter methylation might contribute to impr oved patient stratification and decision making.
Journal Title: Anticancer research

PUBMED ID: 16323194
DOI: doi.org/10.1002/cncr.21582
Titolo: Salvage chemotherapy with cyclophosphamide for recurrent temozolomid e-refractory anaplastic astrocytoma.
Autori: Chamberlain MC., Tsao-Wei DD., Groshen S.
Data di Pubblicazione: 2005-12-03
Abstract: CYC demonstrated modest efficacy with acceptable toxicity in this cohort of adult patients with recurrent anaplastic astrocytoma, all of whom had failed prior TMZ chemotherapy.
Journal Title: Cancer

PUBMED ID: 16283445
DOI: doi.org/10.1007/s11060-005-3030-x
Titolo: Systemic temozolomide combined with loco-regional mitoxantrone in tr eating recurrent glioblastoma.
Autori: Boiardi A., Eoli M., Salmaggi A., Lamperti E., Botturi A., Broggi G. , Bissola L., Finocchiaro G., Silvani A.
Data di Pubblicazione: 2005-11-12
Abstract: Twenty-two recurrent GBM patients were enrolled for second tumor d ebulking with local positioning of a Rickam reservoir, in order to locally d eliver chemotherapy with the aim of controlling local tumor recurrence. We d

esigned a protocol using systemic temozolomide (150 mg/sqm days 1-5 every 28) in association with mitoxantrone, delivered through the reservoir (4 mg/da y 1-5 every 28) positioned into the area of tumor exeresis. After re-operati on a residual tumor mass no larger than 2 cm was identified in 18/22 patient s. The patients were treated with monthly cycles of chemotherapy until evolu tion of the tumor, but in no case for more than 10 cycles. Responses were ev aluated by MRI scans performed every 2 months and images assessed according to MacDonald's criteria. Response rate: no complete responses (CR), 5 partia l responses (PR), 13 stable disease (SD) and 4 progressive disease (PD) occu rred. The median progression-free survival (PFS) and survival time (ST) of t he whole group of treated patients was 7 and 11 months, respectively and mor e than a quarter of the patients survived over 18 months. During the study, the patients' compliance was complete and no dropouts occurred. Hematologica l toxicity was mild and after repeated local injections only minor neurologi cal side-effects occurred. Despite some bias in patients' selection not excl uded in this pilot study, results are interesting: the PFS was as long as th e survival of recurrent GBM reported in the literature.
Journal Title: Journal of neuro-oncology

PUBMED ID: 16267128
DOI: doi.org/10.1073/pnas.0508347102
Titolo: Evaluation of the functional diffusion map as an early biomarker of time-to-progression and overall survival in high-grade glioma.
Autori: Hamstra DA., Chenevert TL., Moffat BA., Johnson TD., Meyer CR., Mukh erji SK., Quint DJ., Gebarski SS., Fan X., Tsien CI., Lawrence TS., Junck L. , Rehemtulla A., Ross BD.
Data di Pubblicazione: 2005-11-04
Abstract: Diffuse malignant gliomas, the most common type of brain tumor, ca rry a dire prognosis and are poorly responsive to initial treatment. The res ponse to treatment is typically evaluated by measurements obtained from radi ographic images several months after the start of treatment; therefore, an e arly biomarker of tumor response would be useful for making early treatment decisions and for prognostic information. Thirty-four patients with malignan t glioma were examined by diffusion MRI before treatment and 3 weeks later. These images were coregistered, and differences in tumor-water diffusion val ues were calculated as functional diffusion maps (fDM), which were correlate d with the radiographic response, time-to-progression (TTP), and overall sur vival (OS). Changes in fDM at 3 weeks were closely associated with the radio graphic response at 10 weeks. The percentage of the tumor undergoing a signi ficant change in the diffusion of water (V(T)) was different between patient s with progressive disease (PD) vs. stable disease (SD) ($P < 0.001$). Patient s classified as PD by fDM analysis at 3 weeks were found to have a shorter T TP compared with SD (median TTP, 4.3 vs. 7.3 months; $P < 0.04$). By using fDM , early patient stratification also was correlated with shorter OS in the PD group compared with SD patients (median survival, 8.0 vs. 18.2 months; $P < 0$ .01). On the basis of fDM, tumor assessment provided an early biomarker for response, TTP, and OS in patients with malignant glioma. Further evaluation of this technique is warranted to determine whether it may be useful in the individualization of treatment or evaluation of the response in clinical pro tocols.
Journal Title: Proceedings of the National Academy of Sciences of the United States of America

PUBMED ID: 16241105
DOI: doi.org/10.3171/foc.2005.19.4.4
Titolo: Emerging concepts in glioma biology: implications for clinical proto cols and rational treatment strategies.
Autori: Wiesner SM., Freese A., Ohlfest JR.

Data di Pubblicazione: 2005-10-26
Abstract: Glioblastoma multiforme (GBM), the most common primary central ner vous system neoplasm, is a complex, heterogeneous disease. The recent identi fication of stem cells in murine tumor xenografts that were capable of recap itulating the tumor phenotype adds a new dimension of complexity to the alre ady challenging treatment of patients with GBMs. Although specific cellular and genetic changes are commonly associated with GBM, the mechanism by which those changes occur may have a significant impact on treatment outcome. Of t he many bioinformatics techniques developed in recent years, gene expression profiling has become a commonly used research tool for investigating tumor c haracteristics, and the development of rationally targeted molecular therapi es has also accelerated following the initial success of specifically design ed inhibitors in the treatment of malignancies. Despite these advances in re search techniques and targeted molecular therapies, however, limited clinica l impact has been achieved in the treatment of infiltrative malignancies suc h as GBMs. Thus, further extension in survival of patients with GBMs may req uire use of multiple analyses of tumors to develop tailored therapies that r eflect the inter- and intratumoral heterogeneity of this disease. In this re view, the authors briefly consider the potential use of expression profiling combined with mutation analysis in the development of treatment modalities t o address the heterogeneity of this complex tumor phenotype.
Journal Title: Neurosurgical focus

PUBMED ID: 16206736
DOI: doi.org/10.3171/ped.2005.102.1.0065
Titolo: Spontaneous regression of a diffuse brainstem lesion in the neonate. Report of two cases and review of the literature.
Autori: Thompson WD., Kosnik EJ.
Data di Pubblicazione: 2005-10-07
Abstract: The authors present two cases of diffuse brainstem lesions that re gressed without treatment. Two newborns presented with cranial nerve palsies and limb weakness at birth. Magnetic resonance (MR) images obtained in the 1 st week of life revealed a large, expansive pontomedullary lesion in each pa tient. Findings of clinical and imaging examinations were highly consistent with the characteristics of diffuse brainstem glioma. After consultation wit h the parents of both infants, all parties agreed to forgo the treatment mod alities available at the time. Neither patient underwent surgery, radiation treatment, or chemotherapy; both underwent routine neurological and MR imagi ng examinations. Within weeks the patient in Case 1 started to improve clini cally and at 4 years of age has reached nearly all developmental milestones. Serial MR images demonstrated a steady decrease in the size of the lesion. T he patient in Case 2 improved in a similar manner and is now 10 years old. T he findings from these two cases should encourage families and clinicians to consider that a subcategory of diffuse lesions may exist, particularly in th e neonatal period. It must be stressed, however, that nearly all patients wi th diffuse brainstem lesions experience a poor outcome, regardless of tumor grade or treatment. Brainstem gliomas, spontaneous regression of central ner vous system tumors, and the differential diagnoses of brainstem lesions are discussed.
Journal Title: Journal of neurosurgery

PUBMED ID: 16156235
DOI: doi.org/10.3171/jns.2005.102.2.0224
Titolo: Atypical external hydrocephalus with visual failure due to occult le ptomeningeal dissemination of a pontine glioma. Case report.
Autori: Tarnaris A., Edwards RJ., Lowis SP., Pople IK.
Data di Pubblicazione: 2005-09-15

Abstract: The authors report on the case of a diffuse pontine glioma in a 5-year-old boy in whom radiologically and cytologically occult leptomeningeal metastases led to the development of an atypical "external" hydrocephalus, a ssociated with grossly elevated intracranial pressure (ICP). Initial neuroim aging demonstrated only mild communicating ventricular dilation associated w ith a noticeable enlargement of the subarachnoid space, particularly over th e surface of the frontal lobes; these features are not usually associated wi th significantly elevated ICP. Possible pathophysiological mechanisms result ing in this unusual clinical presentation are discussed. Early recognition o f the severity of the raised ICP despite the paucity of clinical and radiolo gical signs may have averted the development of blindness due to optic atrop hy.
Journal Title: Journal of neurosurgery

PUBMED ID: 16151595
DOI: doi.org/10.1007/s11060-005-5261-2
Titolo: Multisection 1H magnetic resonance spectroscopic imaging assessment of glioma response to chemotherapy.
Autori: Balmaceda C., Critchell D., Mao X., Cheung K., Pannullo S., DeLaPaz RL., Shungu DC.
Data di Pubblicazione: 2005-09-10
Abstract: This study evaluated the role of proton magnetic resonance spectro scopic imaging (1H MRSI) in assessing the response of low-grade brain tumors to a chemotherapy-only treatment regimen. Specifically, it was of interest t o assess if 1H MRSI could detect early tumor response to therapy prior to ma gnetic resonance imaging (MRI) changes, and to establish which spectral mark ers were sensitive to regional changes within and around a heterogeneous tum or mass. A total of 14 patients with lower-grade gliomas were evaluated by m ultislice 1H MRSI, MRI and clinical examination. Changes associated with che motherapy were assessed by longitudinal comparisons of regional levels of ch oline (Cho), N-acetyl-L-aspartate (NAA), and lactate (Lac) relative to total creatine. These changes were, in turn, compared to changes on pre- and post-contrast MR images and to each patient's clinical status. In enhancing tumor regions, there was a significant association between an increase in Lac/Cr d uring treatment and decreased progression-free survival time. At baseline, a low NAA/Cr in normal-appearing brain tissue adjacent to non-enhancing tumor was associated with decreased progression-free survival time, as was an incr ease in Cho/Cr during chemotherapy. An increase in Cho/Cr and Lac/Cr in norm al-appearing brain regions next to non-enhancing tumor in one patient was no ted 2 months before MRI showed progressive disease. These results suggest th at 1H MRSI can be a powerful adjunct to MRI in the assessment of tumor respo nse to chemotherapy, and that Cho/Cr and Lac/Cr appear to be the most reliab le markers of tumor progression and may predict response prior to MRI change s.
Journal Title: Journal of neuro-oncology

PUBMED ID: 16132503
DOI: doi.org/10.1007/s11060-005-2913-1
Titolo: The efficacy of radiation therapy in the management of grade I astro cytomas.
Autori: Kidd EA., Mansur DB., Leonard JR., Michalski JM., Simpson JR., Perry A.
Data di Pubblicazione: 2005-09-01
Abstract: While this study reports an excellent overall survival, approximat ely one third of patients with grade I astrocytomas had progressive disease following radiation therapy. In particular, patients with supratentorial tum ors and delayed radiation therapy had a worse PFS. Additional investigation is needed to improve the outcome in these patients.

Journal Title: Journal of neuro-oncology

PUBMED ID: 16115932
DOI: doi.org/10.1158/1078-0432.CCR-05-0559
Titolo: Immunologic evaluation of personalized peptide vaccination for patie nts with advanced malignant glioma.
Autori: Yajima N., Yamanaka R., Mine T., Tsuchiya N., Homma J., Sano M., Kur amoto T., Obata Y., Komatsu N., Arima Y., Yamada A., Shigemori M., Itoh K., Tanaka R.
Data di Pubblicazione: 2005-08-24
Abstract: Personalized peptide vaccinations were recommended for the further clinical study to malignant glioma patients.
Journal Title: Clinical cancer research : an official journal of the America n Association for Cancer Research

PUBMED ID: 16086097
DOI: doi.org/10.1007/s10637-005-2464-5
Titolo: Pre-irradiation 9-amino [20s] camptothecin (9-AC) in patients with n ewly diagnosed glioblastoma multiforme.
Autori: Farray D., Ahluwalia MS., Snyder J., Barnett GH., Cohen BH., Suh JH. , Peereboom DM.
Data di Pubblicazione: 2005-08-09
Abstract: 9-AC lacks activity against glioblastoma multiforme (GBM). Further studies looking at the efficacy of 9-AC in GBM may be futile.
Journal Title: Investigational new drugs

PUBMED ID: 16078112
DOI: doi.org/10.1007/s11060-005-0603-7
Titolo: HER1/EGFR tyrosine kinase inhibitors for the treatment of glioblasto ma multiforme.
Autori: Raizer JJ.
Data di Pubblicazione: 2005-08-04
Abstract: Glioblastoma multiforme (GBM) is a highly malignant brain tumor wi th limited therapeutic options, a high recurrence rate and mortality. Standa rd therapy is maximal surgical resection and radiotherapy (RT). Recent data suggest combining temozolomide with RT is better than RT alone. Adjuvant che motherapy has a modest impact on survival. For relapsed patients there is no standard therapy, but options include chemotherapeutic agents or new agents in development. One approach to improve outcome is using targeted agents tha t interfere with cell-surface receptors or intracellular signaling pathways. Between 40% and 50% of GBM tumors show HER1/EGFR dysregulation, and almost h alf co-express the constitutively active mutant receptor subtype EGFRvIII, w hich may contribute to the aggressive and refractory course of GBM. Numerous studies show a relationship between aberrant HER1/EGFR biology and tumorigen icity in GBM cells. Two available HER1/EGFR tyrosine kinase inhibitors (TKIs) are gefitinib (Iressa) and erlotinib (Tarceva); both show antitumor and ra diosensitization effects in vitro and in animal models of GBM. Clinical tria ls in patients with GBM and other gliomas are ongoing. Preliminary and publi shed results from trials of gefitinib in recurrent GBM show no increased tim e to progression or overall survival (OS) compared with historical controls. Studies with erlotinib show greater antitumor activity in patients with GBM than with gefitinib, although the impact of both agents on OS remains unclea r. GBM treatment with HER1/EGFR TKIs alone or combined with other targeted t herapies and conventional modalities deserve further investigation and refin ement, as does our understanding of their mechanisms of action and the role of genetics.
Journal Title: Journal of neuro-oncology

PUBMED ID: 16078107
DOI: doi.org/10.1007/s11060-004-3348-9
Titolo: Primary neurocytoma of the spinal cord: a case report and review of literature.
Autori: Sharma S., Sarkar C., Gaikwad S., Suri A., Sharma MC.
Data di Pubblicazione: 2005-08-04
Abstract: Most central neurocytomas (CN) and spinal neurocytomas (SN) have a bland well-differentiated histologic picture and uneventful clinical course. However, rare examples showing histologic atypia, recurrence and even CSF di ssemination have been reported. Herein we report a case of recurrent spinal neurocytoma in a 24-year-old male who presented with a 2-month history of we akness and numbness of the left upper and lower limbs, and was previously op erated at the same site 10 months ago. MRI revealed a contrast enhancing int ramedullary mass involving C5-T1 region. Radiologic and operative impression at both surgeries was that of a glioma, possibly anaplastic. Histologic and immunohistochemical features in both resections were those of an atypical ne urocytoma. The tumor showed rare mitoses, focal mild vascular proliferation in both specimens, and necrosis in the initial specimen. MIB1 labeling indic es were 9 and 10%, respectively. Based on the analysis of this case and limi ted data from the literature, it is hypothesized that SN shows a histopathol ogic picture, immunoprofile and biologic behavior very similar to CN. Howeve r, the presence of histologic atypia and increased MIB1 index in SN appear t o more closely correlate with tumor recurrence and a worse overall outcome, in part due to their location in the critical region of cervical spinal cord . Therefore, we hypothesize that SN with atypia requires a close clinical fo llow up. As in CN, radiation therapy is perhaps best reserved for atypical, progressive and recurrent SN.
Journal Title: Journal of neuro-oncology

PUBMED ID: 16059612
DOI: doi.org/10.1590/s0004-282x2005000300031
Titolo: [Isolated Richter's syndrome in central nervous system: case report] .
Autori: Resende LS., Bacchi CE., Resende LA., Gabarra RC., Niéro-Melo L.
Data di Pubblicazione: 2005-08-02
Abstract: Diffuse large cell non Hodgkin's lymphoma associated with chronic lymphoid leukemia (CLL), or Richter's syndrome, is a rare and serious compli cation. Isolated Richter's syndrome in the central nervous system is very ra re; only 12 cases have been reported. We describe a 74-year-old patient with diffuse large cell non Hodgkin's lymphoma in the right frontal region with t he appearance of multiform glioblastoma.
Journal Title: Arquivos de neuro-psiquiatria

PUBMED ID: 16054568
DOI: doi.org/10.1016/S1470-2045(05)70252-7
Titolo: Treatment of medulloblastoma with postoperative chemotherapy alone: an SFOP prospective trial in young children.
Autori: Grill J., Sainte-Rose C., Jouvet A., Gentet JC., Lejars O., Frappaz D., Doz F., Rialland X., Pichon F., Bertozzi AI., Chastagner P., Couanet D., Habrand JL., Raquin MA., Le Deley MC., Kalifa C., Kalifa C.
Data di Pubblicazione: 2005-08-02
Abstract: Conventional chemotherapy alone can be used to cure children with non-metastatic medulloblastoma who have gross total resection confirmed by e arly radiological assessment, but is not sufficient for treatment of those w ith metastatic or incompletely resected medulloblastoma. Salvage treatment f

ollowed by posterior-fossa radiotherapy can effectively treat local relapses or progression.
Journal Title: The Lancet. Oncology

PUBMED ID: 16053669
DOI: doi.org/10.1097/00130404-200505000-00012
Titolo: Thalidomide is inactive in heavily pretreated patients with metastatic breast cancer.
Autori: Morabito A., Carillio G., Longo R., Gasparini G.
Data di Pubblicazione: 2005-08-02
Abstract: Experimental studies have demonstrated that thalidomide has anti-tumor activity mediated by blockage of angiogenesis, with clinical efficacy in multiple myeloma, glioblastoma multiforme, and renal cell cancer. We investigated the therapeutic activity and toxicity of thalidomide in patients with progressive metastatic breast cancer pretreated with chemotherapy. Inclusion criteria were metastatic breast cancer in progression of disease after at least two lines of chemotherapy, age > or = 18 years, performance status < or = 2, and adequate hematologic, renal, and hepatic functions. Twelve patients entered the study, eight of whom were pretreated with three or more lines of chemotherapy (66.7%). Thalidomide was well tolerated: the most common side effects were constipation and somnolence (58.3% of patients). No objective response or durable stable disease was observed. Median time to progression and median overall survival were 8 weeks (range, 4-10 weeks) and 16 weeks (range, 8-54 weeks), respectively. In conclusion, thalidomide is an ineffective treatment in patients with progressive metastatic breast cancer heavily pretreated with chemotherapy.
Journal Title: Cancer journal (Sudbury, Mass.)

PUBMED ID: 16033874
DOI: doi.org/10.1093/annonc/mdi317
Titolo: Imatinib and hydroxyurea in pretreated progressive glioblastoma multiforme: a patient series.
Autori: Dresemann G.
Data di Pubblicazione: 2005-07-22
Abstract: The efficacy results, combined with findings that imatinib and hydroxyurea were well tolerated, suggest that this combination shows promise as therapy for GBM.
Journal Title: Annals of oncology : official journal of the European Society for Medical Oncology

PUBMED ID: 16000956
DOI: doi.org/10.1097/01.cji.0000162782.86008.ml
Titolo: Phase I trial of intravenous IL-4 pseudomonas exotoxin protein (NBI-3001) in patients with advanced solid tumors that express the IL-4 receptor.
Autori: Garland L., Gitlitz B., Ebbinghaus S., Pan H., de Haan H., Puri RK., Von Hoff D., Figlin R.
Data di Pubblicazione: 2005-07-08
Abstract: NBI-3001 is a novel immunotoxin of attenuated Pseudomonas exotoxin fused to circularly permutated IL-4, which has shown some antitumor effects in glioblastoma multiforme with intratumoral administration. The authors evaluated the safety and tolerability of NBI-3001 administered intravenously in a dose-escalation design to patients with renal cell and non-small cell lung carcinoma whose tumors showed at least 10% IL-4 receptor expression. Cohorts of three to six patients were treated at dose levels of 0.008, 0.016, and 0.027 mg/m2 daily x 5 days every 28 days. Neutralizing antibody (NAB) titers, plasma levels of NBI-3001, and patient tolerability were monitored sequentially. 14 patients received a total of 36 cycles of NBI-3001 (range 1-6). No d

ose-limiting toxicities were noted at dose levels 0.008 and 0.016 mg/m2. At 0.027 mg/m2, two patients developed self-limiting, grade 3 or 4 transaminase elevation during cycle 1. NAB titers of more than 1:100 were detected in fiv e of the seven patients treated with at least two cycles; the median titer a fter cycle 1 and the median maximum titer in subsequent cycles were 1:50 and approximately 1:1,710, respectively. No objective tumor responses were noted . Eight of 12 evaluable patients with renal cell carcinoma had stable diseas e; four patients had disease progression. High NAB titers resulted in four p atients being withdrawn from the study. The dose-limiting toxicity for intra venous NBI-3001 was transaminase elevation at 0.027 mg/m2. NBI-3001 at 0.016 mg/m2 was well tolerated. Low circulating levels of NBI-3001, coupled with r ising NAB titers, may have contributed to the lack of response in tumors tha t express IL-4R.
Journal Title: Journal of immunotherapy (Hagerstown, Md. : 1997)

PUBMED ID: 15998902
DOI: doi.org/10.1200/JCO.2005.23.622
Titolo: Phase II trial of temsirolimus (CCI-779) in recurrent glioblastoma m ultiforme: a North Central Cancer Treatment Group Study.
Autori: Galanis E., Buckner JC., Maurer MJ., Kreisberg JI., Ballman K., Boni J., Peralba JM., Jenkins RB., Dakhil SR., Morton RF., Jaeckle KA., Scheithau er BW., Dancey J., Hidalgo M., Walsh DJ., Walsh DJ.
Data di Pubblicazione: 2005-07-07
Abstract: Temsirolimus is well tolerated in recurrent GBM patients. Despite the effect of EIACs on temsirolimus metabolism, therapeutic levels were achi eved. Radiographic improvement was observed in 36% of temsirolimus-treated p atients, and was associated with significantly longer TTP. High levels of ph osphorylated p70s6 kinase in baseline tumor samples appear to predict a pati ent population more likely to derive benefit from treatment. These findings should be validated in other studies of mTOR inhibitors.
Journal Title: Journal of clinical oncology : official journal of the Americ an Society of Clinical Oncology

PUBMED ID: 15971308
DOI: doi.org/10.1016/s0167-8140(04)80012-4
Titolo: Overview of clinical experiences on carbon ion radiotherapy at NIRS.
Autori: Tsujii H., Mizoe JE., Kamada T., Baba M., Kato S., Kato H., Tsuji H. , Yamada S., Yasuda S., Ohno T., Yanagi T., Hasegawa A., Sugawara T., Ezawa H., Kandatsu S., Yoshikawa K., Kishimoto R., Miyamoto T.
Data di Pubblicazione: 2005-06-23
Abstract: Carbon ion radiotherapy, due to its physical and biologic advantag es over photons, has provided improved outcome in terms of minimized toxicit y and high local control rates for locally advanced tumors and pathologicall y non-squamous cell type of tumors. Using carbon ion radiotherapy, hypofract ionated radiotherapy with application of larger doses per fraction and a red uction of overall treatment times as compared to conventional radiotherapy w as enabled.
Journal Title: Radiotherapy and oncology : journal of the European Society f or Therapeutic Radiology and Oncology

PUBMED ID: 15930352
DOI: doi.org/10.1158/1078-0432.CCR-05-0120
Titolo: Clinical evaluation of dendritic cell vaccination for patients with recurrent glioma: results of a clinical phase I/II trial.
Autori: Yamanaka R., Homma J., Yajima N., Tsuchiya N., Sano M., Kobayashi T. , Yoshida S., Abe T., Narita M., Takahashi M., Tanaka R.
Data di Pubblicazione: 2005-06-03

Abstract: This study showed the safety and clinical response of autologous t
umor lysate-pulsed dendritic cell therapy for patients with malignant glioma
. Dendritic cell therapy is recommended for further clinical studies in mali
gnant glioma patients.
Journal Title: Clinical cancer research : an official journal of the America
n Association for Cancer Research

PUBMED ID: 15918940
DOI: doi.org/10.1227/01.neu.0000159649.71890.30
Titolo: Safety and feasibility of convection-enhanced delivery of Cotara for
the treatment of malignant glioma: initial experience in 51 patients.
Autori: Patel SJ., Shapiro WR., Laske DW., Jensen RL., Asher AL., Wessels BW
., Carpenter SP., Shan JS.
Data di Pubblicazione: 2005-05-28
Abstract: The majority of Cotara infusions delivered between 90 and 110% of
the prescribed administered activity to the targeted region. This method of
administration has an acceptable safety profile compared with literature rep
orts of other therapeutics delivered by convection-enhanced delivery.
Journal Title: Neurosurgery

PUBMED ID: 15912507
DOI: doi.org/10.1002/cncr.21110
Titolo: A multicenter retrospective study of chemotherapy for recurrent intr
acranial ependymal tumors in adults by the Gruppo Italiano Cooperativo di Ne
uro-Oncologia.
Autori: Brandes AA., Cavallo G., Reni M., Tosoni A., Nicolardi L., Scopece L
., Franceschi E., Sotti G., Talacchi A., Turazzi S., Ermani M.
Data di Pubblicazione: 2005-05-25
Abstract: Cisplatin-based chemotherapy achieved a higher response rate, but
did not prolong disease progression-free survival or OS. More active regimen
s for the salvage treatment of ependymal tumors have yet to be found.
Journal Title: Cancer

PUBMED ID: 15870090
DOI: doi.org/10.1093/annonc/mdi183
Titolo: Neoadjuvant phase II multicentre study of new agents in patients wit
h malignant glioma after minimal surgery. Report of a cohort of 187 patients
treated with temozolomide.
Autori: Brada M., Ashley S., Dowe A., Gonsalves A., Huchet A., Pesce G., Ren
i M., Saran F., Wharram B., Wilkins M., Wilkins P.
Data di Pubblicazione: 2005-05-05
Abstract: The phase II study design of primary chemotherapy in patients with
malignant glioma following biopsy alone is feasible and provides as objectiv
e a method of assessment of efficacy as is currently available. The baseline
data on temozolomide provide a benchmark for assessment of efficacy of other
agents and combinations.
Journal Title: Annals of oncology : official journal of the European Society
for Medical Oncology

PUBMED ID: 15857844
DOI: doi.org/10.1093/annonc/mdi225
Titolo: Temozolomide in combination with BCNU before and after radiotherapy
in patients with inoperable newly diagnosed glioblastoma multiforme.
Autori: Barrié M., Couprie C., Dufour H., Figarella-Branger D., Muracciole X
., Hoang-Xuan K., Braguer D., Martin PM., Peragut JC., Grisoli F., Chinot O.
Data di Pubblicazione: 2005-04-29

Abstract: The combination of BCNU plus temozolomide as neo-adjuvant therapy in inoperable GBM exhibited promising activity with a good safety profile an d warrants further evaluation.
Journal Title: Annals of oncology : official journal of the European Society for Medical Oncology

PUBMED ID: 15831236
DOI: doi.org/10.1215/S1152851704000602
Titolo: Phase 2 study of T138067-sodium in patients with malignant glioma: T rial of the National Cancer Institute of Canada Clinical Trials Group.
Autori: Kirby S., Gertler SZ., Mason W., Watling C., Forsyth P., Aniagolu J. , Stagg R., Wright M., Powers J., Eisenhauer EA.
Data di Pubblicazione: 2005-04-16
Abstract: We studied the activity of T138067-sodium in patients with maligna nt gliomas. T138067-sodium is a unique new chemotherapy agent that inhibits microtubule formation by binding irreversibly and specifically to beta(1), b eta(2)and beta(4) isotypes of 3-tubulin, causing cell arrest at G(2)/M and i nducing apoptosis. Patients with recurrent anaplastic astrocytoma or gliobla stoma multiforme were treated intravenously with 330 mg/m(2) of T138067-sodi um weekly. Treatment was continued until the patient experienced either unac ceptable toxicity or progressive disease. Patients had to have histologicall y proven glioma, have bidimensionally measurable disease at least 1 cm x 1 c m, and have received no more than one prior adjuvant chemotherapy. No chemot herapy or radiotherapy for recurrent disease was permitted. Nineteen patient s entered the trial. One patient was found to be ineligible. There were two patients with anaplastic astrocytoma and 16 with glioblastoma multiforme. On ly two patients had received prior adjuvant chemotherapy. The first seven pa tients had full pharmacokinetic sampling. No dose-limiting toxicity was seen , and pharmacokinetic results were consistent with those from nonglioma pati ents. The most common drug-related effects were fatigue (33%), nausea (28%), neutropenia (28%), and anorexia (17%). No patients stopped the study because of toxicity. No responses were seen in the 15 eligible patients who complete d at least one cycle. Three patients had stable disease with a median durati on of 2.6 months. Our results suggest that given in this dose and schedule T 138067-sodium does not have activity in this population of anaplastic astroc ytoma and glioblastoma multiforme.
Journal Title: Neuro-oncology

PUBMED ID: 15813507
DOI: Mancante
Titolo: Benefit of temozolomide compared to procarbazine in treatment of gli oblastoma multiforme at first relapse: effect on neurological functioning, p erformance status, and health related quality of life.
Autori: Macdonald DR., Kiebert G., Prados M., Yung A., Olson J.
Data di Pubblicazione: 2005-04-09
Abstract: Since high-grade malignant gliomas can seldom be treated curativel y, the main aim of first line therapy is to improve progression free surviva l (PFS), to reduce morbidity, and to preserve, if not restore neurological f unctions and the capacity to perform daily activities. Focusing on a single clinical efficacy parameter in clinical trials may provide a potentially bia sed result, as for patients the overall result of treatment entails a more c omplex picture of weighing and balancing gains and losses on different outco me measures. In this paper we address different clinical outcomes measures s eparately and we illustrate the value of multiple outcome measures using the results of a recent clinical trial comparing temozolomide with procarbazine in the treatment of Glioblastoma Multiforme. Compared with procarbazine, tem ozolomide not only prolonged PFS, but also maintained neurological functioni ng and performance status for a longer period of time, and also improved hea

lth-related quality of life (HRQL). All these statistically significant outc omes demonstrate a remarkable consistency. In addition, temozolomide showed a trend of extending overall survival over procarbazine.
Journal Title: Cancer investigation

PUBMED ID: 15805192
DOI: doi.org/10.1073/pnas.0501532102
Titolo: Functional diffusion map: a noninvasive MRI biomarker for early stra tification of clinical brain tumor response.
Autori: Moffat BA., Chenevert TL., Lawrence TS., Meyer CR., Johnson TD., Don g Q., Tsien C., Mukherji S., Quint DJ., Gebarski SS., Robertson PL., Junck L R., Rehemtulla A., Ross BD.
Data di Pubblicazione: 2005-04-05
Abstract: Assessment of radiation and chemotherapy efficacy for brain cancer patients is traditionally accomplished by measuring changes in tumor size se veral months after therapy has been administered. The ability to use noninva sive imaging during the early stages of fractionated therapy to determine wh ether a particular treatment will be effective would provide an opportunity to optimize individual patient management and avoid unnecessary systemic tox icity, expense, and treatment delays. We investigated whether changes in the Brownian motion of water within tumor tissue as quantified by using diffusio n MRI could be used as a biomarker for early prediction of treatment respons e in brain cancer patients. Twenty brain tumor patients were examined by sta ndard and diffusion MRI before initiation of treatment. Additional images we re acquired 3 weeks after initiation of chemo- and/or radiotherapy. Images w ere coregistered to pretreatment scans, and changes in tumor water diffusion values were calculated and displayed as a functional diffusion map (fDM) for correlation with clinical response. Of the 20 patients imaged during the cou rse of therapy, 6 were classified as having a partial response, 6 as stable disease, and 8 as progressive disease. The fDMs were found to predict patien t response at 3 weeks from the start of treatment, revealing that early chan ges in tumor diffusion values could be used as a prognostic indicator of sub sequent volumetric tumor response. Overall, fDM analysis provided an early b iomarker for predicting treatment response in brain tumor patients.
Journal Title: Proceedings of the National Academy of Sciences of the United States of America

PUBMED ID: 15782008
DOI: doi.org/10.2176/nmc.45.156
Titolo: Primary cerebral angiitis containing marked xanthoma cells with mass ive intraparenchymal involvement--case report--.
Autori: Ishikawa E., Tsuboi K., Takano S., Kimura H., Aoki T., Mashiko R., N agata M.
Data di Pubblicazione: 2005-03-23
Abstract: A 27-year-old woman was referred to our hospital with mild disorie ntation, bilateral abducens nerve palsy, and mild left hemiparesis. Magnetic resonance (MR) imaging revealed diffuse mass lesions resembling malignant gl ioma in the right frontal intraparenchymal region, with enhancement of multi ple meningeal and intraparenchymal nodules. Partial resection of the frontal lesion was performed. Histological examination revealed that the specimens c onsisted of brain tissue, with marked perivascular infiltration of histiocyt es and sheets of xanthomatous cells. The diagnosis was primary cerebral angi itis containing marked xanthoma cells. Steroid therapy was administered over 1 week. MR imaging showed that the remaining lesions resolved gradually, and had disappeared 2 years after surgery. No neurological symptoms or recurrenc e of the tumor has been observed during the 6-year period since the operatio n.
Journal Title: Neurologia medico-chirurgica

PUBMED ID: 15737833
DOI: doi.org/10.1016/S1470-2045(05)01767-5
Titolo: MRI in treatment of adult gliomas.
Autori: Henson JW., Gaviani P., Gonzalez RG.
Data di Pubblicazione: 2005-03-02
Abstract: Diffuse astrocytomas of the adult cerebral hemispheres are unique among tumours in human beings in the extent to which their imaging features are related to histopathological characteristics and clinical behaviour. However, understanding is still restricted about the value of imaging features in the measurement of response and of progression in these tumours. The present approach used in clinical trials, which consists of an anatomical measurement of the enhancing tumour on MRI, has many problems, and might not be acceptable as a surrogate endpoint for survival in patients with glioblastoma who are enrolled in clinical trials. Dynamic imaging techniques, such as capillary permeability mapping, are being used in studies of new drugs that target specific molecular features of gliomas; however, the validity of these techniques has not been elucidated. Diffusion imaging can be valuable for fibre-tract mapping to assist surgical planning and might become useful in measuring early response to treatment in densely cellular tumours. Functional imaging techniques can be used to localise motor, sensory, and language-control areas before surgery. Intraoperative MRI has produced improvements in the extent of tumour resection, and molecular imaging is another technique on the horizon, which could come to have a role in clinical trials in the near future. Thus, as a rapidly expanding sphere of investigation, brain-tumour imaging is producing great excitement. The aim of these new techniques is to aid the identification of more effective treatments.
Journal Title: The Lancet. Oncology

PUBMED ID: 15735921
DOI: doi.org/10.1007/s11060-004-2026-2
Titolo: A Phase II trial of paclitaxel and topotecan with filgrastim in patients with recurrent or refractory glioblastoma multiforme or anaplastic astrocytoma.
Autori: Pipas JM., Meyer LP., Rhodes CH., Cromwell LD., McDonnell CE., Kingman LS., Rigas JR., Fadul CE.
Data di Pubblicazione: 2005-03-01
Abstract: Paclitaxel and topotecan with G-CSF support exhibits modest activity in adults with recurrent or refractory glioblastoma and anaplastic astrocytoma. The significant hematotoxicity encountered, however, cannot justify further investigation of this combination in patients with high grade brain tumors.
Journal Title: Journal of neuro-oncology

PUBMED ID: 15701286
DOI: doi.org/10.1215/S1152851703000589
Titolo: Sustained radiographic and clinical response in patient with bifrontal recurrent glioblastoma multiforme with intracerebral infusion of the recombinant targeted toxin TP-38: case study.
Autori: Sampson JH., Reardon DA., Friedman AH., Friedman HS., Coleman RE., McLendon RE., Pastan I., Bigner DD.
Data di Pubblicazione: 2005-02-11
Abstract: Glioblastoma multiforme remains refractory to conventional therapy, and novel therapeutic modalities are desperately needed. TP-38 is a recombinant chimeric protein containing a genetically engineered form of the cytotoxic Pseudomonas exotoxin fused to transforming growth factor (TGF)-alpha. TGF-alpha binds with high affinity to the epidermal growth factor receptor, w

hich is uniformly overexpressed in malignant gliomas, often because of gene amplification. Prior to therapy with TP-38, the patient described here was c ompletely refractory to multiple other therapies, with radiographic and path ologic evidence of tumor progression. After therapy, she improved clinically , was weaned off steroids and anti-convulsants, and experienced a progressiv e decrease in enhancing tumor volume. Despite multiple prior recurrences, sh e has not progressed for >43 months after TP-38 therapy. Small remaining are as of enhancement demonstrate no evidence of tumor histologically and are hy pometabolic on positron emission tomography. This report describes a dramati c and sustained clinical and radiographic response in a patient with a bifro ntal glioblastoma multiforme treated with intratumoral infusion of a novel t argeted toxin, TP-38.
Journal Title: Neuro-oncology

PUBMED ID: 15701281
DOI: doi.org/10.1215/S1152851704000304
Titolo: Sequential chemotherapy, high-dose thiotepa, circulating progenitor cell rescue, and radiotherapy for childhood high-grade glioma.
Autori: Massimino M., Gandola L., Luksch R., Spreafico F., Riva D., Solero C ., Giangaspero F., Locatelli F., Podda M., Bozzi F., Pignoli E., Collini P., Cefalo G., Zecca M., Casanova M., Ferrari A., Terenziani M., Meazza C., Pola stri D., Scaramuzza D., Ravagnani F., Fossati-Bellani F.
Data di Pubblicazione: 2005-02-11
Abstract: Childhood malignant gliomas are rare, but their clinical behavior is almost as aggressive as in adults, with resistance to therapy, rapid prog ression, and not uncommonly, dissemination. Our study protocol incorporated sequential chemotherapy and high-dose thiotepa in the preradiant phase, foll owed by focal radiotherapy and maintenance with vincristine and lomustine fo r a total duration of one year. The induction treatment consisted of two cou rses of cisplatin (30 mg/m2) plus etoposide (150 mg/m2) x 3 days and of vinc ristine (1.4 mg/m2) plus cyclophosphamide (1.5 g/m2) plus high-dose methotre xate (8 g/m2), followed by high-dose thiotepa (300 mg/m2 x 3 doses), with ha rvesting of peripheral blood progenitor cells after the first cisplatin/etop oside course. From August 1996 to March 2003, 21 children, 14 females and 7 males, with a median age of 10 years were enrolled, 18 presenting with resid ual disease after surgery. Histologies were glioblastoma multiforme in 10, a naplastic astrocytoma in nine, and anaplastic oligodendroglioma in two; site s of origin were supratentorial areas in 17, spine in two, and posterior fos sa in two. Of the 21 patients, 12 have died (10 after relapse, with a median time to progression for the whole series of 14 months; one with intratumoral bleeding at 40 months after diagnosis; and one affected by Turcot syndrome f or duodenal cancer relapse). Four of 12 relapsed children had tumor dissemin ation. At a median follow-up of 57 months, overall survival and progression-free survival at four years were 43% and 46%, respectively. Sequential and h igh-dose chemotherapy can be afforded in front-line therapy of childhood mal ignant glioma without excessive morbidity and rather encouraging results.
Journal Title: Neuro-oncology

PUBMED ID: 15662767
DOI: Mancante
Titolo: Temozolomide chemotherapy of patients with recurrent anaplastic astr ocytomas and glioblastomas.
Autori: Sipos L., Vitanovics D., Afra D.
Data di Pubblicazione: 2005-01-25
Abstract: Temozolomide chemotherapy in patients with recurrent malignant ast rocytoma and glioblastoma proved to be efficacious and similar good results were achieved as with a nitrosourea based combined chemotherapy. Even in tho se patients who received previous chemotherapy temozolomide is well tolerate

d and a relatively long time to progression was achieved in cases of recurre nt malignant gliomas. In a few number of patients where BCNU had been previo usly failed with temozolomide stable disease was achieved. Temozolomide seem s to be a promising drug in the chemotherapy of malignant gliomas and can be applied as a second line chemotherapy, as well.
Journal Title: Ideggyogyaszati szemle

PUBMED ID: 15570079
DOI: doi.org/10.1200/JCO.2004.06.181
Titolo: Second-line chemotherapy with irinotecan plus carmustine in glioblas toma recurrent or progressive after first-line temozolomide chemotherapy: a phase II study of the Gruppo Italiano Cooperativo di Neuro-Oncologia (GICNO) .
Autori: Brandes AA., Tosoni A., Basso U., Reni M., Valduga F., Monfardini S. , Amistà P., Nicolardi L., Sotti G., Ermani M.
Data di Pubblicazione: 2004-12-01
Abstract: The BCNU plus irinotecan regimen seems active and non-cross-resist ant in patients with GBM with recurrence after temozolomide-based chemothera py.
Journal Title: Journal of clinical oncology : official journal of the Americ an Society of Clinical Oncology

PUBMED ID: 15557883
DOI: Mancante
Titolo: Multiple sclerosis and gliomas. Clinical remarks on 10 cases and cri tical review of the literature.
Autori: Isidori A., Caroli E., Frati A., D'Andrea G., Brogna C., Piccirilli M., Salvati M.
Data di Pubblicazione: 2004-11-24
Abstract: The association between multiple sclerosis and tumours of the cent ral nervous system is unusual. The authors analyzed the clinico-pathological elements of the correlation. The pertinent literature on this subject is cri tically reviewed. Ten cases of patients with an history of multiple sclerosi s for more than 15 years and a clinical and radiological evidence of brain t umour were submitted to surgery in order to remove the lesion and/or to chem o- and radiotherapy. The various aspects of the association were studied in detail. A patient with multiple sclerosis, particularly with atypical sympto ms, should be evaluated by an annual MRI investigation with intravenous para magnetic contrast medium. The diagnostic work-up should be: clinical and rad iological assessment; MRI in the event of atypical symptoms; Sstereotactic o r neuronavigation-aided biopsy in any suspected lesions. Patients with multi ple sclerosis and glioma present survival times identical to those observed in patients not suffering from multiple sclerosis. The coexistence of multip le sclerosis and brain tumours does not seem to influence the clinical evolu tion of either of these pathologies. We believe that it is important to achi eve an early diagnosis of brain tumour in such patients with a clinical and neuroradiological follow up, so that they can be treated promptly.
Journal Title: Journal of neurosurgical sciences

PUBMED ID: 15509482
DOI: doi.org/10.1007/s11864-004-0037-z
Titolo: Therapeutic strategies for local recurrent malignant glioma.
Autori: Sills AK., Duntsch C., Weimar J.
Data di Pubblicazione: 2004-10-29
Abstract: Patients with local recurrent malignant gliomas present diagnostic and therapeutic challenges for the neuro-oncology practitioner. Management m ust be individualized depending on the patient's age, performance status, hi

stology, response to initial therapy, type of recurrence (local vs diffuse), and time since original diagnosis. Treatment options may be classified into surgery, additional radiation therapy, or chemotherapy. Results of treatment are often difficult to determine because of limitations of conventional imag ing. Symptom palliation is an important goal that often requires additional adjuvant medical therapy. Quality of life issues are also of paramount impor tance in patients with recurrent malignant glioma and frequently will guide management strategy. Finally, patients with recurrent malignant gliomas shou ld be encouraged to consider participation in a clinical trial in the hopes that better treatment alternatives will be available for this group of patie nts within the next few years.
Journal Title: Current treatment options in oncology

PUBMED ID: 15477552
DOI: doi.org/10.1212/01.wnl.0000140495.33615.ca
Titolo: How effective is BCNU in recurrent glioblastoma in the modern era? A phase II trial.
Autori: Brandes AA., Tosoni A., Amistà P., Nicolardi L., Grosso D., Berti F. , Ermani M.
Data di Pubblicazione: 2004-10-13
Abstract: The activity of this BCNU regimen is comparable with that reported in the past and with the newest therapies, such as temozolomide. However, BC NU toxicity is high and recovery is slow, thus compromising the administrati on of further drugs in patients with progressive disease.
Journal Title: Neurology

PUBMED ID: 15370616
DOI: doi.org/10.1080/02841860410015271
Titolo: Temozolomide treatment in glioma--experiences in two university hosp itals in Finland.
Autori: Mäenpää HO., Aaltonen K., Mäntylä R., Minn H.
Data di Pubblicazione: 2004-09-17
Abstract: Thirty-two patients with relapsing glioma were treated with temozo lomide in two university hospitals in Finland. One patient (3%) had complete response and 9 (28%) partial response, with 8 patients (25%) showing stable disease. Median progression-free survival for these 18 patients (56%) was 7 months (range 2-11+). The remaining either had progressive disease (25%) or only clinical evaluation (19%). Karnofsky score improved in 34% of patients and decreased in 3%. Symptoms were alleviated in 44% and deteriorated in 9%. Grade 3-4 toxicity was detected in 9% of the patients. Only 4% of the days i n treatment were spent in hospital. An average 1.8 neuroradiological investi gations, 6.9 laboratory visits, and 5.3 visits to the oncologist were made. This study confirms that temozolomide has positive effects on the outcome of often heavily pretreated glioma patients. High drug costs are compensated by prolonged home care and even the possibility to maintain working capacity.
Journal Title: Acta oncologica (Stockholm, Sweden)

PUBMED ID: 15323467
DOI: doi.org/10.3171/foc.2003.15.5.10
Titolo: Stereotactic radiosurgery for hemangiomas and ependymomas of the spi nal cord.
Autori: Ryu SI., Kim DH., Chang SD.
Data di Pubblicazione: 2004-08-25
Abstract: Stereotactic radiosurgery for intramedullary spinal tumors is feas ible and safe in selected cases and may prove to be another therapeutic opti on for these challenging lesions.
Journal Title: Neurosurgical focus

PUBMED ID: 15306839
DOI: doi.org/10.1038/sj.gt.3302336
Titolo: Safety and biodistribution studies of an HSV multigene vector follow ing intracranial delivery to non-human primates.
Autori: Wolfe D., Niranjan A., Trichel A., Wiley C., Ozuer A., Kanal E., Kon dziolka D., Krisky D., Goss J., Deluca N., Murphey-Corb M., Glorioso JC.
Data di Pubblicazione: 2004-08-13
Abstract: Malignant glioma is a fatal human cancer in which surgery, chemo- and radiation therapies are ineffective. Therapeutic gene transfer used in c ombination with current treatment methods may augment their effectiveness wi th improved clinical outcome. We have shown that NUREL-C2, a replication-def ective multigene HSV-based vector, is effective in treating animal models of glioma. Here, we report safety and biodistribution studies of NUREL-C2 using rhesus macaques as a model host. Increasing total doses (1 x 10(7) to 1 x 10 (9) plaque forming units (PFU)) of NUREL-C2 were delivered into the cortex w ith concomitant delivery of ganciclovir (GCV). The animals were evaluated fo r changes in behavior, alterations in blood cell counts and chemistry. The r esults showed that animal behavior was generally unchanged, although the chr onic intermediate dose animal became slightly ataxic on day 12 postinjection , a condition resolved by treatment with aspirin. The blood chemistries were unremarkable for all doses. At 4 days following vector injections, magnetic resonance imaging showed inflammatory changes at sites of vector injections concomitant with HSV-TK and TNFalpha expression. The inflammatory response w as reduced at 14 days, resolving by 1 month postinjection, a time point when transgene expression also became undetectable. Immunohistochemical staining following animal killing showed the presence of a diffuse low-grade gliosis with infiltrating macrophages localized to the injection site, which also re solved by 1 month postinoculation. Viral antigens were not detected and inje cted animals did not develop HSV-neutralizing antibodies. Biodistribution st udies revealed that vector genomes remained at the site of injection and wer e not detected in other tissues including contralateral brain. We concluded that intracranial delivery of 1 x 10(9) PFU NUREL-C2, the highest anticipate d patient dose, was well tolerated and should be suitable for safety testing in humans.
Journal Title: Gene therapy

PUBMED ID: 15277636
DOI: doi.org/10.1212/01.wnl.0000130249.41341.58
Titolo: Chemotherapy as initial treatment in gliomatosis cerebri: results wi th temozolomide.
Autori: Levin N., Gomori JM., Siegal T.
Data di Pubblicazione: 2004-07-28
Abstract: The optimal therapy for gliomatosis cerebri is unclear, and the ra te of response to chemotherapy is not known. Eleven radiotherapy-naive patie nts received a median number of 10 treatment cycles of temozolomide. An obje ctive response was documented in 45%, and the median time to tumor progressi on was 13 months with a progression-free survival of 55% at 12 months. These results indicate that radiotherapy to extensive brain regions can be deferre d until progressive disease is observed.
Journal Title: Neurology

PUBMED ID: 15277619
DOI: doi.org/10.1212/01.wnl.0000129985.39973.e4
Titolo: Initial chemotherapy in gliomatosis cerebri.
Autori: Sanson M., Cartalat-Carel S., Taillibert S., Napolitano M., Djafari L., Cougnard J., Gervais H., Laigle F., Carpentier A., Mokhtari K., Tailland

ier L., Chinot O., Duffau H., Honnorat J., Hoang-Xuan K., Delattre JY., Dela ttre JY.
Data di Pubblicazione: 2004-07-28
Abstract: Initial chemotherapy is useful for some patients with gliomatosis cerebri. Temozolomide is well tolerated and appears to be a valuable alterna tive to procarbazine-CCNU-vincristine, especially for those with slow-growin g, low-grade GC.
Journal Title: Neurology

PUBMED ID: 15241528
DOI: doi.org/10.1007/s00066-004-1221-6
Titolo: Immediate postoperative radiotherapy or "watch and wait" in the mana gement of adult low-grade glioma?
Autori: Kortmann RD., Jeremic B., Weller M., Lutterbach J., Paulsen F., Bamb erg M.
Data di Pubblicazione: 2004-07-09
Abstract: The arguments for immediate postoperative irradiation include: low -grade gliomas respond to radiotherapy; the tumors often display an aggressi ve pathobiological behavior; patients with high risk profile may benefit fro m immediate radiotherapy in terms of progression-free and overall survival; modern focal radiotherapy is far less toxic than feared; radiotherapy might be more effective at diagnosis than at progression. Chemotherapy might be an alternative in immediate postoperative treatment. Its role, however, is uncl ear. The forthcoming prospective trial of the EORTC will address this issue in a randomized setting.
Journal Title: Strahlentherapie und Onkologie : Organ der Deutschen Rontgeng esellschaft ... [et al]

PUBMED ID: 15184628
DOI: doi.org/10.1212/01.wnl.0000127617.89363.84
Titolo: One week on/one week off: a novel active regimen of temozolomide for recurrent glioblastoma.
Autori: Wick W., Steinbach JP., Küker WM., Dichgans J., Bamberg M., Weller M .
Data di Pubblicazione: 2004-06-09
Abstract: Twenty-one patients with recurrent or progressive glioblastoma wer e enrolled in a prospective phase II trial to determine the safety and effic acy of a 1-week on/1-week off regimen of temozolomide administered at 150 mg /m2 on days 1 to 7 and days 15 to 21 of 28-day treatment cycles. Two patient s achieved a partial response (10%), and 17 patients (81%) had stable diseas e. The median progression-free survival was 5 months. The progression-free s urvival at 6 months was 48%.
Journal Title: Neurology

PUBMED ID: 15174520
DOI: doi.org/10.1023/b:neon.0000024744.16031.e9
Titolo: Results of contemporary surgical management of radiation necrosis us ing frameless stereotaxis and intraoperative magnetic resonance imaging.
Autori: McPherson CM., Warnick RE.
Data di Pubblicazione: 2004-06-04
Abstract: In this review, frameless stereotaxis was helpful in guiding the s urgeon; however, IOMRI did not provide any additional benefit for the surgic al treatment of radiation necrosis. Surgical treatment of radiation necrosis was associated with high risks of complication or neurologic deficit. Given the success of medical therapies, including hyperbaric oxygen, we believe th at surgical treatment of radiation necrosis should be reserved for symptomat ic patients in whom medical therapy has failed.

Journal Title: Journal of neuro-oncology

PUBMED ID: 15153843
DOI: doi.org/10.1177/107327480401100307
Titolo: Recent progress in immunotherapy for malignant glioma: treatment str ategies and results from clinical trials.
Autori: Ehtesham M., Black KL., Yu JS.
Data di Pubblicazione: 2004-05-22
Abstract: An effective treatment paradigm for malignant gliomas may eventual ly require a multifaceted approach combining two or more different immunothe rapeutic strategies. Such scenarios may involve the use of local cytokine ge ne therapy to enhance glioma-cell immunogenicity in conjunction with dendrit ic cell-based active vaccination to stimulate systemic tumoricidal T-cell im munity. Given the heterogeneity of this disease process and the potential ri sk of immunoediting out a selected, treatment-refractory tumor cell populati on, the concurrent use of multiple modalities that target disparate tumor ch aracteristics may be of greatest therapeutic relevance.
Journal Title: Cancer control : journal of the Moffitt Cancer Center

PUBMED ID: 15140402
DOI: doi.org/10.1593/neo.03349
Titolo: Pretreatment prediction of brain tumors' response to radiation thera py using high b-value diffusion-weighted MRI.
Autori: Mardor Y., Roth Y., Ochershvilli A., Spiegelmann R., Tichler T., Dan iels D., Maier SE., Nissim O., Ram Z., Baram J., Orenstein A., Pfeffer R.
Data di Pubblicazione: 2004-05-14
Abstract: Diffusion-weighted magnetic resonance imaging (DWMRI) is sensitive to tissues' biophysical characteristics, including apparent diffusion coeffi cients (ADCs) and volume fractions of water in different populations. In thi s work, we evaluate the clinical efficacy of DWMRI and high diffusion-weight ed magnetic resonance imaging (HDWMRI), acquired up to b = 4000 sec/mm(2) to amplify sensitivity to water diffusion properties, in pretreatment predictio n of brain tumors' response to radiotherapy. Twelve patients with 20 brain l esions were studied. Six ring-enhancing lesions were excluded due to their d istinct diffusion characteristics. Conventional and DWMRI were acquired on a 0.5-T MRI. Response to therapy was determined from relative changes in tumor volumes calculated from contrast-enhanced T1-weighted MRI, acquired before a nd a mean of 46 days after beginning therapy. ADCs and a diffusion index, R(D), reflecting tissue viability based on water diffusion were calculated fro m DWMRIs. Pretreatment values of ADC and R(D) were found to correlate signif icantly with later tumor response/nonresponse ($r = 0.76$, $P < .002$ and $r = 0.7$ 7, $P < .001$). This correlation implies that tumors with low pretreatment diff usion values, indicating high viability, will respond better to radiotherapy than tumors with high diffusion values, indicating necrosis. These results d emonstrate the feasibility of using DWMRI for pretreatment prediction of res ponse to therapy in patients with brain tumors undergoing radiotherapy.
Journal Title: Neoplasia (New York, N.Y.)

PUBMED ID: 15139066
DOI: doi.org/10.1002/cncr.20224
Titolo: Phase II study of temozolomide without radiotherapy in newly diagnos ed glioblastoma multiforme in an elderly populations.
Autori: Chinot OL., Barrie M., Frauger E., Dufour H., Figarella-Branger D., Palmari J., Braguer D., Hoang-Xuan K., Moktari K., Peragut JC., Martin PM., Grisoli F.
Data di Pubblicazione: 2004-05-13

Abstract: Temozolomide represents a safe, easily administered, and effective therapeutic approach for elderly patients with newly diagnosed GBM.
Journal Title: Cancer

PUBMED ID: 15093907
DOI: doi.org/10.1016/j.ijrobp.2003.10.040
Titolo: Importance of baseline mini-mental state examination as a prognostic factor for patients with low-grade glioma.
Autori: Brown PD., Buckner JC., O'Fallon JR., Iturria NL., O'Neill BP., Brow n CA., Scheithauer BW., Dinapoli RP., Arusell RM., Curran WJ., Abrams R., Sh aw EG., Shaw EG., Shaw EG.
Data di Pubblicazione: 2004-04-20
Abstract: The presence of an abnormal baseline MMSE score was a strong predi ctor of poorer progression-free and overall survival for patients with a low -grade glioma. The baseline MMSE should be considered in future prognostic s coring systems.
Journal Title: International journal of radiation oncology, biology, physics

PUBMED ID: 15073253
DOI: Mancante
Titolo: PET and SPECT for detection of tumor progression in irradiated low-g rade astrocytoma: a receiver-operating-characteristic analysis.
Autori: Henze M., Mohammed A., Schlemmer HP., Herfarth KK., Hoffner S., Hauf e S., Mier W., Eisenhut M., Debus J., Haberkorn U.
Data di Pubblicazione: 2004-04-10
Abstract: (123)I-IMT SPECT imaging of amino acid transport accurately detect s tumor progression in patients with irradiated LGA. In contrast to (123)I-I MT, (18)F-FDG PET was slightly less accurate for classification, and (99m)Tc -MIBI SPECT was of limited value. Imaging of amino acid transport with (123) I-IMT is a valuable additional tool for the follow-up of LGA, allowing early , noninvasive differentiation of lesions with ambiguous morphology after irr adiation.
Journal Title: Journal of nuclear medicine : official publication, Society o f Nuclear Medicine

PUBMED ID: 15022289
DOI: doi.org/10.1002/cncr.20072
Titolo: Salvage chemotherapy with cyclophosphamide for recurrent, temozolomi de-refractory glioblastoma multiforme.
Autori: Chamberlain MC., Tsao-Wei DD.
Data di Pubblicazione: 2004-03-17
Abstract: CYC exhibited modest efficacy with acceptable toxicity in the curr ent cohort of adult patients with recurrent glioblastoma multiforme, all of whom had previously experienced treatment failure after temozolomide chemoth erapy.
Journal Title: Cancer

PUBMED ID: 15022287
DOI: doi.org/10.1002/cncr.20073
Titolo: Pegylated liposomal doxorubicin-efficacy in patients with recurrent high-grade glioma.
Autori: Hau P., Fabel K., Baumgart U., Rümmele P., Grauer O., Bock A., Dietm aier C., Dietmaier W., Dietrich J., Dudel C., Hübner F., Jauch T., Drechsel E., Kleiter I., Wismeth C., Zellner A., Brawanski A., Steinbrecher A., Marie nhagen J., Bogdahn U.
Data di Pubblicazione: 2004-03-17

Abstract: Pegylated liposomal doxorubicin administered alone or in combinati on with tamoxifen is safe and moderately effective in patients with recurren t high-grade glioma. None of the putative predictors for response that were evaluated proved to be significant in this setting.
Journal Title: Cancer

PUBMED ID: 15015788
DOI: doi.org/10.1023/b:neon.0000013479.64348.69
Titolo: Phase II trial of cisplatin plus temozolomide, in recurrent and prog ressive malignant glioma patients.
Autori: Silvani A., Eoli M., Salmaggi A., Lamperti E., Maccagnano E., Broggi G., Boiardi A.
Data di Pubblicazione: 2004-03-16
Abstract: We report a phase II trial of cisplatinum and temozolomide (TMZ) c ombination in recurrent malignant glioma patients. The DNA repair protein O(6)-alkylguanine-DNA alkyltransferase (AGAT) is important in glioblastoma res istance to alkylating antitumor agents. In vitro, cisplatin (CDDP) decreases MGMT activity in a time- and dose-dependent manner. Thirty-three recurrent m alignant glioma patients (20 GBM-13 AA) were treated at recurrence or progre ssion with a CDDP and TMZ association. On days 1 and 2, iv CDDP (40 mg/sqm) was administered. TMZ (at the dose of 200 mg/sqm) was administered as a sing le oral daily-dose on days 2-6 (starting 24 h after the first CDDP dose), th e cycle was repeated every 4 weeks. All patients had been previously treated with surgery followed by radiotherapy and CDDP + BCNU chemotherapy. The prim ary endpoint of the study was progression free survival at 6 months (PFS-6). Secondary endpoints included radiological response and toxicities. Thirty-th ree patients received a total of 113 courses (median 3 range 1-11). Complete responses were not observed, partial responses were 18.8% with an additional 39.9% of stable disease. For the whole group of patients the PFS at 6 and 12 months was 52% and 15% with a median TTP of 33 weeks. PFS-6 for GBM and Anap lastic astrocytoma (AA) were 35% and 69%, respectively. PFS-12 for GBM and A A were 13.8% and 17.3%, respectively. Median TTP was 21.3 and 39.5 weeks, re spectively. The principal toxic effects of the regimen were: neutropenia (5 WHO grade IV), thrombocytopenia (4 WHO grade IV), nausea and vomiting.
Journal Title: Journal of neuro-oncology

PUBMED ID: 15015785
DOI: doi.org/10.1023/b:neon.0000013472.50749.84
Titolo: The efficacy of stereotactic radiosurgery in the management of intra cranial ependymoma.
Autori: Mansur DB., Drzymala RE., Rich KM., Klein EE., Simpson JR.
Data di Pubblicazione: 2004-03-16
Abstract: SRS is an effective treatment for intracranial ependymoma. Further clinical trials are warranted incorporating radiosurgery as a component of i nitial management in selected ependymoma patients.
Journal Title: Journal of neuro-oncology

PUBMED ID: 14770438
DOI: doi.org/10.1002/cncr.20042
Titolo: Second-line treatment with carboplatin for recurrent or progressive oligodendroglial tumors after PCV (procarbazine, lomustine, and vincristine) chemotherapy: a phase II study.
Autori: Soffietti R., Nobile M., Rudà R., Borgognone M., Costanza A., Laguzz i E., Mutani R.
Data di Pubblicazione: 2004-02-11
Abstract: When administered according to a monthly schedule, carboplatin exh ibited modest activity in adult patients with recurrent or progressive oligo

dendroglioma or oligoastrocytoma who experienced treatment failure after PCV chemotherapy; the current treatment regimen also was associated with severe toxicity. Further improvement of second-line chemotherapy for the patient gr oup examined in the current study is necessary.
Journal Title: Cancer

PUBMED ID: 14745879
DOI: doi.org/10.1002/cncr.11949
Titolo: Temozolomide in the treatment of recurrent malignant glioma.
Autori: Chang SM., Theodosopoulos P., Lamborn K., Malec M., Rabbitt J., Page M., Prados MD.
Data di Pubblicazione: 2004-01-28
Abstract: Temozolomide was well tolerated in patients with recurrent maligna nt glioma and had modest efficacy, even at the time of multiple recurrences.
Journal Title: Cancer

PUBMED ID: 14682377
DOI: doi.org/10.1023/b:neon.0000003588.18644.9c
Titolo: Treatment of progressive or recurrent glioblastoma multiforme in adu lts with herpes simplex virus thymidine kinase gene vector-producer cells fo llowed by intravenous ganciclovir administration: a phase I/II multi-institu tional trial.
Autori: Prados MD., McDermott M., Chang SM., Wilson CB., Fick J., Culver KW. , Van Gilder J., Keles GE., Spence A., Berger M.
Data di Pubblicazione: 2003-12-20
Abstract: To determine the safety and evaluate the efficacy of repeated admi nistration of virus-producing cells (GLI 328) containing the herpes simplex virus thymidine-kinase gene followed by ganciclovir treatment in adults with recurrent glioblastoma multiforme, we conducted a phase I/II multi-instituti onal trial. Eligible patients underwent surgical resection of tumor, followe d by injections of vector producing cells (VPC) into the brain adjacent to t he cavity. An Ommaya reservoir placed after surgery was used to inject a fur ther dose of VPC seven days after surgery, followed seven days later by ganc iclovir. Further gene therapy was given at 28-day intervals for up to a tota l of five cycles. Toxicity and anti-tumor effect were assessed. Of 30 patien ts who enrolled in the study, 16 experienced serious adverse events possibly related to the experimental therapy. Laboratory testing, including polymeras e chain reaction analysis to detect replication-competent retrovirus in peri pheral blood lymphocytes and tissues, as well as co-cultivation bioassays, w ere negative. Before receiving ganciclovir, 37% of the patients showed evide nce of transduced peripheral blood leukocytes, but only 12% showed a persist ence of transduced cells at the end of the first cycle of ganciclovir. Media n survival was 8.4 months. Twenty percent of the patients (n = 6) survived m ore than 12 months from the date of study entry. This treatment modality is feasible and appears to have some evidence of efficacy. Toxicity may be rela ted in part to the method of gene delivery.
Journal Title: Journal of neuro-oncology

PUBMED ID: 14666736
DOI: Mancante
Titolo: Recombinant mutant human tumor necrosis factor-alpha (TNF-SAM2) immu notherapy with ranimustine chemotherapy and concurrent radiation therapy for malignant astrocytomas.
Autori: Fukushima T., Yamamoto M., Oshiro S., Tsugu H., Hirakawa K., Soma G.
Data di Pubblicazione: 2003-12-12
Abstract: These results suggest that combined chemotherapy with mutant TNF-a lpha (TNF-SAM2) in this patient population seems to be safe and tolerable an

d may benefit those with anaplastic astrocytoma. These intriguing clinical o bservations warrant further evaluation to determine whether this approach ca n provide therapeutic benefits and improve survival.
Journal Title: Anticancer research

PUBMED ID: 14630676
DOI: doi.org/10.1093/annonc/mdg494
Titolo: Carboplatin and teniposide as third-line chemotherapy in patients wi th recurrent oligodendroglioma or oligoastrocytoma: a phase II study.
Autori: Brandes AA., Basso U., Vastola F., Tosoni A., Pasetto LM., Jirillo A ., Lonardi S., Paris MK., Koussis H., Monfardini S., Ermani M.
Data di Pubblicazione: 2003-11-25
Abstract: Although the response rate of combined carboplatin and teniposide chemotherapy in heavily pretreated oligodendroglial tumors is moderate, the toxicity is manageable, and delay of progression in responders or stable pat ients may still confer a relevant clinical benefit.
Journal Title: Annals of oncology : official journal of the European Society for Medical Oncology

PUBMED ID: 14630675
DOI: doi.org/10.1093/annonc/mdg502
Titolo: Temozolomide chemotherapy for progressive low-grade glioma: clinical benefits and radiological response.
Autori: Pace A., Vidiri A., Galiè E., Carosi M., Telera S., Cianciulli AM., Canalini P., Giannarelli D., Jandolo B., Carapella CM.
Data di Pubblicazione: 2003-11-25
Abstract: The high response rate of 47% (95% CI 31% to 61%) confirms that TM Z chemotherapy is a valid option in the treatment of progressive LGG. The pr esent preliminary results seem interesting and warrant further evaluation of TMZ clinical activity in a larger series of progressive LGG.
Journal Title: Annals of oncology : official journal of the European Society for Medical Oncology

PUBMED ID: 14630674
DOI: doi.org/10.1093/annonc/mdg371
Titolo: Phase II study of primary temozolomide chemotherapy in patients with WHO grade II gliomas.
Autori: Brada M., Viviers L., Abson C., Hines F., Britton J., Ashley S., Sar dell S., Traish D., Gonsalves A., Wilkins P., Westbury C.
Data di Pubblicazione: 2003-11-25
Abstract: Temozolomide has single-agent activity in patients with WHO grade II cerebral glioma, with modest improvement in quality of life and improveme nt in epilepsy control. On present evidence, temozolomide cannot be consider ed as primary therapy without formal comparison with other treatment modalit ies.
Journal Title: Annals of oncology : official journal of the European Society for Medical Oncology

PUBMED ID: 14558604
DOI: doi.org/10.1023/a:1025689004046
Titolo: Loss of heterozygosity for loci on chromosome arms 1p and 10q in oli godendroglial tumors: relationship to outcome and chemosensitivity.
Autori: Thiessen B., Maguire JA., McNeil K., Huntsman D., Martin MA., Horsma n D.
Data di Pubblicazione: 2003-10-16

Abstract: Oligodendroglial tumors frequently have deletions ofchromosomal lo ci on 1p and 19q. Loss of heterozygosity (LOH) of chromosome 10 may be a neg ative prognostic factor. We reviewed 23 patients with oligodendroglial tumor s, to evaluate the frequency of 1p and 10q LOH and correlate with clinical o utcome. Three loci (D1S402, D1S1172, MCT118) on 1p and 2 loci (D10S520 and D 10S521) on 10q were analyzed for LOH using PCR techniques. Sixteen oligodend rogliomas (6 low grade and 10 anaplastic) and 7 oligoastrocytomas (1 low gra de and 6 anaplastic) were studied. Overall 14/22 (64%) showed 1p LOH and 7/2 3 (30%) showed 10q LOH. Of 7 patients with some response to chemotherapy, al l showed 1p LOH and none had 10q LOH. Of 5 patients with stable or progressi ve disease, 1 had 1p LOH and 2 showed 10q LOH. The presence of 1p LOH was si gnificantly associated with response to chemotherapy (p = 0.02). Median prog ression free survival (PFS) was 31 months for 1p intact patients and 118 mon ths for the 1p LOH group (p = 0.014). Median PFS for 10q LOH patients was 31 and 118 months for patients with intact chromosome 10 (p = 0.016).1p LOH is a predictor of response to chemotherapy and a good prognostic factor. 10q LO H is less common in oligodendroglial tumors but predicts for worse outcome. Molecular genotyping of oligodendroglial tumors is recommended as part of th e standard diagnostic workup.
Journal Title: Journal of neuro-oncology

PUBMED ID: 14509949
DOI: doi.org/10.1007/s00066-003-9104-9
Titolo: Current and future strategies in radiotherapy of childhood low-grade glioma of the brain. Part I: Treatment modalities of radiation therapy.
Autori: Kortmann RD., Timmermann B., Taylor RE., Scarzello G., Plasswilm L., Paulsen F., Jeremic B., Gnekow AK., Dieckmann K., Kay S., Bamberg M.
Data di Pubblicazione: 2003-09-27
Abstract: Radiation therapy is an effective treatment modality in children w ith low-grade glioma regarding tumor control and improvement and/or preserva tion of neurologic function or vision, respectively. More prospective studie s are needed to address the impact of modern radiation therapy technologies (including intensity-modulated radiotherapy) on outcome especially in the ve ry young and to define the role of radiation therapy as a part of a comprehe nsive treatment approach. The forthcoming prospective trial SIOP/GPOH LGG RT 2003 is addressing this issue.
Journal Title: Strahlentherapie und Onkologie : Organ der Deutschen Rontgeng esellschaft ... [et al]

PUBMED ID: 12884791
DOI: Mancante
Titolo: [Therapeutic efficacy and prognostic factors in diffuse astrocytomas].
Autori: Watanabe T., Komine C., Yokoyama T., Yoshino A., Katayama Y.
Data di Pubblicazione: 2003-07-30
Abstract: Diffuse astrocytomas are slowly growing tumors with a relatively l ong overall survival. Considerable controversy exists as to the best therape utic management for patients with such tumors. In the present study, we retr ospectively analyzed a series of 64 patients with WHO grade II astrocytomas of the cerebral hemispheres. Gross total resection and interferon-beta thera py were significantly associated with both longer progression free survival (PFS) and overall survival (OS). Immediate postoperative radiation therapy d id not prolong either the PFS or OS. The presence of promoter hypermethylati on of the O6-methylguanine-DNA methyltransferase (MGMT) gene was an independ ent predictor of a shorter PFS. Our data suggest that radical surgery plus i nterferon-beta therapy may offer the best chance for long survival. Since th e presence of MGMT methylation is a probable indication of an increased sens itivity to alkylating chemotherapeutic agents, determining the methylation s

tatus of MGMT could provide a potential basis for logical therapeutic interv
ention in identifying a subgroup of patients who could be candidates for ear
ly chemotherapy.
Journal Title: No shinkei geka. Neurological surgery

PUBMED ID: 12829152
DOI: doi.org/10.1016/s0360-3016(03)00293-1
Titolo: Gliomatosis cerebri: improved outcome with radiotherapy.
Autori: Perkins GH., Schomer DF., Fuller GN., Allen PK., Maor MH.
Data di Pubblicazione: 2003-06-28
Abstract: RT is effective against gliomatosis cerebri. Patients who are youn
g and have a nonglioblastoma tumor histologic subtype perform more favorably
. In this analysis, no role for chemotherapy, extensive surgery, or whole-br
ain RT was found.
Journal Title: International journal of radiation oncology, biology, physics

PUBMED ID: 12805331
DOI: doi.org/10.1200/JCO.2003.12.097
Titolo: Phase II evaluation of temozolomide and 13-cis-retinoic acid for the
treatment of recurrent and progressive malignant glioma: a North American Br
ain Tumor Consortium study.
Autori: Jaeckle KA., Hess KR., Yung WK., Greenberg H., Fine H., Schiff D., P
ollack IF., Kuhn J., Fink K., Mehta M., Cloughesy T., Nicholas MK., Chang S.
, Prados M., Prados M.
Data di Pubblicazione: 2003-06-14
Abstract: TMZ and cRA were active, exceeding our 20% thresholds for PFS 6 su
ccess, assuming 20% improvement over our previously reported database (gliob
lastoma multiforme: expected, 30%; observed, 32%; anaplastic glioma: expecte
d, 40%; observed, 50%).
Journal Title: Journal of clinical oncology : official journal of the Americ
an Society of Clinical Oncology

PUBMED ID: 12778010
DOI: doi.org/10.1097/00001622-200305000-00002
Titolo: The role of gamma knife radiosurgery in the treatment of primary and
metastatic brain tumors.
Autori: Gerosa M., Nicolato A., Foroni R.
Data di Pubblicazione: 2003-06-05
Abstract: With the widespread diffusion of stereotactic radiosurgical proced
ures, GKR treatments have gained considerable momentum as a major therapeuti
c option for patients harboring primary or metastatic brain tumors. Present
results in high grade gliomas indicate a potential palliative role of this t
echnique. The overall low radiosensitivity of these oncotypes and their infi
ltrative nature-with the resulting problems in properly defining the tumor t
arget-are still a major obstacle to further development of the approach. In
this regard, useful contributions are expected from advances in molecular ne
urobiology and functional neuroimaging as shown by preliminary investigation
s with MR spectroscopy. Surgery maintains a dominant role in the therapeutic
armamentarium for low grade gliomas. However, in unfavorable cases (unresect
able tumors, recurrences), GKR seems to be an effective alternative to conve
ntional radiochemotherapy. In grade 2 astrocytomas and specifically in grade
1 pilocytic forms, short-to-mid-term reported studies have documented encour
aging 70 to 93% local tumor control rates, with minimal cerebral toxicity. F
inally, during the last decade, GKR has become a primary treatment choice fo
r patients harboring small-to-medium-size brain metastases, with reasonable
life expectancy and no impending intracranial hypertension. Focal tumor resp
onses are consistently elevated, even in the most radioresistant oncotypes (

melanoma, renal carcinoma); median and actuarial survival rates are far bett
er than with conventional radiation treatments and are comparable to those o
bserved in accurately selected surgical-radiation series.
Journal Title: Current opinion in oncology

PUBMED ID: 12744471
DOI: doi.org/10.1111/j.1750-3639.2003.tb00017.x
Titolo: Promoter hypermethylation of the DNA repair gene O6-methylguanine-DN
A methyltransferase is an independent predictor of shortened progression fre
e survival in patients with low-grade diffuse astrocytomas.
Autori: Komine C., Watanabe T., Katayama Y., Yoshino A., Yokoyama T., Fukush
ima T.
Data di Pubblicazione: 2003-05-15
Abstract: The O6-methylguanine-DNA methyltransferase (MGMT) plays a major ro
le in repairing DNA damage from alkylating agents. In several human neoplasm
s including low-grade diffuse astrocytomas, promoter hypermethylation of MGM
T has been shown to correlate with an increased frequency of p53 mutation. I
n the present study, we analyzed MGMT promoter methylation by the methylatio
n-specific PCR in 49 newly diagnosed WHO grade II astrocytomas and evaluated
its clinical usefulness. MGMT promoter methylation was found in 21 (43%) of
the 49 tumors. A tight correlation existed between MGMT methylation and p53
protein accumulation (P=0.0424). The presence of MGMT methylation was signif
icantly associated with a shorter progression free survival (PFS) on both un
ivariate analysis (P=0.0014) and multivariate analysis (P=0.0081). It was a
more powerful determinant of the PFS than age, sex, performance status, prol
iferative activity, or p53 expression, and was independent of the extent of
surgery. In terms of the overall survival, MGMT methylation demonstrated a p
rognostic utility in the univariate analysis but not in the multivariate ana
lysis. The present findings indicate that aberrant methylation of the MGMT p
romoter independently augurs for an unfavorable clinical course in patients
with low-grade diffuse astrocytomas. Since the presence of MGMT methylation
is expected to predict an increased sensitivity to alkylating chemotherapeut
ic agents, earlier chemotherapy could serve to improve an unfavorable natura
l history in tumors with MGMT methylation.
Journal Title: Brain pathology (Zurich, Switzerland)

PUBMED ID: 12675529
DOI: doi.org/10.1023/a:1022644031905
Titolo: Quantifying efficacy of chemotherapy of brain tumors with homogeneou
s and heterogeneous drug delivery.
Autori: Swanson KR., Alvord EC., Murray JD.
Data di Pubblicazione: 2003-04-05
Abstract: Gliomas are diffuse and invasive brain tumors with the nefarious a
bility to evade even seemingly draconian treatment measures. Here we introdu
ce a simple mathematical model for drug delivery of chemotherapeutic agents
to treat such a tumor. The model predicts that heterogeneity in drug deliver
y related to variability in vascular density throughout the brain results in
an apparent tumor reduction based on imaging studies despite continual sprea
d beyond the resolution of the imaging modality. We discuss a clinical examp
le for which the model-predicted scenario is relevant. The analysis and resu
lts suggest an explanation for the clinical problem of the long-standing con
founding observation of shrinkage of the lesion in certain areas of the brai
n with continued growth in other areas.
Journal Title: Acta biotheoretica

PUBMED ID: 12587796
DOI: doi.org/10.1023/a:1021204616334

Titolo: Clinicopathological study of seven cases of symptomatic supratentori
al subependymoma.
Autori: Im SH., Paek SH., Choi YL., Chi JG., Kim DG., Jung HW., Cho BK.
Data di Pubblicazione: 2003-02-18
Abstract: Subependymomas are rare, slow-growing tumors, the majority of whic
h are found incidentally at postmortem examination. The authors retrospectiv
ely analyzed seven cases of symptomatic supratentorial subependymomas. Five
were females and two were males, ranging in age at operation of 6-50 years (
median 45). The follow-up period ranged from 1.5 to 8.3 years. Tumors were i
ntraventricularly located as a lobulated mass with cystic changes: four in t
he frontal horn, two in the trigone, and one in the third ventricle. Moderat
e to marked enhancement was noted in two tumors of the trigone and in one tu
mor of the frontal horn on both CT scan and MR imaging. MR spectroscopy of a
recurrent subependymoma demonstrated a higher Cho/Cr ratio of 2.66, compared
with a Cho/Cr ratio (0.48) of a non-recurrent subependymoma. Angiography, wh
ich was performed in four patients, revealed no staining in two and delayed
modest staining in two. Radiosurgery was performed in two patients but was i
neffective. Five patients with gross total tumor resection showed no evidenc
e of tumor recurrence to the last follow-up. The two subtotally resected tri
gonal tumors progressed two years after operation. No histological differenc
e except MIB-1 index was noted between recurrent and non-recurrent cases. In
conclusion, we suggest that subependymoma could show progressive biological
behavior, especially in cases of markedly enhancing, irregularly contoured,
large tumors located in the trigone. For symptomatic supratentorial subepend
ymomas, gross total resection is the treatment of choice and radiation has l
ittle effect on tumor control.
Journal Title: Journal of neuro-oncology

PUBMED ID: 12586801
DOI: doi.org/10.1200/JCO.2003.01.009
Titolo: Phase II trial of temozolomide in patients with progressive low-grad
e glioma.
Autori: Quinn JA., Reardon DA., Friedman AH., Rich JN., Sampson JH., Provenz
ale JM., McLendon RE., Gururangan S., Bigner DD., Herndon JE., Avgeropoulos
N., Finlay J., Tourt-Uhlig S., Affronti ML., Evans B., Stafford-Fox V., Zakn
oen S., Friedman HS.
Data di Pubblicazione: 2003-02-15
Abstract: Initial results indicate that Temodar may be active in the treatme
nt of low-grade glioma, and thus, further evaluation of this agent in the tr
eatment of these tumors is warranted.
Journal Title: Journal of clinical oncology : official journal of the Americ
an Society of Clinical Oncology

PUBMED ID: 12449727
DOI: doi.org/10.1081/cnv-120005910
Titolo: CI-980 for the treatment of recurrent or progressive malignant gliom
as: national central nervous system consortium phase I-II evaluation of CI-9
80.
Autori: Kunschner LJ., Fine H., Hess K., Jaeckle K., Kyritsis AP., Yung WK.
Data di Pubblicazione: 2002-11-27
Abstract: These results fail to demonstrate the significant activity of CI-9
80 against recurrent glioma.
Journal Title: Cancer investigation

PUBMED ID: 12397464
DOI: doi.org/10.1007/s00259-002-0896-0

Titolo: Detection of tumour progression in the follow-up of irradiated low-g
rade astrocytomas: comparison of 3-[123I]iodo-alpha-methyl- L-tyrosine and 9
9mTc-MIBI SPET.
Autori: Henze M., Mohammed A., Schlemmer H., Herfarth KK., Mier W., Eisenhut
M., Debus J., Haberkorn U.
Data di Pubblicazione: 2002-10-25
Abstract: Conventional MRI often fails to distinguish between progressive tu
mour and radiation injury, because both appear as mass lesions with unspecif
ic Gd-DTPA enhancement. Furthermore, the sensitivity of FDG PET for the eval
uation of malignant lesions in the brain is limited owing to high cortical u
ptake. The aim of this study was to assess the potential of alternative SPET
tracers in the same group of patients. 35.2+/-20.1 months after stereotactic
radiotherapy (59.3+/-4.2 Gy) of low-grade astrocytomas (median WHO II), 16 p
atients, presenting 25 Gd-DTPA-enhancing lesions on MRI, were examined by SP
ET. Lesions were classified as progressive tumour (PT, n=17) or non-PT (nPT,
n=8) based on prospective follow-up (clinical examination, MRI, proton-MR sp
ectroscopy) for 25.6+/-6.7 months after SPET. SPET scans were performed 15 a
nd 60 min after injection of 694+/-67 MBq hexakis(2-methoxyisobutylisonitril
e)(99m)Tc(I) (MIBI). 3-[(123)I]iodo-alpha-methyl- L-tyrosine (IMT) SPET was
acquired 15 min after injection of 291+/-58 MBq IMT. Lesion-to-normal tissue
ratios (l/n) for IMT (l/n(IMT)) and MIBI (l/n(MIBI)) were calculated using a
reference region mirrored to the contralateral hemisphere. Using IMT, signif
icantly higher ratios (P<0.001) were found in PT (1.7+/-0.4) than in nPT (1
.1+/-0.1). For MIBI, there was no statistically significant difference (P=0
.206) between PT (3.7+/-2.8) and nPT (1.8+/-1.8). Sensitivities for MIBI and
IMT were 53% and 94%, and specificities 75% and 100%, respectively. Positive
predictive values for MIBI and IMT respectively reached 80% and 100%, and ne
gative predictive values were 46% and 90%. In conclusion, in contrast to MIB
I, IMT showed almost no overlap between the PT and the nPT group. The sensit
ivity, specificity and predictive values of IMT SPET were obviously higher t
han those of MIBI SPET. IMT is considered to be a useful tracer for differen
tiating PT from nPT in the follow-up of irradiated low-grade astrocytomas.
Journal Title: European journal of nuclear medicine and molecular imaging

PUBMED ID: 12209758
DOI: doi.org/10.1002/cncr.10710
Titolo: Evaluation of the efficiency of chemotherapy in in vivo orthotopic m
odels of human glioma cells with and without 1p19q deletions and in C6 rat o
rthotopic allografts serving for the evaluation of surgery combined with che
motherapy.
Autori: Branle F., Lefranc F., Camby I., Jeuken J., Geurts-Moespot A., Spren
ger S., Sweep F., Kiss R., Salmon I.
Data di Pubblicazione: 2002-09-05
Abstract: The in vivo models of gliomas of the central nervous system develo
ped in the current work best mimicked clinical reality. They can be used eit
her to identify new therapies against human gliomas or to optimize existing
therapies.
Journal Title: Cancer

PUBMED ID: 12209682
DOI: doi.org/10.1002/cncr.10826
Titolo: Salvage chemotherapy for recurrent spinal cord ependymona.
Autori: Chamberlain MC.
Data di Pubblicazione: 2002-09-05
Abstract: Chronic oral etoposide appears to be well tolerated, has modest to
xicity, and had apparent activity in the small cohort of adults in the curre
nt study with surgically and medically refractory, recurrent, intradural int
ramedullary SCE.

Journal Title: Cancer

PUBMED ID: 12174942
DOI: Mancante
Titolo: Treatment of recurrent malignant supratentorial astrocytomas with ca rboplatin and etoposide combined with recombinant mutant human tumor necrosi s factor-alpha.
Autori: Yamamoto M., Oshiro S., Tsugu H., Hirakawa K., Ikeda K., Soma G., Fu kushima T.
Data di Pubblicazione: 2002-08-15
Abstract: These results suggest that combined therapy with carboplatin, etop oside and recombinant mutant TNF-alpha in this patient population seems to b e safe and acceptable and may benefit those with recurrent anaplastic astroc ytomas. These intriguing clinical observations warrant a properly stratified randomized trial to determine whether this approach can provide therapeutic benefits and improve survival.
Journal Title: Anticancer research

PUBMED ID: 12125988
DOI: doi.org/10.1023/a:1015788814667
Titolo: Temozolomide as second-line chemotherapy for relapsed gliomas.
Autori: Trent S., Kong A., Short SC., Traish D., Ashley S., Dowe A., Hines F ., Brada M.
Data di Pubblicazione: 2002-07-20
Abstract: In the small cohort of patients with recurrent malignant glioma wh o failed PCV chemotherapy temozolomide demonstrated limited activity as seco nd-line treatment although this remains within the confidence intervals of r esponse seen in patients with glioblastoma.
Journal Title: Journal of neuro-oncology

PUBMED ID: 12057097
DOI: doi.org/10.1007/s11864-001-0073-x
Titolo: Neoplastic meningitis.
Autori: Kim L., Glantz MJ.
Data di Pubblicazione: 2002-06-12
Abstract: Neoplastic meningitis is recognized clinically in 4% to 7% of pati ents with extraneural cancer, but it remains dramatically under-diagnosed. T he frequency of neoplastic meningitis is increasing because of heightened cl inical suspicion, improved neuroimaging techniques, and longer survival in p atients with extraneural cancer Longer survival allows residual tumor cells within central nervous system sanctuary sites time to become symptomatic. Af fected patients may present with cerebral, cranial nerve, or spinal signs an d symptoms, depending on the specific sites of central nervous system (CNS) involvement. Magnetic Resonance Imaging (MRI) seems to be sensitive for dete cting metastatic deposits along the neuraxis. However, metastases at a micro scopic level are below the resolution of MRI scanning. As a result, the stan dard diagnostic test for neoplastic meningitis remains the cytologic identif ication of malignant cells in cerebrospinal fluid (CSF). Although CSF cytolo gy is useful, malignant cells are not detected in as many as one third of pa tients who have compelling clinical or radiographic evidence of neoplastic m eningitis. Novel assays are being tested that may enhance the early identifi cation of malignant cells in CSF. Currently, the diagnosis occurs generally after the onset of neurologic manifestations and heralds a rapidly fatal cou rse for most patients. By the time symptoms appear, most tumors have dissemi nated widely within the CNS, due to cortical irritation, compression of nerv ous system structures, or obstruction of CSF flow. At this stage surgery, cr anial irradiation, and chemotherapy are rarely, if ever, curative. The goals

of treatment are to improve or to stabilize the neurologic status of patient s and to prolong survival. A major problem in treating neoplastic meningitis is that the entire neuraxis must be treated. If only symptomatic areas are t reated, reseeding of the neuraxis with tumor cells will occur. Therefore, in trathecal chemotherapy remains a mainstay of therapy. Currently, four therap eutic agents are available for intrathecal treatment: methotrexate, ara-C, s ustained-release ara-C (DepoCyt; Chiron Therapeutics, San Francisco, CA), an d thiotepa. Unfortunately, intrathecal chemotherapy does not treat bulky dis ease in the subarachnoid space, and often is slow to stabilize progressive n eurologic deficits. For these reasons, radiation therapy to sites of symptom atic disease and sites of bulky disease on imaging studies is recommended. H igh dose intravenous methotrexate may be as effective as intrathecal methotr exate. Alternative approaches (which offer less toxicity, enhanced therapeut ic effect, and prolonged survival) are being investigated.
Journal Title: Current treatment options in oncology

PUBMED ID: 11980998
DOI: doi.org/10.1200/JCO.2002.09.084
Titolo: Phase II trial of carmustine plus O(6)-benzylguanine for patients wi th nitrosourea-resistant recurrent or progressive malignant glioma.
Autori: Quinn JA., Pluda J., Dolan ME., Delaney S., Kaplan R., Rich JN., Fri edman AH., Reardon DA., Sampson JH., Colvin OM., Haglund MM., Pegg AE., Mosc hel RC., McLendon RE., Provenzale JM., Gururangan S., Tourt-Uhlig S., Herndo n JE., Bigner DD., Friedman HS.
Data di Pubblicazione: 2002-05-01
Abstract: These results indicate that O(6)-BG plus BCNU at the dose schedule used in this trial is unsuccessful in producing tumor regression in patients with nitrosourea-resistant malignant glioma, although stable disease was see n in five patients for 6, 12, 12, 12, and 18 weeks. Future use of this appro ach will require strategies to minimize dose-limiting toxicity of BCNU such as regional delivery or hematopoietic stem-cell protection.
Journal Title: Journal of clinical oncology : official journal of the Americ an Society of Clinical Oncology

PUBMED ID: 11949830
DOI: doi.org/10.1023/a:1014498225405
Titolo: Intra-arterial carboplatin and intravenous etoposide for the treatme nt of recurrent and progressive non-GBM gliomas.
Autori: Newton HB., Slivka MA., Stevens CL., Bourekas EC., Christoforidis GA ., Baujan MA., Chakeres DW.
Data di Pubblicazione: 2002-04-13
Abstract: Recurrent and progressive non-GBM gliomas are a diverse group of b rain tumors that often respond poorly to adjuvant chemotherapy treatment. Re gional intra-arterial (IA) administration of chemotherapy may result in incr eased tumor uptake of drug, with improvement in response rates and time to p rogression (TTP). Twenty-five patients with recurrent or progressive non-GBM gliomas were treated with IA carboplatin (200 mg/m2/d) and intravenous (IV) etoposide (100 mg/m2/d) for 2 days every 4 weeks. Patients ranged in age fro m 22 to 68 years (mean 37.8). All but one patient had received standard irra diation, and eight patients had attempted prior chemotherapy. Five of 25 pat ients had objective responses (20%), while another 15 patients had stable di sease (60%), receiving a total of 318 IA treatment procedures. There was one complete response (4.0%), three partial responses (12.0%), one minor respons e (4.0%), 15 stable diseases (60.0%), and five progressive diseases (20.0%). The median TTP was 24.2 weeks overall and 32 weeks in responders. Overall me dian survival was 34.2 weeks. Therapy was well tolerated, with mainly hemato logic toxicity. Two patients had embolic complications. Although these are p

reliminary results, IA carboplatin and IV etoposide have modest activity aga inst recurrent and progressive non-GBM gliomas and warrants further study.
Journal Title: Journal of neuro-oncology

PUBMED ID: 11916502
DOI: Mancante
Titolo: A phase II trial of thymidine and carboplatin for recurrent malignan t glioma: a North American Brain Tumor Consortium Study.
Autori: Robins HI., Chang SM., Prados MD., Yung WK., Hess K., Schiff D., Gre enberg H., Fink K., Nicolas K., Kuhn JG., Cloughesy T., Junck L., Mehta M.
Data di Pubblicazione: 2002-03-28
Abstract: This phase II study in recurrent high-grade glioma evaluated the r esponse rate, toxicities, and time to treatment failure of high-dose carbopl atin modulated by a 24-h infusion of thymidine (75 g/m(2)). The trial was ba sed on preclinical data and a prior phase I study (J. Clin. Oncol. 17, 2922 -2931, 1999); a phase II recurrent high-grade glioma study was initiated in July of 1998. Thymidine was given over 24 h; carboplatin was given over 20 m in at hour 20 of the thymidine infusion. The starting dose of carboplatin ha d a value of 7 for the area under the curve (AUC), with allowance for dose e scalation of 1 AUC unit per cycle if grade 2 toxicity was observed. Treatmen t cycles were repeated every 4 weeks. Accrual as of September 1999 was 45 pa tients [4 were unevaluable]: 76% with glioblastoma multiforme (GBM), 20% wit h anaplastic oligodendroglioma, 2% with mixed type, and 2% with anaplastic a strocytoma. Most patients had prior chemotherapy (78%). As observed in the e arlier phase I study (in which carboplatin pharmacokinetics were unaltered b y thymidine or antiseizure medications), thymidine was myeloprotective, resu lting in a minimal need for dose reduction for patients having a >2 grade to xicity (in only 4% of the courses of treatment). Of 101 total courses, the n umber of courses (at the AUCs) was 3 (5), 4 (6), 58 (7), 20 (8), 11 (9), and 5 (10). Grade 3 nonhematologic toxicities included headache (4%), altered co nsciousness (3%), fatigue (1%), and nausea (3%). Responses included 2 partia l (1 oligodendroglioma, 1 GBM; 5%); 3 minor (1 anaplastic astrocytoma, 2 GBM ; 7.3%); 6 stable disease (14.6%); and 30 progressive disease (73.2%). For G BM patients, median survival was 23 weeks (with a 95% confidence interval of 20 to 50 weeks), and progression-free survival was 8 weeks (with a 95% confi dence interval of 7-16 weeks). These results in GBM were comparable to other phase II GBM trials and thus do not represent a therapeutic advance in the t reatment of GBM. Taken collectively, however, results are consistent with co ntinued investigation of thymidine in combination with chemotherapeutic agen ts for high-grade glioma and other malignant diseases. The significant myelo protection afforded by thymidine may have particular relevance to polychemot herapeutic regimens.
Journal Title: Neuro-oncology

PUBMED ID: 11914886
DOI: doi.org/10.1007/s00259-001-0717-x
Titolo: Local injection of the 90Y-labelled peptidic vector DOTATOC to contr ol gliomas of WHO grades II and III: an extended pilot study.
Autori: Schumacher T., Hofer S., Eichhorn K., Wasner M., Zimmerer S., Freita g P., Probst A., Gratzl O., Reubi JC., Maecke R., Mueller-Brand J., Merlo A.
Data di Pubblicazione: 2002-03-27
Abstract: We have previously presented preliminary observations on targeting somatostatin receptor-positive malignant gliomas of all grades by local inje ction of the radiolabelled peptidic vector 90Y-DOTATOC. We now report on our more thorough clinical experience with this novel compound, focussing on low -grade and anaplastic gliomas. Small peptidic vectors have the potential to target invisible infiltrative disease within normal surrounding brain tissue , thereby opening a window of opportunity for early intervention. Five progr

essive gliomas of WHO grades II and III and five extensively debulked low-gr
ade gliomas were treated with varying fractions of 90Y-DOTATOC. The vectors
were locally injected into the resection cavity or into solid tumour. The ac
tivity per single injection ranged from 555 to 1,875 MBq, and the cumulative
activity from 555 to 7,030 MBq, according to tumour volumes and eloquence of
the affected brain area, yielding dose estimates from 76+/-15 to 312+/-62 Gy
. Response was assessed by the clinical status, by steroid dependence and, e
very 4-6 months, by magnetic resonance imaging and fluorine-18 fluorodeoxygl
ucose positron emission tomography. In the five progressive gliomas, lasting
responses were obtained for at least 13-45 months without the need for stero
ids. Radiopeptide brachytherapy had been the only modality applied to counte
r tumour progression. Interestingly, we observed the slow transformation of
a solid, primarily inoperable anaplastic astrocytoma into a resectable multi
-cystic lesion 2 years after radiopeptide brachytherapy. Based on these obse
rvations, we also assessed the feasibility of local radiotherapy following e
xtensive debulking, which was well tolerated. Targeted beta-particle irradia
tion based on diffusible small peptidic vectors appears to be a promising mo
dality for the treatment of malignant gliomas.
Journal Title: European journal of nuclear medicine and molecular imaging

PUBMED ID: 11870183
DOI: doi.org/10.1200/JCO.2002.20.5.1383
Titolo: Phase II trial of temozolomide plus the matrix metalloproteinase inh
ibitor, marimastat, in recurrent and progressive glioblastoma multiforme.
Autori: Groves MD., Puduvalli VK., Hess KR., Jaeckle KA., Peterson P., Yung
WK., Levin VA.
Data di Pubblicazione: 2002-03-01
Abstract: The combination of TMZ and MRM resulted in a PFS at 6 months that
exceeded the literature target by 29%. This drug combination met phase II st
udy criteria; further study in recurrent patients with GBM might be warrante
d. Further study of therapy-induced joint pain is necessary.
Journal Title: Journal of clinical oncology : official journal of the Americ
an Society of Clinical Oncology

PUBMED ID: 11846927
DOI: doi.org/10.1097/00006123-200112000-00002
Titolo: Age and radiation response in glioblastoma multiforme.
Autori: Barker FG., Chang SM., Larson DA., Sneed PK., Wara WM., Wilson CB.,
Prados MD.
Data di Pubblicazione: 2002-02-16
Abstract: Older GM patients are less likely to have good responses to postop
erative external beam radiation therapy. Karnofsky Performance Scale score b
efore radiation treatment and extent of surgical resection are additional pr
edictors of radiographically assessed radiation response in GM.
Journal Title: Neurosurgery

PUBMED ID: 11804278
DOI: doi.org/10.1023/a:1012982303419
Titolo: Gliomatosis cerebri: post-mortem molecular and immunohistochemical a
nalyses in a case treated with thalidomide.
Autori: Mawrin C., Aumann V., Kirches E., Schneider-Stock R., Scherlach C.,
Vogel S., Mittler U., Dietzmann K., Krause G., Weis S.
Data di Pubblicazione: 2002-01-24
Abstract: Gliomatosis cerebri (GC) is a rare tumor of the central nervous sy
stem (CNS) characterized by widespread diffuse infiltration of the brain and
spinal cord by neoplastic glial cells. We report the case of a 17-year-old b
oy with a bioptically diagnosed fibrillary astrocytoma. The administration o

f thalidomide, which was suggested to be beneficial in the treatment of huma n cancers, had no substantial clinical effect on our patient. Autopsy studie s revealed a diffuse infiltration of the frontal and temporal lobes of the r ight hemisphere, brainstem, and the leptomeninges covering the whole spinal cord by an astrocytic tumor, which showed features both of low-grade astrocy toma and glioblastoma multiforme. No mutations in the p53 and PTEN tumor sup pressor genes were found; immunoreactivities for p53, PTEN, and EGFR could n ot be detected.
Journal Title: Journal of neuro-oncology

PUBMED ID: 11772431
DOI: doi.org/10.1093/neuonc/4.1.39
Titolo: A phase II study of extended low-dose temozolomide in recurrent mali gnant gliomas.
Autori: Khan RB., Raizer JJ., Malkin MG., Bazylewicz KA., Abrey LE.
Data di Pubblicazione: 2002-01-05
Abstract: Temozolomide is an effective agent in the treatment of recurrent m alignant gliomas. The standard dosage is 150-200 mg/m2 per day for 5 days in a 28-day cycle. A prior phase I study established a chronic daily temozolomi de dose that significantly increased the total dose administered and suggest ed a superior response rate. In a prospective phase II trial, we treated 35 patients with recurrent malignant gliomas with temozolomide 75 mg/m2 per day for 42 consecutive days in a 70-day cycle. Median age was 55 years (range, 2 7-73 years) and median Karnofsky performance score was 70 (range, 60-90). Tw enty-eight (79%) patients had glioblastoma multiforme, 3 (9%) anaplastic ast rocytoma, 2 (6%) anaplastic oligodendroglioma, and 2 (6%) anaplastic oligoas trocytoma. All but one had prior radiotherapy, and 27 had prior chemotherapy . There were 2 partial (anaplastic astrocytoma) and 3 minor (glioblastoma mu ltiforme) radiographic responses; 17 patients had progressive disease at the end of the first cycle. In 55 cycles of temozolomide, there were 8 episodes of asymptomatic drug-related grade 3 toxicity: 6 lymphopenia, 1 neutropenia, and 1 thrombocytopenia. Median progression-free survival and overall surviva l were 2.5 and 8.7 months (2.3 and 7.7 months in glioblastoma multiforme pat ients). At 6 months, progression-free survival and overall survival rates we re 27% and 67% (19% and 60% in glioblastoma multiforme). Quality of life sco res did not change significantly during treatment. We conclude that the exte nded low-dose schedule of temozolomide is well tolerated in heavily pre-trea ted patients; however, our results do not support an improved rate of respon se or survival.
Journal Title: Neuro-oncology

PUBMED ID: 11694768
DOI: doi.org/10.1159/000055122
Titolo: Therapeutic anti-angiogenesis for malignant brain tumors.
Autori: Kirsch M., Santarius T., Black PM., Schackert G.
Data di Pubblicazione: 2001-11-06
Abstract: Malignant brain tumors, especially malignant gliomas, have a poor prognosis, a fact which has remained unchanged over the last decades despite the employment of multimodal therapeutic approaches. Malignant gliomas are a mong the most vascularized tumors known and the amount of vascularization ha s been correlated to their prognosis. Since tumor growth is dependent on con comitant vascularization, recent experimental studies have focused on the us e of anti-angiogenic molecules as a novel strategy in brain tumor therapy. A ngiogenesis inhibitors target at proliferating endothelial cells and suppres s the formation of a sufficient vascular bed. Inhibitors such as TNP-470, su ramin and angiostatin have shown their therapeutic potential in experimental studies. In a clinical setting, they could be applied for the treatment of m ultiple tumors or postsurgically as an adjuvant therapy to prevent recurrenc

e. This article discusses presently available anti-angiogenic agents, emphas izing on substances already in clinical trials.
Journal Title: Onkologie

PUBMED ID: 11584894
DOI: doi.org/10.1093/neuonc/3.4.246
Titolo: Phase I study of Gliadel wafers plus temozolomide in adults with rec urrent supratentorial high-grade gliomas.
Autori: Gururangan S., Cokgor L., Rich JN., Edwards S., Affronti ML., Quinn JA., Herndon JE., Provenzale JM., McLendon RE., Tourt-Uhlig S., Sampson JH., Stafford-Fox V., Zaknoen S., Early M., Friedman AH., Friedman HS.
Data di Pubblicazione: 2001-10-05
Abstract: Both Gliadel wafers [1,3-bis(2-chloroethyl)-1-nitrosourea] and tem ozolomide (TEMO) have been shown in independent studies to prolong survival of patients with recurrent malignant glioma following surgery and radiothera py. On the basis of preclinical evidence of synergism between Gliadel wafers and TEMO, a phase I study was designed to evaluate the toxicity of combining these 2 agents in the treatment of patients with recurrent supratentorial ma lignant glioma. All patients had surgical resection of the tumor at relapse, and up to 8 Gliadel (3.85%) wafers were placed in the surgical cavity follow ing resection. Two weeks after surgery, TEMO was given orally daily for 5 da ys. Cohorts of 3 patients received TEMO at daily doses of 100 mg/m2, 150 mg/ m2, and 200 mg/m2, respectively. Patients were assessed for toxicity 4 weeks after start of the first course of TEMO. Contrast-enhanced MRI of the brain was used to assesstumor response after the first cycle of TEMO. Patients wit h stable disease or response after the first cycle of TEMO were allowed to c ontinue treatment at the same dose every 4 weeks for 12 cycles or until dise ase progression or unacceptable toxicity. Ten patients with a median age of 47 years (range, 22-66 years) were enrolled in this study. There were 7 pati ents with glioblastoma multiforme and 3 patients with anaplastic astrocytoma . Three patients were treated with TEMO at the first dose level of 100 mg/m2 , 4 at the second dose level of 150 mg/m2, and 3 at the third dose level of 200 mg/m2. The 10 patients received a median of 3 cycles (range, 1-12 cycles) of TEMO following placement of Gliadel wafers. The treatment was well tole rated, with only 1 patient suffering grade III thrombocytopenia at the highe st dose level. Two patients at each dose level had no evidence of disease pr ogression after treatment. Four patients suffered progressive disease on the rapy. Our study demonstrates that TEMO can be given safely after placement o f Gliadel (3.85%) wafers. The recommended dosage for TEMO for a phase II stu dy of this combination is 200 mg/m2 per day for 5 days.
Journal Title: Neuro-oncology

PUBMED ID: 11485231
DOI: doi.org/10.1007/pl00012393
Titolo: Intracerebral ganglioglioma: clinical and radiological study of elev en surgically treated cases with follow-up.
Autori: Ildan F., Tuna M., Göçer IA., Erman T., Cetinalp E.
Data di Pubblicazione: 2001-08-04
Abstract: We conclude that ganglioglioma is a distinct histological phenomen on with mildly predictable clinical symptoms (seizures), mildly characterist ic radiological features, and long-term survival after surgical resection wi thout the need of adjuvant treatment such as radiotherapy.
Journal Title: Neurosurgical review

PUBMED ID: 11463801
DOI: doi.org/10.1093/jjco/hye059

Titolo: Radiotherapy combined with nimustine hydrochloride and etoposide for malignant gliomas: results of a pilot study.
Autori: Tanaka M., Shibui S., Nomura K., Nakanishi Y.
Data di Pubblicazione: 2001-07-21
Abstract: RT with ACNU and etoposide are feasible and well tolerated and the treatment results were comparable to the best results reported in the litera ture.
Journal Title: Japanese journal of clinical oncology

PUBMED ID: 11432894
DOI: doi.org/10.1200/JCO.2001.19.13.3260
Titolo: Toxicity, efficacy, and pharmacology of suramin in adults with recur rent high-grade gliomas.
Autori: Grossman SA., Phuphanich S., Lesser G., Rozental J., Grochow LB., Fi sher J., Piantadosi S., Piantadosi S.
Data di Pubblicazione: 2001-07-04
Abstract: This study demonstrates that suramin is well tolerated by patients with recurrent high-grade gliomas and may have efficacy in this disease. Its pharmacology seems unaffected by anticonvulsants. As a result of this data, suramin and radiation are now being administered concurrently to patients wi th newly diagnosed glioblastoma multiforme, with survival as the primary out come.
Journal Title: Journal of clinical oncology : official journal of the Americ an Society of Clinical Oncology

PUBMED ID: 11394532
DOI: doi.org/10.1089/02724570152057634
Titolo: Phase I clinical evaluation of a neutralizing monoclonal antibody ag ainst epidermal growth factor receptor in advanced brain tumor patients: pre liminary study.
Autori: Crombet T., Torres O., Rodríguez V., Menéndez A., Stevenson A., Ramo s M., Torres F., Figueredo R., Veitía I., Iznaga N., Pérez R., Lage A.
Data di Pubblicazione: 2001-06-08
Abstract: High levels of growth factors and their receptors have been demons trated in human tumors. Gliomas and meningiomas are characterized by overexp ression of epidermal growth factor receptor (EGF-R). Ior egf/r3, is a neutra lizing murine monoclonal antibody (MAb) against EGF-R, and was generated at the Cuban Institute of Oncology. The antibody recognizes EGF-R with high aff inity, inhibiting tyrosine kinase activation. A clinical trial was conducted in brain tumor patients to evaluate toxicity, immunogenicity, and clinical b enefit of escalating doses of the antibody. Nine patients with histologicall y confirmed gliomas or meningiomas, who had active or recurrent disease afte r receiving conventional treatment, received four intravenous doses of ior e gf/r3. Total dosages ranged from 160 to 480 mg. As inclusion criteria, radio immunoscintigraphy with the same MAb labeled with 99mTechnetium (99mTc) was performed. Immune response against the murine antibody was also evaluated. A fter four doses of ior egf/r3 MAb, no significant toxicity was found, except in one patient who developed a grade 4 allergic adverse event. This reaction was probably related with previous sensitization to the same MAb and the dev elopment of human anti-mouse antibodies (HAMA) response. Despite no major ob jective antitumor responses, eight patients had stable disease on the 6-mont h evaluation, and two patients remain alive after four years of MAb therapy.
Journal Title: Hybridoma

PUBMED ID: 11355088
DOI: Mancante

Titolo: Diagnosis and results of treatment with radiation therapy in gliomat
osis cerebri patient: case report.
Autori: Sun LM., Lui CC., Huang SC., Lu K., Wang CJ.
Data di Pubblicazione: 2001-05-18
Abstract: Gliomatosis cerebri (GC) is a rare disease loosely defined as a di
ffusely infiltrating glioma involving extensive areas of the brain. The prog
nosis is poor and no definite treatment has proven effective for GC. Little
information exists regarding the role of radiation therapy (RT) for GC, but
some researchers have suggested that it is a good choice of treatment from t
heir limited experience. In this report, we present a case with imaging and
histological diagnosis of GC and demonstrate the treatment results of RT. Th
e patient was a 39-year-old woman with progressive symptoms of dizziness, un
steady gait, headache, vomiting, and consciousness disturbance for 6 months.
She received a series of radiographic examinations and surgical intervention
s for diagnosis. The definite diagnosis of GC was made by a combination of m
agnetic resonance imaging (MRI) findings and histological examinations. Fort
y Gray (Gy) of whole brain irradiation followed by 14 Gy reduced-field boost
s were given to her. The MRI, following treatment, showed regressive changes
, and clinical symptoms were slightly improved. The patient survived 19 mont
hs after the diagnosis, which is longer than the average survival time of pa
tients without treatment.
Journal Title: Chang Gung medical journal

PUBMED ID: 11349883
DOI: doi.org/10.1023/a:1006441104260
Titolo: Intra-arterial cisplatin plus oral etoposide for the treatment of re
current malignant glioma: a phase II study.
Autori: Ashby LS., Shapiro WR.
Data di Pubblicazione: 2001-05-15
Abstract: Twenty-five adults with recurrent malignant glioma were enrolled i
nto a phase II clinical study. All patients had undergone surgical resection
and had failed radiotherapy and first-line treatment with nitrosourea-based
chemotherapy; five had failed second-line chemotherapy. Our objective was to
test the efficacy of combining intra-arterially (i.a.) infused cisplatin and
oral etoposide. Using conventional angiographic technique to access anterior
/posterior cerebral circulation, cisplatin 60 mg/m2 was administered by i.a.
infusion on day 1 of treatment. Oral etoposide 50 mg/m2/day was given days 1
-21, with a 7 day rest interval between courses. Response to treatment was e
valuated in 20 patients. Two patients with anaplastic astrocytoma had partia
l responses (PR) and six patients experienced stable disease (SD) for an ove
rall response rate (PR +/- SD) of 40%. The median time to disease progressio
n (MTP) following treatment for the responder subgroup was 18 weeks. The med
ian survival time from treatment (MST) for the responders (n = 8) and non-re
sponders (n = 12) was 56.5 weeks and 11 weeks, respectively. Combined i.a. c
isplatin and oral etoposide was well-tolerated, but produced an objective re
sponse in only a minority of patients. Those considered responders (PR + SD)
experienced significant survival advantage when compared to the non-responde
rs. Nonetheless, i.a. delivery of chemotherapy is an expensive and technolog
ically burdensome treatment for most patients to access, requiring proximity
to a major center with neuro-oncological and neuroradiological clinical serv
ices. This is of special concern for patients suffering recurrent disease wi
th progressive neurological symptoms at a time in their course when quality
of life must be safeguarded and palliation of symptoms should be the therape
utic goal. Despite the efforts of previous investigators to use this combina
tion of agents to treat recurrent malignant glioma, we cannot recommend the
use of i.a. chemotherapy for salvage treatment of this disease.
Journal Title: Journal of neuro-oncology

PUBMED ID: 11349879
DOI: doi.org/10.1023/a:1006414804835
Titolo: Thalidomide as an anti-angiogenic agent in relapsed gliomas.
Autori: Short SC., Traish D., Dowe A., Hines F., Gore M., Brada M.
Data di Pubblicazione: 2001-05-15
Abstract: The efficacy of thalidomide in terms of response in recurrent glio mas is low, with a partial response rate of only 6%. Future studies should i nvestigate thalidomide in combination with other agents and at an earlier st age of disease. Methods to assess anti-angiogenic properties such as changes in tumour vasculature could be employed as initial surrogate end-points in t he investigation of efficacy.
Journal Title: Journal of neuro-oncology

PUBMED ID: 11212902
DOI: doi.org/10.1023/a:1006496831144
Titolo: Treosulfan chemotherapy for recurrent malignant glioma.
Autori: Schmidt F., Wick W., Herrlinger U., Dichgans J., Weller M.
Data di Pubblicazione: 2001-02-24
Abstract: Treosulfan is a bifunctional alkylating prodrug with activity agai nst various solid tumors. To improve the outcome for patients with recurrent malignant glioma, we assessed the efficacy of intravenous treosulfan (6-10 g /m2 4-weekly) as salvage therapy for patients with recurrent or progressive glioblastoma (GB, n = 14) or anaplastic astrocytoma (AA, n = 2). All patient s had prior involved-field radiotherapy and adjuvant nitrosourea-based chemo therapy. A total of 56 cycles were administered. Tumor responses were assess ed radiologically and clinically prior to each cycle. All patients were asse ssable for toxicity, response and survival. There were no complete or partia l responses (CR, PR). Two patients progressed after the first cycle, 14 pati ents had initially stable disease (SD). Median progression-free survival was 3.25 months for the GB patients. Five patients were progression-free at 6 mo nths (30%), including the 2 AA patients. The 2 AA patients are stable at 22 months. Myelosuppression was the dose-limiting toxicity in this cohort of ni trosourea-pretreated patients. Treosulfan has modest activity in patients wi th recurrent malignant glioma. Further evaluation of treosulfan in chemonaiv e malignant glioma patients is warranted.
Journal Title: Journal of neuro-oncology

PUBMED ID: 11149242
DOI: doi.org/10.1080/01616412.2000.11740756
Titolo: Analysis of the proliferative potential of tumor cells after stereot actic radiosurgery for recurrent astrocytic tumors.
Autori: Kodera T., Kubota T., Kabuto M., Nakagawa T., Takeuchi H., Arishima H., Sato K., Kobayashi H., Kitabayashi M., Hirose S.
Data di Pubblicazione: 2001-01-10
Abstract: We analyzed the effectiveness of stereotactic radiosurgery (SRS) f or recurrent astrocytic tumors histologically. Five patients were followed b y pathological examination after radiosurgery treatment of recurrent astrocy tic tumors. Histological diagnoses at the time of the last operation before SRS were Daumas-Duport grade II in two patients and grade IV (glioblastoma) in three patients. No histological diagnoses at the time of SRS were identif ied in any patients. Contrast enhanced lesions enlarged gradually on magneti c resonance (MR) images after SRS, and local control by SRS was judged as pr ogressive disease radiologically in all patients. Four of five patients rece ived re-operation after SRS, and the other patient died without re-operation and underwent post-mortem examination. After SRS, Ki-67 labeling indices (LI s) of recurrent astrocytomas initially diagnosed as grade II were 2.6% and 1 .1%. These LIs were relatively lower than those of the control group of pati ents with recurrent grade II astrocytomas that were not treated by SRS. Ki-6

7 LIs of three glioblastomas after SRS were 23.5%, 18.6%, and 17.8%. These L Is were significantly lower than those before SRS (2.3%, 4.5%, and 0.9%). In the autopsy case, there was a significant difference between the LI of tumor cells in the radiosurgically treated region (0.9%) and that in the untreated region (29.2%). These results suggest that the proliferative potential of ma lignant astrocytic tumors in the radiosurgically treated area is reduced aft er SRS, and that radiological enlargement of enhanced lesions on MR images i s due to propagation of the residual tumor cells that were not covered by ra diosurgical target volume or to radiation necrosis. SRS may be a useful ther apeutic tool in multidisciplinary treatment of malignant gliomas.
Journal Title: Neurological research

PUBMED ID: 11130015
DOI: doi.org/10.1080/028418600750063839
Titolo: Radiation therapy approach in gliomatosis cerebri--case reports and literature review.
Autori: Horst E., Micke O., Romppainen ML., Pyhtinen J., Paulus W., Schäfer U., Rübe C., Willich N.
Data di Pubblicazione: 2000-12-29
Abstract: Gliomatosis cerebri is defined as a remarkably diffuse glioma, cha racterized by widespread infiltration of the central nervous system. Clinico pathologic characteristics and imaging findings have been published but vali d classification remains controversial. Few reports exist regarding therapeu tic options in gliomatosis cerebri. Here we review data on 17 patients treat ed with radiation therapy extracted from the literature, in which we focus o ur attention on available details of irradiation and clinical outcome and pr esent the results of three additional patients treated at our two institutio ns. Radiologic-pathologic correlation in gliomatosis cerebri indicates that tumor delineation should be based on T2-weighted MRI. Radiation therapy in g liomatosis cerebri is associated with a temporary improvement in or stabiliz ation of clinical symptoms in the majority of cases. Duration of improvement was > or = 6 months in 50% of treated patients. Survival from onset of sympt oms was 23.8 months (range 8-42). Considerable variation in the natural cour se of the disease precludes conclusions regarding the impact of radiation th erapy on survival.
Journal Title: Acta oncologica (Stockholm, Sweden)

PUBMED ID: 10987250
DOI: doi.org/10.1053/hupa.2000.9086
Titolo: Quantitative telomerase expression in glioblastomas shows regional v ariation and down-regulation with therapy but no correlation with patient ou tcome.
Autori: Kleinschmidt-Demasters BK., Evans LC., Bobak JB., Lopez-Uribe D., Ho pper D., Shroyer AL., Shroyer KR.
Data di Pubblicazione: 2000-09-15
Abstract: Despite the nearly ubiquitous expression of telomerase in almost a ll types of malignant human tumors, studies have shown widely varying positi vity in the highest-grade glioma, the glioblastomas (GBMs), ranging from 26% to 100% of tumors analyzed. We have previously shown significant variability in positive versus negative telomerase expression from region to region with in the same GBM. In this study, we hypothesized that application of new quan titative methodology would extend our previous observations and identify whe ther there is heterogeneity in levels of protein expression even within area s positive for telomerase in high-grade gliomas. Finally, we sought to corre late quantitative telomerase expression with patient outcome and therapeutic response. Quantitative analysis was achieved by polymerase chain-based TRAP assay with phosphorimager analysis and compared with clinical information ob tained from 19 patients, most with primary, untreated GBMs. Results showed u

p to 3-fold variability in telomerase levels across multiple regional sample s from the same patient, as well as between patients. In 5 of 6 patients wit h recurrent tumors who had received intervening radiation therapy or chemoth erapy, telomerase was downregulated in the second, post-therapy sample. Thes e data provide in vivo corroboration of recent in vitro experiments showing telomerase downregulation after radiation therapy or chemotherapy treatment of cell lines. Our finding of variability in levels of telomerase expression in GBMs parallels the known heterogeneity of these tumors for histologic fea tures and cell growth-related factors. Statistical analysis showed no relati onship between TRAP score and either time to clinical progression or time to death.
Journal Title: Human pathology

PUBMED ID: 10955504
DOI: doi.org/10.1111/j.1740-8261.2000.tb02091.x
Titolo: Primary irradiation of canine intracranial masses.
Autori: Spugnini EP., Thrall DE., Price GS., Sharp NJ., Munana K., Page RL.
Data di Pubblicazione: 2000-08-24
Abstract: Twenty-nine dogs received primary radiation therapy for intracrani al lesions and clinical signs suggestive of neoplasia. Presumptive diagnosis and tumor categorization was based on computed tomographic or magnetic reson ance images. Meningioma was the most likely tumor type in 22 dogs and glioma or choroid plexus tumors were tentatively identified in 4 and 3 dogs, respec tively. Cobalt-60 radiation was delivered in 3 Gy fractions on a daily, Mond ay-through-Friday basis for a total dose of 48 Gy (16 fractions) in 28 dogs; one dog received 54 Gy. Two of 29 dogs died during treatment of signs sugges tive of progressive tumor growth but were included in the overall evaluation of response to treatment. Median overall survival was 250 days (range 21-804). Mild acute radiation effects on normal tissue developed and did not influ ence outcome in any dog. Late radiation effects could not be evaluated in th is study. No significant predictive indicators were identified from the clin ical or imaging data. Radiation therapy is superior to medical treatment of brain tumors in dogs with steroids, is useful for tumors that are not curren tly operable and may be preferable to surgical resection in dogs if the mass appears infiltrative. However, 22/29 (76%) dogs died of recurrent progressiv e neuropathy suggestive of tumor regrowth or progression. Thus, alternative methods for delivery of radiation to dogs with brain tumors or novel combina tions of therapy should continue to undergo evaluation.
Journal Title: Veterinary radiology & ultrasound : the official journal of t he American College of Veterinary Radiology and the International Veterinary Radiology Association

PUBMED ID: 10933931
DOI: doi.org/10.1006/mthe.2000.0030
Titolo: Phase I study of adenoviral delivery of the HSV-tk gene and ganciclo vir administration in patients with current malignant brain tumors.
Autori: Trask TW., Trask RP., Aguilar-Cordova E., Shine HD., Wyde PR., Goodm an JC., Hamilton WJ., Rojas-Martinez A., Chen SH., Woo SL., Grossman RG.
Data di Pubblicazione: 2000-08-10
Abstract: Between December 1996 and September 1998, 13 patients with advance d recurrent malignant brain tumors (9 with glioblastoma multiforme, 1 with g liosarcoma, and 3 with anaplastic astrocytoma) were treated with a single in tratumoral injection of 2 x 10(9), 2 x 10(10), 2 x 10(11), or 2 x 10(12) vec tor particles (VP) of a replication-defective adenoviral vector bearing the herpes simplex virus thymidine kinase gene driven by the Rous sarcoma virus promoter (Adv.RSVtk), followed by ganciclovir (GCV) treatment. The VP to inf ectious unit ratio was 20:1. Our primary objective was to determine the safe ty of this treatment. Injection of Adv.RSVtk in doses <==2 x 10(11) VP, foll

owed by GCV, was safely tolerated. Patients treated with the highest dose, 2 x 10(12) VP, exhibited central nervous system toxicity with confusion, hyponatremia, and seizures. One patient is living and stable 29.2 months after treatment. Two patients survived >25 months before succumbing to tumor progression. Ten patients died within 10 months of treatment, 9 from tumor progression and 1 with sepsis and endocarditis. Neuropathologic examination of postmortem tissue demonstrated cavitation at the injection site, intratumoral foci of coagulative necrosis, and variable infiltration of the residual tumor with macrophages and lymphocytes.
Journal Title: Molecular therapy : the journal of the American Society of Gene Therapy

PUBMED ID: 10871815
DOI: doi.org/10.1007/BF02796204
Titolo: Phase II study of temozolomide in patients with relapsing high grade glioma and poor performance status.
Autori: Janinis J., Efstathiou E., Panopoulos C., Samantas E., Aravantinos G., Christodoulou C., Skarlos D.
Data di Pubblicazione: 2000-06-29
Abstract: Temozolomide (SCHS2.365), an oral alkylating agent which penetrates the blood-brain barrier, evolved as an alternative to dacarbazine. The aim of this study was to evaluate the efficacy and safety of temozolomide in terms of overall survival, progression-free survival, clinical benefit and health related quality of life in symptomatic patients with relapsing malignant glioma and a poor performance status. Eleven patients were enrolled in the study. The median age was 44.6 years. Patients were treated with temozolomide per os at a dose of 150-200 mg/m2 daily for 5 consecutive days. Each cycle was repeated every 28 days. The median number of courses given per patient was 3.5. Nine patients were assessable for response. All patients were evaluable for toxicity. Based on radiographic findings 4 patients had stable disease (2 patients after a total of 16 cycles, and 2 patients after a total of 10 cycles). Four patients had progressive disease after 2 to 4 cycles. Of these 3 patients demonstrated a clinical benefit and one patient died after 3 cycles of treatment. Six patients had a significant clinical benefit even after 2 cycles of treatment with improvement of their neurological and performance status. Hematologic toxicity Gr II-III occurred in 3/9 patients. Nonhematologic toxicity consisted of Gr I nausea, and vomiting. In conclusion temozolomide appears to be a useful alternative for patients with relapsing malignant glioma after radiation and surgery and a poor performance status with little or no toxicity and considerable clinical benefit.
Journal Title: Medical oncology (Northwood, London, England)

PUBMED ID: 10778730
DOI: doi.org/10.1023/a:1006293606710
Titolo: Pilot study of local autologous tumor infiltrating lymphocytes for the treatment of recurrent malignant gliomas.
Autori: Quattrocchi KB., Miller CH., Cush S., Bernard SA., Dull ST., Smith M., Gudeman S., Varia MA.
Data di Pubblicazione: 2000-04-25
Abstract: A prospective pilot study was performed in order to assess the safety of treating recurrent malignant gliomas (MGs) with locally infused autologous tumor infiltrating lymphocytes (TILs) and recombinant interleukin-2 (rIL-2). Six patients were entered between June 27, 1994 and June 2, 1995 and followed until July 1, 1998. At surgery an Ommaya reservoir was placed for later infusion of TILs and rIL-2. Following surgery, autologous TILs were expanded in vitro in the presence of rIL-2 and infused on treatment days 1 and 14, with concurrent rIL-2 infusions performed three times each week for one month. Following completion of immunotherapy all patients were offered chemo

therapy. Phenotypic analysis demonstrated TILs to be T-lymphocytes (87-99% CD3+). Of these, 4 of 6 cases (67%) phenotyped as cytotoxic/suppressor T-lymphocytes (CD8+) and 2 of 6 cases (33%) phenotyped as helper/inducer T-lymphocytes (CD4+). TILs demonstrated limited selective cytotoxicity, with dose dependent cytotoxicity against autologous tumor, allogenic tumor and long term MG cell lines. There were no significant (Grade 3 or 4) complications. One patient developed transient low grade fevers, and 2 developed asymptomatic hydrocephalus. All patients developed transient and asymptomatic cerebral swelling, noted on the immediate post-treatment imaging studies. At three and six month follow-up, 3 patients responded with partial response, 2 demonstrated stable disease and 1 patient progressed. At long term follow-up, 1 patient had a complete response (45 month follow-up), 2 had a partial response (48 and 47 month follow-up) and 3 patients expired as a result of progressive disease (at 12, 12 and 18 months following immunotherapy). A relationship between subsequent chemotherapy or extent of resection to outcome was not apparent but could not be excluded. This pilot study demonstrated that locally infused autologous TILs and rIL-2 could be delivered without serious toxicity. Further studies are indicated to determine the safety and long term efficacy of TIL immunotherapy.
Journal Title: Journal of neuro-oncology

PUBMED ID: 10769645
DOI: Mancante
Titolo: Hydroxyurea and trimidox enhance the radiation effect in human pancreatic adenocarcinoma cells.
Autori: Leyden D., Ahmed N., Hassan HT.
Data di Pubblicazione: 2000-04-19
Abstract: The present study demonstrates the superiority of hydroxyurea at non-cytotoxic doses compared to the other two recent RR inhibitors: gemcitabine and trimidox in radio-sensitising human pancreatic cancer cells. Hydroxyurea combined with radiation has significantly improved progression-free survival of advanced cervical cancer and glioblastoma patients and showed clinical benefit in combination with other chemotherapy drugs in advanced pancreatic cancer. The present results suggest the clinical use of hydroxyurea as a radiosensitiser in both pre- and post-operative chemo-radiotherapy in pancreatic cancer patients. Given the demonstrated potent radio-sensitising effect of hydroxyurea at non-cytotoxic doses when administered before or immediately after radiation and its low clinical toxicity, it should be feasible to administer hydroxyurea both before and after radiation in pancreatic cancer patients.
Journal Title: Anticancer research

PUBMED ID: 10738082
DOI: doi.org/10.1016/s0167-8140(00)00149-3
Titolo: Radiation therapy of optico-hypothalamic gliomas (OHG)--radiographic response, vision and late toxicity.
Autori: Grabenbauer GG., Schuchardt U., Buchfelder M., Rödel CM., Gusek G., Marx M., Doerr HG., Fahlbusch R., Huk WJ., Wenzel D., Sauer R.
Data di Pubblicazione: 2000-03-30
Abstract: Postoperative RT with a total dose above 45 Gy should be considered as standard treatment in OHG with documented progression. Close radiographic monitoring and lifelong yearly evaluation for the need of possible hormone replacement are strongly recommended.
Journal Title: Radiotherapy and oncology : journal of the European Society for Therapeutic Radiology and Oncology

PUBMED ID: 10619500

DOI: doi.org/10.1023/a:1006399804896
Titolo: Treatment of meningeal gliomatosis.
Autori: Pradat PF., Hoang-Xuan K., Cornu P., Mokhtari K., Martin-Duverneuil N., Poisson M., Delattre JY.
Data di Pubblicazione: 2000-01-05
Abstract: To evaluate whether vigorous treatment is beneficial for patients with meningeal gliomatosis (MG) we reviewed the case records of 20 consecutive patients treated for a symptomatic MG in our center. All received systemic or intrathecal chemotherapy and six received additional cranial or spinal radiotherapy. Six patients (30%) achieved a partial response (one low-grade astrocytoma, two anaplastic astrocytomas, one anaplastic oligodendroglioma and two glioblastomas). In these cases, clinical improvement was associated with radiological improvement on CT scan or MRI in five and with a major cerebrospinal fluid improvement in three. Three patients (15%) were stable for 3 months or more and 11 (55%) had progressive disease. Median survival was longer for the responding patients (10 months) than for the other patients (2 months). This study suggests that some patients with MG may benefit from a treatment combining radiotherapy to symptomatic areas and chemotherapy with agents that cross the blood-brain barrier or are delivered directly into the CSF.
Journal Title: Journal of neuro-oncology

PUBMED ID: 10576660
DOI: doi.org/10.1038/sj.bjc.6690802
Titolo: Phase I dose-escalation and pharmacokinetic study of temozolomide (SCH 52365) for refractory or relapsing malignancies.
Autori: Brada M., Judson I., Beale P., Moore S., Reidenberg P., Statkevich P., Dugan M., Batra V., Cutler D.
Data di Pubblicazione: 1999-11-27
Abstract: Temozolomide, an oral cytotoxic agent with approximately 100% bioavailability after one administration, has demonstrated schedule-dependent clinical activity against highly resistant cancers. Thirty patients with minimal prior chemotherapy were enrolled in this phase I trial to characterize the drug's safety, pharmacokinetics and anti-tumour activity, as well as to assess how food affects oral bioavailability. To determine dose-limiting toxicities (DLT) and the maximum tolerated dose (MTD), temozolomide 100-250 mg m(-2) was administered once daily for 5 days every 28 days. The DLT was thrombocytopenia, and the MTD was 200 mg m(-2) day(-1). Subsequently, patients received the MTD to study how food affects the oral bioavailability of temozolomide. When given orally once daily for 5 days, temozolomide was well tolerated and produced a non-cumulative, transient myelosuppression. The most common non-haematological toxicities were mild to moderate nausea and vomiting. Clinical activity was observed against several advanced cancers, including malignant glioma and metastatic melanoma. Temozolomide demonstrated linear and reproducible pharmacokinetics and was rapidly absorbed (mean Tmax approximately 1 h) and eliminated (mean t1/2 = 1.8 h). Food produced a slight reduction (9%) in absorption of temozolomide. Temozolomide 200 mg m(-2) day(-1) for 5 days, every 28 days, is recommended for phase II studies.
Journal Title: British journal of cancer

PUBMED ID: 10404133
DOI: doi.org/10.1002/(sici)1096-9098(199907)71:3<167::aid-jso6>3.0.co;2-v
Titolo: Carboplatin and etoposide for recurrent malignant glioma following surgical and radiotherapy failure: A clinical study conducted at the Northern Israel Oncology Center.
Autori: Stein ME., Kuten A., Drumea K., Goldsher D., Tzuk-Shina Z.
Data di Pubblicazione: 1999-07-15

Abstract: This phase II regimen proved to be ineffective in recurrent malign ant glioma. Further studies incorporating innovative drug regimens and sched ules are warranted. J. Surg. Oncol., 1999;71:167-170.
Journal Title: Journal of surgical oncology

PUBMED ID: 10069350
DOI: doi.org/10.4065/74.2.137
Titolo: Phase II study of antineoplastons A10 (NSC 648539) and AS2-1 (NSC 62 0261) in patients with recurrent glioma.
Autori: Buckner JC., Malkin MG., Reed E., Cascino TL., Reid JM., Ames MM., T ong WP., Lim S., Figg WD.
Data di Pubblicazione: 1999-03-09
Abstract: Although we could not confirm any tumor regression in patients in this study, the small sample size precludes definitive conclusions about tre atment efficacy. Antineoplaston-related toxicity was acceptable in most pati ents with appropriate dose modification, although severe neurocortical toxic ity may occur. Steady-state plasma concentrations of phenylacetate with use of A10 and AS2-1 were similar to those reported with use of similar doses of phenylacetate alone.
Journal Title: Mayo Clinic proceedings

PUBMED ID: 9989521
DOI: doi.org/10.1016/s0360-3016(98)00370-8
Titolo: Concurrent twice-a-week docetaxel and radiotherapy: a dose escalatio n trial with immunological toxicity evaluation.
Autori: Koukourakis MI., Giatromanolaki A., Schiza S., Kakolyris S., Georgou lias V.
Data di Pubblicazione: 1999-02-16
Abstract: Docetaxel radiochemotherapy is a promising therapeutic approach fo r locally advanced cancer. The recommended dose of docetaxel for chest and p elvic cancer patients is 15 mg/m2 twice a week. Patients with brain tumors c an be safely treated with higher doses of docetaxel (23 mg/m2 twice a week) without toxicity. The severe immunologic toxicity observed suggests that gra nulocyte-macrophage colony-stimulating factor (GM-CSF) and immunoglobulin ad ministration may be important in the efficacy and tolerance of taxane-based radiochemotherapy. Randomized trials are required to assess whether the effi cacy of docetaxel radiochemotherapy depends on the frequency of docetaxel ad ministration during radiation treatment.
Journal Title: International journal of radiation oncology, biology, physics

PUBMED ID: 9861650
DOI: doi.org/10.1007/s001170050441
Titolo: [Brain stem glioma].
Autori: Wietelmann D., Schumacher M., Muendel J.
Data di Pubblicazione: 1998-12-23
Abstract: Brain-stem gliomas occur mainly in childhood and are localized in the mesencephalon, pons and medulla oblongata. Diagnosis is a domain of MRI, requiring T2, T1 and KM. CT shows hemorrhage and calcification well. The cri teria are the primary site, size, tumor growth, brain-stem enlargement, deli neation, intralesional structure, exophytic components and enhancement. Seco ndary criteria are herniation, hydrocephalus and liquorgenic seeding. In CT glioma are hypodense, in MRI hyperintense in T2 and hypointense in T1. Enhan cement is seen in 25-60% and does not allow differentiation of tumor vs nont umor or gradings. Factors influencing poor outcome are high grade, a short h istory, cranial nerve involvement, severe brain-stem enlargement, pontine si te, diffuse growth and recurrency. The 5-year-survival rate is 30% (after ra diation: focal tumors 85%, diffuse 20%). Most frequent are symptoms of brain

pressure, cerebellum, cranial nerves and pyramidal tract. There is no agreem ent on whether biopsy is necessary or not. A diagnosis of tumor is highly su ggestive if classical MRI findings fit the clinical history.
Journal Title: Der Radiologe

PUBMED ID: 9810441
DOI: doi.org/10.1007/s007010050176
Titolo: Gliomatosis cerebri: clinical features, treatment, and prognosis.
Autori: Kim DG., Yang HJ., Park IA., Chi JG., Jung HW., Han DH., Choi KS., C ho BK.
Data di Pubblicazione: 1998-11-12
Abstract: To clarify clinical features and to elucidate prognostic factors a nd prognosis, the authors retrospectively analyzed 16 cases of gliomatosis c erebri treated at Seoul National University Hospital between January 1988 an d December 1995. Age at diagnosis ranged from 19 to 62 (median 34) years and male to female ratio was 10:6. Most presented with headache or seizure, and the mean duration of symptoms was 12.8 months. A poorly defined diffuse high signal intensity lesion, extending in T2-weighted images for two lobes or mo re, was the characteristic magnetic resonance (MR) image finding. On postcon trast T1-weighted MR imaging, focal enhancement of the lesion was detected i n five cases. All patients underwent histological confirmation by craniotomy (9 cases) or stereotactic biopsy (7 cases). Histologically, all patients had compatible findings of gliomatosis cerebri which are the widespread infiltra tion of neoplastic glial cells with minimal destruction of pre-existing stru ctures. After histological diagnosis, external radiation therapy was begun e xcept in one case, who declined this treatment. Fourteen patients completed the whole procedure and received the planned dose (mean 5780 cGy). Median su rvival time after diagnosis was 38.4 months. In univariate analysis, the Ki-67 labelling index (> 1) showed significant correlation with the length of s urvival (p = 0.006). It is suggested that 1) gliomatosis cerebri can be diag nosed by a combination of MR imaging findings and histological examination; 2) histological diagnosis and external radiation therapy might be a good tre atment modality; 3) the Ki-67 labelling index correlates significantly with survival time.
Journal Title: Acta neurochirurgica

PUBMED ID: 9802850
DOI: doi.org/10.1097/00006123-199811000-00035
Titolo: PCV chemotherapy for recurrent oligodendrogliomas and oligoastrocyto mas.
Autori: Soffietti R., Rudà R., Bradac GB., Schiffer D.
Data di Pubblicazione: 1998-11-05
Abstract: These results suggest that chemotherapy with PCV is effective in t he treatment of recurrent low-grade oligodendrogliomas and oligoastrocytomas .
Journal Title: Neurosurgery

PUBMED ID: 9740547
DOI: doi.org/10.1023/a:1006043332368
Titolo: A phase II study of temozolomide in advanced untreated pancreatic ca ncer.
Autori: Moore MJ., Feld R., Hedley D., Oza A., Siu LL.
Data di Pubblicazione: 1998-09-18
Abstract: Temozolomide (SCH 52365) is an imidazotetrazine derivative which e xhibits broad spectrum activity against murine tumors and is structurally re lated to dacarbazine (DTIC). Temozolomide cytotoxicity is schedule dependent in vivo with a daily x 5 schedule showing the highest activity. Oral temozol

omide is rapidly and completely absorbed with minimal interpatient and intra patient variability in pharmacokinetics. Clinical studies have demonstrated activity against melanoma and glioma. The present study examined the activit y of oral temozolomide against patients with pancreatic cancer. Patients wit h advanced pancreatic adenocarcinoma previously untreated with chemotherapy received temozolomide 200 mg/m2/day once daily orally for 5 days with cycles repeated every 28 days. There were 16 patients entered on study with 15 eval uable for response and toxicity. There were no responses seen in 15 evaluabl e patients with 14 manifesting progressive disease within 2 months of starti ng therapy. Toxicity was primarily hematological with 3 patients experiencin g > or = grade 3 neutropenia and thrombocytopenia respectively. Other toxici ties were relatively modest. In conclusion, temozolomide in the once daily x 5 schedule is inactive against adenocarcinoma of the pancreas.
Journal Title: Investigational new drugs

PUBMED ID: 9667273
DOI: doi.org/10.1200/JCO.1998.16.7.2522
Titolo: Methylphenidate therapy improves cognition, mood, and function of br ain tumor patients.
Autori: Meyers CA., Weitzner MA., Valentine AD., Levin VA.
Data di Pubblicazione: 1998-07-17
Abstract: This study demonstrated improved patient function in the setting o f a progressive neurologic illness. Methylphenidate should be more widely co nsidered as adjuvant brain tumor therapy.
Journal Title: Journal of clinical oncology : official journal of the Americ an Society of Clinical Oncology

PUBMED ID: 9626222
DOI: doi.org/10.1200/JCO.1998.16.6.2202
Titolo: Iodine-131-labeled antitenascin monoclonal antibody 81C6 treatment o f patients with recurrent malignant gliomas: phase I trial results.
Autori: Bigner DD., Brown MT., Friedman AH., Coleman RE., Akabani G., Friedm an HS., Thorstad WL., McLendon RE., Bigner SH., Zhao XG., Pegram CN., Wikstr and CJ., Herndon JE., Vick NA., Paleologos N., Cokgor I., Provenzale JM., Za lutsky MR.
Data di Pubblicazione: 1998-06-17
Abstract: The MTD for administration of 131I-labeled 81C6 into the SCRCs of previously irradiated patients with recurrent primary or metastatic brain tu mors was 100 mCi. The dose-limiting toxicity was neurologic toxicity. We are encouraged by the minimal toxicity and survival in this phase I trial. Radio labeled mAbs may improve the current therapy for brain tumor patients.
Journal Title: Journal of clinical oncology : official journal of the Americ an Society of Clinical Oncology

PUBMED ID: 9619354
DOI: doi.org/10.1097/00001622-199805000-00004
Titolo: Advances in brain tumor chemosensitivity.
Autori: Balmaceda C.
Data di Pubblicazione: 1998-06-10
Abstract: Despite advances in surgery and radiation, most malignant central nervous system tumours recur. Chemotherapy has assumed an important role in treatment, particularly for responsive tumors such as primary central nervou s system lymphoma and oligodendrogliomas. The design of sound chemotherapeut ic trials for brain tumors requires an understanding of drug resistance. Dru g sensitivity may be improved in a variety of ways: through the use of agent s at higher than conventional doses or in new treatment schedules, through t he use of localized resistance to modulators, and even through genetic manip

ulation of malignant cells. As treatment with chemotherapy for central nervo us system tumors becomes more successful, new measurements of tumor response may need to be developed to replace or complement standard criteria.
Journal Title: Current opinion in oncology

PUBMED ID: 9584959
DOI: doi.org/10.3109/13550289809114522
Titolo: Management of malignant glioma: role of surgery in relation to multi modality therapy.
Autori: Black P.
Data di Pubblicazione: 1998-05-19
Abstract: The goals of surgery for malignant glioma are to establish a histo logical diagnosis and to achieve mechanical cytoreduction to reduce intracra nial pressure (ICP) and possibly alter tumor kinetics. There is controversy concerning the question whether the glioma is a focal or diffuse process; it appears that there may be variability between the two extremes in individual cases. The question of the value of surgery has also been controversial. Rev iew of the literature suggests that both early and long-term postoperative o utcome after radical surgical resection are better than the results of eithe r partial resection or simple biopsy, in terms of neurological status and du ration of survival. Similarly, reoperation for recurrence of glioma offers r easonable extension of quality survival. Despite the desirability of extensi ve cytoreductive surgery for malignant gliomas, the presence of viable infil trative cells beyond the margins of the resection necessitate that surgery b e a part of an aggressive multimodality therapeutic approach. Adjunctive mea sures to control the infiltrative component include newer forms of radiother apy (such as stereotaxic radiosurgery) and newer delivery techniques for che motherapy (agents impregnated in biodegradable polymers implanted in the tum or bed after surgical resection), and possibly immunotherapy and gene therap y as they may become feasible in the future. The strategy for management of malignant glioma thus consists of a combination of extensive surgical resect ion to reduce the accessible tumor burden, followed in rapid sequence by mea sures to control the infiltrative portion of the tumor. It is recommended th at these measures be offered 'up front' rather than delaying treatment until there is clinical or radiographic evidence of tumor recurrence.
Journal Title: Journal of neurovirology

PUBMED ID: 9538158
DOI: doi.org/10.3892/or.5.3.597
Titolo: Quick response of advanced cancer to chemoradiation therapy with ant ineoplastons.
Autori: Tsuda H., Sata M., Kumabe T., Hara H., Eriguchi N., Sugita Y., Nagam atsu H.
Data di Pubblicazione: 1998-05-09
Abstract: Antineoplastons A10 and AS2-1 exhibit growth inhibition of cancer cells by diverse modes of action. We observed antitumor responses within 2-3 weeks of a combination treatment of chemoradiation therapy and antineoplasto ns A10 and AS2-1 in phase I clinical study being conducted in Kurume Univers ity Hospital. We reviewed 3 clinical cases of advanced cancer (multiple meta static lung cancer, thalamic glioma and primary lung cancer) in which we bel ieved antineoplaston A10 and AS2-1 may be contributing to the rapid antitumo r response. The possible use of this combination for induction therapy in ad vanced cancer is discussed.
Journal Title: Oncology reports

PUBMED ID: 9549488
DOI: doi.org/10.1093/brain/121.1.59

Titolo: A study of medial pallidotomy for Parkinson's disease: clinical outc ome, MRI location and complications.
Autori: Samuel M., Caputo E., Brooks DJ., Schrag A., Scaravilli T., Branston NM., Rothwell JC., Marsden CD., Thomas DG., Lees AJ., Quinn NP.
Data di Pubblicazione: 1998-04-29
Abstract: We have studied the effects of unilateral ventral medial pallidoto my in 26 patients with medically intractable Parkinson's disease with marked drug-induced dyskinesias. Preoperatively, all patients were assessed during one 5-day admission according to the Core Assessment Programme for Intracere bral Transplantation (CAPIT) protocol, including rating in the 'practically defined off' and 'best on' states before and during a single-dose levodopa c hallenge. Motor performance was assessed with subset categories of the Unifi ed Parkinson's Disease Rating Scale (UPDRS), timed motor tests and a standar d dyskinesia rating scale. Pallidotomy was performed under stereotaxic CT gu idance with intra-operative extracellular microelectrode recording made from the basal ganglia. All patients were re-assessed 3 months postoperatively an d a subgroup (n = 9) have so far also been re-assessed after 1 year. Pre- an d postoperative performance scores were compared in order to determine which categories of performance improved postoperatively. Significance was accepte d at P < 0.005 in order to take into account the multiple number of comparis ons performed. Patient medication was compared pre- and postoperatively and the morbidity associated with surgery was also recorded. The most significan t improvement postoperatively was the diminution of 'on' dyskinesias contral aterally (67%, P = 0.0001); however, ipsilateral (45%, P = 0.0006) and axial (50%, P = 0.0008) dyskinesias also improved. Contralateral to pallidotomy, t he median 'off' motor UPDRS score improved by 27% (P = 0.001) and a signific ant improvement was also observed in contralateral rigidity by 25% (P = 0.00 1). There were trends towards improvement in contralateral tremor (33%, P = 0.016) and bradykinesia (24%, P = 0.013) scores. Ipsilateral rigidity improv ed by 22% (P = 0.005), but other ipsilateral motor scores did not alter sign ificantly. The 'off' gait/postural instability score and 'off' walking time showed marginally significant improvements by 7% (P = 0.007) and 29% (P = 0. 014), respectively. On medication, no significant postoperative improvements in parkinsonism were detected. Anti-parkinsonian medication increased by 11% postoperatively. In the subgroup who were available for assessment 1 year po stoperatively, responses were generally maintained. Two (7.7%) of the 26 pat ients had fatal complications (one cerebral haemorrhage and one haemorrhagic infarct) directly related to surgery. Among the remaining 24 patients, four (15.4% of the total 26) had major complications (two persisting and two tran sient). Ten patients (38.5%) had minor complications. The majority of the co mplications (major and minor) occurred in the earlier operated patients and the complication rate subsequently declined with increasing operative experi ence. The remaining 10 patients (38.5%) had no significant side-effects. One of these 10 patients died from an incidental malignant glioma 6 months posto peratively. These findings confirm that levodopa-induced dyskinesias are dra matically reduced following ventral medial pallidotomy and constitute the pr incipal indication for pallidotomy. Improvements in underlying parkinsonism were of smaller magnitude. Pallidotomy may also offer some patients an oppor tunity to increase antiparkinsonian medication. Patient selection for medial pallidotomy should, therefore, be based largely on anticipated improvements in levodopa-induced dyskinesias, but this must be balanced against the assoc iated morbidity and mortality.
Journal Title: Brain : a journal of neurology

PUBMED ID: 9531367
DOI: doi.org/10.1016/s0360-3016(97)00891-2
Titolo: Boron neutron-capture therapy (BNCT) for glioblastoma multiforme (GB M) using the epithermal neutron beam at the Brookhaven National Laboratory.

Autori: Chadha M., Capala J., Coderre JA., Elowitz EH., Iwai J., Joel DD., L iu HB., Wielopolski L., Chanana AD.
Data di Pubblicazione: 1998-04-08
Abstract: It is feasible to safely deliver a single fraction of BPA-based BN CT. At the dose prescribed, the patients did not experience any morbidity. T o further evaluate the therapeutic efficacy of BNCT, a dose-escalation study delivering a minimum target volume dose of 17 Gy-Eq is in progress.
Journal Title: International journal of radiation oncology, biology, physics

PUBMED ID: 9524096
DOI: doi.org/10.1023/a:1005826323652
Titolo: High dose oral tamoxifen and subcutaneous interferon alpha-2a for re current glioma.
Autori: Chang SM., Barker FG., Huhn SL., Nicholas MK., Page M., Rabbitt J., Prados MD.
Data di Pubblicazione: 1998-04-02
Abstract: Chemotherapeutic regimens in present use for recurrent glioma have substantial toxicity. Activity against recurrent gliomas has been reported f or both tamoxifen and interferon alpha, agents that have more acceptable tox icity profiles and that can be administered in an outpatient setting. We tes ted the efficacy and toxicity of the combination of high-dose tamoxifen and interferon alpha in adults with recurrent glioma in a phase II trial. Eligib le patients had radiographically measurable recurrent gliomas of any grade a fter initial radiation therapy. Interferon-alpha [6 x 10(6) U subcutaneously three times per week] and tamoxifen (240 mg/m2/day orally) were administered continuously. Treatment response was assessed at 6 week intervals using clin ical and radiographic criteria. Eighteen patients (11 males and 7 females) w ere enrolled. Median age was 41 years (range 23-61 years). All patients had gliomas that progressed after radiation therapy and nitrosourea chemotherapy . The histologic diagnosis of the original tumor was glioblastoma multiforme in 8 patients, anaplastic astrocytoma in 5 patients, astrocytoma in 4 patien ts and mixed malignant glioma in 1 patient. Reversible moderate to severe ne urological toxicity manifested by dizziness and unsteady gait was seen at ta moxifen doses of 240 mg/m2/day. Although the initial tamoxifen dose was redu ced to 120 mg/m2/day, moderate neurotoxicity was noted at this dose as well and the trial was closed early. The combination of oral tamoxifen (120 to 24 0 mg/m2/day) and subcutaneous interferon-alpha [6 x 10(6) U three times per week] was associated with significant neurotoxicity in this group of recurre nt glioma patients, resulting in early study closure. Of 16 evaluable patien ts, 12 had progressive disease after one cycle of treatment, 3 had stable di sease, and there was one minor response. Gradual dose escalation may be requ ired if similar patients are to be treated with high dose tamoxifen in conju nction with interferon.
Journal Title: Journal of neuro-oncology

PUBMED ID: 9498252
DOI: doi.org/10.1007/s001170050314
Titolo: [Profile of ambulatory radiosurgery with the gamma knife system. 2: Report of clinical experiences].
Autori: Wowra B., Horstmann GA., Cibis R., Czempiel H.
Data di Pubblicazione: 1998-03-14
Abstract: Gamma Knife radiosurgery (GKRS) was applied in 500 consecutive tre atments for 445 patients within 2 years. Indications were arterio-venous mal formations (93 patients), schwannomas of cranial nerves (75 patients), menin giomas (79 patients; 73 of the tumors involving the skull base), pituitary a denomas (40 patients), craniopharyngiomas (13 cases), gliomas (13 cases), ra re indications (12 cases), and brain metastases (126 patients). In arterio-v enous malformations two complications were observed whereas two other patien

ts underwent surgery due to intracranial hemorrhage in the latent period aft er GKRS. In all cases follow-up with MRI showed evidence of an active oblite ration process. Out of 24 patients with a follow-up over 1 year, angiography revealed complete obliteration in 9 patients so far. A partial obliteration was evidenced by MRI in 15 cases. In benign tumors (meningiomas and vestibul ar schwannomas) tumor control rates of 88% and 89% were achieved, respective ly. Treatment related side effects were mild and rare; no facial palsy occur ed after primary Gamma Knife treatment. GKRS was particularly effective in i noperable skull base meningiomas. Cerebral metastases were controlled in 89. 5% by a single Gamma Knife treatment. The mean survival period was 11.8 mont hs. In patients receiving a single Gamma Knife treatment the mean survival t ime was 9.1 months. For patients undergoing multiple (up to 5) sessions of G KRS (because of new tumors) the mean survival period was 17.2 months. MRI sh owed evidence of adverse radiation reactions in 10/124 patients (8.1%) which were symptomatic in 3 patients (0.8%). The results obtained in patients with cerebral metastases emphasize that GKRS alone is as effective as the combine d treatment of these lesions by surgery and fractionated radiotherapy. Our r esults demonstrated an attractively high therapeutic gain factor of Gamma Kn ife treatment in key indications of radiosurgery.
Journal Title: Der Radiologe

PUBMED ID: 9215830
DOI: doi.org/10.1200/JCO.1997.15.7.2596
Titolo: Phase II study of continuous infusion carmustine and cisplatin follo wed by cranial irradiation in adults with newly diagnosed high-grade astrocy toma.
Autori: Grossman SA., Wharam M., Sheidler V., Kleinberg L., Zeltzman M., Yue N., Piantadosi S.
Data di Pubblicazione: 1997-07-01
Abstract: This chemotherapy regimen appears to have significant activity and may prolong survival in adults with newly diagnosed high-grade astrocytoma.
Journal Title: Journal of clinical oncology : official journal of the Americ an Society of Clinical Oncology

PUBMED ID: 9167741
DOI: doi.org/10.1097/00000421-199706000-00002
Titolo: Fractionated stereotactic radiotherapy with cis-platinum radiosensit ization in the treatment of recurrent, progressive, or persistent malignant astrocytoma.
Autori: Glass J., Silverman CL., Axelrod R., Corn BW., Andrews DW.
Data di Pubblicazione: 1997-06-01
Abstract: External beam irradiation of malignant astrocytoma often provides temporary local tumor control, but dose is limited by potential toxicity to normal brain. Fractionated stereotactic radiotherapy (SRT) provides addition al radiation to the tumor with less dose deposition in adjacent normal brain . We administered a potential radiosensitizer, cis-platinum (CDDP), to optim ize the therapeutic index. CDDP (40 mg/m2) was given weekly, with SRT once o r twice weekly, to 20 patients. One had a partial response, 11 stable diseas e, and eight progressed despite therapy. Acute toxicities were manageable. F ive patients required surgery for tumor progression or radiation necrosis. M edian response duration was 18.5 weeks and median survival was 55 weeks. SRT combined with CDDP is safe, with durable responses in some patients. Further investigations to determine optimal SRT and CDDP doses and scheduling are ju stified.
Journal Title: American journal of clinical oncology

PUBMED ID: 9153469

DOI: doi.org/10.1212/wnl.48.5.1336
Titolo: Chemotherapy response criteria in malignant glioma.
Autori: Grant R., Liang BC., Slattery J., Greenberg HS., Junck L.
Data di Pubblicazione: 1997-05-01
Abstract: No one has ever proven a relationship between the extent of respon se to chemotherapy in malignant glioma and time to progression or survival. We studied the predictive value of "imaging response" following two courses of nitrosourea-based chemotherapy in 136 patients with recurrent astrocytoma /malignant glioma. We performed image analysis by blinded side-to-side compa rison of sequential studies, and categorized response into: partial response (PR) (>50% reduction), minor response (MR) (25-50% reduction), stable diseas e (SD) (<25% change), progressive disease (PD) (>25% increase). Patients wit h PR, MR, and SD did not differ with respect to time to progression (TTP) (p > 0.2) or survival (p > 0.2). Median TTP was 27 weeks for SD, 43 weeks for M R, and 30 weeks for PR. Patients with PD had a significantly reduced surviva l (p < 0.001). Median survival was 21 weeks for PD, 53 weeks for SD, 63 week s for MR, and 48 weeks for PR. The lack of relationship between response and TTP may be due to early relapses in patients with response, a cytostatic ben efit of chemotherapy in some patients who do not have an objective response, or a relatively favorable natural history in some tumors that do not respond to chemotherapy. Our data do not support the validity of current response gr ading, assessed after two courses of chemotherapy. Further research and vali dation of response criteria is necessary.
Journal Title: Neurology

PUBMED ID: 9092863
DOI: doi.org/10.1097/00006123-199704000-00042
Titolo: Second-look surgery for incompletely resected fourth ventricle epend ymomas: technical case report.
Autori: Foreman NK., Love S., Gill SS., Coakham HB.
Data di Pubblicazione: 1997-04-01
Abstract: For patients in whom complete excision of fourth ventricle ependym omas is not possible at initial surgery, second-look procedures may enable m acroscopic clearance to be achieved with little morbidity. A larger study is needed to evaluate this approach to treatment.
Journal Title: Neurosurgery

PUBMED ID: 9045344
DOI: Mancante
Titolo: Intensive radiation therapy concurrent with up to 7-week continuous- infusion paclitaxel for locally advanced solid tumors: phase I studies.
Autori: Rosenthal DI., Okani O., Truelson JM., Fathallah-Shaykh H., Vuitch F M., Gazdar AF., Griener J., Landay M., Mendelsohn D., Tourville J., Hamilton L., Orr KY., McWhorter J., Carbone DP.
Data di Pubblicazione: 1997-02-01
Abstract: Patients with locally advanced solid tumors of the lung, head and neck, and malignant astrocytomas usually succumb to their disease despite ag gressive standard therapy. Laboratory data suggest that the addition of 1.0 to 10 nmol/L paclitaxel (Taxol; Bristol-Myers Squibb Company, Princeton, NJ) , a microtubule stabilizing drug, to radiation therapy may result in signifi cant radiation sensitization, perhaps due to accumulation of cells at G2/M. Relatively low concentrations (1.0 to 10 nmol/L) appear to be optimal for di rect cytotoxicity and radiosensitization in vitro. Within this dose range, m ore prolonged exposure seems to result in higher response rates. The phase I trials reported here are designed to test the combination of paclitaxel, adm inistered by continuous intravenous infusion (24 hours a day, 7 days a week) , and standard, curative-intent radiation therapy. The ultimate goal of this study is to improve local and systemic control and survival for patients wit

h these three tumor types. To date, 39 evaluable patients are enrolled in th is study; there has been no dose-limiting toxicity up to 6.5 mg/m2/d. Observ ed toxicities include anemia, lymphopenia, mucositis, and cutaneous toxiciti es.
Journal Title: Seminars in oncology

PUBMED ID: 9368733
DOI: doi.org/10.1016/s0936-6555(05)80071-8
Titolo: Intradural drop metastases in oligodendrogliomas.
Autori: Shah N., Pigott K., Bradford R.
Data di Pubblicazione: 1997-01-01
Abstract: The case history is presented of a patient with primary intracereb ral oligodendroglioma, who received multiple therapies for local recurrence. Four years following the initial diagnosis, the patient presented with spina l cord compression due to intradural metastases. The patterns of recurrence and metastases in oligodendroglioma are discussed.
Journal Title: Clinical oncology (Royal College of Radiologists (Great Brita in))

PUBMED ID: 9816151
DOI: Mancante
Titolo: Treatment of recurrent malignant gliomas with high-dose 13-cis-retin oic acid.
Autori: Yung WK., Kyritsis AP., Gleason MJ., Levin VA.
Data di Pubblicazione: 1996-12-01
Abstract: Malignant gliomas account for more than 60% of all primary brain t umors in adults. Adjuvant chemotherapy in addition to radical surgery and ra diation therapy has provided only a modest increase in survival. Retinoic ac id has been shown to have growth-inhibitory activity against glioma cells in culture. This provides the rationale for a Phase II study using 13-cis-retin oic acid (CRA) in patients with recurrent malignant brain tumors. The object ive of this study was to determine the clinical activity of CRA in patients with a histologically proven diagnosis of malignant brain tumor and document ed progressive or recurrent disease after radiation and chemotherapy. Fifty patients with documented recurrent disease were treated with CRA as a single agent p.o. at a dose of 60-100 mg/m2 per day. Three weeks of treatment were followed by 1 week of rest. Of the 43 patients who received more than 4 week s of therapy, 3 (7%) achieved partial response, 7 (16%) achieved minor respo nse, 13 (30%) remained stable, and 20 (47%) had disease progression. The med ian time from onset of treatment to disease progression for the whole group of 43 patients was 16 weeks (19 weeks for glioblastomas and 11 weeks for ana plastic glioma), whereas that for the 23 patients with partial response and minor response and who remained stable was 66 weeks, and that for the 20 pat ients with progressive disease was only 8 weeks. The median survival time fo r glioblastoma was 58 weeks, and 34 weeks for anaplastic astrocytoma. Toxici ty was mainly dermatological, with dry skin and cheilitis. These preliminary results suggest that 13-cis-retinoic acid is active against malignant glioma s and is very well tolerated.
Journal Title: Clinical cancer research : an official journal of the America n Association for Cancer Research

PUBMED ID: 8862843
DOI: doi.org/10.1017/s031716710003852x
Titolo: Focal midbrain glioma: long term survival in a cohort of 16 patients and the implications for management.
Autori: Hamilton MG., Lauryssen C., Hagen N.
Data di Pubblicazione: 1996-08-01

Abstract: Patients with focal midbrain gliomas require symptom control aimed at treatment of hydrocephalus, or mass effect from the tumor. However the extended survival of this population suggests that routine aggressive surgical debulking is often not required. Furthermore, the routine use of radiation therapy or chemotherapy for all such patients is questioned.
Journal Title: The Canadian journal of neurological sciences. Le journal canadien des sciences neurologiques

PUBMED ID: 8844206
DOI: doi.org/10.1089/hum.1996.7.12-1465
Titolo: Treatment of advanced CNS malignancies with the recombinant adenovirus H5.010RSVTK: a phase I trial.
Autori: Eck SL., Alavi JB., Alavi A., Davis A., Hackney D., Judy K., Mollman J., Phillips PC., Wheeldon EB., Wilson JM.
Data di Pubblicazione: 1996-08-01
Abstract: Primary CNS malignancies are responsible for approximately 12,000 deaths annually in the United States. There has been little change in the outcome for adults with malignant brain tumors over the past few decades, despite improvements in surgical techniques and advances in radiation therapy. These tumors are uniformly fatal one to two years after diagnosis. The morbidity and mortality of this disease arise from the effects of a locally invasive, non-metastasizing lesion. The patients may suffer from seizures, paralysis, incoordination, aphasia, confusion, memory loss, sensory deficits or visual loss, depending on the regions of the brain affected. In addition, they usually require large doses of corticosteroids early and late in their illness, and may experience disabling side effects of this treatment, such as edema, proximal myopathy, diabetes, fungal infections or deep vein thrombosis. Few patients in the older age group are able to work after the diagnosis. Most of the patients are incapable of self-care for several months before death. The localized transfer of new genes into cancer cells potentially permits the expression of proteins with specific biologic functions that may provide a means to alter the biology of tumor growth through a variety of mechanisms including increasing tumor immunogenicity, inducing the local expression of toxic agents, and sensitization of tumors to chemotherapeutic agents. Gene therapy with the transfer of the drug susceptibility gene Herpes virus thymidine kinase (HSV-TK) has shown promise in a number of animal models, including CNS tumors. This study will evaluate the use of adenovirus-mediated transfer of the HSV-TK gene into primary human brain tumors followed by systemic treatment with ganciclovir. The goals of this phase I study are to evaluate the overall safety and efficacy of this treatment and to gain insight into the parameters that may limit the general applicability of this approach. In this phase I study, patients with recurrent gliomas will receive stereotactic-guided injections of the virus into the brain tumor, followed by intravenous ganciclovir for 14 days. Patients eligible to undergo a palliative debulking procedure will receive the same treatment followed by resection on day 7. At the time of resection a second dose of virus will be administered intra-operatively into the residual, unresectable portion of the tumor, and intravenous ganciclovir will be continued for additional 14 days. Tissue removed at the time of resection will be analyzed for evidence of adenovirus infection, thymidine kinase expression and signs of inflammation. The size and metabolic activity of all tumors will be followed by volumetric MRI scans and Position Emission Tomography Scans, respectively. Patients will be enrolled in groups of three, with each group receiving successively larger doses of adenovirus. This study will quantify the toxicity of this therapy, and provide evidence as to the duration of transgene expression and virus induced inflammation.
Journal Title: Human gene therapy

PUBMED ID: 8777179
DOI: doi.org/10.1093/oxfordjournals.annonc.a010550
Titolo: Phase II study of topotecan in patients with recurrent malignant gli oma. National Clinical Institute of Canada Clinical Trials Group.
Autori: Macdonald D., Cairncross G., Stewart D., Forsyth P., Sawka C., Wainm an N., Eisenhauer E.
Data di Pubblicazione: 1996-02-01
Abstract: Topotecan in this dose and schedule has only modest activity in re current glioblastoma and anaplastic astrocytoma.
Journal Title: Annals of oncology : official journal of the European Society for Medical Oncology

PUBMED ID: 8571175
DOI: Mancante
Titolo: Hyperthermia--its actual role in radiation oncology. Part IV: Thermo -radiotherapy for malignant brain tumors.
Autori: Seegenschmiedt MH., Feldmann HJ., Wust P., Molls M.
Data di Pubblicazione: 1995-10-01
Abstract: The encouraging results of clinical trials may be biased by favour able tumor and patient selection. Randomized clinical trials comparing RT al one versus combined RT-HT for advanced and recurrent brain tumors are justif ied. Part I has covered biological and technical fundamentals of clinical hy perthermia and has been published in Strahlenther. Onkol. 168 (1992), 183-19 0. Part II has covered clinical fundamentals and results in superficial tumo rs of clinical hyperthermia and has been published in Strahlenther. Onkol. 1 69 (1993), 633-654. Part III has covered clinical rationale and results in d eep seated tumors and has been published in Strahlenther. Onkol. 171 (1995), 251-264.
Journal Title: Strahlentherapie und Onkologie : Organ der Deutschen Rontgeng esellschaft ... [et al]

PUBMED ID: 7674024
DOI: doi.org/10.3171/jns.1995.83.4.0724
Titolo: Primary diffuse leptomeningeal oligodendroglioma. Case report.
Autori: Chen R., Macdonald DR., Ramsay DA.
Data di Pubblicazione: 1995-10-01
Abstract: The authors describe a case of a diffuse primary leptomeningeal ol igodendroglioma in a 17-year-old girl who presented with raised intracranial pressure and hydrocephalus. She underwent imaging studies and a left frontot emporal craniotomy that revealed a cystic oligodendroglioma in the suprasell ar cistern and spread of neoplastic cells to the spinal leptomeninges. The t umor showed little response to maximum radiotherapy and chemotherapy, and th e patient died from complications of high-dose chemotherapy 2 years after di agnosis. Postmortem examination of the brain and spinal cord revealed diffus e meningeal infiltration by neoplastic cells and no evidence of an intrapare nchymal origin. Glial heterotopias were noted at several sites along the bra in base, adding circumstantial support to the theory that leptomeningeal gli omas are derived from ectopic glial tissue in the subarachnoid space.
Journal Title: Journal of neurosurgery

PUBMED ID: 7897511
DOI: doi.org/10.3171/jns.1995.82.4.0530
Titolo: Stereotactic radiosurgery for glioblastoma: a final report of 31 pat ients.
Autori: Masciopinto JE., Levin AB., Mehta MP., Rhode BS.
Data di Pubblicazione: 1995-04-01

Abstract: From February 1989 to December 1992, 31 patients who presented wit
h an initial pathological diagnosis of glioblastoma multiforme underwent tum
or debulking or biopsy, stereotactic radiosurgery, and standard radiation th
erapy as part of their primary treatment. Presenting characteristics in the
22 men and nine women included a median age of 57 years, Karnofsky Performan
ce Scale score median of 80, and median tumor volume of 16.4 cm3. Stereotact
ic radiosurgery delivered a central dose of 15 to 35 Gy with the isocenter l
ocation, collimator size, and beam paths individualized by means of three-di
mensional software developed at the University of Wisconsin. The peripheral
isodose line varied from 40% to 90% with a median of 72.5% and a mode of 80%
. The mean follow-up period was 12.84 months with a median of 9.5 months. St
atistical analysis was performed using Kaplan-Meier analysis and log-rank co
mparison of risk factor groups. The parameters of age, initial Karnofsky Per
formance Scale score, and biopsy were significantly different in patient sur
vival from debulking; but no difference was noted between single and multipl
e isocenters and patterns of steroid requirement. Radiographic recurrences w
ere divided by location into the following categories: central (within centr
al stereotactic radiosurgery dose), 0; peripheral (within 2 cm of central do
se), 19; and distant (> 2 cm), 4. There is no evidence of recurrence in five
surviving patients. Actuarial 12-month survival was 37%, with a median survi
val of 9.5 months. These values are similar to previous results for surgery
and standard radiotherapy alone. The results suggest that the curative value
of radiosurgery is significantly limited by peripheral recurrences.
Journal Title: Journal of neurosurgery

PUBMED ID: 8729851
DOI: Mancante
Titolo: [Extracerebral metastases of a glioblastoma, in the absence of surge
ry].
Autori: Chretien F., Gray F., Funalot B., Authier FJ., Peltier E., Lange F.,
Degos JD., Poirier J.
Data di Pubblicazione: 1995-01-01
Abstract: A 50 y.o. male presented with a right parietal tumor which was a g
lioblastoma on stereotactic biopsy. He was treated by radiation and steroids
, with clinical improvement. Four months later, he presented with a left pre
auricular mass and cervical lymphadenopathy. CT scan showed destruction of t
he left mastoid and filling of the left tympanic cavity. One month later, he
suffered progressive dyspnea. Chest X ray showed a mediastinal mass on the r
ight side and numerous bilateral interstitial opacities in the lungs. A bron
chial biopsy was inconclusive. His general condition worsened, and he died.
Postmortem showed continuous neoplastic infiltration of the left part of the
base of skull, extending into the neck. Numerous metastases were present in
mediastinal lymph nodes, lung parenchyma, pleura and pleural aspect of the d
iaphragm. There were no subdiaphragmatic metastases. Neuropathological exami
nation confirmed a poorly differentiated highly malignant glioblastoma with
severe necrosis involving the internal part of the parietal lobe extending t
o the dura mater of the convexity and falx cerebri with invasion of the supe
rior longitudinal sinus which was entirely occluded. The biopsy scar was not
infiltrated. Visceral tumors were morphologically identical to the brain tum
or. They were strongly GFAP positive and cytokeratin negative. Extraneural m
etastases of glioblastoma in the absence of surgery are uncommon in adults.
Involvement of the dura mater and/or superior longitudinal sinus is an almos
t constant feature. In our case, this may have led to invasion of the base o
f skull and secondary regional, lymphatic, and hematogenous spread.
Journal Title: Archives d'anatomie et de cytologie pathologiques

PUBMED ID: 7673984
DOI: doi.org/10.1007/BF01059953

Titolo: Leukoencephalopathy associated with intra-arterial ACNU in patients with gliomas.
Autori: Tsuboi K., Yoshii Y., Hyodo A., Takada K., Nose T.
Data di Pubblicazione: 1995-01-01
Abstract: Thirty cases of gliomas treated by surgery, radiotherapy and intra-arterial (IA) ACNU were reviewed with a focus on the late side-effect known as leukoencephalopathy. All cases were classified into three groups; remission (10 cases), regrowth (15 cases) and leukoencephalopathy (5 cases) from their outcome. The average total doses of IA ACNU were 49.8 mg/sqm body surface area in the remission group, 157.3 mg/sqm in the regrowth group and 203.1 mg/sqm in the leukoencephalopathy group. There were significant differences in the total IA ACNU doses between the remission group and both regrowth and leukoencephalopathy groups, while no significant differences were noticed in the dose of radiation given. There was a correlation between the total dose of IA ACNU and the occurrence of leukoencephalopathy. An autopsy of a typical case of leukoencephalopathy revealed various degrees of myelin breakdown and thickening of arterial walls, which probably manifested progressive dementia accompanied by urinary incontinence and gait disturbance.
Journal Title: Journal of neuro-oncology

PUBMED ID: 7623074
DOI: doi.org/10.1007/BF01058464
Titolo: Phase II study of amonafide in patients with recurrent glioma.
Autori: Levitt R., Buckner JC., Cascino TL., Burch PA., Morton RF., Westberg MW., Goldberg RM., Gallagher JG., O'Fallon JR., Scheithauer BW.
Data di Pubblicazione: 1995-01-01
Abstract: Amonafide, a novel imide derivative with broad preclinical antitumor activity, achieves significant cerebrospinal fluid levels in animal models. In order to test its antitumor activity in patients with recurrent diffuse infiltrative glioma of the astrocytic and oligodendroglial type, we performed a phase II clinical trial. Of the 22 eligible and evaluable patients treated, 2 (9%) experienced tumor regression lasting more than one year. No other patients experienced tumor regression; one remained stable more than six months. Toxicities consisted primarily of myelosuppression, vomiting, and venous irritation at the infusion site. We conclude that amonafide has minimal activity in recurrent glioma patients. Further investigations are not warranted in this study population.
Journal Title: Journal of neuro-oncology

PUBMED ID: 8153288
DOI: Mancante
Titolo: Delayed cerebral radiation necrosis.
Autori: Morris JG., Grattan-Smith P., Panegyres PK., O'Neill P., Soo YS., Langlands AO.
Data di Pubblicazione: 1994-02-01
Abstract: The clinical features and long-term outcome of seven patients with delayed cerebral radiation necrosis (DCRN) are described. Radiotherapy had been given for pituitary tumour (1), astrocytoma (2), pinealoma (2), craniopharyngioma (1) and parotid carcinoma (1). The mean latency to onset of the first neurological symptoms was 22 months (range 6-40 months), and mean duration of follow-up was 86 months (range 60-126). Three patients died at a mean of 84 months after radiotherapy (range 62-98). A fourth patient probably died from metastatic disease. Three patients remain alive, albeit severely disabled, after 5-10 years. The illness typically ran a stepwise course, with fits and stroke-like episodes occurring against a background of progressive dementia and somnolence. CT and MRI scans showed progressive ventricular dilatation associated with cerebral atrophy and diffuse or focal changes in the white matter. Four patients had had two or more neurosurgical procedures afte

r the radiotherapy. In only one of the seven patients was the diagnosis made at presentation. DCRN produces a distinctive clinical picture, yet remains a poorly recognized complication of cranial irradiation.
Journal Title: The Quarterly journal of medicine

PUBMED ID: 7807192
DOI: doi.org/10.1007/BF01052725
Titolo: High dose chemotherapy for the treatment of malignant brain tumors.
Autori: Petersdorf SH., Livingston RB.
Data di Pubblicazione: 1994-01-01
Abstract: Conventional treatment of malignant high grade gliomas includes maximal resection followed by external beam radiotherapy. The addition of adjuvant chemotherapy has provided little improvement in the median duration of survival for these patients, particularly those patients with glioblastoma multiforme. The failure of conventional dose chemotherapy to improve the outcome of patients with high grade brain tumors has led several investigators to utilize high dose chemotherapy in order to overcome the limited benefit seen with conventional dose therapy which is due to intrinsic drug resistance as well as the impermeability of blood brain barrier. The majority of published studies utilizing this approach suggest that the addition of high dose chemotherapy with bone marrow transplant is of marginal benefit. However, most of these trials include small numbers of patients with advanced, refractory disease. A few trials have been reported utilizing high dose therapy in an adjuvant setting and the data from these studies are somewhat more promising. This review will analyze these studies and also discuss possible modifications of this approach in order to improve this aggressive treatment for patients who otherwise would have a dismal prognosis.
Journal Title: Journal of neuro-oncology

PUBMED ID: 7519356
DOI: doi.org/10.1007/978-3-642-85039-4_10
Titolo: Radiosurgery/stereotactic external beam radiotherapy for malignant brain tumours: the Royal Marsden Hospital experience.
Autori: Brada M., Laing R.
Data di Pubblicazione: 1994-01-01
Abstract: SRT is a high-precision technique of radiotherapy which delivers focused irradiation to small target volumes. In the context of external beam radiotherapy it can be described as stereotactically guided conformal radiotherapy. As the technique originated from neurosurgical technology, it has initially been limited to single fraction treatment. However, with the use of relocatable fixation devices the way ahead particularly in its application in the treatment of brain tumours is in fractionated SRT. Currently, single fraction SRT/radiosurgery is of proven value only in the treatment of small inoperable arteriovenous malformations. It is being exploited in the management of brain tumours but so far remains as experimental treatment. We have demonstrated that fractionated SRT in patients with gliomas is a non-invasive equivalent to brachytherapy and in patients with solitary metastases a non-invasive alternative to surgical excision. However, the treatment is not without side effects, and the long-term effectiveness and toxicity of SRT, particularly with the use of unconventional fractionation, is not defined. The future use of SRT in the treatment of brain tumours should not be guided simply by the technical possibilities but by a rational appraisal of all treatment options to achieve the best disease control, survival and toxicity. Although there is potential for benefit in a number of small tumours, SRT cannot at present be recommended as the primary treatment in any tumour. In addition, its use should be discouraged in the treatment of unbiopsied brain lesions and as the major form of treatment of pineal germinomas. The technology of stereotactic radiotherapy is evolving, and it is likely that SRT will be inte

grated into conventional radiotherapy practice to become simply a high-preci sion technique of radiotherapy delivery in everyday use.
Journal Title: Recent results in cancer research. Fortschritte der Krebsfors chung. Progres dans les recherches sur le cancer

PUBMED ID: 8514549
DOI: doi.org/10.1016/0360-3016(93)90973-y
Titolo: The effect of advanced age on the efficacy of radiation therapy for early breast cancer, local prostate cancer and grade III-IV gliomas.
Autori: Peschel RE., Wilson L., Haffty B., Papadopoulos D., Rosenzweig K., F eltes M.
Data di Pubblicazione: 1993-06-15
Abstract: This study strongly supports the use of standard radiation therapy programs for early breast and prostate cancer patients age 70 years or more. However, our study raises questions about the efficacy of radiation therapy in patients over the age of 70 years with Grade 3-4 gliomas.
Journal Title: International journal of radiation oncology, biology, physics

PUBMED ID: 8509817
DOI: doi.org/10.1007/BF01053933
Titolo: Intracranial ependymoma long term outcome, patterns of failure.
Autori: Kovalic JJ., Flaris N., Grigsby PW., Pirkowski M., Simpson JR., Roth KA.
Data di Pubblicazione: 1993-02-01
Abstract: We analyzed 31 patients with intracranial ependymoma, all verified by secondary neuropathology review. There were 12 patients with ependymomas and 19 patients with anaplastic ependymoma by the WHO classification. Eight patients received craniospinal irradiation, 22 patients received cranial irr adiation alone, and one patient was treated with chemotherapy alone. The med ian follow-up time was 11 years. The 5- and 10-year progression-free surviva ls (PFS) were 60% and 48%. Those with anaplastic tumors had a decreased 10 y ear PFS over those with low grade lesions: 26% vs. 55% (p = 0.02). Deliverin g spinal irradiation in addition to cranial irradiation did not improve outc ome. There were relapses in 16 patients. All patients relapsed at the primar y intracranial sites with no spinal failures. Patients treated with whole br ain irradiation had decreased 10 year PFS over those treated with local fiel ds: 19% vs. 64% (p = 0.006). Those patients treated to > or = 50 Gy had an i mproved long-term PFS (p = 0.04). Multivariate analysis was undertaken with the following variables: extent of cranial irradiation, pathology, anatomic site of ependymoma, cranial irradiation dose, extent of surgery, and whether spinal irradiation was given. With PFS as the endpoint, only extent of crani al irradiation (favoring local fields) and pathology (favoring low grade epe ndymoma) were significant prognosticators. We conclude that carefully outlin ed local field irradiation is the therapy of choice, and elective spinal irr adiation is of questionable benefit.
Journal Title: Journal of neuro-oncology

PUBMED ID: 1460488
DOI: doi.org/10.1007/BF00172601
Titolo: Multiple-fraction-per-day external beam radiotherapy for adults with supratentorial malignant gliomas.
Autori: Halperin EC.
Data di Pubblicazione: 1992-11-01
Abstract: The prognosis following therapy for adults with supratentorial mal ignant gliomas is poor. Standard therapy of 60 Gy of external beam radiother apy with chemotherapy achieves a median survival time of 35 to 51 weeks foll owing surgery. A variety of innovative therapies have been considered for th

erapy of malignant gliomas. Multiple-fraction-per-day (MFD) external beam ra diotherapy has been evaluated by many investigators. The rationale for MFD t eletherapy is based upon exploiting differences in the recovery capacity for radiation damage between slowly and rapidly proliferating tissues and/or sho rtening the overall treatment time. A large number of clinical trials have, for the most part, failed to show any survival benefit from MFD radiotherapy . These trials have utilized b.i.d. and t.i.d. radiotherapy with fraction si zes of 0.89 to 2 Gy to total doses of 30-81.6 Gy. The linear quadratic model of the radiation cell survival curve suggests that a biological effective tu moricidal dose > or = 10% higher than standard daily radiotherapy, with appr oximately isoeffective normal tissue damage, could be achieved at 1.2 Gy b.i .d. to a total dose of approximately 72 Gy. Trials of low dose per fraction MFD radiotherapy, to total doses less than 72 Gy, would be predicted to be i nadequate to the task.
Journal Title: Journal of neuro-oncology

PUBMED ID: 1506881
DOI: doi.org/10.3171/jns.1992.77.3.0355
Titolo: Adult intramedullary astrocytomas of the spinal cord.
Autori: Epstein FJ., Farmer JP., Freed D.
Data di Pubblicazione: 1992-09-01
Abstract: In this series, 25 adult patients with intramedullary astrocytomas were treated by radical excision alone. Six patients proved to have anaplast ic astrocytoma; five of them died within approximately 2 years and the sixth has demonstrated disease progression. The other 19 patients were diagnosed a s having low-grade astrocytoma (16 cases) or ganglioglioma (three cases); tw o of these had advanced preoperative neurological disability and died of med ical complications. Fifteen of the remaining 17 patients have no clinical ev idence of tumor recurrence after a mean follow-up period of 50.2 months; the other two have a small residual neoplasm that demonstrates no progression. O f these 17 patients, seven had previously received radiation therapy, but ha d clear evidence of tumor growth subsequently. This experience suggests that surgery is not beneficial for anaplastic spinal astrocytoma. However, in cas es of low-grade tumor, radical excision is associated with minimal morbidity and an excellent long-term prognosis when carried out before significant dis ability occurs.
Journal Title: Journal of neurosurgery

PUBMED ID: 1607975
DOI: doi.org/10.3171/jns.1992.77.1.0078
Titolo: Clinical effect of intra-arterial tumor necrosis factor-alpha for ma lignant glioma.
Autori: Yoshida J., Wakabayashi T., Mizuno M., Sugita K., Yoshida T., Hori S ., Mori T., Sato T., Karashima A., Kurisu K.
Data di Pubblicazione: 1992-07-01
Abstract: Recombinant human tumor necrosis factor-alpha was administered int ra-arterially to treat 20 cases of malignant gliomas, mostly progressive or recurrent. The optimum dosage was determined to be 1 x 10(5) U/sq m/day. Amo ng the 10 evaluable patients treated at this dosage, two responded (one comp letely and one partially), resulting in a 20% response rate. Side effects we re mild and easily controllable. Improvement of neurological symptoms was no ted in 47% of the patients a few days after treatment, even when computerize d tomography showed no tumor regression. This might have been due to the ple iotypic biological activity of tumor necrosis factor-alpha. Neuroradiographi c observations revealed narrowing of the tumor-feeding artery, a decrease in tumor staining ability, and necrosis in the central part of a tumor. The aut hors suggest that intra-arterial administration of tumor necrosis factor-alp

ha may be an effective treatment for malignant glioma, including recurrent c
ases.
Journal Title: Journal of neurosurgery

PUBMED ID: 1919696
DOI: doi.org/10.3171/jns.1991.75.5.0740
Titolo: Long-term outcome of 89 low-grade brain-stem gliomas after interstit
ial radiation therapy.
Autori: Mundinger F., Braus DF., Krauss JK., Birg W.
Data di Pubblicazione: 1991-11-01
Abstract: Between 1974 and 1985, 89 patients suffering from histologically c
onfirmed, nonresectable low-grade astrocytomas located in the brain stem wer
e entered into a retrospective study. Iodine-125 (125I) was implanted in 29
patients and iridium-192 (192Ir) in 26 patients. Computerized tomography rev
ealed that 78% of the tumors in these patients were located chiefly in the m
esencephalic region, 70% were circumscribed, and 78% were contrast-enhanced.
Thirty-four patients underwent biopsy without prior aggressive tumor-specifi
c therapy such as chemotherapy or external beam irradiation. Among these, 70
% of the tumors were located predominantly in the pons, 74% were diffuse, an
d 59% were hypodense or isodense after contrast enhancement. Long-term follo
w-up investigations indicated that life expectancy after interstitial radiat
ion therapy with 125I implanted directly by catheter either permanently or t
emporarily showed a more favorable trend than that after treatment with 192I
r. Interstitial radiation therapy with 125I appears to be an effective treat
ment for slowly proliferating, differentiated, well-delineated, nonresectabl
e brain-stem gliomas. This technique makes it possible to achieve radiosurgi
cal tumor control and, when carefully applied, represents the least traumati
c treatment. Reduction of the tumor mass brings about improvement of the cli
nical symptoms. Further investigations on the biological behavior of brain-s
tem gliomas and prospective randomized long-term follow-up studies are neces
sary to evaluate the different kinds of treatment available for these patien
ts.
Journal Title: Journal of neurosurgery