BANGLADESH SOCIETY FOR BREAST CANCER STUDY BSBCS

OncoEdu
Research | Education | Treatment

CME on

Management of Brain tumors in New Era 2025

Sunday, 27th July, 2025 || 2:00 to 4:00 PM (Lunch will be served from 2:00 PM)

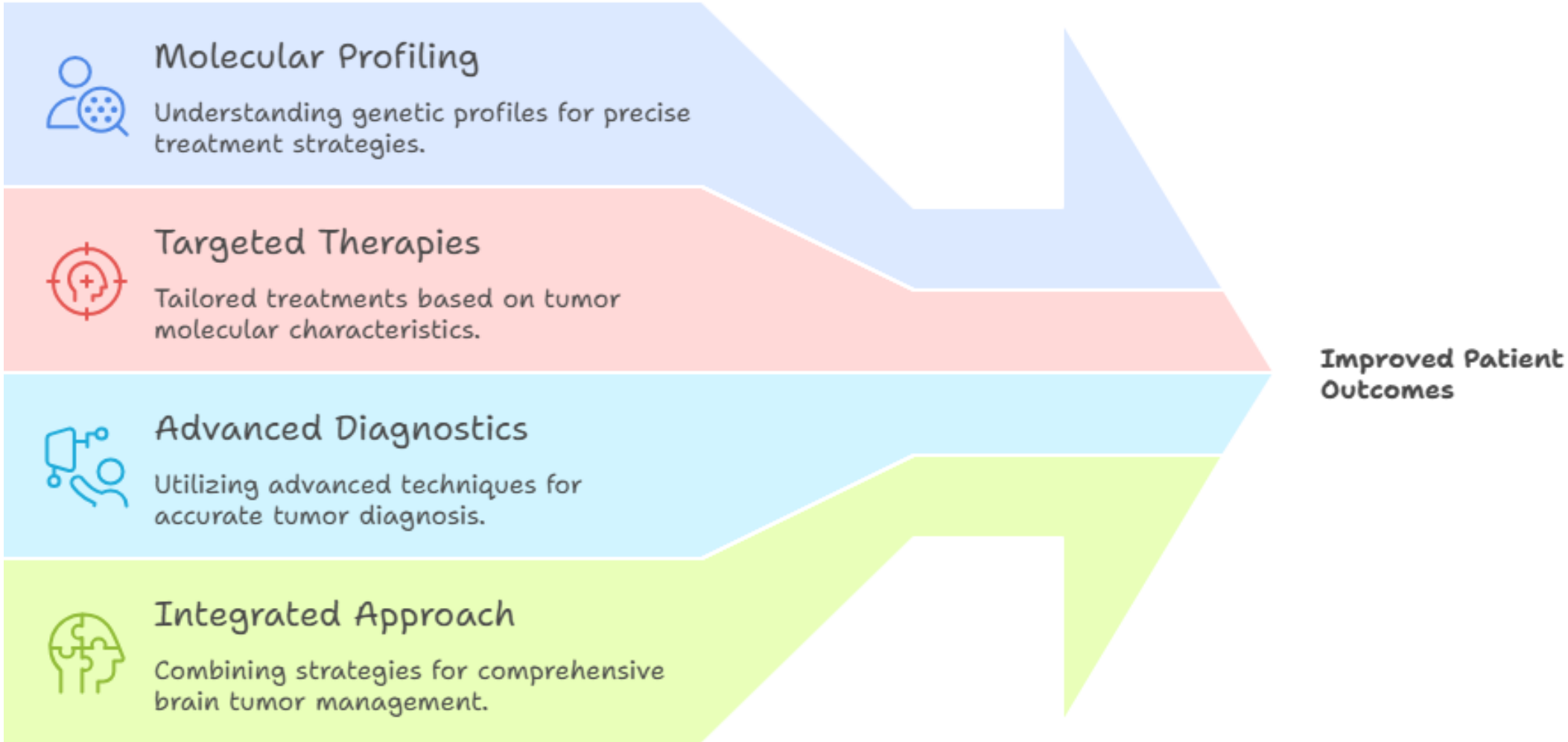
Dr. Mukut Hall, Bangladesh Specialized Hospital PLC

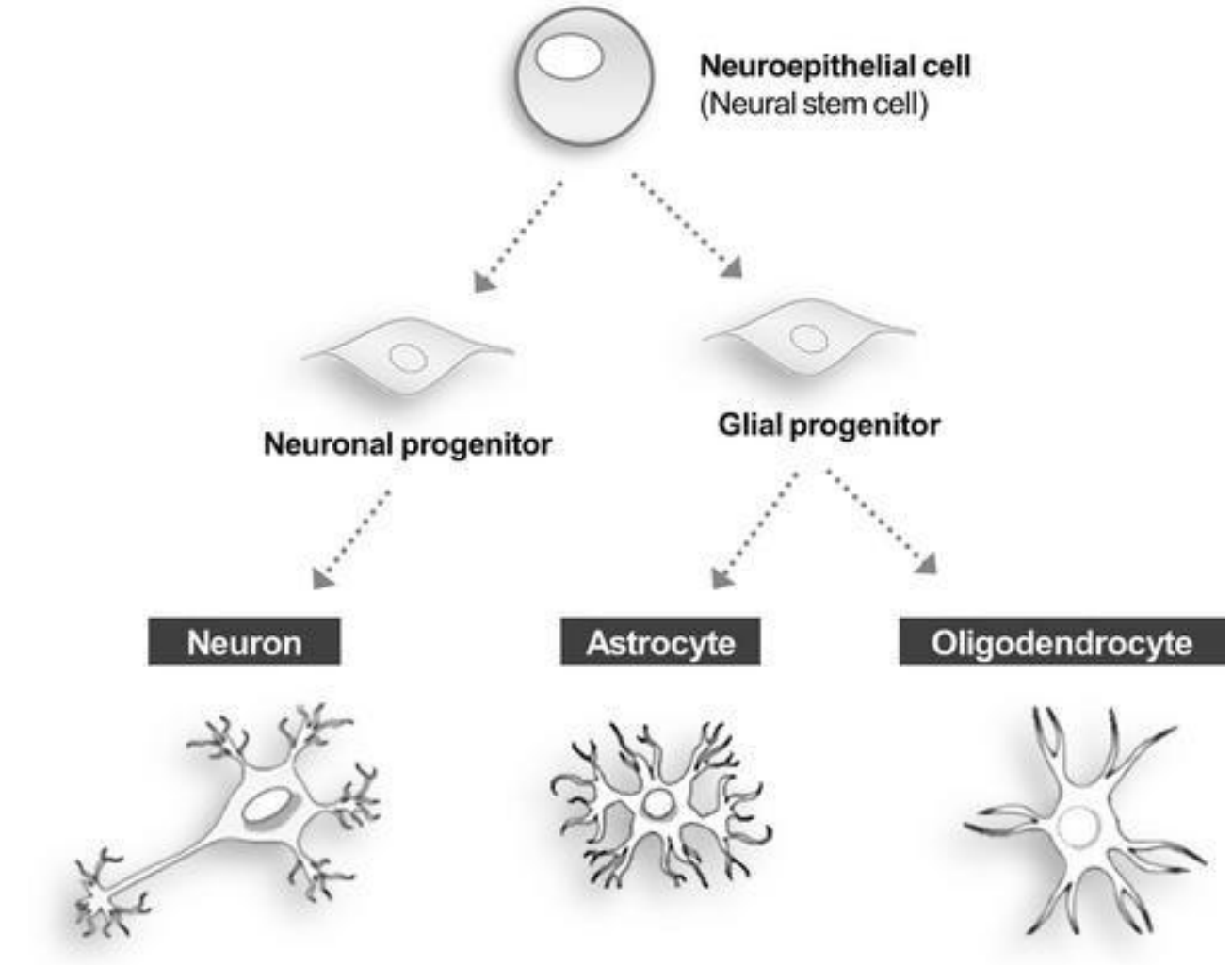
Integrated Management of Brain tumors based on Molecular signature

Dr Rajesh Balakrishnan
Professor - Radiation Oncology
DMG - Breast / Neuro-oncology / Paed Rad Onc
CMC Vellore

rajeshb@cmcvellore.ac.in

Precision in Brain Tumor Management

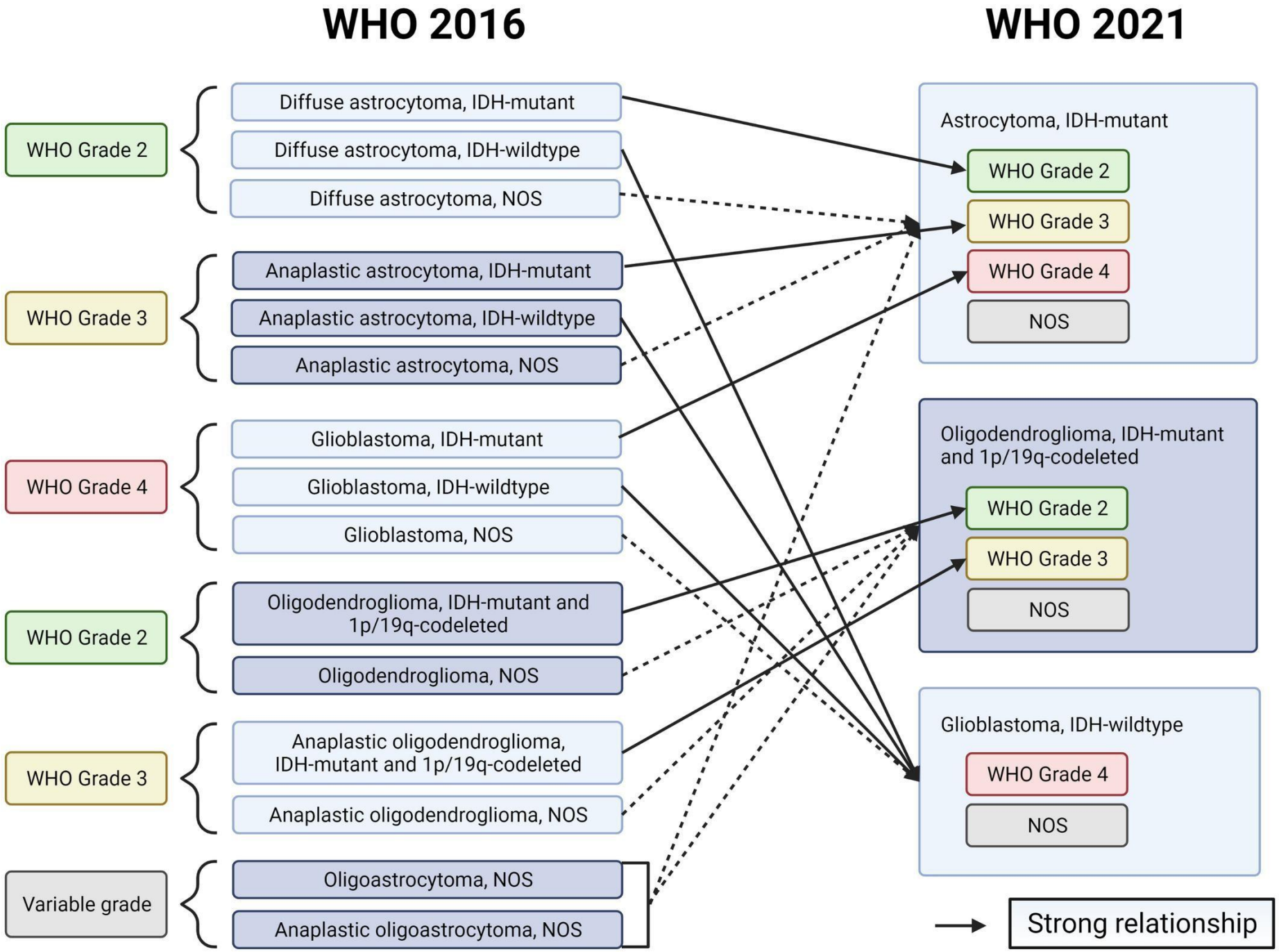




Glioneuronal Tumors | Gliomas | Oligodendrogliomas

https://onlinelibrary.wiley.com/doi/full/10.1002/jmri.29016

2016 Vs 2021



OncoEdu
Research | Education | Treatment

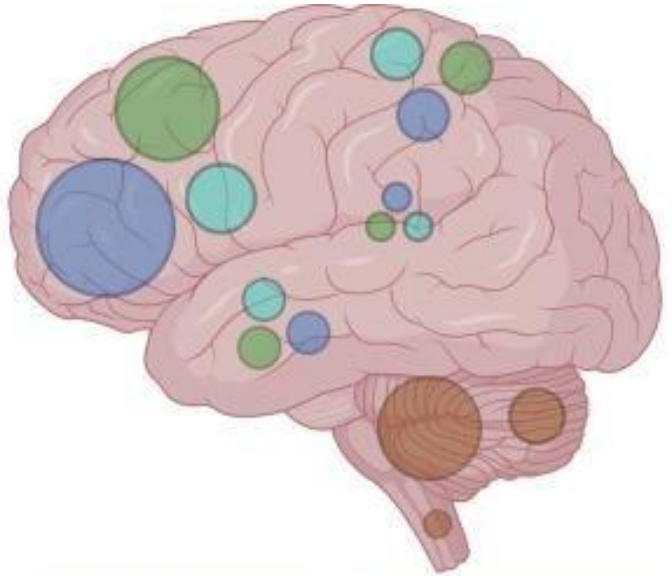
7 Molecular tests required
Classification - Gliomas - (WHO 2021)

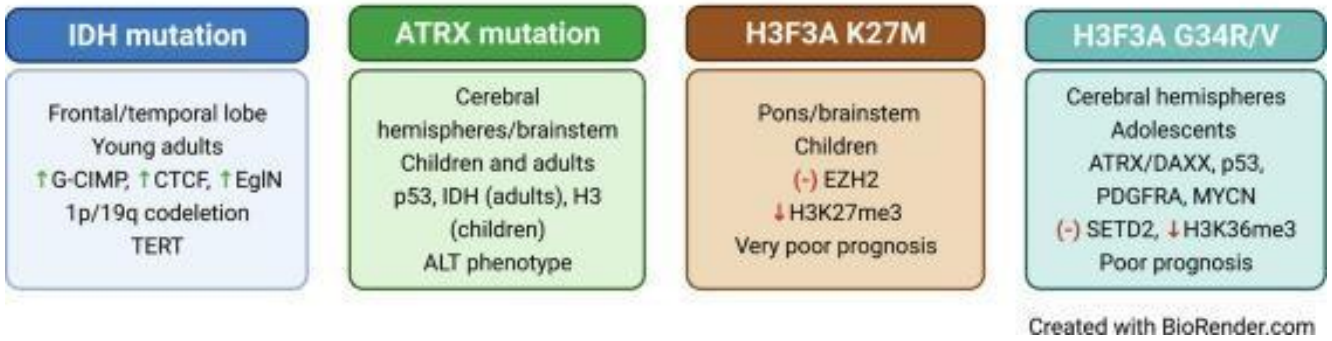
Isocitrate Dehydrogenase (IDH 1/ IDH2) mutations	IHC
Alpha Thalassemia /Mental retardation syndrome X related gene Expression (ATRX)	IHC
1p /19 q codeletion	MLPA /FISH
CDKN2A/B homozygous deletion on 9p21	MLPA /FISH
TERT mutation /EGFR Gene amplification and/or Chromosome 7 gain and 10 loss (+7/ -10)	MLPA /FISH
Histone H3 K27M mutations	IHC
Histone H3 G34R/V mutations	IHC

Multiplex Ligation dependent Probe Amplification

Location of Tumors and Mutations

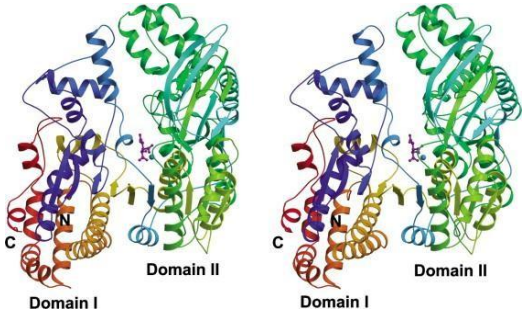
IDH mutations – Frontal / Temporal lobes
ATRX mutations – Brainstem / Cerebral hemispheres
H3K27 mutations – Midline – pons / brainstem
H3G34 mutations – Cerebral hemispheres

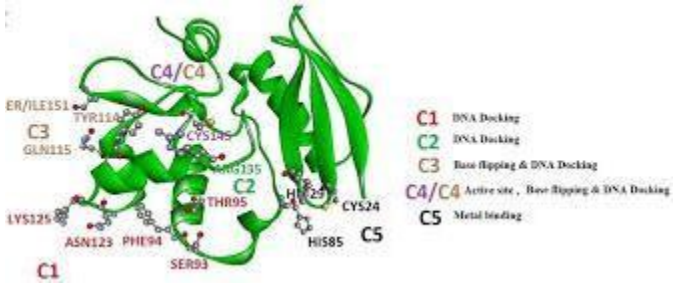


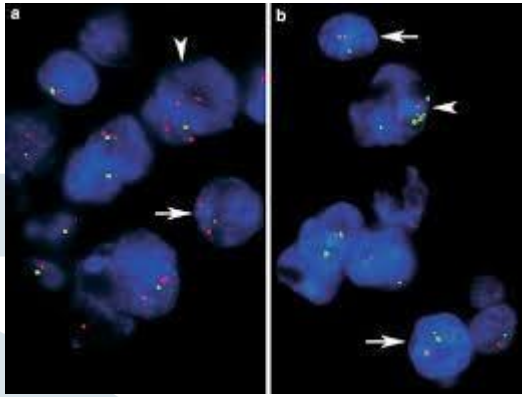


OncoEdu
Research | Education | Treatment

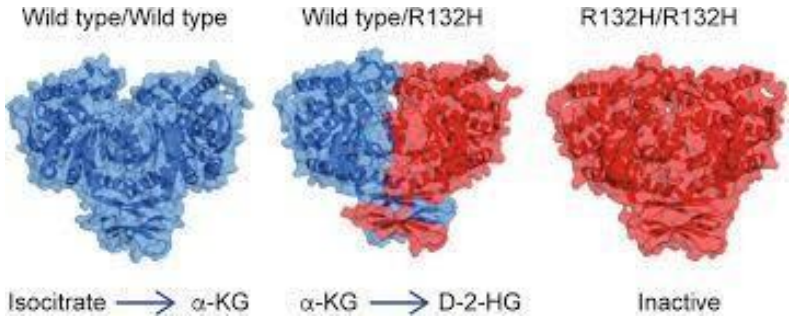
Dharmaiah S, Huse JT. The epigenetic dysfunction underlying malignant glioma pathogenesis. Laboratory Investigation. 2022 Jul 1;102(7):682-90.





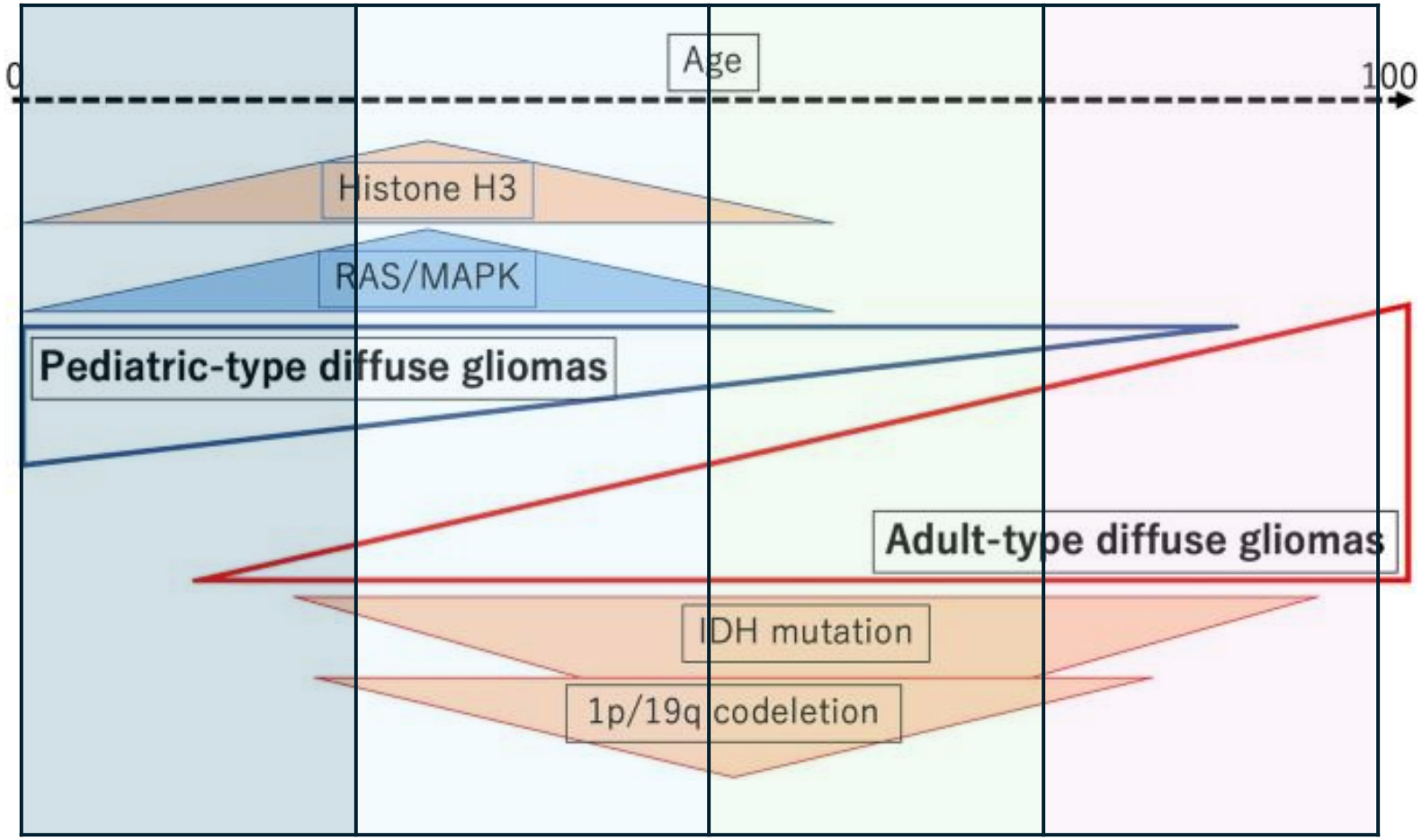


Management based on Molecular classification



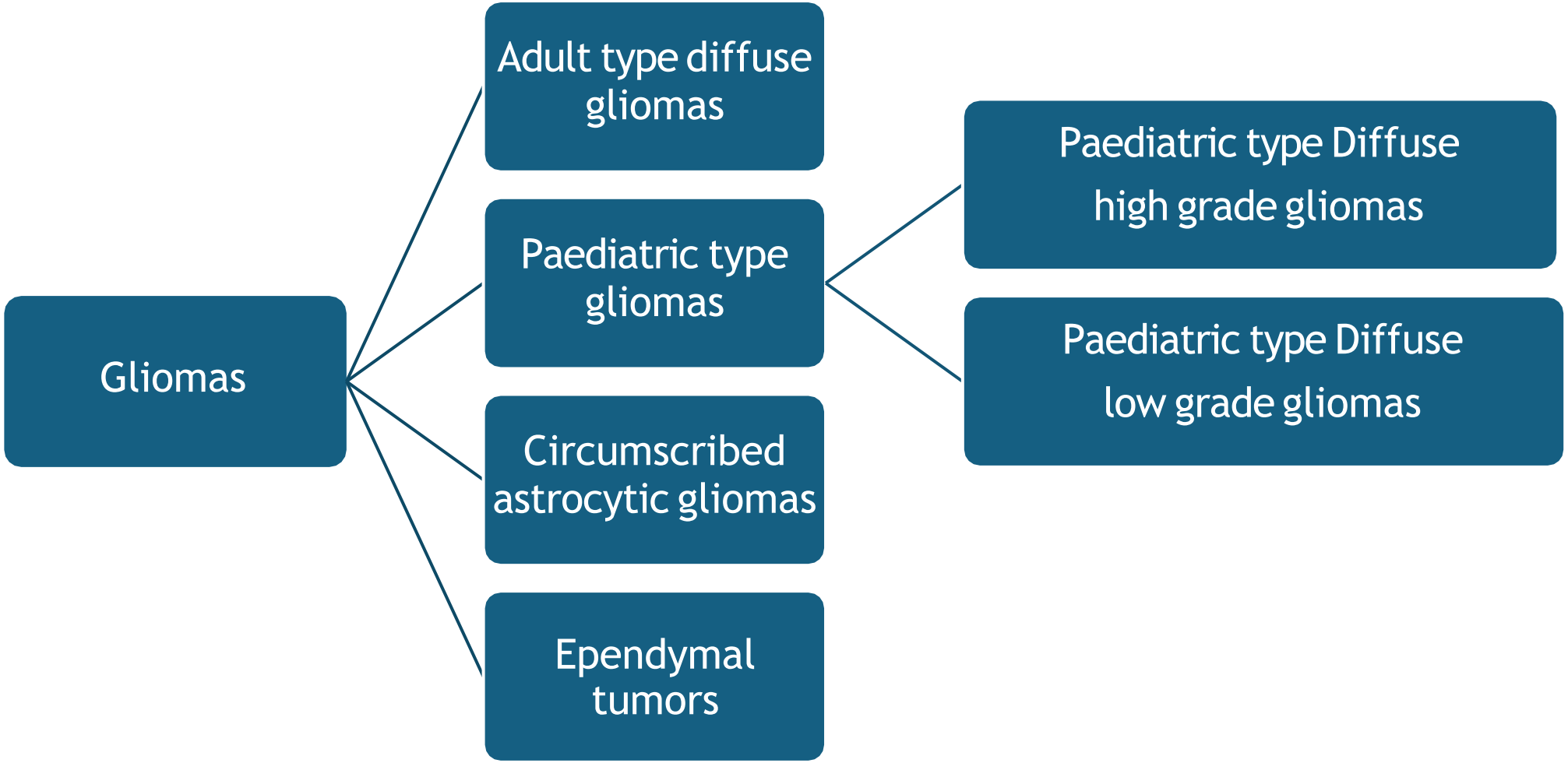
OncoEdu
Research | Education | Treatment

Note that the pediatric type may occur in adults, and vice versa

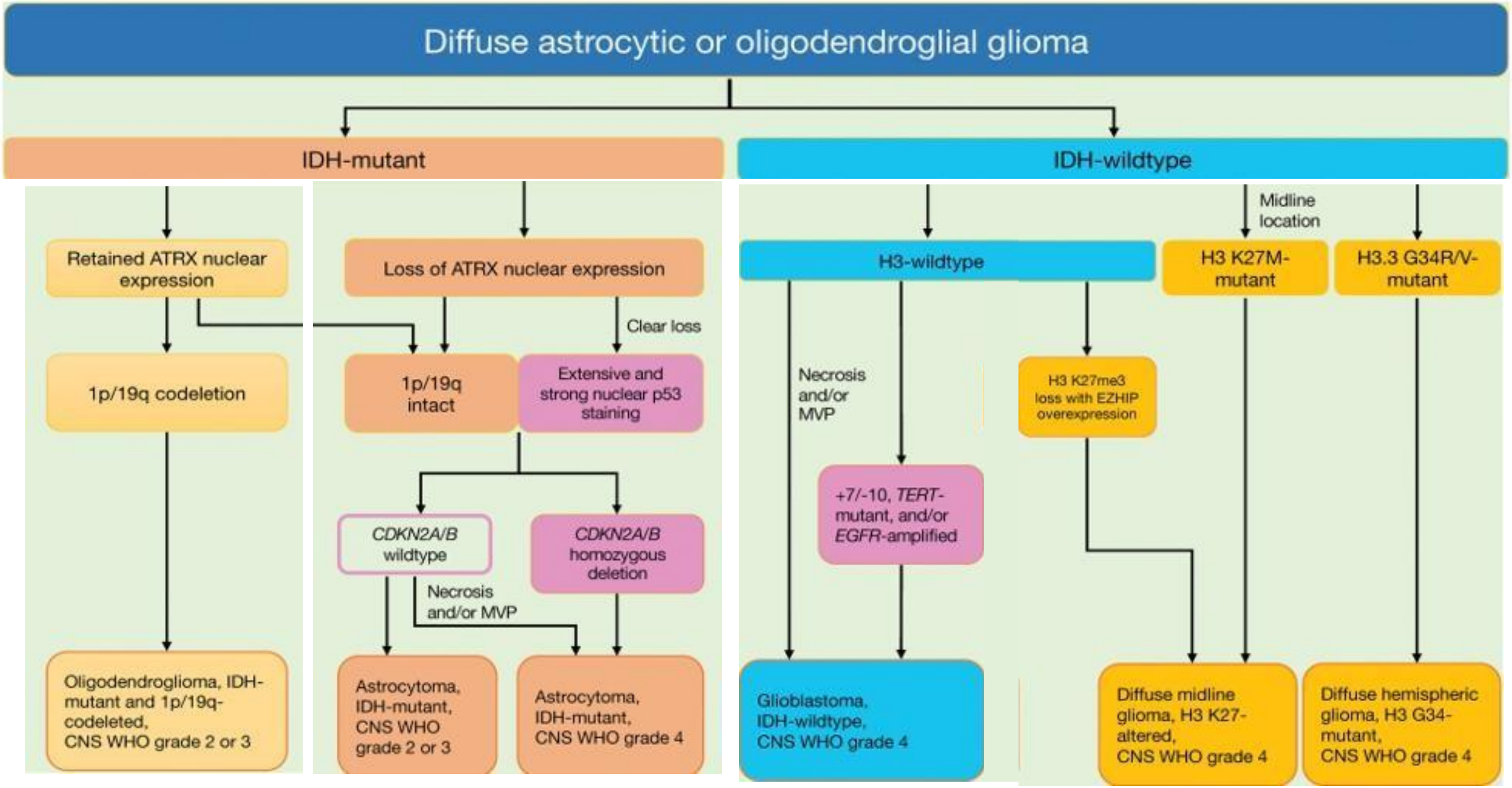


Komori T. The molecular framework of pediatric-type diffuse gliomas: shifting toward the revision of the WHO classification of tumors of the CNS. Brain Tumor Pathology. 2021 Jan;38(1):1-3.

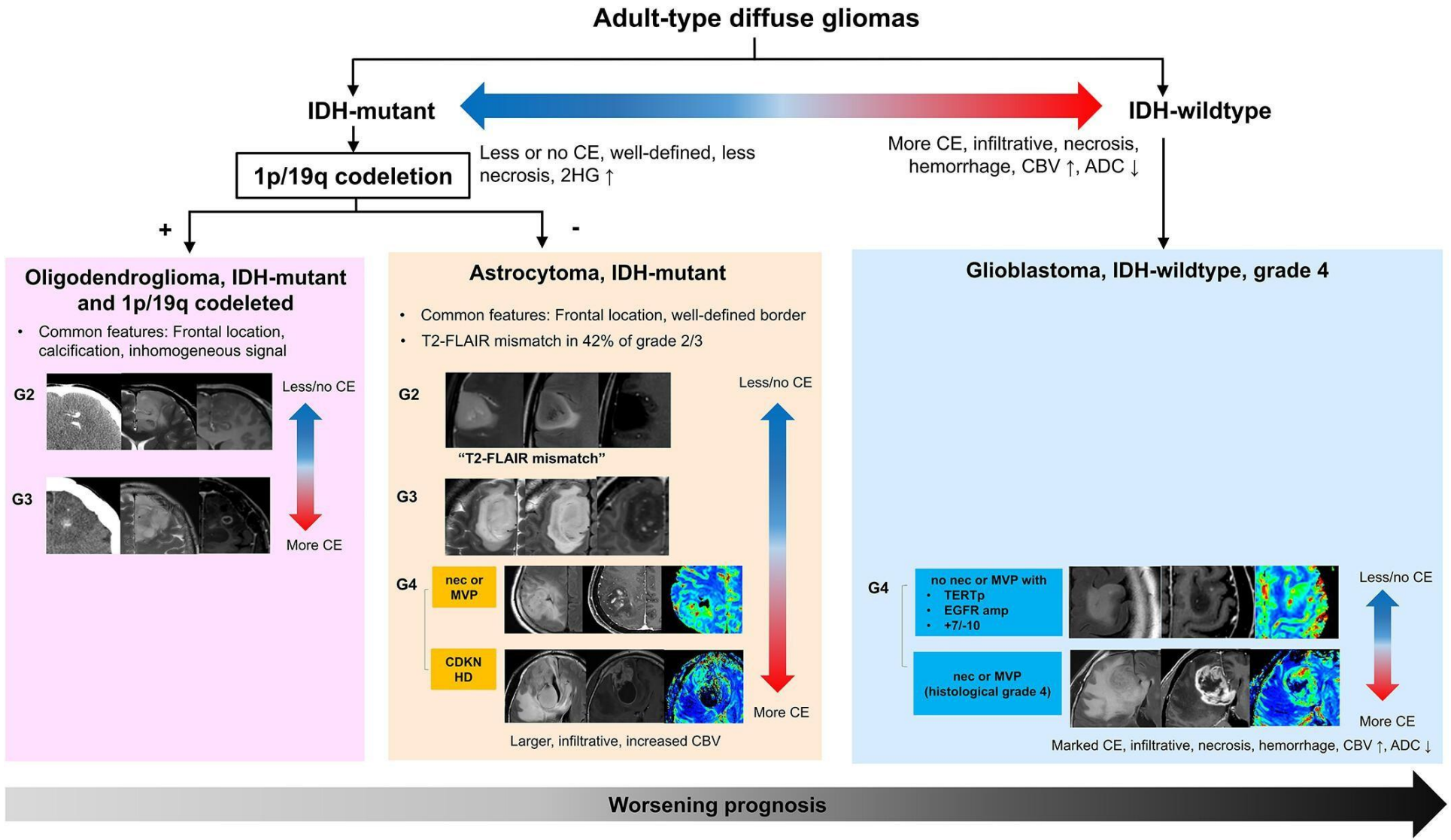
WHO CNS 5 - 2021 Classification



Kurokawa R. Published Online: July 08, 2022
https://doi.org/10.1148/rg.210236

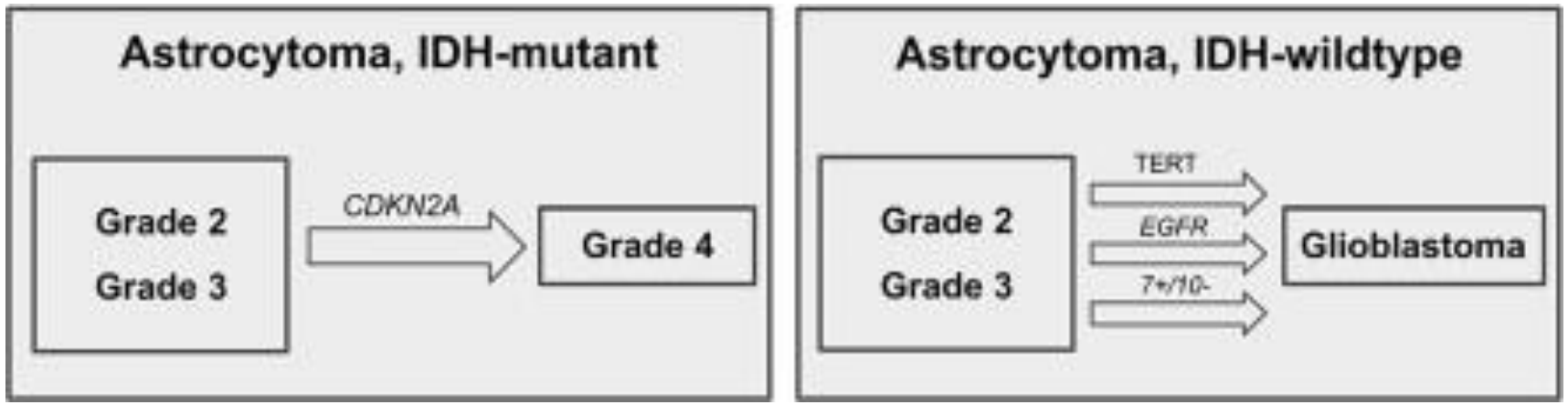


Adult-Type Diffuse Gliomas



OncoEdu
Research | Education | Treatment

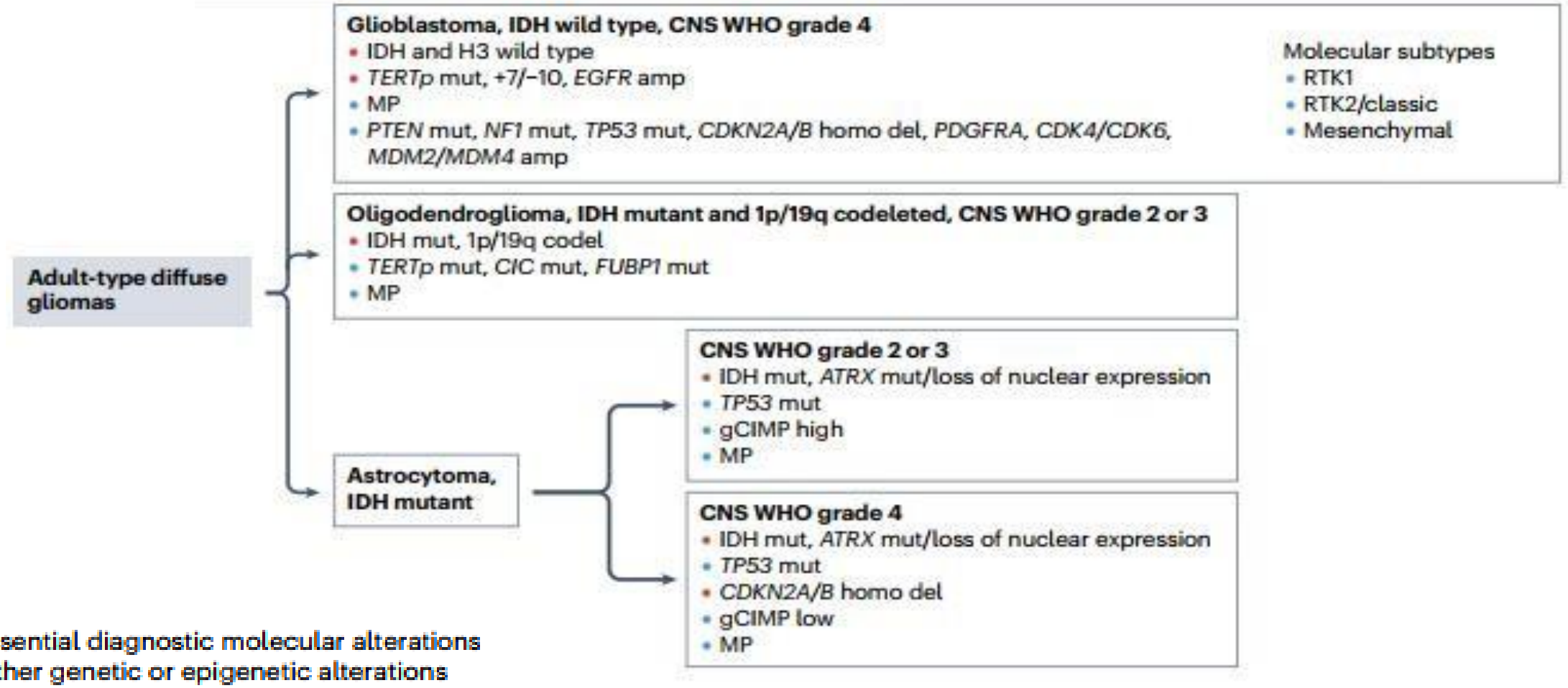
Astrocytoma grading based on genetic alterations WHO CNS5 2021



https://link.springer.com/article/10.1007/s40291-022-00612-3

OncoEdu
Research | Education | Treatment

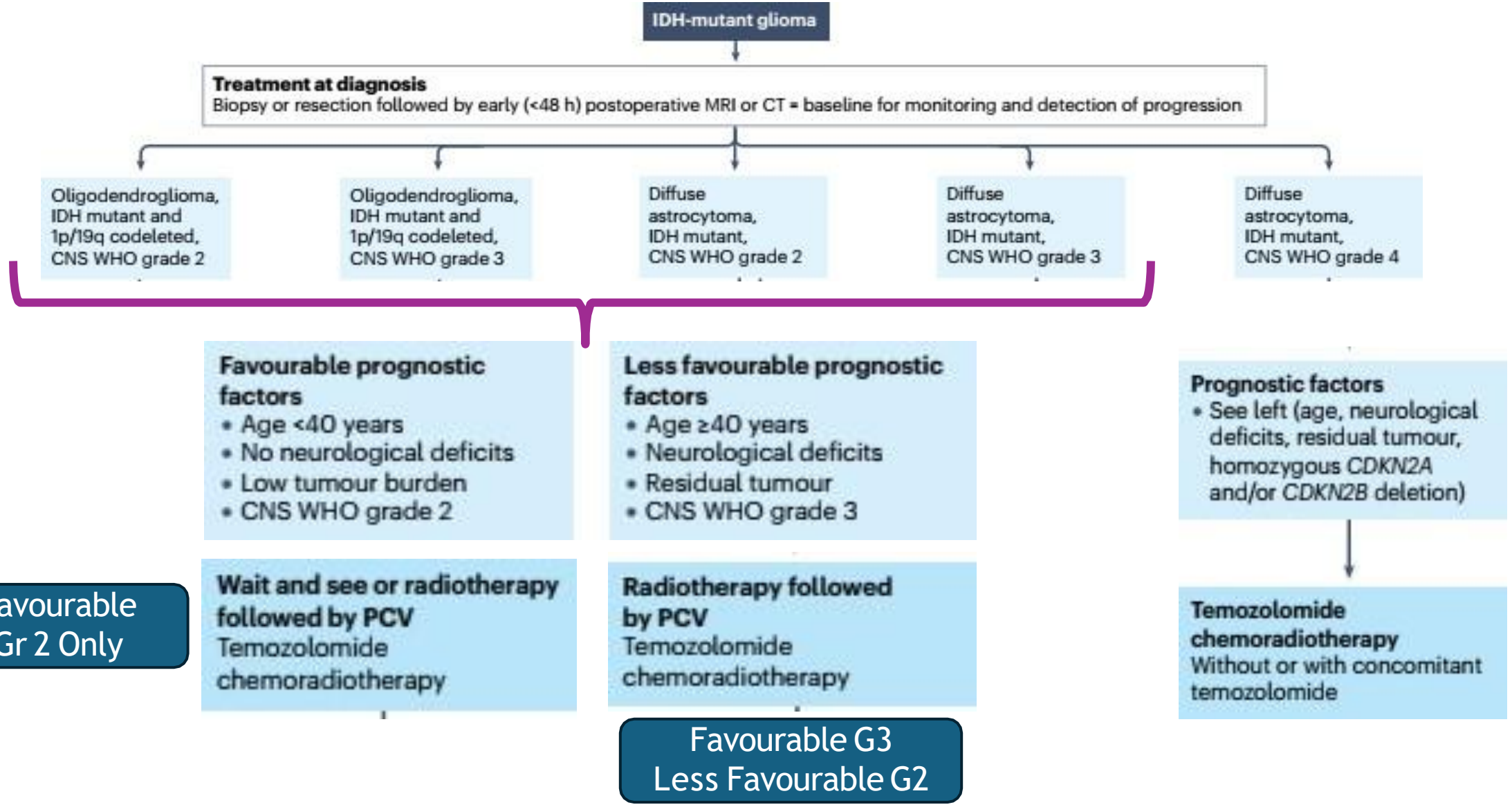
Adult Type Diffuse Gliomas



OncoEdu
Research | Education | Treatment

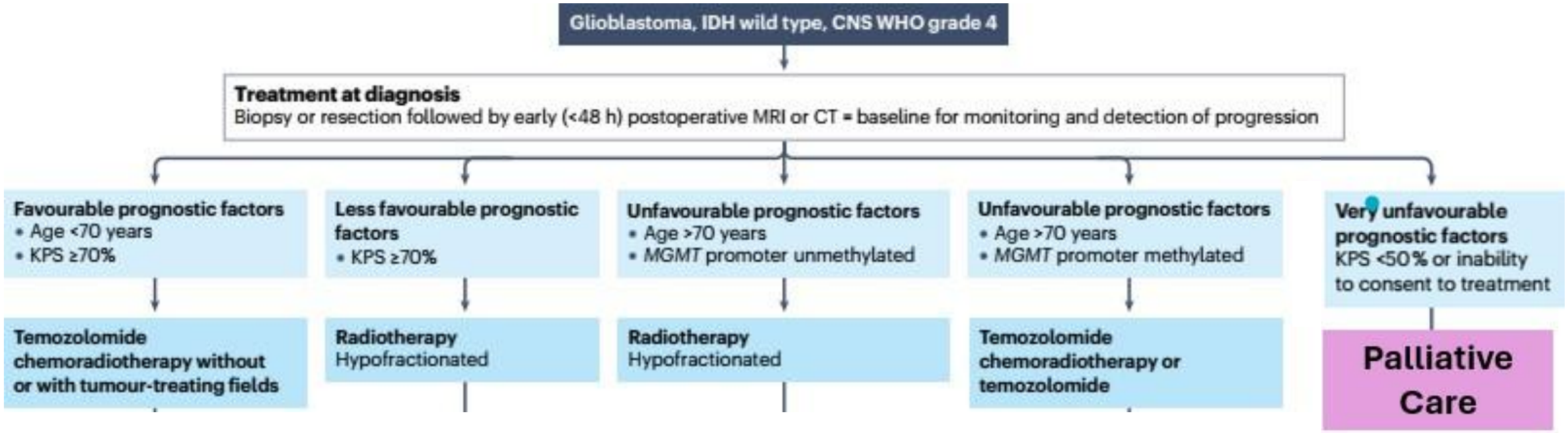
Nature Reviews Disease Primers | (2024) 10:33

IDH Mutant Glioma
Management



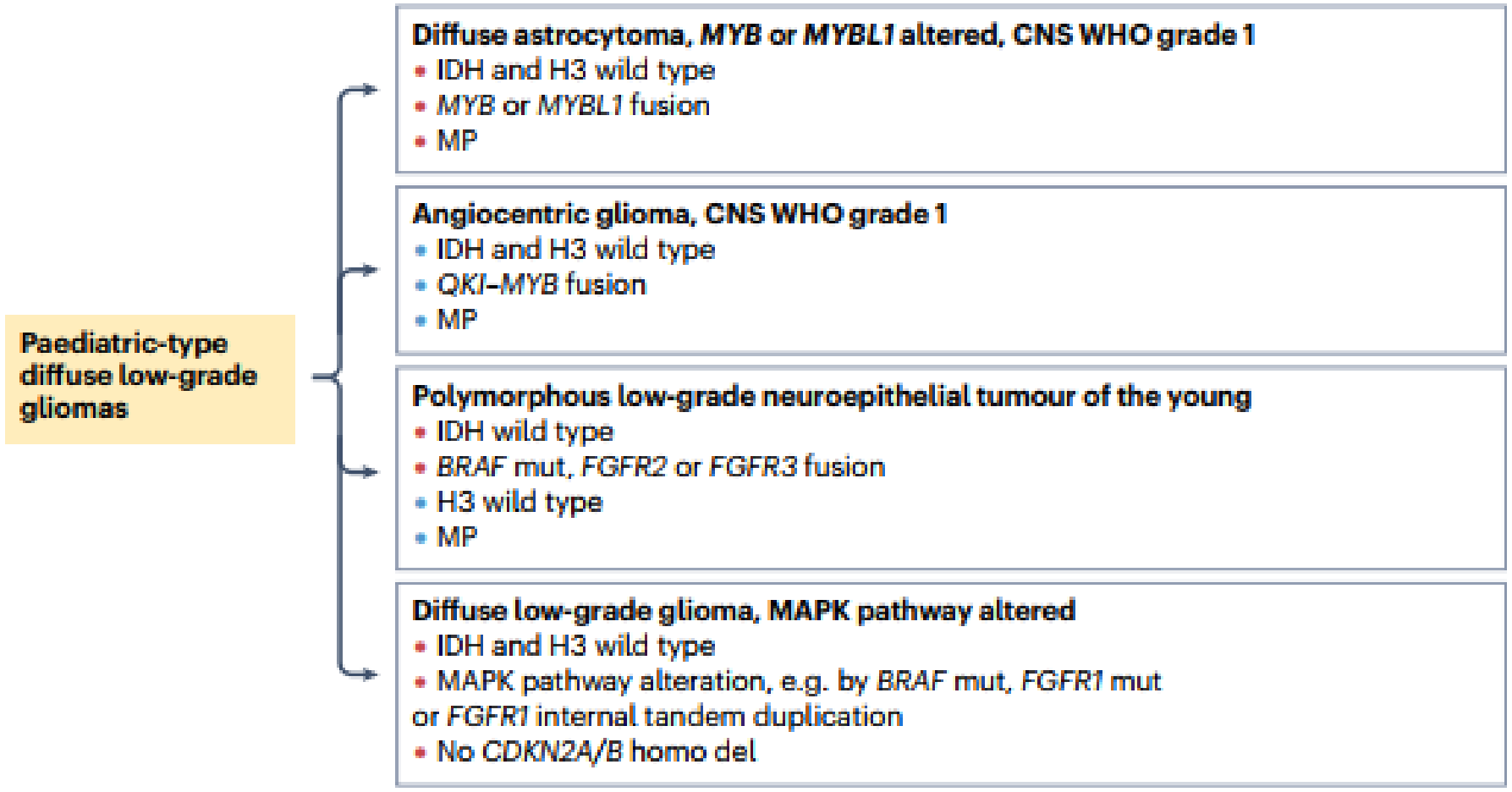
OncoEdu
Research | Education | Treatment

IDH wt / Glioblastoma
Management



OncoEdu
Research | Education | Treatment

Paediatric Type Diffuse Low Grade Gliomas

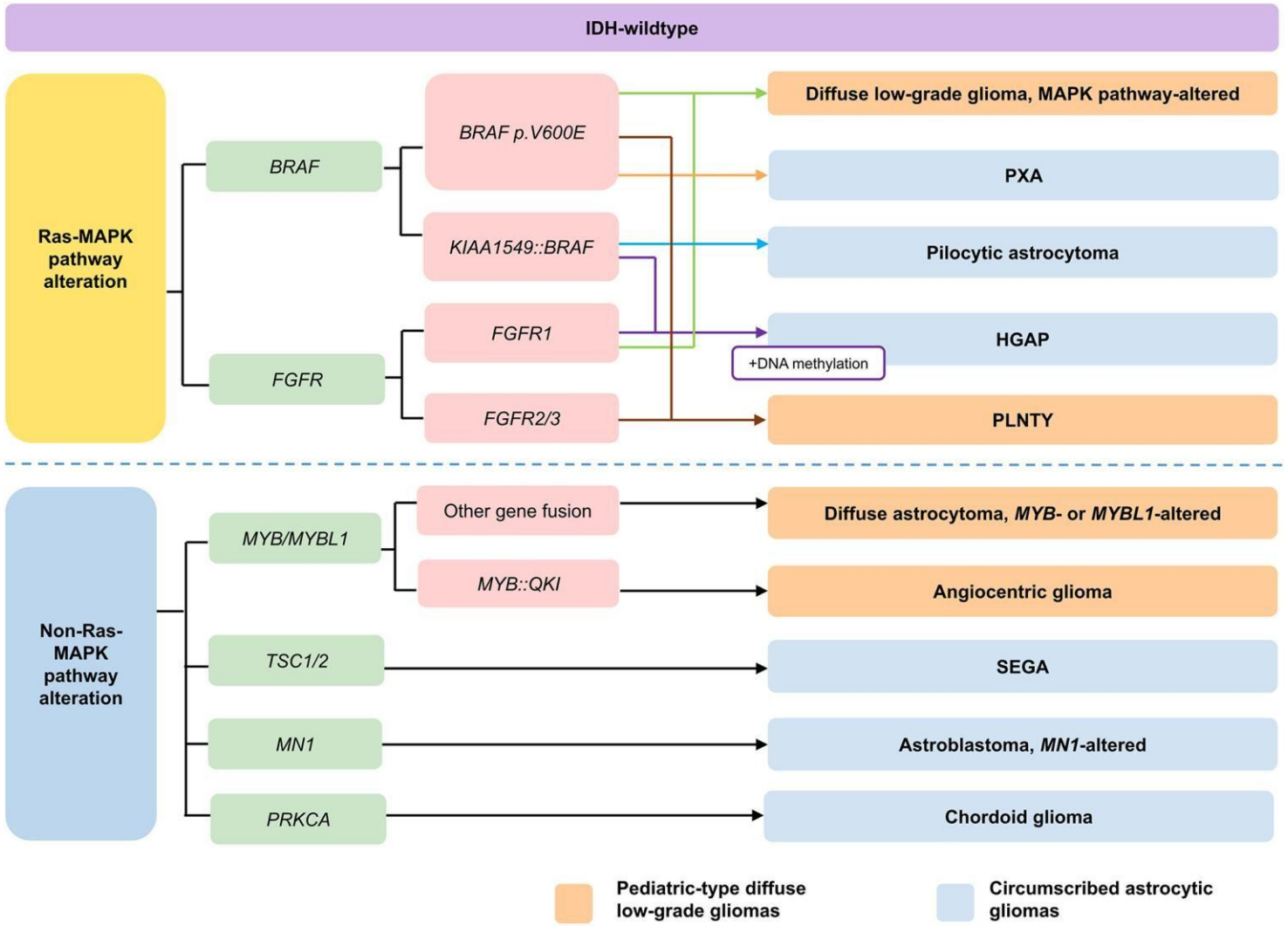


- Essential diagnostic molecular alterations
- Other genetic or epigenetic alterations

OncoEdu
Research | Education | Treatment

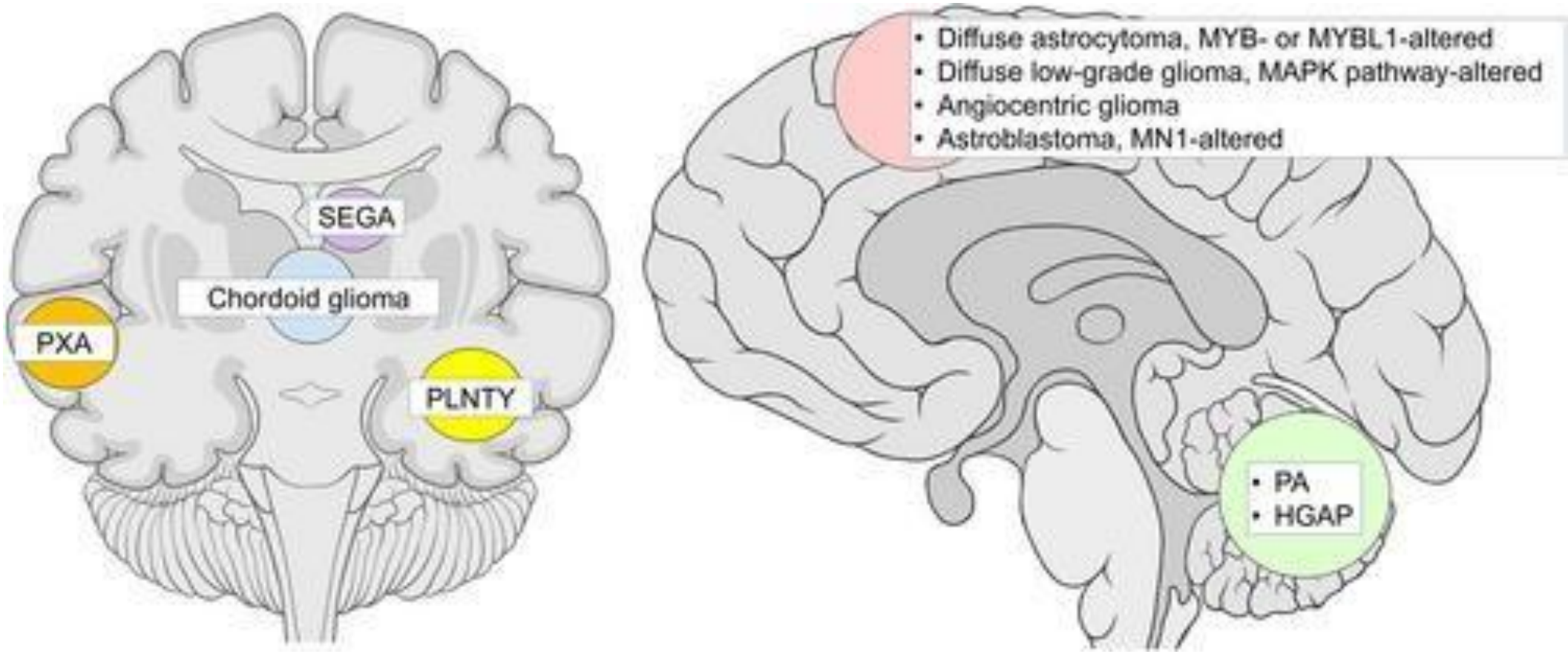
Nature Reviews Disease Primers | (2024) 10:33

Paediatric Type Diffuse Low Grade Gliomas



https://doi.org/10.1002/jmri.28740

Paediatric Type Diffuse Low Grade Gliomas



https://doi.org/10.1002/jmri.28740

Paediatric-type Diffuse Low grade gliomas
Management

Low Risk for Progression

High Risk for Progression

1

Carboplatin and Vincristine

Carboplatin and Vincristine are used for high-risk, traditional chemotherapy.

2

MEK Inhibitors

MEK Inhibitors are effective for high-risk, targeted therapy.

3

Monitoring

Monitoring is suitable for low-risk, traditional management.

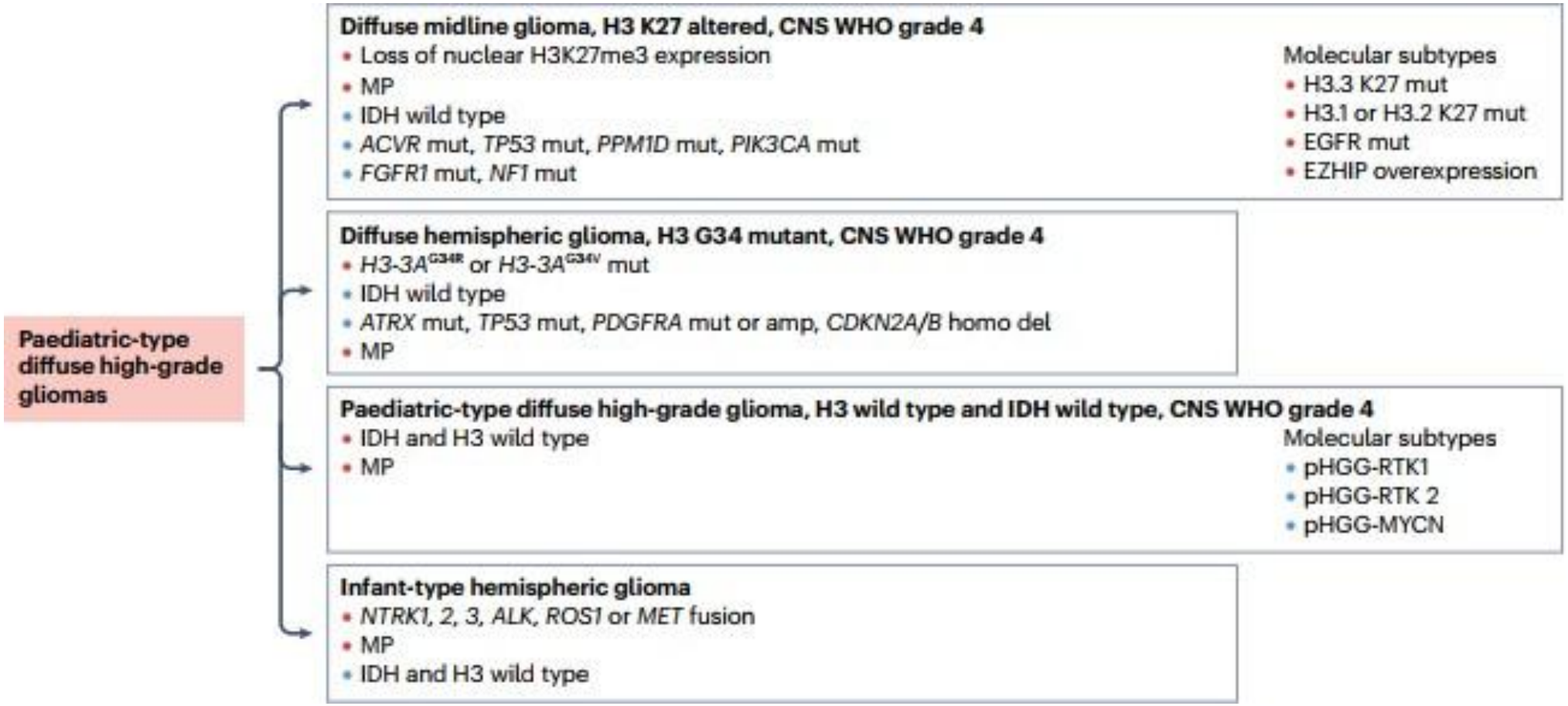
4

Molecularly Targeted Agents

Molecularly Targeted Agents are effective for low-risk, targeted therapy.

OncoEdu
Research | Education | Treatment

Paediatric Type Diffuse High Grade Gliomas

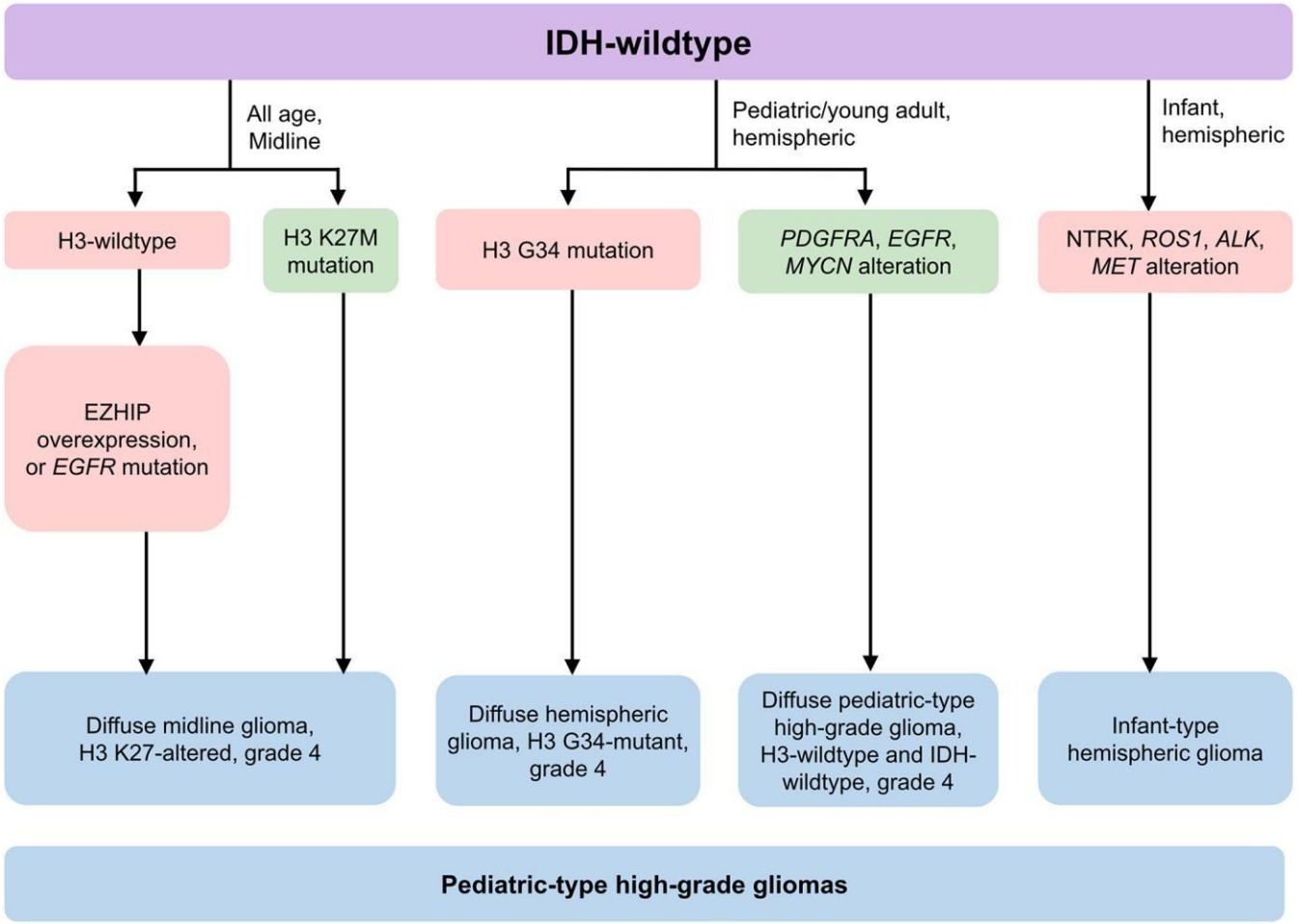


- Essential diagnostic molecular alterations
- Other genetic or epigenetic alterations

OncoEdu
Research | Education | Treatment

Nature Reviews Disease Primers | (2024) 10:33

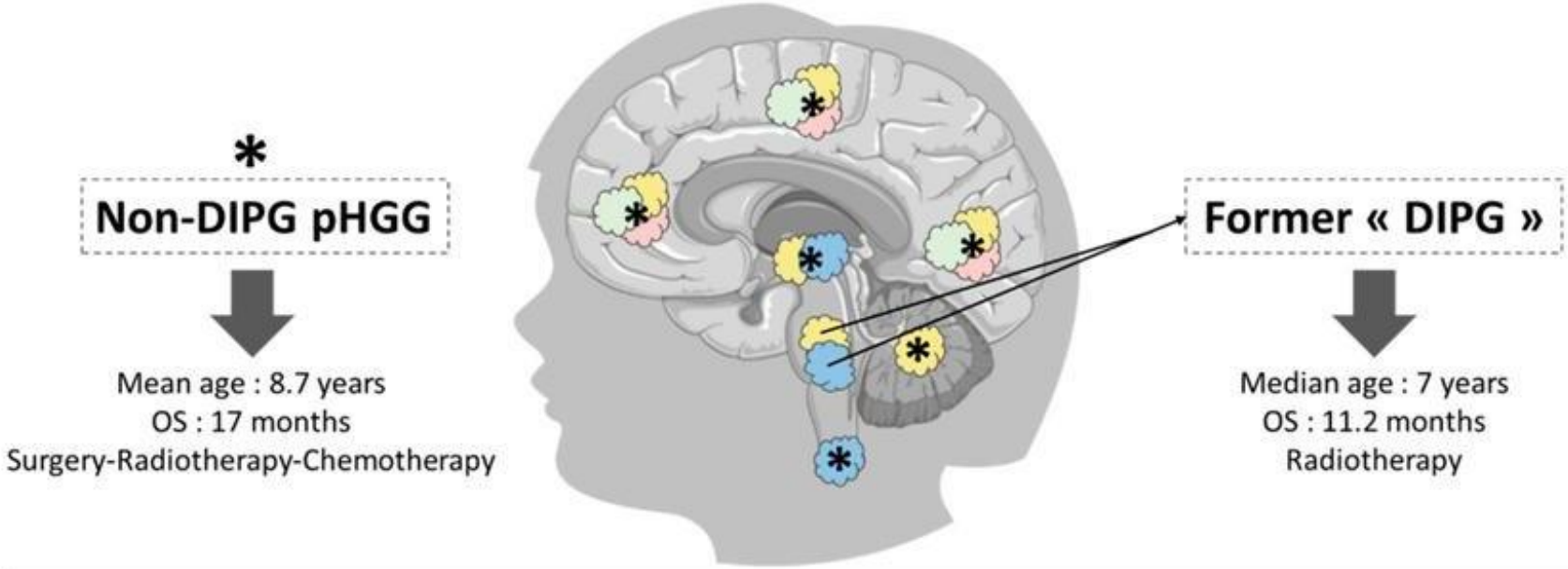
Paediatric Type Diffuse High Grade Gliomas
Classification



https://doi.org/10.1002/jmri.28740

OncoEdu
Research | Education | Treatment

Paediatric Type Diffuse High Grade Gliomas
Prognosis

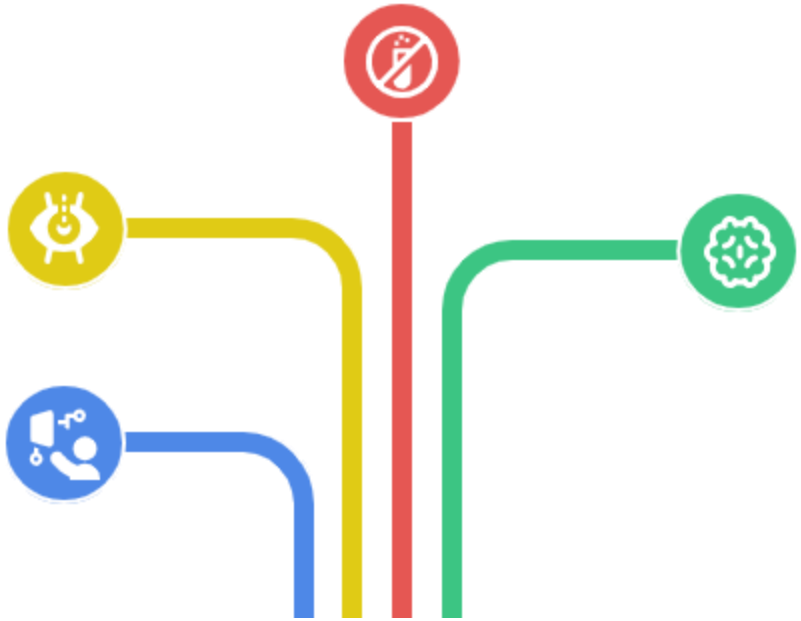


WHO CNS5 pHGG subtypes	Locations	Molecular characteristics
(a) DMG H3 K27-Altered	Thalamus, brainstem or spinal cord	Mutation K27M in *H3F3A* or *HIST1H3B* ; *EZHIP* overexpression
(b) Diffuse hemispheric glioma, H3 G34-mutant	Cerebral hemispheres	Mutation G34R or G34V in *H3F3A*
(c) Diffuse pHGG H3-WT and IDH-WT	Supratentorial, brain stem or cerebellum	MYCN or RTK1 or RTK2 amplification etc.
(d) Infant-type hemispheric glioma	Cerebral hemispheres	Fusion genes *ALK*, *ROS1*, *NTRK1/2/3*, or *MET*

Paediatric-type diffuse High grade gliomas
H3K27 Altered / Diffuse midline glioma
Management

Avoid Chemotherapy

Traditional chemotherapeutics like TMZ are ineffective due to lack of MGMT promoter methylation.



Focal Radiotherapy

Standard of care for these tumours.

Stereotactic Biopsy

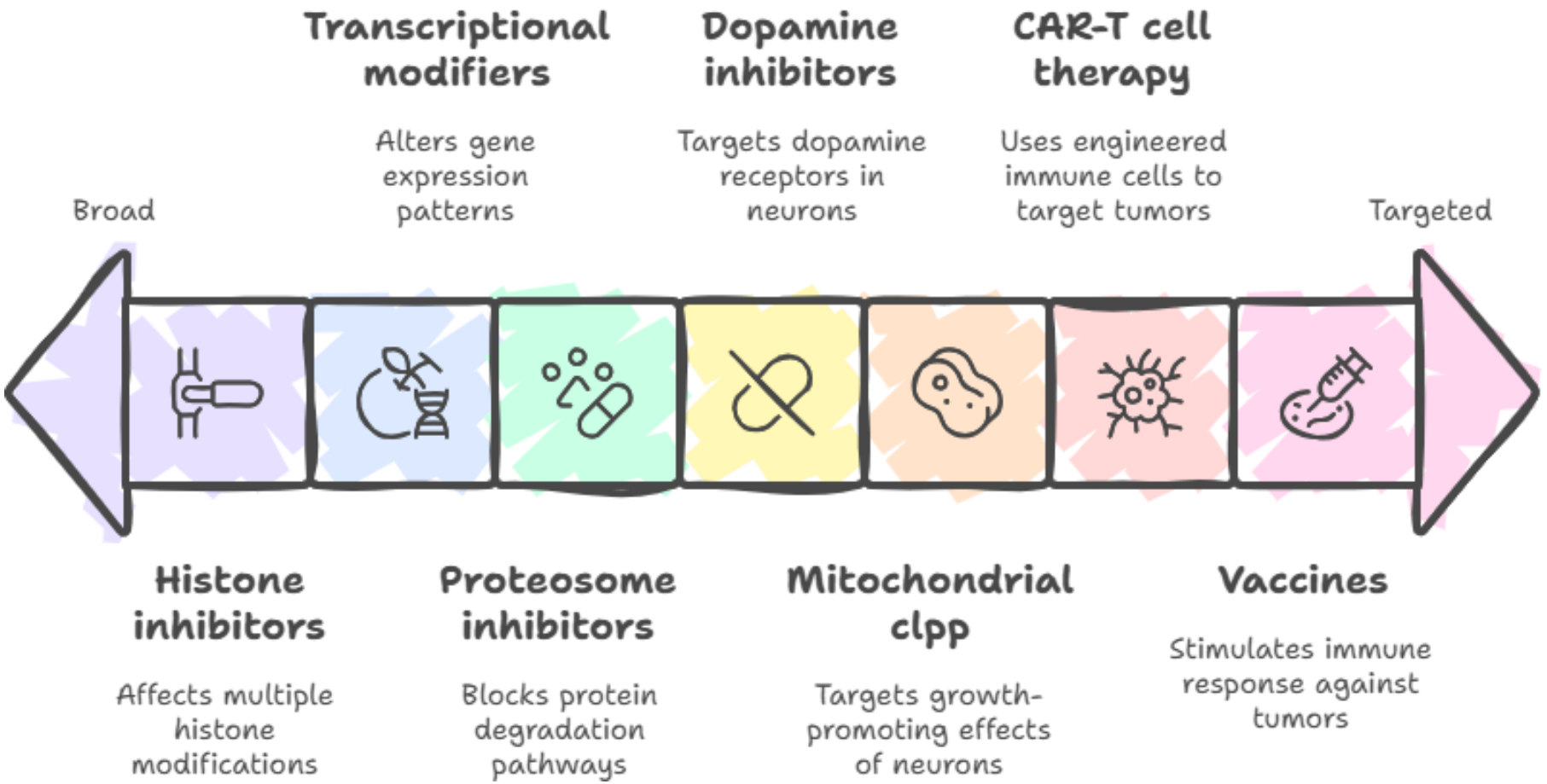
Essential for molecular diagnosis and clinical trial enrolment due to infeasibility of surgical resection.

Re-irradiation

Offers potential benefits in symptom improvement and survival at progression.

OncoEdu
Research | Education | Treatment

Paediatric-type diffuse High grade gliomas
Management - Epigenetic Therapy



OncoEdu
Research | Education | Treatment

H3 G34-mutant Diffuse hemispheric gliomas
Management

Disseminated Disease

Whole-Brain Radiotherapy

Whole-brain radiotherapy addresses widespread disease with low methylation.

MGMT Unmethylated

Focal Radiotherapy

Local field radiotherapy targets localized disease with low methylation.

Limited Disease

Temozolomide with Radiotherapy

Temozolomide enhances radiotherapy effectiveness in widespread, methylated tumors.

MGMT Methylated

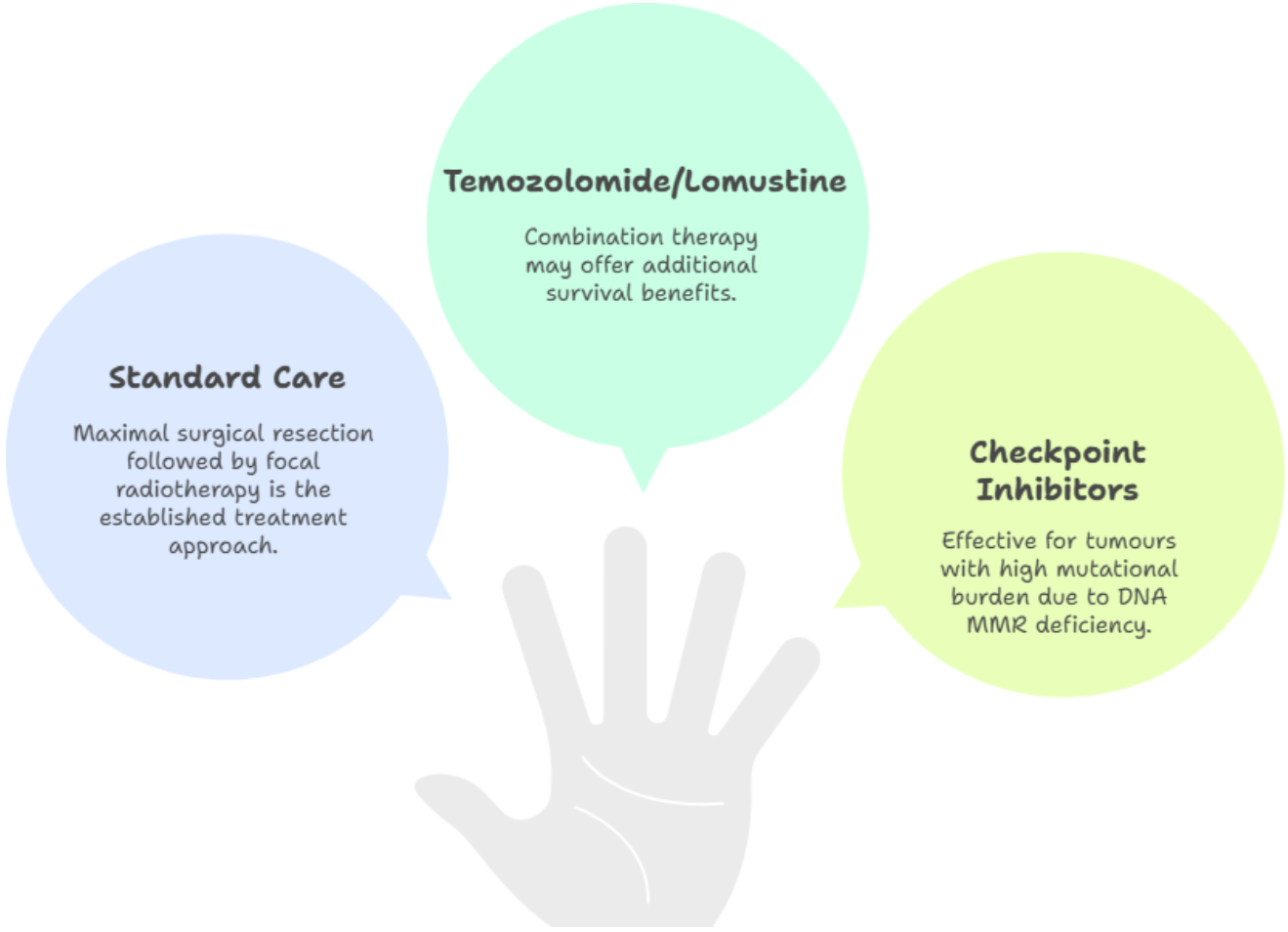
Surgical Resection

Surgical resection is effective for localized, methylated tumors.

OncoEdu
Research | Education | Treatment

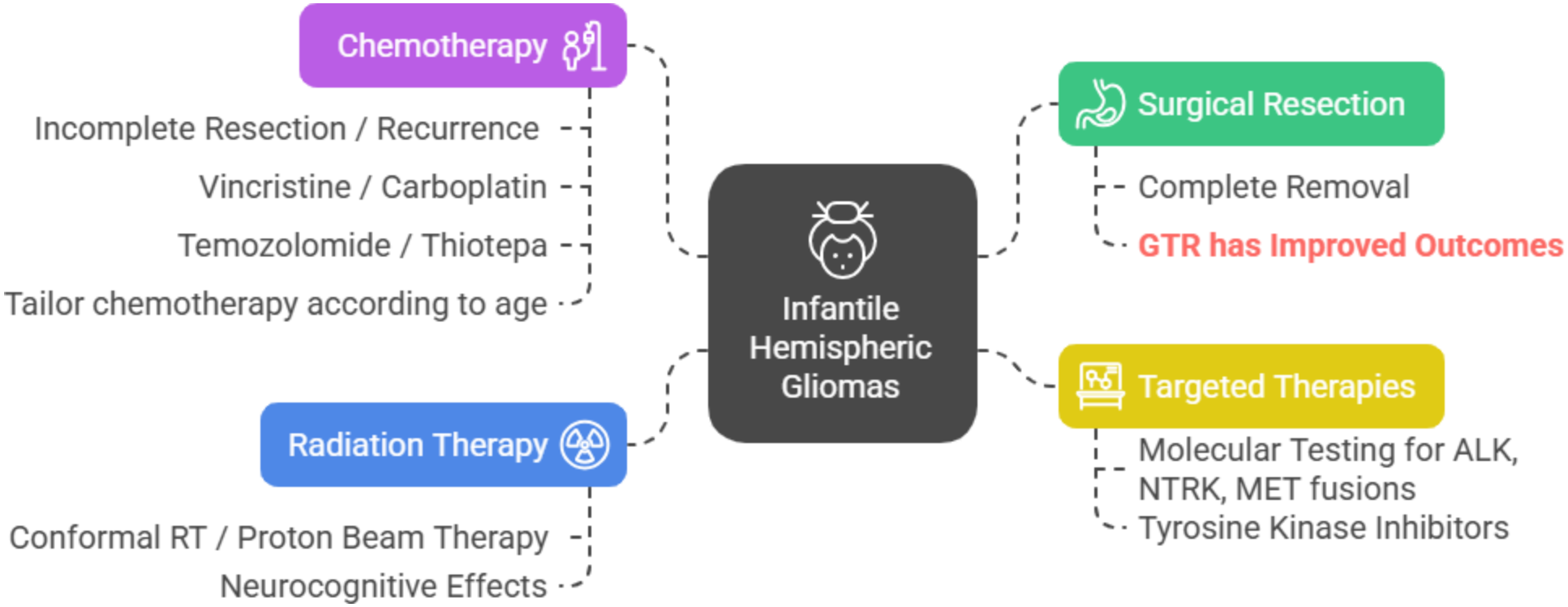
Paediatric-type diffuse High grade gliomas H3 Wild type / IDH wt

Management



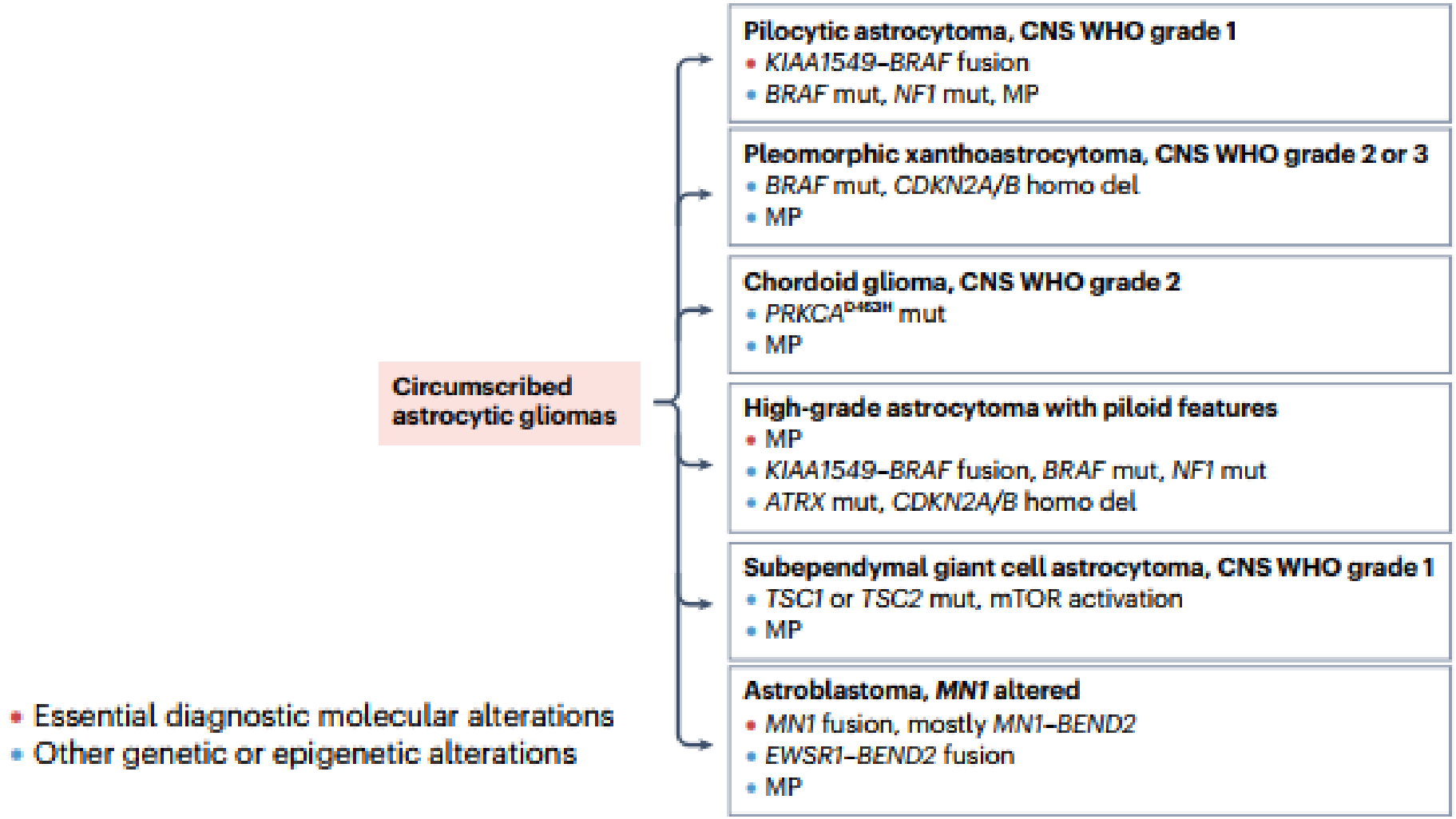
OncoEdu
Research | Education | Treatment

Paediatric-type diffuse High grade gliomas
Infantile Hemispheric Gliomas
Management



OncoEdu
Research | Education | Treatment

Circumscribed Astrocytic Gliomas

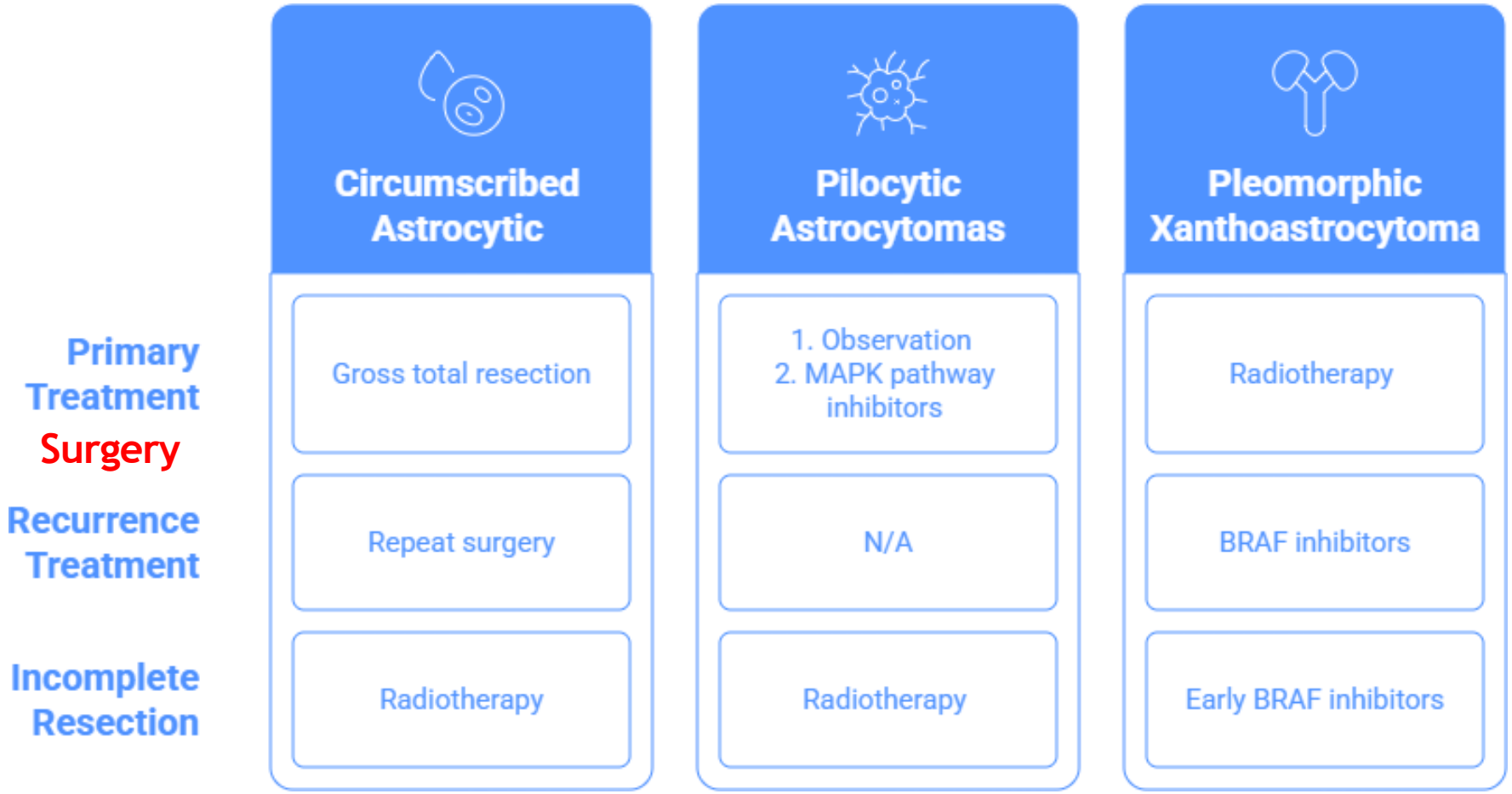


OncoEdu
Research | Education | Treatment

Nature Reviews Disease Primers | (2024) 10:33

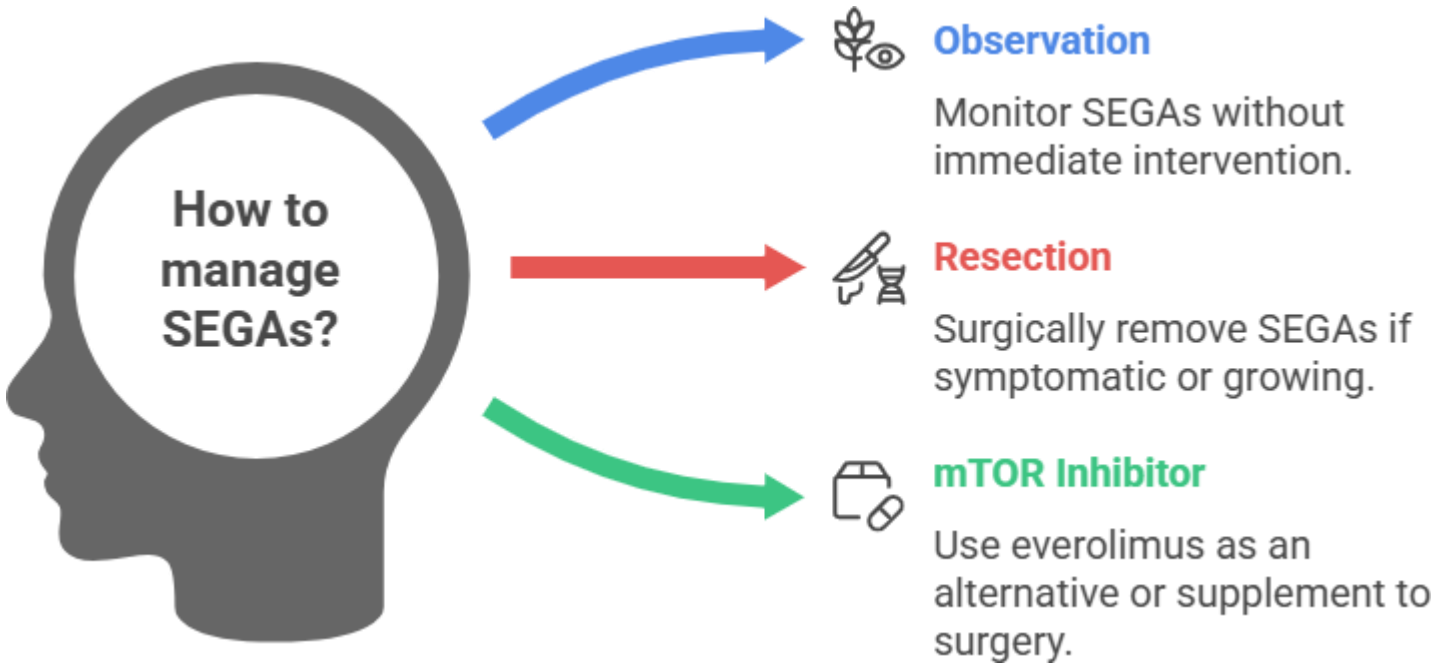
Circumscribed astrocytic gliomas

Management

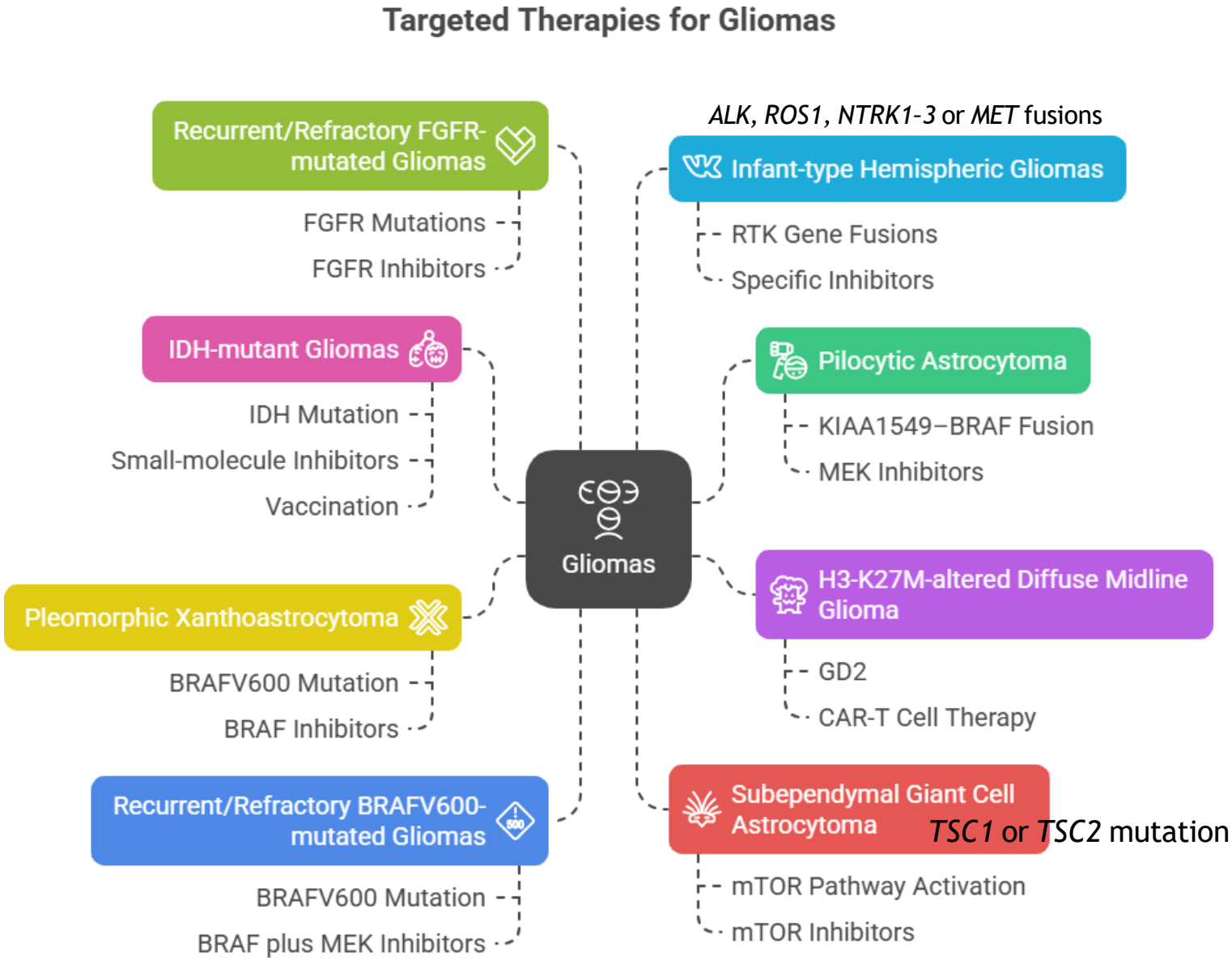


Circumscribed astrocytic gliomas

Management



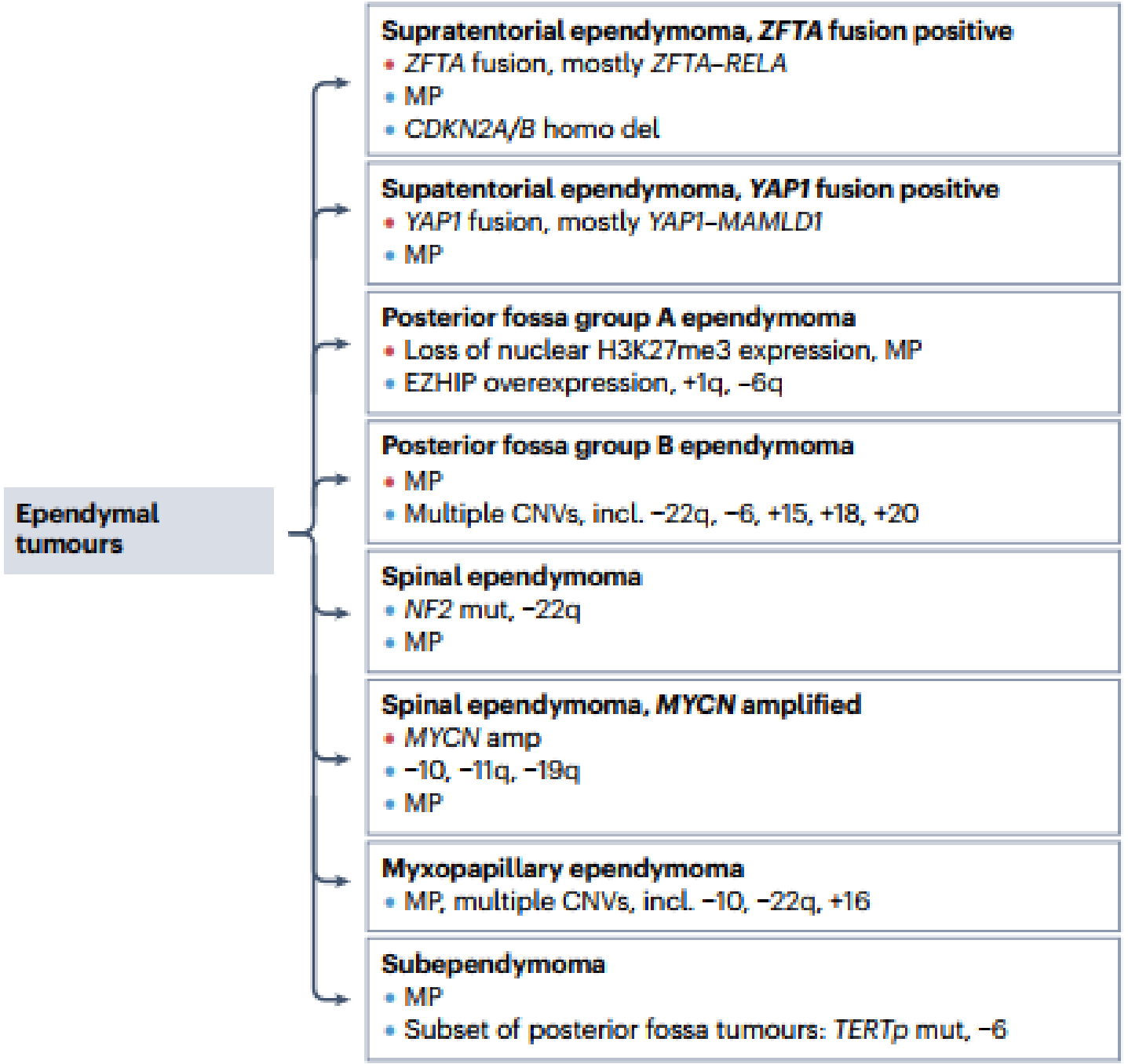
Emerging molecularly targeted treatment options for patients with glioma



OncoEdu
Research | Education | Treatment

Ependymal Tumors

- Essential diagnostic molecular alterations
- Other genetic or epigenetic alterations



Ependymomas
Workup required

- History C Physical Examination – evaluate for symptoms of elevated ICP

- **Imaging –** MRI of brain C spine with and without contrast
- Lumbar puncture for CSF cytology
- If Raised ICT – Consider Endoscopic Third ventriculostomy Vs VP Shunt

If ICP elevated, wait 10-14 days postop to do LP to avoid risk of herniation

- **Maximal safe resection!!**
- Postoperative MRI to assess extent of resection (Within 48 hrs)
- CSF Cytology if not done preoperatively (After 2 weeks postop)
- MRI Spine with contrast if not done preoperatively (After 2 weeks postop)

European standard clinical practice recommendations for newly diagnosed ependymoma of childhood and adolescence. EJC Paediatric Oncology. 2025 Apr 9:100227

Ependymomas
Staging - Residual disease and metastases

Residual disease stage	Definition
R0	No residual tumour
R1	No residual tumour based on imaging, but small remaining lesion described by neurosurgeon; or unknown neurosurgical result
R2	Residual tumour <5mm in all diameters, not measurable in 3 planes
R3	Measurable residual tumour in 3 planes or one diameter ≥5mm
R4	No relevant changes compared to pre-surgery imaging
RX	Presence of residual tumour cannot be assessed

Metastatic stage	Definition
M0	No evidence of metastatic disease
M1	Microscopic tumour cells found in CSF
M2	Gross nodular seeding in cerebellum, cerebral subarachnoid space, or in the third or fourth ventricles
M3	Gross nodular seeding in spinal subarachnoid space
M4	Metastasis outside the central nervous system

European standard clinical practice recommendations for newly diagnosed ependymoma of childhood and adolescence. EJC Paediatric Oncology. 2025 Apr 9:100227

Ependymomas
Management

Maximal Safe Resection
Prognostic!

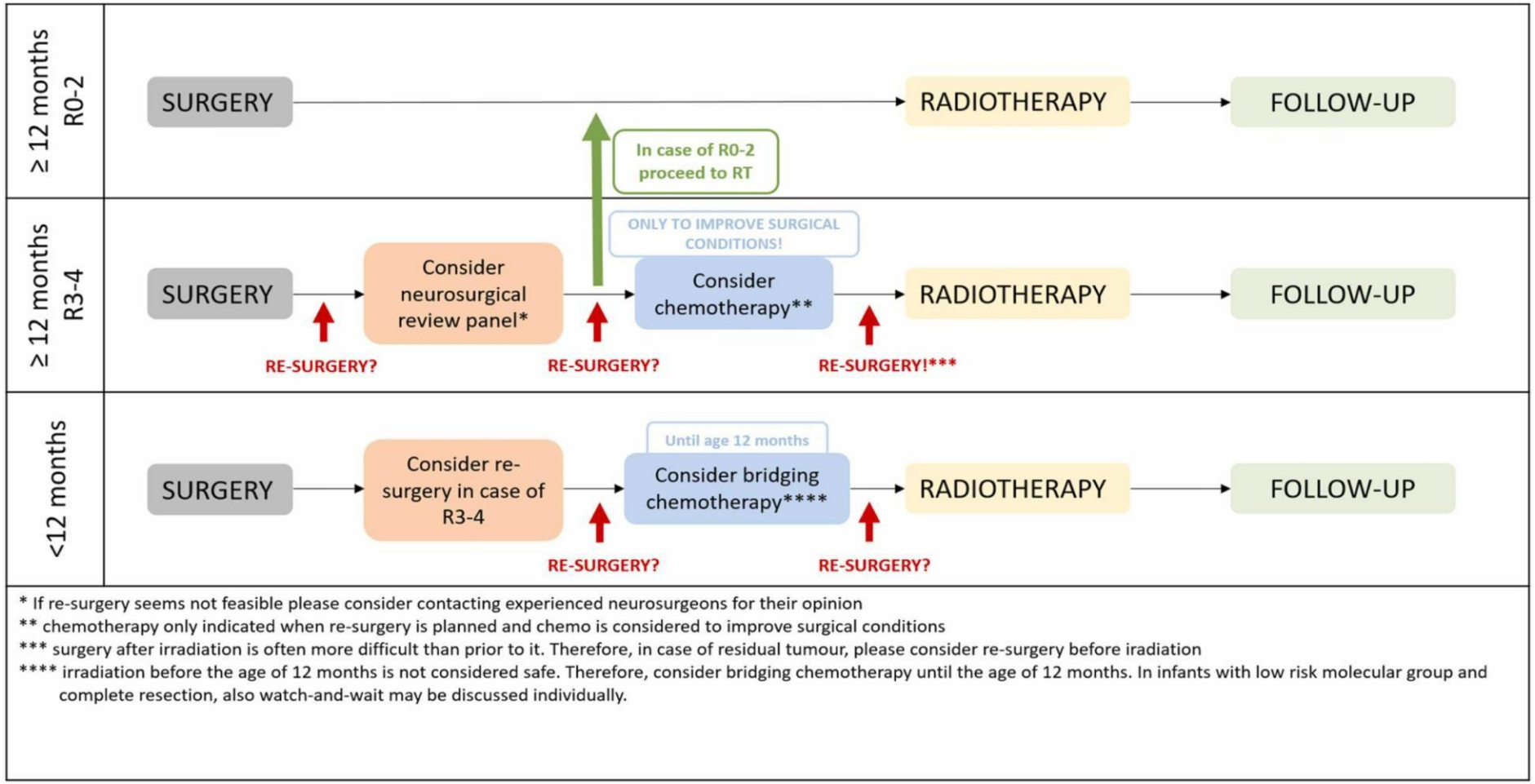
	5 yr OS	5 yr PFS
GTR	67 - 80%	51 - 75 %
STR	22 - 47 %	0-26 %

Surgery	Aim for GTR	STR is worse [Think of Resurgery Chemo→ Surgery]	
Complete workup s determine stage/risk	MRI spine (Staging)	MRI brain (postop within 72 hours) To assess Residual	LP postop (10–14 days postop) Staging
Radiation	Tumor bed 59.4 Gy (54 Gy if 12-18 mon)	CSI to 36 Gy if M+	Start 1 month postop
Chemotherapy	To convert STR to resectable disease, or on trial	Bridging Chemotherapy if Age < 12 months	Pre- or post-RT, not concurrent

OncoEdu
Research | Education | Treatment

Intracranial ependymomas
Management

R Stage	Definition
R0	No residual tumor
R1	No residual on imaging. Surgeon describes a small residual
R2	Residual <5mm. Not measurable in 3 planes
R3	Residual > 5mm in one plane OR Measurable in 3 planes
R4	Same as Presurgery
Rx	Cannot be assessed



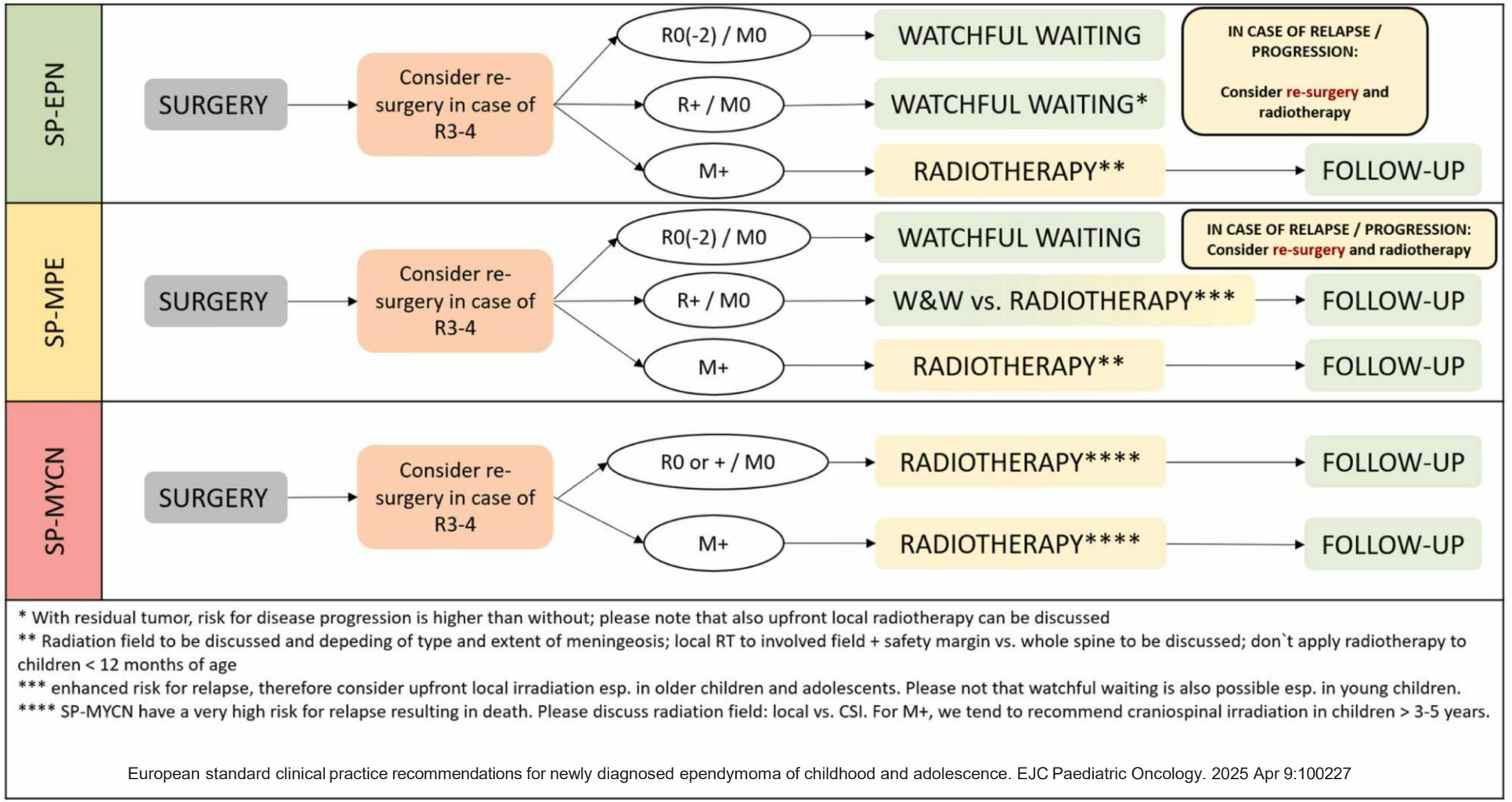
* If re-surgery seems not feasible please consider contacting experienced neurosurgeons for their opinion
** chemotherapy only indicated when re-surgery is planned and chemo is considered to improve surgical conditions
*** surgery after irradiation is often more difficult than prior to it. Therefore, in case of residual tumour, please consider re-surgery before iradiation
**** irradiation before the age of 12 months is not considered safe. Therefore, consider bridging chemotherapy until the age of 12 months. In infants with low risk molecular group and complete resection, also watch-and-wait may be discussed individually.

European standard clinical practice recommendations for newly diagnosed ependymoma of childhood and adolescence. EJC Paediatric Oncology. 2025 Apr 9:100227

OncoEdu
Research | Education | Treatment

Spinal ependymomas
Management

R Stage	Definition
R0	No residual tumor
R1	No residual on imaging. Surgeon describes a small residual
R2	Residual <5mm. Not measurable in 3 planes
R3	Residual > 5mm in one plane OR Measurable in 3 planes
R4	Same as Presurgery
Rx	Cannot be assessed



European standard clinical practice recommendations for newly diagnosed ependymoma of childhood and adolescence. EJC Paediatric Oncology. 2025 Apr 9:100227

OncoEdu
Research | Education | Treatment

Ependymomas
RT Doses and Margin

Trial	Trial Period	Age Restriction (months)	Target Volume	CTV Margin (cm)	Dose (cGy/CcGE)
US Cooperative Group Studies					
POG-9132	1991-1994[43]	> 36	Preoperative	2.0	69.6/1.2 BID
CCG-9942	1995-1999[42]	> 36	Preoperative	1.5	59.4/1.8 55.8/1.8
ACNS0121	2003-2007[2]	> 12	Postoperative	1.0	59.4/1.8 54.0/1.8
ACNS0831	2010-present[3]	> 12	Postoperative	0.5	59.4/1.8 54.0/1.8
Single- or multi-institutional studies					
St Jude Children's Research Hospital	1997-2003[5]	> 12	Postoperative	1.0	59.4/1.8 54.0/1.8
PSI	2004-2013[39]	> 12	Postoperative	0.5-1.0	59.4/1.8
French cohort	2000-2013[40]	> 36	No details	No details	59.4/1.8 54.0/1.8
Italian cohort	2003-present[41]	> 36	No details	No details	59.4/1.8 67.8/1.8-2.0

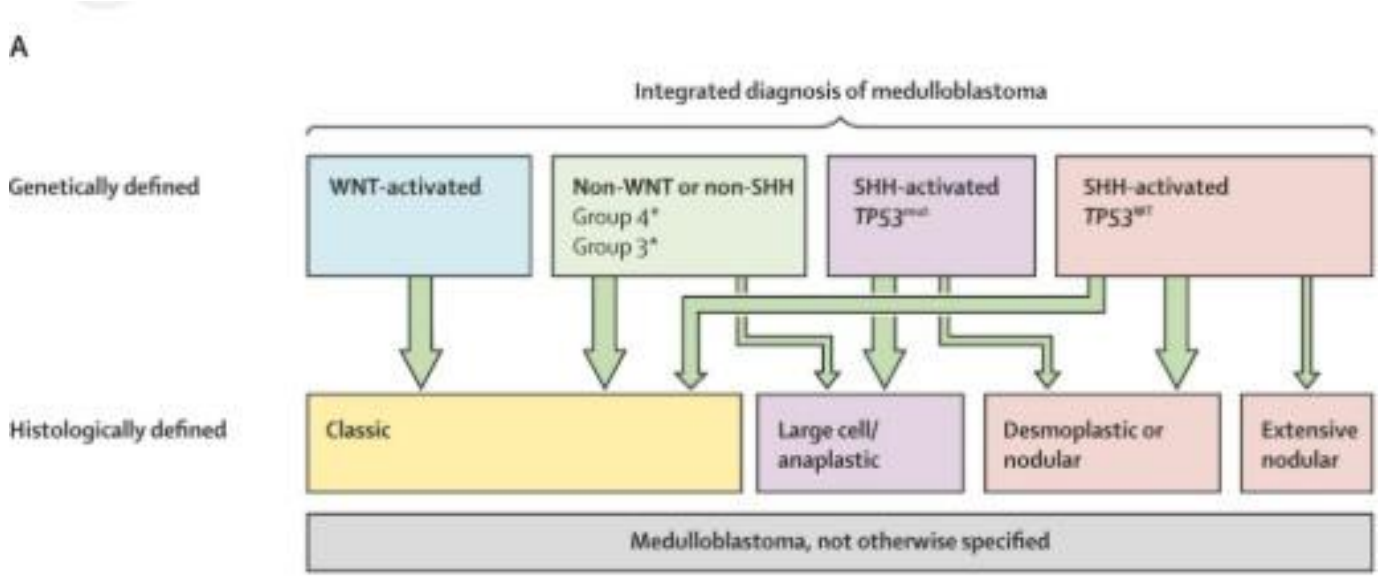
GTV
CTV
PTV

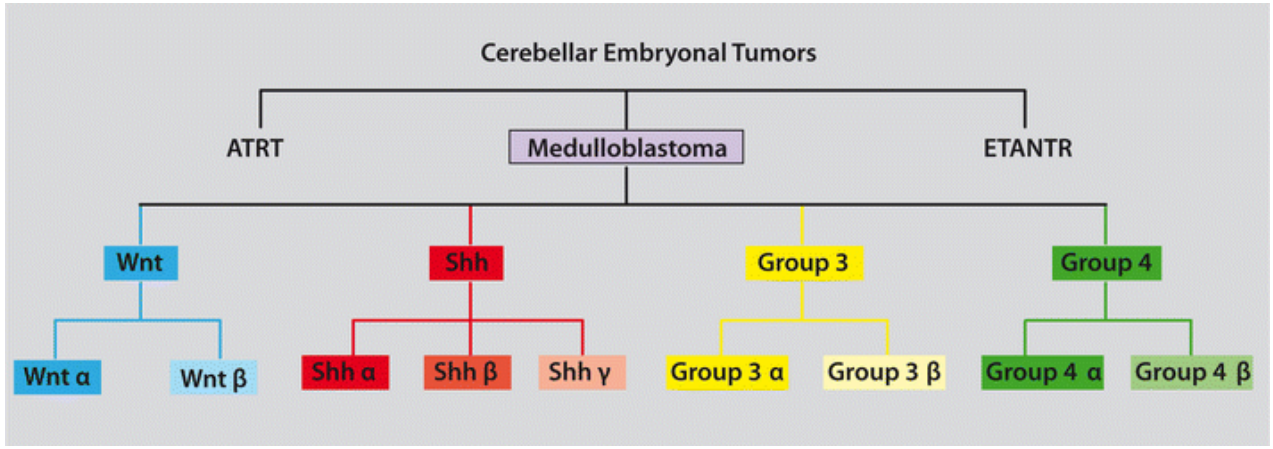
Photons 59.4 Gy
Age < 18m - 54 Gy
Protons 54 Gy

Ependymomas
Management – Focal RT Vs CSI

Scenario / Factor	Preferred RT Modality	Rationale / Notes
Age < 3 years	Generally avoid CSI	CSI is generally avoided in this age group. When used protons preferable
PF-A ependymoma, localized	Focal RT	Poor prognosis, but CSI not standard unless disseminated.
ST-ZFTA, localized (ST-EPN)	Focal RT	No CSI even with molecular risk factors, unless metastases are present.
ST-YAP1 (ST-EPN)	Focal RT	Excellent prognosis; de-escalation may be considered in clinical trials.
MYCN-amplified spinal ependymoma	CSI + boost	Aggressive behavior; CSI considered, due to frequent dissemination.
Disseminated myxopapillary ependymoma	CSI + boost	Especially in sacrococcygeal variants with high dissemination risk.
Metastatic disease (M1+, M2, M3)	CSI + boost	CSI recommended.
1q gain alone (PF-A)	Borderline	Does not indicate CSI by itself.
13q loss (PF-B)	Borderline	Does not indicate CSI by itself.

Medulloblastoma Classification





https://doi.org/10.1016/S1470-2045(19)30669-2

Medulloblastoma
Risk Stratification - Developing Countires

Table 3
Risk stratification in Medulloblastoma as per the SIOP Pediatric Oncology in Developing Countries (PODC) Committee.

Standard risk Medulloblastoma	High-risk Medulloblastoma
All of the following:	**Any one** of the following
➢ > 3yrs of age	➢ < 3yrs of age
➢ < 1.5cm2 residual tumor after resection (complete resection)	➢ >1.5cm2 residual (Subtotal resection)
➢ CSF negative for tumor cells	➢ CSF positive for tumor cells
➢ MRI spine negative for leptomeningeal spread	➢ MRI spine with leptomeningeal spread
➢ Classic or Desmoplastic pathology	➢ Large cell or anaplastic subtype
➢ Complete staging if possible	➢ Incomplete staging

Pediatric Hematology Oncology Journal
Volume 8, Issue 2, June 2023, Pages 121-128

Medulloblastoma
Risk Stratification - Molecular Era

Chromosome 11 - Group 4 (Loss is Good)

Chromosome 14 - SHH (Loss is Bad)

	Low risk (<90% survival)	Standard risk (75-90% survival)	High risk (50-75% survival)	Very high risk (<50% survival)
WNT	Non-metastatic			
SHH		Non-metastatic **AND** *TP53* WT **AND** No *MYCN* amplification **No Chr 14 loss**	Metastatic **AND** *TP53* WT **-- OR --** Non-metastatic **AND** *MYCN* amplification	*TP53* mutation **Chr 14 loss**
Group 3		Non-metastatic **AND** No *MYC* amplification		Metastatic **AND** *MYC* amplification
Group 4	Non-metastatic **AND** Chromosome 11 loss	Non-metastatic **AND** No chromosome 11 loss	Metastatic	

Fig. 2. Patient risk stratication based on molecular and outcome criteria[61]. WNT : wingless, SHH : sonic hedgehog, M : male, F : female.

Medulloblastoma Management

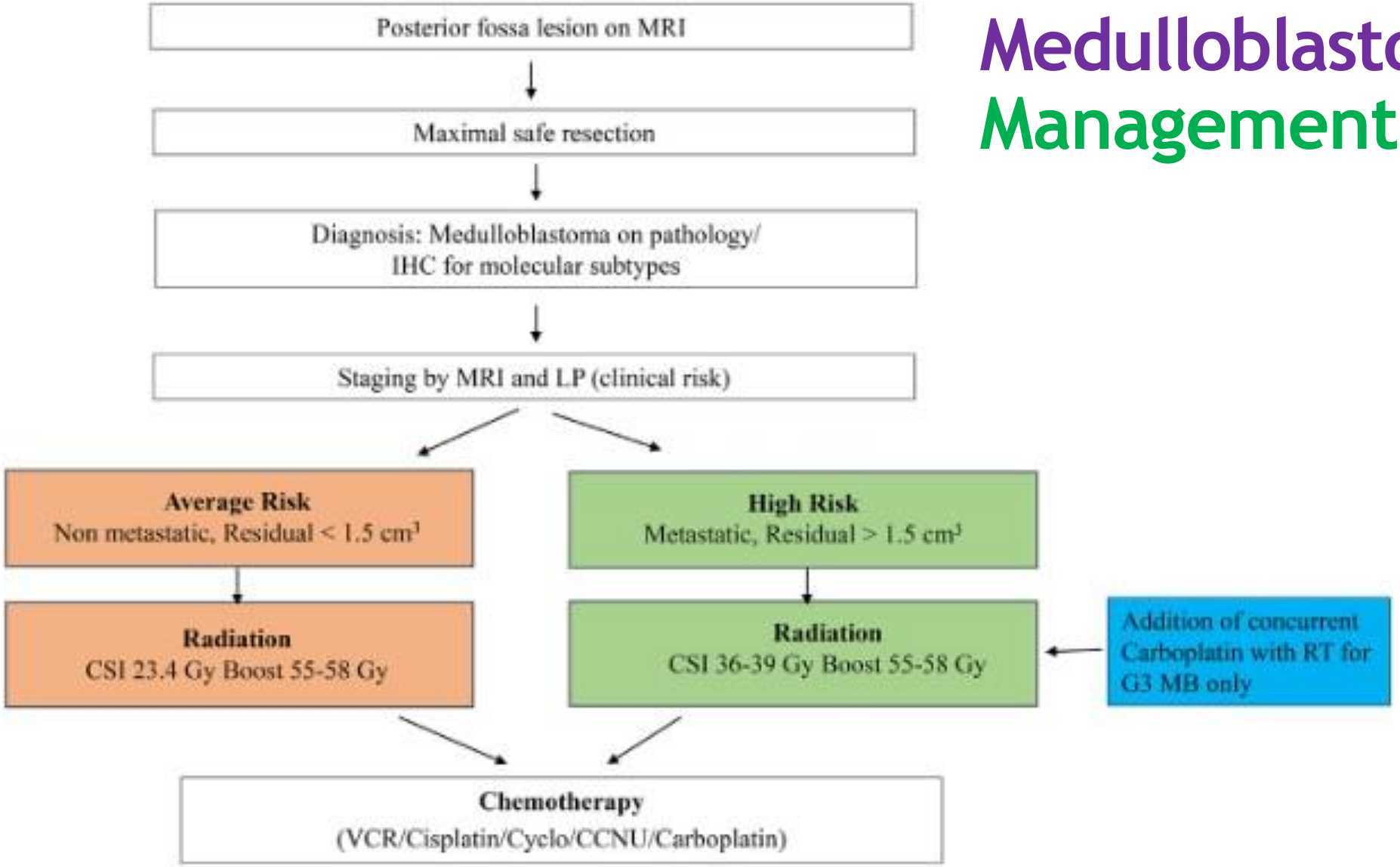


Fig. 1. Current schematic treatment for childhood MB (3yrs–21yrs).

Pediatric Hematology Oncology Journal
Volume 8, Issue 2, June 2023, Pages 121-128

Meningioma Classification

Grade 1 / Benign

Mitosis < 4 per 10 HPF

Grade 2 / Atypical

Mitosis 4-19 per 10 HPF

OR

Clear cell or chordoid histology
Brain invasion

OR

3/5 of the following
1. Necrosis
2. High NC ratio
3. Prominent Nucleoli
4. Architectural Sheeting
5. Hypercellularity

Grade3 / Anaplastic

Mitosis ≥20 per HPF

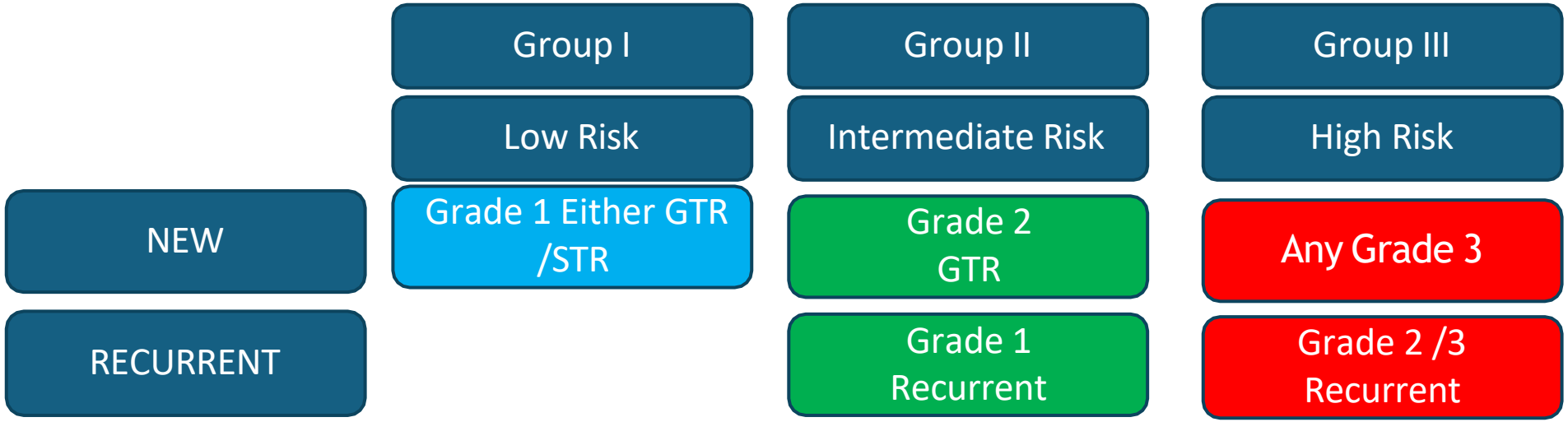
OR

Papillary or Rhabdoid histology

OR

Anaplasia

Meningiomas
RTOG 053G - Risk Categories

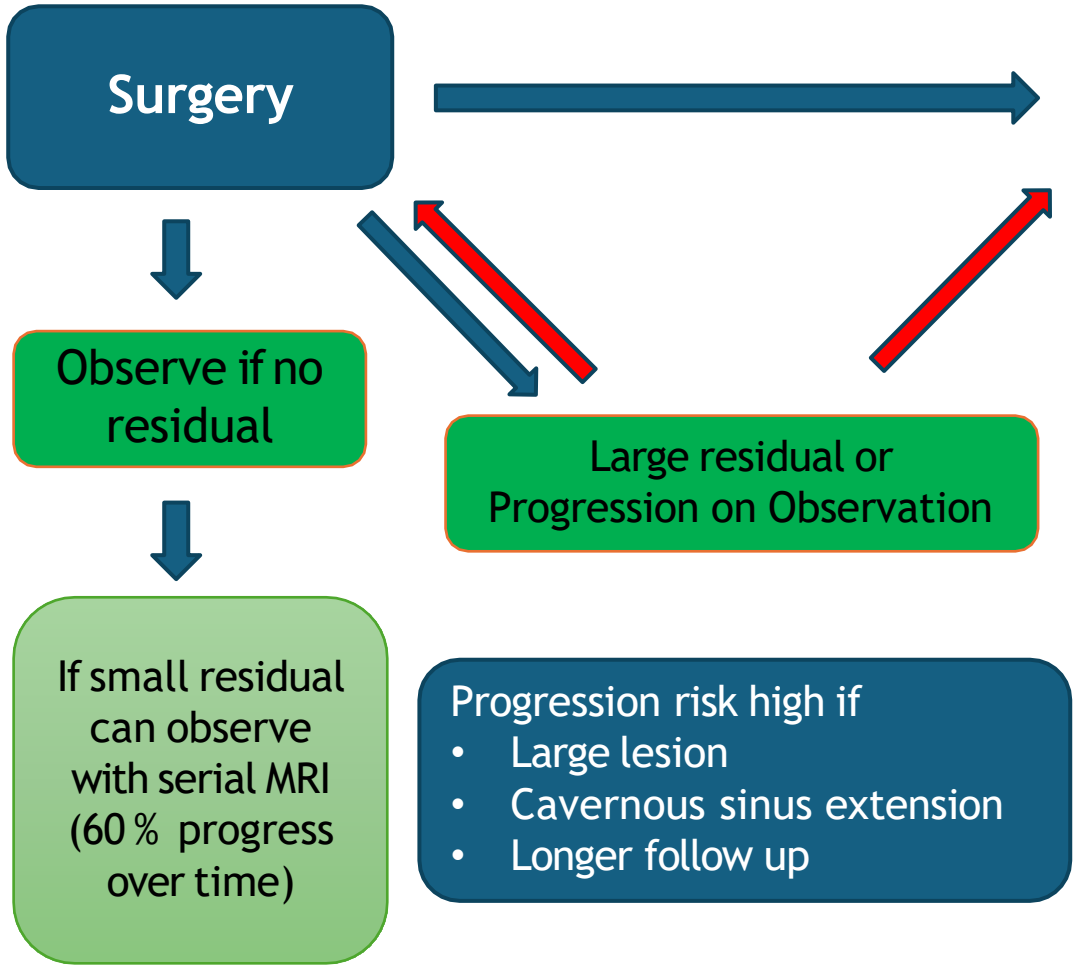


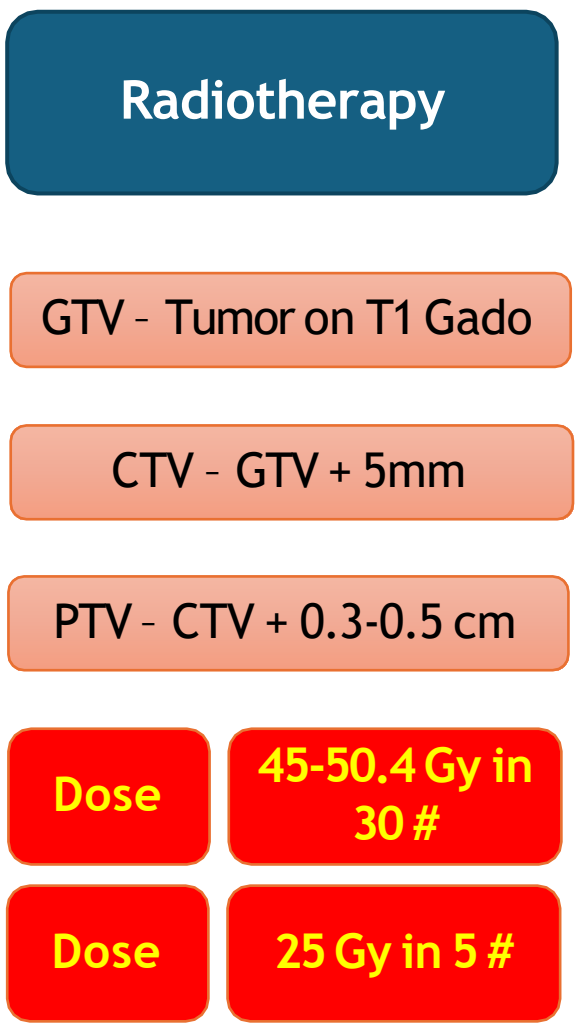
Meningiomas

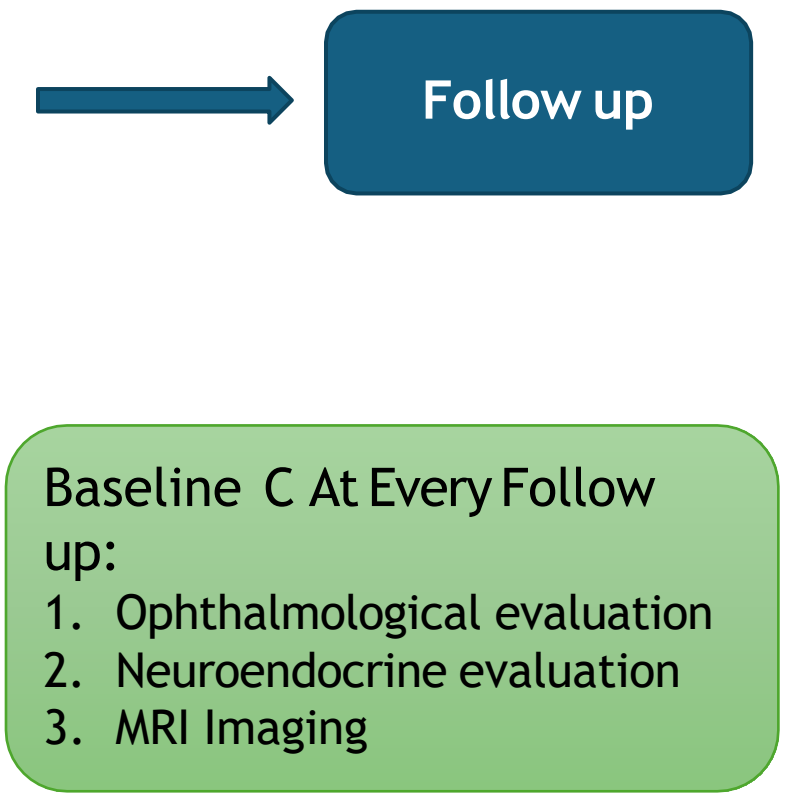
Management as per RTOG 053G - Risk Categories

Group I	Group II	Group III
Low Risk	Intermediate Risk	High Risk
GTR – Observation	3DCRT /SRT /IMRT /Proton	IMRT - SIB
STR – Observation SRS RT	54 Gy in 30 #	PTV 60 : 60Gy in 30 fractions, 2 Gy/ # PTV 54 : 54Gy in 30 fractions, 1.8 Gy/#

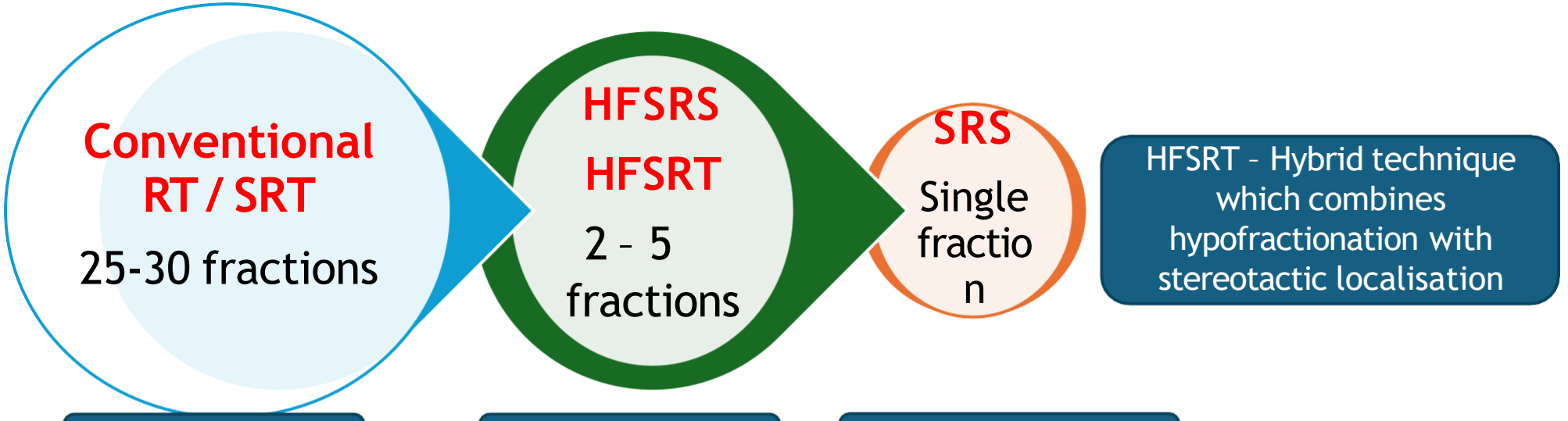
Pituitary Adenomas
Management







Pituitary Adenomas
Fractionation Schedules



Craniopharyngiomas
Management

Maximal Safe Surgery → Radiotherapy if residual → Follow up

Maximal Safe Surgery → Observe if no residual

Radiotherapy if residual:

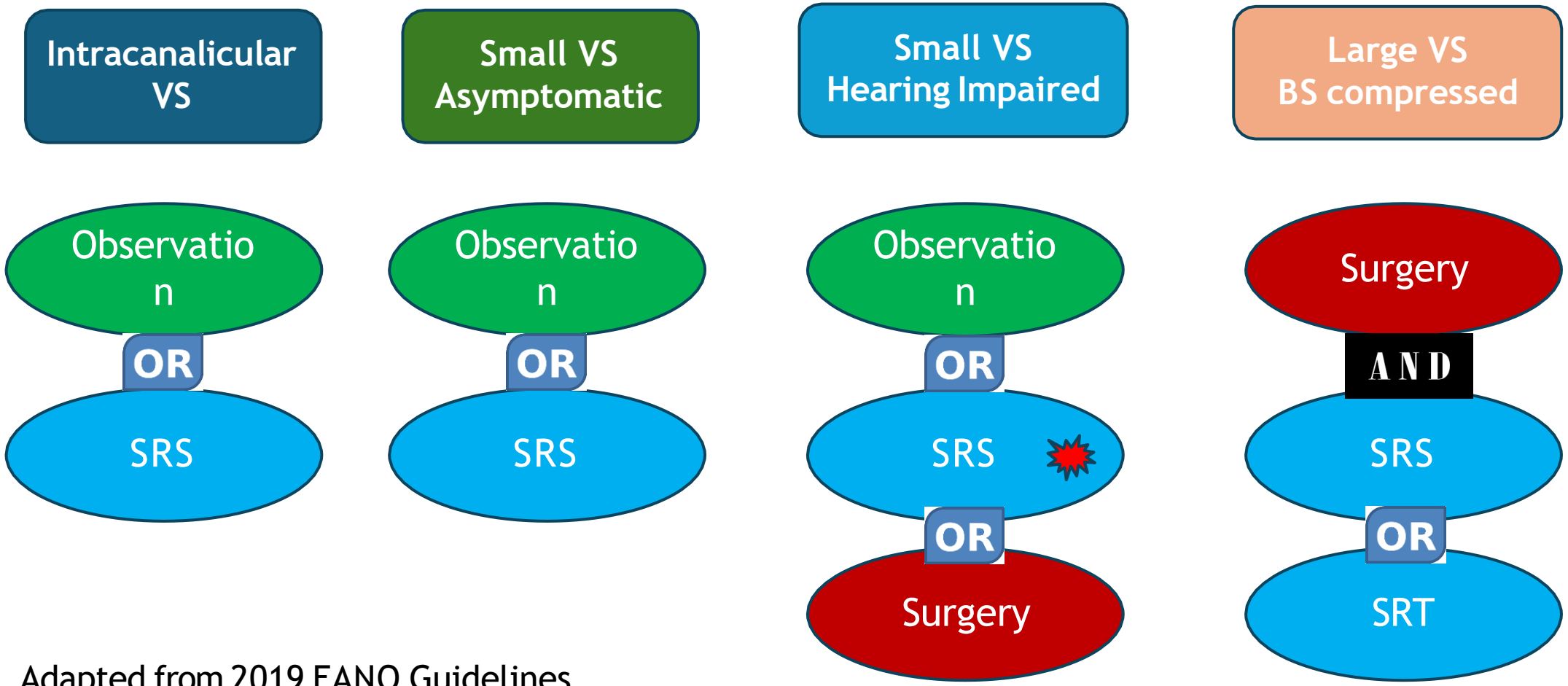
- GTV – Tumor on T1 Gado
- CTV – GTV + 5mm
- PTV – CTV + 0.3-0.5 cm
- Dose: 54 Gy in 30 #
- Interim CT Scan If Cystic

Follow up:

Baseline C At Every Follow up:

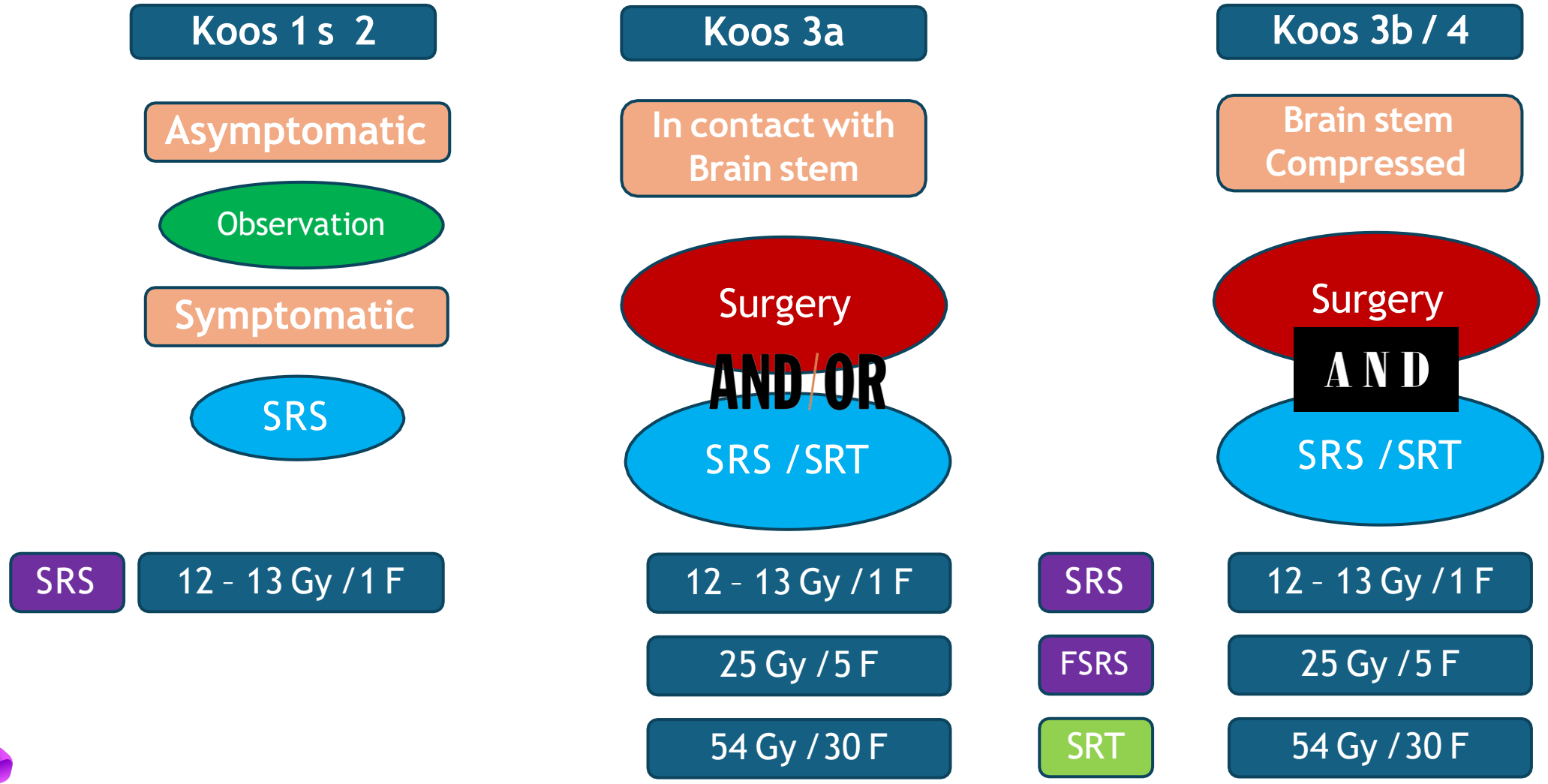
1. Ophthalmological evaluation
2. Neuroendocrine evaluation
3. MRI Imaging

Vestibular Schwannomas
Management

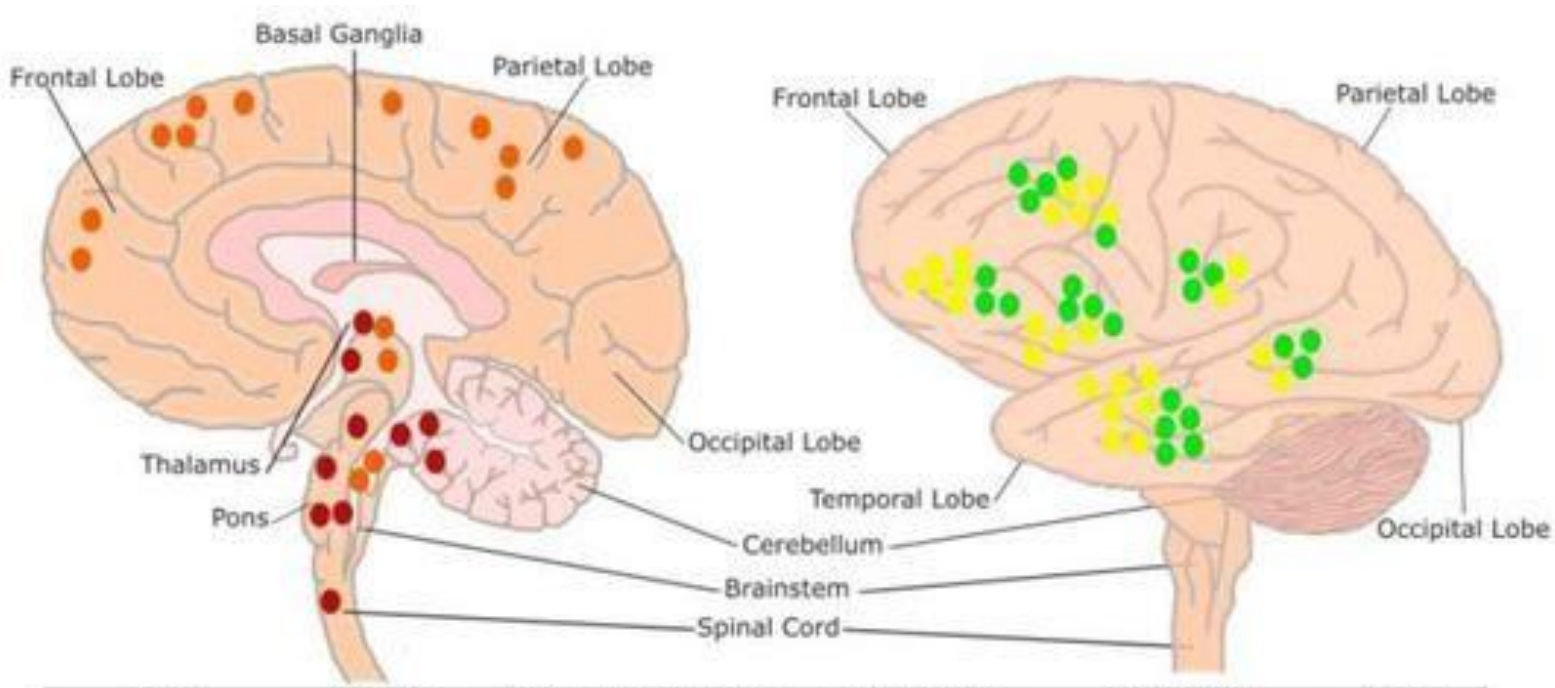


Adapted from 2019 EANO Guidelines

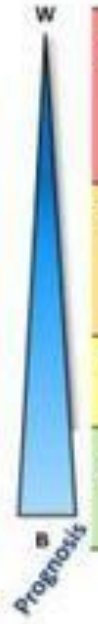
Vestibular Schwannomas
Fractionation Schedules



Paediatric Type Diffuse High Grade Gliomas Prognosis

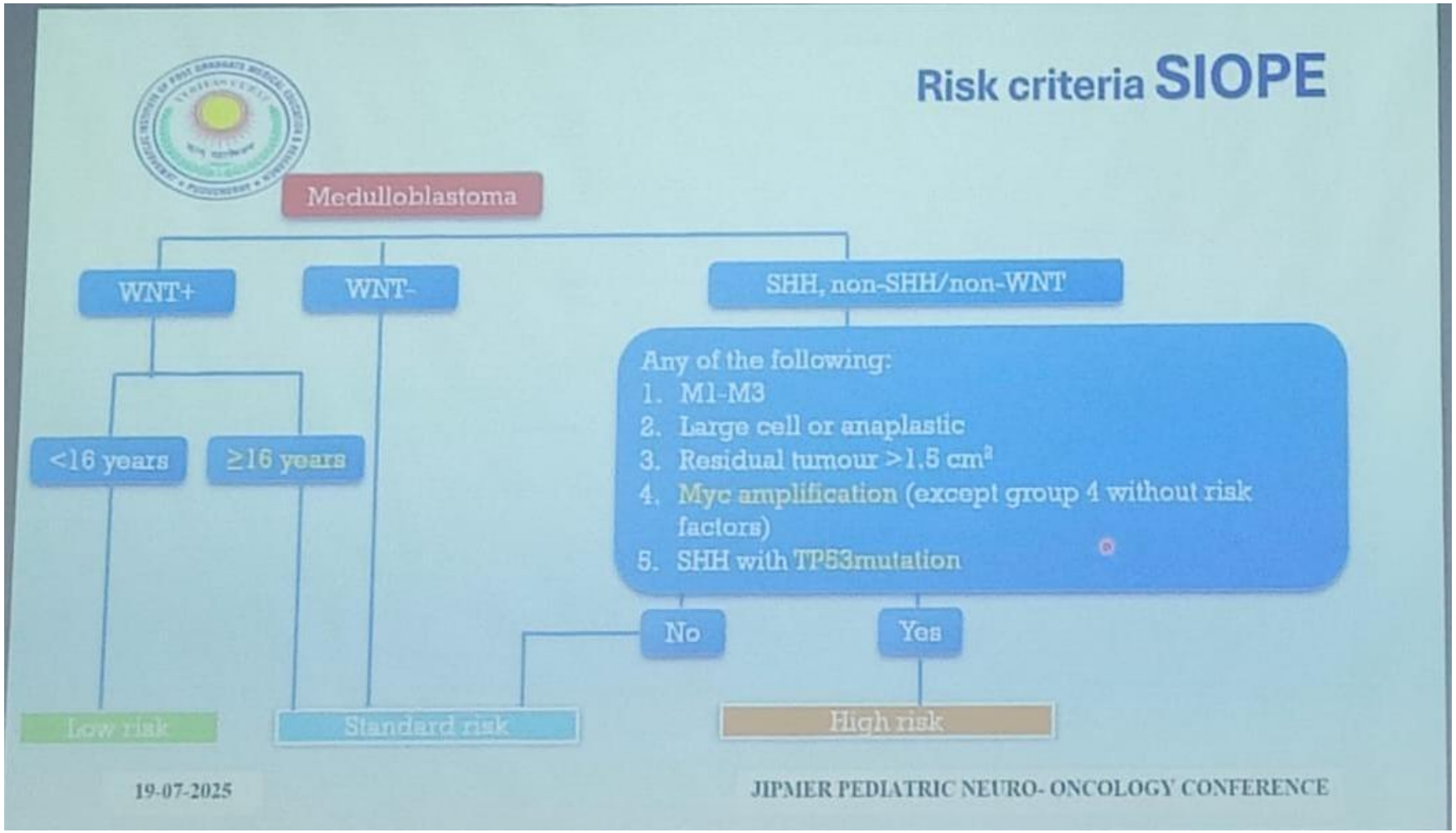


Subtype	Molecular characteristics	Associated somatic mutations	Histopathological classification	Growth pattern	Grade according to WHO
Diffuse Midline Gliomas H3 K27-altered	H3.1K27M	HIST1H3B, *PI3K, ACVR1, ATRX*	Astrocytic morphology with oligodendroglial-like features	Midline structure (thalamus, brainstem, cerebellum, pons), spinal cord	4
	H3.3K27M	H3F3A, *FGFR1, TP53, PPMD1, PDGFRalpha, CCND2, TOP3A, EZHIP, EGFR*			4
Diffuse paediatric-type high-grade glioma, H3-wildtype and IDH wildtype	H3K27WT	*MYCN, EGFR, PDGFRA*, H3-wildtype, IDH-wildtype	Astrocytic morphology with oligodendroglial-like features	Cerebral hemispheres and midline structures	4
Infant-type hemispheric glioma	NTRK family	NTRK family, *ALK, ROS, MET*	Astrocytic morphology	Cerebral hemispheres	4
Diffuse hemispheric glioma, H3 G34- mutant	H3.3G34R/V	H3F3A, *TP53, ATRX, FBXW7, MGMT promoter methylation*	Neuro-glial heterogeneity	Cerebral hemispheres	4



OncoEdu
Research | Education | Treatment

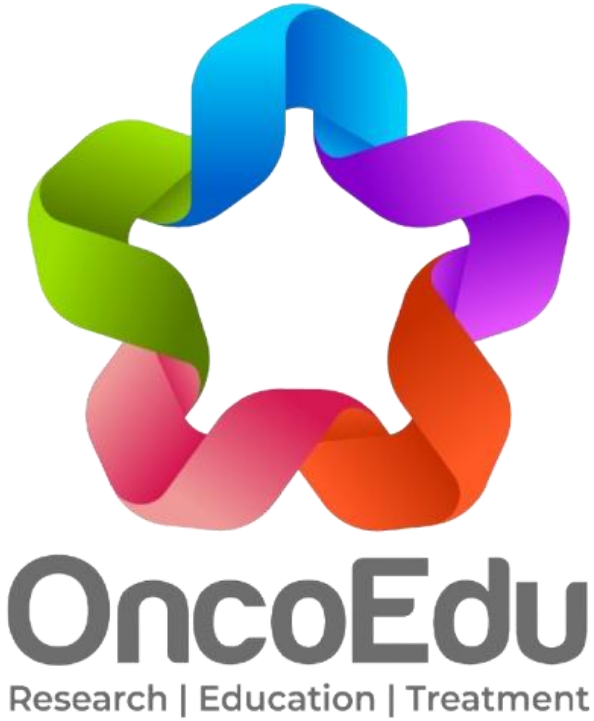
Medulloblastoma
Risk Stratification – Molecular Era



Slide Courtesy – Dr Thankamma Ajitkumar

RTOG 053G - Volume Delineation

	Group II /Intermediate Risk	Group III / High Risk
	3DCRT /SRT /IMRT	IMRT - SIB
	54 Gy in 30 #	PTV 60 : **60Gy** in 30 fractions, 2 Gy/ # PTV 54 : **54Gy** in 30 fractions, 1.8 Gy/#
GTV	1. Tumor bed on post op MRI 2. Any residual nodular enhancement 3. Hyperostotic or directly invaded bone	1. Tumor bed on post op MRI 2. Any residual nodular enhancement 3. Hyperostotic or directly invaded bone
CTV	GTV + 1 cm (reduced to 0.5 cm around natural barriers to tumor growth such as skull)	CTV 60: GTV + 1 cm CTV 54: GTV + 2 cm (reduce to 1cm at natural barriers)
PTV	CTV + 0.3cm	CTV + 0.3cm



Note from the presenter:

Kindly note that if you plan to use or refer to any part of the presentation, please acknowledge the source properly.

- Dr Rajesh Balakrishnan

Professor – Radiation Oncology
DMG – Breast /Neuro-oncology /Paed Rad Onc
CMC Vellore