ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE

ANNALS OF ONCOLOGY driving innovation in oncology

MELANOMA AND OTHER SKIN TUMOURS

1081O ctDNA reduction and clinical efficacy of the darovasertib + crizotinib (daro + crizo) combination in metastatic uveal melanoma (MUM)

M. Mckean[1], B. Chmielowski[2], M.O. Butler[3], R. Carvajal[4], J. Rodon[5], M. Carlino[6], K.B. Kim[7], T. Wise-draper[8], S. Khan[9], A.K.S. Salama[10], J. Moser[11], J. Reeves[12], K.D. Wilner[13], M. Maurer[14], M. Abed[15], B. Mitchell[16], D. Beaupre[17], M. Orloff[18]

[1]Drug Development Unit, Sarah Cannon Research Institute, Nashville, TN, USA; [2]Division of Hematology-Medical Oncology, Jonsson Comprehensive Cancer Center, University of California Los Angeles, Los Angeles, CA, USA; [3]Medical Oncology and Hematology Department, UHN - University Health Network - Princess Margaret Cancer Centre, Toronto, ON, Canada; [4]Medicine, Northwell Health Cancer Institute, Lake Success, NY, USA; [5]Investigational Cancer Therapeutics, The University of Texas MD Anderson Cancer Center, Houston, TX, USA; [6]Medical Oncology Department, Crown Princess Mary Cancer Centre Westmead, Westmead, NSW, Australia; [7]Oncology, California Pacific Medical Center Research Institute, San Francisco, CA, USA; [8]Hematology Oncology Dept., Vontz Center for Molecular Studies, Cincinnati, OH, USA; [9]Medical Oncology, HICCC - Herbert Irving Comprehensive Cancer Center - Columbia University, New York, NY, USA; [10]Duke Cancer Center, Duke University, Durham, NC, USA; [11]Drug Development and Medical Oncology, HonorHealth Research Institute, Scottsdale, AZ, USA; [12]Medical Oncology, Sarah Cannon Research Institute at Florida Cancer Specialists, Cape Coral, FL, USA; [13]Global Product Development, Pfizer Inc., San Diego, CA, USA; [14]Medical Oncology, IDEAYA Biosciences, South San Francisco, CA, USA; [15]Translational, IDEAYA Biosciences, South San Francisco, CA, USA; [16]Clinical Development, IDEAYA Biosciences, South San Francisco, CA, USA; [17]Clinical Development, Biosplice Therapeutics, Inc., San Diego, CA, USA; [18]Medical Oncology, Thomas Jefferson Univ Hospital, Philadelphia, PA, USA

Background: MUM has limited effective therapies. Driver mutations in *GNAQ/11* occur in >95% of MUM, activating protein kinase C (PKC) signaling. Darovasertib (IDE196), an oral PKC inhibitor, has clinical activity in MUM (*Br J Cancer.* 2023;128(6):1040-1051). Crizotinib, an oral c-MET inhibitor, showed synergy with Daro pre-clinically. This phase 1/2 study evaluated the combination in first line (1L) and pretreated MUM.

Methods: Eligibility included RECIST 1.1 measurable disease, ECOG 0-1 and adequate organ function. Dose escalation used a 3 + 3 design with 3 escalation cohorts, followed by expansion at 300 mg BID Daro + 200 mg BID Crizo. Safety, efficacy, and circulating tumor (ct) DNA were assessed.

Results: At 08Mar2023 data cut-off, of 68 MUM pts treated at the expansion dose (safety population (SP)) as of September 2022, 63 were evaluable for response (per-protocol efficacy population (PPEP)). The PPEP had a large tumor burden: 66% with largest metastatic lesion > 3cm, 64% with hepatic + extrahepatic disease, & 60% with elevated LDH. HLA-A2*02:01 status (n=51 tested): 63% neg., 37% pos. In the SP, the most common drug-related adverse events (AEs) (>30%) were diarrhea, nausea, edema, fatigue, hypotension & rash. AEs were largely Grade 1-2. Related Serious AEs were seen in 6 (9%) pts and AEs leading to discontinuation in 4 (6%) pts. In the PPEP, 30% had a confirmed partial response (cPR) with 92% of patients having tumor shrinkage. First-line (1L) pts (n=20) had a cPR of 45% with 95% of patients having tumor shrinkage. Median PFS (mPFS) in both PPEP and 1L pts was ~7 months. In pts with hepatic only disease (n=20 pts, 1L and pretreated), an ORR of 35% and mPFS was 11 months. Clinical efficacy was seen in both HLA-A2 pos. and neg. pts. There were deep & sustained ctDNA molecular responses in the majority of pts.

Conclusions: Initial evaluation of Daro + Crizo in both 1L & pretreated pts with MUM showed a manageable safety profile and clinical efficacy that appears superior to current standards of care. ctDNA was reduced in almost all pts. These data support the registrational phase II/III study for potential accelerated approval in 1L HLA-A2 neg. MUM, where there are no FDA approved therapies.

Clinical trial identification: NCT03947385.

Legal entity responsible for the study: The authors.

Funding: IDEAYA Biosciences.

Disclosure: M. Mckean: Financial Interests, Institutional, Other, Consulting: Pfizer, Castle Biosciences, Eisai, IQVIA, Merck, Moderna; Financial Interests, Personal, Other, Consulting: iTeos; Financial Interests, Institutional, Research Grant: Ascentage Pharma Group, Bicycle Therapeutics, Dragonfly Therapeutics, Epizyme, Exelixis, Genentech, GSK, IDEAYA Biosciences, Ikena Oncology, Infinity Pharmaceuticals, Jacobio Pharmaceuticals, Moderna, NBE Therapeutics, Novartis, Oncorus, Plexxicon, Prelude Therapeutics, Regeneron, Sapience Therapeutics, Seattle Genetics, Tizona Therapeutics, Tmunity Therapeutics, TopAlliance Biosciences, Aadi Biosciences, Alpine Immune Sciences, Arcs Biosciences, Bayer, Arvinas, ASCO, Astellas, BioMed Valley Discoveries, BioNTech, C4 Therapeutics, EMD Serono, Erasca, Foghorn Therapeutics, G1 Therapeutics, Gilead Sciences, ImmVira Pharma, Kechow Pharma, Kezar Life Sciences, Kinnate BioPharma, MedImmune, Mereo BioPharma, Metabomed, Nektar, OncoC4, PACT Pharma, Pfizer, Poseida, Pyramid Biosciences, Scholar Rock, Synthrox, Takeda Pharmaceuticals, Teneobio, Tempest Therapeutics, Xilio. B. Chmielowski: Financial Interests, Personal, Other, DMC: Nektar; Financial Interests, Personal, Advisory Board: Novartis, Delcath Systems, Instil Bio, Replimune; Financial Interests, Institutional, Local PI, Clinical trial support: Bristol Myers Squibb, Macrogenics, Karyopharm Therapeutics, Infinity Pharmaceuticals, Advenchen Biotherapeutics, Xencor, Compugen, Iovance, PACT Pharma, RAPT Therapeutics, Immunocore, Ascentage, Atreca, Replimune, IDEAYA Biosciences, Instil Bio; Financial Interests, Institutional, Local PI, clinical trial support: Adagene, TriSalus Life Sciences, Kinnate Biopharma, PTC Therapeutics, Xilio Therapeutics, Kezar Life Sciences. M.O. Butler: Financial Interests, Personal, Speaker's Bureau: Bristol Myers Squibb, Merck, Novartis, Sanofi, Pfizer; Financial Interests, Personal, Advisory Board: Merck, Bristol Myers Squibb, Novartis, Adaptimmune, Instil Bio, Iovance, Sun Pharma, GSK, Sanofi, LaRoche Possey, Pfizer, Medison, IDEAYA, Regeneron; Financial Interests, Personal, Research Grant: Merck, Takara Bio, Novartis. R. Carvajal: Financial Interests, Personal, Advisory Board: Alkermes, Bristol Myers Squibb, Castle Biosciences, Delcath, Eisai, Hengrui, IDEAYA, Immunocore, InxMed, Iovance, Merck, Novartis, OncoSec, Pierre Fabre, Puretech Health, Regeneron, Sanofi, TriSalus. J. Rodon: Financial Interests, Personal, Advisory Board: Ellipses Pharma, iOnctura SA; Financial Interests, Personal, Other, Consultancy: Aadi Bioscience, Clarion Healthcare, Debiopharm, Monte Rosa Therapeutics, Cullgen, Pfizer, Merus N.V., Macrogenics, Oncology One, Envision Pharma, Columbus Venture Partners, Sardona Therapeutics, Avoro Capital Advisors, Vall d'Hebron Institute of Oncology/Ministero de Empleo y Seguridad, Chinese University of Hong Kong, Boxer Capital LLC, Tang Advisors LLC, Incyte; Financial Interests, Institutional, Other, Clinical Research: Novartis, Spectrum Pharmaceuticals, Symphogen, BioAtla, Pfizer, GenMab, CytomX, Kelun-Biotech, Takeda-Millennium, GSK; Financial Interests, Institutional, Other, Research Funding: Blueprint Medicines, Black Diamond, Merck Sharp & Dohme; Financial Interests, Institutional, Research Grant, Research Funding/Clinical Research: Hummingbird, Yingli; Financial Interests, Institutional, Research Grant, Research Funding: Vall d'Hebron Institute of Oncology/Cancer Core Europe; Financial Interests, Institutional, Research Grant, Clinical Research: Bicycle Therapeutics, Taiho, Roche Pharmaceuticals, Merus, Curis, Aadi Bioscience, Nuvation, Fore Biotherapeutics, BioMed Valley Discoveries, Loxo Oncology, Hutchinson MediPharma, Cellestia, Deciphera, IDEAYA, Amgen, Tango Therapeutics, Mirati, Linnaeus Therapeutics, Bayer; Other, Travel: European Society for Medical Oncology; Other: VHIO/Ministero de Empleo y Seguridad Social. M. Carlino: Financial Interests, Personal, Advisory Board, Consultant Advisor: MSD, BMS, Novartis, Amgen, OncoSec, Merck, Sanofi, IDEAYA, Pierre Fabre, Eisai, Nektar, Regeneron. K.B. Kim: Financial Interests, Personal, Advisory Board: Bristol Myers Squibb, Merck, Aveo, Regeneron, Sanofi; Financial Interests, Personal, Invited Speaker: Bristol Myers Squibb; Financial Interests, Personal, Stocks/Shares: Arvinas; Financial Interests, Institutional, Funding, Moderna has provided funding to the institution for conducting a clinical trial of Moderna's drug: Moderna. T. Wise-draper: Financial Interests, Personal, Other, Consultant: Shattuck Labs, Need Inc.; Financial Interests, Personal, Advisory Board: Exicure, Rakuten Medical, Merck & Co.; Financial Interests, Personal, Invited Speaker: Physician Education Resource; Financial Interests, Personal, Other, Consultant for Molecular Tumor Board: Caris Life Sciences; Financial Interests, Personal, Ownership Interest: High Enroll; Financial Interests, Personal, Research Grant: BMS, Merck & Co., Tesaro/GSK, AstraZeneca, Janssen; Financial Interests, Personal and Institutional, Local PI: BMS, EMD Serono, Replimune, AstraZeneca, Alkermes, Exicure, Shattuck Labs, Boston Medical, Debio Pharm, Eli Lilly, Epizyme, Iovance, Agenus, SQZ Biotech, Triumvera, Adlai Nortye, Yingli, Vyriad, IDEAYA, MINK, Sinogen. S. Khan: Financial Interests, Personal, Advisory Board: Castle Biosciences, Replimune Inc. A.K.S. Salama: Financial Interests, Personal, Advisory Board: Bristol Myers Squibb, Iovance, Regeneron, Replimune, Novartis, Pfizer; Financial Interests, Institutional, Local PI: Bristol Myers Squibb, Ascentage, IDEAYA, Immunocore, Merck, Regeneron, Replimune, Seagen; Financial Interests, Institutional, Trial Chair: Olatec. J. Moser: Financial Interests, Personal, Advisory Board: BMS, Amunix, Thirona Bio, Adagene, IQVIA, Incyte, Boxer Capital, Oberland Capital; Financial Interests, Personal, Other, Consultant: Imaging Endpoints; Financial Interests, Personal, Invited Speaker: Immunocore, Caris Life Sciences; Financial Interests, Personal, Other, Molecular Tumor Board Member: Caris Life Sciences; Financial Interests, Institutional, Coordinating PI: Novocure; Financial Interests, Institutional, Local PI: Genentech, Alpine Immune Sciences, Amgen, Trishula Therapeutics, FujiFilm, ImmunSensor, Simcha Therapeutics, Repertoire Immune Sciences, Nektar Therapeutics, Synthorx Inc., Istari Oncology, IDEAYA Biosciences, Rubius Therapeutics, University of Arizona, Senwha Biosciences, Storm Therapeutics, Werewolf Therapeutics, Fate Therapeutics, Y-mab Therapeutics, Agenus; Financial Interests, Personal, Local PI: Bioeclipse Therapeutics. M. Maurer: Financial Interests, Personal, Other, Independent Medical Consultant for ongoing Healthy Volunteer study: The Global Health Drug Discovery Institute (GHDDI); Financial Interests, Personal, Full or part-time Employment, Full time employee of IDEAYA Biosciences; Financial Interests, Personal, Stocks/Shares, Own stock in BMS (BMY): BMS; Financial Interests, Personal, Stocks/Shares, Own stock and stock options in IDEAYA Biosciences (IDYA); Non-Financial Interests, Member, Regular member: ASCO. M. Abed: Financial Interests, Personal, Full or part-time Employment: IDEAYA Biosciences, Zentalis. B. Mitchell: Financial Interests, Personal, Full or part-time Employment, Employee of IDEAYA. Biosciences; Financial Interests, Personal, Stocks/Shares, Employee Stock Options: IDEAYA Biosciences. D. Beaupre: Financial Interests, Personal, Full or part-time Employment, Employee: IDEAYA; Financial Interests, Personal, Stocks/Shares, Stock: IDEAYA; Non-Financial Interests, Leadership Role, CMO of organization: IDEAYA; Non-Financial Interests, Institutional, Proprietary Information, Access to company confidential information: IDEAYA. M. Orloff: Financial Interests, Personal, Advisory Board: Tirsalus, Delcath, Replimune, IDEAYA Biosciences; Financial Interests, Personal, Speaker's Bureau: Immunocore. All other authors have declared no conflicts of interest.

https://doi.org/10.1016/j.annonc.2023.09.2215

1082O Concurrent intrathecal (IT) and intravenous (IV) nivolumab (N) for melanoma (MM) patients (pts) with leptomeningeal disease (LMD)

I.C. Glitza[1], S. Phillips[1], I. John[1], R.L. Bassett[2], R. Lin[2], M.L. Rohlfs[1], J. Richard[1], M. Iqbal[1], T. Hennegan[1], I.E. McCutcheon[3], S. Ferguson[3], B. O'Brien[4], S. Tummala[4], N. Guha-Thakurta[5], M. Debnam[5], H.A. Tawbi[1], E. Burton[6], M. Davies[1]

[1]Melanoma Medical Oncology Department, The University of Texas MD Anderson Cancer Center, Houston, TX, USA; [2]Biostatistics, MD Anderson Cancer Center, Houston, TX, USA; [3]Neurosurgery, The University of Texas MD Anderson Cancer Center, Houston, TX, USA; [4]Neuro-Oncology, The University of Texas MD Anderson Cancer Center, Houston, TX, USA; [5]Neuro-Radiology, The University of Texas MD Anderson Cancer Center, Houston, TX, USA; [6]Genomic Medicine, The University of Texas MD Anderson Cancer Center, Houston, TX, USA

Background: Pts with LMD have dismal prognosis and few clinical trial options. We previously reported safety and efficacy of the dose escalation (DE) phase of an open label, single arm, single center phase I/IB trial (NCT03025256) for MM pts with LMD. Concurrent IT/IV N was well tolerated, no new or unexpected CNS toxicities. 50mg IT N was the recommended dose (RD) for expansion accrual. Here we report the updated safety and efficacy results for the escalation and expansion cohorts.

Methods: Study design methods were previously reported (Glitza, *Nat Med,* 2023). Primary objectives were to determine safety and RD of IT/IV N and safety in RD expansion cohort. Secondary objectives included overall survival (OS).

Results: Fifty pts total were treated (48 pts with MM, 2 pts with NSCLC), including 31 pts with IT N 50 mg. Median age at LMD diagnosis was 49 (19-74); 27 pts are male. All pts had radiographic evidence of LMD; 26 pts had positive CSF cytology at baseline. Median follow-up and OS is shown in the table. Safety profile remained consistent with prior reports: 9 pts (18%) experienced gr 3 AEs, none had gr 4 or 5. Nausea (46%), rash (40%), vomiting (34%), diarrhea (20%), and dizziness (20%) were the most common AEs. Thirty pts (60%) experienced AEs after IT N administration, including 2 gr 3 (vasogenic edema, elevated ALT); remainder were gr 1/2.

Table: 1082O

	Med follow up wks (range)	Median OS Wks (95% CI)	OS 13 wks	OS 26 wks	OS 52 wks
All	27.3 (2, 251)	30 (19, 64)	68%	54%	35%
<50 mg	25 (5, 251)	25 (15, 143)	68%	47%	26%
50 mg	30 (2, 140)	41 (13, 65)	68%	58%	43%

Conclusions: This updated analysis confirms the safety of IT (50mg)/IV N. There were no significant differences in OS between the tx groups and no unexpected toxicities were observed at RD. These results support further evaluation of IT immunotherapy strategies for pts with LMD. Insights gained from translational studies on CSF samples will aid in the development of future IT immunotherapy strategies for these patients.

Clinical trial identification: NCT03025256.

Legal entity responsible for the study: The authors.

Funding: Bristol Myers Squibb.

Disclosure: I.C. Glitza: Financial Interests, Institutional, Speaker, Consultant, Advisor: Bristol Meyers Squibb, Array, Novartis, Sintetica; Financial Interests, Institutional, Principal Investigator: Bristol Meyers Squibb, Merck, Pfizer. S. Ferguson: Financial Interests, Institutional, Research Funding: Codiak. H.A. Tawbi: Financial Interests, Institutional, Speaker, Consultant, Advisor: Bristol Meyers Squibb, Genentech, Novartis, Merck, Boxer Capital, Karyopharm, Iovance, Eisai Jazz, Medicenna; Financial Interests, Institutional, Principal Investigator: Bristol Meyers Squibb, Novartis, Merck, Genentech, GSK, EMD Serono, Eisai, Dragonfly Therapeutics, RAPT Therapeutics. M. Davies: Financial Interests, Institutional, Speaker, Consultant, Advisor: Roche/Genentech, Array, Pfizer, Novartis, Bristol Meyers Squibb, GSK, Sanofi-Aventis, Vaccinex, Apexigen, Eisai, ABM Therapeutics; Financial Interests, Institutional, Principal Investigator: Roche/Genentech, GSK, Sanofi-Aventis, Merck, Myriad, Oncothyreon. All other authors have declared no conflicts of interest.

https://doi.org/10.1016/j.annonc.2023.09.2216

1085O Atezolizumab, bevacizumab, and cobimetinib (TACo) in patients (pts) with PD1 refractory melanoma brain metastases (MBM)

E. Burton[1], V. Honaker[2], D. Milton[3], I.C. Glitza[4], R. Amaria[2], S. Patel[2], A. Diab[4], M. Wong[4], J. Mcquade[4], C. Chung[5], J.S. Wefel[6], J. Li[7], M. Davies[4], H.A. Tawbi[4]

[1]Genomic Medicine, The University of Texas MD Anderson Cancer Center, Houston, TX, USA; [2]Melanoma Medical Oncology, The MD Anderson Cancer Center, Houston, TX, USA; [3]Department of Biostatistics, The University of Texas MD Anderson Cancer Center, Houston, TX, USA; [4]Melanoma Medical Oncology Department, The University of Texas MD Anderson Cancer Center, Houston, TX, USA; [5]Radiation Oncology, MD Anderson Cancer Center, Houston, TX, USA; [6]Neuro-Oncology, The University of Texas MD Anderson Cancer Center, Houston, TX, USA; [7]Radiation Oncology Department, The University of Texas MD Anderson Cancer Center - Main Building, Houston, TX, USA

Background: Combination immune checkpoint blockade (ICB) achieves frequent durable responses in pts with untreated MBM. However, systemic treatments (tx) after ICB failure are limited, especially in BRAF wild-type pts. We investigated the novel TACo regimen in ICB- refractory MBM based on biological insights that (1) VEGF can drive ICB resistance, and (2) MEK inhibition can increase MHC I expression and T cell infiltration to potentially synergize with ICB. We hypothesized this regimen would be safe and demonstrate efficacy in pts with MBM.

Methods: In this single-center phase II study evaluating TACo in pts with MBM (NCT03175432), primary objectives included safety and efficacy (intracranial response rate (ICRR) by modified RECIST 1.1). Secondary objectives included IC clinical benefit rate (ICCBR), progression free (PFS) and overall survival (OS), and duration on tx (DoT). Prior PD1 tx and $\geq$1 non irradiated lesion (5-30mm) were required. BRAF mutated pts were allowed after BRAF/MEK tx (3-month washout). Pts on $\leq$4m/day PO of dexamethasone or equivalent were allowed. Tx schedule: atezolizumab 840mg IV every 2 weeks (wks), bevacizumab 5mg/kg every 2 wks, cobimetinib 60mg PO daily for 3 wks followed by 1 wk off. MRIs were obtained prior to cycles 1-3, and 5.

Results: Of the 20 pts treated, 70% were male, median age 59.5 yrs (34-78), and 2 pts were BRAFV600E mutated. 11 pts had $\geq$ 1 prior tx for MBM. Median follow up was 8.2 mos (0.4-39.2). Median DoT was 8 wks (0.6-63.8). 18 pts experienced tx related adverse events (AEs), most commonly rash (70%), diarrhea (D) (55%), hypertension (HTN) (25%), proteinuria (25%). 35% pts had gr 3/4 AEs: HTN (15%), D (10%) were most common. 2 pts stopped tx due to toxicity. 18 pts were evaluable for IC response: ICRR was 39% (1 CR, 6 PR) and ICCBR was 56% (+SD). Median PFS was 2.7 mos (95% CI 0.9,7.3) and median OS was 9.3 (95% CI 3.8,20.9). 7 (35%) pts continued on tx post progression for $\geq$ 3 wks (3-55 wks).

Conclusions: In this heavily pretreated MBM pt population with no available standard systemic therapy options, TACo regimen was tolerable, demonstrated IC clinical benefit, and provided clinical benefit beyond progression, warranting further evaluation.

Clinical trial identification: NCT03175432.

Legal entity responsible for the study: MD Anderson Cancer Center - PI Hussein Tawbi.

Funding: Genentech.

Disclosure: V. Honaker: Financial Interests, Institutional, Full or part-time Employment, Research nurse: MD Anderson Cancer Center; Financial Interests, Personal, Stocks/Shares: Pfizer. I.C. Glitza: Financial Interests, Personal, Speaker, Consultant, Advisor: BMS, Array, Novartis, Sintetica; Financial Interests, Institutional, Research Funding: BMS, Merck, Pfizer. R. Amaria: Financial Interests, Personal, Advisory Board: Iovance Biotherapeutics, Novartis, Erasca; Financial Interests, Institutional, Coordinating PI: Merck, Bristol Myers Squibb, Novartis; Financial Interests, Institutional, Local PI: Iovance, Roche; Financial Interests, Institutional, Trial Chair: Obsidian. S. Patel: Financial Interests, Personal, Advisory Board: TriSalus, Cardinal Health, Castle Biosciences, Novartis, BMS, Pfizer, Immatics; Financial Interests, Personal, Other, Consultant for educational materials: Advance Knowledge in Healthcare; Financial Interests, Personal, Advisory Board, Advisory Board and Corporate Day speaker (unbranded): Delcath; Financial Interests, Personal, Other, Independent Data Monitoring Committee: Immunocore; Financial Interests, Personal, Other, Consultant: Guidepoint Global; Financial Interests, Institutional, Trial Chair: Provectus Biopharmaceuticals, Bristol Myers Squibb; Financial Interests, Institutional, Local PI: Lyvgen, InxMed, Foghorn Therapeutics, IDEAYA, Novartis, Seagen, Syntrix Bio; Financial Interests, Institutional, Steering Committee Member: TriSalus Life Sciences; Non-Financial Interests, Member: ASCO, AACR, International Society of Ocular Oncology, Society for Melanoma Research; Non-Financial Interests, Leadership Role: SWOG. A. Diab: Financial Interests, Institutional, Research Funding: BMS. M. Wong: Financial Interests, Personal, Speaker, Consultant, Advisor: Merck, Pfizer, BMS, Regeneron, EMD Serono, ExiCure, Castle Biosciences. J. Mcquade: Financial Interests, Personal, Speaker, Consultant, Advisor: BMS, Merck, Roche. C. Chung: Financial Interests, Personal, Officer, Vice-Chair: Quantitative Imaging Biomarker Alliance RSNA; Financial Interests, Institutional, Coordinating PI, Research funding: Siemens Healthineers; Financial Interests, Institutional, Coordinating PI, Research and Co-development Funding: RaySearch Laboratories; Non-Financial Interests, Leadership Role, Co-Chair of ICRU committee report: International Commission on Radiation Units and Measures (ICRU). J.S. Wefel: Financial Interests, Personal, Advisory Board: Bayer; Financial Interests, Institutional, Other, Neurocognitive outcomes consultant: GT Medical Technologies, Novocure; Non-Financial Interests, Advisory Role: American

Brain Tumor Association; Non-Financial Interests, Leadership Role: International Cognition and Cancer Task Force. M. Davies: Financial Interests, Personal, Advisory Board: Roche, Pfizer, Novartis, BMS, Sanofi-Aventis, GSK, Vaccinex, Apexigen, Eisai, Iovance, Merck, ABM Therapeutics; Financial Interests, Institutional, Coordinating PI: Pfizer; Financial Interests, Institutional, Research Grant: ABM Therapeutics, Lead Pharma, Genentech, GSK, Sanofi-Aventis, Merck, Oncothyreon; Financial Interests, Research Grant: Myriad. H.A. Tawbi: Financial Interests, Personal, Advisory Board: Bristol Myers Squibb, Merck, Novartis, Genentech, Eisai, Karyopharm, Iovance, Pfizer, Jazz Pharmaceuticals; Financial Interests, Institutional, Trial Chair: Bristol Myers Squibb; Financial Interests, Institutional, Local PI: Merck, RAPT Pharmaceuticals; Financial Interests, Institutional, Steering Committee Member: Novartis, Genentech; Financial Interests, Institutional, Funding: GSK, Eisai. All other authors have declared no conflicts of interest.

https://doi.org/10.1016/j.annonc.2023.09.2219

1083MO Brain metastases and survival evaluation in the SECOMBIT trial

P.A. Ascierto[1], M. Mandalà[2], P.F. Ferrucci[3], M. Guidoboni[4], P. Rutkowski[5], V. Ferraresi[6], A.M. Arance Fernandez[7], M. Guida[8], E. Maiello[9], H. Gogas[10], E. Richtig[11], M.T. Fierro[12], C. Lebbe[13], H. Helgadottir[14], I. Melero[15], G. Palmieri[16], D. Giannarelli[17], A.M. Grimaldi[18], R. Dummer[19], V. Chiarion Sileni[20]

[1]Melanoma, Cancer Immunotherapy & Developmental Therapeutics, Istituto Nazionale Tumori - IRCCS - Fondazione Pascale, Naples, Italy; [2]Medicine and Surgery Department, Università degli Studi di Perugia, Perugia, Italy; [3]Oncology Dept., IEO - Istituto Europeo di Oncologia, Milan, Italy; [4]Oncology, IRST - Istituto Scientifico Romagnolo per lo Studio e la Cura dei Tumori IRCCS S.r.l., Meldola, Italy; [5]Department of Soft Tissue/Bone Sarcoma and Melanoma, Maria Sklodowska-Curie National Research Institute of Oncology, Warsaw, Poland; [6]Sarcomas and Rare Tumors Unit, IRCCS Regina Elena National Cancer Institute (IRE), Rome, Italy; [7]Medical Oncology Department, Hospital Clinic y Provincial de Barcelona, Barcelona, Spain; [8]Oncology, Istituto Tumori Giovanni Paolo II, Bari, Italy; [9]Oncology Unit, IRCCS Fondazione Casa Sollievo della Sofferenza, San Giovanni Rotondo, Italy; [10]First Department of Medicine, National and Kapodistrian University of Athens - School of Medicine, Athens, Greece; [11]Dermatology Dept., Universitätsklinik für Dermatologie und Venerologie, Graz, Austria; [12]Department of Medical Sciences, University of Turin, Turin, Italy; [13]Dermatology Dept., Hopital Saint Louis AP-HP, Paris, France; [14]Department of Oncology, Karolinska Institutet - Cancer Center Karolinska (CCK), Solna, Sweden; [15]Laboratory of Immunology, Clinica Universitaria de Navarra, Pamplona, Spain; [16]Immuno-Oncology & Targeted Cancer Biotherapies, University of Sassari, Sassari, Italy; [17]Biostatistical Unit, Fondazione Policlinico Universitario Agostino Gemelli IRCCS, Rome, Italy; [18]Medical Oncology Unit, AORN "San Pio", Naples, Italy; [19]Dermatology Department, Universitätsspital Zürich - Klinik für Dermatologie, Zurich, Switzerland; [20]Clinical and Experimental Oncology Dept., IOV - Istituto Oncologico Veneto IRCCS, Padua, Italy

Background: Despite the availability of effective systemic therapies, a significant number of advanced melanoma patients develop brain metastases. In the SECOMBIT study patients received the combination of encorafenib/binimetinib (E+B) as targeted therapy (T-T) or the combination of ipilimumab/nivolumab (I+N) as immunotherapy (I-O). In the present analysis, we updated survival outcomes and investigated if the incidence of and timing to brain metastasis onset were significantly different in patients receiving T-T (Arm A) or I-O (Arm B) as first line with switch at progression, as well as the "sandwich" strategy with T-T first preplanned switched to combo I-O after 8 weeks, returning back to T-T after progression (Arm C). In our previous reports, 4-year survival outcomes confirmed long-term benefit in ARM B and C pts. We also described preliminary biomarkers analyses where the loss-of-function affecting JAK or low baseline levels of serum interferon gamma (IFNγ) are correlated to PFS and OS.

Methods: From Nov 2016 to May 2019, of 251 pts enrolled, 69 were randomized in ARM A, 71 pts in ARM B and 69 pts in ARM C. BMFS (Brain Metastasis Free Survival) was defined as time from start of first systemic therapy until new brain metastasis detection or last pts contact (censored BMFS). The Kaplan-Meier method was used to estimate OS and PFS. The median follow up was 43 months (IQR: 37-51).

Results: Pts treated in arm B and C had a lower risk to develop brain metastasis compared to pts in arm A. Brain metastasis occurred during first line treatment, in 17, 6, and 8 patients, respectively, treated in ARM A, B and C. During the study, an intracranial progression was detected in a total of 23, 11 and 9 patients in ARM A, B and C. The exploratory HR for BMFS was of 0.51 (0.25-1.04) for ARM B vs ARM A, and 0.37 (0.17-0.81) for ARM C vs ARM A. In the biomarker analysis, pts with high tumor mutational burden (TMB, $\geq$10 mut/mb) had an improved BMFS compared with pts with low TMB [HR 0.20 (0.05-0.95)]. JAK mutated pts had a better BMFS compared to wild type pts [HR 0.26 (0.06-1.12)].

Conclusions: Patients in ARM B and C had a longer BMFS compared with pts who started treatment with T-T. BMFS rate at 4 years was better in TMB high and in JAK mutated pts. At the time of the meeting it will also be reported the 5-years OS data.

Clinical trial identification: NCT02631447.

Legal entity responsible for the study: Fondazione Melanoma.

Funding: This study was supported by unconditioned grants from Bristol Myers Squibb (Princeton, NJ) and Array Biopharma Inc./Pfizer (Boulder, CO).

Disclosure: P.A. Ascierto: Financial Interests, Personal, Advisory Board: Bristol Myers Squibb, Roche-Genentech, Merck Sharp & Dohme, Novartis, Merck Serono, Pierre Fabre, AstraZeneca, Sun Pharma, Sanofi, Idera, Sandoz, Immunocore, 4SC, Italfarmaco, Nektar, Boehringer Ingelheim, Eisai, Regeneron, Daiichi Sankyo, Pfizer, OncoSec, Nouscom, Lunaphore, Seagen, iTeos, Medicenna. All other authors have declared no conflicts of interest.

https://doi.org/10.1016/j.annonc.2023.09.2217

1084MO Nivolumab plus ipilimumab in melanoma patients with asymptomatic brain metastases: 7-year outcomes and quality of life from the multicenter phase III NIBIT-M2 trial

A.M. Di Giacomo[1], V. Chiarion Sileni[2], M. Del Vecchio[3], P.F. Ferrucci[4], M. Guida[5], P. Quaglino[6], M. Guidoboni[7], P. Marchetti[8], E. Simonetti[9], G. Amato[10], A. Covre[9], R. Camerini[11], L. Calabro[12], M. Valente[10], M. Mandalà[13], D. Giannarelli[14], M. Maio[1]

[1]Oncology, University of Siena, Center for Immuno-Oncology, University Hospital of Siena, Siena, Italy; [2]Melanoma Oncology Unit, Veneto Institute of Oncology IOV-IRCCS, Padua, Italy; [3]Unit of Melanoma, Medical Oncology, Department of Medical Oncology and Hematology, Istituto Nazionale dei Tumori, Milan, Italy; [4]Cancer Biotherapy Unit, Department of Experimental Oncology, European Institute of Oncology, IRCCS, Milan, Italy; [5]Rare Tumors and Melanoma Unit, IRCCS Istituto Tumori "Giovanni Paolo II", Bari, Italy; [6]Dermatology Clinic, Department of Medical Science, University of Turin, Turin, Italy; [7]Immunotherapy - Cell Therapy and Biobank Unit, Istituto Scientifico Romagnolo per lo Studio e la Cura dei Tumori (IRST) IRCCS, Meldola, Italy; [8]Department of Clinical and Molecular Medicine, Sapienza University of Rome, Rome, Italy; [9]Oncology, University of Siena, Siena, Italy; [10]Oncology, Center for Immuno-Oncology, University Hospital of Siena, Siena, Italy; [11]Oncology, NIBIT Foundation Onlus, Genoa, Italy; [12]Oncology, University of Ferrara, Ferrara, Italy; [13]Oncology, University of Perugia, Santa Maria della Misericordia, University Hospital of Perugia, Perugia, Italy; [14]Statistics, Fondazione Policlinico Universitario A. Gemelli, IRCCS, Rome, Italy

Background: The phase III NIBIT-M2 study showed a 41% 5-year overall survival (OS) of melanoma patients (pts) with asymptomatic brain metastases (BM) treated with ipilimumab (I) plus nivolumab (N) (I+N) (*Di Giacomo AM, CCR 2021*). In spite of the significant efficacy of I combined with N, no data are available on long-term survival, and patient-reported outcomes (PROs) and quality of life (QoL) in this patient population. Here, we report the 7-year efficacy outcomes and HRQoL analyses of the NIBIT-M2 study.

Methods: The NIBIT-M2 study recruited melanoma pts with active, untreated, asymptomatic BM from 9 Italian Centers that were randomized (1:1:1) to fotemustine (F) (Arm A), I+F (Arm B), or I+N (Arm C). Primary endpoint was OS; among secondary endpoints were intracranial progression-free survival (iPFS) and HRQoL. PROs were assessed at week (W) 1 and W12 using the EORTC Quality of Life Questionnaire (QLQ)-C30 Version 3.

Results: From Jan 2013 to Sept 2018 , 80 pts were enrolled: 76 received F (23), I+F (26), or I+N (27). As of May 1, 2023, at a median follow-up of 67 months (mo), median OS was 8.5 (95% CI: 6.6-10.3), 8.2 (95% CI: 2.1-14.3) and 29.2 (95% CI: 0-69.9) mo for Arm A, B, and C respectively. The 7-y OS rate was 10.0% (95% CI: 0-22.5) in Arm A, 10.3% (95% CI: 0-22.6) in Arm B, and 42.8% (95% CI: 23.4-62.2) in Arm C. Median iPFS was 3.0 (95% CI: 2.3-3.6), 3.3 (95%CI: 1.2-5.4) and 8.7 (95% CI: 0-19.9) for Arm A, B, and C, respectively. The 7-year iPFS rate was 4.3% (95% CI: 0-12.7) in Arm A, 7.7% (95% CI: 0-17.9) in Arm B, and 28.6% (95% CI: 11.2-46.0) in Arm C. Seventy-two pts (compliance 95%) and 34 pts (compliance 45%) completed the baseline and the W12 QLQ C-30 assessment. HRQoL was preserved in all treatment arms; no significant differences were observed in global health score. Most functional scales evaluated were preserved from baseline to W12, with a lower mean score decrease in pts receiving I+N.

Conclusions: The 7-year results of the NIBIT-M2 study, with the longest follow-up available to date in melanoma pts with asymptomatic BM treated with I+N, continue to show persistent therapeutic efficacy. HRQoL was preserved in all treatment arms and I+N induced a lower decrease in mean functional scales.

Clinical trial identification: NCT02460068.

Legal entity responsible for the study: NIBIT Foundation ONLUS.

Funding: Bristol Myers Squibb.

Disclosure: A.M. Di Giacomo: Financial Interests, Personal, Advisory Board: Bristol Myers Squibb, MSD, Pierre Fabre, Novartis; Financial Interests, Personal, Invited Speaker: Sanofi. V. Chiarion Sileni: Financial Interests, Personal, Advisory Board, analysis of treatment modality (diagnosis, stanging, surgery, radiotherapy, systemic therapy for Merkel cell carcinoma in Italy: Merck-Serono; Financial Interests, Institutional, Invited Speaker, Treatment option for BRAF mutated melanoma: Novartis; Financial Interests, Institutional, Invited Speaker, Treatment choices for BRAF mutated melanoma, evidence-based, and biologically supported: Pierre Fabre; Financial Interests, Institutional, Invited Speaker, Immunotherapy for melanoma treatment present and future: Bristol Myers Squibb; Financial Interests, Personal, Other, Travel, registration, and accommodation to attend ASCO annual meetings: Pierre Fabre. M. Del Vecchio: Financial Interests, Personal, Advisory Board: BMS, MSD, Sanofi, Pierre Fabre, Novartis. P.F. Ferrucci: Financial Interests, Personal, Advisory Board: BMS, Roche, Pierre Fabre, MSD, Novartis. M. Guida: Financial Interests, Personal, Advisory Board: Bristol Meyer Squibb, Novartis, Merck Sharp & Dohme. P. Quaglino: Non-Financial Interests, Personal, Advisory Board: BMS, Novartis; Financial Interests, Personal, Advisory Board: Pierre Fabre, MSD. M. Guidoboni: Financial Interests, Personal, Advisory Board: Bristol Myers Squibb, Merck Sharp & Dohme, Novartis, Pierre Fabre; Financial Interests, Personal, Research Grant: Merck Sharp & Dohme. P. Marchetti: Other, Personal, Advisory Board: BMS, Roche, MSD, Novartis, AstraZeneca, Pfizer; Financial Interests, Personal, Advisory Board: Bristol Myers Squibb, Novartis, Pfizer, Merck Sharp & Dohme, AstraZeneca, Boehringer Ingelheim, Celgene, Roche. A. Covre: Other, Personal, Advisory Board: EpiGen Therapeutics srl. R. Camerini: Financial Interests, Personal, Advisory Board: Bristol Meyer Squibb; Other, Personal, Advisory Board: Reithera srl, Alfasigma SPA, Cosmo Nbv, EpiGen Therapeutics. L. Calabro: Other, Personal, Advisory Board: BMS, AstraZeneca, MSD, Sanofi, Roche. M.

Mandalà: Financial Interests, Personal, Advisory Board: MSD, Novartis, Sanofi, BMS, Pierre Fabre; Financial Interests, Personal, Invited Speaker: Sun Pharma. D. Giannarelli: Financial Interests, Personal, Other, Educational Course in Biostatistics: Amgen; Financial Interests, Personal, Other, Course on GRADE system in Hematology: AstraZeneca. M. Maio: Financial Interests, Personal, Advisory Board: BMS, Roche, GSK, Sanofi, Alfasigma, Amgen, Sciclone, Eli Lilly, MSD, Incyte, Pierre Fabre, AstraZeneca; Financial Interests, Personal, Stocks/Shares: EpiGen, Theravance. All other authors have declared no conflicts of interest.

https://doi.org/10.1016/j.annonc.2023.09.2218

1086MO Lifileucel tumor-infiltrating lymphocyte (TIL) cell therapy in patients (pts) with advanced mucosal melanoma after progression on immune checkpoint inhibitors (ICI): Results from the phase II C-144-01 study

G-U. Grigoleit[1], H. Kluger[2], S. Thomas[3], J.A. Chesney[4], E. Domingo-Musibay[5], M.F. Sanmamed[6], T. Medina[7], M. Ziemer[8], E. Whitman[9], F. Graf Finckenstein[10], J. Chou[10], X. Wu[11], G. Sulur[10], W. Shi[10], A. Sarnaik[12]

[1]Hematology & Oncology, Helios Klinikum Duisburg, Duisburg, Germany; [2]Medical Oncology, Yale Cancer Center, New Haven, CT, USA; [3]Hematology & Oncology, Orlando Health Cancer Institute, Orlando, FL, USA; [4]Medical Oncology & Hematology, Brown Cancer Center University of Louisville, Louisville, KY, USA; [5]Medicine Department, University of Minnesota, Minneapolis, MN, USA; [6]Medical Oncology, Clinica Universidad de Navarra, Pamplona, Spain; [7]Medical Oncology, University of Colorado Cancer Center, Aurora, CO, USA; [8]Dermatologie, Venerologie und Allergologie, Universitätsklinikum Leipzig - Klinik und Poliklinik für Frauenheilkunde, Leipzig, Germany; [9]Surgical Oncology, Atlantic Health System, Morristown, NJ, USA; [10]Clinical Science, Iovance Biotherapeutics, Inc., San Carlos, CA, USA; [11]Biostatistics, Iovance Biotherapeutics, Inc., San Carlos, CA, USA; [12]Cutaneous Oncology, H. Lee Moffitt Cancer Center & Research Institute - Magnolia Campus, Tampa, FL, USA

Background: Advanced mucosal melanoma is rare and difficult to treat, with worse outcomes after anti—PD-1 therapy than nonmucosal melanoma (median ORR: 19%—23%; median OS: 11.3—13.4 mo in large pooled analyses [D'angelo *JCO* 2017 , Mignard *J Oncol* 2018 , Hamid *Br J Can* 2018]). Lifileucel, a one-time autologous TIL cell therapy, had an ORR of 31.4% in 153 pts with heavily pretreated advanced melanoma (only uveal excluded) in the C-144-01 study (NCT02360579; Chesney *JITC* 2022). We report outcomes of pts with advanced mucosal melanoma treated with lifileucel in C-144-01.

Methods: Pts (coh 2+4) must have progressed after anti—PD-1/PD-L1 therapy. Pts had $\geq$1 lesion resected for lifileucel manufacturing, then received lymphodepleting chemotherapy (cyclophosphamide 60 mg/kg/d $\times$ 2d; fludarabine 25 mg/m^2/d $\times$ 5d), a single lifileucel infusion, and up to 6 doses of high-dose IL-2. Responses were assessed by IRC per RECIST v1.1.

Results: Fifteen pts with mucosal melanoma were enrolled; lifileucel was manufactured for all 15 (100%), and lymph nodes were the most common source (47%). Twelve pts received lifileucel (median target lesion SOD: 118.9 mm; median prior lines of therapy: 2 [range: 1—6]; LDH >ULN: 42%; liver and/or brain metastases: 42%). Median number of TIL infused was 26 $\times$ 10^9 cells. ORR was 50% (95% CI: 21%—79%). At median study follow-up of 35.7 months, median DOR was not reached (NR; 95% CI: 12.5 mo—NR), median PFS was NR (95% CI: 1.4 mo—NR), and median OS was 19.4 mo (95% CI: 7.9—NR). TEAEs were consistent with known safety profiles of lymphodepleting chemotherapy and IL-2. The most common ($\geq$30%) G3/4 non-hematologic TEAEs were febrile neutropenia (58%) and hypotension (33%). Translational data will be presented.

Conclusions: In C-144-01, the activity of lifileucel in this small subset of pts with the difficult-to-treat mucosal melanoma subtype was clinically meaningful and durable (ORR: 50%; median DOR: NR) with anti-tumor activity that was consistent with the overall post-anti—PD-1/PD-L1 advanced melanoma population. These data further support the potential benefit of lifileucel as a one-time treatment that is differentiated from other immunotherapies.

Editorial acknowledgement: Writing assistance was provided by Amanda Kelly (Iovance Biotherapeutics, Inc.).

Legal entity responsible for the study: Iovance Biotherapeutics, Inc.

Funding: Iovance Biotherapeutics, Inc.

Disclosure: H. Kluger: Financial Interests, Institutional, Research Funding: Apexigen, BMS, Merck; Financial Interests, Personal, Advisory Role: BMS, Clinigen, Shionogi, Chemocentryx, Calithera, Signatero, Merck, Iovance. S. Thomas: Financial Interests, Personal, Speaker's Bureau: BMS, Merck, Pfizer, Ipsen, Amgen, Genentech, Foundation One; Financial Interests, Personal, Other, Travel, Accommodations, Expenses: BMS, Merck, Pfizer, Ipsen, Amgen, Genentech, Foundation One; Financial Interests, Personal, Advisory Role: BMS, Merck, Pfizer, Ipsen, Amgen, Genentech, Foundation One; Financial Interests, Institutional, Research Funding: BMS, Merck, Pfizer, Ipsen, Amgen, Genentech, Foundation One. J.A. Chesney: Financial Interests, Personal, Speaker, Consultant, Advisor: Amgen; Financial Interests, Institutional, Research Funding: Replimune, Amgen, Iovance Biotherapeutics, Inc., FATE. E. Domingo-Musibay: Financial Interests, Institutional, Other, Grants or contracts: Instil Bio. M.F. Sanmamed: Non-Financial Interests, Personal, Advisory Board: Numab, BMS, Pieris; Non-Financial Interests, Institutional, Research Funding: Roche, BMS; Financial Interests, Personal, Speaker's Bureau: MSD, Replimune; Financial Interests, Personal, Other, Grant travel: Roche, BMS, AZ. T. Medina: Financial Interests, Personal, Advisory Role: Merck, Bristol Myers Squibb, Iovance Biotherapeutics, Inc., Moderna, Nektar, Regeneron, Exicure, Checkmate, BioAtla, Xencor, Replimune, Day One Pharmaceuticals, Pfizer, Taiga. E. Whitman: Financial Interests, Personal, Advisory Board: Merck; Financial Interests, Personal, Speaker, Consultant, Advisor: Merck; Financial Interests, Personal, Speaker's Bureau: Merck, Bristol Myers Squibb, Regeneron, Castle BioSciences. F. Graf Finckenstein: Financial Interests, Personal, Leadership Role: Iovance Biotherapeutics, Inc.; Financial Interests, Personal, Stocks/Shares: Iovance Biotherapeutics, Inc.; Financial Interests, Personal, Full or part-time Employment: Iovance Biotherapeutics, Inc.; Financial Interests, Personal, Officer: Iovance Biotherapeutics, Inc. J. Chou, X. Wu, G. Sulur, W. Shi: Financial Interests, Personal, Full or part-time Employment: Iovance Biotherapeutics, Inc.; Financial Interests, Personal, Stocks/Shares: Iovance Biotherapeutics, Inc. A. Sarnaik: Non-Financial Interests, Institutional, Non-financial benefits: Iovance Biotherapeutics, Inc.; Financial Interests, Institutional, Royalties: Iovance Biotherapeutics, Inc.; Financial Interests, Personal, Speaker, Consultant, Advisor: Iovance Biotherapeutics, Inc., Guidepoint, Defined Health, Boxer Capital, Huron Consulting Group, Keyquest Health, Istari, Rising Tide, Gerson Lehram Group; Financial Interests, Personal, Speaker's Bureau: Society for ImmunoTherapy of Cancer, Physicians' Education Resource, Medscape, WebMD, MedStart Health; Financial Interests, Personal, Other, Support for attending meetings and/or travel: Iovance Biotherapeutics, Inc., Provectus Biopharmaceuticals; Financial Interests, Personal, Other, Patents: Moffitt Cancer Center, Provectus Biopharmaceuticals; Financial Interests, Institutional, Other, Receipt of equipment, materials, drugs, medical writing, gifts or other services: Bristol Myers Squibb, Genentech. All other authors have declared no conflicts of interest.

https://doi.org/10.1016/j.annonc.2023.09.2220

1087MO A single arm phase II, multicenter trial to evaluate the clinical activity and safety of avelumab plus cetuximab in unresectable stage III or IV cutaneous squamous cell carcinoma: First results from the AliCe study

J.C. Becker[1], B. Schilling[2], U. Leiter-Stoppke[3], L. Zimmer[4], J.C. Hassel[5], I. von Wasielewski[6], M. Ziemer[7], M. Fluck[8], F. Meier[9], A. Spillner[10], A. Gesierich[2], T. Eigentler[11], E. Livingstone[12], M. Albers[13], Y. Angela[14], R. Gutzmer[15]

[1]Translational Skin Cancer Research, German Cancer Consortium (DKTK), Essen, Germany; [2]Dermatology, UKW - University Hospital Würzburg, Würzburg, Germany; [3]Dermatology, Universitaetsklinik Tuebingen, Tuebingen, Germany; [4]Dermatology, Universitätsklinikum Essen, Essen, Germany; [5]Section of Dermato-Oncology, NCT - Nationales Zentrum für Tumorerkrankungen, Heidelberg, Germany; [6]Dermatology, MHH - Medizinische Hochschule Hannover, Hannover, Germany; [7]Dermatology, Universitätsklinikum Leipzig - Klinik und Poliklinik für Frauenheilkunde, Leipzig, Germany; [8]Internistischen Onkologie, Fachklinik Hornheide, Münster, Germany; [9]Skin Cancer Center, National Center for Tumor Diseases, Dept. of Dermatology, Universitaetsklinikum Carl Gustav Carus Dresden, Dresden, Germany; [10]Data Management, Alcedis GmbH, Giessen, Germany; [11]Dermatology, Charité - Universitätsmedizin Berlin, Berlin, Germany; [12]Dermatology Department, University Hospital Essen Westdeutsches Tumorzentrum, Essen, Germany; [13]Statistics, Alcedis GmbH, Giessen, Germany; [14]Dermatology, Johannes Weseling Klinikum, Minden, Germany; [15]Dermatology, Skin Cancer Center, Ruhr University Bochum Medizinische Universitätsklinik, Bochum, Germany

Background: In cutaneous squamous cell carcinoma (cSCC), both PD-1 and EGFR-inhibitors are effective, but durable tumor control, especially in anogenital cSCC, is still limited. For the latter, and refractory patients (pts), there is an unmet medical need.

Methods: Pts with unresectable stage III/IV cSCC were treated with PD-L1 inhibitor avelumab (10 mg/kg q2w) plus EGFR-inhibitor cetuximab (500 mg/m^2 q2w) for up to 1 year. The Safety Analysis (SAF) set was defined as pts who received at least 1 administration of study treatment, the per protocol (PP) set if treated for at least 12 weeks.

Results: 54 pts were registered (SAF Set: 51 pts; PP Set: 37 pts). Two-thirds of pts had prior systemic treatment for cSCC, i.e. chemotherapy or PD-1 inhibition. 31.4% (SAF) and 21.6% (PP) of primaries were anogenital cSCC. Within a median follow up of $\sim$ 2.5 years, median PFS/OS were 8.4/17.4 months in the SAF and 9.2/25.4 months in the PP set, respectively. No significant differences in PFS and OS were observed when subgroups for tumor stage (III vs. IV), location of primary (anogenital vs. elsewhere), or prior treatment (yes vs. no) were analyzed. Adverse events (AE) >= grade 3 were common, but adverse drug reactions (ADR) >= grade 3 occurred only in $\sim$ 20% of pts, which is explained by the frailty of pts with advanced cSCC. Only two pts discontinued treatment due to ADR (abnormal ECG, sarcoid-like lesions).

Table: 1087MO

Baseline characteristics and outcome data	SAF set (n=51)	PP set (n=37)
Mean age (years)	71.8	73.2
Sex female	33.3%	32.4%
ECOG > = 1	37.3%	43.2%
Stage (III/IV)	21.6%/78.4%	24.3%/75.7%
Anogenital primary	31.4%	21.6%
Prior systemic treatment	66.7%	67.6%
Response rate	45.1%	56.8%
Median PFS (95% CI), months	8.4 (4.5-10.2)	9.2 (8.3-12.5)
Median OS (95% CI), months	17.4 (11.1-33.1)	25.4 (13.9-NR)
AE > = grade 2	43 (84.3%)	32 (86.5%)
Adverse drug reactions (ADR) > = grade 3	10 (19.6%)	6 (16.2%)

Conclusions: Avelumab plus cetuximab is a feasible treatment option in patients with cSCC. This combination shows remarkable activity even in patients in whom PD-1 blockade has low efficacy, such as anogenital cSCC, or after failure of anti-PD-1 monotherapy.

Clinical trial identification: EudraCT 2018-001708-12.

Legal entity responsible for the study: Dermatologic Cooperative Oncology Group (DeCOG/ADO).

Funding: Merck KGaA/EMD.

Disclosure: J.C. Becker: Financial Interests, Personal, Advisory Board: Amgen, Merck, Recordati, Sanofi, Boehringer Ingelheim, InProTher, Almirall; Financial Interests, Personal, Other, Member of a DMSB: 4SC; Financial Interests, Institutional, Research Grant: IQVIA, Alcedis, Merck; Non-Financial Interests, Institutional, Product Samples: 4SC. L. Zimmer: Financial Interests, Personal, Advisory Board: Bristol Myers Squibb, Novartis, MSD, Sun Pharma, Pierre Fabre, Sanofi; Financial Interests, Personal, Other, Travel Support: Bristol Myers Squibb, MSD, Sun Pharma, Pierre Fabre, Sanofi, Novartis, Amgen; Financial Interests, Personal, Invited Speaker: Novartis, MSD, Pierre Fabre, Roche; Financial Interests, Personal and Institutional, Research Grant: Novartis; Non-Financial Interests, Member: German Cancer Society, Dermatologic Cooperative Oncology Group. J.C. Hassel: Financial Interests, Personal, Invited Speaker: BMS, Novartis, Sanofi, MSD, Sun Pharma, Almirall, Roche, Amgen, GSK, Pierre Fabre; Financial Interests, Personal, Advisory Board: MSD, Pierre Fabre, Sun Pharma, GSK; Financial Interests, Institutional, Advisory Board: Novartis, BMS, Immunocore, Nektar, Philogen; Financial Interests, Institutional, Research Grant: BMS, Sun Pharma; Financial Interests, Institutional, Local PI: Philogen, Genentech, 4SC, BioNTech, Idera, Iovance, Nektar, Pierre Fabre, Regeneron, Sanofi; Financial Interests, Institutional, Coordinating PI: BMS, Immunocore, Novartis; Financial Interests, Institutional, Steering Committee Member: Immunocore; Non-Financial Interests, Leadership Role: DeCOG; Non-Financial Interests, Member: ASCO. All other authors have declared no conflicts of interest.

https://doi.org/10.1016/j.annonc.2023.09.2221

1088MO A phase II study of neoadjuvant cemiplimab for stage II to IV cutaneous squamous cell carcinoma (CSCC): One-year follow-up

N. Gross[1], D.M. Miller[2], N.I. Khushalani[3], V. Divi[4], E. Ruiz[5], E.J. Lipson[6], F. Meier[7], Y.B. Su[8], P.L. Swiecicki[9], J.L. Atlas[10], J.L. Geiger[11], A. Hauschild[12], J.H. Choe[13], B.G.M. Hughes[14], S-Y. Yoo[15], M.D. Mathias[16], H. Han[16], M.G. Fury[16], D. Rischin[17]

[1]Head and Neck Surgery, The University of Texas MD Anderson Cancer Center, Houston, TX, USA; [2]Division of Hematology/Oncology, Beth Israel Deaconess Medical Center, Boston, MA, USA; [3]Department of Cutaneous Oncology, Moffitt Cancer Centre, Tampa, FL, USA; [4]Department of Otolaryngology-Head and Neck Surgery, Stanford University School of Medicine, Stanford, CA, USA; [5]Department of Dermatology, Brigham and Women's Hospital, Harvard Medical School, Boston, MA, USA; [6]Bloomberg ~ Kimmel Institute for Cancer Immunotherapy and Sidney Kimmel Comprehensive Cancer Centre, Johns Hopkins, Baltimore, MD, USA; [7]Skin Cancer Center, National Center for Tumor Diseases, Dept. of Dermatology, Universitaetsklinikum Carl Gustav Carus Dresden, Dresden, Germany; [8]Head and Neck Medical Oncology, Nebraska Cancer Specialists - Midwest Cancer Center-Legacy, Omaha, NE, USA; [9]Rogel Comprehensive Cancer Centre, University of Michigan, Ann Arbor, MI, USA; [10]Levine Cancer Institute, Carolinas HealthCare System/Atrium Health, Charlotte, NC, USA; [11]Solid Tumor Oncology, Cleveland Clinic, Cleveland, OH, USA; [12]Department of Dermatology, Schleswig-Holstein University Hospital, Kiel, Germany; [13]Medical Oncology, Duke Cancer Institute, Durham, NC, USA; [14]Department of Cancer Care Services, Royal Brisbane and Women's Hospital and University of Queensland, Herston, QLD, Australia; [15]Biostatistics, Regeneron Pharmaceuticals, Inc., Tarrytown, NY, USA; [16]Oncology Department, Regeneron Pharmaceuticals, Inc., Tarrytown, NY, USA; [17]Department of Medical Oncology, Peter MacCallum Cancer Centre and University of Melbourne, Melbourne, VIC, Australia

Background: We previously reported a high rate of pathologic complete response (pCR) or major pathologic response (MPR) to neoadjuvant (neoadj) cemiplimab (anti-programmed cell death-1) among 79 patients (pts) with locoregionally advanced, resectable CSCC. Here, we present 1-year follow-up data, with event-free, disease-free and overall survival (EFS, DFS, OS; NCT04154943).

Methods: This non-randomised multicentre phase II study had 2 parts. In part 1, pts with resectable stage II–IV (M0) CSCC received neoadj cemiplimab 350 mg every 3 weeks (Q3W) for up to 4 doses followed by curative-intent surgery. In Part 2, per investigator discretion, pts received adjuvant cemiplimab for up to 48 weeks or radiotherapy (RT) or observation only. EFS (time from first dose of neoadj cemiplimab to progressive disease precluding surgery, inability to undergo complete resection, disease recurrence, or death due to any cause); DFS (time from surgery until CSCC recurrence or death due to any cause) and OS were summarised by the Kaplan-Meier method.

Results: At December 1, 2022 data cut-off, median duration of follow-up was 18.7 months (range: 1.3–30.4) for all 79 pts. Among 70 pts who had surgery, the most common choices for subsequent care were observation only (n=29), cemiplimab (n=16), or RT (n=12) or other (Table). None of 40 pts with pCR and 1 of 10 pts with MPR experienced recurrence. Estimated 12-month EFS was 89% (95% confidence interval [CI]: 79–94%) for all pts and 95% (95% CI: 81–99%) for pts with pCR. Of 70 pts who completed surgery, 12-month DFS was 92% (95% CI: 82–97%). For all 79 pts: estimated 12-month OS rate was 92% (95% CI: 83–96%). Of 16 pts who received cemiplimab in part 2, there were 2 serious adverse events: grade 3 cardiomyopathy and grade 3 hypophysitis.

Table: 1088MO

n (%)	Pathology response by independent central pathology review: pCR (n = 40)	MPR (n = 10)	Non-pCR/non-MPR (n=20)
Adjuvant treatment in part 2			
Cemiplimab	12 (30)	1 (10)	3 (15)
Radiotherapy	1 (3)	5 (50)	6 (30)
Observation only[a]	24 (60)	3 (30)	2 (10)
Other			
Survival follow up	0	0	2 (10)
Imaging only[b]	0	0	6 (30)
Not applicable[c]	3 (8)	1 (10)	1 (5)
CSCC recurrence	0 (0)	1 (10)	2 (10)

[a]Patients in the "observation only" group had 4 doses of cemiplimab in Part 1. [b]Patients in the "imaging only" group had <4 doses of cemiplimab due to progressive disease in Part 1. [c]Included: lost to follow up (n=2), withdrawal of consent (n=1), fatal post-op COVID pneumonia (n=1), post-op death prior to starting Part 2 (n=1).

Conclusions: In pts with resectable stage II–IV CSCC, neoadj cemiplimab demonstrated favourable EFS, DFS and OS rates, and no recurrences in pts with pCR at a median follow-up of 18.7 months. There were no new safety signals with cemiplimab.

Clinical trial identification: NCT04154943.

Editorial acknowledgement: Medical writing support was provided by Jenna Lee, MSc, of Prime, Knutsford, UK, funded by Regeneron Pharmaceuticals, Inc., Sanofi.

Legal entity responsible for the study: Regeneron Pharmaceuticals, Inc., and Sanofi.

Funding: Regeneron Pharmaceuticals, Inc., and Sanofi.

Disclosure: N. Gross: Financial Interests, Institutional, Funding: Regeneron Pharmaceuticals, Inc.; Financial Interests, Personal, Advisory Board: PDS Biotechnology, Shattuck Labs, DragonFly Therapeutics, Sanofi, Merck, Genzyme; Financial Interests, Personal, Advisory Role: PDS Biotechnology, Shattuck Labs, DragonFly Therapeutics, Sanofi, Merck, Genzyme. D.M. Miller: Financial Interests, Personal, Advisory Role: Castle Biosciences, EMD Serono, Merck KGaA, Merck Sharpe & Dohme, Pfizer, Regeneron Pharmaceuticals, Inc., Sanofi Genzyme; Financial Interests, Personal, Stocks/Shares: Checkpoint Therapeutics, Avstera Therapeutics Corp; Financial Interests, Institutional, Funding: Kartos Therapeutics, NeoImmune Tech, Inc., Regeneron Pharmaceuticals, Inc. N.I. Khushalani: Financial Interests, Personal, Advisory Board: Regeneron Pharmaceuticals, Inc., Bristol Myers Squibb, Merck, Novartis, Iovance, Instil Bio, Castle Biosciences, Nektar, Incyte (data safety monitoring committee), AstraZeneca (data safety monitoring committee), Jounce Therapeutics; Financial Interests, Personal, Research Grant: Regeneron Pharmaceuticals, Inc., Bristol Myers Squibb, Merck, Novartis, Replimune, GSK, HUYA, Celgene; Financial Interests, Personal, Other, Honoraria: Genzyme, NCCN (from Pfizer), Nektar (study steering committee); Financial Interests, Personal, Stocks or ownership: Bellicum Pharmaceuticals, Amarin, Transenetrix. V. Divi: Financial Interests, Institutional, Research Funding: Genentech; Financial Interests, Personal, Advisory Board: Regeneron Pharmaceuticals, Inc. E. Ruiz: Financial Interests, Personal, Advisory Board: Genentech, Leo Pharmaceuticals, Regeneron Pharmaceuticals, Inc., Sanofi; Financial Interests, Personal, Advisory Role: Genentech, Leo Pharmaceuticals, Regeneron Pharmaceuticals, Inc., Sanofi; Financial Interests, Personal, Member of Board of Directors: Checkpoint Therapeutics. E.J. Lipson: Financial Interests, Personal, Advisory Board: Bristol Myers Squibb, Merck, Sanofi, Regeneron, Genentech, Eisai, Instil Bio, Natera, Nektar Therapeutics, Pfizer, Rain Therapeutics, CareDx, Immunocore, Novartis, Replimune, HUYA Bioscience International; Financial Interests, Personal, Other, Consultant: OncoSec; Financial Interests, Institutional, Coordinating PI: Bristol Myers Squibb; Financial Interests, Institutional, Local PI: Regeneron, Merck, Sanofi. F. Meier: Financial Interests, Personal, Other, Travel support, speaker's fees or advisor's honoraria: Bristol Myers Squibb, Merck Sharp & Dohme, Novartis, Pierre Fabre, Roche, Sanofi; Financial Interests, Institutional, Research Funding: Novartis, Roche. P.L. Swiecicki: Financial Interests, Institutional, Research Grant: Ascentage Pharma, Pfizer; Financial Interests, Personal, Advisory Board: Elevar Therapeutics, Prelude Therapeutics, Regeneron Pharmaceuticals, Inc. J.L. Atlas: Financial Interests, Personal, Advisory Board: Bristol Myers Squibb, Castle Biosciences, Pfizer, Regeneron Pharmaceuticals, Inc., Sanofi; Financial Interests, Personal, Advisory Role: Bristol Myers Squibb, Castle Biosciences, Pfizer, Regeneron Pharmaceuticals, Inc., Sanofi. J.L. Geiger: Financial Interests, Institutional, Research Funding: Alkermes, Merck, Regeneron Pharmaceuticals, Inc., Roche/Genentech; Financial Interests, Institutional, Sponsor/Funding: EMD Serono; Financial Interests, Personal, Advisory Board: Astellas, Exelixis, Merck, Regeneron Pharmaceuticals, Inc.; Financial Interests, Personal, Advisory Role: Astellas, Exelixis, Merck, Regeneron Pharmaceuticals, Inc. A. Hauschild: Financial Interests, Personal, Advisory Board: BMS, MSD, Philogen, Pierre Fabre, Regeneron, Roche, Sanofi, Novartis, Eisai, Immunocore, Replimune, Seagen, Dermagnostix, Neracare, IO Biotech, Incyte, Highlight Therapeutics, Agenus; Financial Interests, Personal, Invited Speaker: Merck, Pfizer; Financial Interests, Institutional, Local PI: BMS, MSD, Pierre Fabre, Amgen, Roche, Agenus; Financial Interests, Institutional, Coordinating PI: Regeneron, Novartis. J.H. Choe: Financial Interests, Personal, Advisory Role: Exelixis, Coherus Biosciences, Merck Sharp & Dohme, Regeneron Pharmaceuticals, Inc.; Financial Interests, Institutional, Research Funding: Genmab A/S, Arcus Biosciences. B.G.M. Hughes: Financial Interests, Personal, Advisory Role: AstraZeneca, Bristol Myers Squibb, Eisai, Merck Sharp & Dohme, Pfizer, Roche; Financial Interests, Institutional, Research Funding: Amgen. S. Yoo, M.D. Mathias, H. Han, M.G. Fury: Financial Interests, Personal, Full or part-time Employment: Regeneron Pharmaceuticals, Inc.; Financial Interests, Personal, Stocks/Shares: Regeneron Pharmaceuticals, Inc. D. Rischin: Financial Interests, Institutional, Research Grant: Regeneron Pharmaceuticals, Inc., Genentech, Sanofi, Kura Oncology, Roche, Merck Sharp & Dohme, Merck KGaA, Bristol Myers Squibb, GSK, ALX Oncology; Non-Financial Interests, Personal, Advisory Board: Merck Sharp & Dohme, Regeneron Pharmaceuticals, Inc., Sanofi, GSK, Bristol Myers Squibb; Non-Financial Interests, Personal, Steering Committee Member: Merck Sharp & Dohme, Regeneron Pharmaceuticals, Inc., Sanofi, GSK, Bristol Myers Squibb. All other authors have declared no conflicts of interest.

https://doi.org/10.1016/j.annonc.2023.09.2222

1089P Adjuvant nivolumab (NIVO) vs ipilimumab (IPI) in resected stage III/IV melanoma: 7-y results from CheckMate 238

P.A. Ascierto[1], M. Del Vecchio[2], B. Merelli[3], H. Gogas[4], A.M. Arance Fernandez[5], S. Dalle[6], C.L. Cowey[7], M. Schenker[8], J.J. Grob[9], V. Chiarion Sileni[10], I. Marquez-Rodas[11], M.O. Butler[12], A.M. Di Giacomo[13], M. Pe Benito[14], R. Soomro[14], M. Askelson[14], J.S. Weber[15], J. Larkin[16]

[1]Melanoma, Cancer Immunotherapy & Developmental Therapeutics, Istituto Nazionale Tumori IRCCS Fondazione Pascale, Naples, Italy; [2]Medical Oncology, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy; [3]Oncology, ASST Papa Giovanni XXIII Bergamo, Bergamo, Italy; [4]First Department of Medicine, National and Kapodistrian University of Athens, Athens, Greece; [5]Medical Oncology, Hospital Clínic Barcelona, Barcelona, Spain; [6]Medical Oncology, Hospices Civils de Lyon, Pierre Benite, France; [7]Medical Oncology, Texas Oncology-Baylor Charles A. Sammons Cancer Center, Dallas, TX, USA; [8]Medical Oncology, Oncology Center Sf Nectarie Ltd., Craiova, Romania; [9]Medical Oncology, Aix-Marseille University, AP-HM de la Timone Hospital, Marseille, France; [10]Clinical and Experimental Oncology Dept., Veneto Institute of Oncology IOV — IRCCS 4, Padua, Italy; [11]Medical Oncology, General University Hospital Gregorio Marañón & CIBERONC, Madrid, Spain; [12]Medical Oncology and Hematology Department, Princess Margaret Cancer Centre, Department of Medical Oncology and Hematology, University of Toronto, Toronto, ON, Canada; [13]Medical Oncology and Immunotherapy, University of Siena and Center for Immuno-Oncology, University Hospital of Siena, Siena, Italy; [14]Medical Oncology, Bristol Myers Squibb, Princeton, NJ, USA; [15]Perlmutter Cancer Center, Laura and Isaac Perlmutter Cancer Center, New York, NY, USA; [16]Medicine Department, The Royal Marsden NHS Foundation Trust, London, UK

Background: In the phase III CheckMate 238 trial, NIVO showed improved recurrence-free survival (RFS) and distant metastasis-free survival (DMFS) vs IPI in pts with high-risk, resected stage IIIB—C or IV melanoma, sustained for 5 y; no significant difference was observed in OS. Updated 7-y results are presented.

Methods: Pts aged > 15 y (stratified by disease stage and PD-L1 status) were randomized 1:1 to NIVO 3 mg/kg Q2W (n = 453) or IPI 10 mg/kg Q3W for 4 doses then Q12W (n = 453), for up to 1 y or until disease recurrence/unacceptable toxicity. Endpoints included RFS, OS, DMFS in stage III pts, and safety. Progression-free survival through next-line therapy (PFS2) and melanoma-specific survival (MSS) are post hoc analyses presented here for the first time.

Results: At 7-y, RFS remained superior with NIVO vs IPI (HR 0.74; 95% CI 0.62—0.88) with DMFS and PFS2 also favoring NIVO (Table). New recurrence events since 5 y included 12 new events (2 regional, 7 distant, 2 new primary, 1 death) for NIVO and 7 new events (1 local, 2 distant, 4 deaths) for IPI; 6% and 5% of at-risk pts relapsed after yr 5. For NIVO vs IPI respectively, there were a total of 13 and 12 new deaths overall (8 and 10 due to melanoma). Subsequent systemic therapy was less frequent with NIVO than IPI (36% vs 44%), including subsequent immunotherapy in 26% vs 36% of pts. No new voluntarily reported late-emergent treatment-related adverse events were reported since the 4-y database lock, and overall rates remain low.

Conclusions: At 7-y follow-up, the longest follow-up of any anti—PD-1 therapy in this setting, NIVO showed superior long-term RFS vs IPI in pts with stage IIIB—C or IV resected melanoma. DMFS and PFS2 also favored NIVO, and OS and MSS rates were high in both arms, with no significant difference between arms. The additional recurrences at 7-y vs 5-y follow-up may indicate a clinical consideration for imaging and follow-up visits beyond 5 y.

Table: 1089P

	NIVO (n = 453)	IPI (n = 453)
	7-y rates, % (95% CI) HR[a] (95% CI)	
RFS	45 (40—50) 0.74 (0.62—0.88)	38 (33—42)
OS	71 (66—75) 0.89 (0.70—1.14)	69 (64—73)
MSS	75 (70—79) 0.89 (0.68—1.16)	72 (68—76)
DMFS[b]	54 (48—60) 0.82 (0.66—1.01)	50 (44—55)
PFS2	59 (54—64) 0.76 (0.62—0.93)	52 (48—57)

[a]NIVO vs IPI (Stratified Cox proportional hazards model). [b]In stage III patients (NIVO = 307; IPI = 366).

Clinical trial identification: NCT02388906.

Editorial acknowledgement: Professional medical writing and editorial assistance were provided by Jessica Augello, PhD, and Michele Salernitano of Ashfield MedComms, an Inizio company, and funded by Bristol Myers Squibb.

Legal entity responsible for the study: Bristol Myers Squibb.

Funding: Supported by Bristol Myers Squibb Company and ONO Pharmaceutical.

Disclosure: P.A. Ascierto: Financial Interests, Personal, Other, Consultant and Advisory Role: BMS, Roche Genentech, MSD, Novartis, Merck Serono, Pierre Fabre, AstraZeneca, Sun Pharma, Sanofi, Idera, Sandoz, Immunocore, 4SC, Nektar, Boehringer Ingelheim, Regeneron; Financial Interests, Personal, Other, Consultant and Advisory Role. Travel support: Pfizer/Array; Financial Interests, Personal, Other, Consultant Role: Italfarmaco; Financial Interests, Personal, Other, Advisory Role: Eisai, Seagen; Financial Interests, Personal, Other, Consultant Role: Daiichi Sankyo, Pfizer, OncoSec, Nouscom, Lunaphore; Financial Interests, Personal, Other, Consultant role: Medicenna; Financial Interests, Personal, Other, Consultant role and travel support: Bio-AI Health; Financial Interests, Personal, Advisory Board, Consultant and Advisory Role: iTeos; Financial Interests, Personal, Advisory Board, Consultant and Advisory role: ValoTx; Financial Interests, Personal, Advisory Board, Consultant and Advisor role. Travel support: Replimune; Financial Interests, Personal, Advisory Board, Advisor role: Bayer; Financial Interests, Institutional, Funding, Clinical Trial: Pfizer/Array, Roche Genentech, Sanofi; Financial Interests, Personal, Advisory Board: Erasca; Financial Interests, Institutional, Funding, Clinical trial and translational research: BMS; Non-Financial Interests, Leadership Role, President since 2010: Fondazione Melanoma Onlus Italy; Non-Financial Interests, Leadership Role, President since 2014: Campania Society of ImmunoTherapy of Cancer (SCITO) Italy; Non-Financial Interests, Other, Member of Steering Committee since 2016: Society for Melanoma Research (SMR); Non-Financial Interests, Member of Board of Directors, November 2017 - December 2021: Society for Immunotherapy of Cancer (SITC); Non-Financial Interests, Member: ASCO, SITC, EORTC Melanoma Cooperative Group, SMR, AIOM. M. Del Vecchio: Financial Interests, Personal, Advisory Board: BMS, MSD, Novartis, Pierre Fabre, Immunocore. H. Gogas: Financial Interests, Personal, Advisory Board: MSD, BMS, Pierre Fabre, Sanofi; Financial Interests, Personal, Invited Speaker: MSD, BMS, Novartis, Pierre Fabre, Sanofi; Financial Interests, Steering Committee Member: Amgen, Replimune; Financial Interests, Institutional, Local PI: Amgen, MSD, BMS, Replimune, Iovance, Bayer; Financial Interests, Institutional, Research Grant: BMS, Pfizer, Lilly, Pierre Fabre. A.M. Arance Fernandez: Financial Interests, Personal, Advisory Board, Consultant /Advisory/Speaker/Travel, Accommodation, Expenses/: Pierre Fabre, Novartis, Roche, BMS, MSD, Merck, Sanofi; Financial Interests, Institutional, Other, Research Funding: Pierre Fabre, Novartis, MSD, BMS, Merck, Roche, Sanofi, Amgen. S. Dalle: Financial Interests, Institutional, Research Grant: BMS, MSD, Pierre Fabre; Financial Interests, Personal, Financially compensated role: BMS, MSD, Pierre Fabre; Financial Interests, Personal, Stocks/Shares: Sanofi. C.L. Cowey: Financial Interests, Personal, Speaker, Consultant, Advisor: Merck, EMD Serono, Eisai, Regeneron, Iovance. M. Schenker: Financial Interests, Institutional, Research Grant: BMS, AbbVie, Amgen, Astellas, AstraZeneca, Bayer, BeiGene, Clovis, Eli Lilly, Gilead, GSK, Merck, MSD, Mylan, Novartis, Pfizer, PharmaMar, Regeneron, Roche, Samsung Pharmaceuticals, Serono, Tesaro. J.J. Grob: Financial Interests, Personal, Advisory Board: BMS, MSD, Pierre Fabre, Sanofi, Novartis, Philogen. V. Chiarion Sileni: Financial Interests, Personal, Advisory Board, analysis of treatment modality (diagnosis, staging, surgery, radiotherapy, systemic therapy for Merkel cell carcinoma in Italy: Merck-Serono; Financial Interests, Institutional, Invited Speaker, treatment option for BRAF mutated melanoma: Novartis; Financial Interests, Institutional, Invited Speaker, Treatment choices for BRAF mutated melanoma, evidence-based, and biologically supported: Pierre Fabre; Financial Interests, Institutional, Invited Speaker, Immunotherapy for melanoma treatment present and future: Bristol Myers Squibb; Financial Interests, Personal, Other, Travel, registration, and accommodation to attend ASCO annual meetings: Pierre Fabre. I. Marquez-Rodas: Financial Interests, Personal, Advisory Board: BMS, MSD, Novartis, Pierre Fabre, Roche, GSK, AstraZeneca, Celgene, Regeneron, Sanofi, Merck Serono, Highlight Therapeutics, Bioline Rx, Sun Pharma, Immunocore; Financial Interests, Personal and Institutional, Coordinating PI, GEM1802 clinical trial: Pierre Fabre; Financial Interests, Institutional, Coordinating PI, GEM1801 clinical study: Novartis, BMS, Roche, Pierre Fabre, Incyte, MSD; Financial Interests, Institutional, Coordinating PI, National coordinator of Spotlight 203 clinical trial: Highlight Therapeutics; Non-Financial Interests, Member of Board of Directors: Spanish Melanoma Group. M.O. Butler: Financial Interests, Personal, Speaker's Bureau: BMS, Merck, Novartis, Sanofi, Pfizer; Financial Interests, Personal, Advisory Board: Merck, BMS, Novartis, Adaptimmune, Instil Bio, Iovance, Sun Pharma, GSK, Sanofi, LaRoche Possey, Pfizer, Medison, IDEAYA, Regeneron; Financial Interests, Personal, Research Grant: Merck, Takara Bio, Novartis. A.M. Di Giacomo: Financial Interests, Personal, Advisory Board: Bristol Myers Squibb, MSD, Pierre Fabre, Novartis; Financial Interests, Personal, Invited Speaker: Sanofi. M. Pe Benito, M. Askelson: Financial Interests, Personal, Full or part-time Employment: Bristol Myers Squibb; Financial Interests, Personal, Stocks/Shares: Bristol Myers Squibb. J.S. Weber: Financial Interests, Personal, Advisory Board, Ad Boards: BMS; Financial Interests, Personal, Advisory Board: Merck, GSK, Incyte, Genentech, Pfizer, Biond, OncoC4, AstraZeneca, Regeneron, ImCheck, Novartis; Financial Interests, Personal, Stocks/Shares: Biond, Evaxion, Instil Bio, OncoC4; Financial Interests, Personal, Royalties: Moffitt Cancer Center; Financial Interests, Institutional, Local PI: BMS, Regeneron; Financial Interests, Institutional, Coordinating PI: Merck, Novartis; Non-Financial Interests, Principal Investigator: Moderna, BMS; Non-Financial Interests, Member: ASCO. J. Larkin: Financial Interests, Personal, Invited Speaker: BMS, Pfizer, Roche, Pierre Fabre, AstraZeneca, Novartis, EUSA Pharma, MSD, Merck, GSK, Ipsen, Aptitude, Eisai, Calithera, Ultimovacs, Seagen, Goldman Sachs, eCancer, Inselgruppe, Agence Unik; Financial Interests, Personal, Other, Consultancy: Incyte, iOnctura, Apple Tree, Merck, BMS, Eisai, Debiopharm; Financial Interests, Personal, Other, Honorarium: touchIME, touchEXPERTS, VJOncology, RGCP, Cambridge Healthcare Research, Royal College of Physicians; Financial Interests, Institutional, Funding: BMS, MSD, Novartis, Pfizer, Achilles, Roche, Nektar, Covance, Immunocore, Pharmacyclics, Aveo. All other authors have declared no conflicts of interest.

https://doi.org/10.1016/j.annonc.2023.09.2223

1090P Outcome impact of time from complete resection to start of adjuvant immunotherapy in stage III-IV melanoma patients

S. Martinez Recio[1], M.A. Molina Pérez[1], E. Muñoz Couselo[2], A.R. Sevillano Tripero[3], J. Martin-Liberal[4], M. Orrillo[4], A.M. Arance Fernandez[5], F. Aya Moreno[5], L.A. Fernández-Morales[6], M. Quindos Varela[7], R. Lesta[7], A. Barba Joaquín[1], I.G. Sullivan[1], M. Majem[1]

[1]Medical Oncology Department, Hospital de la Santa Creu i Sant Pau, Barcelona, Spain; [2]Medical Oncology Department, Vall d'Hebron University Hospital, Barcelona, Spain; [3]Medical Oncology Department, Hospital Universitario San Cecilio, Granada, Spain; [4]Medical Oncology Department, Institut Català d'Oncologia l'Hospitalet, L'Hospitalet de Llobregat, Spain; [5]Medical Oncology Department, Hospital Clinic y Provincial de Barcelona, Barcelona, Spain; [6]Medical Oncology Department, Hospital Universitario Parc Taulí, Sabadell, Spain; [7]Medical Oncology Department, CHUAC - Complexo Hospitalario Universitario A Coruña, A Coruña, Spain

Background: Adjuvant therapy with immune checkpoint inhibitors improves outcomes in patients with resected melanoma. However, clinical trials included patients that started treatment within a maximum of three months after complete resection. The objective of this study is to analyze whether starting adjuvant therapy beyond 3 months after surgery could impact on efficacy.

Methods: This is a multicenter retrospective study of patients with completely surgically resected stage III to IV melanoma that have been treated with PD-1 inhibitors (either alone or in combination). We compared efficacy and pattern of recurrence according to the period of time from last resection to the start of immunotherapy (more -group A- or less -group B- than three months).

Results: We included 214 patients, group A included 31 (14%) patients and group B 183 (86%) patients; baseline characteristics were similar between both groups. With a median follow up of 20 months, 22 (71%) patients in group A and 76 (42%) patients in group B have recurred; the median disease free survival (DFS) was 8,4 months (95% CI 2-14,8) in group A and 43,4 months (95%CI 26-60,7) in group B (log rank p=0,002). After multivariate analysis Hazard Ratio (HR) was 3,8 (95% CI 2,1-6,8, p<0,001). Patients in group A presented higher rate of distant recurrence (86% vs 73%) and visceral non-pulmonary recurrence (18% vs 8%) than group B, without differences in central nervous system (CNS) recurrence (18% vs 15%). For patients with distant recurrence that received systemic therapy (18 in group A and 51 in group B), both groups showed similar overall response rate (40% vs 42%) and DFS (median 6,6 vs 8,9 months, p>0,05). Group A showed a trend to shorter overall survival (OS) than group B (median OS NR in both groups; OS at 18 and 24 months were 81% and 69% in group A vs 91% and 87% in group B, respectively).

Conclusions: Starting adjuvant PD-1 inhibitors after more than 3 months from last resection surgery negatively impacts in DFS in patients with resected melanoma, with a higher proportion of distant recurrence.

Legal entity responsible for the study: Hospital de la Santa Creu i Sant Pau.

Funding: Has not received any funding.

Disclosure: S. Martinez Recio: Financial Interests, Personal, Invited Speaker: Pierre Fabre, Sanofi; Other, Other, Travel fees, meeting registration expenses: Merck; Other, Other, Accommodation expenses: Sanofi; Other, Other, Travel fees: Lilly. E. Muñoz Couselo: Financial Interests, Personal, Advisory Role: BMS, MSD, Pierre Fabre, Sanofi, Roche, Immunocore; Financial Interests, Personal, Invited Speaker: Novartis, BMS, MSD, Pierre Fabre, Sanofi; Financial Interests, Personal, Other, Travels, accommodations, expenses: MSD; Financial Interests, Personal, Other, Travels, accommodations, Expenses: BMS. J. Martin-Liberal: Financial Interests, Personal, Invited Speaker: Astellas, Bristol Myers Squibb, MSD, Novartis, Pierre Fabre, Pfizer, Roche, Sanofi; Financial Interests, Personal, Advisory Board: Bristol Myers Squibb, Novartis, Pierre Fabre, Roche, Sanofi, Highlight Therapeutics; Financial Interests, Personal, Other, Travel grant: Bristol Myers Squibb, MSD, Novartis, Pierre Fabre, Pfizer, Roche, Ipsen. A.M. Arance Fernandez: Financial Interests, Personal, Advisory Board, Consultant /Advisory/Speaker/Travel, Accommodations, Expenses: Pierre Fabre, Novartis, Roche, BMS, MSD, Merck, Sanofi; Financial Interests, Institutional, Other, Research Funding: Pierre Fabre, Novartis, MSD, BMS, Merck, Roche, Sanofi, Amgen. F. Aya Moreno: Financial Interests, Personal, Invited Speaker: MSD, Novartis; Financial Interests, Personal, Other, Scientific Coordinator and Communication Officer: GETICA; Non-Financial Interests, Other, ASEICA Young committee member: ASEICA. L.A. Fernández-Morales: Financial Interests, Personal, Invited Speaker: BMS, MSD, Pierre Fabre, Roche, Novartis, Pfizer; Financial Interests, Personal, Advisory Role: Novartis, Pfizer. M. Quindos Varela: Financial Interests, Personal, Speaker, Consultant, Advisor: BMS, Novartis; Financial Interests, Personal, Speaker's Bureau: Pierre Fabre, MSD, Sanofi. R. Lesta: Financial Interests, Personal, Invited Speaker: Rovi, Sanofi; Financial Interests, Personal, Other, Travel, accommodation, expenses: Roche, GSK, AstraZeneca, MSD, Pierre Fabre. A. Barba Joaquín: Financial Interests, Personal, Invited Speaker: Pfizer, MSD, Sanofi, BMS, Novartis, Roche, AstraZeneca, Pierre Fabre; Financial Interests, Personal, Advisory Board: BMS, Sanofi; Non-Financial Interests, Principal Investigator, PI - Clinical Trial C4221016: Pfizer. I.G. Sullivan: Financial Interests, Personal, Advisory Board: Roche, Novartis, Boehringer Ingelheim, Takeda, Sanofi, Bristol Myers Squibb; Financial Interests, Personal, Invited Speaker: Roche, AstraZeneca, Takeda, Pfizer, Merck Sharp & Dohme; Financial Interests, Personal, Other, Travel grant: Roche, Takeda, Lilly, AstraZeneca. M. Majem: Financial Interests, Personal, Advisory Board: Amgen, Roche, AstraZeneca, Takeda, Janssen, Casen Recordati, BMS; Financial Interests, Personal, Invited Speaker: Amgen, Roche, AstraZeneca, Pfizer, Takeda, Helsinn; Financial Interests, Institutional, Funding: BMS, AstraZeneca, Roche. All other authors have declared no conflicts of interest.

https://doi.org/10.1016/j.annonc.2023.09.2224

1091P Relapse-free survival with adjuvant dabrafenib/trametinib therapy after relapse on a prior adjuvant checkpoint inhibitor and subsequent surgical resection in patients with BRAF V600-mutated stage III/IV melanoma

J.S. Weber[1], W. Haque[1], S.N. Markovic[2], A.K.S. Salama[3], I. Mehmi[4], R.J. Sullivan[5], Y.G. Najjar[6], A.C.J. van Akkooi[7], A.M. Menzies[8], G.V. Long[8], A.M. Taylor[8], J.B.A.G. Haanen[9], L. Zijlker[10], K. Davis[11], S. Karanth[11], R. Shah[12], L. Connolly[13], D. Norton[14]

[1]Laura and Isaac Perlmutter Cancer Center, NYU Langone Health, New York, NY, USA; [2]Medical Oncology, Mayo Clinic - Rochester, Rochester, MN, USA; [3]Duke Cancer Center, Duke University, Durham, NC, USA; [4]Dept. of Medicine, The Angeles Clinic & Research Institute, Los Angeles, CA, USA, Santa Monica, CA, USA; [5]Cancer Center, MGH - Massachusetts General Hospital, Boston, MA, USA; [6]Hillman Cancer Center, University of Pittsburgh Medical Center, Pittsburgh, PA, USA; [7]Surgical Oncology Dept., Melanoma Institute Australia, Wollstonecraft, NSW, Australia; [8]Medical Oncology, Melanoma Institute Australia, Wollstonecraft, NSW, Australia; [9]Medical Oncology Dept., NKI-AVL - Netherlands Cancer Institute/Antoni van Leeuwenhoek Hospital, Amsterdam, Netherlands; [10]Surgical Oncology, NKI-AVL - Netherlands Cancer Institute/Antoni van Leeuwenhoek Hospital, Amsterdam, Netherlands; [11]Health Economics, RTI Health Solutions, Research Triangle Park, NC, USA; [12]Thoracic Surgery Dept., Novartis Pharmaceuticals Corporation, East Hanover, NJ, USA; [13]Real-World Evidence, Novartis Ireland Limited, Dublin, Ireland; [14]Oncology, Novartis Pharmaceuticals Corporation, East Hanover, NJ, USA

Background: In BRAF mutant resected melanoma, both targeted therapy and immunotherapy have shown durable clinical benefit as 1st line (1L) adjuvant therapy. However, there are no clinical studies evaluating 2nd line (2L) adjuvant targeted therapy in patients with locoregional relapse and complete surgical resection following initial adjuvant immunotherapy.

Methods: This was a retrospective, multicenter chart review study of BRAF V600-mutated stage III/IV melanoma patients in the United States, Australia, and The Netherlands who received 1L adjuvant checkpoint inhibitor therapy, then relapsed locoregionally or distantly, were again resected to NED, and then treated with dabrafenib/trametinib (dab/tram) as 2L adjuvant therapy. The primary endpoint was relapse-free survival (RFS-2) after initiation of dab/tram therapy. Secondary endpoints included overall survival (OS) and distant metastasis-free survival (DMFS). Analyses were descriptive with event time endpoints (RFS-2, OS, DMFS) estimated using the Kaplan-Meier method.

Results: A total of 37 patients were included (median age 51 years, 62% male, 89% stage III, median follow-up of 19 months from dab/tram initiation). Median time to dab/tram initiation after repeat resection to NED was 0.9 months (range: 0.2 — 2.8 months). A majority (73%) had discontinued dab/tram by last follow-up, with median therapy duration of 10.1 months (range: 1 day — 22.7 months). Median (95% confidence interval [CI]) RFS-2 was 18.9 (14.9 — 28.1) months, with 91% and 81% remaining relapse-free at 12 and 18 months, respectively; most patients also remained distant metastasis-free at 6 months (97%) and 12 months (85%). Only 2 patients were deceased at last follow-up, with nearly all patients (97%) still alive at 18 months; median OS was not reached.

Conclusions: More than 80% of patients remained relapse- and metastasis-free for at least 12 months after initiation of dab/tram. Longer follow-up and a larger patient cohort is needed in future studies to confirm efficacy of 2L adjuvant dab/tram in this population.

Legal entity responsible for the study: Novartis.

Funding: Novartis.

Disclosure: J.S. Weber: Financial Interests, Personal, Advisory Board, Ad Boards: BMS; Financial Interests, Personal, Advisory Board: Merck, GSK, Incyte, Genentech, Pfizer, Biond, OncoC4, AstraZeneca, Regeneron, ImCheck, Novartis; Financial Interests, Personal, Stocks/Shares: Biond, Evaxion, Instil Bio, OncoC4; Financial Interests, Personal, Royalties: Moffitt Cancer Center; Financial Interests, Institutional, Local PI: BMS, Regeneron; Financial Interests, Institutional, Coordinating PI: Merck, Novartis; Non-Financial Interests, Principal Investigator: Moderna, BMS; Non-Financial Interests, Member: ASCO. S.N. Markovic: Financial Interests, Institutional, Royalties: Sorrento; Financial Interests, Institutional, Research Grant: Sorrento; Non-Financial Interests, Institutional, Research Grant: BMS; Non-Financial Interests, Institutional, Local PI: BMS. A.K.S. Salama: Financial Interests, Personal, Advisory Board: Bristol Myers Squibb, Iovance, Regeneron, Replimune, Novartis, Pfizer; Financial Interests, Institutional, Invited Speaker: Bristol Myers Squibb, Ascentage, IDEAYA, Immunocore, Merck, Olatec, Regeneron, Replimune, Seagen. I. Mehmi: Financial Interests, Personal, Invited Speaker: BMS; Financial Interests, Personal, Advisory Board: AstraZeneca. R.J. Sullivan: Financial Interests, Personal, Advisory Board: Merck, Novartis, Bristol Myers Squibb, Eisai, Iovance, OncoSec, Pfizer, Replimune, Marengo; Financial Interests, Personal, Royalties: Up-To-Date; Financial Interests, Institutional, Research Grant: Merck; Financial Interests, Institutional, Invited Speaker: GSK, Pfizer, Sanofi, Moderna, Roche-Genentech, BioMed Valley Discoveries, Astex, Compugen, Beigene, Novartis, Rubius, Alkermes, Simcha Therapeutics, OnKure, Marengo, Synthekine. Y.G. Najjar: Financial Interests, Personal, Advisory Board: Immunocore, InterVenn Bio, Merck, BMS, Pfizer, Novartis; Financial Interests, Personal, Invited Speaker: Immunocore, Pfizer; Non-Financial Interests, Institutional, Funding: Merck, Pfizer, BMS, Replimune. A.C.J. van Akkooi: Financial Interests, Institutional, Advisory Board: Amgen, Bristol Myers Squibb, Novartis, MSD-Merck, Merck-Pfizer, Pierre Fabre, Sanofi, Sirius Medical, 4SC, Provectus; Financial Interests, Institutional, Research Grant, NIVEC study: Amgen; Financial Interests, Institutional, Research Grant: Merck-Pfizer. A.M. Menzies: Financial Interests, Personal, Advisory Board, advisory board: BMS, MSD, Novartis, Roche, Pierre Fabre, QBiotics. G.V. Long: Other, Personal, Advisory Role: Agenus Inc., Amgen Inc., Array Biopharma, Boehringer Ingelheim, BMS, Evaxion Biotech, Hexal AG, Highlight Therapeutics, Innovent Biologics, MSD, Novartis Pharmaceuticals, OncoSec, PHMR, Pierre Fabre, Provectus, QBiotics, Regeneron. J.B.A.G. Haanen: Financial Interests, Institutional, Advisory Board: Bristol Myers Squibb, Achilles Therapeutics, Ipsen, Merck Sharp & Dohme, Merck Serono, Pfizer, Molecular Partners, Novartis, Roche, Sanofi, Third Rock Venture, Iovance Biotherapeutics; Financial Interests, Institutional,

Advisory Board, SAB member: BioNTech, Immunocore, Gadeta, Instil Bio, PokeAcel, T-Knife; Financial Interests, Personal, Advisory Board, SAB member: Neogene Therapeutics, Scenic; Financial Interests, Personal, Stocks/Shares: Neogene Therapeutics; Financial Interests, Institutional, Research Grant: Bristol Myers Squibb, BioNTech US, Merck Sharp & Dohme, Amgen, Novartis, Asher Bio; Non-Financial Interests, Member: ASCO, AACR, SITC; Other, Other, Editor-in-Chief IOTECH: ESMO; Other, Other, Editorial Board ESMO Open: ESMO; Other, Other, Editorial Board: Kidney Cancer. K. Davis: Financial Interests, Institutional, Funding: Novartis, AstraZeneca, Eisai, Gilead, Pfizer, Merck, Bristol Myers Squibb. S. Karanth: Financial Interests, Institutional, Funding, Full-time employee of RTI Health Solutions, an independent non-profit research organization, which was retained by Novartis to conduct the research that is being submitted to ESMO. Compensation is unconnected to the studies on which I work: Novartis; Financial Interests, Institutional, Funding, Full-time employee of RTI Health Solutions, an independent non-profit research organization, which was retained by Pfizer to conduct the research that is being submitted to ESMO. Compensation is unconnected to the studies on which I work: Pfizer. R. Shah: Financial Interests, Personal, Full or part-time Employment, Medical Director at Novartis: Novartis. L. Connolly: Financial Interests, Personal, Stocks/Shares: Novartis. D. Norton: Financial Interests, Institutional, Full or part-time Employment, work as head of Medical team for GI in the US: Novartis; Financial Interests, Institutional, Stocks/Shares, work as head of Medical team for GI in the US: Novartis; Financial Interests, Institutional, Funding, work as head of Medical team for GI in the US: Novartis; Non-Financial Interests, Leadership Role, work as head of Medical team for GI in the US: Novartis. All other authors have declared no conflicts of interest.

https://doi.org/10.1016/j.annonc.2023.09.2225

1092P Adjuvant treatment with anti-PD-1 in acral melanoma patients: A nationwide study

M. Bloem[1], O.J. van Not[2], J.B.A.G. Haanen[3], C.U. Blank[3], M.J.B. Aarts[4], F.W.P.J. Van den Berkmortel[5], J.W. de Groot[6], G.A.P. Hospers[7], E. Kapiteijn[8], D. Piersma[9], R.S. van Rijn[10], M. Stevense-den Boer[11], A.A.M. Van der Veldt[12], G. Vreugdenhil[13], H. Bonenkamp[14], M.J. Boers-Sonderen[15], W.A. Blokx[16], F. Van Den Eertwegh[17], K.P.M. Suijkerbuijk[18], M. Wouters[19]

[1]Biomedical Data Sciences, LUMC-Leiden University Medical Center, Leiden, Netherlands; [2]Medical Oncology Department, UMC - University Medical Center Utrecht, Utrecht, Netherlands; [3]Medical Oncology Dept., NKI-AVL - Netherlands Cancer Institute/Antoni van Leeuwenhoek Hospital, Amsterdam, Netherlands; [4]Medical Oncology, Maastricht University Medical Center (MUMC), Maastricht, Netherlands; [5]Department of Medical Oncology, Zuyderland Medical Center, Sittard-Geleen, Netherlands; [6]Oncology Center, Isala, Zwolle, Netherlands; [7]Department of Medical Oncology, University Medical Center Groningen, Groningen, Netherlands; [8]Department of Medical Oncology, Leiden University Medical Center, Leiden, Netherlands; [9]Department of Internal Medicine, Medisch Spectrum Twente, Enschede, Netherlands; [10]Hematology Department, MCL - Medisch Centrum Leeuwarden, Leeuwarden, Netherlands; [11]Department of Internal Medicine, Amphia Ziekenhuis, Breda, Netherlands; [12]Department of Medical Oncology, Erasmus Medical Center, Rotterdam, Netherlands; [13]Internal Medicine, Maxima Medisch Centrum - Veldhoven, Veldhoven, Netherlands; [14]Surgery, Radboud University Medical Center, Nijmegen, Netherlands; [15]Medical Oncology, Radboud University Medical Center, Nijmegen, Netherlands; [16]Pathology, UMC - University Medical Center Utrecht, Utrecht, Netherlands; [17]Medical Oncology, Amsterdam UMC - Vrije University Medical Centre (VUmc), Amsterdam, Netherlands; [18]Department of Medical Oncology, University Medical Center Utrecht, Utrecht, Netherlands; [19]Surgical Oncology Department, Netherlands Cancer Institute/Antoni van Leeuwenhoek Hospital (NKI-AVL), Amsterdam, Netherlands

Background: Previous studies demonstrate limited efficacy of immune checkpoint inhibitors in patients with irresectable acral melanoma (AM) compared to cutaneous melanoma (CM) in other locations. However, little is known about the outcomes of adjuvant therapy for resectable stage III-IV AM. This study aims to compare clinical outcomes after treatment with adjuvant anti-PD-1 in resectable stage III-IV AM and compare them to CM.

Methods: All patients with stage III-IV AM and CM who received adjuvant anti-PD-1 after complete resection between 2017 and 2022 were included from the prospective nationwide Dutch Melanoma Treatment Registry. We described baseline characteristics and analyzed the recurrence-free survival (RFS). A multivariable Cox regression analysis was performed to account for potential confounders age, performance status (ECOG), AJCC 8th edition disease stage, mutation status. Type of recurrence (locoregional or distant metastases) and toxicity rates will be presented at the conference.

Results: In total, 1977 patients (86 AM and 1891 CM) were included. At baseline, *KIT* mutations were more common in AM patients. In addition, AM patients more often had higher AJCC 8 disease stages. No other significantly different baseline characteristics were identified. Median follow-up was 16.4 months. The median RFS was 14.8 months (95%CI: 11.5-29.7) for the AM cohort and 37.4 months (95%CI: 32.1 - NR) for the CM cohort (p=.002)). After correcting for potential confounders, AM remained associated with higher risk of recurrence than CM (HR_{adj} 1.55; 95%CI: 1.09-2.19; p=.014).

Table: 1092P Baseline characteristics and median RFS stratified by melanoma type.

		AM (n=86)	CM (n=1891)	P-value
Median age (IQR)		65 [54, 72]	64 [54, 73]	.984
Gender (n (%) female)		45 (52.3)	793 (41.9)	.160
AJCC8 stage (n (%))	IIIA	5 (5.7)	130 (6.9)	.001
	IIIB	17 (19.5)	599 (31.7)	
	IIIC	58 (66.7)	713 (37.7)	
	IIID	2 (2.3)	37 (2.0)	
	IV	2 (2.3)	170 (9.0)	
	Unknown	3 (3.4)	241 (12.8)	
Mutation (n (%))	BRAF	23 (26.7)	804 (42.5)	.001
	NRAS	9 (10.5)	441 (23.3)	
	KIT	7 (8.1)	12 (0.6)	
Median RFS (months; 95% CI)		14.8 (11.5-29.3)	37.4 (32.1-NA)	.002

Conclusions: This study suggests that AM patients treated with adjuvant anti-PD-1 have shorter RFS than CM patients receiving the same treatment. Longer follow-up is needed to investigate overall survival and distant-metastasis-free survival.

Legal entity responsible for the study: The authors.

Funding: Has not received any funding.

Disclosure: J.B.A.G. Haanen: Financial Interests, Institutional, Advisory Board: Bristol Myers Squibb, Achilles Therapeutics, Ipsen, Merck Sharp & Dohme, Merck Serono, Pfizer, Molecular Partners, Novartis, Roche, Sanofi, Third Rock Venture, Iovance Biotherapeutics; Financial Interests, Institutional, Advisory Board, SAB member: BioNTech, Immunocore, Gadeta, Instil Bio, PokeAcel, T-Knife; Financial Interests, Personal, Advisory Board, SAB member: Neogene Therapeutics, Scenic; Financial Interests, Personal, Stocks/Shares: Neogene Therapeutics; Financial Interests, Institutional, Research Grant: Bristol Myers Squibb, BioNTech US, Merck Sharp & Dohme, Amgen, Novartis, Asher Bio; Non-Financial Interests, Member: ASCO, AACR, SITC; Other, Other, Editorial Board ESMO Open: ESMO; Other, Other, Editor-in-Chief IOTECH: ESMO; Other, Editorial Board: Kidney Cancer. C.U. Blank: Financial Interests, Institutional, Advisory Board: BMS, MSD, Roche, Novartis, GSK, AZ, Pfizer, Lilly, GenMab, Pierre Fabre; Financial Interests, Personal, Advisory Board: Third Rock Ventures; Financial Interests, Personal, Stocks/Shares: Immagene; Financial Interests, Personal, Stocks/Shares, intention to develop IFN signature algorithm: NewCo, no name yet; Financial Interests, Institutional, Coordinating PI: BMS, Novartis, NanoString, 4SC; Other, pending patent: WO 2021/177822 A1. M.J.B. Aarts: Financial Interests, Advisory Board: Amgen, BMS, Novartis, MSD-Merck, Merck-Pfizer, Pierre Fabre, Sanofi, Astellas, Bayer; Financial Interests, Institutional, Research Grant: Merck-Pfizer. J.W. de Groot: Financial Interests, Advisory Role: BMS, Pierre Fabre, Servier, MSD, Novartis. G.A.P. Hospers: Financial Interests, Advisory Role: Amgen, BMS, Roche, MSD, Pfizer, Novartis, Pierre Fabre; Financial Interests, Institutional, Research Grant: BMS, Seerave. E. Kapiteijn: Financial Interests, Institutional, Advisory Board: BMS, Novartis, Pierre Fabre, Merck, Delcath, Bayer, Lilly; Financial Interests, Institutional, Coordinating PI: BMS, Pierre Fabre, Delcath. R.S. van Rijn: Financial Interests, Advisory Board: Pfizer; Financial Interests, Other, expert meeting fee: Roche. A.A.M. Van der Veldt: Financial Interests, Institutional, Advisory Role: BMS, Roche, Novartis, Pierre Fabre, Pfizer, Sanofi, Ipsen, Eisai, Merck; Financial Interests, Institutional, Advisory Board: MSD. M.J. Boers-Sonderen: Financial Interests, Advisory Role: Pierre Fabre, MSD, Novartis. F. Van Den Eertwegh: Financial Interests, Institutional, Research Grant, Grant for national trial: Roche; Financial Interests, Institutional, Research Grant, Grant for research project: BMS; Financial Interests, Institutional, Research Grant, Research grant for trial: Sanofi, Idera; Financial Interests, Institutional, Research Grant, Grant for trial: Teva; Non-Financial Interests, Advisory Role: BMS, Novartis, Pierre Fabre, MSD, Pfizer, Amgen, Ipsen, Merck. K.P.M. Suijkerbuijk: Financial Interests, Institutional, Advisory Board: Novartis, BMS, AbbVie, Pierre Fabre, MSD; Financial Interests, Institutional, Invited Speaker: Roche; Financial Interests, Institutional, Research Grant: Novartis, TigaTx. All other authors have declared no conflicts of interest.

https://doi.org/10.1016/j.annonc.2023.09.2226

1093P Neoadjuvant (NeoAd) intratumoral (IT) TAVO-EP (plasmid IL-12 electro gene transfer) in combination with nivolumab (NIVO) for patients (pts) with operable locoregionally advanced melanoma

A. Tarhini[1], Z. Eroglu[2], E. Castellano[3], J.S. Zager[2], R.J. Gonzalez[4], A. Sarnaik[2], C.W. Cruse[5], D.B. De Aquino[5], E. Abraham[5], A. Richards[5], D. Kalos[6], Y.A. Chen[6], E. Browning[7], D. Canton[7], P-L. Chen[8], J.L. Messina[9], V.K. Sondak[2]

[1]Cutaneous Oncology and Immunology, H. Lee Moffitt Cancer Center & Research Institute - Magnolia Campus, Tampa, FL, USA; [2]Cutaneous Oncology, H. Lee Moffitt Cancer Center & Research Institute - Magnolia Campus, Tampa, FL, USA; [3]Chemistry, Emory University, Atlanta, GA, USA; [4]Sarcoma, Moffitt Cancer Center, Tampa, FL, USA; [5]Cutaneous Oncology, Moffitt Cancer Center, Tampa, FL, USA; [6]Biostatistics and Bioinformatics, Moffitt Cancer Center, Tampa, FL, USA; [7]Research, OncoSec Medical Incorporated, Pennington, NJ, USA; [8]Pathology, Moffitt Cancer Center, Tampa, FL, USA; [9]Pathology, H. Lee Moffitt Cancer Center & Research Institute - Magnolia Campus, Tampa, FL, USA

Background: IT TAVO-EP (tavokinogene telseplasmid delivered by electroporation) results in localized expression of IL-12 in the tumor microenvironment. This phase II study (NCT04526730) was designed to evaluate NeoAd TAVO-EP in combination with NIVO in subjects with operable, locoregionally advanced melanoma. Pts provided an IRB-approved (Advarra IRB Pro00041794) written informed consent.

Methods: The NeoAd phase comprised up to 3 x4-week cycles of TAVO-EP on days 1, 8 and 15 (optional) concurrently with 480 mg NIVO iv on day 8 of each cycle. Surgery followed and later adjuvant NIVO was initiated. Primary endpoint was pathologic complete response (pCR), secondary endpoints included near pCR (≤10% viable tumor), pathologic major response (pMR; pCR + near pCR) and nonresponse (pNR), among others. Biomaterials were collected at screening, C1D8, C2D1, pre-surgery and during adjuvant phase.

Results: 16 pts (7 female, 9 male, cutaneous primary, age 30 – 88) were treated; 9 Stage IIIB, 5 IIIC, 2 IV (M1a) as clinically assessed. Highest-grade (Gr3) treatment-related adverse events included 1 hyponatremia, 2 diarrhea/colitis, 1 pancreatitis, 1 hypertension. One pt currently in NeoAd phase. Among the 15 pts who completed NeoAd phase, median number of NeoAd NIVO was 3 (range 1 - 3) and TAVO-EP 7 (3 - 9). Preoperative response rate (RECIST, unconfirmed) was 9/15 (60%; 95% CI: 55.7-68.3%); 2 PD, 4 SD, 6 PR, 3 CR. One pt with PR declined surgery and 1 with early distant PD did not have surgery. Among 13 pts who had surgery: 2 pNR, 3 near pCR, 8 pCR; pMR rate was 11/14 (78.6%; 95%CI: 73.7—81.9%). Among those with pMR, there was no melanoma relapse to date with a median follow up of 11.4 months (range 0.9 – 24.6) from surgery. At baseline, many pts had low levels of CD8+ TIL, PD-L1, and IFN-gamma signature scores. Combination therapy induced local and systemic proinflammation changes, including increases in immune-related gene expression profiles, CD8+ TIL and peritumoral T cells.

Conclusions: NeoAd IT TAVO-EP and iv NIVO exhibited promising clinical activity and a favorable safety profile. Enhanced immune activation in responding patients supports the proposed immune mechanisms.

Clinical trial identification: NCT04526730.

Legal entity responsible for the study: Moffitt Cancer Center.

Funding: OncoSec.

Disclosure: A. Tarhini: Financial Interests, Institutional, Funding, Contracted Research: OncoSec, Genentech-Roche, Regeneron; Financial Interests, Institutional, Advisory Board, Contracted Research: Bristol Myers Squib, Sanofi-Genzyme, Clinigen, Nektar, Merck, Acrotech, Pfizer, Scholar Rock, Checkmate; Financial Interests, Personal, Advisory Board: OncoSec, Bristol Myers Squibb, Merck, Eisai, Instil Bio, Regeneron, Sanofi-Genzyme, Novartis, Partner Therapeutics, Genentech/Roche, BioNTech, Concert AI, AstraZeneca, Pfizer. E. Browning, D. Canton: Financial Interests, Personal, Financially compensated role, Employee: OncoSec. V.K. Sondak: Financial Interests, Personal, Advisory Board: Merck, Bristol Myers Squibb, Iovance, OncoSec, Regeneron, Ultimovacs; Financial Interests, Personal, Other, Independent Data Safety Monitoring Committee: Alkermes, Novartis; Financial Interests, Personal, Other, Independent medical monitor for clinical trial: Genesis Drug Discovery & Development; Financial Interests, Institutional, Research Grant, Research grant to institution: Turnstone Biologics; Financial Interests, Institutional, Coordinating PI, Per patient funding to institution to support clinical trial: Skyline DX; Financial Interests, Institutional, Local PI, Research grant to institution: Neogene Therapeutics. All other authors have declared no conflicts of interest.

https://doi.org/10.1016/j.annonc.2023.09.2227

1094P Relapse free survival (RFS) at 3 years by pathological (path) response to neoadjuvant systemic treatment (NST) in patients (pts) with surgically resectable, high-risk melanoma

E. Burton[1], D. Milton[2], L. Simpson[3], M. Tetzlaff[4], I.C. Glitza[5], M.I. Ross[6], J.E. Gershenwald[6], J. Mcquade[5], M. Wong[3], S. Patel[3], A. Diab[5], M. Postow[7], C.E. Ariyan[8], J. Lee[6], S. Fisher[6], V. Prieto[9], M. Davies[5], H.A. Tawbi[5], J. Wargo[6], R. Amaria[3]

[1]Genomic Medicine & Melanoma Medical Oncology Dept., The MD Anderson Cancer Center, Houston, TX, USA; [2]Biostatistics, The University of Texas MD Anderson Cancer Center, Houston, TX, USA; [3]Melanoma Medical Oncology Department, The MD Anderson Cancer Center, Houston, TX, USA; [4]Pathology, UCSF - University of California San Francisco, San Francisco, CA, USA; [5]Melanoma Medical Oncology Department, The University of Texas MD Anderson Cancer Center, Houston, TX, USA; [6]Surgical Oncology, The University of Texas MD Anderson Cancer Center, Houston, TX, USA; [7]Medicine, Memorial Sloan Kettering 60th Street Outpatient Center, New York, NY, USA; [8]Surgery, Memorial Sloan Kettering Cancer Center, New York, NY, USA; [9]Pathology, The University of Texas MD Anderson Cancer Center, Houston, TX, USA

Background: For pts with high-risk, surgically resectable melanoma, NST demonstrated improved outcomes compared to upfront surgery and adjuvant therapy. Outcomes are most improved in pts who achieve a pathologic complete response (pCR) with any NST [targeted therapy (TT) or immune checkpoint blocked (ICB)]. Prior studies in ICB NST suggest improved outcomes associated with any path response. We evaluated updated data from 2 previously reported NST studies for long-term outcomes by path response, determined by percent tumor viability (TV).

Methods: We analyzed 2 trials in for clinical stage III/IV, resectable melanoma: NST [2 months (mo)] + adjuvant (10 mo) dabrafenib + trametinib (DT) (NCT02231775) and ICB, (NCT02519322). ICB trial arms were 8-9 wks of NST: nivolumab (nivo) (Arm A), ipilimumab 3mg/kg plus nivo 1mg/kg (Arm B) both followed by adjuvant nivo for 6 mo, and nivo + relatlimab (2 mos NST, 10 mos adjuvant) (Arm C). RFS was estimated using Kaplan Meier (KM) method and differences by path responses were evaluated by the log-rank test.

Results: 97 pts of 103 treated pts underwent surgery and were evaluable for analysis by detailed path response: 49 pts on DT and 48 on ICB (11 Arm A, 10 Arm B, 28 Arm C). Median follow up for all pts was 34.5 mos (3.8-94.8). Median RFS in mos for any pt with pCR was not reached and 23.7 mos (95% CI: 11.3, 30.5) for pts with <pCR (p<0.001). The table reports 36 mos RFS by NST and path response: >50% TV (pNR), 11-50% TV (pPR), 1 - ≤10% TV near pCR, and 0% TV pCR. Additional clinical data and outcomes will be reported at the meeting.

Table: 1094P 36 mos RFS KM rates

Path response	All pts			TT pts			ICB pts		
	n	Rate		n	Rate		n	Rate	
pCR	42	83%	p < 0.001	17	65%	p < 0.001	25	96%	p = 0.005
near pCR	10	53%		7	36%		3	100%	
pPR	16	24%		12	0%		4	75%	
pNR	29	32%		13	8%		16	49%	

Conclusions: At 3 years, RFS in pts treated with NST TT and ICB with pCR continues to be superior to those with <pCR. Any path response to ICB NST (pCR, near pCR, pPR) is associated with improved RFS, but only pCR predicts durable RFS in TT NST. It is critical to understand associations between NST, path response, and outcomes to support personalization of adjuvant approaches and improve overall outcomes.

Clinical trial identification: NCT02231775 and NCT02519322.

Legal entity responsible for the study: The authors.

Funding: Novartis, BMS, MRA/Rising Tide Fondation.

Disclosure: I.C. Glitza: Financial Interests, Personal, Speaker, Consultant, Advisor: BMS, Array, Novartis, Sintetica; Financial Interests, Institutional, Research Funding: BMS, Merck, Pfizer. M.I. Ross: Financial Interests, Institutional, Research Funding: Amgen; Financial Interests, Personal, Speaker, Consultant, Advisor: Amgen, Castle Biosciences, Merck, Novartis. J.E. Gershenwald: Financial Interests, Personal, Other, consultant, advisory board, scientific advisory board: Merck; Financial Interests, Personal, Other, consultant: Regeneron; Financial Interests, Personal, Royalties, author/coauthor of several chapters for this online clinical resource: UpToDate. J. Mcquade: Financial Interests, Personal, Speaker, Consultant, Advisor: Merck, BMS, Roche. M. Wong: Financial Interests, Personal, Speaker, Consultant, Advisor: Merck, Pfizer, BMS, Regeneron, EMD Serono, ExiCure, Castle Biosciences. S. Patel: Financial Interests, Personal, Advisory Board: TriSalus, Cardinal Health, Castle Biosciences, Novartis, BMS, Pfizer, Immatics; Financial Interests, Personal, Other, Consultant for educational materials: Advance Knowledge in Healthcare; Financial Interests, Personal, Advisory Board, Advisory Board and Corporate Day speaker (unbranded): Delcath; Financial Interests, Personal, Other, Independent Data Monitoring Committee: Immunocore; Financial Interests, Personal, Other, Consultant: Guidepoint Global; Financial Interests, Institutional, Trial Chair: Provectus Biopharmaceuticals, Bristol Myers Squibb; Financial Interests, Institutional, Local PI: Lyvgen, InxMed, Foghorn Therapeutics, IDEAYA, Novartis, Seagen, Syntrix Bio; Financial Interests, Institutional, Steering Committee Member: TriSalus Life Sciences; Non-Financial Interests, Member: ASCO, AACR, International Society of Ocular Oncology, Society for Melanoma Research; Non-Financial Interests, Leadership Role: SWOG. A. Diab: Financial Interests, Institutional, Research Funding: BMS. M. Postow: Financial Interests, Personal, Advisory Board: BMS, Chugai, Merck, Nektar, Pfizer; Financial Interests, Institutional, Coordinating PI: BMS; Financial Interests, Institutional, Local PI: Merck, Novartis. C.E. Ariyan: Financial Interests, Personal, Advisory Board: Merck, Iovance; Financial Interests, Personal, Stocks/Shares: Pfizer. V. Prieto: Financial Interests, Personal, Other, Consultant: Orlucent, Merck, Castle Biosciences, Novartis. M. Davies: Financial Interests, Personal, Advisory Board: Roche, Pfizer, Novartis, BMS, Sanofi-Aventis, GSK, Vaccinex, Apexigen, Eisai, Iovance, Merck, ABM Therapeutics; Financial Interests, Institutional, Coordinating PI: Pfizer; Financial Interests, Institutional, Research Grant: ABM Therapeutics, Lead Pharma, Genentech, GSK, Sanofi-Aventis, Merck, Oncothyreon; Financial Interests, Research Grant: Myriad. H.A. Tawbi: Financial Interests, Personal, Advisory Board: Bristol Myers Squibb, Merck, Novartis, Genentech, Eisai, Karyopharm, Iovance, Pfizer, Jazz Pharmaceuticals; Financial Interests, Institutional, Trial Chair: Bristol Myers Squibb; Financial Interests, Institutional, Local PI: Merck, RAPT Pharmaceuticals; Financial Interests, Institutional, Steering Committee Member: Novartis, Genentech; Financial Interests, Institutional, Funding: GSK, Eisai. J. Wargo: Financial Interests, Personal, Invited Speaker: Dava Oncology, Omniprex, Illumina, Gilead, PeerView, Physician Education Resource, MedImmune, Exelixis, Bristol Meyers Squibb, Medscape; Financial Interests, Personal, Advisory Board: Roche Genentech, Novartis, AstraZeneca, GSK, Merck; Financial Interests, Personal, Stocks/Shares: Micronoma, OSE therapeutics; Other, J.A.W. is an inventor on a US patent application (PCT/US17/53.717) submitted by the University of Texas MD Anderson Cancer Center which covers methods to enhance immune checkpoint blockade responses by modulating the microbiome: University of Texas MD Anderson Cancer Center. R. Amaria: Financial Interests, Personal, Advisory Board: Iovance Biotherapeutics, Novartis, Erasca; Financial Interests, Institutional, Coordinating PI: Merck, Bristol Myers Squibb, Novartis; Financial Interests, Institutional, Local PI: Iovance, Roche; Financial Interests, Institutional, Trial Chair: Obsidian. All other authors have declared no conflicts of interest.

https://doi.org/10.1016/j.annonc.2023.09.2228

1095P Associations between baseline biomarkers and 3-year survival in the PRADO trial testing neoadjuvant ipilimumab and nivolumab in stage III melanoma

I. Reijers[1], P. Dimitriadis[2], A.M. Menzies[3], E. Kapiteijn[4], A.A.M. Van der Veldt[5], K.P.M. Suijkerbuijk[6], G.A.P. Hospers[7], W. Van Houdt[8], R. Saw[9], A. Broeks[10], S. Cornelissen[11], L. Grijpink-Ongering[12], T. Pennington[13], A. Colebatch[14], B. van de Wiel[15], R. Scolyer[16], A.C.J. van Akkooi[8], G.V. Long[17], C.U. Blank[18]

[1]Medical Oncology Department, Netherlands Cancer Institute, Amsterdam, Netherlands; [2]Tumor Immunology Department, NKI-AVL - Netherlands Cancer Institute/Antoni van Leeuwenhoek Hospital, Amsterdam, Netherlands; [3]Medical Oncology Department-Suite 5/6, Melanoma Institute Australia, Wollstonecraft, NSW, Australia; [4]Medical Oncology Dept., Leiden University Medical Center (LUMC), Leiden, Netherlands; [5]Medical Oncology Department, Erasmus MC - University Medical Center, Rotterdam, Netherlands; [6]Medical Oncology Dept., UMC-University Medical Center Utrecht, Utrecht, Netherlands; [7]Medical Oncology Dept., UMCG - University Medical Center Groningen, Groningen, Netherlands; [8]Surgical Oncology Department, NKI-AVL - Netherlands Cancer Institute/Antoni van Leeuwenhoek Hospital, Amsterdam, Netherlands; [9]Department of Melanoma & Surgical Oncology, Royal Prince Alfred Hospital, Camperdown, NSW, Australia; [10]Core Facility Molecular Pathology & Biobanking, Netherlands Cancer Institute/Antoni van Leeuwenhoek Hospital (NKI-AVL), Amsterdam, Netherlands; [11]Core Facility Molecular Pathology & Biobanking, Netherlands Cancer Institute, Amsterdam, Netherlands; [12]Department of Biometrics, Netherlands Cancer Institute, Amsterdam, Netherlands; [13]Surgical Oncology, Melanoma Institute Australia, Wollstonecraft, NSW, Australia; [14]Pathology Department, Melanoma Institute Australia, Wollstonecraft, NSW, Australia; [15]Pathology Department, NKI-AVL - Netherlands Cancer Institute/Antoni van Leeuwenhoek Hospital, Amsterdam, Netherlands; [16]Pathology Department, Royal Prince Alfred Hospital, Camperdown, NSW, Australia; [17]Medical Oncology Dept., Melanoma Institute Australia, Wollstonecraft, NSW, Australia; [18]Medical Oncology Dept., NKI-AVL - Netherlands Cancer Institute/Antoni van Leeuwenhoek Hospital, Amsterdam, Netherlands

Background: PRADO tested neoadjuvant ipilimumab plus nivolumab in 99 stage III melanoma patients (pts) followed by omission of therapeutic lymph node dissection (TLND) and adjuvant therapy in pts achieving a major pathologic response (MPR) in their index lymph node, and addition of adjuvant therapy after TLND in non-responding (pNR) pts. Previous analyses of PRADO and its previous OpACIN-neo trial showed that a high interferon-gamma (IFN-γ) signature, PD-L1 expression and tumor mutational burden (TMB) were associated with major pathologic response (PD-L1 expression only in PRADO). Here, we report the association between these biomarkers and 3-year (3y) survival of PRADO.

Methods: The IFN-γ signature, PD-L1 expression and TMB were analyzed on baseline tumor biopsies using mRNA sequencing (n=80), anti-PD-L1 mAb (clone 22C3) (n=76), and whole exome sequencing (n=75). Cutoffs between high and low cohorts were calculated using ROC curves on MPR. Event-free (EFS), relapse-free (RFS), distant metastasis-free (DMFS) and overall (OS) survival curves were generated and compared using the Kaplan-Meier and log-rank method.

Results: Pts with a high baseline IFN-γ signature or a PD-L1 expression of ≥1% had a significantly higher 3y EFS rate than pts with low levels (85% vs 61%, p=0.006 and 91% vs 67%, p=0.005, respectively) (Table). Pts with a high TMB had a numerically higher 3y EFS rate (81% vs 64%, p=0.072). The correlation between baseline IFN-γ signature and PD-L1 expression and EFS translated into a numerical benefit in RFS, DMFS and OS (OS was statistically significant for PD-L1). However, no association with RFS, DMFS or OS was observed for TMB.

Table: 1095P

	3-year survival rate estimate		Log-rank p-value
Registration-to-event analyses			
IFN-γ	High (n=39)	Low (n=41)	
EFS	85%	61%	0.006
OS	95%	80%	0.059
PDL1	≥1% (n=33)	<1% (n=43)	
EFS	91%	67%	0.005
OS	100%	81%	0.010
TMB	High (n=31)	Low (n=44)	
EFS	81%	64%	0.072
OS	87%	86%	0.940
Surgery-to-event analyses*			
IFN-γ	High (n=39)	Low (n=34)	
RFS	85%	70%	0.066
DMFS	90%	73%	0.053
PDL1	≥1% (n=32)	<1% (n=37)	
RFS	91%	78%	0.068
DMFS	94%	84%	0.130
TMB	High (n=29)	Low (n=39)	
RFS	83%	72%	0.210
DMFS	86%	77%	0.320

*Patients with an event prior to surgery (n=6) or who did not undergo surgery (n=1) were excluded.

Conclusions: The IFN-γ signature seems to be the most robust baseline biomarker for long-term (event-free) survival across different cohorts. In contrast to results from the previous OpACIN-neo trial, PD-L1 expression was also associated with survival in PRADO, while TMB was not significantly associated.

Clinical trial identification: NCT02977052.

Legal entity responsible for the study: Netherlands Cancer Institute.

Funding: BMS.

Disclosure: I. Reijers: Financial Interests, Personal, Licensing Fees, I.L.M.R reports financial interest in Signature Oncology, and will receive some possible revenues if the IFN-γ signature is being developed as clinical companion diagnostic: Signature Oncology. P. Dimitriadis: Financial Interests, Personal, Licensing Fees, P.D. reports financial interest in Signature Oncology, and will receive some possible revenues if the IFN-γ signature is being developed as clinical companion diagnostic: Signature Oncology. A.M. Menzies: Financial Interests, Personal, Advisory Board, advisory board: BMS, MSD, Novartis, Roche, Pierre Fabre, QBiotics. E. Kapiteijn: Financial Interests, Institutional, Advisory Board: BMS, Novartis, Pierre Fabre, Merck, Delcath, Bayer, Lilly; Financial Interests, Institutional, Coordinating PI: BMS, Pierre Fabre, Delcath. A.A.M. Van der Veldt: Financial Interests, Institutional, Advisory Board: BMS, MSD, Merck, Roche, Eisai, Pfizer, Sanofi, Novartis, Pierre Fabre, Ipsen. K.P.M. Suijkerbuijk: Financial Interests, Institutional, Advisory Board: Novartis, BMS, AbbVie, Pierre Fabre, MSD; Financial Interests, Institutional, Invited Speaker: Roche; Financial Interests, Institutional, Research Grant: Novartis, TigaTx. G.A.P. Hospers: Financial Interests, Institutional, Advisory Board: Amgen, Roche, MSD, BMS, Pfizer, Novartis, Pierre Fabre; Financial Interests, Institutional, Research Grant: BMS, Seerave. W. Van Houdt: Financial Interests, Institutional, Invited Speaker: Amgen; Financial Interests, Institutional, Advisory Board: Belpharma, Sanofi, MSD; Financial Interests, Personal, Other, travel grant: Novartis; Financial Interests, Institutional, Local PI: BMS. R. Saw: Financial Interests, Institutional, Advisory Board: MSD, Novartis, QBiotics; Financial Interests, Institutional, Speaker, Consultant, Advisor: BMS, Novartis. B. van de Wiel: Financial Interests, Institutional, Advisory Board: BMS. R. Scolyer: Financial Interests, Institutional, Advisory Board: F. Hoffmann-La Roche, Evaxion, Provectus Biopharmaceuticals Australia, QBiotics, Novartis, MSD, NeraCare, Amgen, BMS, Myriad Genetics, GSK. A.C.J. van Akkooi: Financial Interests, Institutional, Advisory Board: Amgen, Bristol Myers Squibb, Novartis, MSD - Merck, Merck-Pfizer, Pierre Fabre, Sanofi, Sirius Medical, 4SC, Provectus; Financial Interests, Institutional, Research Grant, NIVEC study: Amgen; Financial Interests, Institutional, Research Grant: Merck-Pfizer. G.V. Long: Financial Interests, Institutional, Advisory Board: Agenus, Amgen, Array Biopharma, AstraZeneca, Boehringer Ingelheim, BMS, Evaxion, Hexal AG, Highlight Therapeutics, Innovent Biologics, MSD, Novartis, OncoSec, PHMR Ltd., Pierre Fabre, Provectus, QBiotics, Regeneron Pharmaceuticals. C.U. Blank: Financial Interests, Institutional, Advisory Board: BMS, MSD, Roche, Novartis, GSK, AZ, Pfizer, Lilly, GenMab, Pierre Fabre; Financial Interests, Personal, Advisory Board: Third Rock Ventures; Financial Interests, Personal, Stocks/Shares: Immagene; Financial Interests, Personal, Stocks/Shares, intention to develop IFN signature algorithm: NewCo, no name yet; Financial Interests, Institutional, Coordinating PI: BMS, Novartis, NanoString, 4SC; Other, pending patent: WO 2021/177822 A1. All other authors have declared no conflicts of interest.

https://doi.org/10.1016/j.annonc.2023.09.2229

1096P Prolonged follow-up confirms durability of favorable outcomes after neoadjuvant ipilimumab plus nivolumab in melanoma

M.W. Lucas[1], E.A. Rozeman[1], J.M. Versluis[2], A.M. Menzies[3], H. Eriksson[4], B. van de Wiel[5], R. Scolyer[6], H.V. van Thienen[2], H. Mallo[2], M. Gonzalez[7], L. Landman[8], A. Torres Acosta[8], L. Grijpink-Ongering[9], J.B.A.G. Haanen[1], A.C.J. van Akkooi[10], G.V. Long[11], C.U. Blank[1]

[1]Medical Oncology Department, NKI-AVL - Netherlands Cancer Institute/Antoni van Leeuwenhoek Hospital, Amsterdam, Netherlands; [2]Medical Oncology Department, Netherlands Cancer Institute, Amsterdam, Netherlands; [3]Medical Oncology Department-Suite 5/6, Melanoma Institute Australia, Wollstonecraft, NSW, Australia; [4]Oncology-Pathology Department, Karolinska University Hospital-Solna, Solna, Sweden; [5]Pathology Department, NKI-AVL - Netherlands Cancer Institute/Antoni van Leeuwenhoek Hospital, Amsterdam, Netherlands; [6]Department of Pathology, Royal Prince Alfred Hospital, Camperdown, NSW, Australia; [7]Clinical Trials, Melanoma Institute Australia, Wollstonecraft, NSW, Australia; [8]Scientific Administration, NKI-AVL - Netherlands Cancer Institute/Antoni van Leeuwenhoek Hospital, Amsterdam, Netherlands; [9]Scientific Administration, Netherlands Cancer Institute, Amsterdam, Netherlands; [10]Surgical Oncology Dept., Melanoma Institute Australia, Wollstonecraft, NSW, Australia; [11]Medical Oncology Department, Melanoma Institute Australia, Wollstonecraft, NSW, Australia

Background: A paradigm shift in the treatment of resectable stage III melanoma is expected, given the superior results of neoadjuvant (neoadj) immune checkpoint inhibition (ICI) in the SWOG S1801 trial and with the 1st phase III trial (NCT04949113) on its way. In this rapidly evolving field, long-term outcomes of neoadj ICI are scarce. Here we report the 4- and 6-yr survival update of the OpACIN and OpACIN-neo.

Methods: In the randomized OpACIN trial, 20 patients (pts) with resectable stage III melanoma were treated with ipilimumab (IPI) 3mg/kg + nivolumab (NIVO) 1mg/kg; in the adjuvant (adj) arm 4 cycles after therapeutic lymph node dissection (TLND) and in the neoadj arm 2 cycles before and 2 after TLND. In the OpACIN-neo trial, 86 pts were randomized between neoadj IPI 3mg/kg + NIVO 1mg/kg (2x; arm A), IPI 1mg/kg + NIVO 3 mg/kg (2x; arm B) and IPI 3mg/kg (2x) > NIVO 3mg/kg (2x; arm C), followed by TLND without adj therapy. Event-free survival (EFS) was defined as time from randomization to progression, recurrence or death.

Results: Median follow-up (FU) for OpACIN was 84.0 mo. Estimated 6-yr EFS was 60% for both the adj and neoadj arm, while OS was 70% and 90% respectively. Only 1 recurrence has been observed after the 3-yr landmark. Median FU for OpACIN-neo was 60.7 mo. Estimated 4-yr EFS was 80% (see table for EFS/OS). After the 3-yr

landmark, 1 new recurrence was observed and 1 non-melanoma related death. Major- and partial pathological responders (MPR/pPR) had 4-yr EFS rates of 96% and 92%, versus 33% in non-responders (pNR). Combining data from both trials, the median time to recurrence was 6.2 mo for the 16 pts that relapsed after pNR, while this was 37.7 mo for the 3 pts that relapsed after MPR/pPR.

Table: 1096P

	6-year EFS (95% CI)	6-year OS (95% CI)
OpACIN — adjuvant	60% (36-100)	70% (47-100)
OpACIN - neoadjuvant	60% (36-100)	90% (73-100)
	4-year EFS (95% CI)	**4-year OS (95% CI)**
OpACIN-neo	80% (43-89)	92% (86-98)
Arm A	87% (75-100)	90% (80-100)
Arm B	77% (63-93)	93% (85-100)
Arm C	77% (62-95)	92% (83-100)

Conclusions: Although the EFS rates are similar for the neoadj and adj arms after 6 yrs in the OpACIN trial, the favorable EFS and OS rates observed in the larger OpACIN-neo support the durability of response to neoadj IPI plus NIVO. The pathological response may serve as predictor for long-term outcome.

Clinical trial identification: NCT02437279; NCT02977052.

Legal entity responsible for the study: Netherlands Cancer Institute.

Funding: Bristol Myers Squibb.

Disclosure: A.M. Menzies: Financial Interests, Personal, Advisory Board, advisory board: BMS, MSD, Novartis, Roche, Pierre Fabre, QBiotics. B. van de Wiel: Financial Interests, Institutional, Advisory Role: BMS. R. Scolyer: Financial Interests, Institutional, Advisory Role: F. Hoffmann-La Roche Ltd., Evaxion, Provectus Biopharmaceuticals Australia, QBiotics, Novartis, Merck Sharp & Dohme, NeraCare, Amgen Inc., Bristol Myers Squibb, Myriad Genetics, GSK. J.B.A.G. Haanen: Financial Interests, Institutional, Advisory Board: Bristol Myers Squibb, Achilles Therapeutics, Ipsen, Merck Sharp & Dohme, Merck Serono, Pfizer, Molecular Partners, Novartis, Roche, Sanofi, Third Rock Venture, Iovance Biotherapeutics; Financial Interests, Institutional, Advisory Board, SAB member: BioNTech, Immunocore, Gadeta, Instil Bio, PokeAcel, T-Knife; Financial Interests, Personal, Advisory Board, SAB member: Neogene Therapeutics, Scenic; Financial Interests, Personal, Stocks/Shares: Neogene Therapeutics; Financial Interests, Institutional, Research Grant: Bristol Myers Squibb, BioNTech US, Merck Sharp & Dohme, Amgen, Novartis, Asher Bio; Non-Financial Interests, Member: ASCO, AACR, SITC; Other, Editor-in-Chief IOTECH: ESMO; Other, Editorial Board ESMO Open: ESMO; Other, Editorial Board: Kidney Cancer. A.C.J. van Akkooi: Financial Interests, Institutional, Advisory Board: Amgen, Bristol Myers Squibb, Novartis, MSD - Merck, Merck-Pfizer, Pierre Fabre, Sanofi, Sirius Medical, 4SC, Provectus; Financial Interests, Institutional, Research Grant, NIVEC study: Amgen; Financial Interests, Institutional, Research Grant: Merck-Pfizer. G.V. Long: Financial Interests, Institutional, Advisory Role: Agenus, Amgen, Array Biopharma, AstraZeneca, Boehringer Ingelheim, Bristol Myers Squibb, Evaxion, Hexal AG (Sandoz Company), Highlight Therapeutics, Innovent Biologics, MSD, Novartis, OncoSec, PHMR Ltd., Pierre Fabre, Provectus, QBiotics, Regeneron Pharmaceuticals. C.U. Blank: Financial Interests, Institutional, Advisory Board: BMS, MSD, Roche, Novartis, GSK, AZ, Pfizer, Lilly, GenMab, Pierre Fabre; Financial Interests, Personal, Advisory Board: Third Rock Ventures; Financial Interests, Personal, Stocks/Shares: Immagene; Financial Interests, Institutional, Coordinating PI: NanoString, BMS, Novartis, 4SC; Financial Interests, Personal, Stocks/Shares, intention to develop IFN signature algorithm: NewCo, no name yet; Other, pending patent: WO 2021/177822 A1. All other authors have declared no conflicts of interest.

https://doi.org/10.1016/j.annonc.2023.09.2230

1097P Durable relapse-free survival in stage IV melanoma patients (pts) treated with neoadjuvant immune-checkpoint inhibitor (ICI) followed by local procedures

D. Belkadi-Sadou[1], A. Marchand[1], B. Archambaud[2], A. Cavalcanti[3], Y. Tao[4], L. Tselikas[5], S. Roy[1], E. Routier[1], C. Boutros[1], C. Robert[1]

[1]Dermatology Unit, Department of Medicine, Gustave Roussy Cancer Campus, Villejuif, France; [2]Biostatistics, Gustave Roussy - Cancer Campus, Villejuif, France; [3]Department of Surgery, Gustave Roussy Cancer Campus, Villejuif, France; [4]Department of Radiotherapy, Gustave Roussy Cancer Campus, Villejuif, France; [5]Interventional Radiology Department, Gustave Roussy Cancer Campus, Villejuif, France

Background: Achieving a complete response (CR) with ICI is associated with a long term survival in advanced melanoma pts. The long term outcome of pts for which the CR is obtained by a local procedure (LP) such as surgery, radiotherapy or interventional radiology following ICI is not known. We report here long term relapse-free survival (RFS) and overall survival (OS) data of a cohort of pts in this situation.

Methods: RFS and OS of melanoma pts with a CR obtained by ICI + LP were estimated from the time of LP to progression or death using the Kaplan-Meier method. Pts with no viable cells in the resected metastases were excluded.

Results: 40 pts (57.5% males) with a mean age of 52.4 years achieved a CR after receiving ICI combined by an additional LP on 1 to 3 stable or progressing metastatic sites including lymph nodes, skin, lung, liver and brain. Most pts had received previous treatment lines (mean: 2.9). 23 (57.5%) pts were in progression according to RECIST 1.1 before the LP, 5 (12.5%) pts were in partial response, and 1(2.5%) pt in stable disease. 4 (10%) pts had a dissociated response and for 7 (17.5%) pts the response was not evaluable. Median duration between ICI onset and LP was 8.9 months [3.9—16.4]. After a median duration of follow-up of 5.4 years from LP, the median duration of response was not reached, 5 years RFS and OS rates were 58.65% [44.52—77.27] and 88.57% [78.63—99.76] respectively. Median RFS and OS were not reached. Relapses occurred in 14 (35%) pts, most often on a site different from that treated by the LP.

Conclusions: This real life study shows that long term RFS and OS can be achieved when ICI is given before a LP at oligometastatic sites in spite of tumor progression following ICI and suggests that neoadjuvant ICI should be evaluated in stage IV pts.

Legal entity responsible for the study: Caroline Robert.

Funding: Has not received any funding.

Disclosure: E. Routier: Financial Interests, Personal and Institutional, Other, Compensation: BMS, Novartis, Pierre Fabre; Financial Interests, Personal and Institutional, Invited Speaker: BMS, Novartis, Pierre Fabre. C. Boutros: Financial Interests, Personal and Institutional, Advisory Board: BMS; Financial Interests, Personal and Institutional, Invited Speaker: MSD; Financial Interests, Personal and Institutional, Other, Meeting fees: Pierre Fabre. C. Robert: Financial Interests, Personal and Institutional, Advisory Role: BMS, Novartis, Pierre Fabre, MSD, Roche, Sanofi, AstraZeneca, Merck; Financial Interests, Personal, Other, Cofounder of Ribonexus. All other authors have declared no conflicts of interest.

https://doi.org/10.1016/j.annonc.2023.09.2231

1098P Anti-PD1-based neoadjuvant therapy in resectable stage III or IV melanoma patients: A systematic review and meta-analysis

T.M. Madeira[1], F. Cezar A Moraes[2], J.N. Priantti[3], E. Moisés de Lima Santiago[4], M.F. Ribeiro[5], M. Silveira Vilbert[5]

[1]Intenal Medicine, UFMG - Universidade Federal de Minas Gerais, Belo Horizonte, Brazil; [2]Department of Internal Medicine, UFPA - Universidade Federal do Pará, Belém, Brazil; [3]Internal Medicine Department, Universidade Federal do Amazonas - Faculdade de Medicina, Manaus, Brazil; [4]Department of Internal Medicine, HU/EBSERH/UFMS, Campo Grande, Brazil; [5]Medical Oncology and Hematology Department, UHN - University Health Network - Princess Margaret Cancer Centre, Toronto, ON, Canada

Background: Neoadjuvant therapy (NAT) with immunotherapy (anti-PD1-based) has shown promising event-free survival (EFS) and pathologic complete response (pCR) in resectable melanoma patients. We performed a systematic review and meta-analysis to evaluate anti-PD1-based NAT for stage III and IV resectable melanoma.

Methods: We searched PubMed, Scopus, and Cochrane Library databases for clinical trials and observational cohort studies. Outcomes of interest were pCR, major pathologic response (MPR), EFS, and overall survival (OS). Subgroups analysis included clinical stages and mucosal and acral melanomas (MM/AM) subpopulation. Heterogeneity was examined with I2 statistics; We used a DerSimonian and Laird random effects model.

Results: Eleven studies were included, comprising nine phase II/Ib clinical trials and two observational cohort studies with 486 patients. Of them, 85% had cutaneous melanoma, and 15% had MM/AM. Overall, 43% received single-agent NAT. In a pooled analysis, the pCR rate was 35.1% (95%CI 25.7-44.4). Stage III patients achieved a pCR of 36.9% (95%CI 28.9-71.5), whereas studies including stages III/IV reported pCR in 34.1% (95%CI 19.9-48.4). Single-agent therapy led to pCR in 30.5% (95%CI 20.2-40.9) of patients, while those treated with combination therapy had a pCR rate of 42.1% (95%CI 25.6-58.5). MPR was reached in 49.0% (95% 39.6-58.5) of patients. 231 (82.4%) remained free-of-events with a minimum follow-up of 14.6 months. OS was 90.1% (95%CI 86.0-93.1) in two years (27 deaths). Overall pathological response (CR+MPR+PR) was seen in 71.2% (95%CI 63.5-79.0) of patients, and the overall radiographic response in 50.8% (95%CI 45.0-56.5). According to pCR, responders had a greater EFS than non-responders with an OR of 0.10 (95%CI 0.02-0.49 p=0.004). Among MM/AM, 19.9% (95%CI 7.8-34.9) of patients had pCR. There were no treatment-related deaths or delays of surgery.

Conclusions: Our study supports anti-PD1-based NAT anti-tumor activity in patients with resectable melanoma. Patients with pCR and stage III seem to benefit most from NAT, while rare melanomas still have a worse response. Other ongoing studies and more mature data are needed to confirm our findings.

Legal entity responsible for the study: The authors.

Funding: Has not received any funding.

Disclosure: M.F. Ribeiro: Financial Interests, Personal, Invited Speaker: Bristol Myers Squibb. All other authors have declared no conflicts of interest.

https://doi.org/10.1016/j.annonc.2023.09.2232

1099P Long-term survival follow-up from the REDUCTOR trial: Neoadjuvant cytoreductive treatment with BRAF/MEK inhibition of prior unresectable regionally advanced melanoma to allow complete surgical resection

F.H. Burgers[1], S. Blankenstein[2], M. Rohaan[1], T. Seijkens[1], M. Klop[3], B. van der Hiel[4], M. Lahaye[5], B. van de Wiel[6], A. Sari[7], W. Van Houdt[2], A.C.J. van Akkooi[2], J.B.A.G. Haanen[1]

[1]Department of Medical Oncology, Antoni van Leeuwenhoek-The Netherlands Cancer Institute, Amsterdam, Netherlands; [2]Department of Surgical Oncology, Antoni van Leeuwenhoek-The Netherlands Cancer Institute, Amsterdam, Netherlands; [3]Department of Head and Neck Surgery and Oncology, Antoni van Leeuwenhoek-The Netherlands Cancer Institute, Amsterdam, Netherlands; [4]Department of Nuclear Medicine, Antoni van Leeuwenhoek-The Netherlands Cancer Institute, Amsterdam, Netherlands; [5]Department of Radiology, Antoni van Leeuwenhoek-The Netherlands Cancer Institute, Amsterdam, Netherlands; [6]Department of Pathology, Antoni van Leeuwenhoek-The Netherlands Cancer Institute, Amsterdam, Netherlands; [7]Department of Biometrics, Antoni van Leeuwenhoek-The Netherlands Cancer Institute, Amsterdam, Netherlands

Background: The REDUCTOR trial demonstrated that neoadjuvant dabrafenib (D) plus trametinib (T) allowed radical (R0) resections in 81% of patients with prior unresectable locally advanced BRAF-mutated melanoma. Major pathologic responses were seen in 9/18 patients undergoing surgery. Recurrences were observed in 50% of patients and usually occurred shortly after surgery. Here, we present an update of long-term relapse-free survival (RFS), progression-free survival (PFS) and overall survival (OS).

Methods: In this single-arm phase II trial, 21 patients with unresectable, BRAF-mutated, locally advanced stage IIIC or oligometastatic stage IV melanoma were treated with neoadjuvant D+T for 8 weeks. PET/CT and physical examination were performed to evaluate response. If sufficient downsizing of the tumor was observed, surgical resection was performed. Adjuvant therapy was not routinely given. The primary endpoint was the percentage of patients achieving a R0 resection. Secondary endpoints were RFS, PFS and OS.

Results: At a median follow-up of 80.9 months (IQR 38.6-89.7 months), the median RFS in patients that underwent surgery was 15.4 months (95% CI 8.89-not reached). The median PFS in all patients was 12.4 months (95% CI 8.68-not reached). Recurrences were seen in 10/18 patients undergoing surgery, most of which occurred in the first year after resection (8/10). One patient recurred after 1 year and one after 5 years. The median OS was not reached. The 1-year, 2-year, 3-year and 4-year OS were 100%, 85% (95% CI 70.7-100.0), 85% (95% CI 70.7-100.0) and 75% (95% CI 58.2-96.6), respectively. In total, 1/6 patients (17%) with a pathologic complete response (pCR) developed recurrence, compared to 4/5 patients (80%) with a pathologic non-response (pNR). Late recurrences (after >1 year) were seen in a patient with a near-pCR and a patient with a pNR.

Conclusions: These data confirm favorable long-term survival rates after neoadjuvant D+T and surgical resection without adjuvant therapy in prior unresectable locally advanced BRAF-mutated melanoma patients. Most patients remain disease-free if no recurrence occurs in the first year after treatment.

Clinical trial identification: EudraCT: 2013-002616-28.

Legal entity responsible for the study: Netherlands Cancer Institute, Amsterdam, The Netherlands.

Funding: Netherlands Cancer Institute and Novartis.

Disclosure: W. Van Houdt: Financial Interests, Institutional, Invited Speaker: Amgen; Financial Interests, Institutional, Advisory Board: Belpharma, Sanofi, MSD; Financial Interests, Personal, Other, travel grant: Novartis; Financial Interests, Institutional, Local PI: BMS. A.C.J. van Akkooi: Financial Interests, Institutional, Advisory Board: Amgen, Bristol Myers Squibb, Novartis, MSD - Merck, Merck-Pfizer, Pierre Fabre, Sanofi, Sirius Medical, 4SC, Provectus; Financial Interests, Institutional, Research Grant, NIVEC study: Amgen; Financial Interests, Institutional, Research Grant: Merck-Pfizer. J.B.A.G. Haanen: Financial Interests, Institutional, Advisory Board: Bristol Myers Squibb, Achilles Therapeutics, Ipsen, Merck Sharp & Dohme, Merck Serono, Pfizer, Molecular Partners, Novartis, Roche, Sanofi, Third Rock Venture, Iovance Biotherapeutics; Financial Interests, Institutional, Advisory Board, SAB member: BioNTech, Immunocore, Gadeta, Instil Bio, PokeAcel, T-Knife; Financial Interests, Personal, Advisory Board, SAB member: Neogene Therapeutics, Scenic; Financial Interests, Personal, Stocks/Shares: Neogene Therapeutics; Financial Interests, Institutional, Research Grant: Bristol Myers Squibb, BioNTech US, Merck Sharp & Dohme, Amgen, Novartis, Asher Bio; Non-Financial Interests, Member: ASCO, AACR, SITC; Other, Editor-in-Chief IOTECH: ESMO; Other, Editorial Board ESMO Open: ESMO; Other, Editorial Board: Kidney Cancer. All other authors have declared no conflicts of interest.

https://doi.org/10.1016/j.annonc.2023.09.2233

1100P Open-label non-randomized phase IB study to characterize the safety, tolerability and recommended dose of tinostamustin in combination with nivolumab in patients with advanced melanoma (ENIGMA)

M. Joerger[1], S. Diem[2], N. Wyss[1], K-L. Koster[1], D. Hess[2], Y. Metaxas[3], M-C. Flynn[1], S. Aeppli[4], T.P. El Saadany[5], S. Mane[6], E. Hiendlmeyer[7], R.A.F. von Moos[8], L. Flatz[9]

[1]Medical Oncology and Hematology Department, Kantonsspital St. Gallen, St. Gallen, Switzerland; [2]Oncology/Hematology Department, Kantonsspital St. Gallen, St. Gallen, Switzerland; [3]Oncology/Hematology Department, Spital Thurgau AG - Kantonsspital Muensterlingen, Muensterlingen, Switzerland; [4]Medical Oncology and Hematology, Brustzentrum Kantonsspital St. Gallen, St. Gallen, Switzerland; [5]Department of Medical Oncology and Hematology, Cantonal Hospital, Chur, Switzerland; [6]Dermatology, University Hospital Tuebingen, Tuebingen, Germany; [7]Clinical Trial Unit, Kantonsspital St. Gallen, St. Gallen, Switzerland; [8]Oncology/Hematology Dept., KSGR - Kantonsspital Graubünden, Chur, Switzerland; [9]Dermatology, Universitätsklinikum Tübingen, Tuebingen, Germany

Background: Melanoma patients (pts) progressing after immune checkpoint inhibitors (ICI) and BRAF targeting therapy have a poor prognosis. We explored the feasibility of a combination of the alkylating deacetylase inhibition fusion molecule tinostamustine in sub-chemotherapeutic concentrations and nivolumab.

Methods: This study was initiated to characterize dose-limiting toxicity (DLT) and the recommended phase-2 dose (RP2D) of tinostamustine and nivolumab in pts with advanced melanoma. Tinostamustine was administered at escalating doses of 15 and 30 mg/m^2 in a 3-plus-3 design, nivolumab was added at a dose of 3 mg/kg on day 15, both given i.v. every 2 weeks until toxicity or tumor progression (with the option of treatment-beyond progression).

Results: 17 pts were included into the study including 4 pts treated with tinostamustine 15 mg/m^2 over 60 min and 13 pts treated with tinostamustine 30 mg/m^2 over 60 min. 13/17 pts (77%) received prior ICI, 7/17 pts (41%) had unfavorable melanoma types (acral, mucosal, uveal) and 10/17 pts (59%) elevated baseline lactate dehydrogenase (LDH). No DLT was documented and the RP2D for tinostamustine in combination with nivolumab was defined as 30mg/m^{2}over 60 min. We observed one nivolumab-associated serious adverse event (SAE) of immune-related pneumonitis. Mean treatment duration was 22 weeks; 3 patients received $\leq$4 weeks of study treatment due to early progression. Disease stabilization among 15 evaluable pts was 47%, including 3pts (20%) with a confirmed partial response. Median progression-free survival was 8.3 weeks (95% CI 2.4 to 15.4 weeks), median overall survival 19.1 weeks (95% CI 2.4 to 41 weeks). No severe myelosuppression was observed except a single case of grade 3 leucocytopenia.Ex vivo T-cell stimulation and ELISA from blood samples revealed induction of adaptive T-cell and antibody responses against tumor-associated antigens.

Conclusions: Tinostamustine at an immune-modulatory dose of 30 mg/m^2 over 60 min is safe when co-administered with nivolumab 3mg/kg and resulted in 47% disease stabilization and 20% objective radiological responses in pts with advanced melanoma failing standard ICI treatment.

Clinical trial identification: NCT03903458.

Legal entity responsible for the study: Clinical Trial Unit, Cantonal Hospital, 9007 St. Gallen, Switzerland.

Funding: Mundipharma.

Disclosure: M. Joerger: Financial Interests, Institutional, Coordinating PI, Clinical study activity: Basilea, Bayer, BMS, Immunophotonics, MSD, Novartis, Roche; Financial Interests, Institutional, Other, Clinical study activity: Daiichi Sankyo; Financial Interests, Institutional, Local PI, Clinical study activity: InnoMedica; Non-Financial Interests, Advisory Role: Novartis, AstraZeneca, Basilea, Bayer, BMS, Debiopharm, MSD, Roche, Sanofi. K. Koster: Other, Personal, Other, Travel grant: Jansen; Other, Personal, Officer, Travel grant: Takeda. D. Hess: Financial Interests, Personal, Stocks/Shares: Novartis, Roche. Y. Metaxas: Financial Interests, Personal, Other, Travel grant: Roche. S. Aeppli: Financial Interests, Institutional, Advisory Board: BMS, Pfizer, Merck. T.P. El Saadany: Non-Financial Interests, Personal, Writing Engagement: Merck, Pfizer. R.A.F. von Moos: Non-Financial Interests, Personal, Advisory Board: Gilead, Merck, Eli Lilly, Pierre Fabre, MSD, Vifor, GSK, PharmaMar, Sanofi; Financial Interests, Institutional, Research Funding: Bayer; Financial Interests, Personal, Other, Travel grant: Takeda, Pierre Fabre. All other authors have declared no conflicts of interest.

https://doi.org/10.1016/j.annonc.2023.09.2234

1101P The effect of LNS8801 in combination with pembrolizumab in patients with treatment-refractory cutaneous melanoma

J. Rodon[1], M.F. Chaney[2], J. Cohen[3], T.K. Garyantes[4], J. Ishizuka[5], J.J. Lin[6], P. Lorusso[7], A. Mita[8], M. Mita[9], C. Muller[10], C. Natale[11], M. Orloff[12], K.P. Papadopoulos[13], S. Patel[14], A.N. Shoushtari[15]

[1]Drug Development Department, The University of Texas MD Anderson Cancer Center, Houston, TX, USA; [2]Early Clinical Development, Merck & Co. Inc - MRL Labs - Upper Gwynedd Campus, North Wales, PA, USA; [3]Abramson Cancer Center, University of Pennsylvania, Philadelphia, PA, USA; [4]R&D, Linnaeus Therapeutics, Haddonfield, NJ, USA; [5]Melanoma Medical Oncology, Yale University, New Haven, CT, USA; [6]Thoracic Oncology Department, MGH - Massachusetts General Hospital, Boston, MA, USA; [7]Medical Oncology Department, Yale School of Medicine - Radiology and Biomedical Imaging, New Haven, CT, USA; [8]Medicine Department, Samuel Oschin Comprehensive Cancer Institute Cedars-Sinai Medical Center, Los Angeles, CA, USA; [9]Cancer, Samuel Oschin Comprehensive Cancer Institute Cedars-Sinai Medical Center, Los Angeles, CA, USA; [10]Gynecologic Oncology, University of New Mexico, Albuquerque, NM, USA; [11]Research, Linnaeus Therapeutics, Haddonfield, NJ, USA; [12]Medical Oncology, Thomas Jefferson Univ Hospital, Philadelphia, PA, USA; [13]Clinical Research Department, South Texas Accelerated Research Therapeutics (START), San Antonio, TX, USA; [14]Melanoma Medical Oncology, MD Anderson Cancer Center, Houston, TX, USA; [15]Medicine, MSKCC - Memorial Sloan Kettering Cancer Center, New York, NY, USA

Background: LNS8801 is an oral G-protein coupled estrogen receptor (GPER) agonist. LNS8801 treatment results in increased melanocytic differentiation, reduced c-Myc protein levels, inhibition of proliferation, and enhancement of immune recognition of cancer cells in the first-in-human study, LNS8801 was safe and tolerable alone and in combination with pembrolizumab in patients with advanced solid tumors (NCT04130516). LNS8801 also demonstrated monotherapy activity in cutaneous melanoma (CM) patients, including a patient that is on treatment for over 3 years with no evidence of active or recurrent disease.

Methods: Patients with treatment-refractory CM received LNS8801 (125 mg, QD, PO) and pembrolizumab (200 mg, Q3W, IV) (NCT04130516). The primary objective was safety and tolerability. Secondary endpoints include pharmacokinetic, pharmacodynamics, objective response rate (ORR) and disease control rate (DCR, CR+PR+SD). Presence of a consensus, fully-functional, germline GPER coding sequence was assessed as a potential predictive biomarker.

Results: As of 4/15/23, 10 CM patients were treated. All patients received prior PD-1 and CTLA-4 directed ICIs, and were treated with a median of 2.5 prior lines of systemic therapies. 8 of 10 patients had AEs possibly related to study drugs (n=4 with grades 1-2 and n=4 with grade 3), with AST/ALT elevation, diarrhea, or fatigue occurring in more than 1 patient. Regarding efficacy, 2 had partial responses (PR), 4 had stable disease (SD), and 1 patient has not been evaluated, resulting in an ORR of 20% and DCR of 60%. Both patients with PRs remained on treatment for greater than 24 weeks. Consensus germline GPER was present in 7 of 10 sequenced patients. Of patients positive for this biomarker, 2 had PR and 3 had SD, resulting in an ORR of 29% and DCR of 71%.

Conclusions: LNS8801 and pembrolizumab is tolerable and has encouraging activity in patients with treatment-refractory CM, including patients who enrolled immediately after confirmed progression on ICIs. Consensus germline GPER is a promising predictive biomarker, and is associated with improved outcomes in patients treated with LNS8801. These data support further development of LNS8801 in combination with pembrolizumab treat advanced CM patients.

Clinical trial identification: NCT04130516.

Legal entity responsible for the study: Linnaeus Therapeutics Inc.

Funding: Linnaeus Therapeutics.

Disclosure: J. Rodon: Financial Interests, Personal, Advisory Board: Ellipses Pharma, iOnctura SA; Financial Interests, Personal, Other, Consultancy: Aadi Bioscience, Clarion Healthcare, Debiopharm, Monte Rosa Therapeutics, Cullgen, Pfizer, Merus N.V., Macrogenics, Oncology One, Envision Pharma, Columbus Venture Partners, Sardona Therapeutics, Avoro Capital Advisors, Vall d'Hebron Institute of Oncology/Ministero de Empleo Y Seguridad, Chinese University of Hong Kong, Boxer Capital, LLC, Tang Advisors, LLC, Incyte; Financial Interests, Institutional, Other, Clinical Research: Novartis, Spectrum Pharmaceuticals, Symphogen, BioAtla, Pfizer, GenMab, CytomX, Kelun-Biotech, Takeda-Millennium, GSK; Financial Interests, Institutional, Other, Research Funding: Blueprint Medicines, Black Diamond, Merck Sharp & Dohme; Financial Interests, Institutional, Research Grant, Research Funding/Clinical Research: Hummingbird, Yingli; Financial Interests, Institutional, Research Grant, Research Funding: Vall d'Hebron Institute of Oncology/Cancer Core Europe; Financial Interests, Institutional, Research Grant, Clinical Research: Bicycle Therapeutics, Taiho, Roche Pharmaceuticals, Merus, Curis, Aadi Bioscience, Nuvation, Fore Biotherapeutics, BioMed Valley Discoveries, Loxo Oncology, Cellestia, Deciphera, IDEAYA, Amgen, Tango Therapeutics, Mirati, Linnaeus Therapeutics, Bayer, Hutchinson MediPharma; Other: VHIO/Ministero de Empleo y Seguridad Social; Other, Travel: European Society for Medical Oncology. M.F. Chaney: Financial Interests, Personal, Full or part-time Employment: Merck and Co., Inc.; Financial Interests, Personal, Stocks/Shares: Merck and Co., Inc.; Non-Financial Interests, Member: ASCO, AACR. J. Cohen: Financial Interests, Personal, Advisory Role: Regeneron, Sanofi; Financial Interests, Institutional, Research Funding: Linnaeus Therapeutics. T.K. Garyantes: Financial Interests, Personal, Full or part-time Employment: Linnaeus Therapeutics. J. Ishizuka: Financial Interests, Personal, Stocks or ownership: Jounce Therapeutics, Kronos Bio; Financial Interests, Personal, Advisory Role: Danger Bio, Phenomic AI, Rheos Medicines, Tango Therapeutics, Two River Group; Financial Interests, Personal, Research Funding: AstraZeneca; Financial Interests, Institutional, Research Funding: Linnaeus Therapeutics. J.J. Lin: Financial Interests, Personal, Other, Consulting: Turning Point Therapeutics, Nuvalent, Elevation Oncology, C4 Therapeutics, Bayer, Novartis, Mirati Therapeutics, Regeneron, CLaiM Therapeutics; Financial Interests, Personal, Advisory Board, Consulting: Blueprint Medicines, Genentech; Financial Interests, Personal, Other, Honorarium, travel: Pfizer; Financial Interests, Institutional, Local PI: Turning Point Therapeutics, Neon Therapeutics, Relay Therapeutics, Bayer, Elevation Oncology, Roche/Genentech, Novartis, Hengrui Therapeutics, Pfizer, Nuvalent. P. Lorusso: Financial Interests, Personal, Advisory Board: AbbVie, Genmab, Genentech, CytomX, Takeda, Cybrexa, Agenus, IQVIA, TRIGR, Pfizer, ImmunoMet, Black Diamond, Glaxo-Smith Kline, QED Therapeutics, AstraZeneca, EMD Serono, Shattuck, Astellas, Salarius, Silverback, MacroGenics, Kyowa Kirin, Kineta, Zentalis, Molecular Templates, ABL Bio, STCube, Bayer, Seagen, imCheck, Relay Therapeutics, Stemline, Compass BADX, Mekanist, Mersana, Roivant Sciences, BAKX Therapeutics, Scenic Biotech, Qualigen, NeuroTrials; Financial Interests, Personal, Other, Data Safety Monitoring Board: Agios, Five Prime, Halozyme; Financial Interests, Personal, Other, imCORE Alliance: Roche-Genentech; Financial Interests, Personal, Other, Consultant: SOTIO, SK Life; Financial Interests, Personal, Other, Data Safety Monitoring Committee: Tyme; Financial Interests, Personal, Advisory Board, Advisory Board & Consultant: I-Mab; Financial Interests, Personal, Stocks/Shares: BAXK; Financial Interests, Institutional, Local PI: AbbVie, ADC Therapeutics, ALX Oncology, Astellas Pharma, Black Diamond, Astex Pharmaceuticals, AstraZeneca, Bayer, Boehringer Ingelheim, Calico Life Sciences, Corvus Pharmaceuticals, CytomX Therapeutics, Eisai Pharmaceuticals, Eli Lilly, EMD Serono, Five Prime, FLX Bio, F-Star Delta Limited, Genentech, Genmab, Incyte, Linnaeus Therapeutics, MedImmune, Merck Sharp & Dohme, Moderna Therapeutics, NextCure, Pfizer, Ribon Therapeutics, SOTIO, Stemline Therapeutics, Takeda, Tesaro, Jounce; Non-Financial Interests, Other, AACI Clinical Research Innovation Steering Committee - Member: Association of American Cancer Institutes; Non-Financial Interests, Other, Molecular Cancer Therapeutics Editorial Board - Member: American Association for Cancer Research; Non-Financial Interests, Other, AACR Methods in Clinical Cancer Research Workshop - Co-Director: American Association for Cancer Research; Non-Financial Interests, Other, AACR Annual Report Committee - Member: American Association for Cancer Research; Non-Financial Interests, Other, Continuing Medical Education Committee - Member: American Association for Cancer Research; Non-Financial Interests, Other, ASCO Conquer Cancer Young Investigator Award Grand Selection Committee - Member: American Society of Clinical Oncology; Non-Financial Interests, Other, New Drugs in Oncology Seminar Planning Committee - Member: American Society of Clinical Oncology; Non-Financial Interests, Other, New Agents Committee: Translational Research Panel - Chair: Cancer Research Unite Kingdom; Non-Financial Interests, Other, Scientific Advisory Board - Member: Targeted Anti-Cancer Therapies; Non-Financial Interests, Other, Chair - Phase 0 Task Force: American Association of Cancer Research; Non-Financial Interests, Member: American Association for Cancer Research, ASCO; Other, Investigational Drug Steering Committee - Committee Member: National Cancer Institute; Other, Phase I Special Emphasis Panel - Grant Reviewer/Discussion Leader: National Cancer Institute; Other, NeXT Special Emphasis Panel - Grant Reviewer: National Cancer Institute/National Institute of Health; Other, Board of Scientific Counselors, Clinical Sciences & Epidemiology: National Cancer Institute; Other, Young Investigator Meeting, Cancer Therapy Evaluation Program - Professor: National Cancer Institute; Other, Academic Advisory Board SPORE GI Malignancies - Case Western Reserve University: Case Western Reserve University; Other, External Advisory Board - Member: University of Arizona; Other, External Scientific Advisory Board - Member: University of New Mexico; Other, Scientific External Advisory Board - Member: University of California at San Diego. A. Mita: Financial Interests, Personal, Speaker's Bureau: Genentech. M. Mita: Financial Interests, Institutional, Research Funding: Linnaeus Therapeutics. C. Muller: Financial Interests, Personal, Advisory Role: GSK; Financial Interests, Institutional, Research Funding: Agenus, AstraZeneca, Incyte, Linnaeus Therapeutics, Merck, Roche, TapImmune, VBL Therapeutics. C. Natale: Financial Interests, Personal, Full or part-time Employment: Linnaeus Therapeutics. M. Orloff: Financial Interests, Institutional, Research Funding: Bristol Myers Squibb, Delcath Systems, IDEAYA Biosciences, Immunocore, Linnaeus Therapeutics, Plexxikon. K.P. Papadopoulos: Financial Interests, Personal, Advisory Board: Turning Point Therapeutics, Bicycle, Basilia; Financial Interests, Institutional, Full or part-time Employment: START; Financial Interests, Personal, Ownership Interest: START; Financial Interests, Institutional, Local PI, For conduct of clinical trial: 3D Medicines, AbbVie, ADC Therapeutics, Amgen, AnHeart Therapeutics, Bayer, Daiichi Sankyo, EMD Serono, F-Star, Incyte, Jounce Therapeutics, Lilly, Linnaeus Therapeutics, Merck, Mersana, Mirati Therapeutics, Pfizer, Regeneron Pharmaceuticals, Revolution Medicines, Syros Pharmaceuticals, Tempest Therapeutics, Treadwell Therapeutics. S. Patel: Financial Interests, Personal, Advisory Board: TriSalus, Cardinal Health, Castle Biosciences, Novartis, BMS, Pfizer, Immatics; Financial Interests, Personal, Other, Consultant for educational materials: Advance Knowledge in Healthcare; Financial Interests, Personal, Advisory Board, Advisory Board and Corporate Day speaker (unbranded): Delcath; Financial Interests, Personal, Other, Independent Data Monitoring Committee: Immunocore; Financial Interests, Personal, Other, Consultant: Guidepoint Global; Financial Interests, Institutional, Trial Chair: Provectus Biopharmaceuticals, Bristol Myers Squibb; Financial Interests, Institutional, Local PI: Lyvgen, InxMed, Foghorn Therapeutics, IDEAYA, Novartis, Seagen, Syntrix Bio; Financial Interests, Institutional, Steering Committee Member: TriSalus Life Sciences; Non-Financial Interests, Member: International Society of Ocular Oncology, ASCO, AACR, Society for Melanoma Research; Non-Financial Interests, Leadership Role: SWOG. A.N. Shoushtari: Financial Interests, Personal, Advisory Board: Bristol Myers Squibb, Immunocore, Novartis; Financial Interests, Personal, Royalties: UpToDate; Financial Interests, Institutional, Local PI: Bristol Myers Squibb, Immunocore, Pfizer, Novartis, Checkmate Pharmaceuticals, Linnaeus Therapeutics, Prelude Therapeutics; Financial Interests, Institutional, Coordinating PI: Polaris, Xcovery, Targovax ASA; Financial Interests, Personal, Local PI: Foghorn Therapeutics; Non-Financial Interests, Member: ASCO.

https://doi.org/10.1016/j.annonc.2023.09.2235

1102P Evaluation of surrogate endpoints for overall survival within the RELATIVITY-047 trial

P. Mohr[1], P. Squifflet[2], E.D. Saad[3], J. Larkin[4], M. Kurt[5], A. Moshyk[5], F. Ejzykowicz[5], M.E. Buyse[6]

[1]Dermatology, Elbe-Kliniken, Buxtehude, Germany; [2]Biostatistics, IDDI, Ottignies (Céroux-Mousty), Belgium; [3]Consultants, International Drug Development Institute, Louvain-la-Neuve, Belgium; [4]Medicine Department, The Royal Marsden Hospital - NHS Foundation Trust, London, UK; [5]Worldwide Health Economics and Outcomes Research, Bristol Myers Squibb, Lawrenceville, NJ, USA; [6]Biostatistics, International Drug Development Institute, Louvain-la-Neuve, Belgium

Background: Advances in the first-line treatment of metastatic melanoma raised the need for earlier assessment of clinical trials using intermediate endpoints that may reach statistical maturity sooner than overall survival (OS) without being influenced by subsequent treatments.

Methods: We evaluated progression-free survival (PFS), time-to-next-treatment-or-death (TNTD) and objective response rate (ORR) as potential surrogate endpoints (SEs) for OS within the phase II/III RELATIVITY-047 trial (n=714) using patient-level data with ≥21 months of follow-up. Individual-level (IL) correlations with OS were derived from copula functions and measured by Spearman's (ρ) and Kendall's (τ) rank

correlation coefficients for PFS and TNTD, and by an odds ratio (OR) for ORR. Patients were clustered in 8 non-overlapping regions according to their country of enrolment for trial-level (TL) surrogacy assessment. Within each region treatment effects on PFS, TNTD and OS were calculated by Cox-proportional-hazards models. TL correlations between the SEs and OS were estimated by weighted linear regression and measured by coefficient of determination (R^2). Sensitivity of the results were tested with respect to alternative geographic clustering.

Results: At the IL, ORR and TNTD were strongly correlated with OS, whereas PFS showed moderate correlation with OS. At the TL, PFS and ORR showed moderate correlation with OS with wide uncertainty whereas TNTD had strong correlation with OS with narrower margin of uncertainty. Alternative geographic clustering of patients had marginal impact on the IL ($\leq$ 0.02 change in all measures for all SEs) and modest impact on TL correlations ($\leq$ 0.08 change in R^2 for all SEs).

Table: 1102P

Correlation	IL		TL
	ρ [95% CI]	τ [95% CI]	R^2 [95% CI]
PFS - OS	0.70 [0.68, 0.72]	0.51 [0.45, 0.58]	0.71 [0.35, 1.00]
TNTD - OS	0.84 [0.81, 0.86]	0.66 [0.63, 0.69]	0.95 [0.87, 1.00]
ORR - OS	**OR**		
	10.60 [6.77-14.43]		0.64 [0.21, 1.00]

Conclusions: Within the RELATIVITY-047 trial, TNTD-OS surrogacy was stronger and more stable than PFS-OS and ORR-OS surrogacy. The strength of each surrogacy relationship analyzed in this study and their relative order were consistent with those previously reported from other immune-checkpoint inhibitor studies.

Clinical trial identification: Phase II/III study: RELATIVITY-047 (CA224-047), NCT03470922.

Editorial acknowledgement: Writing of the abstract was led by Dr. Murat Kurt (co-author). All other co-authors provided comments on the abstract draft. Final version of the document was shaped by a consensus of all co-authors.

Legal entity responsible for the study: Bristol Myers Squibb.

Funding: Bristol Myers Squibb.

Disclosure: P. Mohr: Financial Interests, Personal, Advisory Board: Bristol Myers Squibb, Merck Sharp & Dohme, Novartis, GSK, Pierre Fabre, Sanofi; Financial Interests, Personal, Invited Speaker: Amgen, Bristol Myers Squibb, Merck Sharp & Dohme, Novartis, Roche, Pierre Fabre, Sanofi, Sun Pharma; Financial Interests, Institutional, Funding: Bristol Myers Squibb, Merck Sharp & Dohme, Novartis; Non-Financial Interests, Principal Investigator: Bristol Myers Squibb, Merck Sharp & Dohme, Regeneron, Sanofi, Novartis, Sun Pharma. P. Squifflet: Financial Interests, Institutional, Speaker, Consultant, Advisor, Pierre Fabre; Squifflet is an employee of IDDI and received consultancy fees from Bristol Myers Squibb through IDDI: Bristol Myers Squibb. E.D. Saad: Financial Interests, Institutional, Speaker, Consultant, Advisor, Everardo Saad is an employee of IDDI and received consultancy fees from Bristol Myers Squibb through IDDI: Bristol Myers Squibb. J. Larkin: Financial Interests, Personal, Invited Speaker: BMS, Pfizer, Roche, Pierre Fabre, AstraZeneca, Novartis, EUSA Pharma, MSD, Merck, GSK, Ipsen, Aptitude, Eisai, Calithera, Ultimovacs, Seagen, Goldman Sachs, eCancer, Inselgruppe, Agence Unik; Financial Interests, Personal, Other, Consultancy: Incyte, iOnctura, Apple Tree, Merck, BMS, Eisai, Debiopharm; Financial Interests, Personal, Other, Honorarium: touchIME, touchEXPERTS, VJOncology, RGCP, Cambridge Healthcare Research, Royal College of Physicians; Financial Interests, Institutional, Funding: BMS, MSD, Novartis, Pfizer, Achilles, Roche, Nektar, Covance, Immunocore, Pharmacyclics, Aveo. M. Kurt, A. Moshyk, F. Ejzykowicz: Financial Interests, Personal, Full or part-time Employment: Bristol Myers Squibb; Financial Interests, Personal, Stocks or ownership: Bristol Myers Squibb. M.E. Buyse: Financial Interests, Institutional, Speaker, Consultant, Advisor, Marc Buyse is an employee of IDDI and received consultancy fees from Bristol Myers Squib through IDDI: Bristol Myers Squibb.

https://doi.org/10.1016/j.annonc.2023.09.2236

1103P Nivolumab (NIVO) plus relatlimab (RELA) vs NIVO in previously untreated metastatic or unresectable melanoma: 2-year subgroup analyses from RELATIVITY-047

G.V. Long[1], F.S. Hodi[2], E.J. Lipson[3], D. Schadendorf[4], P.A. Ascierto[5], F.A. Medina Soto[6], M. Maio[7], M. Hernberg[8], J. Mackiewicz[9], S. Prey[10], M.K. Mujika Eizmendi[11], V.G. Atkinson[12], J.C. Hassel[13], G. Cinat[14], B. Ratto[15], S. Rodriguez[16], P.T. Wang[17], S. Dolfi[18], H.A. Tawbi[19]

[1]Medical Oncology, Melanoma Institute Australia, University of Sydney, Royal North Shore and Mater Hospitals, Wollstonecraft, NSW, Australia; [2]Melanoma, Dana-Farber Cancer Institute, Boston, MA, USA; [3]Oncology Department, Johns Hopkins University School of Medicine, Baltimore, MD, USA; [4]Department of Dermatology - Hautklinik, University Hospital Essen, Essen, Germany; [5]Melanoma, Cancer Immunotherapy & Developmental Therapeutics, Istituto Nazionale dei Tumori IRCCS "Fondazione G. Pascale", Naples, Italy; [6]Oncology, Axis Cancer Center, Mexico City, Mexico; [7]Medical Oncology, AOUS Policlinico Santa Maria alle Scotte, Siena, Italy; [8]Comprehensive Cancer Center, Helsinki University Hospital, Helsinki, Finland; [9]Department of Medical and Experimental Oncology, Institute of Oncology, Poznan University of Medical Sciences, Poznan, Poland; [10]Dermatology, Bordeaux Institute of Oncology, Bordeaux, France; [11]Medical Oncology, Onkologikoa of San Sebastián, San Sebastian, Spain; [12]Division of Cancer Services, Greenslopes Private Hospital, Woolloongabba, QLD, Australia; [13]Section of Dermato-Oncology, University Clinic Heidelberg, Heidelberg, Germany; [14]Melanoma and Sarcoma Department, Fundación Cidea/Instituto Alexander Fleming, Buenos Aires, Argentina; [15]Medical Oncology, Bristol Myers Squibb, Lawrenceville, NJ, USA; [16]HQMO - Lung, Head & Neck Department, Bristol Myers Squibb, Princeton, NJ, USA; [17]GBDS Medical Affairs - Oncology, Bristol Myers Squibb, Princeton, NJ, USA; [18]Clinical Research, Bristol Myers Squibb, Princeton, NJ, USA; [19]Melanoma Medical Oncology Department, MD Anderson Cancer Center, Houston, TX, USA

Background: In RELATIVITY-047 (NCT03470922), NIVO + RELA previously demonstrated a statistically significant improvement in the primary endpoint of PFS per BICR vs NIVO, with a clinically meaningful (non-significant) statistical improvement in OS and a numerically higher ORR (secondary endpoints) in pts with previously untreated metastatic or unresectable melanoma. Post hoc analyses exploring the efficacy of NIVO + RELA vs NIVO according to baseline (BL) sites of metastasis (mets) and the time to development of CNS mets are reported herein.

Methods: Pts were randomized 1:1 to receive NIVO 480 mg + RELA 160 mg fixed-dose combination (FDC) or NIVO 480 mg intravenously Q4W. Exploratory post hoc analyses were performed for PFS, OS, ORR, and melanoma-specific survival (MSS) by the no. of mets sites and the presence or absence of liver and lung mets. Time to development of new CNS mets per BICR was also assessed in both arms. Follow-up (f/u) brain imaging was not mandated per protocol.

Results: Median f/u was 25.3 mo; 581/714 pts were included in the BL mets analysis (mucosal and acral pts were excluded). Efficacy favored NIVO + RELA over NIVO in the majority of subgroups analyzed (Table). In pts without CNS mets at BL (348 in each arm), 17 pts (5%) in the NIVO + RELA arm and 31 pts (9%) in the NIVO arm developed new CNS mets per BICR over the course of tumor assessment f/u. Median time to the development of new CNS mets per BICR was 11.1 mo (range, 2.0–31.5) with NIVO + RELA and 6.6 mo (range, 0.6–32.7) with NIVO.

Conclusions: Efficacy outcomes generally favored NIVO + RELA over NIVO in pts with BL liver or lung mets and regardless of no. of BL sites of disease. Fewer pts on NIVO + RELA vs NIVO developed new CNS mets (and took a longer time to develop them), suggesting CNS activity with the FDC; however, incidence was low. Activity of NIVO + RELA in pts with CNS mets needs to be confirmed in a dedicated CNS study. Additional analyses will be presented.

Clinical trial identification: NCT03470922.

Editorial acknowledgement: Jessica R. Augello, PhD, Ashfield MedComms.

Legal entity responsible for the study: Bristol Myers Squibb.

Funding: Bristol Myers Squibb.

Disclosure: G.V. Long: Financial Interests, Personal, Speaker, Consultant, Advisor: Agenus Inc., Amgen Inc., Array Biopharma, Boehringer Ingelheim International GmbH, BMS, Evaxion Biotech A/S,

Table: 1103P

	n	PFS	OS	MSS	ORR
		HR (95% CI)	HR (95% CI)	HR (95% CI)	ORR difference, % (95% CI)
No. of mets sites					
1	184	0.85 (0.57–1.27)	0.92 (0.56–1.52)	0.85 (0.48–1.51)	14.1 (-0.3 to 27.8)
2–3	286	0.71 (0.53–0.95)	0.69 (0.49–0.98)	0.59 (0.40–0.88)	11.5 (0.1 to 22.4)
≥ 4	109	0.91 (0.59–1.42)	0.74 (0.46–1.21)	0.77 (0.46–1.28)	-0.1 (-17.6 to 17.1)
Liver mets					
Present	122	0.81 (0.53–1.23)	0.62 (0.37–1.03)	0.72 (0.41–1.27)	9.4 (-7.7 to 25.6)
Absent	459	0.81 (0.64–1.02)	0.84 (0.64–1.11)	0.72 (0.53–0.99)	9.3 (0.2 to 18.1)
Lung mets					
Present	254	0.77 (0.57–1.05)	0.72 (0.50–1.04)	0.71 (0.47–1.05)	12.8 (0.7 to 24.4)
Absent	327	0.85 (0.64–1.12)	0.84 (0.61–1.17)	0.73 (0.5–1.07)	6.8 (-4.0 to 17.3)

Unstratified HR; NIVO + RELA vs NIVO.

Hexal AG (Sandoz Company), Highlight Therapeutics S.L, Innovent Biologics USA Inc., Merck Sharp & Dohme (Australia) Pty Limited, Novartis Pharma AG; Financial Interests, Personal, Invited Speaker: BMS, Pierre Fabre; Financial Interests, Personal, Advisory Board: Agenus Inc., Amgen Inc., Array Biopharma, Boehringer Ingelheim International GmbH, BMS, Evaxion Biotech A/S, Hexal AG (Sandoz Company), Highlight Therapeutics S.L, Innovent Biologics USA Inc., Merck Sharp & Dohme (Australia) Pty Limited, Novartis Pharma AG. F.S. Hodi: Financial Interests, Institutional, Research Grant: BMS, Novartis; Financial Interests, Personal, Speaker, Consultant, Advisor: BMS, Merck, Novartis, Genentech/Roche, CatalYm, Immunocore, Kairos, Zumutor, Corner Therapeutics, Curis, AstraZeneca; Financial Interests, Personal, Advisory Board: BioEntre, Iovance, Gossamer, Rheos, Surface, Compass Therapeutics, Apricity, Bicara, Checkpoint Therapeutics. E.J. Lipson: Financial Interests, Personal, Advisory Board: Bristol Myers Squibb, Merck, Sanofi, Regeneron, Genentech, Eisai, Instil Bio, Natera, Nektar Therapeutics, Pfizer, Rain Therapeutics, CareDx, Immunocore, Novartis, Replimune, HUYA Bioscience International; Financial Interests, Personal, Other, Consultant: OncoSec; Financial Interests, Institutional, Coordinating PI: Bristol Myers Squibb; Financial Interests, Institutional, Local PI: Regeneron, Merck, Sanofi. D. Schadendorf: Financial Interests, Personal, Invited Speaker: BMS, Novartis, MSD, Roche, Merck Serono, Sanofi; Financial Interests, Personal, Advisory Board: BMS, Novartis, MSD, Immunocore, Pierre Fabre, Sanofi/Regeneron, Pfizer, Philogen, Neracare; Financial Interests, Personal, Steering Committee Member: Novartis, BMS, MSD; Financial Interests, Institutional, Coordinating PI: Novartis, BMS, MSD, Pierre Fabre; Financial Interests, Institutional, Research Grant: BMS, MSD; Financial Interests, Institutional, Local PI: Sanofi, Philogen; Non-Financial Interests, Member of Board of Directors: EORTC-MG. P.A. Ascierto: Financial Interests, Personal, Other, Consultant and Advisory Role: BMS, Roche Genentech, MSD, Novartis, Merck Serono, Pierre Fabre, AstraZeneca, Sun Pharma, Sanofi, Idera, Sandoz, Immunocore, 4SC, Nektar, Boehringer Ingelheim, Regeneron; Financial Interests, Personal, Other, Consultant and Advisory Role. Travel support: Pfizer/Array; Financial Interests, Personal, Other, Consultant Role: Italfarmaco; Financial Interests, Personal, Other, Advisory Role: Eisai, Seagen; Financial Interests, Personal, Other, Consultant Role: Daiichi Sankyo, Pfizer, OncoSec, Nouscom, Lunaphore; Financial Interests, Personal, Other, Consultant role: Medicenna; Financial Interests, Personal, Other, Consultant role and travel support: Bio-AI Health; Financial Interests, Personal, Advisory Board, Consultant and Advisory Role: iTeos; Financial Interests, Personal, Advisory Board, Consultant and Advisory role: ValoTx; Financial Interests, Personal, Advisory Board, Consultant and Advisor role. Travel support: Replimune; Financial Interests, Personal, Advisory Board, Advisor role: Bayer; Financial Interests, Personal, Advisory Board: Erasca; Financial Interests, Institutional, Funding, Clinical trial and translational research: BMS; Financial Interests, Institutional, Funding, Clinical Trial: Roche Genentech, Pfizer/Array, Sanofi; Non-Financial Interests, Leadership Role, President since 2010: Fondazione Melanoma Onlus Italy; Non-Financial Interests, Leadership Role, President since 2014: Campania Society of ImmunoTherapy of Cancer (SCITO) Italy; Non-Financial Interests, Other, Member of Steering Committee since 2016: Society for Melanoma Research (SMR); Non-Financial Interests, Member of Board of Directors, November 2017 - December 2021: Society for Immunotherapy of Cancer (SITC); Non-Financial Interests, Member: ASCO, SITC, EORTC Melanoma Cooperative Group, AIOM, SMR. M. Maio: Financial Interests, Personal, Advisory Board: BMS, Roche, GSK, Sanofi, Alfasigma, Amgen, SciClone, Eli Lilly, MSD, Incyte, Pierre Fabre, AstraZeneca; Financial Interests, Personal, Stocks/Shares: EpiGen, Theravance. M. Hernberg: Financial Interests, Personal, Advisory Board: BMS, Pierre Fabre, MSD, Novartis, Med Engine; Financial Interests, Personal, Invited Speaker: Novartis, MSD, BMS. S. Prey: Financial Interests, Institutional, Advisory Board: BMS, MSD, Novartis. V.G. Atkinson: Financial Interests, Personal, Advisory Board: BMS, MSD, Nektar, Novartis, Pierre Fabre, QBiotics; Financial Interests, Personal, Invited Speaker: BMS, MSD, Novartis, Pierre Fabre, Limbic; Financial Interests, Personal, Other, Travel Support: BMS. J.C. Hassel: Financial Interests, Personal, Invited Speaker: BMS, Novartis, Sanofi, MSD, Sun Pharma, Amgen, GSK, Pierre Fabre, Immunocore; Financial Interests, Personal, Advisory Board: MSD, Pierre Fabre, Sun Pharma, GSK, Onkowissen; Financial Interests, Institutional, Advisory Board: Novartis, BMS, Immunocore, Philogen, Sanofi; Financial Interests, Institutional, Research Grant: BMS, Sun Pharma; Financial Interests, Institutional, Local PI: Philogen, Genentech, 4SC, BioNTech, Idera, Iovance, Nektar, Pierre Fabre, Regeneron, Sanofi, Replimune; Financial Interests, Institutional, Coordinating PI: BMS, Immunocore, Novartis, Genmab; Financial Interests, Personal, Steering Committee Member: Immunocore, IO Biotech; Non-Financial Interests, Leadership Role: DeCOG; Non-Financial Interests, Member: ASCO. G. Cinat: Financial Interests, Personal, Advisory Board: Bristol Myers Squibb, Novartis, Merck Sharp & Dohme (MSD); Financial Interests, Personal, Expert Testimony: Bristol Myers Squibb, Novartis, Merck Sharp & Dohme (MSD); Financial Interests, Personal, Invited Speaker: Bristol Myers Squibb, Novartis, Merck Sharp & Dohme (MSD), Roche; Financial Interests, Personal, Other, Concensus Conference: Americas Health Foundation; Financial Interests, Personal, Full or part-time Employment: Angel H. Roffo Oncology Institute, University of Buenos Aires; Financial Interests, Personal, Local PI: Bristol Myers Squibb (BMS), Novartis, Merck Sharp & Dohme (MSD), Pfizer; Non-Financial Interests, Personal, Member: ASCO, Argentina Association of Clinical Oncology (Asociación Argentina de Oncología Clínica - AAOC). B. Ratto, S. Rodriguez, S. Dolfi: Financial Interests, Personal, Full or part-time Employment: Bristol Myers Squibb; Financial Interests, Personal, Stocks/Shares: Bristol Myers Squibb. P.T. Wang: Financial Interests, Personal, Full or part-time Employment, Biostatistician employed full-time: BMS (Bristol Myers Squibb); Financial Interests, Personal, Stocks/Shares: BMS (Bristol Myers Squibb). H.A. Tawbi: Financial Interests, Personal, Advisory Board: Bristol Myers Squibb, Merck, Novartis, Genentech, Eisai, Karyopharm, Iovance, Pfizer, Jazz Pharmaceuticals; Financial Interests, Institutional, Trial Chair: Bristol Myers Squibb; Financial Interests, Institutional, Local PI: Merck, RAPT Pharmaceuticals; Financial Interests, Institutional, Steering Committee Member: Novartis, Genentech; Financial Interests, Institutional, Funding: GSK, Eisai. All other authors have declared no conflicts of interest.

https://doi.org/10.1016/j.annonc.2023.09.2237

1104P Efficacy of immune checkpoint inhibition in metastatic or non-resectable melanoma after failure of adjuvant anti-PD1 treatment: A EUMelareg real-world evidence study

M. Weichenthal[1], D. Schadendorf[2], L. Bastholt[3], I. Gavrilova[4], J.B.A.G. Haanen[5], J. Mangana[6], E. Espinosa[7], I-M. Svane[8], M. Wouters[9], E. Ellebæk[10], P. Mohr[11], I. Marques Rodas[12], N. Asher[13], R. Dummer[14], C. Gaudy Marqueste[15], F. Aya[16], H. Gogas[17], C. Lebbe[18], P. Rutkowski[19], P.A. Ascierto[20]

[1]Dermatology Department, Christian-Albrechts-University Kiel, Kiel, Germany; [2]Department of Dermatology - Hautklinik, University Hospital Essen Westdeutsches Tumorzentrum, Essen, Germany; [3]Dept. of Oncology, OUH - Odense University Hospital, Odense, Denmark; [4]Oncodermatology, Bulgarian National Cancer Registry, Sofia, Bulgaria; [5]Medical Oncology Dept., NKI-AVL - Netherlands Cancer Institute/Antoni van Leeuwenhoek Hospital, Amsterdam, Netherlands; [6]Dermatologie, Universitätsspital Zürich - Klinik für Dermatologie, Zurich, Switzerland; [7]Oncology Department, Hospital Universitario La Paz, Madrid, Spain; [8]Department of Oncology, Herlev and Gentofte Hospital, Herlev, Denmark; [9]Scientific Department, DICA - Dutch Institute for Clinical Auditing, Leiden, Netherlands; [10]Oncology Department, Herlev and Gentofte Hospital, Herlev, Denmark; [11]Dermato-Oncology Department, Dermatologic Center Buxtehude, Buxtehude, Germany; [12]Medical Oncology Dept., Hospital Universitario de La Paz, Madrid, Spain; [13]Sheba Medical Center, The Ella Institute for Treatment and Research of Melanoma and Skin Cancer - Sheba Medical Center, Ramat Gan, Israel; [14]Dermatology Department, Universitätsspital Zürich - Klinik für Dermatologie, Zurich, Switzerland; [15]Medical Oncology Dept., AP-HM - CHU La Timone Enfants, Marseille, France; [16]Medical Oncology Dept., Hospital Clinic y Provincial de Barcelona, Barcelona, Spain; [17]First Department of Medicine, National and Kapodistrian University of Athens - School of Medicine, Athens, Greece; [18]Dermatology Dept., Hopital Saint Louis AP-HP, Paris, France; [19]Department of Soft Tissue/Bone Sarcoma and Melanoma, Maria Sklodowska-Curie National Research Institute of Oncology, Warsaw, Poland; [20]Melanoma, Cancer Immunotherapy & Developmental Therapeutics, Istituto Nazionale Tumori - IRCCS - Fondazione Pascale, Naples, Italy

Background: Adjuvant immune checkpoint inhibition (ICI) with anti-PD1 antibodies in high-risk resected melanoma has been shown to improve recurrence-free survival by about 50 percent. It is unclear, whether adjuvant pre-treatment with anti-PD1 antibodies would impair response to ICI in metastatic patients with recurrence after adjuvant ICI.

Methods: From the adjuvant study platform of the European Melanoma Treatment Registry (EUMelaReg) we analysed cases with recurrence following adjuvant anti-PD1 ICI. In those, receiving ICI in the first-line setting, response rates and progression-free survival were compared to patients selected from the EMelaReg database by matching for relevant prognostic factors in the first-line non-adjuvant setting.

Results: A total of 389 melanoma patients with first-line ICI after failure from adjuvant anti-PD1 antibody treatment could be matched 1:1 for several prognostic covariates to first-line ICI cases without adjuvant pre-treatment. Overall response rate was significantly lower after adjuvant anti-PD1 treatment failure (32.9% vs. 40.0%) and progression free survival was 4.6 months for patients with adjuvant pre-treatment as compared to 10.1 months for PD1-naive patients ($p<0.0001$). This contrast was independent from usage of single agent anti-PD1 or combined ICI with anti-PD1 and anti-CTLAE4 in the first-line setting.

Conclusions: Adjuvant pre-treatment with anti-PD1 antibodies was related to an inferior response and progression-free survival in patients with metastatic or non-resectable melanoma receiving ICI in the first-line setting.

Legal entity responsible for the study: The European Melanoma Treatment Registry.

Funding: Merck/MSD, BMS, Novartis.

Disclosure: M. Weichenthal: Financial Interests, Personal, Advisory Board: MSD. D. Schadendorf: Financial Interests, Personal, Invited Speaker: BMS, Novartis, MSD, Roche, Merck Serono, Sanofi; Financial Interests, Personal, Advisory Board: BMS, Novartis, MSD, Immunocore, Pierre Fabre, Sanofi/Regeneron, Pfizer, Philogen, NeraCare; Financial Interests, Personal, Steering Committee Member: Novartis, BMS, MSD; Financial Interests, Institutional, Coordinating PI: Novartis, BMS, MSD, Pierre Fabre; Financial Interests, Institutional, Research Grant: BMS, MSD; Financial Interests, Institutional, Local PI: Sanofi, Philogen; Non-Financial Interests, Member of Board of Directors: EORTC-MG. L. Bastholt: Non-Financial Interests, Advisory Role, Scientific committee under Danish Medicines Agency regarding new treatments of melanoma, skin cancer and thyroid cancer: Danish Medicines Agency. I. Gavrilova: Financial Interests, Advisory Board: MSD, Roche, Merck, Novartis, BMS, Sanofi. J.B.A.G. Haanen: Financial Interests, Institutional, Advisory Board: Bristol Myers Squibb, Achilles Therapeutics, Ipsen, Merck Sharp & Dohme, Merck Serono, Pfizer, Molecular Partners, Novartis, Roche, Sanofi, Third Rock Venture, Iovance Biotherapeutics; Financial Interests, Institutional, Advisory Board, SAB member: BioNTech, Immunocore, Gadeta, Instil Bio, PokeAcel, T-Knife; Financial Interests, Personal, Advisory Board, SAB member: Neogene Therapeutics, Scenic; Financial Interests, Personal, Stocks/Shares: Neogene Therapeutics; Financial Interests, Institutional, Research Grant: Bristol Myers Squibb, BioNTech US, Merck Sharp & Dohme, Amgen, Novartis, Asher Bio; Non-Financial Interests, Member: ASCO, AACR, SITC; Other, Editor-in-Chief IOTECH: ESMO; Other, Editorial Board ESMO Open: ESMO; Other, Editorial Board: Kidney Cancer. J. Mangana: Financial Interests, Advisory Board: Merck, Pfizer, MSD, Novartis, Roche, Pierre Fabre, Amgen, BMS. E. Espinosa: Financial Interests, Personal, Advisory Board: BMS, MSD; Financial Interests, Personal, Invited Speaker: BMS, MSD, Pierre Fabre, Novartis. I. Svane: Financial Interests, Personal, Advisory Board: BMS, Pierre Fabre, Novartis; Financial Interests, Personal, Invited Speaker: MSD, Pierre Fabre, Novartis, Roche, BMS; Financial Interests, Personal, Writing Engagement: MSD; Financial Interests, Personal, Stocks/Shares, Cofounder and Founder warrents: IO Biotech; Financial Interests, Institutional, Research Grant: Adaptimmune, Enara Bio, Lytix Biopharma, TILT Biotherapeutics; Financial Interests, Institutional, Funding: Evaxion; Non-Financial Interests, Principal Investigator: BMS, Roche, TILT Biotherapeutics, Lytix Biopharma, Novartis. E. Ellebæk: Financial Interests, Personal, Invited Speaker: Pierre Fabre, BMS, Novartis, MSD, Pfizer; Other, Travel and conference expenses: MSD, Pierre Fabre. P. Mohr: Financial Interests, Personal, Advisory Board: Bristol Myers Squibb, Merck Sharp & Dohme, Merck Sharp & Dohme, Novartis, GSK, Pierre Fabre, Sanofi; Financial Interests,

Personal, Invited Speaker: Amgen, Bristol Myers Squibb, Merck Sharp & Dohme, Merck Sharp & Dohme, Novartis, Roche, Pierre Fabre, Sanofi, Sun Pharma; Financial Interests, Institutional, Funding: Bristol Myers Squibb, Merck Sharp & Dohme, Novartis; Non-Financial Interests, Principal Investigator: Bristol Myers Squibb, Merck Sharp & Dohme, Regeneron, Sanofi, Novartis, Sun Pharma. N. Asher: Financial Interests, Advisory Board: Medison, BMS, MSD, Novartis, NucleAI, Teva, OncoHost. R. Dummer: Financial Interests, Personal, Other, Consulting and/or advisory role: Novartis, Merck Sharp & Dohme (MSD), Bristol Myers Squibb (BMS), Roche, Amgen, Takeda, Pierre Fabre, Sun Pharma, Sanofi, CatalYm, Second Genome, Regeneron, Alligator, MaviVAX SA, touchIME, T3 Pharma, Pfizer, Simcere. C. Gaudy Marqueste: Financial Interests, Advisory Board: Pierre Fabre, BMS, MSD. F. Aya: Financial Interests, Advisory Board: Novartis, MSD. H. Gogas: Financial Interests, Personal, Advisory Board: MSD, BMS, Pierre Fabre, Sanofi; Financial Interests, Personal, Invited Speaker: MSD, BMS, Novartis, Pierre Fabre, Sanofi; Financial Interests, Steering Committee Member: Amgen, Replimune; Financial Interests, Institutional, Local PI: Amgen, MSD, BMS, Replimune, Iovance, Bayer; Financial Interests, Institutional, Research Grant: BMS, Pfizer, Lilly, Pierre Fabre. C. Lebbe: Financial Interests, Personal, Advisory Board: Bristol Myers Squibb, MSD, Novartis, Amgen, Roche, Merck Serono, Sanofi, Pierre Fabre; Financial Interests, Personal, Funding: Roche, Bristol Myers Squibb; Non-Financial Interests, Advisory Role: Bristol Myers Squibb, MSD, Novartis, Amgen, Roche, Merck Serono, Sanofi, Pierre Fabre; Other, Honoraria, Speaker's Bureau, Research funding: Roche; Other, Honoraria, Speaker's bureau, Travel, Accommodation, Expenses, Research funding, Board: Bristol Myers Squibb; Other, Honoraria, Speaker's bureau, Travel, Accommodations, Expenses, Board: Novartis, MSD; Other, Honoraria, Speaker's bureau: Amgen; Other, Honoraria, Travel, Accommodations, Expenses, Board: Pierre Fabre; Other, Honoraria: Pfizer; Other, Honoraria: Incyte; Other, Travel, accommodations, Expenses, Board: Sanofi; Other, Board: Avantis Medical Systems, Jazz Pharmaceuticals; Other, Participation on a Data Safety Monitoring Board or Advisory Board: InflaRx. P. Rutkowski: Financial Interests, Personal, Invited Speaker, honoraria for lectures: MSD, BMS, Pierre Fabre; Financial Interests, Personal, Advisory Board: MSD, BMS, Pierre Fabre, Merck, Sanofi, Blueprint Medicines, Philogen; Financial Interests, Personal, Invited Speaker: Merck, Sanofi, Novartis, AstraZeneca; Financial Interests, Institutional, Research Grant, research grant for ISS: Pfizer; Financial Interests, Institutional, Funding, research grant for institution: BMS; Non-Financial Interests, Member of Board of Directors: Polish Society of Surgical Oncology; Non-Financial Interests, Member of Board of Directors, President: Polish Oncological Society. P.A. Ascierto: Financial Interests, Personal, Other, Consultant and Advisory Role: BMS, Roche Genentech, MSD, Novartis, Merck Serono, Pierre Fabre, AstraZeneca, Sun Pharma, Sanofi, Idera, Sandoz, Immunocore, 4SC, Nektar, Boehringer Ingelheim, Regeneron; Financial Interests, Personal, Other, Consultant and Advisory Role, Travel support: Pfizer/Array; Financial Interests, Personal, Other, Consultant Role: Italfarmaco; Financial Interests, Personal, Other, Advisory Role: Eisai, Seagen; Financial Interests, Personal, Other, Consultant Role: Daiichi Sankyo, Pfizer, OncoSec, Nouscom, Lunaphore; Financial Interests, Personal, Other, Consultant role: Medicenna; Financial Interests, Personal, Other, Consultant role and travel support: Bio-AI Health; Financial Interests, Personal, Advisory Board, Consultant and Advisory Role: iTeos; Financial Interests, Personal, Advisory Board, Consultant and Advisory role: ValoTx; Financial Interests, Personal, Advisory Board, Consultant and Advisor role. Travel support: Replimune; Financial Interests, Personal, Advisory Board, Advisor role: Bayer; Financial Interests, Institutional, Funding, Clinical Trial: Pfizer/Array, Roche Genentech, Sanofi; Financial Interests, Personal, Advisory Board: Erasca; Financial Interests, Institutional, Funding, Clinical trial and translational research: BMS; Non-Financial Interests, Leadership Role, President since 2010: Fondazione Melanoma Onlus Italy; Non-Financial Interests, Leadership Role, President since 2014: Campania Society of ImmunoTherapy of Cancer (SCITO) Italy; Non-Financial Interests, Other, Member of Steering Committee since 2016: Society for Melanoma Research (SMR); Non-Financial Interests, Member of Board of Directors, November 2017 - December 2021: Society for Immunotherapy of Cancer (SITC); Non-Financial Interests, Member: ASCO, SITC, EORTC Melanoma Cooperative Group, SMR, AIOM. All other authors have declared no conflicts of interest.

https://doi.org/10.1016/j.annonc.2023.09.2238

1105P First-line nivolumab plus ipilimumab in advanced melanoma patients previously treated with adjuvant systemic therapy

K. Kozak[1], P. Teterycz[1], L. Galus[2], J. Mackiewicz[2], P. Brandys[3], B. Cybulska-Stopa[4], N. Kempa-Kaminska[4], M. Ziętek[5], J. Zubrowska[6], R. Dziura[6], P. Sobczuk[1], A.M. Czarnecka[7], P. Rutkowski[1]

[1]Department of Soft Tissue/Bone Sarcoma and Melanoma, Maria Sklodowska-Curie National Research Institute of Oncology, Warsaw, Poland; [2]Department of Medical and Experimental Oncology, Institute of Oncology, Poznan University of Medical Sciences, Poznan, Poland; [3]Department of Clinical Oncology, Maria Sklodowska-Curie National Research Institute of Oncology, Krakow Branch, Krakow, Poland; [4]Department of Clinical Oncology, Lower Silesian Center of Oncology, Hematology and Pulmonology, Wroclaw, Poland; [5]Department of Surgical Oncology, Wroclaw Comprehensive Cancer Center, Wroclaw, Poland; [6]Deparment of Clinical Oncology, Holy Cross Cancer Center, Kielce, Poland; [7]Department of Soft Tissue/Bone Sarcoma and Melanoma & Department of Experimental Pharmacology, Maria Sklodowska-Curie National Research Institute of Oncology & Medical Research Centre Polish Academy of Science, Warsaw, Poland

Background: The combination of nivolumab and ipilimumab (NIVO+IPI) is associated with the most durable responses and the highest overall survival rates in patients (pts) with advanced melanoma. However, this regimen is increasingly being used in a different patient population than in clinical trials, namely after prior adjuvant treatment. The objective of this study is to evaluate the efficacy and safety of NIVO+IPI in pts who have relapsed despite adjuvant treatment.

Methods: This retrospective analysis included pts with unresectable stage III and stage IV melanoma treated with NIVO+IPI between 01/2021-10/2022 at 5 cancer centers in Poland according to uniform criteria. All pts received prior adjuvant therapy (immunotherapy or BRAF/MEK inhibitors) for stage III/IV melanoma.

Results: A total of 70 pts were identified. The median age was 53 years, 32% of pts were female, 46% had *BRAF* mutation. At baseline, 18.5% of pts had unresectable stage III disease, 21.2% had stage M1a, 18.2% M1b, 34.8% M1c and 7.6% M1d. Most pts (81.4%) received anti-PD1 in the adjuvant setting. In 70% of pts, the disease relapsed during adjuvant therapy. Median follow-up time was 12.6 months. The objective response rate was 24%. A higher response rate was observed in pts who were immunotherapy-naive (33%) than in pts who received anti-PD1 in the adjuvant setting (22%). Median progression-free survival (mPFS) was 3.9 (95%CI 3.0—9.7) months. Although not statistically significant, a higher median PFS of NIVO+IPI was observed in patients who received BRAF/MEK inhibitors as compared to those who were treated with anti-PD1 antibodies in the adjuvant setting (11.1 vs 3.7 months, p=0.53). Overall survival rate at 12 months was 59% (95%CI 47—74). Treatment-related adverse events (TRAEs) of any grade were observed in 97% of pts and grade 3/4 TRAEs occurred in 24% of pts.

Conclusions: NIVO+IPI shows lower efficacy in advanced melanoma pts who have relapsed despite adjuvant treatment comparing to clinical trial data. The population of pts with a particularly poor prognosis are those previously treated with adjuvant anti-PD-1 antibodies, as disease recurrence indicates some resistance to immunotherapy difficult to overcome by adding anti-CTLA4 antibody to anti-PD-1 therapy.

Legal entity responsible for the study: The authors.

Funding: Has not received any funding.

Disclosure: K. Kozak: Financial Interests, Personal, Invited Speaker: Bristol Myers Squib, MSD, Novartis, Pierre Fabre, Sanofi. P. Teterycz: Financial Interests, Personal, Other: BMS, MSD. L. Galus: Financial Interests, Invited Speaker: BMS, MSD, Novartis, Pierre Fabre. J. Mackiewicz: Financial Interests, Personal, Invited Speaker: BMS, MSD, Roche, Novartis. B. Cybulska-Stopa, N. Kempa-Kaminska, M. Ziętek, A.M. Czarnecka: Financial Interests, Personal, Invited Speaker: BMS, MSD, Novartis, Pierre Fabre. P. Sobczuk: Financial Interests, Personal, Other, Travel grant: Novartis; Financial Interests, Personal, Other, Travel Grant: MSD, BMS; Financial Interests, Personal, Invited Speaker: Swixx BioPharma, BMS, Gilead; Financial Interests, Personal, Advisory Board: Sandoz; Financial Interests, Personal, Stocks/Shares: CelonPharma; Non-Financial Interests, Institutional, Product Samples: Immutep; Non-Financial Interests, Leadership Role, Board Member, Chair of Young Oncologists Section: Polish Society of Clinical Oncology. P. Rutkowski: Financial Interests, Personal, Invited Speaker, honoraria for lectures: MSD, BMS, Pierre Fabre; Financial Interests, Personal, Advisory Board: MSD, BMS, Pierre Fabre, Merck, Sanofi, Blueprint Medicines, Philogen; Financial Interests, Personal, Invited Speaker: Merck, Sanofi, Novartis, AstraZeneca; Financial Interests, Institutional, Research Grant, research grant for ISS: Pfizer; Financial Interests, Institutional, Funding, research grant for institution: BMS; Non-Financial Interests, Member of Board of Directors: Polish Society of Surgical Oncology; Non-Financial Interests, Member of Board of Directors, President: Polish Oncological Society. All other authors have declared no conflicts of interest.

https://doi.org/10.1016/j.annonc.2023.09.2239

1106P Anti-PD-1 (PD1) monotherapy or in combination with anti-CTLA-4 for metastatic melanoma (MM) patients (pts) with liver metastases (mets)

I. Pires da Silva[1], I. Li[2], S. Ugurel-Becker[3], P. Serra-Bellver[4], A. Andhale[4], H. Burnette[5], F. Aya[6], J. Conway[7], M. Carlino[8], A.M. Menzies[9], M. Weichenthal[10], P. Mohr[11], R. Gutzmer[12], A.M. Arance Fernandez[6], D. Johnson[13], P. Lorigan[14], D. Schadendorf[15], S. Lo[2], G.V. Long[9]

[1]Medical Oncology, Melanoma Institute Australia, Wollstonecraft, NSW, Australia; [2]Statistics, Melanoma Institute Australia, Wollstonecraft, NSW, Australia; [3]Dermatology, University Hospital Essen, University of Duisburg-Essen & German Cancer Consortium, Heidelberg, Germany; [4]Dept. of Medical Oncology, The Christie NHS Foundation Trust, Manchester, UK; [5]Medical Oncology Department, Vanderbilt University Medical Center, Nashville, TN, USA; [6]Medical Oncology Department, Hospital Clinic y Provincial de Barcelona, Barcelona, Spain; [7]Melanoma Medical Oncology and Translational Research, Melanoma Institute Australia, Wollstonecraft, NSW, Australia; [8]Medical Oncology Department, Crown Princess Mary Cancer Centre Westmead, Westmead, NSW, Australia; [9]Melanoma Medical Oncology and Translational Research, Melanoma Institute Australia, University of Sydney, Royal North Shore and Mater Hospitals, Wollstonecraft, NSW, Australia; [10]Dermatology Department, Christian-Albrechts-University Kiel, Kiel, Germany; [11]Dermato-Oncology Department, Dermatologic Center Buxtehude, Buxtehude, Germany; [12]Dermatology, Skin Cancer Center, Ruhr University Bochum Medizinische Universitätsklinik, Bochum, Germany; [13]Medical Oncology, Vanderbilt University Medical Center, Nashville, TN, USA; [14]Medical Oncology Dept., The Christie NHS Foundation Trust, Manchester, UK; [15]Department of Dermatology - Hautklinik, University Hospital Essen Westdeutsches Tumorzentrum, Essen, Germany

Background: Liver mets have been associated with poor response and survival in pts with MM treated with PD1 alone or in combination with anti-CTLA-4 (ipilimumab; PD1+IPI). Whether these pts benefit from PD1+IPI over PD1 is unknown. In MM pts with liver metastases, we sought to: a) determine objective response rate (ORR), progression-free survival (PFS) and overall survival (OS) to PD1 vs PD1+IPI, and b) identify clinical predictors of response and survival to PD1+/-IPI.

Methods: MM pts with liver mets treated with 1st line PD1 or PD1+IPI were included. Demographics, patient and disease characteristics, baseline blood parameters and clinical outcomes were examined. Univariate and multivariate (MVA) analyses were performed to identify clinical predictors of response and survival.

Results: Of 533 MM pts treated with 1st line PD1 or PD1+IPI; 284 (53%) had PD1 and 249 (47%) had PD1+IPI. PD1 group had more ECOG PS $\geq$1 (53% vs 34%), but less BRAF V600 mutation (15% vs 33%) and stage M1D (15% vs 31%). Median follow-up from commencement of PD1+/-IPI was 47 months (42—51); ORR was 41%, higher in PD1+IPI (47%) vs PD1 (35%) (p=0.0027). PFS and OS at 1 year were 68% and 40%, respectively; non statistically higher with PD1+IPI (69%/43%) vs PD1 (67%/38%) (p>0.05). However, on MVA with multiple imputation for missing values and adjusting for predefined variables including age, gender, melanoma subtype (cutaneous non-acral, acral and mucosal), mutation status, ECOG PS, LDH and M1 substage

(M1c versus M1d), PD1+IPI was associated with higher ORR (OR 2.21, 1.46 − 3.36; p<0.001), PFS (HR 0.73, 0.57 − 0.92; p=0.009) and OS (HR 0.71, 0.54 − 0.94; p=0.018) compared to PD1. Age (ORR, PFS), ECOG PS (OS), LDH (PFS, OS), M1 substage (ORR, PFS, OS), mutation status (PFS), melanoma subtype (OS) were also independent predictors of response and/or survival. Most pts ceased treatment due to progression (262 [53%]), and more pts stopped treatment due to toxicity in the PD1+IPI (n=77, 31%) vs PD1 (n=36, 14%) group.

Conclusions: In pts with liver metastases, 1st line PD1+IPI showed higher ORR and improved survival compared with PD1 alone. These data will help guide treatment selection for pts with melanoma liver metastases.

Legal entity responsible for the study: The authors.

Funding: Has not received any funding.

Disclosure: I. Pires da Silva: Financial Interests, Personal, Invited Speaker: BMS, MSD, Roche; Financial Interests, Personal, Other, Travel Support: BMS, Roche. S. Ugurel-Becker: Financial Interests, Personal, Research Funding: Bristol Myers Squibb, Merck Serono; Financial Interests, Personal, Speaker, Consultant, Advisor: Bristol Myers Squibb, Merck Sharp & Dohme, Merck Serono, Novartis; Financial Interests, Personal, Other, meeting and travel support: Almirall, Bristol Myers Squibb, IGEA Clinical Biophysics, Merck Sharp & Dohme, Novartis, Pierre Fabre, Sun Pharma. M. Carlino: Financial Interests, Personal, Advisory Board: Amgen, BMS, Eisai, IDEAYA, MSD, Nektar, Novartis, OncoSec, Pierre Fabre, QBiotics, Regeneron, Roche, Merck, Sanofi; Financial Interests, Personal, Invited Speaker: BMS, MSD, Novartis. A.M. Menzies: Financial Interests, Personal, Advisory Board, advisory board: BMS, MSD, Novartis, Roche, Pierre Fabre, QBiotics. M. Weichenthal: Financial Interests, Personal, Speaker, Consultant, Advisor: Merck Sharp & Dohme, Roche, Novartis, Bristol Myers Squibb, Sanofi; Financial Interests, Personal, Advisory Role: Sun Pharma, Pierre Fabre; Financial Interests, Institutional, Research Funding: Merck Sharp & Dohme, Millennium, Bristol Myers Squibb, Johnson & Johnson, Novartis. P. Mohr: Financial Interests, Personal, Speaker, Consultant, Advisor: Bristol Myers Squibb, Merck Sharp & Dohme, Roche/Genentech, Novartis, Amgen, Pierre Fabre, Merck, Sanofi; Financial Interests, Institutional, Research Funding: Merck Sharp & Dohme, Bristol Myers Squibb, Novartis; Financial Interests, Personal, Other, Travel, Accommodations, Expenses: Bristol Myers Squibb, Merck Sharp & Dohme, Novartis, Pierre Fabre, Amgen, Roche, Sun Pharma, Sanofi. R. Gutzmer: Financial Interests, Personal, Speaker, Consultant, Advisor: Bristol Myers Squibb, Merck Sharp & Dohme, Roche/Genentech, Novartis, Merck Serono, Almirall Hermal GmbH, Amgen, Sun Pharma, Pierre Fabre, Sanofi, Immunocore, 4SC; Financial Interests, Institutional, Research Funding: Pfizer, Novartis, Johnson & Johnson, Amgen, Merck Serono, Sun Pharma, Sanofi; Financial Interests, Personal, Other, Travel, Accommodations, Expenses: Bristol Myers Squibb, Roche, Merck Serono, Pierre Fabre, Sun Pharma. A.M. Arance Fernandez: Financial Interests, Personal, Advisory Board, Consultant /Advisory/Speaker/Travel, Accommodation, Expenses/: Pierre Fabre, Novartis, Roche, BMS, MSD, Merck, Sanofi; Financial Interests, Institutional, Other, Research Funding: Pierre Fabre, Novartis, MSD, BMS, Merck, Roche, Sanofi, Amgen. D. Johnson: Financial Interests, Personal, Advisory Board: BMS, Catalyst Biopharma, Iovance, Jansen, Mallinckrodt, Merck, Mosaic ImmunoEngineering, Novartis, OncoSec, Pfizer, Targovax, Teiko; Financial Interests, Personal, Funding: BMS, Incyte. P. Lorigan: Financial Interests, Personal, Speaker, Consultant, Advisor: Novartis, Pierre Fabre, BMS, MSD, Melagenix GmbH, Ultimovacs, MLA Diagnostics; Financial Interests, Personal, Research Funding: BMS, Pierre Fabre. D. Schadendorf: Financial Interests, Personal, Invited Speaker: BMS, Novartis, MSD, Roche, Merck Serono, Sanofi; Financial Interests, Personal, Advisory Board: BMS, Novartis, MSD, Immunocore, Pierre Fabre, Sanofi/Regeneron, Pfizer, Philogen, Neracare; Financial Interests, Personal, Steering Committee Member: Novartis, BMS, MSD; Financial Interests, Institutional, Coordinating PI: Novartis, BMS, MSD, Pierre Fabre; Financial Interests, Institutional, Research Grant: BMS, MSD; Financial Interests, Institutional, Local PI: Sanofi, Philogen; Non-Financial Interests, Member of Board of Directors: EORTC-MG. G.V. Long: Financial Interests, Personal, Speaker, Consultant, Advisor: Agenus, Amgen, Array Biopharma, Boehringer Ingelheim, BMS, Evaxion Biotech, Hexal AG, Highlight Therapeutics, Innovent Biologics, MSD, Novartis Pharma, OncoSec, PHMR, Pierre Fabre, Provectus, QBiotics, Regeneron. All other authors have declared no conflicts of interest.

https://doi.org/10.1016/j.annonc.2023.09.2240

1107P BRAF mutation status does not impact outcomes with tebentafusp in advanced cutaneous melanoma

A.N. Shoushtari[1], M.R. Middleton[2], O. Hamid[3], F. Meier[4], T. Bauer[5], A.K.S. Salama[6], J.M. Kirkwood[7], P.A. Ascierto[8], P. Lorigan[9], C. Mauch[10], M. Orloff[11], R. Edukulla[12], H. Goodall[13], J.C. Hassel[14], T.R.J. Evans[15]

[1]Medicine, MSKCC - Memorial Sloan Kettering Cancer Center, New York, NY, USA; [2]Oncology Department, Churchill Hospital, Oxford, UK; [3]Research Department, The Angeles Clinic and Research Institute - West Los Angeles, Los Angeles, CA, USA; [4]Skin Cancer Center, National Center for Tumor Diseases, Dept. of Dermatology, Universitaetsklinikum Carl Gustav Carus Dresden, Dresden, Germany; [5]Oncology, Tennessee Oncology, Chattanooga, USA; [6]Medicine, Duke University, Durham, NC, USA; [7]Melanoma Program, UPMC Hillman Cancer Center, Pittsburgh, PA, USA; [8]Melanoma, Cancer Immunotherapy & Developmental Therapeutics, Istituto Nazionale Tumori - IRCCS - Fondazione Pascale, Naples, Italy; [9]Medical Oncology Dept., The Christie NHS Foundation Trust, Manchester, UK; [10]Oncology, University Hospital Cologne, Cologne, Germany; [11]Medical Oncology, Thomas Jefferson Univ Hospital, Philadelphia, PA, USA; [12]Biometrics, Immunocore LLC, Conshohocken, PA, USA; [13]Medical Affairs Department, Immunocore Ltd., Abingdon-on-Thames, UK; [14]Section of DermatoOncology, NCT - Nationales Zentrum für Tumorerkrankungen, Heidelberg, Germany; [15]Institute of Cancer Sciences, University of Glasgow, Glasgow, UK

Background: Tebentafusp (tebe), a bispecific (gp100 x CD3) ImmTAC, targets gp100 peptide-HLA-A*02:01 complexes overexpressed in melanoma. In a phase (Ph) 1b study (NCT02535078), pts with metastatic cutaneous melanoma (mCM) who relapsed or were refractory to prior anti-PD(L)1 and received tebe combined with durvalumab (durva) with or without tremelimumab (treme) (n=58), had a 1-year (yr) OS of 75%, comparing favorably with recent benchmarks (38%-57%) [1-3]. Nearly half of pts with mCM harbor activating BRAF mutations and sequencing of BRAF inhibitor regimens (BRAFi) with immunotherapies may be important [4]. Here we present tebe efficacy and safety in pts with mCM by BRAF mutation status.

Methods: In the Ph 1b study, HLA-A*02:01+, pre-treated mCM pts received weekly tebe (IV) monotherapy in arm 4 or in combination with durva and/or treme (IV) Q4W (arms 1-3). Primary objective was RP2D. Secondary objectives were safety and efficacy. OS was obtained using Kaplan-Meier methods. Tumor assessments were performed according to RECIST v1.1. This analysis was performed on all pts in arms 1-4 with data cut-off Oct 7 2022 and median follow up of 14.8 months.

Results: 38/112 (34%) pts had an activating V600 BRAF mutation (BRAFm); of whom, 24 (63%) had received a prior BRAFi regimen. Baseline parameters (e.g., ECOG, LDH, anti-PD(L)1 exposure) were similar between the BRAFm and BRAF wild type (BRAFwt) pts. OS and tumor shrinkage were similar in BRAFm and BRAFwt pts with 1-yr OS of 68% and 62% and tumour shrinkage in 42% and 38% of pts, respectively. The safety profile of tebe was similar in BRAFm and BRAFwt pts. Among BRAFm pts, OS trended longer in those who did not receive prior BRAFi versus those who did (1-yr OS 84% vs 59%).

Conclusions: In this study, promising OS was seen in pretreated mCM pts with or without BRAFm, although OS trended longer in BRAFm pts who had not received prior BRAFi compared with those who did. An ongoing trial (NCT05549297) is investigating tebe as monotherapy and in combination with pembrolizumab in pts with previously treated advanced melanoma including both BRAFwt and BRAFm. 1. Zimmer L, et al. Eur J Cancer 75:47−55, 2017 2. Silva IPD, et al. J Clin Oncol 38:10005−10005, 2020 3. Arance AM et al. J Clin Oncol 39:S9504, 2021 4. Atkins MB, et al. J Clin Oncol 41(2):186-197, 2023.

Clinical trial identification: NCT02535078.

Legal entity responsible for the study: Immunocore Ltd.

Funding: Immunocore Ltd.

Disclosure: A.N. Shoushtari: Financial Interests, Personal, Advisory Board: Bristol Myers Squibb, Immunocore, Novartis; Financial Interests, Personal, Royalties: UpToDate; Financial Interests, Institutional, Invited Speaker: Bristol Myers Squibb, Immunocore, Polaris, Xcovery, Pfizer, Novartis, Targovax ASA, Checkmate Pharmaceuticals, Linnaeus Therapeutics, Prelude Therapeutics; Financial Interests, Personal, Invited Speaker: Foghorn Therapeutics; Non-Financial Interests, Member: ASCO. M.R. Middleton: Financial Interests, Personal, Speaker, Consultant, Advisor: Bristol Myers Squibb, Immunocore, BioLineRx, Boehringer Ingelheim, Alkermes, Bayer; Financial Interests, Institutional, Research Funding: Immunocore, Novartis, AstraZeneca, Roche, Amgen, Bristol Myers Squibb, Merck, Pfizer, Replimune, Regeneron, GRAIL, BioLineRx, SalvaRx, Vaccitech, GRAIL; Non-Financial Interests, Personal, Other: GenesisCare. O. Hamid: Financial Interests, Personal, Advisory Board: Alkermes, Amgen, BMS, Bactonix, Beigene, Bioatla, Eisai, GSK, Georgiamune, GigaGen, Grit Bio, IO Biotech, Idera, Idera, Immunocore, Incyte, Instil Bio, Iovance, Janssen, KSQ, Merck, Nextcure, Novartis, Obsidian, Pfizer, Roche Genentech, Seagen, Sanofi/Regeneron, Tempus, Vial, Zelluna; Financial Interests, Personal, Invited Speaker: BMS, Immunocore, Novartis, Pfizer, Sanofi/Regeneron; Financial Interests, Personal, Stocks/Shares: Bactonix; Financial Interests, Institutional, Invited Speaker: Aduro, Akeso, Amgen, Arcus, BMS, Bioatla, CytomX, Exelixis, GSK, Idera, Immunocore, Incyte, Iovance, Merck, Merck Serono, Moderna, Nextcure, Novartis, Pfizer, Roche Genentech, Rubius, Seagen, Sanofi/Regeneron, Torque, Zelluna. F. Meier: Financial Interests, Personal, Speaker, Consultant, Advisor: Roche, Bristol Myers Squibb, Novartis, MSD, Amgen, Merck, Sanofi, Pierre Fabre; Financial Interests, Personal, Other, Travel, Accommodations, Expenses: Novartis, Roche, Bristol Myers Squibb, MSD, Amgen, Merck, Sanofi, Pierre Fabre; Financial Interests, Personal, Other, Honoraria: Roche, Bristol Myers Squibb, Novartis, MSD, Amgen, Merck, Sanofi; Financial Interests, Institutional, Research Funding: Novartis, Roche. T. Bauer: Financial Interests, Personal, Full or part-time Employment: Tennessee Oncology; Financial Interests, Personal, Speaker, Consultant, Advisor: Pfizer, Bayer, Lilly, Sanofi; Financial Interests, Personal, Speaker's Bureau: Bayer, Lilly; Financial Interests, Personal, Other, Travel, Accommodations, Expenses: Pfizer; Financial Interests, Institutional, Research Funding: Daiichi Sankyo, Incyte, Mirati Therapeutics, MedImmune, AbbVie, AstraZeneca, MabVax, Merck, Lilly, GSK, Novartis, Pfizer, Genentech/Roche, Immunogen, Immunocore, Roche, Bristol Myers Squibb, Amgen, Moderna Therapeutics, Sanofi, Boehringer Ingelheim, Astellas Pharma, Top Alliance BioScience, Loxo, Janssen, Takeda, Onyx, Foundation Medicine. A.K.S. Salama: Financial Interests, Personal, Advisory Board: Bristol Myers Squibb, Iovance, Regeneron, Replimune, Novartis, Pfizer; Financial Interests, Institutional, Local PI: Bristol Myers Squibb, Ascentage, IDEAYA, Immunocore, Merck, Regeneron, Replimune, Seagen; Financial Interests, Institutional, Trial Chair: Olatec. J.M. Kirkwood: Financial Interests, Personal, Speaker, Consultant, Advisor: Novartis, Amgen, Harbour BioMed, ISTARI Oncology, Scopus BioPharma, Pfizer, AXIO Research, Immunocore, Natera, DermTech, Ankyra Therapeutics, Becker Pharmaceutical Consulting, Fenix Group International, IQVIA, Merck, Replimune, SR One Capital Management, Iovance Biotherapeutics, Checkmate Pharmaceuticals, OncoSec, OncoCyte, Cancer Network, Takeda, Applied Clinical Intelligence, PathAI, Magnolia Innovation, iOnctura, Jazz Pharmaceuticals, Regeneron; Financial Interests, Personal, Other, Travel, Accommodations, Expenses: Checkmate Pharmaceuticals, Bristol Myers Squibb, Regeneron, Ankyra Therapeutics, Iovance Biotherapeutics; Financial Interests, Personal, Other, Honoraria: Bristol Myers Squibb; Financial Interests, Institutional, Research Funding: Amgen, Bristol Myers Squibb, Checkmate Pharmaceuticals, Immunocore, Iovance Biotherapeutics, Novartis, Immvira, Harbour BioMed, Takeda, Verastem, Lion Biotechnologies. P.A. Ascierto: Financial Interests, Personal, Other, Consultant and Advisory Role: BMS, Roche Genentech, MSD, Novartis, Merck Serono, Pierre Fabre, AstraZeneca, Sun Pharma, Sanofi, Idera, Sandoz, Immunocore, 4SC, Nektar, Boehringer Ingelheim, Regeneron; Financial Interests, Personal, Other, Consultant and Advisory Role, Travel support: Pfizer/Array; Financial Interests, Personal, Other, Consultant Role: Italfarmaco; Financial Interests, Personal, Other, Advisory Role: Eisai, Seagen; Financial Interests, Personal, Other, Consultant Role: Daiichi Sankyo, Pfizer, OncoSec, Nouscom, Lunaphore; Financial Interests, Personal, Other, Consultant role and travel support: Bio-AI Health; Financial Interests, Personal, Other, Consultant role: Medicenna; Financial Interests, Personal, Advisory Board, Consultant and Advisory Role: iTeos; Financial Interests, Personal, Advisory Board, Consultant and Advisory role: ValoTx; Financial Interests, Personal, Advisory Board, Consultant and Advisor role. Travel support: Replimune; Financial Interests, Personal, Advisory Board, Advisor role: Bayer; Financial Interests, Institutional, Funding, Clinical Trial: Pfizer/Array, Roche Genentech, Sanofi; Financial Interests, Personal, Advisory Board: Erasca; Financial Interests, Institutional, Funding, Clinical trial and translational research: BMS; Non-Financial Interests, Leadership Role, President since 2010: Fondazione Melanoma Onlus Italy; Non-Financial Interests, Leadership Role, President since 2014: Campania Society of ImmunoTherapy of Cancer (SCITO) Italy; Non-Financial Interests, Other, Member of Steering Committee since 2016: Society for Melanoma Research (SMR); Non-Financial Interests, Member of Board of Directors, November 2017 - December 2021: Society for Immunotherapy of Cancer (SITC); Non-Financial Interests, Member: ASCO, SITC, EORTC Melanoma Cooperative Group, SMR, AIOM. P. Lorigan: Financial Interests, Personal, Speaker, Consultant, Advisor: Merck Sharp & Dohme, Bristol Myers Squibb, Amgen, Pierre

Fabre, Novartis, Nektar; Financial Interests, Personal, Speaker's Bureau: Merck Sharp & Dohme, Novartis, Bristol Myers Squibb, Pierre Fabre; Financial Interests, Personal, Other, Travel, Accommodations, Expenses: Merck Sharp & Dohme, Bristol Myers Squibb; Financial Interests, Personal, Other, Honoraria: Novartis, Pierre Fabre, Merck, Bristol Myers Squibb, MSD, NeraCare GmbH, Amgen, Roche, Oncology Education, Nektar; Financial Interests, Institutional, Research Funding: Bristol Myers Squibb, Pierre Fabre. C. Mauch: Financial Interests, Personal, Other, Travel, Accommodations, Expenses: Bristol Myers Squibb, Sanofi; Financial Interests, Personal, Other, Honoraria: Bristol Myers Squibb, Sanofi, Roche. M. Orloff: Financial Interests, Personal, Speaker's Bureau: Bristol Myers Squibb; Financial Interests, Personal, Speaker, Consultant, Advisor: IDEAYA Biosciences, Immunocore, Trisalus Life Sciences, Delcath Systems; Financial Interests, Institutional, Research Funding: Bristol Myers Squibb, Immunocore, Delcath Systems, Plexxikon, IDEAYA Biosciences, Linnaeus Therapeutics, IDEAYA Biosciences. R. Edukulla, H. Goodall: Financial Interests, Personal, Full or part-time Employment: Immunocore; Financial Interests, Personal, Stocks/Shares: Immunocore. J.C. Hassel: Financial Interests, Personal, Invited Speaker: BMS, Novartis, Sanofi, MSD, Sun Pharma, Amgen, GSK, Pierre Fabre, Immunocore; Financial Interests, Personal, Advisory Board: MSD, Pierre Fabre, Sun Pharma, GSK, Onkowissen; Financial Interests, Institutional, Advisory Board: Novartis, BMS, Immunocore, Philogen, Sanofi; Financial Interests, Institutional, Research Grant: BMS, Sun Pharma; Financial Interests, Institutional, Local PI: Philogen, Genentech, 4SC, BioNTech, Idera, Iovance, Nektar, Pierre Fabre, Regeneron, Sanofi, Replimune; Financial Interests, Institutional, Coordinating PI: BMS, Immunocore, Novartis, Genmab; Financial Interests, Personal, Steering Committee Member: Immunocore, IO Biotech; Non-Financial Interests, Leadership Role: DeCOG; Non-Financial Interests, Member: ASCO. T.R.J. Evans: Financial Interests, Institutional, Advisory Board, Advisory Board for GI Cancers and Melanoma (Immune Checkpoint Inhibitors): Bristol Myers Squibb; Financial Interests, Institutional, Invited Speaker, Invited speaker - GI Cancers, Melanoma, Immunotherapy: Bristol Myers Squibb; Financial Interests, Institutional, Advisory Board, Advisory Boards - GI cancers, melanoma: Roche/Genentech; Financial Interests, Institutional, Invited Speaker, Invited speaker GI cancer, melanoma: Roche/Genentech; Financial Interests, Institutional, Advisory Board, Advisory Board (lenvatinib): Eisai; Financial Interests, Institutional, Invited Speaker, Speaker's fees (lenvatinib): Eisai; Financial Interests, Institutional, Advisory Board, advisory board: MSD, AstraZeneca, Bayer, Bicycle Therapeutics, Clovis; Financial Interests, Institutional, Invited Speaker, Speaker's fees: MSD, AstraZeneca, Bayer; Financial Interests, Institutional, Advisory Board, Advisory board: Nucana; Financial Interests, Institutional, Invited Speaker, speaker's fees: Nucana; Financial Interests, Institutional, Advisory Board, advisory board; Chair of Scientific Advisory Council (HCC & MIV-818): Medivir; Financial Interests, Institutional, Invited Speaker, speaker's fees (and presentation to potential investors): Medivir; Financial Interests, Personal, Other, Support to attend international conferences: Bristol Myers Squibb, Roche/Genentech, MSD, Nucana, Bayer, Celgene, Pierre Fabre; Financial Interests, Institutional, Advisory Board, Advisory Board for Upper GI Cancer: Ascelia; Financial Interests, Institutional, Advisory Board, Advisory Board for Oesophageal Cancer: Seagen; Financial Interests, Institutional, Coordinating PI, Educational grant (supply of study agents) for investigator-led study and reimbursement of study costs for commercial studies: AstraZeneca; Financial Interests, Institutional, Local PI, reimbursement of study costs for commercial studies: Astellas, Bayer, Basilea, Celgene, GSK, Roche, Immunocore, Medivir, Starpharma, Novartis, Sapience Therapeutics, MiNa Therapeutics, Lilly, Bicycle Therapeutics, Sierra, CytomX, Beigene, Pfizer, Johnson & Johnson, UCB, Codiak, Avacta, Nurix, T3P; Financial Interests, Institutional, Coordinating PI, reimbursement of study costs for commercial studies: Adaptimmune, Bristol Myers Squibb, Eisai, MSD, Nucana, Sanofi, iOnctura; Financial Interests, Institutional, Local PI, support for non-commercial investigator-led study: Verastem; Financial Interests, Institutional, Local PI, reimbursement for costs of commercial studies: Boehringer Ingelheim; Financial Interests, Institutional, Local PI, reimbursement of costs of commercial study: Seagen; Non-Financial Interests, Member, Cancer Society Member: American Society of Clinical Oncology, America Association for Cancer Research, British Association for Cancer Research, Association of Cancer Physicians (UK), European Association for Cancer Research, International Liver Cancer Association; Non-Financial Interests, Other, Member of Scientific Advisory Panel: Pancreatic Cancer Research Fund; Non-Financial Interests, Other, Annual Meeting abstracts committee: International Liver Cancer Association; Non-Financial Interests, Institutional, Product Samples, Supply of investigational and licensed compounds for a non-commercial study for which I'm Chief Investigator: AstraZeneca; Other, Editor-in-Chief: British Journal of Cancer; Other, Chair of Independent Data Monitoring Committee for a phase I trial - honorarium payable to the employing institution: Genmab; Other, Chair and panel member, Scientific Evaluation Committee: Early phase trials (Amgen, Merck, AstraZeneca): Institut National du Cancer (France).

https://doi.org/10.1016/j.annonc.2023.09.2241

1108P Outcomes of patients with unresectable or metastatic melanoma after cessation of immunotherapy following complete response or toxicities

N.S. Zulkifli, L. Tam, A. Mclean, V.G. Atkinson

Medical Oncology Department, Princess Alexandra Hospital - Metro South Health, Woolloongabba, QLD, Australia

Background: Checkpoint inhibitors (CPI) have changed the treatment paradigm for patients (pts) with advanced melanoma with significant improvements in overall survival. This study evaluated the outcomes of patients with advanced melanoma who were treated with CPI and had cessation of treatment due to either complete response (CR) or toxicities (tox).

Methods: From January 2015 to December 2021, 699 pts with unresectable stage III or stage IV melanoma were treated by a single prescriber across two centres in Brisbane, Queensland. In this retrospective study, we analysed 237 pts who had ceased CPI either due to CR, defined trial protocol or tox. We performed descriptive analyses of outcomes following cessation of CPI and subsequent treatment received after documented disease recurrence.

Results: Of the 237 pts who had ceased CPI, 176 pts had CR, 53 pts had treatment related tox and 8 pts had completed trial protocol. The average age of pts treated with CPI was 63 years old and the mean duration of treatment was 448 days. In this study, 71.3% of pts were BRAF wild-type, 27.4% of pts had a BRAF mutation and 1.3% of pts with uveal melanoma. 59.5% of pts had monotherapy CPI while 40.5% of pts had combination CPI. 182 pts (76.8%) had ongoing CR whilst 55 pts (23.2%) relapsed following cessation of therapy. In the cohort that relapsed, 36 pts had stopped CPI due to CR or defined trial protocol and 19 pts stopped following treatment related tox. The relapse rate was higher in pts stopped CPI due to tox (35.8%) compared to the cohort of pts who ceased due to CR or defined trial protocol (19.6%). Of those 55 pts who had relapsed, 22 were rechallenged with response, 12 were rechallenged with no response, 2 were rechallenged but ceased due to tox, 1 was rechallenged and is awaiting restaging, 7 had local therapy with either radiation therapy or surgery, 3 had different systemic therapy. 8 pts received best supportive cares.

Conclusions: Patients who had ceased CPI following CR had durable responses and a lower rate of relapse compared to pts with treatment related tox. On recurrence, retreatment with immunotherapy demonstrated response and could be considered a viable treatment option.

Legal entity responsible for the study: The authors.

Funding: Has not received any funding.

Disclosure: V.G. Atkinson: Financial Interests, Personal, Advisory Board: BMS, MSD, Nektar, Novartis, Pierre Fabre, QBiotics; Financial Interests, Personal, Invited Speaker: BMS, MSD, Novartis, Pierre Fabre, Limbic; Financial Interests, Personal, Other, Travel Support: BMS. All other authors have declared no conflicts of interest.

https://doi.org/10.1016/j.annonc.2023.09.2242

1109P Second-line pembrolizumab (pembro) in Chinese patients (pts) with advanced melanoma: Long-term follow-up of the phase I KEYNOTE-151 study

L. Si[1], X. Zhang[2], Y. Shu[3], H. Pan[4], D. Wu[5], J. Liu[6], L. Mao[1], X. Wang[1], X. Wen[7], Y. Gu[8], L. Zhu[9], S. Lan[10], X. Cai[11], S. Diede[12], S.S. Chen[13], H. Hu[14], J. Guo[1]

[1]Melanoma and Sarcoma, Key Laboratory of Carcinogenesis and Translational Research, Ministry of Education/Beijing, Peking University Cancer Hospital and Institute, Beijing, China; [2]State Key Laboratory of Oncology in South China, Sun Yat-sen University Cancer Centre, Guangzhou, China; [3]Oncology, The First Affiliated Hospital of Nanjing Medical University, Nanjing, China; [4]Medical Oncology, Sir Run Run Shaw Hospital School of Medicine Zhejiang University, Hangzhou, China; [5]Oncology, The First Hospital of Jilin University, Changchun, Jilin, China; [6]Oncology Department, The First Affiliated Hospital of Dalian Medical University, Dalian, China; [7]Melanoma and Sarcoma Unit, Sun Yat-sen University Cancer Center, Guangzhou, China; [8]Medical Oncology, Jiangsu Province Hospital, Nanjing, China; [9]Oncology, Jiangsu Province Hospital, Nanjing, China; [10]Medical Oncology, The First Hospital of Jilin University, Changchun, China; [11]Oncology, The First Affiliated Hospital of Dalian Medical University, Dalian, China; [12]Medical Oncology, Merck & Co., Inc., Rahway, NJ, USA; [13]Clinical Research, MSD (China) Co., Ltd., Shanghai, China; [14]Biostatistics and Research Decision Science (BARDS), MSD (China) Co., Ltd., Beijing, China

Background: At the 3-y follow-up of KEYNOTE-151 (NCT02821000), second-line pembro showed manageable safety and clinically meaningful antitumor activity in Chinese pts with advanced melanoma. Results from more than 5 y of follow-up are presented.

Methods: Adults who had histologically confirmed locally advanced or metastatic melanoma, who were of Chinese descent, and whose disease progressed with first-line therapy received pembro 2 mg/kg IV Q3W for ≤35 cycles (~2 y) or until disease progression or unacceptable toxicity. Pts with SD or better who discontinued pembro could receive a second course of pembro (≤17 cycles) upon disease progression. Primary end points were safety and tolerability and ORR per RECIST v1.1 by blinded independent central review (BICR). Secondary end points were DOR and PFS per RECIST v1.1 and irRECIST by BICR, ORR per irRECIST by BICR, and OS. Safety and OS were analyzed in pts who received ≥1 dose of pembro. Other efficacy end points were assessed in pts who received ≥1 dose of pembro and had measurable disease per RECIST v1.1 at baseline.

Results: One hundred three pts received pembro (102 with measurable disease at baseline). Median age was 52 y, 57.3% of the pts were female, 51.5% had PD-L1 positive disease, and 14.6% had mucosal melanoma. Median follow-up at data cutoff (Nov 30, 2022) was 73.2 mo (IQR, 67.6-74.8). No new safety signals were reported. Grade 3-5 treatment-related AEs occurred in 12.6% of pts; no pts died of treatment-related AEs. ORR per RECIST v1.1 was 17.6% (95% CI, 10.8-26.4; 1 CR, 17 PR); DCR was 38.2% (95% CI, 28.8-48.4). Median DOR per RECIST v1.1 was 13.8 mo (range, 2.7-69.4+); an estimated 37.7% of pts had DOR ≥60 mo. Median PFS was 2.8 mo (95% CI, 2.7-3.5); 60-mo PFS was 5.0%. One additional pt had PR per irRECIST (ORR, 18.6%; 95% CI, 11.6-27.6). Median OS was 13.2 mo (95% CI, 10.4-16.5); 60-mo OS was 13.4%. One pt with PR as the best overall response per RECIST v1.1 received second-course pembro.

Conclusions: After more than 5 y of follow-up, second-line pembro continued to show manageable safety and clinically meaningful antitumor activity in Chinese pts with advanced melanoma. These results support the continued use of pembro in this population.

Clinical trial identification: NCT02821000.

Editorial acknowledgement: Medical writing and/or editorial assistance was provided by Jemimah Walker, PhD, and Rob Steger, PhD, of ApotheCom (Yardley, PA, USA).

Legal entity responsible for the study: Merck Sharp & Dohme LLC, a subsidiary of Merck & Co., Inc., Rahway, NJ, USA.

Funding: Merck Sharp & Dohme LLC, a subsidiary of Merck & Co., Inc., Rahway, NJ, USA.

Disclosure: L. Si: Financial Interests, Personal, Invited Speaker: MSD, Novartis, Oriengene, Roche, Shanghai Junshi Biosciences; Financial Interests, Personal, Advisory Board: MSD, Novartis, Shanghai Junshi Biosciences. S. Diede: Financial Interests, Personal, Full or part-time Employment: Merck. S.S. Chen, H. Hu: Financial Interests, Personal, Full or part-time Employment: MSD. J. Guo: Financial Interests, Personal, Advisory Board: MSD, Roche, Pfizer, Bayer, Novartis, Simcere, Shanghai Junshi Biosciences, Oriengene. All other authors have declared no conflicts of interest.

https://doi.org/10.1016/j.annonc.2023.09.2243

1110P A phase II clinical trial of SHR-1701 combined with temozolomide for advanced melanoma

T. Hu[1], Y. Xu[1], W. Sun[1], S. Wang[2], W. Yan[1], C. Wang[1], H. Li[3], Y. Chen[1]

[1]Department of Musculoskeletal Oncology, Fudan University Shanghai Cancer Center, Shanghai, China; [2]Department of Radiology, Fudan University Shanghai Cancer Center, Shanghai, China; [3]Department of Clinical Research & Development, Jiangsu Hengrui Pharmaceutical Co., Ltd., Shanghai, China

Background: Immune checkpoint inhibitors (ICIs) have limited efficacy in advanced melanoma in Asians, and chemotherapy is still an important option. Temozolomide (TMZ) has been recommended in guidelines for treatment of melanoma. SHR-1701 is a bifunctional fusion protein composed of a mAb against PD-L1 fused to the extracellular domain of TGF-β receptor II. Here, we report the safety and efficacy of SHR-1701 combined with TMZ in advanced melanoma.

Methods: In this single-center, phase II study, patients(pts) with advanced melanoma were eligible. Prior ICIs plus TMZ and progressed within 6 months was not permitted. Pts received SHR-1701(30 mg/kg IV Q3W) combined with TMZ (150 mg/m^2 IV, Days 1-5 Q3W) until disease progression or unacceptable toxicity. The primary endpoint was objective response rate (ORR) per RECIST1.1. Secondary endpoints included progression free survival (PFS), disease control rate (DCR), overall survival (OS), and safety. A standard Simon two-stage design was used. If there were more than 5 responses in 21 pts in stage I, the study would continue to 31 pts in stage II.

Results: As of March 31, 2023, 21 pts were enrolled. Various histology subtypes were included (16 acral, 2 mucosal, 2 cutaneous, 1 unknown histology subtype). The median age was 54 years (range, 34-73), most patients were male (52.4%), 18 pts (85.7%) were ECOG PS 1, 15 pts (71.4%) were stage IV. Received previous 0/1/2 lines of systemic treatment were 14(66.7%)/4(19.0%)/3(14.3%) pts. The median follow-up was 4.4 months (range, 0.5 to 12.7 months). At the data cutoff, 12 pts remained on treatment. Of 16 evaluable pts, 7 pts had partial response, and 6 pts had stable disease. The unconfirmed ORR and DCR were 43.8% and 81.3%, respectively. After treatment, 3 pts with solitarily metastatic lesions received curative surgery. Of 21 pts, the incidence of treatment-related adverse events (TRAEs) was 47.6%, most commonly anemia, γ-glutamyltransferase increase and rash (14.3% each). The incidence of grade 3 TRAEs was 14.3%. No grade $\geq$ 4 TRAEs occurred.

Conclusions: SHR-1701 plus TMZ showed promising antitumor activity in advanced melanoma pts, and was generally well tolerated.

Clinical trial identification: NCT05106023; released in November 3, 2021.

Legal entity responsible for the study: The authors.

Funding: Has not received any funding.

Disclosure: All authors have declared no conflicts of interest.

https://doi.org/10.1016/j.annonc.2023.09.2244

1111P A randomised phase II study of intermittent versus continuous dosing of targeted therapy in patients with BRAFV600 mutant advanced melanoma (INTERIM)

A. Gupta[1], R.N. Matin[2], A. Dayimu[3], J. Nobes[4], R.E. Board[5], M. Payne[6], A.R. Rao[7], A. Fusi[8], S. Danson[9], B.K. Eccles[10], J. Carser[11], C. O'Hanlon Brown[12], N. Steven[13], G.J. Burghel[14], L. Demain[15], E.C. Baker[15], J. Wulff[16], S. Twelves[16], M.R. Middleton[17], P.G. Corrie[18]

[1]Department of Medical Oncology, The Christie NHS Foundation Trust, Manchester, UK; [2]Churchill Hospital, Old Road, Headington, Oxford University Hospitals NHS Foundation Trust - Churchill Hospital, Oxford, UK; [3]Department of Oncology, CRUK - Cancer Research UK Cambridge Institute - University of Cambridge, Cambridge, UK; [4]Oncology, Norfolk and Norwich University Hospital NHS Foundation Trust, Norwich, UK; [5]Medical Oncology, Royal Preston Hospital, Preston, Lancashire, UK; [6]Oncology and Haematology, Oxford University Hospitals NHS Foundation Trust - Churchill Hospital, Oxford, UK; [7]Oncology Department, Nottingham City Hospital, Nottingham, UK; [8]Medical Oncology, St George's University of London, London, UK; [9]Oncology and Metabolism Department, Weston Park Hospital - Sheffield Teaching Hospitals NHS Foundation Trust, Sheffield, UK; [10]Oncology Department, University Hospitals Dorset, Poole, UK; [11]Oncology Department, Northern Ireland Cancer Centre - Belfast Health & Social Care Trust, Belfast, UK; [12]Oncology Department, St James's Hospital, Dublin, Ireland; [13]Cancer Centre, Queen Elizabeth Hospital - University Hospitals Birmingham NHS Foundation Trust, Birmingham, UK; [14]North West Genomic Laboratory Hyb, GLH - The North West Genomic Laboratory Hub, Manchester, UK; [15]North West Genomic Laboratory Hub, Manchester University NHS Foundation Trust, Manchester, UK; [16]CCTU Cancer Theme, Cambridge University Hospitals NHS Foundation Trust, Cambridge, UK; [17]Department of Oncology, University of Oxford, Oxford, UK; [18]Oncology Department, Cambridge University Hospitals NHS Foundation Trust, Cambridge, UK

Background: BRAF+MEK inhibitors extend life expectancy of BRAF V^{600} mutant advanced melanoma patients; acquired resistance limits duration of benefit. Preclinical and case studies suggested that intermittent dosing could enable patients to remain on treatment longer, delay onset of disease progression and offer improved quality of life (QoL). INTERIM was a UK randomised multicentre phase II trial testing an intermittent dosing regimen.

Methods: Patients with BRAFV^{600} mutant advanced melanoma with ECOG PS 0-1 due to start dabrafenib+trametinib were randomised to receive dabrafenib (150mg bid) and trametinib (2mg od) either continuously (CONT) or intermittently (INT; dabrafenib d1-22+trametinib d1−15) on a 28 day cycle. Prior immunotherapy and brain involvement was allowed. Patient recruitment, treatment compliance, QoL and progression-free survival (PFS) were evaluated for the primary endpoint. Secondary endpoints included response rate (ORR), overall survival (OS) and toxicity. The prognostic and predictive value of mutant BRAFV^{600E} ctDNA was measured by droplet digital PCR (ddPCR), using mutant allele frequency of >1% as the detection threshold.

Results: 79 patients (39 INT, 40 CONT) were recruited from Dec '17−Feb '20; median age 67 years, 52% PS 1, 65% AJCC (7th ed) M1c, 29% had brain metastases and 46% had LDH > ULN. With median follow-up of 19 months, INT was inferior in all efficacy measures: median PFS 8.5 vs 10.7mo (HR 1.39, 95% CI 0.79−2.45, p = 0.255); median OS 18.1 mo vs not reached (HR 1.69, 95% CI 0.87−3.28, p = 0.121), ORR 57% vs 77%. INT patients experienced fewer treatment related AEs (76% vs 88%), but a higher proportion of grade >3 AEs (53% vs 42%). QoL at 6 months favoured CONT. 66 patients had baseline plasma collected for ctDNA analysis and 27 (41%) of these had detectable BRAFV^{600E} ctDNA. Detection prior to treatment correlated with worse OS (HR 2.55, 95%CI 1.25-5.21, p=0.01) and higher disease burden (LDH>ULN; p<0.001). A change to undetected during treatment did not significantly predict better OS.

Conclusions: The UK INTERIM study is consistent with other national studies suggesting that intermittent dosing does not improve efficacy of BRAF+MEKi.

Clinical trial identification: Protocol Number: INTERIM17; Final version and date: V4.0 01 August 2019 EudraCT Number: 2016-005228-27; ISRCTN Number: 18183156.

Legal entity responsible for the study: Cambridge University Hospitals NHS Foundation Trust.

Funding: National Institute for Health and Care Research & Cancer Research UK.

Disclosure: A. Gupta: Financial Interests, Personal, Invited Speaker: Bristol Myers Squibb; Financial Interests, Personal, Writing Engagement: Novartis; Financial Interests, Personal, Advisory Board: Amgen; Financial Interests, Institutional, Local PI: Alkermes, AstraZeneca, Merck, Novartis; Financial Interests, Institutional, Coordinating PI: Bristol Myers Squibb. R.E. Board: Non-Financial Interests, Advisory Role: Melanoma Focus. M. Payne: Financial Interests, Personal, Advisory Board, clinical advisor for advisory board: BMS; Financial Interests, Personal, Invited Speaker, Invited speaker: BMS; Non-Financial Interests, Other, Received funding towards conference fess and travel for ESMO 2022: Pierre Fabre. S. Danson: Financial Interests, Institutional, Full or part-time Employment, National Specialty Lead for Early Phase Cancer: NIHR; Financial Interests, Institutional, Other, Consultancy: Oxcia, Orion; Financial Interests, Institutional, Coordinating PI, Dante lead: NIHR; Financial Interests, Institutional, Coordinating PI, Fortitude pi: Amgen; Financial Interests, Institutional, Research Grant, Ecmc lead: Cancer research UK; Non-Financial Interests, Leadership Role, Lion steering group chair: NIHR; Non-Financial Interests, Leadership Role, Concorde steering group member: Cancer Research UK. J. Carser: Financial Interests, Personal, Invited Speaker, speaker fee: Merck. C. O'Hanlon Brown: Financial Interests, Personal, Advisory Board: Gilead, Daiichi Sankyo. G.J. Burghel: Financial Interests, Personal, Invited Speaker, I was compensated for educational presentations: AstraZeneca. S. Twelves: Financial Interests, Personal, Full or part-time Employment, Partner is employee of GSK; Financial Interests, Personal, Stocks/Shares, Partner owns GSK shares. M.R. Middleton: Financial Interests, Personal and Institutional, Research Grant: Roche, AstraZeneca, Immunocore, GRAIL; Financial Interests, Institutional, Research Funding, trials fees paid to institution: Novartis, Immunocore, BMS, Pfizer, Merck/MSD, Regeneron, BioLineRx, Replimune. P.G. Corrie: Financial Interests, Personal, Advisory Board: Merck Sharp & Dohme; Financial Interests, Personal, Invited Speaker: Bristol Myers

Squibb, Pierre Fabre; Financial Interests, Personal, Other, Consultancy: Microbiotica; Financial Interests, Institutional, Local PI: Bristol Myers Squibb, Novartis, Achilles, AstraZeneca, Array Pharmaceuticals, Merck Sharp & Dohme; Financial Interests, Institutional, Research Grant: Pierre Fabre. All other authors have declared no conflicts of interest.

https://doi.org/10.1016/j.annonc.2023.09.2245

1112P Five-year survival after intermittent targeted therapy and anti-PD1 in stage IV melanoma: An update of the IMPemBra trial

L. Hoeijmakers[1], E.A. Rozeman[1], M. Lopez-Yurda[2], L. Grijpink-Ongering[2], B. Heeres[3], B. van de Wiel[4], C. Flohil[4], A. Sari[5], S. Heijmink[3], D. Van Den Broek[6], A. Broeks[7], J.W. de Groot[8], M. Vollebergh[1], S. Wilgenhof[1], H.V. van Thienen[1], J.B.A.G. Haanen[1], C.U. Blank[1]

[1]Medical Oncology Department, NKI-AVL - Netherlands Cancer Institute/Antoni van Leeuwenhoek Hospital, Amsterdam, Netherlands; [2]Department of Biometrics, Netherlands Cancer Institute, Amsterdam, Netherlands; [3]Radiology, NKI-AVL - Netherlands Cancer Institute/Antoni van Leeuwenhoek Hospital, Amsterdam, Netherlands; [4]Pathology Department, NKI-AVL - Netherlands Cancer Institute/Antoni van Leeuwenhoek Hospital, Amsterdam, Netherlands; [5]Department of Biometrics, NKI-AVL - Netherlands Cancer Institute/Antoni van Leeuwenhoek Hospital, Amsterdam, Netherlands; [6]Laboratory Medicine, Netherlands Cancer Institute/Antoni van Leeuwenhoek Hospital (NKI-AVL), Amsterdam, Netherlands; [7]Core Facility Molecular Pathology & Biobanking, Netherlands Cancer Institute/Antoni van Leeuwenhoek Hospital (NKI-AVL), Amsterdam, Netherlands; [8]Oncology Center Department, Isala Ziekenhuis, Zwolle, Netherlands

Background: IMPemBra was the first trial testing intermittent, short-term, dabrafenib and trametinib (DT) plus pembrolizumab (PEM) in patients with stage IV melanoma, with the concept of inducing stronger immune infiltration in the tumor, translating in better long-term outcome. The adverse event (AE) rate of intermittent DT was lower than for continuous triple therapy. While addition of DT only slightly increased the best overall response from 75% to 88%, the 3-year progression free survival (PFS) and overall survival (OS) was higher for the DT+PEM cohorts as compared to PEM only (53% vs 25%, and 64% vs 33%, respectively), no statistically significant differences were found probably due to small patient cohorts. Here we present the updated 5-year PFS and OS data from patients enrolled in the IMPemBra trial.

Methods: 32 treatment-naïve patients with stage IV melanoma harboring a BRAFV600E/K mutated melanoma were enrolled. All patients started with 2 cycles of PEM 200mg (Q3W), followed by randomization to either PEM monotherapy (cohort 1); PEM in combination with either dabrafenib (D) 150 mg BID + trametinib (T) 2mg QD intermittent for 2x1 week (cohort 2), 2x2 weeks (cohort 3) or continuously for 6 weeks (cohort 4). From week 12 and onwards, all cohorts continued PEM for a maximum of in total 2 years.

Results: With a median follow-up of 59.6 months, the estimated 5-year RFS and OS rates were 25% and 50% in cohort 1, 63% and 63% in cohort 2, 38% and 75% in cohort 3, and 60% and 75% in cohort 4, respectively, as shown in the table. We observed no differences in the quantity and type of subsequential therapies between the cohorts. No new safety signals were identified.

Table: 1112P

5-year clinical outcomes

	5-year PFS (95% CI)	5-year OS (95% CI)
All patients (n=32)	46% (32.5-67.3)	66% (51.1-84.3)
Cohort 1 (n=8)	25% (7.5-83.0)	50% (25.0-100)
Cohort 2 (n=8)	63% (36.5-100.0)	63% (36.5-100)
Cohort 3 (n=8)	38% (15.3-91.7)	75% (50.3-100)
Cohort 4 (n=8)	60% (33.1-100)	75% (50.3-100)

Subsequential therapies

	Subsequential treatment	Anti-PD1	Anti-CTLA-4	Anti-CTLA-4 + anti-PD1	Targeted therapy	Surgery	Other
All patients	**18 (56%)**	6 (33%)	2 (11%)	7 (39%)	14 (78%)	2 (11%)	1 (6%)
Cohort 1	**6 (75%)**	1 (13%)	1 (13%)	3 (38%)	5 (63%)		1 (13%)
Cohort 2	**3 (38%)**			2 (25%)	3 (38%)		
Cohort 3	**5 (63%)**	3 (38%)			3 (38%)	1 (13%)	
Cohort 4	**4 (50%)**	2 (25%)	1 (13%)	2 (25%)	3 (38%)	1 (13%)	

Conclusions: This update from the IMPemBra trial confirms the previous findings indicating that the addition of short-term DT to PEM can induce long-lasting responses upon PEM that appears to be superior compared to PEM monotherapy. This improved PFS translated also into a promising increase in 5-year OS compared to PEM in first line therapy.

Clinical trial identification: NCT02625337.

Legal entity responsible for the study: Netherlands Cancer Institute - Antoni van Leeuwenhoek Amsterdam.

Funding: MSD.

Disclosure: B. van de Wiel: Non-Financial Interests, Personal, Advisory Role: BMS. D. Van Den Broek: Financial Interests, Institutional, Advisory Role: Roche Diagnostics. S. Wilgenhof: Financial Interests, Institutional, Advisory Board: Eisai, Pfizer, Novartis, Pierre Fabre; Financial Interests, Institutional, Invited Speaker: Bristol Myers Squibb. J.B.A.G. Haanen: Financial Interests, Institutional, Advisory Board: Bristol Myers Squibb, Achilles Therapeutics, Ipsen, Merck Sharp & Dohme, Merck Serono, Pfizer, Molecular Partners, Novartis, Roche, Sanofi, Third Rock Venture, Iovance Biotherapeutics; Financial Interests, Institutional, Advisory Board, SAB member: BioNTech, Immunocore, Gadeta, Instil Bio, PokeAcel, T-Knife; Financial Interests, Personal, Advisory Board, SAB member: Neogene Therapeutics, Scenic; Financial Interests, Personal, Stocks/Shares: Neogene Therapeutics; Financial Interests, Institutional, Research Grant: Bristol Myers Squibb, BioNTech US, Merck Sharp & Dohme, Amgen, Novartis, Asher Bio; Non-Financial Interests, Member: ASCO, AACR, SITC; Other, Editorial Board ESMO Open: ESMO; Other, Editor-in-Chief IOTECH: ESMO; Other, Editorial Board: Kidney Cancer. C.U. Blank: Financial Interests, Institutional, Advisory Board: BMS, MSD, Roche, Novartis, GSK, AZ, Pfizer, Lilly, GenMab, Pierre Fabre; Financial Interests, Personal, Advisory Board: Third Rock Ventures; Financial Interests, Personal, Stocks/Shares: Immagene; Financial Interests, Personal, Stocks/Shares, intention to develop IFN signature algorithm: NewCo, no name yet; Financial Interests, Institutional, Coordinating PI: BMS, Novartis, NanoString, 4SC; Other, pending patent: WO 2021/177822 A1. All other authors have declared no conflicts of interest.

https://doi.org/10.1016/j.annonc.2023.09.2246

1113P COLUMBUS 7-year update: A randomized, open-label, phase III trial of encorafenib (enco) + binimetinib (bini) vs vemurafenib (vemu) or enco in patients (pts) with BRAF V600–mutant melanoma

D. Schadendorf[1], R. Dummer[2], K.T. Flaherty[3], C. Robert[4], A.M. Arance Fernandez[5], J.W. de Groot[6], C. Garbe[7], H. Gogas[8], R. Gutzmer[9], I. Krajsova[10], G. Liszkay[11], C. Loquai[12], M. Mandalà[13], N. Yamazaki[14], C.A. Guenzel[15], A. Polli[16], M. Thakur[17], A. di Pietro[18], P.A. Ascierto[19]

[1]Department of Dermatology - Hautklinik, University Hospital Essen Westdeutsches Tumorzentrum, Essen, Germany; [2]Dermatology Department, Universitätsspital Zürich - Klinik für Dermatologie, Zurich, Switzerland; [3]Oncology, MGH - Massachusetts General Hospital, Boston, MA, USA; [4]Dermatology Department, Institut Gustave Roussy, Villejuif, France; [5]Medical Oncology Department, Hospital Clinic y Provincial de Barcelona, Barcelona, Spain; [6]Oncology Center Department, Isala Ziekenhuis, Zwolle, Netherlands; [7]Dermatologische Onkologie, Universitaets-Hautklinik Tuebingen, Tuebingen, Germany; [8]First Department of Medicine, National and Kapodistrian University of Athens - School of Medicine, Athens, Greece; [9]Dermatology, Skin Cancer Center, Ruhr University Bochum Medizinische Universitätsklinik, Bochum, Germany; [10]First Faculty of Medicine, Charles University, Prague, Czech Republic; [11]Dermato-Oncology Dept., National Institute of Oncology, Budapest, Hungary; [12]Dermatology, Universitätsmedizin der Johannes Gutenberg-Universität Mainz, Mainz, Germany; [13]Medicine and Surgery Department, Università degli Studi di Perugia, Perugia, Italy; [14]Dermatologic Oncology Dept., National Cancer Center - Tsukiji Campus, Chuo-ku, Japan; [15]Oncology, Pfizer, Inc., New York, NY, USA; [16]Oncology Statistics Department, Pfizer Italy, Milan, Italy; [17]Pfizer Inc., New York, NY, USA; [18]GPD Immuno-Oncology Department, Pfizer Italia S.r.l., Milan, Italy; [19]Melanoma, Cancer Immunotherapy & Developmental Therapeutics, Istituto Nazionale Tumori - IRCCS - Fondazione Pascale, Naples, Italy

Background: In the randomized, 2-part, multicenter, open-label, phase III COLUMBUS study, enco + bini (approved in the US, EU, and other countries) and enco alone improved PFS and OS rates vs vemu in patients with BRAF V600–mutant metastatic melanoma. Here we report data from the 7-year analysis of COLUMBUS part 1.

Methods: Pts with advanced or metastatic BRAF V600–mutant melanoma were randomized 1:1:1 to enco 450 mg QD + bini 45 mg BID, vemu 960 mg BID, or enco 300 mg QD. Pts were treatment (tx)-naive or had progression after 1L immunotherapy. No prior BRAF/MEKi was allowed. Randomization was stratified by cancer stage (IIIB + IIIC + IVM1a + IVM1b vs IVM1c), ECOG PS (0 vs 1), and prior 1L immunotherapy (yes vs no).

Results: 577 pts were randomized to enco + bini (n=192), vemu (n=191), or enco alone (n=194). Updated analyses were conducted after >93 mo of minimum follow-up (cutoff: Jan 13, 2023). The 7-year PFS and OS rates (95% CI) were 21.2% (14.7, 28.4) and 27.4% (21.2, 33.9) in the enco + bini arm and 6.4% (2.1, 14.0) and 18.2% (12.8, 24.3) in the vemu arm, respectively. TEAEs (≥30% with enco + bini) were nausea, diarrhea, vomiting, arthralgia, and fatigue. Grade 3/4 TEAEs (≥5% with enco + bini) were γ-glutamyltransferase increased, blood CPK increased, hypertension, ALT increased, and anemia. Across arms, 16% to 20% of pts discontinued tx due to AEs. After tx discontinuation, 15% of pts from the enco + bini arm, 42% from the vemu arm, and 28% from the enco alone arm received BRAF/MEKi tx; 42% from the enco + bini arm, 49% from the vemu arm, and 43% from the enco alone arm received checkpoint inhibitors.

Conclusions: With a median duration of follow-up of 100 mo, the 7-year analysis from COLUMBUS part 1 confirms the long-term, sustained efficacy and known safety profile of enco + bini, with no new safety signals emerging, in pts with BRAF V600—mutant metastatic melanoma.

Table: 1113P

By BICR	Enco + bini (n = 192)	Vemu (n = 191)	Enco alone (n = 194)
mPFS, mo (95% CI)	14.9 (11.0, 20.2)	7.3 (5.6, 7.9)	9.6 (7.4, 14.8)
mOS, mo (95% CI)	33.6 (24.4, 39.2)	16.9 (14.0, 24.5)	23.5 (19.6, 33.6)
7-year PFS rate, % (95% CI)	21.2 (14.7, 28.4)	6.4 (2.1, 14.0)	15.8 (9.3, 23.8)
7-year OS rate, % (95% CI)	27.4 (21.2, 33.9)	18.2 (12.8, 24.3)	31.7 (24.9, 38.7)
Best overall response, n (%)			
CR	29 (15.1)	16 (8.4)	17 (8.8)
PR	94 (49.0)	62 (32.5)	83 (42.8)
SD[a]	54 (28.1)	77 (40.3)	63 (32.5)
PD[b]	15 (7.8)	36 (18.9)	31 (16.0)
ORR, % (95% CI)	64.1 (56.8, 70.8)	40.8 (33.8, 48.2)	51.5 (44.3, 58.8)
DCR, % (95% CI)	92.2 (87.4, 95.6)	81.2 (74.9, 86.4)	84.0 (78.1, 88.9)

[a]Includes non-CR/non-PD. [b]Includes best response of unknown or no assessment.

Clinical trial identification: NCT01909453 CMEK162B2301 C4221004 (Other Identifier: Alias Study Number) 2013-001176-38 (EudraCT Number) Last Update Posted: April 24, 2023.

Editorial acknowledgement: The authors would like to thank Joe Kleha of Pfizer for his contribution to the data analysis and interpretation. Medical writing support was provided by Asu Erden, PhD, of Health Interactions, Nucleus Global, and was funded by Pfizer.

Legal entity responsible for the study: The COLUMBUS study was sponsored by Array BioPharma, which was acquired by Pfizer in July 2019.

Funding: Pfizer, Inc.

Disclosure: D. Schadendorf: Financial Interests, Personal, Invited Speaker: BMS, Novartis, MSD, Roche, Merck Serono, Sanofi, Novartis, BMS, MSD; Financial Interests, Personal, Advisory Board: BMS, Novartis, MSD, Immunocore, Pierre Fabre, Sanofi/Regeneron, Pfizer, Philogen, Neracare; Financial Interests, Institutional, Invited Speaker: Novartis, BMS, MSD, Pierre Fabre, Sanofi, Philogen; Financial Interests, Institutional, Research Grant: BMS, MSD; Non-Financial Interests, Member of Board of Directors: EORTC-MG. R. Dummer: Financial Interests, Personal, Other, Consulting and/or advisory role: Novartis, Merck Sharp & Dohme (MSD), Bristol Myers Squibb (BMS), Roche, Amgen, Takeda, Pierre Fabre, Sun Pharma, Sanofi, CatalYm, Second Genome, Regeneron, Alligator, MaviVAX SA, touchIME, T3 Pharma, Pfizer, Simcere. K.T. Flaherty: Financial Interests, Personal, Other, Consultant: Takeda, Transcode Therapeutics, Novartis; Financial Interests, Personal, Member of Board of Directors: Clovis Oncology, Strata Oncology, Checkmate Pharmaceuticals, Kinnate BioPharma, Scorpion Therapeutics; Financial Interests, Personal, Stocks/Shares: Clovis Oncology, Strata Oncology, Checkmate Pharmaceuticals, Kinnate BioPharma, Scorpion Therapeutics, PIC Therapeutics, Apricity, Tvardi, xCures, Monopteros, Vibliome, ALX Oncology, Fog Pharma, Soley Therapeutics; Financial Interests, Personal, Ownership Interest: Nextech; Financial Interests, Institutional, Invited Speaker: Novartis, Pfizer. C. Robert: Financial Interests, Personal, Other, Consultancy fees: BMS, Roche, Pierre Fabre, Novartis, Sanofi, MSD, AstraZeneca, Pfizer. A.M. Arance Fernandez: Financial Interests, Personal, Advisory Board, Consultant /Advisory/Speaker/Travel, Accommodation, Expenses/: Pierre Fabre, Novartis, Roche, BMS, MSD, Merck, Sanofi; Financial Interests, Institutional, Other, Research Funding: Pierre Fabre, Novartis, MSD, BMS, Merck, Roche, Sanofi, Amgen. J.W. de Groot: Other, Institutional, Advisory Board: Bristol Myers Squibb, MSD, Pierre Fabre, Servier. C. Garbe: Other, Institutional, Advisory Board: Amgen, Bristol Myers Squibb, MSD, NeraCare, Novartis, Pfizer, Philogen, Pierre Fabre, Roche, Sanofi. H. Gogas: Other, Institutional, Advisory Board: Bristol Myers Squibb, MSD, Pierre Fabre; Financial Interests, Institutional, Invited Speaker: Bristol Myers Squibb, MSD, Novartis, Pierre Fabre; Other, Institutional, Other, Steering Committee Member: Amgen; Financial Interests, Institutional, Principal Investigator: Amgen, Bristol Myers Squibb, MSD; Financial Interests, Institutional, Other, Research Support: Bristol Myers Squibb, Pfizer. R. Gutzmer: Other, Institutional, Invited Speaker: Almirall, Amgen, Bristol Myers Squibb, Merck Serono, MSD, Novartis, Pierre Fabre, Roche, Sanofi, Sun Pharma; Other, Institutional, Other, Clinical Study Fees: Amgen, Bristol Myers Squibb, Merck, Serono, MSD, Novartis, Pfizer, Philogen, Pierre Fabre, Roche, Sanofi, Sun Pharma; Other, Institutional, Advisory Board: 4SC, Almirall, Amgen, Bayer, Bristol Myers Squibb, Merck Serono, MSD, Novartis, Pfizer, Pierre Fabre, Roche, Sanofi, Sun Pharma; Other, Institutional, Other, Research Support: Amgen, Johnson & Johnson, Merck Serono, Novartis, Pfizer, Sanofi, Sun Pharma; Other, Institutional, Other, Travel/Meeting Support: Bristol Myers Squibb, Merck Serono, Pierre Fabre, Roche, Sun Pharma. G. Liszkay: Other, Institutional, Invited Speaker: Bristol Myers Squibb, MSD, Novartis, Pfizer, Roche; Other, Institutional, Principal Investigator: Bristol Myers Squibb, MSD, Novartis, Pfizer, Roche, Incyte; Other, Institutional, Advisory Board: Bristol Myers Squibb, MSD, Novartis, Pfizer, Roche. C. Loquai: Other, Institutional, Advisory Board: Almirall, BioNTech, Bristol Myers Squibb, Merck, MSD, Novartis, Pierre Fabre, Roche, Sanofi, Sun Pharma; Other, Institutional, Speaker's Bureau: Bristol Myers Squibb, Merck, MSD, Novartis, Pierre Fabre, Roche, Sanofi, Sun Pharma; Other, Institutional, Other: Almirall, BioNTech, Bristol Myers Squibb, Kyowa Kirin, Merck, MSD, Novartis, Pierre Fabre, Roche, Sanofi, Sun Pharma. M. Mandalà: Financial Interests, Personal, Advisory Board: MSD, Novartis, Sanofi, BMS, Pierre Fabre; Financial Interests, Personal, Invited Speaker: Sun Pharma. N. Yamazaki: Financial Interests, Personal, Invited Speaker, Advisory Board: Ono Pharmaceutical, MSD; Financial Interests, Personal, Advisory Board: Chugai Pharma; Financial Interests, Personal, Invited Speaker: Novartis, Bristol Myers Squibb Japan; Financial Interests, Institutional, Research Grant: Ono Pharmaceutical, Bristol Myers Squibb Japan, Novartis, Astellas Amgen Biopharma, Merck Serono, Takara Bio. C.A. Guenzel, A. Polli, M. Thakur, A. di Pietro: Other, Institutional, Full or part-time Employment: Pfizer, Inc. P.A. Ascierto: Financial Interests, Personal, Other, Consultant and Advisory Role: BMS, Roche Genentech, MSD, Novartis, Merck Serono, Pierre Fabre, AstraZeneca, Sun Pharma, Sanofi, Idera, Sandoz, Immunocore, 4SC, Nektar, Boehringer Ingelheim, Regeneron; Financial Interests, Personal, Other, Consultant and Advisory Role, Travel support: Pfizer/Array; Financial Interests, Personal, Other, Consultant Role: Italfarmaco; Financial Interests, Personal, Other, Advisory Role: Eisai, Seagen; Financial Interests, Personal, Other, Consultant Role: Daiichi Sankyo, Pfizer, OncoSec, Nouscom, Lunaphore; Financial Interests, Personal, Other, Consultant role: Medicenna; Financial Interests, Personal, Other, Consultant role and travel support: Bio-AI Health; Financial Interests, Personal, Advisory Board, Consultant and Advisory Role: iTeos; Financial Interests, Personal, Advisory Board, Consultant and Advisory role: ValoTx; Financial Interests, Personal, Advisory Board, Consultant and Advisor role. Travel support: Replimune; Financial Interests, Personal, Advisory Board, Advisor role: Bayer; Financial Interests, Personal, Advisory Board: Erasca; Financial Interests, Institutional, Funding, Clinical trial and translational research: BMS; Financial Interests, Institutional, Funding, Clinical Trial: Roche Genentech, Pfizer/Array, Sanofi; Non-Financial Interests, Leadership Role, President since 2010: Fondazione Melanoma Onlus Italy; Non-Financial Interests, Leadership Role, President since 2014: Campania Society of ImmunoTherapy of Cancer (SCITO) Italy; Non-Financial Interests, Other, Member of Steering Committee since 2016: Society for Melanoma Research (SMR); Non-Financial Interests, Member of Board of Directors, November 2017 - December 2021: Society for Immunotherapy of Cancer (SITC); Non-Financial Interests, Member: ASCO, SITC, EORTC Melanoma Cooperative Group, AIOM, SMR. All other authors have declared no conflicts of interest.

https://doi.org/10.1016/j.annonc.2023.09.2247

1114P Encorafenib (E) plus binimetinib (B) in unresectable advanced or metastatic BRAFV600-mut melanoma, real-world evidence in Spain (GEM 2002 - BECARE)

A. Soria[1], P. Sanchez Mauriño[2], R. García Galindo[3], S. Sequero[4], L. Gutiérrez Sanz[5], G. Crespo[6], R. Díaz-Beveridge[7], T. Puértolas[8], P. López[9], J. Fra Rodríguez[10], R. López Castro[11], C. Aguayo[12], J. Valdivia[13], A. Cunquero-Tomás[14], G. Benítez[15], P. Ayala de Miguel[16], E. Espinosa[17], E. Muñoz-Couselo[18], B. Campos[19], P. Cerezuela-Fuentes[20]

[1]Medical Oncology, Hospital Universitario Ramón y Cajal, Madrid, Spain; [2]Medical Oncology, Hospital Universitario Reina Sofia, Córdoba, Spain; [3]Medical Oncology, Hospital Universitario de Jerez de la Frontera, Jerez de la Frontera, Spain; [4]Medical Oncology, Hospital Universitario San Cecilio, Granada, Spain; [5]Medical Oncology, Hospital Universitario Puerta de Hierro, Majadahonda, Spain; [6]Medical Oncology, Hospital Universitario de Burgos, Burgos, Spain; [7]Medical Oncology, Hospital Universitario y Politécnico la Fe de Valencia, Valencia, Spain; [8]Medical Oncology Department, Hospital Universitario Miguel Servet, Zaragoza, Spain; [9]Medical Oncology, Complejo Hospitalario de Jaén, Jaén, Spain; [10]Medical Oncology, Hospital Universitario Río Hortega, Valladolid, Spain; [11]Medical Oncology, Hospital Clínico Universitario de Valladolid, Valladolid, Spain; [12]Medical Oncology, Hospital Universitario Infanta Sofía, San Sebastián de los Reyes, Spain; [13]Medical Oncology, Hospital Universitario Virgen de las Nieves, Granada, Spain; [14]Medical Oncology, Hospital General Universitario de Valencia, Valencia, Spain; [15]Medical Oncology, Complejo Hospitalario Universitario Insular-Materno infantil de Gran Canaria, Las Palmas de Gran Canaria, Spain; [16]Medical Oncology, Hospital Universitario San Pedro de Alcántara, Cáceres, Spain; [17]Medical Oncology, Hospital Universitario La Paz - CIBERONC, Madrid, Spain; [18]Medical Oncology, Hospital Universitario Vall d'Hebron, Barcelona, Spain; [19]Medical Oncology, Hospital Universitario Lucus Augusti de Lugo, Lugo, Spain; [20]Medical Oncology, Hospital Clínico Universitario Virgen de la Arrixaca, IMIB-Arrixaca, Murcia, Spain

Background: Combined BRAF/MEK inhibitors have demonstrated efficacy and tolerability in phase III clinical trials, and is standard of care for advanced/metastatic BRAF-mutated melanoma. However there is limited evidence in the real-world.

Methods: BECARE is a retrospective study of EB in unresectable advanced/metastatic $BRAF^{V600}$-mut melanoma in 21 sites from Spain. The study includes melanoma patients (pts) treated according to standard clinical practice with EB in the 1st or after progression to a 1st line with immune checkpoint inhibitors (IT) for advanced or metastatic stage. Previous BRAF- and/or MEK- inhibitor (other than adjuvant ended $\geq$ 6 m before EB) or chemotherapy was not allowed. The primary objective is to characterize the population of pts receiving EB and assess treatment efficacy and tolerability in the real world.

Results: From Sep 2021 to Mar 2023, 117 pts were included. Median age was 59 years (range: 23-89), 59.8% were male, 64.1% had ECOG 0, all pts had metastasis at inclusion, and 21.4% brain metastasis. LDH was elevated in 35.9% of pts. The median follow-up was 13.1 m (95% CI: 11.4-15.1). EB was administered as the 2nd line after IT in 28 (23.9%) pts. The median PFS and OS for pts with brain metastasis treated with EB in the 1st line was 6.3 m (95% CI: 6.2-12) and 10 m (95% CI: 7.4-NR), respectively. Treatment-related adverse events of grade 3-4 were reported in 17 (14.5%) pts, being the most common elevated liver enzymes (6%), diarrhea (2.6%) and fatigue (1.7%). Creatinine was increased in 3 (2.6%) pts, and eye disorders present in 6 (5.1%). EB was administered for a median of 10.7 m (95% CI: 8.2-12.6) and required dose reductions or interruptions due to AEs in 29 (24.8%) and 37 (31.6%) pts, respectively. Treatment was ended due to toxicity in 6 (5.1%) pts.

Table: 1114P

EB treatment	ORR; n (%)	median PFS (95% CI); months	median OS (95% CI); months
1st line	63 (75)	12 (9.4-21.6)	24.6 (14.8-NR)
2nd line after IT	21 (77.8)	12.5 (6.6-NR)	13.9 (10.5-NR)

Conclusions: EB confirmed efficacy in the real-world including pts with worse prognosis than clinical trials. EB is also a feasible option after IT. Toxicity consistent with previous experience.

Editorial acknowledgement: Mfar Clinical Research staff for their assistance in the development of this abstract.

Legal entity responsible for the study: Grupo Español Multidisciplinar en Melanoma (GEM).

Funding: Grupo Español Multidisciplinar en Melanoma (GEM) as Sponsor with Industry partner Pierre Fabre Ibérica.

Disclosure: A. Soria: Financial Interests, Personal, Other, Honoraria: MSD, Merck Serono, Novartis Pharma, Bristol Myers Squibb, Pierre Fabre, Sanofi; Financial Interests, Personal, Speaker, Consultant, Advisor: MSD, Merck Serono, Novartis Pharma, Bristol Myers Squibb, Pierre Fabre, Sanofi. S. Sequero: Financial Interests, Personal, Speaker, Consultant, Advisor: Novartis, Pierre Fabre, Roche, MSD, Takeda, Pfizer, AstraZeneca, Incyte, Gilead. T. Puértolas: Financial Interests, Personal, Advisory Role: Bristol, Immunocore, Novartis, Seagen; Financial Interests, Personal, Other, Travel, Accommodation, Expenses: Novartis, MSD, Pierre Fabre. J. Fra Rodríguez: Financial Interests, Personal, Speaker, Consultant, Advisor: Amgen, Roche, Sanofi, Merck, Novartis, GSK, Pierre Fabre, Servier, BMS, PharmaMar, AAA. C. Aguayo: Financial Interests, Personal, Advisory Board: Pierre Fabre; Financial Interests, Personal, Other, Honoraria for Continuous Medical Education: Pfizer, Novartis, MSD, Pierre Fabre, BMS, Roche. G. Benítez: Financial Interests, Personal, Advisory Board: Sun Pharma; Financial Interests, Personal, Speaker, Consultant, Advisor: Merck, AstraZeneca, MSD, Bristol, Novartis, Pierre Fabre; Financial Interests, Personal, Principal Investigator: Pierre Fabre. P. Ayala de Miguel: Financial Interests, Personal, Speaker, Consultant, Advisor: MSD, Novartis, Sanofi, Pierre Fabre, BMS. E. Muñoz-Couselo: Financial Interests, Personal, Speaker, Consultant, Advisor: BMS, MSD, Novartis, Pierre Fabre, Sanofi, Roche. B. Campos: Financial Interests, Personal, Speaker, Consultant, Advisor: Roche, BMS, AstraZeneca, Sanofi, Novartis, Merck, Pierre Fabre, Rovi, Leo Pharma, Sun Pharma. All other authors have declared no conflicts of interest.

https://doi.org/10.1016/j.annonc.2023.09.2248

1115P Comparison of efficacy and toxicity of dabrafenib/trametinib versus vemurafenib/cobimetinib therapy in routine medical practice: Eight years of BRAF/MEK inhibitor use in routine clinical practice

K. Piejko[1], B. Cybulska-Stopa[2], A.M. Czarnecka[3], K. Ostaszewski[4], M. Ziętek[5], L. Galus[6], W. Bal[7], T. Kubiatowski[8], G. Kaminska-Winciorek[9], R. Suwinski[10], J. Mackiewicz[6], R. Dziura[11], E. Rutkowska[11], T. Switaj[12], P. Rogala[4], N. Kempa-Kaminska[2], P. Blonski[4], M.K. Zielińska[4], P. Rutkowski[12]

[1]Department of Clinical Oncology, Clinical Oncology Clinic, Maria Sklodowska-Curie National Research Institute of Oncology, Cracow Branch, Kraków, Poland; [2]Department of Clinical Oncology, Lower Silesian Center of Oncology, Hematology and Pulmonology, Wroclaw, Poland; [3]Department of Soft Tissue/Bone Sarcoma and Melanoma & Department of Experimental Pharmacology, Maria Sklodowska-Curie National Research Institute of Oncology & Medical Research Centre Polish Academy of Science, Warsaw, Poland; [4]Department of Soft Tissue/Bone Sarcoma and Melanoma, Maria Sklodowska-Curie National Research Institute of Oncology, Warsaw, Poland; [5]Department of Surgical Oncology, Wroclaw Comprehensive Cancer Center, Wroclaw, Poland; [6]Department of Medical and Experimental Oncology, Institute of Oncology, Poznan University of Medical Sciences, Poznan, Poland; [7]Outpatient Chemotherapy Department, National Oncology Institute Maria Sklodowska-Curie National Research Institute, Gliwice Branch, Gliwice, Poland; [8]Department of Oncology and Immuno-Oncology, Warmian-Masurian Cancer Center of the Ministry of the Interior and Administration's Hospital, Olsztyn, Poland; [9]The Skin Cancer and Melanoma Team, Department of Bone Marrow Transplantation and Hematology-Oncology, Maria Sklodowska Curie National Research Institute of Oncology Gliwice Branch, Gliwice, Poland; [10]Radiotherapy and Chemotherapy Clinic and Teaching Hospital, National Oncology Institute Maria Sklodowska-Curie National Research Institute, Gliwice Branch, Gliwice, Poland; [11]Deparment of Clinical Oncology, Holy Cross Cancer Center, Kielce, Poland; [12]Soft Tissue, Bone Sarcoma and Melanoma, Maria Sklodowska-Curie National Research Institute of Oncology, Warsaw, Poland

Background: BRAF inhibitors (BRAFi) and MEK inhibitors (MEKi) significantly changed the prognosis of patients with advanced melanoma. Our aim was to compare long-term treatment outcomes in patients treated with vemurafenib + cobimetinib (V+C) and dabrafenib + trametinib (D+T) in real world practise.

Methods: Consecutive patients with unresectable or metastatic *BRAF*-mutated melanoma started treatment with V+C and D+T between 01/Jan/2014 and 30/Jun/2021 according to national drug reimbursement programme. Clinical factors including age, sex, primary location of melanoma, ECOG performance status, baseline LDH level, metastasis location, response to treatment, adverse events (AEs) were analysed. Survival analyses were performed using the Kaplan-Meier method, Log-rank and chi-square tests were used for comparison between groups.

Results: In total 583 patients were enroled, 178 (31%) received first-line V+C, while 405 (69%) D+T. The patients with V + C were significantly younger (median 56 vs 62; p=0.0001) and had more frequent brain metastases (40% vs 30%, p = 0,023). The estimated median OS (mOS) in *V+C* group was 12.0 month while in D+T - 12.5 months (p=0.79; HR=1.03, CI 95% 0.8-1.3). The estimated progression free survival (mPFS) group V+C was 7.8 month while in D+T - 7.2 months (p=0.81; HR=1.02, CI 95% 0.8-1.2). 5- and 7-years OS rates was 21%/19% and 17%/13% and PFS rates 11%/11% and 8%/8% in V+C and D+T group, respectively. In multivariate analysis a significant positive effect on OS and PFS had normal LDH level, no brain metastases and ECOG 0 in both groups, in addition only in D+T group a significant positive effect on OS had age $\geq$ 65 years. The percentage of patients with any grade of AEs was similar in boths groups (p=0,8088). Skin AEs and nephrotoxicity were more frequent in V+C group (p=0.0004 and p=0.01, respectively); fever were more frequent in D+C group (p = 0.035).

Conclusions: The analysis did not show differences in median OS and PFS between patients treated in the first line with *V+C* and *D+T*. In the V+C group there were more skin AEs and nephrotoxicity, and in D+T fever was more common, however the treatment was well tolerated in nonselected patients.

Legal entity responsible for the study: The authors.

Funding: Has not received any funding.

Disclosure: B. Cybulska-Stopa: Financial Interests, Personal, Advisory Board, Advisory Boards outside of the scope of the study: BMS, Novartis, Roche, Pierre Fabre, MSD; Financial Interests, Personal, Invited Speaker: BMS, Novartis, Roche, Pierre Fabre, MSD. A.M. Czarnecka: Financial Interests, Personal, Advisory Board, Advisory Boards outside of the scope of the study: BMS, Novartis, Roche, Merck; Financial Interests, Personal, Invited Speaker: BMS, Novartis, Roche, Merck. M. Ziętek: Financial Interests, Personal, Advisory Board, Advisory Boards outside of the scope of the study: BMS, MSD, Novartis; Financial Interests, Personal, Invited Speaker: BMS, MSD, Novartis. L. Galus: Financial Interests, Personal, Advisory Board, Advisory Boards outside of the scope of the study: BMS, Roche, MSD, Novartis, Pierre Fabre; Financial Interests, Personal, Invited Speaker: BMS, Roche, MSD, Novartis, Pierre Fabre. W. Bal: Financial Interests, Personal, Advisory Board, Department of Clinical Oncology: BMS, Novartis, Roche, Pierre Fabre, MSD; Financial Interests, Personal, Invited Speaker: BMS, Novartis, Roche, Pierre Fabre, MSD. T. Kubiatowski: Financial Interests, Personal, Advisory Board, Advisory Boards outside of the scope of the study: BMS, Novartis, Roche, Pierre Fabre, MSD; Financial Interests, Personal, Invited Speaker: BMS, Novartis, Roche, Pierre Fabre, MSD. G. Kaminska-Winciorek: Financial Interests, Personal, Advisory Board, Advisory Boards outside of the scope of the study: BMS, Novartis, Roche, Pierre Fabre, MSD; Financial Interests, Personal, Invited Speaker: BMS, Novartis, Roche, Pierre Fabre, MSD. R. Suwinski: Financial Interests, Personal, Advisory Board, Advisory Boards outside of the scope of the study: BMS, MSD, Astellas Pharma; Financial Interests, Personal, Invited Speaker: BMS, MSD, Astellas Pharma. J. Mackiewicz: Financial Interests, Personal, Research Grant: BMS, BMS; Financial Interests, Personal, Speaker, Consultant, Advisor: MSD, MSD; Financial Interests, Personal, Advisory Board, Advisory Boards outside of the scope of the study: GSK, Roche, Novartis, Pierre Fabre; Financial Interests, Personal, Invited Speaker: GSK, Roche, Novartis, Pierre Fabre. R. Dziura: Financial Interests, Personal, Advisory Board, Advisory Boards outside of the scope of the study: BMS, Novartis, Roche, Pierre Fabre, MSD; Financial Interests, Personal, Invited Speaker: BMS, Novartis, Roche, Pierre Fabre, MSD. N. Kempa-Kaminska: Financial Interests, Personal, Advisory Board, Advisory Boards outside of the scope of the study: BMS, Roche; Financial Interests, Personal, Invited Speaker: BMS, Roche. P. Rutkowski: Financial Interests, Personal, Invited Speaker, honoraria for lectures: MSD, BMS, Pierre Fabre; Financial Interests, Personal, Advisory Board: MSD, BMS, Pierre Fabre, Merck, Sanofi, Blueprint Medicines, Philogen; Financial Interests, Personal, Invited Speaker: Merck, Sanofi, Novartis, AstraZeneca; Financial Interests, Institutional, Research Grant, research grant for ISS: Pfizer; Financial Interests, Institutional, Funding, research grant for institution: BMS; Non-Financial Interests, Member of Board of Directors: Polish Society of Surgical Oncology; Non-Financial Interests, Member of Board of Directors, President: Polish Oncological Society. All other authors have declared no conflicts of interest.

https://doi.org/10.1016/j.annonc.2023.09.2249

1116P Long term outcome of complete responders to immune checkpoint inhibitors (ICI) or target therapy (TT) in advanced melanoma

C. Boutros[1], D. Belkadi-Sadou[1], B. Archambaud[2], A. Vallet[1], A. Dutheil[1], A. Marchand[1], S. Roy[1], E. Routier[1], C. Robert[1]

[1]Dermatology Unit, Department of Medicine, Gustave Roussy Cancer Campus, Villejuif, France; [2]Biostatistics, Gustave Roussy - Cancer Campus, Villejuif, France

Background: Achieving a CR with ICI or with TT is associated with long-term survival in advanced melanoma pts. This is a retrospective study of the characteristics and long-term outcome of complete responders to ICI or TT.

Methods: Clinical data were collected between October 2010 and July 2022. Progression-free survival (PFS) and overall survival (OS) were estimated using the Kaplan-Meier method. Cox multivariate proportional hazard regression model was applied to analyze association between clinical characteristics and PFS.

Results: A CR was achieved by 197 pts after ICI (anti-PD-1+/-anti-CTLA-4) for 168 (85.3%) and TT (anti-BRAF+/-anti-MEK) for 26 (13.2%) pts respectively. Median follow-up (FU) was 72 months (mos) [range=8;132]. Median duration of treatment (tx) was 11.1 mos [IQR=5.9;19.3] with ICI and 19.4 mos [IQR=8.5;30.4] with TT. Median duration to achieve the 1st CR was 9 mos with ICI and 13.9 mos with TT. Median duration of response was not reached (NR) with ICI and 2.28 mos [95%CI=1.15;NA] with TT. Relapses occurred in 38 (22.6%) and 16 (61.5%) of pts respectively, meaning a significantly higher relapse risk with TT than with ICI (HR=2.58 [95%CI=1.23 ;5.43], p=0.012). Median PFS was NR with ICI and 2.97 mos [95%CI=2.65;NA] with TT. PFS rate at 72 mos was 73.3% with ICI [95%CI=65.84;81.67] and 33.9% with TT [95% CI=18.27;63.21]. Number of lines, LDH, BRAF/NRAS mutation status were not statistically associated with relapse. Relapse occurred during tx in 6 (16.2%) and 8 (53.3%) pts and after tx discontinuation in 31 (83.8%) and 7 (46.4%) pts with ICI and TT respectively. The brain was a site of relapse in 2.9 % and 19.2% of responders to ICI and TT respectively (p: 0.0046, Fisher exact test). Among relapsing pts, 23 pts were rechallenged with ICI and 5 with TT, a new CR occurring in 3 and 2 pts respectively. Median OS was NR in both groups. After a median FU of 72 mos, 87.1% [95% CI=81.38;93.40] pts and 64.6% [95%CI=45.23;92.31] were alive respectively.

Conclusions: In this real life long-term study of patients in CR, 6 year PFS rates were 73.3% with ICI vs 33.9% with TT and 87.2% vs 64.6 % were alive with ICI and TT respectively. Brain relapses were significantly more frequent in the TT responder group than with ICI.

Legal entity responsible for the study: Caroline Robert.

Funding: Has not received any funding.

Disclosure: C. Boutros: Financial Interests, Personal and Institutional, Advisory Board: BMS; Financial Interests, Personal and Institutional, Speaker, Consultant, Advisor: MSD; Financial Interests, Personal, Other, conference fee: Pierre Fabre; Financial Interests, Personal, Other, conference fees: Viatris. E. Routier: Financial Interests, Personal and Institutional, Other, conference fees: BMS, Pierre Fabre; Financial Interests, Personal and Institutional, Other, conference fee: Novartis; Financial Interests, Personal and Institutional, Other, compensation: BMS, Pierre Fabre, Novartis. C. Robert: Financial Interests, Personal and Institutional, Advisory Role: BMS, Pierre Fabre, Novartis, MSD, Roche, Sanofi, AstraZeneca, Merck; Financial Interests, Personal and Institutional, Other, cofounder: Ribonexus. All other authors have declared no conflicts of interest.

https://doi.org/10.1016/j.annonc.2023.09.2250

1117P Overall survival (OS) in patients with metastatic BRAF V600-mutant melanoma treated with encorafenib plus binimetinib (ENCO+BINI): Comparing real-world vs clinical trial data

G.K. In[1], K. Chen[2], G. Sajeev[3], R. Simpson[3], S. Kalia[3], D. Christensen[4], D. Liu[3], N. Rezai[5], A. di Pietro[6], J. Signorovitch[3]

[1]Division of Oncology, University of Southern California, Norris Comprehensive Cancer Center, Los Angeles, CA, USA; [2]Global Access and Value Oncology, Pfizer Inc., Cambridge, MA, USA; [3]Health Economics and Outcomes Research, Analysis Group, Inc., Boston, MA, USA; [4]Health Economics and Outcomes Research, Analysis Group, Inc., New York, NY, USA; [5]Medical Oncology, Pfizer Inc., New York, NY, USA; [6]GPD Immuno-Oncology Department, Pfizer Srl, Milan, Italy

Background: ENCO+BINI, a combination BRAF and MEK inhibitor therapy, prolonged OS in patients with BRAF V600-mutant metastatic melanoma in the multinational, phase III COLUMBUS clinical trial. We assessed how the real-world effectiveness of ENCO+BINI compares to efficacy observed in clinical trials after accounting for differences in patient profiles across these settings.

Methods: Patients treated with ENCO+BINI were drawn from the COLUMBUS trial and from Flatiron Health, an EMR-derived database of academic and community cancer clinics in the US. Included patients were adults with metastatic BRAF V600E/K mutated melanoma without central nervous system metastases who were untreated or had prior 1L immunotherapy (IO) and ECOG performance status (PS) of 0/1. OS was compared between ENCO+BINI patients treated in Flatiron vs. COLUMBUS, adjusting for age, sex, race, BMI, ECOG PS, LDH, prior 1L IO, prior medication/surgery, time since metastasis, and time from initial diagnosis to metastasis.

Results: This study included 275 patients treated with ENCO+BINI (192 from COLUMBUS, 83 from Flatiron). At baseline, patients in Flatiron had worse LDH (42% > ULN vs 29%), worse ECOG (46% vs 29% with ECOG PS of 1), and were more likely to have had prior 1L IO (36% vs 9%). Fewer patients in Flatiron had therapies after ENCO+BINI discontinuation (28% vs 43%). Survival at one (75% vs 75%) and 2 years (52% vs 58%) was similar, while median OS was numerically shorter in Flatiron (24.0 vs 33.6 months; p=0.35). OS was not significantly different between Flatiron and COLUMBUS in adjusted analyses (HR: 1.03 [0.62, 1.72]; p=0.90). Adjustments for sites/number of metastases and subsequent therapies, which may impact longer-term OS, may warrant consideration in the future.

Conclusions: Real world data suggests that clinical outcomes, including OS, for patients with metastatic BRAF V600-mutant melanoma treated with ENCO+BINI, are similar to those from trials, after accounting for differences in patient profiles. This indicates that clinical trial efficacy of ENCO+BINI translates to effectiveness in a broader real-world population, including patients treated with prior 1L IO.

Legal entity responsible for the study: The authors.

Funding: Pfizer Inc.

Disclosure: G.K. In: Financial Interests, Personal, Principal Investigator: Pfizer; Financial Interests, Personal, Speaker's Bureau: Merck; Financial Interests, Personal, Advisory Board: Novartis, Bristol Myers Squibb, Regeneron, Sanofi, Castle Biosciences, Array; Financial Interests, Institutional, Principal Investigator: Regeneron, Idera, Array Biosciences, Xencor, Checkmate Pharmaceuticals, Instil Bio. K. Chen: Other, Institutional, Full or part-time Employment: Pfizer Inc. G. Sajeev, R. Simpson, S. Kalia, D. Christensen, D. Liu, J. Signorovitch: Other, Institutional, Full or part-time Employment: Analysis Group, Inc. which received consulting fees from Pfizer for this research. N. Rezai: Financial Interests, Institutional, Full or part-time Employment: Pfizer Inc. A. di Pietro: Financial Interests, Institutional, Full or part-time Employment: Pfizer Slr.

https://doi.org/10.1016/j.annonc.2023.09.2251

1118P Real-world treatment patterns and outcomes among patients with BRAF+ metastatic melanoma refractory to first-line immunotherapy

T-G. Truong[1], S. Chandra[2], L. Connolly[3], R. Shah[4], C. Byrne[5], J. Tang[5], Z. Eroglu[6]

[1]Hematology and Oncology Department, Kaiser Permanente Vallejo Medical Center, Vallejo, CA, USA; [2]Division of Hematology Oncology, Robert. H. Lurie Cancer Center of Northwestern University, Chicago, IL, USA; [3]Real-World Evidence, Novartis Ireland Limited, Dublin, Ireland; [4]Oncology, Novartis Pharmaceuticals Corporation, East Hanover, NJ, USA; [5]HEOR, Asclepius Analytics, New York, NY, USA; [6]Oncology, H. Lee Moffitt Cancer Center & Research Institute - Magnolia Campus, Tampa, FL, USA

Background: Many patients with BRAF+ metastatic melanoma (MM) experience tumor progression during first-line (1L) immunotherapy (IO). This real-world study evaluated the characteristics, treatment patterns, and outcomes among BRAF+ MM patients who experienced disease progression while on 1L IO.

Methods: This retrospective cohort study used Flatiron Health data from 1/1/2014 to 9/30/2021. Included patients were age ≥18 years with BRAF+ MM and were 1L IO-refractory, defined as having documented disease progression within 6 months of 1L IO initiation. Therapy use post-progression was defined as 2L, regardless of whether it was a new therapy or the same as 1L. Patient characteristics and treatment patterns were evaluated descriptively. The Kaplan-Meier method was used to describe overall survival (OS) and time to progression or death (TTPD) in patients who continued to receive IO (2L IO) and those who switched to targeted therapy (2L TT), from the start of 2L therapy.

Results: A total of 325 patients (mean age 60 years, 65% male) were included. Median time from 1L IO initiation to first disease progression was 64 days. Post-progression, 157 patients (48%) were treated with 2L IO within a median of 0 days and 83 (26%) initiated 2L TT within a median of 13 days. The median duration of 2L therapy for patients treated with 2L IO and 2L TT was 127 vs 182 days, respectively. Patients on 2L IO had improved median OS compared to those who received 2L TT (27.2 vs 10.5 months; p<0.0001) as well as improved time to next progression at 1 (32 vs 11%) and 2 years (23 vs 2%). Median TTPD was similar for patients treated with 2L IO and 2L TT (4.1 vs 4.8 months; p=0.078), despite patients receiving 2L TT having evidence of more severe disease (higher ECOG, elevated lactate dehydrogenase, and more liver metastases).

Conclusions: Outcomes among patients with 1L IO-refractory BRAF+ MM are poor and many patients progress on 2L therapy. While 2L IO appeared to lead to more durable treatment responses for some patients, 2L TT was associated with a similar TTPD despite patients having more severe disease. Earlier use of TT (i.e., 1L TT+IO combinations) should be considered for this group with especially poor prognosis.

Legal entity responsible for the study: Novartis Pharmaceuticals Corporation.

Funding: Novartis Pharmaceuticals Corporation.

Disclosure: T. Truong, S. Chandra, Z. Eroglu: Financial Interests, Personal, Speaker, Consultant, Advisor: Novartis. L. Connolly, R. Shah: Financial Interests, Personal, Full or part-time Employment: Novartis. C. Byrne, J. Tang: Financial Interests, Institutional, Speaker, Consultant, Advisor: Novartis.

https://doi.org/10.1016/j.annonc.2023.09.2252

1119P Stage IIIA melanoma with isolated tumor cells in lymph nodes: Time for reviewing the AJCC v8 classification

T.M.S. Amaral[1], L. Nanz[2], R. Stadler[3], A. Forschner[2], A. Meiwes[1], F. Meraz-torres[1], F. Wolfsperger[1], E. Chatziioannou[2], L. Flatz[2], C. Garbe[2], U. Leiter-Stoppke[2]

[1]Dermato-Oncology Department, Skin Cancer Clinical Trials Center, University of Tuebingen, Tuebingen, Germany; [2]Department of Dermatology, Eberhard Karls University, Tuebingen, Germany; [3]Dermatology, Johannes Wesling Klinikum, Minden, Germany

Background: The classification of stage III melanoma has significantly changed in the American Joint Committee on Cancer 8th version (AJCC v8). Besides including four new substages, AJCC v8 defines that lymph nodes (LN) with metastatic tumor cells, regardless of the size and the technic used to identify it, should be considered tumor-involved LN. This implies that even thin melanomas with isolated tumor cells (ic) in LN will be classified as stage IIIA, potentially upstaging patients (pts) with good prognosis.

Methods: Patients with cutaneous melanoma diagnosed with stage I-III between 2000-2020 at the Centre of Dermatooncology, University-Hospital of Tuebingen, were included. A cohort of stage IIIA (ic) pts from the DeCOG trial was used as a validation cohort. Relapse-free survival (RFS) and distant metastasis-free survival (DMFS) were evaluated using Kaplan-Meier estimates. Data on pts and tumor characteristics will also be presented.

Results: The Tuebingen cohort included 106 pts with stage IIIA (ic) and 132 pts with stage IIIA with a LN metastasis >0.1 mm (from now on stage IIIA). The validation cohort from the DeCOG trial consisted of 39 pts with melanoma IIIA (ic) and 104 pts with stage IIIA. The median follow-up (mFU) for stage IIIA (ic) and IIIA in the CMMR cohort was 64 and 60 months (95% CI 34-97 and 35-106), respectively. The mFU for stage IIIA (ic) and IIIA in the DeCOG cohort was 64 and 62 months (95%CI 47-95 and 37-86), respectively. In the Tuebingen cohort, 10y RFS rates for stage IIIA (ic) and IIIA

were 82% (95% CI 72-92) and 48% (95% CI 38-58), respectively (p<0.001). The 10y DMFS rates for stage IIIA (ic) and IIIA were 87% (95% CI 79-96) and 55% (95% CI 44-66), respectively; (p<0.001). In the DeCOG cohort, 10y RFS for stage IIIA (ic) and stage IIIA were 88% (95% CI 77-99) and 35% (95% CI 7-62), respectively; (p=0.009). The 10y DMFS for stage IIIA (ic) and IIIA was 88% (95% CI 77-99) and 60% (95% CI 39-80), respectively (p=0.061).

Conclusions: AJCCv8 Stage IIIA (ic) melanoma has a prognosis similar to stage IB, statistically significantly better than Stage IIIA. LN with isolated tumor cells should not be considered tumor-involved LN, and this should be reviewed in the new AJCC edition.

Legal entity responsible for the study: The authors.

Funding: Has not received any funding.

Disclosure: T.M.S. Amaral: Financial Interests, Personal, Writing Engagement: CeCaVa; Financial Interests, Personal, Invited Speaker: BMS, Novartis, Pierre Fabre; Financial Interests, Institutional, Funding: Novartis, Neracare, Sanofi, Skyline-Dx; Financial Interests, Institutional, Research Grant: Novartis, iFIT; Financial Interests, Institutional, Local PI: IO Biotech, MSD, University Hospital, Essen, Roche; Financial Interests, Institutional, Coordinating PI: Unicancer; Non-Financial Interests, Member: Portuguese Society for Medical Oncology, ASCO; Other, Clinical expert: INFARMED. R. Stadler: Financial Interests, Personal, Advisory Board: Kyowa Kirin, Stemline, 4SC. A. Forschner: Financial Interests, Personal and Institutional, Invited Speaker: Pierre Fabre, Novartis, MSD, BMS; Financial Interests, Institutional, Advisory Board: Immunocore, Pierre Fabre, MSD, BMS, Novartis; Financial Interests, Institutional, Research Grant: BMS Stiftung Immunonkologie; Financial Interests, Personal, Other, Travel, Accommodation, Expenses: Pierre Fabre, Novartis. L. Flatz: Financial Interests, Personal, Stocks or ownership: Hookipa Pharma; Financial Interests, Personal, Invited Speaker: BMS, Novartis, Sanofi; Financial Interests, Personal, Advisory Board: BMS, Novartis, Sanofi, Philogen; Financial Interests, Institutional, Research Funding: Hookipa Pharma; Financial Interests, Personal, Royalties: Hookipa Pharma. C. Garbe: Financial Interests, Personal, Advisory Board: CeCaVa, Novartis, NeraCare, BMS, Philogen, Roche, Sanofi, MSD. U. Leiter-Stoppke: Financial Interests, Institutional, Research Grant: MSD; Financial Interests, Personal, Invited Speaker: MSD, Novartis, Sun Pharma, Allmiral Hermal, Sanofi; Financial Interests, Personal, Other, Travel support: Sun Pharma; Financial Interests, Personal, Advisory Board: MSD, Novartis, Sun Pharma, Allmiral Hermal, Sanofi; Non-Financial Interests, Personal, Other, Board member: ADO (DECOG). All other authors have declared no conflicts of interest.

https://doi.org/10.1016/j.annonc.2023.09.2253

1120P Development and external validation of a clinical prediction model to predict recurrence-free survival and melanoma-specific survival in patients with melanoma after sentinel lymph node biopsy

R.C. Stassen[1], C. Maas[2], A.A.M. Van der Veldt[3], S. Lo[4], R. Saw[5], A. Varey[6], R. Scolyer[7], G.V. Long[8], J. Thompson[9], P. Rutkowski[10], U. Keilholz[11], A.C.J. van Akkooi[12], C. Verhoef[1], D. van Klaveren[2], D. Gruenhagen[1]

[1]Surgical Oncology, Erasmus MC - Daniel den Hoed Cancer Center, Rotterdam, Netherlands; [2]Public Health, Erasmus MC, Rotterdam, Netherlands; [3]Medical Oncology Department, Erasmus MC - University Medical Center, Rotterdam, Netherlands; [4]Melanoma Institute Australia, The University of Sydney School of Public Health, Sydney, NSW, Australia; [5]Department of Melanoma & Surgical Oncology, Royal Prince Alfred Hospital, Camperdown, NSW, Australia; [6]Plastic & Reconstructive Surgery, Melanoma Institute Australia, Wollstonecraft, NSW, Australia; [7]Pathology, Royal Prince Alfred Hospital, Camperdown, NSW, Australia; [8]Medical Oncology, Melanoma Institute Australia, Wollstonecraft, NSW, Australia; [9]Surgical Oncology, Melanoma Institute Australia, Wollstonecraft, NSW, Australia; [10]Department of Soft Tissue/Bone Sarcoma and Melanoma, Maria Sklodowska-Curie National Research Institute of Oncology, Warsaw, Poland; [11]Charité Comprehensive Cancer Center, Charité - Universitätsmedizin Berlin, Berlin, Germany; [12]Surgical Oncology Dept., Melanoma Institute Australia, Wollstonecraft, NSW, Australia

Background: The introduction of adjuvant systemic treatment for patients with high-risk melanoma has increased the importance of adequate melanoma staging. However, inconsistencies in outcomes between disease stages exist, as an increase in stage does not necessarily correspond to improved recurrence-free survival (RFS) or melanoma-specific survival (MSS). Therefore, there is a need for a tool that can predict patient-specific outcomes rather than grouping patients according to outcome.

Methods: A total of 4071 patients who underwent sentinel lymph node biopsy between 1997 and 2013 in four European melanoma centers were included in the development cohort. A prognostic model and nomogram were developed to predict recurrence and melanoma-specific mortality (MSM) on a continuous scale in patients with >pT1a melanomas. From this model, individual values for RFS and MSS were derived. For the purpose of external validation, a cohort consisting of 4822 patients was provided by the Melanoma Institute of Australia. Model performance was assessed by discrimination (C-index) and calibration.

Results: The prediction model for recurrence and MSM contained six prognostic factors: positive sentinel node (SN) status, Breslow depth, ulceration, age, location and SN tumor burden. The C-index for the recurrence model was 0.76, and was 0.79 for the MSM model. External validation showed good calibration for both outcomes with a C-index of 0.74 for recurrence and 0.76 for MSM.

Conclusions: This EORTC-MIA prediction model and nomogram provides patient-specific risk probabilities for recurrence and MSM and consequently RFS and MSS using only readily-available variables. The nomogram can support clinical decision-making for adjuvant treatment in patients with high-risk melanomas.

Legal entity responsible for the study: The authors.

Funding: Has not received any funding.

Disclosure: A.A.M. Van der Veldt: Financial Interests, Institutional, Speaker, Consultant, Advisor: BMS, MSD, Merck, Roche, Novartis, Pfizer, Sanofi, Pierre Fabre, Ipsen, Eisai. J. Thompson: Financial Interests, Institutional, Advisory Board: BMS, MSD, GSK, Provectus; Financial Interests, Institutional, Other, travel & conference support: GSK, Provectus, Novartis. P. Rutkowski: Financial Interests, Personal, Invited Speaker, honoraria for lectures: MSD, BMS, Pierre Fabre; Financial Interests, Personal, Advisory Board: MSD, BMS, Pierre Fabre, Merck, Sanofi, Blueprint Medicines, Philogen; Financial Interests, Personal, Invited Speaker: Merck, Sanofi, Novartis, AstraZeneca; Financial Interests, Institutional, Research Grant, research grant for ISS: Pfizer; Financial Interests, Institutional, Funding, research grant for institution: BMS; Non-Financial Interests, Member of Board of Directors: Polish Society of Surgical Oncology; Non-Financial Interests, Member of Board of Directors, President: Polish Oncological Society. A.C.J. van Akkooi: Financial Interests, Institutional, Advisory Board: Amgen, Bristol Myers Squibb, Novartis, MSD - Merck, Merck-Pfizer, Pierre Fabre, Sanofi, Sirius Medical, 4SC, Provectus; Financial Interests, Institutional, Research Grant, NIVEC study: Amgen; Financial Interests, Institutional, Research Grant: Merck-Pfizer. All other authors have declared no conflicts of interest.

https://doi.org/10.1016/j.annonc.2023.09.2254

1121P Interferon-gamma (IFNy) gene signature as a predictive biomarker for response in lactate dehydrogenase (LDH) low advanced melanoma patients

L. Hoeijmakers[1], P. Dimitriadis[2], A. van Vliet[2], J.M. Versluis[1], D. Peeper[2], C.U. Blank[1]

[1]Medical Oncology Department, NKI-AVL - Netherlands Cancer Institute/Antoni van Leeuwenhoek Hospital, Amsterdam, Netherlands; [2]Molecular Oncology and Immunology, NKI-AVL - Netherlands Cancer Institute/Antoni van Leeuwenhoek Hospital, Amsterdam, Netherlands

Background: In current clinical practice, LDH level is widely used as decision tool between anti-PD1 monotherapy (LDH low) versus combination of anti-PD1 and anti-CTLA4 (LDH high). However, approximately only 50% of LDH low patients respond to anti-PD1. In stage III melanoma patients (generally LDH low) the interferon (IFN)g signature has been identified as strongest baseline marker for response to neo-adjuvant combination immunotherapy. Therefore, we addressed the question whether an IFNg signature could serve as additional biomarker for treatment decisions in LDH low advanced melanoma patients.

Methods: Advanced melanoma patients participating in biobank study in the Netherlands Cancer Institute (NKI), treated with anti-PD1 monotherapy between April 2014 and June 2016 were retrospectively identified. The IFNg-signature was analyzed on baseline paraffine tumor biopsies using mRNA sequencing. The cutoff between IFNg-high and IFNg-low cohorts was calculated using ROC curves on the objective response (OR).

Results: Forty-nine patients were included: the majority had cutaneous (98%) and BRAF wild type (53%) melanoma and stage M1c disease (39%, AJCC 8th edition). Patients with a high IFNg-signature at baseline showed a higher response rate to anti-PD1 (OR 86% vs 43%; p=0.016) and an improved progression free survival (p=0.046) and overall survival (p=0.064).

Table: 1121P

	IFNg low (n=46)	IFNg high (n=19)
Objective response	15 (43%)	12 (86%)
median PFS (m, IQR)	7.0 (2.0, 23.5)	25.5 (7.0, 72.0)
median OS (m, IQR)	23.0 (12.0, 76.0)	60.5 (37.0, 76.8)
24 m PFS (%)	27% (CI: 15.4-46.8)	50% (CI: 29.6-84.4)
60 m PFS (%)	15% (CI: 6.7-33.4)	43% (CI: 23.4-78.5)
24 m OS (%)	46% (CI: 31.9-65.6)	78% (CI: 59.8-100)
60 m OS (%)	31% (CI: 19.3-51.3)	50% (CI: 29.6-84.4)

PFS, progression free survival; OS, overall survival; m, months; IQR, interquartile range; CI, 95% confidence interval.

Conclusions: Our results suggest that the IFNg-signature could become a biomarker for treatment decisions in LDH low patients directing towards anti-PD1 monotherapy (in IFNg high patients) versus combination therapy, with either anti-LAG3 or anti-CTLA-4 in IFNg low patients. However, confirmation in larger cohorts and in other combination therapies is needed.

Legal entity responsible for the study: Christian Blank's group.

Funding: Has not received any funding.

Disclosure: P. Dimitriadis: Financial Interests, Personal, Advisory Role, will receive some possible revenues if the IFN-γ signature is being developed as clinical companion diagnostic: Signature oncology. D. Peeper: Financial Interests, Personal, Ownership Interest, o-founder, shareholder, and advisor: Immagene. C.U. Blank: Financial Interests, Institutional, Advisory Board: BMS, MSD, Roche, Novartis, GSK, AZ, Pfizer, Lilly, GenMab, Pierre Fabre; Financial Interests, Personal, Advisory Board: Third Rock Ventures; Financial Interests, Personal, Stocks/Shares: Immagene; Financial Interests, Personal, Stocks/Shares, intention to develop IFN signature algorithm: NewCo, no name yet; Financial Interests, Institutional, Coordinating PI: BMS, Novartis, NanoString, 4SC; Other, pending patent: WO 2021/177822 A1. All other authors have declared no conflicts of interest.

https://doi.org/10.1016/j.annonc.2023.09.2255

1122P Neutrophil/lymphocyte ratio and systemic inflammatory index as prognostic biomarkers in metastatic melanoma patients under immune checkpoint inhibitors: Could any of them be used?

M.B. Menezes[1], L. Goncalves[2], I.Q. Dunões[1], P. Semedo[2], S.L. Lobo Martins[3], A.G. da Silva Oliveira[4], G.M. Baió[5], C. Alvim[2], I.S. Soares de Pinho[6], T. Barroso[2], V.D.C. Patel[7], M. Esperanca-Martins[8], R.L. Brás[9], A.R. Teixeira Sousa[9], A.B. Mansinho[10], S. Torres[11], M.M. Inácio[12], L. Costa[13], R.D. Dinis[14]

[1]Medical Oncology, Hospital Espírito Santo de Évora, Évora, Portugal; [2]Medical Oncology, HSM - Hospital Santa Maria - Centro Hospitalar Universitario de Lisboa Norte E.P.E., Lisbon, Portugal; [3]Medical Oncology, Hospital São Francisco Xavier, Lisbon, Portugal; [4]Oncology Department, Hospital Espírito Santo, EPE-SNS - Évora, Évora, Portugal; [5]Oncologia, Hospital Espírito Santo, EPE-SNS - Évora, Évora, Portugal; [6]Oncologia Médica, Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal; [7]Oncology Department, HSM - Hospital Santa Maria - Centro Hospitalar Universitario de Lisboa Norte E.P.E., Lisbon, Portugal; [8]Medical Oncology, Centro Hospitalar Universitário Lisboa Norte, Lisbon, Portugal; [9]Oncology Department, HSM - Hospital Santa Maria - Centro Hospitalar de Lisboa Norte E.P.E., Lisbon, Portugal; [10]Start Lisbon, HSM - Hospital Santa Maria - Centro Hospitalar Universitario de Lisboa Norte E.P.E., Lisbon, Portugal; [11]Medical Oncology, Hospital Santa Maria, Lisbon, Portugal; [12]Medical Oncology, Hospital Espírito Santo, EPE — Évora, Evora, Portugal; [13]START Lisbon, Medical Oncology, HSM - Hospital Santa Maria - Centro Hospitalar de Lisboa Norte E.P.E., Lisbon, Portugal; [14]Oncology Service Department, Hospital Espírito Santo, EPE-SNS - Évora, Évora, Portugal

Background: Immune checkpoint inhibitors (ICI) targeting cytotoxic T-lymphocyte-associated protein 4 and programmed cell death protein 1 are now the standard of care for patients with advanced melanoma, with an improvement in overall survival (OS) and quality of life. Elevated neutrophil to lymphocyte ratio (NLR) and systemic inflammatory index (SII) have been reported associated with poor survival in cancer patients, including those with ICI. The aim of this study was to determine the clinical significance of pre-treatment NLR and SII as prognostic indicator in metastatic melanoma patients treated with ICI.

Methods: Retrospective, multicentric study of metastatic melanoma patients who received ICI between 2016-2022 in two hospitals in Portugal. The SII [platelets x neutrophil/lymphocyte ratio] and NLR were calculated before the beginning of ICI. SII was considered high if $>$ 572 and NLR was considered high if $>$5. Data was collected from clinical records. Statistical analysis was performed with SPSSv26. Progression free survival (PFS) and OS were assessed using Kaplan-Meier plots and log-rank testing.

Results: Eighty-nine patients were enrolled, 57 were male, mean age 68 years old. Seventy-six patients had cutaneous, 10 mucosal and 3 uveal melanoma. The type of ICI was nivolumab in 36 patients, ipilimumab/nivolumab in 34 and pembrolizumab in 19. With a median follow-up of 19 months, the median PFS and OS was 11 and 15 months, respectively. NLR was high in 12 patients. The median PFS was 3 months in NLR high vs 25 months in NLR low patients and OS was 13 months in NLR high vs 32 months. However, these differences were not statistically significant. A total of 53 patients were presented with SII high. In this group, the median PFS was 10 months vs 22 months in SII low patients (p=0.017) and the median OS was 17 months vs 32 months (p=0.032).

Conclusions: The present study suggests that elevated SII may be associated with a worse PFS and OS in metastatic melanoma patients, however, this association was not demonstrated for NLR. Thus, SII could be a prognostic value on advanced/metastatic melanoma in patients under ICI and could be an important tool in the management of these patients.

Legal entity responsible for the study: The authors.

Funding: Has not received any funding.

Disclosure: All authors have declared no conflicts of interest.

https://doi.org/10.1016/j.annonc.2023.09.2256

1123P Baseline tumor-infiltrating lymphocytes and response to immune checkpoint inhibition in advanced melanoma

M. Schuiveling[1], I. van Duin[1], L.S. ter Maat[1], F.W.P.J. Van den Berkmortel[2], M.J. Boers-Sonderen[3], J.W. de Groot[4], E. Kapiteijn[5], M. Labots[6], D. Piersma[7], A.M.R. Schrader[8], G. Vreugdenhil[9], H.M. Westgeest[10], J. Pluim[11], M. Veta[11], W.A. Blokx[12], P.J. van Diest[12], K.P.M. Suijkerbuijk[1]

[1]Medical Oncology, UMC-University Medical Center Utrecht, Utrecht, Netherlands; [2]Medical Oncology, Zuyderland Medical Center, Heerlen, Netherlands; [3]Medical Oncology, Radboud University Medical Center, Nijmegen, Netherlands; [4]Oncology Center, Isala, Zwolle, Netherlands; [5]Medical Oncology, Leiden University Medical Center (LUMC), Leiden, Netherlands; [6]Medical Oncology, Amsterdam UMC, Location VUmc, Amsterdam, Netherlands; [7]Internal Medicine, Medisch Spectrum Twente (MST) - Radiology, Enschede, Netherlands; [8]Pathology, Leiden University Medical Center (LUMC), Leiden, Netherlands; [9]Internal Medicine, Maxima Medisch Centrum - Veldhoven, Veldhoven, Netherlands; [10]Internal Medicine, Amphia Ziekenhuis - Location Langendijk, Breda, Netherlands; [11]Biomedical Engineering, Eindhoven University of Technology, Eindhoven, Netherlands; [12]Pathology, UMC - University Medical Center Utrecht, Utrecht, Netherlands

Background: Although the presence of tumor-infiltrating lymphocytes (TILs) in pathological specimens has been associated with prolonged survival in melanoma, it is largely unknown whether TILs can predict response to immune checkpoint inhibition (ICI) in advanced melanoma. Therefore, we investigated the association between treatment response and TILs in the largest cohort to date.

Methods: Patients who received first-line anti-PD1 ± anti-CTLA4 for advanced cutaneous melanoma were retrospectively identified from nine hospitals in the Netherlands. TILs were scored as absent, non-brisk or brisk on hematoxylin and eosin (H&E) slides of primary melanoma and pre-treatment metastases. The primary outcome was clinical response to ICI according to RECIST 1.1. Univariable and multivariable logistic regression analyses were performed and Kaplan-Meier methods were used for survival analyses.

Results: Metastatic melanoma specimens were available for 676 patients, whereas primary melanomas were available from 436 patients. TILs were absent in 347, non-brisk in 260 and brisk in 69 metastases. Compared to patients with absent TILs, both patients with non-brisk TILs (odds ratio [OR] 1.74, 95% confidence interval [CI] 1.25-2.43) and brisk TILs (OR 3.58, 95%CI 2.01-6.64) had a higher probability of response to ICI. This association remained in multivariable analysis, adjusted for age, sex, disease stage, lactate dehydrogenase level and World Health Organisation performance score (see table). Patients with absent TILs had a shorter median progression-free survival (PFS) compared to patients with non-brisk TILs and brisk TILs (6.2, 10.6 and 19.3 months, respectively [p=0.003]). No significant association was found between TILs in primary melanoma specimens and response.

Table: 1123P Objective response rate (ORR), odds ratio (OR) and adjusted OR for response, median progression-free survival (PFS) and overall survival (OS) in months, stratified by TIL score on 676 pre-treatment metastatic specimens of advanced melanoma patients treated with ICI

	TIL score			
	Absent	Non-brisk	Brisk	*p-value*
ORR	45%	58%	74%	
OR [95% CI] for response (univariable)	REF	1.74 [1.25-2.43]	3.58 [2.01-6.64]	<0.001
OR [95% CI] for response (multivariable)	REF	1.61 [1.13-2.32]	3.09 [1.68-5.92]	<0.001
Median PFS [95% CI]	6.2 [5.4-9.0]	10.6 [6.4-not reached]	19.3[9.5-not reached]	0.003
Median OS [95% CI]	19.8 [15.4-29.4]	49.4 [25.7-not reached]	40.8[23.5-not reached]	0.003

Conclusions: The presence of non-brisk and brisk TILs in pre-treatment metastatic H&E histopathology specimens is associated with better response to ICI and survival outcomes.

Legal entity responsible for the study: The authors.

Funding: Hanarth Fonds.

Disclosure: M. Labots: Financial Interests, Institutional, Advisory Role: Bristol Myers Squibb, Janssen-Cilag B.V. K.P.M. Suijkerbuijk: Financial Interests, Institutional, Advisory Board: Novartis, BMS, AbbVie, Pierre Fabre, MSD; Financial Interests, Institutional, Invited Speaker: Roche; Financial Interests, Institutional, Research Grant: Novartis, TigaTx. All other authors have declared no conflicts of interest.

https://doi.org/10.1016/j.annonc.2023.09.2257

1124P IL-6 as prognostic factor in adjuvant or metastatic skin cancer patients treated with immunotherapy: A deep biomarker analysis

D. Mallardo[1], S. Arpino[2], M.G. Vitale[1], A. Minopoli[2], M. Tuffanelli[1], C. Trojaniello[1], M. Mallardo[1], M. Ottaviano[1], G. D'Angelo[1], V. Vanella[1], F. Sparano[1], E. Cioli[1], B. Alfano[1], L. Festino[1], A. Budillon[3], E. Simeone[1], C. Caracò[4], E. Cavalcanti[2], P.A. Ascierto[1]

[1]Melanoma, Cancer Immunotherapy and Development Therapeutics Department, Istituto Nazionale Tumori - IRCCS - Fondazione Pascale, Naples, Italy; [2]Division of Laboratory Medicine, Istituto Nazionale Tumori IRCCS - Fondazione G. Pascale, Naples, Italy; [3]Translational Research, Istituto Nazionale Tumori - IRCCS - Fondazione Pascale, Naples, Italy; [4]Division of Surgery of Melanoma and Skin Cancer, Istituto Nazionale Tumori - IRCCS - Fondazione Pascale, Naples, Italy

Background: The immune checkpoint inhibitors (ICIs) revolutionized cancer therapeutic landscape and substantially improved the survival of patients (pts) with advanced malignancies, especially in skin cancer pts. IL-6 is a key inflammatory molecule secreted by M2 macrophages after polarization, mediating the progression of pancreatic and colorectal cancer. The purpose of this study is to retrospectively investigate the relationships between IL-6 and outcome in skin cancer patients treated with immunotherapy.

Methods: IL-6 levels were analyzed in two independent cohorts, in cohort 1 serum IL-6 were evaluated from 386 consecutive skin cancer pts before start ICIs. IL-6 was measured by Electrochemiluminescence immunoassays (ECLIA) from Cobas C6000 (Roche). In cohort 2 we conducted a gene profile analysis with Nanostring from PBMCs of 121 metastatic melanoma pts. All pts signed informed consent. Patient's characteristics and treatment are listed in the table.

Table: 1124P

Patient characteristics	Cohort 1 N = 386	Cohort 2 N = 121
Median age	62 (range 23-96)	62 (range 27-91)
Gender: female/male, n (%)	146/240 (38/62)	53/68 (38/62)
BRAF Status, Mutation, n (%)	126 (32)	22 (32)
Line of treatment in mtx pts	N = 288	
1st line treatment, anti-PD1	145 (38)	88 (73)
1st line treatment, anti-CTLA4	15 (4)	33 (27)
1st line treatment, ipi+nivo	28 (7)	36 (30)
1st line treatment, cemiplimab in CSCC	40 (10)	
ORR, n (%)	48 (64)	
Resected stage III/IV melanoma, anti-PD1	N = 98	
Progression disease, n (%)	26 (27)	

Results: Among 507 pts, in cohort 1 lower serum IL-6 was associated with a better Progression Free Survival (PFS) 18.67 months (95% CI 16.6-20.7) versus 10.31 months (95% CI 8.5-12.0), HR = 0.45 (CI 0,3-0,5, p<0.0001); Overall Survival (OS) (27.59 months (95% CI 25.9-29.2) versus 20.12 months (95% CI 17.7-22.4), HR = 0.32 (CI 0,23-0,47, p<0.0001) and Overall Response Rate (ORR) (p<0.001). Similarly, IL-6 and previous therapy are associated with OS and PFS in multivariate analysis (p <0.01). We also confirmed the association between IL-6 and outcomes in all subgroups. In cohort 2 we observed a similar trend in pts with lower IL-6 expression. Moreover, higher IL-6 was associated to MAP3K12, EGFR, SELL, FPR1 genes.

Conclusions: We found that lower levels of both serum and gene expression of IL-6 are associated with better OS, PFS and ORR. Furthermore, IL-6 is associated to higher expression of genes relate to cell cycle, proliferation and metastasis. Further investigations are needed to get additional information.

Legal entity responsible for the study: The authors.

Funding: Italian Ministry of Health (IT-MOH).

Disclosure: P.A. Ascierto: Financial Interests, Advisory Role, consultant/advisory role: Bristol Myers Squibb; Financial Interests, Other, consultant/advisory role: Roche-Genentech, Merck Sharp & Dohme, Novartis, Merck Serono, Pierre Fabre, AstraZeneca, Sun Pharma, Sanofi, Idera, Sandoz, Immunocore, 4SC, Italfarmaco, Nektar, Boehringer Ingelheim, Eisai, Regeneron, Daiichi Sankyo, Pfizer, OncoSec, Nouscom, Lunaphore, Seagen, iTeos; Financial Interests, Officer, consultant/advisory role: Medicenna, Bio-Al Health. All other authors have declared no conflicts of interest.

https://doi.org/10.1016/j.annonc.2023.09.2258

1125P Identification of a subset of metastatic melanoma patients demonstrating germline determined insensitivity to immunotherapy

B.P. Fairfax[1], C. Taylor[2], R.A. Watson[1], W. Ye[1], O. Tong[1], F. Matos Santo[3], N.A. Coupe[4], M.R. Middleton[5], M. Payne[6]

[1]Department of Oncology, The MRC Weatherall Institute of Molecular Medicine Oxford, Oxford, UK; [2]WIMM, Department of Oncology, University of Oxford, Oxford, UK; [3]Department of Oncology, John Radcliffe Hospital University of Oxford, Oxford, UK; [4]Oncology Department, Churchill Hospital, Oxford, UK; [5]Oncology Department, Churchill Hospital, Oxford, UK; [6]Oncology, Churchill Hospital - Oxford University Hospitals NHS Foundation Trust, Oxford, UK

Background: Long-term clinical outcomes post immune checkpoint blockade (ICB) for metastatic melanoma (MM) are highly variable. Whilst this is in part reflects inter-tumour heterogeneity, the degree patient germline genetic variation influences ICB responses is poorly characterised. Previous pan-tumour patient cohort studies suggested that homozygosity at Class I MHC alleles is associated with reduced survival post ICB, although these observations have not been reproduced in meta-analyses. Here we explore the relationship between homozygosity at one, two and three alleles at Class I MHC in a longitudinal follow-up cohort of patients receiving ICB for MM, integrating observations with immunological and transcriptomic data at single-cell resolution.

Methods: 232 MM patients receiving standard of care ICB were HLA typed using genome-wide genotyping and followed for up to 9 years. Pre-treatment and on treatment CD8 T cells RNA and T cell receptor (TCR) sequencing of was performed for all samples (n>500), as well as focused single-cell RNA seq. The relationship between homozygosity at HLA-A, HLA-B and HLA-C and survival parameters were explored with results integrated with transcriptomic and immunophenotyping.

Results: 50.9% of patients survived for >5 years. Notably, no effect of homozygosity at either one or two Class I HLA alleles on outcomes was noted (60.5% vs. 49.8% - no homozygosity, P=0.17). However, patients homozygous at three alleles (3.0% cohort) have catastrophic outcomes, independent of tumour features, with 1 year survival 17.8% vs. 75.2%, P<0.0001. Pre-treatment these patients have reduced CD8 TCR diversity, and marked immune dysregulation. Single-cell RNA sequencing demonstrates impaired responses to ICB from treatment initiation.

Conclusions: Understanding ICB resistance is of vital importance in stratifying MM treatments. We find homozygosity at one or two Class I MHC alleles does not impact outcomes. Conversely, we demonstrate a subset of MM patients have homozygosity at all three Class I MHC alleles. They show markedly impaired immunological and transcriptomic responses to ICB, with very poor clinical outcomes. This work marks the first description of germline encoded ICB resistance.

Legal entity responsible for the study: University of Oxford.

Funding: Wellcome Trust, Cancer Research UK.

Disclosure: All authors have declared no conflicts of interest.

https://doi.org/10.1016/j.annonc.2023.09.2259

1126P REtrospective Study of definitive therapy for head and neck mUcosal MElanoma: The RESUME study

M. Nomura[1], N. Kiyota[2], Y. Shimizu[3], A. Motegi[4], T. Akimoto[4], T. Mukaigawa[5], T. Fujii[6], N. Tsushima[7], K. Shiga[8], T. Koyama[9], D. Kawakita[10], A. Ohkoshi[11], M. Nakahira[12], N. Hanai[13], S. Murono[14], T. Ueda[15], H. Mitani[16], A. Homma[7]

[1]Clinical Oncology, Kyoto University Hospital, Kyoto, Japan; [2]Medical Oncology and Hematology Department, Kobe University Hospital, Kobe, Japan; [3]Medical Oncology, Hokkaido University Hospital, Sapporo, Japan; [4]Division of Radiation Oncology, National Cancer Center Hospital East, Kashiwa, Japan; [5]Division of Head and Neck Surgery, Shizuoka Cancer Center, Shizuoka, Japan; [6]Head and Neck Surgery, OICI - Osaka International Cancer Institute, Osaka, Japan; [7]Otolaryngology-Head and Neck Surgery, Hokkaido University Hospital, Sapporo, Japan; [8]Otolaryngology-Head and Neck Surgery, Iwate Medical University School of Medicine, Morioka, Japan; [9]Medical Oncology - Hematology, Kobe University Hospital, Kobe, Japan; [10]Otorhinolaryngology, Head and Neck Surgery, Nagoya City University, Nagoya, Japan; [11]Otorhinolaryngology, Head and Neck Surgery, Tohoku University School of Medicine, Sendai, Japan; [12]Head and Neck Oncology/Ear, Nose and Throat, Saitama Medical University International Medical Center, Saitama, Japan; [13]Head and Neck Surgery, Aichi Cancer Center Hospital, Nagoya, Japan; [14]Otolaryngology, Fukushima Medical University, Fukushima, Japan; [15]Otolaryngology, Head and Neck Surgery, Hiroshima University Hospital, Hiroshima, Japan; [16]Head and Neck Surgery, The Cancer Institute Hospital of JFCR, Koto-ku, Japan

Background: Head and neck mucosal melanoma (HNMM) is a rare clinical subtype of melanoma. The aim of this study was to compare survival following surgery-based treatment (S group) versus radiotherapy-based treatment (RT group) and to assess the efficacy of the addition of adjuvant immune checkpoint inhibitor (adj-ICI) after definitive treatment for locally advanced HNMM patients.

Methods: This was a multi-institutional retrospective study which enrolled patients treated for locally advanced HNMM patients between October 2014 and March 2022.

Treatment efficacy was compared between the S and RT groups and between those with and without adj-ICI.

Results: Among 294 patients, 148 patients were in the S group and 146 in the RT group. In the RT group, 80 patients received proton RT and 43 received carbon ion RT. Patient characteristics between the S and RT groups were mostly similar, except for patients with nasal and paranasal sinus primary sites (77% in S group vs. 91% in RT group) and clinical-T4 stage disease (25% in S group vs. 51% in RT group). Overall, 29 in the S group and 43 in the RT group received adj-ICI. Among patients without adj-ICI, the S group tend to have longer progression-free survival (PFS) than the RT group (hazard ratio [HR] 1.34, 95% confidence interval [CI] 0.98-1.84). However, there was no significant difference in overall survival (OS) between the S and RT groups (HR 1.02, 95% CI 0.64-1.62). Patients with adj-ICI experienced significantly longer PFS than those without adj-ICI (HR 0.68, 95% CI 0.48-0.96) irrespective of definitive treatment (HR 0.65, 95% CI 0.37-1.13 in S group; HR 0.65, 95% CI 0.41-1.03 in RT group). However, OS did not significantly differ between those with and without adj-ICI (HR 0.96, 95% CI 0.59-1.56).

Conclusions: There were no significant differences in PFS and OS between the S and RT groups. Although the addition of adj-ICI yielded longer PFS in locally advanced HNMM patients, adj-ICI might not lead to a benefit in OS.

Legal entity responsible for the study: The authors.

Funding: National Cancer Center Research and Development Fund (2023-J-03) of Japan.

Disclosure: All authors have declared no conflicts of interest.

https://doi.org/10.1016/j.annonc.2023.09.2260

1127P Efficacy of immune checkpoint inhibitors (ICIs) in advanced mucosal melanoma (MM): A systematic review and meta-analysis

J.P. Pham[1], J. Hurwitz[1], R. Cosman[1], S.M. Goldinger[2], H-W. Sim[1], R. Dummer[3], A.M. Joshua[1]

[1]Medical Oncology, The Kinghorn Cancer Centre, Sydney, NSW, Australia; [2]Dermatology, University Hospital Zurich, Zurich, Switzerland; [3]Dermatology Department, USZ - University Hospital Zürich, Zurich, Switzerland

Background: Unresectable or metastatic MM has been associated with worse survival and inferior treatment responses than cutaneous melanoma. ICIs are commonly used to treat advanced MM; however, robust conclusions on their efficacy are limited by small studies with heterogeneous patient populations.

Methods: A systematic review and meta-analysis was conducted to benchmark the efficacy of ICIs in advanced MM. PubMed, Medline, Embase, Web of Science and CENTRAL were searched in April 2023 using a combination of ICI and MM search terms, restricted to primary studies with at least 5 patients. Logit-transformed objective response rates (ORR) and adverse event (AE) rates were pooled using a random effects model and the inverse variance methods. Progression-free survival (PFS) and overall survival (OS) Kaplan-Meier curves were digitalised and used to construct summary plots, from which median estimates were derived. Results are reported with 95% confidence intervals.

Results: 28 studies reporting on ICIs in advanced MM were identified (n=2008). 37 treatment types were reported – 10 anti-CTLA4 (n=212), 21 anti-PD1 (n=1428) and 6 anti-CTLA4 plus anti-PD1 (n=368). 62% of patients were treatment-naïve. Pooled ORR was 10% (7-13) for anti-CTLA4, 23% (22-28) for anti-PD1 and 31% (28-35) for anti-CTLA4 plus anti-PD1 ($P<0.001$). Median PFS was 3.5 months (2.7-4.7) for anti-CTLA4, 4.0 months (2.9-5.2) for anti-PD1 and 4.7 months (3.6-6.6) for anti-CTLA4 plus anti-PD1 ($P<0.001$). Median OS was 7.2 months (5.7-10.6) for anti-CTLA, 14.4 months (10.8-17.5) for anti-PD1 and 19.4 (13.8-21.2) for anti-CTLA4 plus anti-PD1 ($P<0.001$). Grade 3 and higher AEs occurred in 36% (1-95) of patients for anti-CTLA4, 14% (11-18) for anti-PD1 and 50% (33-58) for anti-CTLA4 plus anti-PD1.

Conclusions: ICIs are associated with modest activity in patients with advanced MM. Although efficacy is slightly greater with combined anti-CTLA4/anti-PD1 compared to anti-PD1 alone, this was associated with a significantly high risk of grade 3+ AEs. Recommendations for combination ICI therapy should involve a risk-benefit analysis for individual patients. Research to identify predictive molecular biomarkers for ICI efficacy may help with treatment selection for advanced MM.

Legal entity responsible for the study: The authors.

Funding: Has not received any funding.

Disclosure: R. Dummer: Financial Interests, Personal, Other, Consulting and/or advisory role: Novartis; Financial Interests, Personal, Other, Consulting and/or advisory role: Merck Sharp & Dohme (MSD); Financial Interests, Personal, Other, Consulting and/or advisory role: Bristol Myers Squibb (BMS); Financial Interests, Personal, Other, Consulting and/or advisory role: Roche; Financial Interests, Personal, Other, Consulting and/or advisory role: Amgen; Financial Interests, Personal, Other, Consulting and/or advisory role: Takeda; Financial Interests, Personal, Other, Consulting and/or advisory role: Pierre Fabre; Financial Interests, Personal, Other, Consulting and/or advisory role: Sun Pharma; Financial Interests, Personal, Other, Consulting and/or advisory role: Sanofi; Financial Interests, Personal, Other, Consulting and/or advisory role: CatalYm; Financial Interests, Personal, Other, Consulting and/or advisory role: Second Genome; Financial Interests, Personal, Other, Consulting and/or advisory role: Regeneron; Financial Interests, Personal, Other, Consulting and/or advisory role: Alligator; Financial Interests, Personal, Other, Consulting and/or advisory role: Mavi-VAX SA; Financial Interests, Personal, Other, Consulting and/or advisory role: Simcere; Financial Interests, Personal, Other, Consulting and/or advisory role: touchIME; Financial Interests, Personal, Other, Consulting and/or advisory role: T3 Pharma; Financial Interests, Personal, Other, Consulting and/or advisory role: Pfizer. All other authors have declared no conflicts of interest.

https://doi.org/10.1016/j.annonc.2023.09.2261

1128P A phase I dose escalation and expansion study of FHD-286, a novel BRG1/BRM (SMARCA4/SMARCA2) inhibitor, for the treatment of metastatic uveal melanoma

S. Patel[1], M. Mckean[2], S. Piperno-Neumann[3], A.N. Shoushtari[4], L. Hernandez-Aya[5], M. Orloff[6], S. Khan[7], K. Montazeri[8], E. Kapiteijn[9], E. Buchbinder[10], S. Agresta[11], S. Reilly[11], C.M. Patriquin[11], D. Hickman[11], D. Corrigan[11], L. Granlund[11], M. Hentemann[12], J. Piel[13], P. Martin[14], I. Mehmi[15]

[1]Melanoma Medical Oncology, MD Anderson Cancer Center, Houston, TX, USA; [2]Drug Development Unit, Sarah Cannon Research Institute, Nashville, TN, USA; [3]Medical Oncology Dept., Institut Curie, Paris, France; [4]Medicine, Memorial Sloan Kettering Cancer Center, New York, NY, USA; [5]Medical Oncology, University of Miami Miller School of Medicine, Sylvester Comprehensive Cancer Center, Miami, FL, USA; [6]Medical Oncology, Thomas Jefferson University Hospital, Philadelphia, PA, USA; [7]Medical Oncology, Herbert Irving Comprehensive Cancer Center - Columbia University, New York, NY, USA; [8]Dept. of Medicine, Massachusetts General Hospital Cancer Center, Harvard Medical School, Boston, MA, USA; [9]Medical Oncology Dept., Leiden University Medical Center (LUMC), Leiden, Netherlands; [10]Medical Oncology Department, Dana-Farber Cancer Institute, Boston, MA, USA; [11]Clinical Development, Foghorn Therapeutics, Inc., Cambridge, MA, USA; [12]Program Management, Foghorn Therapeutics, Inc., Cambridge, MA, USA; [13]Translational, Foghorn Therapeutics, Inc., Cambridge, MA, USA; [14]Integrated Drug Development, Certara, Sheffield, UK; [15]Dept. of Medicine, The Angeles Clinic & Research Institute, Los Angeles, CA, USA

Background: The BRG/Brahma-associated factors (BAF) family of chromatin remodeling complexes regulates the chromatin landscape of the genome. Through its ATP-dependent chromatin remodeling activity, BAF regulates the accessibility of gene-control elements, allowing for the binding of transcription factors. FHD-286 is a first-in-class, orally administered compound that potently and selectively inhibits the ATPase components of the BAF complex, SMARCA4 and SMARCA2 (BRG1 and BRM, respectively).

Methods: As of a 31 December 2022 data cutoff, FHD-286 was administered in patients with metastatic uveal melanoma at escalating doses either on a daily dosing regimen ranging from 2.5 mg QD to 10 mg QD or an intermittent regimen of 1-week-on/1-week-off at 10 mg or 15 mg doses. Primary endpoints were safety, tolerability, dose-limiting toxicities (DLTs), and determination of the recommended phase II dose(s) (RP2D). Secondary endpoints included pharmacokinetic (PK) and preliminary efficacy.

Results: At data cutoff, 52 patients had received at least 1 dose of FHD-286. Any grade (Gr) treatment-related adverse events (TRAEs) occurred in 83% of patients, most commonly dysgeusia (39%), fatigue (31%), AST increased (29%), nausea/vomiting (29%), dry mouth (25%) and rash (25%). Gr $\geq$ 3 TRAEs occurred in 25% of patients, most commonly anemia, asthenia, ALP increased, hypokalemia, muscular weakness and rash each occurring in 4% of patients. One patient with Gr 3 keratitis and 2 patients with Gr 3 rash met DLT criteria at the 7.5 mg QD dose level. These AEs were non-serious and improved with dose interruption. No treatment-related deaths occurred. Ongoing PK analysis indicates that FHD-286 accumulates with QD dosing and PK exposure increases with increasing dose. One patient assigned to the 10 mg QD dosing cohort achieved a partial response and remained on treatment for 16 months; prolonged stable disease and reductions in tumor burden have also been observed across dose levels.

Conclusions: FHD-286 has been generally well-tolerated and preliminary anti-tumor activity has been observed. The RP2D(s) has not yet been established. Updated dosing, safety, tolerability, PK and anti-tumor activity data will be shared at the meeting.

Clinical trial identification: NCT04879017 (May 10, 2021) EudraCT Number: 2021-001529-35.

Legal entity responsible for the study: Foghorn Therapeutics Inc.

Funding: Foghorn Therapeutics Inc.

Disclosure: S. Patel: Financial Interests, Personal, Advisory Board: TriSalus, Cardinal Health, Castle Biosciences, Novartis, BMS, Pfizer, Immatics; Financial Interests, Personal, Other, Consultant for educational materials: Advance Knowledge in Healthcare; Financial Interests, Personal, Advisory Board, Advisory Board and Corporate Day speaker (unbranded): Delcath; Financial Interests, Personal, Other, Independent Data Monitoring Committee: Immunocore; Financial Interests, Personal, Other, Consultant: Guidepoint Global; Financial Interests, Institutional, Trial Chair: Provectus Biopharmaceuticals, Bristol Myers Squibb; Financial Interests, Institutional, Local PI: Lyvgen, InxMed, Foghorn Therapeutics, IDEAYA, Novartis, Seagen, Syntrix Bio; Financial Interests, Institutional, Steering Committee Member: TriSalus Life Sciences; Non-Financial Interests, Member: ASCO, AACR, International Society of Ocular Oncology, Society for Melanoma Research; Non-Financial Interests,

Leadership Role: SWOG. M. Mckean: Financial Interests, Institutional, Other, Consulting: Pfizer, Castle Biosciences, Eisai, IQVIA, Merck, Moderna; Financial Interests, Personal, Other, Consulting: iTeos; Financial Interests, Institutional, Research Grant: Ascentage Pharma Group, Bicycle Therapeutics, Dragonfly Therapeutics, Epizyme, Exelixis, Genentech, GSK, IDEAYA Biosciences, Ikena Oncology, Infinity Pharmaceuticals, Jacobio Pharmaceuticals, Moderna, NBE Therapeutics, Novartis, Oncorus, Plexxicon, Prelude Therapeutics, Regeneron, Sapience Therapeutics, Seattle Genetics, Tizona Therapeutics, Tmunity Therapeutics, TopAlliance Biosciences, Aadi Biosciences, Alpine Immune Sciences, Arcs Biosciences, Arvinas, ASCO, Astellas, Bayer, BioMed Valley Discoveries, BioNTech, C4 Therapeutics, EMD Serono, Erasca, Foghorn Therapeutics, G1 Therapeutics, Gilead Sciences, ImmVira Pharma, Kechow Pharma, Kezar Life Sciences, Kinnate BioPharma, MedImmune, Mereo BioPharma, Metabomed, Nektar, OncoC4, PACT Pharma, Pfizer, Poseida, Pyramid Biosciences, Scholar Rock, Synthrox, Takeda Pharmaceuticals, Teneobio, Tempest Therapeutics, Xilio. S. Piperno-Neumann: Financial Interests, Personal, Advisory Board: Immunocore, Pierre Fabre, Atlanthera. A.N. Shoushtari: Financial Interests, Personal, Advisory Board: Bristol Myers Squibb, Immunocore, Novartis, Erasca; Financial Interests, Personal, Royalties: UpToDate; Financial Interests, Institutional, Local PI: Bristol Myers Squibb, Immunocore, Pfizer, Novartis, Checkmate Pharmaceuticals, Linnaeus Therapeutics, Foghorn Therapeutics, Prelude Therapeutics, Iovance Biotherapeutics; Financial Interests, Institutional, Coordinating PI: Polaris, Xcovery, Targovax ASA; Non-Financial Interests, Member: ASCO. L. Hernandez-Aya: Financial Interests, Personal and Institutional, Advisory Board: BMS, CASTLE Bioscience, Replimune; Non-Financial Interests, Institutional, Principal Investigator: Foghorn Therapeutics, Immatics, Syntrix Pharmaceuticals. M. Orloff: Financial Interests, Personal, Advisory Board: Trisalus, Delcath, Replimune, IDEAYA, Immunocore; Financial Interests, Personal, Speaker, Consultant, Advisor: Immunocore. S. Khan: Financial Interests, Personal, Advisory Board: Castle Biosciences, Replimune Inc. K. Montazeri: Financial Interests, Personal, Speaker, Consultant, Advisor: Immunocore. E. Kapiteijn: Financial Interests, Institutional, Advisory Board: BMS, Novartis, Pierre Fabre, Merck, Delcath, Bayer, Lilly; Financial Interests, Institutional, Coordinating PI: BMS, Pierre Fabre, Delcath. E. Buchbinder: Financial Interests, Personal, Advisory Board: Instilbio, Nektar, Novartis, BMS, Iovance, Merck, Sanofi, Xilio; Financial Interests, Institutional, Coordinating PI: Genentech, Partners therapeutics; Other, Spouse employment: AstraZeneca, Takeda. S. Agresta: Financial Interests, Personal, Full or part-time Employment: Foghorn Therapeutics; Financial Interests, Personal, Stocks/Shares: Foghorn Therapeutics; Financial Interests, Personal, Officer: Foghorn Therapeutics. S. Reilly: Financial Interests, Personal, Full or part-time Employment: Foghorn Therapeutics; Financial Interests, Personal, Stocks/Shares: Foghorn Therapeutics, Adaptimmune Therapeutics, Johnson & Johnson, Procter & Gamble; Financial Interests, Personal, Other, Investor: Luna Genetics. C.M. Patriquin: Financial Interests, Personal, Stocks/Shares: Foghorn Therapeutics, Roche; Financial Interests, Personal, Full or part-time Employment: Foghorn Therapeutics. D. Hickman, L. Granlund, M. Hentemann, J. Piel: Financial Interests, Personal, Full or part-time Employment: Foghorn Therapeutics; Financial Interests, Personal, Stocks/Shares: Foghorn Therapeutics. D. Corrigan: Financial Interests, Personal, Stocks/Shares: Foghorn Therapeutics. P. Martin: Financial Interests, Personal, Full or part-time Employment: Certara. I. Mehmi: Financial Interests, Personal, Speaker, Consultant, Advisor: BMS; Financial Interests, Personal, Advisory Board: AZ.

https://doi.org/10.1016/j.annonc.2023.09.2262

1129P Effect of subsequent therapies including checkpoint inhibitors on overall survival in a phase III randomized trial of tebentafusp in first-line metastatic uveal melanoma: Long-term follow-up

M. Orloff[1], C. Watkins[2], R.D. Carvajal[3], A.N. Shoushtari[4], J.J. Sacco[5], M. Schlaak[6], J. Gama[7], M.O. Butler[8]

[1]Medical Oncology, Thomas Jefferson Univ Hospital, Philadelphia, PA, USA; [2]Biometrics, Clarostat Consulting Ltd., Cheshire, UK; [3]Division of Hematology/Oncology, Columbia University Medical Center College of Physicians & Surgeons - New York Presbyterian Hospital, New York, NY, USA; [4]Medicine, MSKCC - Memorial Sloan Kettering Cancer Center, New York, NY, USA; [5]Medical Oncology Department, Clatterbridge Cancer Center - NHS Foundation Trust, Wirral, UK; [6]Clinic for Dermatology, Venerology and Allergology, Charité - Universitaetsmedizin Berlin, Berlin, Germany; [7]Medical Affairs, Immunocore Limited, Abingdon-on-Thames, UK; [8]Medical Oncology and Hematology Department, UHN - University Health Network - Princess Margaret Cancer Centre, Toronto, ON, Canada

Background: Tebentafusp (tebe) is a bispecific consisting of an affinity-enhanced T cell receptor fused to an anti-CD3 effector that can redirect T cells to target gp100+ cells. Tebe significantly improved overall survival (OS) compared to investigator's choice of pembrolizumab, ipilimumab or dacarbazine (HR 0.51) in first line (1L) mUM [NCT03070392]. Here we evaluated the impact of subsequent therapy on long-term survival.

Methods: Analyses were conducted on HLA-A*02:01+ patients with first line mUM recruited to the randomized phase III study (Study 202, N=378). Crossover to tebe was not permitted until the planned interim analysis demonstrated significant OS benefit. Inverse probability of censoring weighting (IPCW) was used to compare the tebentafusp and investigator's choice (IC) arms by removing the effects of subsequent therapies (any versus CPI only). OS from the start of subsequent therapy was compared between arms using Cox regression models adjusted for prognostic baseline covariates.

Results: After a median follow-up of 37.8 months, a similar percentage of patients, ~ 62%, received subsequent therapy in each arm. Median time to first subsequent therapy was longer for tebe pts (6.4 mo) vs. IC pts (4.5 mo). The most frequent subsequent therapy was CPI in both arms (received by 49% of tebe pts and 34% of IC pts); 17% of IC pts received subsequent tebe. When adjusting for the effect of subsequent therapy (any or CPI), the OS benefit from the ITT analysis was maintained. In an analysis of survival from the start of any first subsequent therapy, prior tebe patients tended to have longer OS compared to prior IC patients, HR (95% CI) 0.75 (0.55, 1.04). This difference was also seen when restricting to patients who received subsequent CPI therapy, HR (95% CI) 0.72 (0.48, 1.09).

Conclusions: Based on IPCW analysis, the OS benefit in first line HLA-A*02:01+ mUM patients is predominantly due to tebentafusp and not due to subsequent therapy. This reinforces the use of tebentafusp in the first line setting. Updated data with a minimum 3 years of follow-up will be presented. 1. Yang J. et al. ASCO 2019 , *J. Clin Oncol* 37:15_suppl, 9592.

Clinical trial identification: NCT03070392.

Legal entity responsible for the study: Immunocore Ltd.

Funding: Immunocore Ltd.

Disclosure: M. Orloff: Financial Interests, Personal, Speaker's Bureau: Bristol Myers Squibb; Financial Interests, Personal, Speaker, Consultant, Advisor: IDEAYA Biosciences, Immunocore, TriSalus Life Sciences, Delcath Systems; Financial Interests, Institutional, Research Funding: Bristol Myers Squibb, Immunocore, Delcath Systems, Plexxikon, IDEAYA Biosciences, Linnaeus Therapeutics. C. Watkins: Financial Interests, Personal, Speaker, Consultant, Advisor: Celgene/Bristol Myers Squibb, Roche, Immunocore, Ascelia, Humanigen, Astellas Pharma, F2G, Amylyx, Kite/Gilead, Novo Nordick, Neurovalens, Medical Developments International, Servier, EQRx. R.D. Carvajal: Financial Interests, Personal, Speaker, Consultant, Advisor: Alkermes, Bristol Myers Squibb, Castle Biosciences, Delcath, Eisai, Hengrui, IDEAYA, Immunocore, InxMed, Iovance, Merck, Novartis, OncoSec, Pierre Fabre, PureTech Health; Financial Interests, Institutional, Speaker, Consultant, Advisor: Regeneron, Sanofi Genzyme, Trisalus Clinical; Financial Interests, Institutional, Advisory Board: Aura Biosciences, Chimeron, Rgenix. A.N. Shoushtari: Financial Interests, Personal, Advisory Board: Bristol Myers Squibb, Immunocore, Novartis; Financial Interests, Personal, Royalties: UpToDate; Financial Interests, Institutional, Invited Speaker: Bristol Myers Squibb, Immunocore, Polaris, Xcovery, Pfizer, Novartis, Targovax ASA, Checkmate Pharmaceuticals, Linnaeus Therapeutics, Prelude Therapeutics; Financial Interests, Personal, Invited Speaker: Foghorn Therapeutics; Non-Financial Interests, Member: ASCO. J.J. Sacco: Financial Interests, Personal, Speaker, Consultant, Advisor: Immunocore, Bristol Myers Squibb, MSD, Delcath, Amgen; Financial Interests, Personal, Speaker's Bureau: Bristol Myers Squibb, MSD, Pierre Fabre; Financial Interests, Institutional, Research Grant: Immunocore, Bristol Myers Squibb, MSD, Amgen, AstraZeneca, Replimune. M. Schlaak: Financial Interests, Personal, Advisory Board: Bristol Myers Squibb, Novartis, Merck/MSD, Roche, Pierre Fabre, Kyowa Kirin, Immunocore, Sanofi Genzyme; Financial Interests, Personal, Other, Travel expenses: Sun Pharma. J. Gama: Financial Interests, Personal, Full or part-time Employment: Immunocore. M.O. Butler: Financial Interests, Personal, Speaker, Consultant, Advisor: Merck, Bristol Myers Squibb, Novartis, Sanofi, Pfizer, Adaptimmune, GSK, Immunocore, EMD Serono, Sun Pharma; Financial Interests, Personal and Institutional, Research Grant: Merck; Financial Interests, Personal, Research Grant: Takara Bio; Financial Interests, Institutional, Research Grant: Bristol Myers Squibb, Novartis, Sanofi, Adaptimmune, Immunocore, Regeneron, Lilly, Amgen, OncoSeq.

https://doi.org/10.1016/j.annonc.2023.09.2263

1130P Tebentafusp (tebe) in an ongoing cohort of 72 French patients (pts) with metastatic uveal melanoma (mUM)

L. Mailly-Giacchetti[1], T. Ramtohul[2], S. Renault[3], M. Saint-Ghislain[4], M. Pracht[5], J-C. Thery[6], P-F. Combe[7], N. Litrowski[8], H. Martin[9], C. Dutriaux[10], L. De Koning[1], V. Servois[11], S. Piperno-Neumann[12], M.J. Rodrigues[12]

[1]Department of Clinical Oncology, Curie Institute, Paris, France; [2]Radiology Department, Institut Curie, Paris, France; [3]Translational Research, Institut Curie, Paris, France; [4]Department of Drug Development and Innovation (D3i), Institut Curie, Paris, France; [5]Medical Oncology Department, Centre Eugene - Marquis, Rennes, France; [6]Medical Oncology, Centre Henri Becquerel, Rouen, France; [7]Oncology, Pôle Santé Léonard de Vinci, Chambray-lès-Tours, France; [8]Dermatology, Hopital Jacques Monod, Montivilliers, France; [9]Medical Oncology Department, CHR Metz-Thionville - Hopital Bel-Air, Thionville, France; [10]Medical Oncology Department, CHU Bordeaux - Hopital St. André, Bordeaux, France; [11]Radiology Department, Université de Paris, Paris, France; [12]Medical Oncology Dept., Institut Curie, Paris, France

Background: Tebe, a bispecific T-cell engager, showed a benefit in response rate, progression-free survival (PFS) and overall survival (OS) in HLA A*02-01^{pos} mUM pts in the IMCgp100-202 phase III trial. Prior to approval, French Health Authorities allowed an early access to Tebe in May 2021 to mUM pts. We report here our real-world experience with Tebe and analyses of potential prognostic and predictive biomarkers.

Methods: Ongoing ambispective cohort of mUM pts treated with Tebe. Tumor sizes were evaluated according to RECIST 1.1. Circulating tumor DNA (ctDNA) analyses were performed on this cohort and on the 18 pts enrolled in the IMCgp100-202 trial and randomized to Tebe, at Institut Curie. ctDNA was measured by digital droplet PCR (ddPCR) targeting codons 183 & 209 of both *GNAQ* and *GNA11*.

Results: 72 pts were included from May 26th 2021 to December 12th 2022. With a median follow-up of 48 weeks, patients received a median of 22 weeks of Tebe. Out of 60 assessable pts, 33 (55%) showed stable disease and 5 (8%) partial response according to RECIST 1.1. Median PFS (mPFS) was 28 weeks (confidence interval 95% [CI_{95}]: 8-56). OS at 12 months (OS_{12m}) was 72%. No new, unexpected safety event occurred. Elevated baseline LDH was correlated with poorer OS (Spearman rho= -0.26, p<0.01). 63 pts had mUM carrying somatic mutations detectable by ddPCR (ie *GNAQ/GNA11* mutations). Of these, 39 pts (62%) had detectable ctDNA at baseline. Pts with detectable ctDNA at baseline had poorer PFS (mPFS 4.0 vs 14.0 months; HR=2.83, CI_{95}[1.48-5.41]) and OS (OS_{12m} of 51.5% vs 95.4%; HR=6.11, CI_{95}[2.04-18.3]) than those with undetectable ctDNA. 22 pts cleared their ctDNA at first assessment (12 weeks) and had numerically better OS_{12m} than those who did not (70% vs 60%; HR = 1.83 CI_{95}[0.92-13.9]).

Conclusions: In this real-world cohort of mUM pts, Tebe is associated with clinical outcomes in lin withthe IMCgp100-202 trial. Baseline ctDNA and LDH are prognostic factors while ctDNA clearance might predict benefit from Tebe. Other analyses are ongoing to identify new predictive biomarkers.

Legal entity responsible for the study: The authors.

Funding: INSERM.

Disclosure: M. Saint-Ghislain: Financial Interests, Invited Speaker: Oncotream. J. Thery: Financial Interests, Invited Speaker: PharmaMar; Financial Interests, Advisory Board: Pfizer, AstraZeneca. P. Combe: Financial Interests, Invited Speaker: Eisai, BMS GmbH&Co.KG, Novartis, Clovis Oncology, AstraZeneca. C. Dutriaux: Financial Interests, Advisory Board: Bristol Myers Squibb, MSD, Pierre Fabre. S. Piperno-Neumann: Financial Interests, Personal, Advisory Board: Immunocore, Pierre Fabre, Atlanthera. M.J. Rodrigues: Financial Interests, Personal, Invited Speaker: Immunocore; Financial Interests, Personal, Advisory Board: GSK, AstraZeneca; Financial Interests, Institutional, Coordinating PI: Johnson & Johnson; Non-Financial Interests, Institutional, Product Samples: MSD. All other authors have declared no conflicts of interest.

https://doi.org/10.1016/j.annonc.2023.09.2264

1131P Management of metastatic uveal melanoma (MUM) patients on tebentafusp in a real-world setting

M.F. Ribeiro[1], I. Hirsch[1], E.C. Koch[1], L. Mantle[1], T. Pimentel Muniz[1], M. Silveira Vilbert[1], K. Abdulalem[1], D.P. Arteaga Ceballos[1], S. Genta[1], P. Spiliopoulou[1], O. Vornicova[1], C. Fournier[2], E. Giovannetti[1], H. Krema[3], S. Saibil[1], A. Spreafico[1], M.O. Butler[1]

[1]Medical Oncology and Hematology Department, UHN - University Health Network - Princess Margaret Cancer Centre, Toronto, ON, Canada; [2]Dermatology, UHN - University Health Network - Princess Margaret Cancer Centre, Toronto, ON, Canada; [3]Ocular Oncology, UHN - University Health Network - Princess Margaret Cancer Centre, Toronto, ON, Canada

Background: Tebentafusp (TEBE), a bispecific T-cell engager targeting HLA-presented gp100 peptide, was approved for treatment-naïve (TN) MUM HLA-A*02:01+ pts. In its pivotal trial, pts attended weekly outpatient (OP) visits and the duration of premedication was not defined. Additional data on drug administration, safety, and efficacy of a tertiary center may provide insight into optimal premedication and an ideal follow-up schedule in the real-world setting.

Methods: We assessed MUM pts treated with TEBE at our center from Jun/2021-Nov/2022. Data on adverse events (AE), OP visits and discontinuation of premedication were analyzed. Efficacy outcomes included OS, PFS, time-to-TEBE discontinuation (TTD), and best response (BOR - clinician's assessment). Survival was estimated using Kaplan-Meier; categorical variables were analyzed using logistic regression, Chi-square/Fisher's exact tests.

Results: We identified 36 pts. Median age was 64 (30-90); 21 (58.4%) were male. At TEBE initiation, 22 (61%) pts had M1a disease. 20 pts (55.6%) had only 1 metastatic site, and 19 (53%) presented with liver-only disease. Extrahepatic involvement occurred in 17 (47%) pts. 25 pts (69.4%) were TN. Tumor reduction (TR) occured in 5 (14%) and disease control (DC) in 23 (64%) pts. The 1y OS was 68% (median: NR). Median PFS and TTD were, respectively, 6 (95%CI 3.8-8.1) and 9 mo (95%CI 4.6-13.3), with 1y PFS and TTD of 14% and 35.4%. Pts whose BOR was TR or SD had longer TTD when compared with those experiencing PD (12 vs 4 mo, $p<0.01$). All pts developed AE, most frequently rash (n=33), fever (n=23), and pruritus (n=14); 30.5% had G3/4 AE, with rash and hypoxemia occurring in 45% and 27%, respectively. M1a stage was associated with higher DC rate ($p=0.03$) and lower incidence of fever ($p<0.01$); rash was the only factor associated with DC in the multivariate analysis ($p<0.01$). The median number of inpatient doses was 4 (3-18). In the OP setting, 19 pts (53%) were switched to q3 week visits after a median of 6 doses (6-39). For 19 pts (53%), premedications were successfully stopped after a median of 7 doses (4-27).

Conclusions: Our data supports the reduction of OP visits and holding premedication after the resolution of AE. The promising activity of TEBE was confirmed in this cohort mostly comprised of TN pts.

Legal entity responsible for the study: The authors.

Funding: Has not received any funding.

Disclosure: M.F. Ribeiro: Financial Interests, Invited Speaker: Bristol Myers Squibb. S. Saibil: Financial Interests, Advisory Board: Janssen, Novartis, Sanofi, Immunocore; Financial Interests, Funding: Iovance Biotherapeutics. A. Spreafico: Financial Interests, Advisory Board: Merck, Bristol Myers Squibb, Oncorus, Janssen, Medison, Immunocore; Financial Interests, Research Grant: Novartis, Symphogen, Bristol Myers Squibb, AstraZeneca/MedImmune, Merck, Bayer, Surface Oncology, Northern Biologics, Janssen Oncology/Johnson and Johnson, Roche, Regeneron, Alkermes, Array Biopharma/Pfizer, GSK, NuBiyota, Oncorus, Treadwell, Amgen, ALX Oncology, Genentech, Seagen, Servier. M.O. Butler: Financial Interests, Research Grant: Merck, Takara Bio, Novartis; Financial Interests, Advisory Board: Merck, Bristol Myers Squibb, Novartis, Adaptimmune, InstilBio, Iovance, Sun Pharma, GSK, Sanofi, LaRoche Posay, Pfizer, Medison, IDEAYA, Regeneron; Financial Interests, Invited Speaker: Bristol Myers Squibb, Novartis, Sanofi, Pfizer, Merck. All other authors have declared no conflicts of interest.

https://doi.org/10.1016/j.annonc.2023.09.2265

1132P Chemokine expression in uveal melanoma and association with tumor genetics and response to immunotherapy

A. Nallagangula[1], Y. Baca[2], A. Elliott[2], P. Walker[2], F. Abdulla[3], J. Moser[4], Y. Shao[5], J. Lutzky[6]

[1]Hematology Oncology, University of Arizona Cancer Center, Tucson, AZ, USA; [2]Clinical and Translational Research, Caris Life Sciences - Headquarters, Phoenix, AZ, USA; [3]POA, Caris Life Sciences - Headquarters, Phoenix, AZ, USA; [4]Drug Development and Medical Oncology, HonorHealth Research Institute, Scottsdale, AZ, USA; [5]Hematology and Oncology, Wayne State University School of Medicine; Barbara Ann Karmanos Cancer Institute, Detroit, MI, USA; [6]Cutaneous Oncology, University of Miami Sylvester Comprehensive Cancer Center, Miami, FL, USA

Background: Uveal melanoma (UM) is a rare form of melanoma having poor responses to currently available systemic agents. Our goal is to understand differences in chemokine expression in relation to tumor genetics and response to immunotherapy.

Methods: UM patient tumors (N=278, 41 primary, 174 liver mets and 63 other mets) were profiled by NGS DNA/RNA at Caris Life Sciences (Phoenix, AZ). Chemokine expression, high/Low (H/L) defined as samples with >75th- or <25th-percentile of transcripts per million (TPM). Tumor microenvironment (TME) cell fraction estimated by RNA, with median fold changes (H/L) or proportion of samples with non-zero fraction reported (Table). PDL1+ (SP142) tested by IHC. Survival data obtained from insurance claims.

Results: Primary tumors had increased expression of *CXCR4, CXCR1, CXCR2, CCL27* and *CXCL13* compared to liver mets (FC range 1.2-4.2), while *CXCL2* expression was increased in liver mets (2.3, $p<0.01$). In liver mets, increased infiltration of immunosuppressive cells was observed for *CXCR4*-H and *CXCL12*-H tumors(Table). Only M1 macrophages, CD8+ T cells and B cells were increased for *CXCR4*-H and *CXCL12*-H primary tumors. PDL1+ rates were increased in *CXCR4*-H tumors overall (H 36% vs L 13%, $p<0.05$). In liver mets, *SF3B1* mutation was associated with lower *CXCL1* and *CXCL2* expression compared to WT (0.35- and 0.47-fold, respectively, p-<0.01). *BAP1*-mutated liver mets showed increased *CXCL1* expression (2.0-fold, p-0.04), whereas *CCR10* expression was increased in *BAP1*-mutated primary tumors (2.6-fold, p-0.02). Among immunotherapy treated patients with liver mets, there was a trend for improved survival for *CXCL12* H (n=13) vs L (n=12) (HR 0.51 (0.21-1.3), p=0.14) and *CXCR4* H (n=13) vs L (n=12) (HR 0.49 (0.20-1.2), p=0.12) though not significant.

Table: 1132P TME (liver mets): CXCR4/CXCL12 median fold change (H/L) (where median is 0, % non-zero H vs L).

Immune Cell	*CXCR4* Median FC (H/L) or non-zero%	p-value	*CXCL12* Median FC (H/L) or non-zero%	p-value
Monocyte	13% vs 0%	0.01	37% vs 11%	0.31
Treg	2.9	<0.01	2.9	<0.01
T cell CD8	70% vs 28%	<0.01	67% vs 34%	<0.01
T cell CD4	32% vs 13%	0.02	37% vs 11%	0.01
NK cell	1.4	<0.001	1.5	<0.001
Macrophage M2	1.3	0.002	1.3	<0.001
Macrophage M1	92% vs 50%	<0.01	96% vs 49%	<0.001
B cell	1.6	<0.01	1.3	0.02

Conclusions: Our results suggest chemokines are differentially expressed in tumors harboring the common alterations associated with medium risk of distant metastases.

Legal entity responsible for the study: The authors.

Funding: Caris Life Sciences.

Disclosure: Y. Baca, A. Elliott, P. Walker, F. Abdulla: Financial Interests, Institutional, Financially compensated role: Caris Life Sciences. All other authors have declared no conflicts of interest.

https://doi.org/10.1016/j.annonc.2023.09.2266

1133P SF3B1 mutation predicts improved overall survival in metastatic uveal melanoma patients: Molecular and clinical correlates

L.P. del Carpio Huerta[1], M. Varela[2], M. Goma[2], E. Purqueras[2], D. Lorenzo[3], C. Gutierrez[4], A. Slocker[4], J. Caminal[3], J.M. Piulats Rodriguez[1]

[1]Medical Oncology, ICO - Institut Català d'Oncologia l'Hospitalet (Hospital Duran i Reynals), Hospitalet de Llobregat, Spain; [2]Pathology, Hospital Universitari de Bellvitge, Hospitalet de Llobregat, Spain; [3]Ophthalmology, Hospital Universitari de Bellvitge, Hospitalet de Llobregat, Spain; [4]Radiotherapy, ICO - Institut Català d'Oncologia - Hospital Duran i Reynals, Hospitalet de Llobregat, Spain

Background: Metastatic uveal melanoma (MUM) is a rare and lethal disease with varied clinical course. Despite the existence of well-characterized molecular drivers none have been associated with clinical outcomes in MUM. We aimed to study how uveal melanoma genetic alterations affect MUM prognosis.

Methods: From a prospective database of MUM patients, we analysed molecular alterations of primary tumors, including mutations (GNAQ/GNA11 and SF3B1) and chromosomal imbalances (chr3 monosomy (M3),chr8q amplification (+8q), chr8p deletion (-8p),chr8p amplification (+8p), chr1p deletion (-1p), chr6p deletion (-6p), and chr6q amplification (+6q)). Relevant clinical features at the time of MUM diagnosis, such as age, sex, disease-free survival from primary tumor, ECOG score, size of liver metastasis, and levels of LDH, alkaline phosphatase (ALP), bilirubin (BIL), aspartate aminotransferase (AST), alanine aminotransferase (ALT), and gamma-glutamyltransferase (GGT) were recorded. Survival analysis was calculated from MUM diagnosis to death or last follow-up.

Results: Molecular data was obtained from 59 of 119 MUM patients treated at our institution from 2007 to 2022. The mutational driver profile was: 46% GNAQ and 40% GNA11; 42% Q209P and 44% Q209L; 19% SF3B1 mutation being 10% R625H, and 9% R625C. Chromosomal alterations were: M3 81%, +8q 60%, +8p 15%, -8p 12%, -1p 30%, -6q 17%, and +6p 17%. The median overall survival (mOS) for the entire cohort was 16 months(m). Among all genetic alterations, only SF3B1 had a significant impact on mOS: 13m (95% CI 10-15) for wild-type (WT) vs 31.6 m (95% CI 16-46) for mutant (MUT), p=0.01, HR=0.32. Survival probability was higher at 12, 24, and 48m for WT vs MUT (57% vs 81%, 17% vs 70%, and 6% vs 37%). SF3B1 mutation was not statistically associated with any clinical variable. In the multivariate analysis using all clinical variables and SF3B1 status, only DFS ≥2y (HR=2.3), elevated LDH (HR=3.5), elevated ALP (HR=6.1), and SF3B1 MUT (HR=0.2, 95%CI 0.1-0.8, p=0.02) remained significant.

Conclusions: SF3B1 mutation is independently associated with improved OS in MUM patients. Results may affect MUM care, treatment development, and trial stratification. More research is needed to confirm these findings.

Legal entity responsible for the study: The authors.

Funding: Has not received any funding.

Disclosure: All authors have declared no conflicts of interest.

https://doi.org/10.1016/j.annonc.2023.09.2267

1134P Safety and efficacy of low dose (LD) ipilimumab (Ipi) + pembrolizumab (pem) in checkpoint inhibitor (CPI) naïve patients (pts) with melanoma brain metastases (MBM)

I.C. Glitza[1], D. Milton[2], V. Honaker[1], S. Turner[1], T. Hennegan[1], T. Beckham[3], R. Amaria[1], S. Patel[1], A. Diab[1], M. Wong[1], J. Mcquade[1], C. Yee[1], M. Davies[1], E. Burton[1], H.A. Tawbi[1]

[1]Melanoma Medical Oncology Department, The University of Texas MD Anderson Cancer Center, Houston, TX, USA; [2]Biostatistics, The University of Texas MD Anderson Cancer Center, Houston, TX, USA; [3]Radiation Oncology, The University of Texas MD Anderson Cancer Center, Houston, TX, USA

Background: The CPI combination of standard dose (SD) Ipi (3mg/kg) and nivolumab 1mg/kg (N) has dramatically improved outcomes in pts with MBM but is associated with frequent grade (gr) 3/4 adverse events (AEs). In pts without MBM, LD Ipi (at 1mg/kg) + anti-PD1 with N or Pem has demonstrated promising efficacy with reduced toxicity. We hypothesized this approach would have activity in pts with MBM.

Methods: We conducted a phase II, single arm and site trial (NCT03873818) evaluating LD Ipi + Pem in pts with MBM. Pts received up to 4 cycles of LD Ipi + Pem, followed by Pem only. At least 1 MBM >/= 5mm was required. CPI naïve (Cohort A) and prior PD-1 (Cohort B) were allowed. Primary objective included intracranial (IC) benefit rate (CBR) − complete response (CR) + partial response (PR) + stable disease (SD) ≥ 6 months (mos) by mRECIST 1.1. Secondary objectives were overall (OS) and progression free (PFS) survival. Study was terminated early due to accrual challenges. Here we report the efficacy results of cohort A.

Results: A total 19 of a planned 25 (76%) pts were treated in Cohort A. 58% (11) were male, median age was 63 years (23-88), 7 had BRAF V600 mutation. Median number of MBM was 3 (1-20), median diameter of largest MBM 8 mm (5-28). Pts received a median 4 cycles (1-4) of the combination, median total cycles received was 6 (1-35). IC CBR was 58% (32% CR, 11% PR, 16% SD). At a median follow-up of 14.5 mos (0.5-43), median IC PFS was 8.0 mos (95% CI 1.4- not reached) and median OS has not been reached. 11 (58%) pts in cohort A are alive at time of data lock. 25% (4/16) of pts stopped tx due to progression. 7 pts (37%) stopped tx for AEs. 16 pts experienced AEs at least possibly related to tx, most commonly rash (53%), fatigue (42%), and elevated liver enzymes (32%). Gr 3/4 AEs were observed in 6 (32%) pts, including rash (16%), elevated liver enzymes (11%), nausea, pneumonitis, anorexia, and colitis (5% each).

Conclusions: LD Ipi/Pem was well tolerated in CPI naïve pts with MBM, with no new or unexpected AEs, and with promising efficacy. The results support a larger study to confirm benefit.

Clinical trial identification: NCT03873818.

Legal entity responsible for the study: The authors.

Funding: Merck.

Disclosure: I.C. Glitza: Financial Interests, Institutional, Speaker, Consultant, Advisor: Bristol Meyers Squibb, Array, Novartis, Sintetica; Financial Interests, Institutional, Principal Investigator: Bristol Meyers Squibb, Merck, Pfizer. R. Amaria: Financial Interests, Institutional, Principal Investigator: Bristol Meyers Squibb, Iovance, Obsidian, Merck. S. Patel: Financial Interests, Institutional, Principal Investigator: Bristol Meyers Squibb, Foghorn Therapeutics, InxMed, Novartis, Provectus, Reata Pharmaceuticals, TriSalus Life Sciences; Financial Interests, Personal, Advisory Board: Cardinal Health, Castle Biosciences; Financial Interests, Institutional, Other, Data Safety Monitoring Board: Immunocore; Financial Interests, Personal, Speaker, Consultant, Advisor: Advance Knowledge in Healthcare. A. Diab: Financial Interests, Institutional, Principal Investigator: Bristol Meyers Squibb. M. Wong: Financial Interests, Institutional, Advisory Board: Merck, Pfizer, Bristol Myers Squibb, Regeneron, EMD-Serono, ExiCure, Castle Biosciences. J. Mcquade: Financial Interests, Institutional, Speaker, Consultant, Advisor: Merck; Financial Interests, Personal, Other, Honorarium: Bristol Myer Squibb, Roche. C. Yee: Financial Interests, Institutional, Speaker, Consultant, Advisor: Grey Wolf Therapeutics, Immatics, RootPath, T-Cypher Bio, GenomeFrontier Therapeutics, Achelios Oncology. M. Davies: Financial Interests, Institutional, Speaker, Consultant, Advisor: Roche/Genentech, Array, Pfizer, Novartis, Bristol Meyers Squibb, GSK, Sanofi-Aventis, Vaccinex, Apexigen, Eisai, ABM Therapeutics; Financial Interests, Institutional, Principal Investigator: Roche/Genentech, GSK, Sanofi-Aventis, Merck, Myriad, Oncothyreon. H.A. Tawbi: Financial Interests, Institutional, Speaker, Consultant, Advisor: Bristol Meyers Squibb, Genentech, Novartis, Merck, Boxer Capital, Karyopharm, Iovance, Eisai Jazz, Medicenna; Financial Interests, Institutional, Principal Investigator: Bristol Meyers Squibb, Novartis, Merck, Genentech, GSK, EMD Serono, Eisai, Dragonfly Therapeutics, RAPT Therapeutics. All other authors have declared no conflicts of interest.

https://doi.org/10.1016/j.annonc.2023.09.2268

1135P Comparison of intracranial (IC) response assessment criteria in patients (pts) with melanoma brain metastases (MBM) treated with combination nivolumab (NIVO) plus ipilimumab (IPI) in CheckMate 204

R. Huang[1], G. Youssef[2], T. Nelson[2], P. Wen[2], P. Forsyth[3], F.S. Hodi[4], K.A. Margolin[5], A.P. Algazi[6], O. Hamid[7], C.D. Lao[8], M.S. Ernstoff[9], S.J. Moschos[10], M.B. Atkins[11], M. Postow[12], D.A. Reardon[2], D.J. Grootendorst[13], M. Askelson[13], C. Ritchings[14], H.A. Tawbi[15]

[1]Department of Radiology, Brigham and Women's Hospital, Boston, MA, USA; [2]Center for Neuro-Oncology, Dana-Farber Cancer Institute, Boston, MA, USA; [3]Department of Neuro-Oncology, Moffitt Cancer Center, Tampa, FL, USA; [4]Medical Oncology, Massachusetts General Hospital, Boston, MA, USA; [5]Department of Medical Oncology, Saint John's Cancer Institute, Santa Monica, CA, USA; [6]Department of Medicine, UCSF Helen Diller Family Comprehensive Cancer Center, San Francisco, CA, USA; [7]Research Department, Cedars-Sinai-The Angeles Clinic and Research Institute, Los Angeles, CA, USA; [8]Department of Dermatology, University of Michigan Comprehensive Cancer Center, Ann Arbor, MI, USA; [9]Department of Immuno-Oncology, Division of Cancer Treatment and Diagnosis, National Cancer Institute at the National Institutes of Health, Rockville, MD, USA; [10]Medical Oncology, University of North Carolina Lineberger Comprehensive Cancer Center, Chapel Hill, NC, USA; [11]Department of Medical Oncology, Georgetown Lombardi Comprehensive Cancer Center, Washington, DC, USA; [12]Medicine, Memorial Sloan Kettering Cancer Center, New York, NY, USA; [13]Medical Oncology, Bristol Myers Squibb, Princeton, NJ, USA; [14]Medical, Bristol Myers Squibb, Princeton, NJ, USA; [15]Melanoma Medical Oncology Department, The University of Texas MD Anderson Cancer Center, Houston, TX, USA

Background: In CheckMate 204, NIVO + IPI showed high IC mRECIST objective response rates (ORRs) in pts with asymptomatic, unirradiated MBM and a lower but durable response in pts with symptomatic and/or steroid-requiring MBM. Response as a surrogate for progression-free survival (PFS)/overall survival (OS) has prompted the use of various response assessment criteria and cutoffs for target lesion size in MBM. In this exploratory analysis, ORRs and correlation of response to survival were examined by mRECIST, RANO-BM, RECIST, and volumetric response.

Methods: Pts with metastatic melanoma and ≥ 1 unirradiated MBM (diameter, 0.5−3 cm) received NIVO 1 mg/kg + IPI 3 mg/kg Q3W × 4, followed by NIVO 3 mg/kg Q2W for ≤ 24 mo. IC ORRs were assessed using mRECIST (5 mm target lesion cutoff), RECIST (10 mm), RANO-BM (5 or 10 mm), and volumetric response (5 or 10 mm), per blinded review. IC PFS and OS using a 6-wk landmark were compared for responders vs nonresponders.

Results: IC ORR was numerically higher with mRECIST or volumetric assessment compared with RANO-BM or RECIST (Table). Responder vs nonresponder PFS and OS were significantly better across the different assessment criteria; mRECIST and volumetric response showed the strongest correlations (Table). mRECIST responders who were not RANO-BM 5 mm responders (n = 14) had similar OS to RANO-BM 5 mm responders. Among 41 pts with only target lesions < 10 mm, mRECIST ORR, and OS for the responders, was similar to the overall CheckMate 204 ITT population.

Conclusions: This analysis supports mRECIST as a reliable assessment scale by showing strong differentiation of long-term benefit for responders vs nonresponders. Volumetric response also correlated with PFS/OS supporting future trial exploratory use. Responders with only MBM < 10 mm derived comparable PFS/OS benefit to ITT, supporting the inclusion of pts with smaller MBM in future trials.

Table: 1135P

	All pts (n = 119)					
	mRECIST 5 mm	RECIST 10 mm	RANO-BM 5 mm	RANO-BM 10 mm	Volumetric[b] 5 mm	Volumetric[b] 10 mm
ORR, % (95% CI)	45 (36–55)	27 (19–36)	34 (26–44)	26 (18–35)	40 (31–50)	39 (31–49)
PFS HR,[a] (95% CI)	0.06 (0.02–0.16)	0.18 (0.06–0.56)	0.13 (0.06–0.29)	0.25 (0.11–0.59)	0.04 (0.01–0.11)	0.07 (0.03–0.19)
OS HR,[a] (95% CI)	0.18 (0.07–0.45)	0.22 (0.07–0.75)	0.26 (0.10–0.71)	0.34 (0.12–1.00)	0.10 (0.03–0.35)	0.11 (0.03–0.36)

[a]Responder vs nonresponder; Cox proportional hazard model was used for hazard ratio (HR) calculation. [b]Volumetric response was defined as a 65% decrease in target lesions and progression as a 73% increase.

Clinical trial identification: NCT02320058.

Editorial acknowledgement: Professional medical writing and editorial assistance were provided by Melissa Kirk, PhD, and Michele Salernitano of Ashfield MedComms, an Inizio company, and funded by Bristol Myers Squibb.

Legal entity responsible for the study: Bristol Myers Squibb.

Funding: Bristol Myers Squibb.

Disclosure: R. Huang: Financial Interests, Personal, Advisory Board: Vysioneer; Financial Interests, Personal, Other, Consultant: Nuvation Bio; Financial Interests, Institutional, Research Grant: Bristol Myers Squibb. P. Forsyth: Financial Interests, Personal, Speaker, Consultant, Advisor: Novocure, AbbVie, BTG, Ziopharm Oncology, Tocagen, Boehringer Ingelheim, BMS, National Brain Tumor Society, Novartis, Midatech Pharma; Financial Interests, Personal, Research Grant: Department of Defense, Pfizer, Bankhead-Coley Cancer Research, Florida Academic Cancer Center Alliance, NIH, NCI, BMS, MSCCoE, Florida Breast Cancer Foundation; Financial Interests, Personal, Financially compensated role: AbbVie, NIH, BTG, Inovio Pharmaceuticals, Physical Sciences Oncology Network, NCI, Bayer, National Cancer Research Institute, BMS, NCCN. F.S. Hodi: Financial Interests, Personal, Other, Consultant: BMS, Merck, Novartis, Genentech/Roche, CatalYm, Immunocore, Kairos, Zumator, Corner Therapeutics, Curis, AstraZeneca; Financial Interests, Personal, Advisory Board: BioEntre, Iovance, Rheos; Financial Interests, Institutional, Research Grant: BMS, Novartis; Financial Interests, Personal, Advisory Board, equity: Apricity, Bicara, Checkpoint Therapeutics. K.A. Margolin: Financial Interests, Personal, Coordinating PI, PI and advisor, Ph IIb study of CD8 PET tracer: ImaginAb; Financial Interests, Personal, Other, Consultant on ad hoc basis: Werewolf, Xilio; Financial Interests, Personal, Other, DSMB: Iovance, Elicio; Financial Interests, Institutional, Local PI, Industry-sponsored trial: Regeneron; Financial Interests, Institutional, Local PI, Industry-sponsored trial: Agenus, Moderna, Medicenna. A.P. Algazi: Financial Interests, Personal, Advisory Board: OncoSec, Onchilles, Sensei, Bluesphere, Tentarix, Venn, IAG, WWCT, Ascendis; Financial Interests, Personal, Stocks/Shares: Valitor, OncoSec, Sensei, Onchilles; Financial Interests, Personal, Local PI: BMS, Merck, AstraZeneca, Incyte, Ascendis, Genentech, Vaccinex; Financial Interests, Institutional, Research Grant: BMS, Merck, AstraZeneca, Incyte, Ascendis, Genentech, Vaccinex. O. Hamid: Financial Interests, Personal, Advisory Board: Alkermes, Amgen, BMS, Bactonix, Beigene, Bioatla, Eisai, GSK, Georgiamune, GigaGen, Grit Bio, IO Biotech, Idera, Idera, Immunocore, Incyte, Instil Bio, Iovance, Janssen, KSQ, Merck, Nextcure, Novartis, Obsidian, Pfizer, Roche Genentech, Seagen, Sanofi-Regeneron, Tempus, Vial, Zelluna; Financial Interests, Personal, Invited Speaker: BMS, Immunocore, Novartis, Pfizer, Sanofi/Regeneron; Financial Interests, Personal, Stocks/Shares: Bactonix; Financial Interests, Institutional, Local PI: Aduro, Akeso, Amgen, Arcus, BMS, Bioatla, CytomX, Exelixis, GSK, Idera, Immunocore, Incyte, Iovance, Merck, Merck Serono, Moderna, Nextcure, Novartis, Pfizer, Roche Genentech, Rubius, Seagen, Sanofi/Regeneron, Torque, Zelluna. C.D. Lao: Financial Interests, Personal, Advisory Board: BMS; Financial Interests, Institutional, Local PI, Research funding: BMS, Novartis, Genentech, OncoSec. M.B. Atkins: Financial Interests, Personal, Advisory Board: BMS, Merck, Novartis, Eisai, Aveo, Pfizer, Werewolf, Fathom, Pyxis Oncology, PACT, Elpis, X4Pharma, ValoHealth, ScholarRock, Surface, Takeda, Roche, SAB Bio, Exelixis, Iovance, COTA, Idera, Agenus, Asher Bio, AstraZeneca, Calithera, Seagen, Sanofi, OncoRe; Financial Interests, Personal, Stocks/Shares: Werewolf, Pyxis Oncology; Financial Interests, Institutional, Coordinating PI: BMS, Merck, Agenus. M. Postow: Financial Interests, Personal, Advisory Board: BMS, Chugai, Merck, Nektar, Pfizer; Financial Interests, Institutional, Coordinating PI: BMS; Financial Interests, Institutional, Local PI: Merck, Novartis. D.A. Reardon: Financial Interests, Personal, Advisory Board: Agios, AnHeart Therapeutics, Avita Biomedical, Blue Rock Therapeutics, Bristol Myers Squibb, Boston Biomedical, CureVac AG, Del Mar Pharma, DNATrix, Hoffmann-LaRoche, Ltd., ImVax, Janssen, Kiyatec, Medicenna, Neuvogen, Novartis, Novocure, Pyramid, Sumitomo Dainippon, Vivacitas Oncology, Inc-Y-Mab Therapeutics; Financial Interests, Institutional, Research Grant: Agenus, Bristol Myers Squibb, Celldex, EMD Serono, Enterome, Epitopoietic Research Corporation, Incyte, Insightec, Novartis, Omniox, Tragara; Financial Interests, Institutional, Coordinating PI: Inovio, Merck. D.J. Grootendorst: Financial Interests, Personal, Full or part-time Employment, Employee of Bristol Myers Squibb: Bristol Myers Squibb; Financial Interests, Personal, Stocks/Shares: Bristol Myers Squibb. M. Askelson, C. Ritchings: Financial Interests, Personal, Full or part-time Employment: BMS; Financial Interests, Personal, Stocks/Shares: BMS. H.A. Tawbi: Financial Interests, Personal, Advisory Board: Bristol Myers Squibb, Merck, Novartis, Genentech, Eisai, Karyopharm, Iovance, Pfizer, Jazz Pharmaceuticals; Financial Interests, Institutional, Trial Chair: Bristol Myers Squibb; Financial Interests, Institutional, Local PI: Merck, RAPT Pharmaceuticals; Financial Interests, Institutional, Steering Committee Member: Novartis, Genentech; Financial Interests, Institutional, Funding: GSK, Eisai. All other authors have declared no conflicts of interest.

https://doi.org/10.1016/j.annonc.2023.09.2269

1136P Regorafenib combined with BRAF-/MEK-inhibitors for the treatment of refractory melanoma brain metastases

I. Dirven, A-S. Vander Mijnsbrugge, J. Tijtgat, M. Vounckx, B. Neyns

Department of Medical Oncology, Vrije Universiteit Brussel (VUB), Universitair Ziekenhuis Brussel (UZ Brussel), Jette, Belgium

Background: There are no active treatment options for patients (pts) with progressive melanoma brain metastases (MBM) who have failed treatment with immune checkpoint blockade (ICB) and BRAF-/MEK-inhibitors (BRAF/MEKi). Regorafenib (REGO), an oral multi-target kinase inhibitor (incl. inhibition of RAF-dimers), has single-agent activity in pretreated melanoma (VD Mijnsbrugge et al. SMR 2022).

Methods: We report our single center retrospective review of prospectively registered pts with refractory MBM treated with REGO and BRAF/MEKi.

Results: 17 pts with stage IV-M1d melanoma were included (8F; med age 54y [33-75]; WHO PS: 0/1/2/3 resp. n=3/6/6/2 pts; 13 pts BRAFmt (12 BRAF V600mt, 1 BRAF fusion), 4 pts NRAS Q61mt). All pts previously progressed on ICB, BRAF/MEKi (all BRAFmt pts), chemotherapy (4 pts), T-VEC (2 pts), REGO mono (3 pts), and REGO + ICB (2 pts). At baseline, 15 pts had active MBM (8 pts were on steroids); 4 pts had intracranial evaluable disease only. BRAFmt pts were treated with REGO (40-80 mg QD) combined with BRAF/MEKi, NRASmt pts with REGO + MEKi (+ low-dose BRAFi to mitigate skin toxicity). There were no grade $\geq$4 TRAE. Grade 3 TRAE included arterial hypertension (n=4), and hepatotoxicity (n=2). None of the 2 pts without active MBM at baseline progressed intra-cranially. The best objective intracranial response (according to RANO-BM) in 17 response evaluable pts was: PR in 5 pts (29%; incl. 4 BRAFmt pts), and SD in 5 pts (29%; incl. 4 BRAFmt pts). In 5 pts intra- and extracranial disease control (PR, SD) were concordant. 3 pts with PR intra- had SD extra-cranially; 2 pts with SD intra- had PD extra-cranially. Assuming a potential clinical benefit of therapy beyond first PD, 10 out of 16 progressive pts continued treatment and remained clinically stable for an additional 3-48 weeks (w) (median 7w). Median time on REGO+BRAF/MEKi in BRAFmt pts was 13w [range 3-62], and 27.5w [range 3-56] on REGO + MEKi in NRASmt pts. In 3 pts treatment is ongoing (9-62w after initiation). Median PFS and OS is resp. 8.4w and 24.6w in BRAFmt pts; 8.6w and 10.1w in NRASmt pts.

Conclusions: In heavily pretreated patients with refractory MBM, REGO combined with BRAF/MEKi demonstrated promising anti-tumor activity. Further investigation in a prospective trial is warranted.

Legal entity responsible for the study: Bart Neyns.

Funding: Has not received any funding.

Disclosure: I. Dirven: Non-Financial Interests, Institutional, Product Samples, Drug support only for investigator-sponsored single-centre clinical trial: Bayer; Non-Financial Interests, Institutional, Non-financial benefits, Travel, accommodation, and expenses: AstraZeneca. J. Tijtgat: Financial Interests, Institutional, Advisory Board: Novartis. B. Neyns: Financial Interests, Institutional, Advisory Board: Novartis, Bristol Myers Squibb, Pierre Fabre, MSD (Merck Sharp & Dohme); Financial Interests, Institutional, Research Grant: Novartis, Pfizer; Non-Financial Interests, Institutional, Product Samples: Bayer. All other authors have declared no conflicts of interest.

https://doi.org/10.1016/j.annonc.2023.09.2270

1137P Treatment strategies and survival outcomes in a nationwide, population-based cohort of patients with melanoma brain metastases: The role of planned shift in systemic therapy and postoperative stereotactic radiotherapy

S. Pedersen[1], E.L. Johansen[2], K. Højholt[3], M.H. Wett[3], A.M. Mogensen[4], S.K. Petersen[2], R.B. Friis[3], M. Donia[1], C.A. Haslund[4], H. Schmidt[3], L. Bastholt[2], I-M. Svane[1], E. Ellebæk[1]

[1]Department of Oncology, Herlev Hospital - National Center for Cancer Immune Therapy (CCIT-DK), Herlev, Denmark; [2]Dept. of Oncology, OUH - Odense University Hospital, Odense, Denmark; [3]Department of Oncology, Aarhus University Hospital, Aarhus, Denmark; [4]Department of Oncology, Aalborg University Hospital, Aalborg, Denmark

Background: Modern therapies have significantly improved outcome for patients with melanoma brain metastases (MBM). Still, the prognosis is poor, and the optimal treatment strategy is not well defined. Here, we report on the survival outcomes of systemic and locoregional treatments in an unselected, nationwide population-based cohort of patients with MBM.

Methods: All patients diagnosed with MBM in Denmark between 2015-2022 were retrospectively included. Patients were identified using the Danish Metastatic Melanoma Database (DAMMED) and local records of surgery and radiotherapy. Data were obtained from patient records.

Results: A total of 838 patients were included. Median overall survival (mOS) of the entire cohort was 9.0 months, and 112 patients were alive >3 years after diagnosis of MBM. Treatment with immune checkpoint inhibitors (ICI), ipilimumab + nivolumab, resulted in an intracranial overall response rate (icORR) of 46%, and a 2-year OS of 49% whereas BRAF/MEK-inhibitors (BRAF/MEKi) resulted in an icORR of 56%, and 2-year OS of 20%. A subgroup of patients with symptomatic MBM, treated initially with BRAF/MEKi with planned shift to ICI, had an icORR of 70%, 2-year OS of 50% and reached the longest mOS of 26 months. Patients with meningeal carcinomatosis (n=67) had a mOS of 8.4 months. Systemic therapy significantly improved OS for these patients, but no survival benefit was observed for patients receiving ICI compared to BRAF/MEKi. In total, 230 patients underwent surgery for MBM; of these, 30 received postoperative stereotactic radiosurgery (SRS). Baseline characteristics were balanced between the two groups. No benefit in OS or intracranial progression free survival was observed for patients receiving postoperative SRS.

Conclusions: Modern systemic therapies have improved survival for real-world patients with MBM; BRAF/MEKi had the highest icORR while ICI generated more durable responses. Planned shift from BRAF/MEKi to ICI can lead to long-term survival in selected patients. Postoperative SRS for patients undergoing surgery for MBM is questioned as a standard procedure.

Legal entity responsible for the study: The authors.

Funding: Has not received any funding.

Disclosure: R.B. Friis: Non-Financial Interests, Personal, Other, Travel and conference expenses: MSD. M. Donia: Financial Interests, Personal, Invited Speaker, Teaching: Novartis, Roche; Financial Interests, Personal, Other, Advisor: Achilles Therapeutics; Non-Financial Interests, Other, Sub-investigator of clinical trial with connected translational research: Bristol Myers Squibb; Non-Financial Interests, Personal, Proprietary Information, Proprietary data access: Bristol Myers Squibb; Non-Financial Interests, Personal, Proprietary Information, Proprietary Data Access: Genentech; Other, Chairman of the Melanoma and Non-melanoma Skin Cancer Scientific Committee: Danish Medicines Council (Medicinrådet). C.A. Haslund: Financial Interests, Personal, Invited Speaker: MSD, GSK, BMS; Financial Interests, Institutional, Local PI: BMS, Tesaro, MSD, IO Biotech, Chimerix, Incyte; Financial Interests, Institutional, Coordinating PI: GSK, Celgene Aps. H. Schmidt: Other, Institutional, Other: Danish Medicines Council, Member of the Melanoma and Non-Melanoma Skin Cancer Scientific Committee. L. Bastholt: Non-Financial Interests, Advisory Role, Scientific committee under Danish Medicines Agency regarding new Treatments of Melanoma, Skin Cancer and Thyroid Cancer: Danish Medicines Agency. I. Svane: Financial Interests, Personal, Advisory Board: BMS, Pierre Fabre, Novartis; Financial Interests, Personal, Invited Speaker: MSD, Pierre Fabre, Novartis, Roche, BMS; Financial Interests, Personal, Writing Engagement: MSD; Financial Interests, Personal, Stocks/Shares, Cofounder and Founder Warrants: IO Biotech; Financial Interests, Institutional, Research Grant: Adaptimmune, Enara Bio, Lytix Biopharma, TILT Biotherapeutics; Financial Interests, Institutional, Funding: Evaxion; Non-Financial Interests, Principal Investigator: BMS, Novartis, Roche, TILT Biotherapeutics, Lytix Biopharma. E. Ellebæk: Financial Interests, Personal, Invited Speaker: Pierre Fabre, BMS, Novartis, MSD, Pfizer; Other, Travel and conference expenses: MSD, Pierre Fabre. All other authors have declared no conflicts of interest.

https://doi.org/10.1016/j.annonc.2023.09.2271

1138P Intralesional administration of L19IL2/L19TNF in difficult-to-treat non-melanoma skin cancer shows a favorable safety profile and preliminary clinical activity

L. Flatz[1], U. Leiter-Stoppke[1], F. Meraz-Torres[2], F. Wolfsperger[2], A. Meiwes[2], N. Wagner[3], L. Nadal[4], E. Puca[4], G. Elia[5], A. Covelli[5], D. Neri[6], C. Antonio[7], T.M.S. Amaral[2]

[1]Department of Dermatology, University Hospital Tuebingen, Tuebingen, Germany; [2]Dermato-Oncology Department, Skin Cancer Clinical Trials Center, University of Tuebingen, Tuebingen, Germany; [3]Dermatology, Kantonsspital St. Gallen, St. Gallen, Switzerland; [4]Philogen, Sovicille, Italy; [5]Clinical Dept., Philochem AG, Otelfingen, Switzerland; [6]Chemistry and Applied Biosciences Department, Philogen S.p.A. - Administrative Office, Sovicille, Italy; [7]Dermatology, Cantonal Hospital, St. Gallen, Switzerland

Background: Non-melanoma skin cancers (NMSC), including squamous cell carcinoma (SCC) and basal cell carcinoma (BCC), are the most common forms of skin cancer, with a rising incidence due to deficient sun protection and growing life expectancy. Treatment options include surgery, radiotherapy, immunotherapy, targeted therapy, or chemotherapy. Surgery typically offers high cure rates; however, surgery's suitability and/or effectiveness in certain patients (pts) may be limited by disease factors (location, functional and cosmetic impairment) or pts factors (age, comorbidities, personal preferences). Initial intralesional treatment with immunostimulatory drugs may be another therapeutic approach, potentially curing NMSC or making surgery less invasive. Here we investigate a combination of 2 immune cytokines (Bifikafusp alfa (L19IL2) and Onfekafusp alfa (L19TNF) targeting the extra domain B of fibronectin (EDB) for selective delivery of immunostimulatory payloads to the tumor site. EDB is virtually absent in healthy adult tissues but highly expressed in tumors, including NMSC.

Methods: In a single-arm, ongoing, phase II study (NCT04362722), pts with locally advanced, non-metastatic, node-negative, single or multifocal NMSC, not eligible for surgery or radiotherapy or who refuse it, are treated with 4 weekly intratumoral administrations of L19IL2/IL19TNF. 14 pts (11 BCC and 3 cSCC) have been treated and are evaluable for safety and efficacy.

Results: Administration of L19IL2/L19TNF was well tolerated with no grade 4-5 adverse events (AE). The most common treatment-related AEs were flu-like symptoms (36.4%), pyrexia (27.3%), face edema, chills, and injection site reaction (13.6%), all transient, managed with symptomatic therapy. In BCC cohort, ORR was assessed on day 36 with a 27.3% RR. In the follow-up, 5/11pts achieved pathological complete response (pCR) with an average time to pCR of 66 days from the first administration. In the 3 SCC pts, ORR was 33.3 % with 1 pCR.

Conclusions: The tolerable safety profile of L19IL2/L19TNF and the results obtained in pts with NMSC justify further exploring the potential of intralesional administration of immunostimulatory drugs in this setting.

Clinical trial identification: EudraCT 2020-003299-42, NCT 04362722.

Legal entity responsible for the study: Philogen SpA.

Funding: Philogen SpA.

Disclosure: L. Flatz: Financial Interests, Personal, Stocks or ownership: Hookipa Pharma; Financial Interests, Personal, Invited Speaker: BMS, Novartis, Sanofi; Financial Interests, Personal, Advisory Board: BMS, Novartis, Sanofi, Philogen; Financial Interests, Institutional, Research Funding: Hookipa Pharma; Financial Interests, Personal, Royalties: Hookipa Pharma. U. Leiter-Stoppke: Financial Interests, Institutional, Research Grant: MSD; Financial Interests, Personal, Invited Speaker: MSD, Novartis, Sun Pharma, Allmiral Hermal, Sanofi; Financial Interests, Personal, Other, Travel Support: Sun Pharma; Financial Interests, Personal, Advisory Board: MSD, Novartis, Sun Pharma, Allmiral Hermal, Sanofi; Financial Interests, Personal, Member, Board member: ADO (DECOG). N. wagner: Financial Interests, Personal, Speaker, Consultant, Advisor: Novartis, Sanofi; Financial Interests, Personal, Advisory Board: Pierre Fabre; Other, Personal and Institutional, Principal Investigator: Sanofi, Regeneron, Pierre Fabre, Philogen; Other, Personal, Member: SITC; Financial Interests, Personal, Other, Travel Support: Amgen. L. Nadal, E. Puca, G. Elia: Financial Interests, Personal, Officer, Employee: Philogen S.p.A. A. Covelli: Financial Interests, Personal, Other, Member of the Scientific Board: Cellestia Biotech AG, Basel, Italfarmaco S.p.A., Milano, Peptomyc S.L, Barcelona; Financial Interests, Personal, Officer, Chief Medical Officer: Philogen S.p.A., Siena. D. Neri: Financial Interests, Personal, Member of Board of Directors: Philogen S.p.A; Financial Interests, Personal, Stocks or ownership: Philogen S.p.A. C. Antonio: Financial Interests, Personal, Advisory Board: AbbVie, Sanofi, Eli Lilly, Philogen. T.M.S. Amaral: Financial Interests, Personal, Writing Engagement: CeCaVa; Financial Interests, Personal, Invited Speaker: BMS, Novartis, Pierre Fabre; Financial Interests, Institutional, Funding: Novartis, Neracare, Sanofi, Skyline-Dx; Financial Interests, Institutional, Research Grant: Novartis, iFIT; Financial Interests, Institutional, Local PI: IO Biotech, MSD, University Hospital, Essen, Roche; Financial Interests, Institutional, Coordinating PI: Unicancer; Non-Financial Interests, Member: Portuguese Society for Medical Oncology, ASCO; Other, Clinical expert: Infarmed. All other authors have declared no conflicts of interest.

https://doi.org/10.1016/j.annonc.2023.09.2272

1139P Final results of a phase II study of pembrolizumab as first-line treatment in advanced cutaneous squamous cell carcinomas (CSCCs)

E. Maubec[1], M. Boubaya[2], L. Deschamps[3], M. Beylot-Barry[4], P. Petrow[5], I. Scheer-Senyarich[1], N. Basset-Seguin[6], C. Gaudy Marqueste[7], G. Quereux[8], C. Bloch-Queyrat[9], M-T. Leccia[10], A. Stefan[11], P. Saiag[12], F. Grange[13], N. Meyer[14], S. Dalac Rat[15], C. Alloux[16], I. Lopez[17], A. Tibi[16], V. Levy[18]

[1]Dermatology Department, Hopital Avicenne AP-HP, Bobigny, France; [2]Unité de Recherche Clinique, Hopital Avicenne AP-HP, Bobigny, France; [3]Pathology, Hôpital Bichat APHP, Paris, France; [4]Dermatology Department, CHU Bordeaux - Hopital St. André, Bordeaux, France; [5]Radiology, Polyclinique Saint Côme, Compiegne, France; [6]Dermatology Oncologist, Hopital Saint Louis AP-HP, Paris, France; [7]Dermatology Department, AP-HM - CHU La Timone Enfants, Marseille, France; [8]Dermatology, CHU du Nantes - Hôtel-Dieu, Nantes, France; [9]Resarch Clinic Unit, Hôpital Avicenne AP-HP, Bobigny, France; [10]Dermatology, CHU Grenoble Alpes - Site Nord (La Tronche), La Tronche, France; [11]Dermatology, CHU de Caen - Hôpital Cote de Nacre, Caen, France; [12]Dermatology and Oncology Department, Hôpital Ambroise Pare AP-HP, Boulogne-Billancourt, France; [13]Dermatology, Centre Hospitalier de Valence, Valence, France; [14]Dermatology, Centre Hospitalier Universitaire de Toulouse - Hôpital Larrey, Toulouse, France; [15]Dermatology, CHU Dijon, Dijon, France; [16]Pharmacy, APHP, Agence Générale des Equipements et Produits de Santé, Paris, France; [17]Radiology, Polyclinique Saint Côme - Association de Cabinet de Radiologie et d'Imagerie Medicale, Compiègne, France; [18]Clinical Research, Hôpital Avicenne, Bobigny, France

Background: In the CARSKIN study (NCT02883556), first line pembrolizumab demonstrated promising activity and manageable safety in patients (pts) with advanced CSCC. Here we report BOR and survival endpoints.

Methods: Eligible pts with unresectable locally advanced or metastatic CSCC received pembrolizumab. The imaging assessment per RECIST v1.1 was blinded with independent central review. Objectives were BOR, PFS, DOR, OS, and safety in the ITT population; exploratory objectives were BOR and survival endpoints by PD-L1 status in the PP population excluding 2 untreated pts, 1 early non related death and 3 pts tested only with 1 assay. PD-L1 status was centrally assessed by 2 blinded independent pathologists, one using the anti—PD-L1 E1L3N clone (TPS_{E1L3N}), the other using the 22C3 antibody (TPS_{22C3} and CPS_{22C3}) with a cutoff of 1%.

Results: With a median follow-up of 26 mo, BOR was 47% with 15 PR (26%) and 12 CR (21%); 1y-PFS and OS were 49% and 72% (Table). BOR was significantly higher in PD-L1+ pts than in PD-L1 − pts using TPSE1L3N (p=0.02) or CPS22C3 (p=0.038) but not TPS22C3 (p=0.76). The optimal cutoff of CPS22C3 for BOR using a ROC curve was estimated to be ≥ 7% (Se=0.70, Sp=0.75). Pts with PD-L1+ CSCCs have a significantly better 1y-PFS using TPSE1L3N (p=0.004) but not CPS22C3 and a better 1y-OS with both antibodies (p<0.03). Severe TRAEs occurred in 10 patients (17.5%); 1 pt died of a fatal 2nd aggressive HNSCC.

Table: 1139P

Outcome [95%CI]	ITT population #57	PP population #51	TPS (EILN3)		CPS (22C3)	
			PD-L1+ pts #40	PD-L1− pts #11	PD-L1+ pts #41	PD-L1− pts #10
Best ORR	47% [34-61]	51% [34-62]	60% [43-75]	18% [2-52]	59% [42-74]	20% [3-56]
Median PFS	10.1 [4.8-NR]	13.7 [4.6 -NR]	19.6 [6.1-NR]	2.1 [1.9-NR]	13.8 [5.6-NR]	4.3 [2.0-NR]
1y-PFS	49% [37-64]	50% [38-66]	57% [43-72]	27% [10-72]	53% [39-71]	40% [19-86]
Median OS	25.3 [16.5-NR]	25.3 [16.5-NR]	NR	10.0 [4.0-NR]	NR	10.0 [2.0-NR]
1y-OS	72% [61-85]	73% [61-86]	82% [70-95]	42% [20-87]	79% [67-93]	50% [27-93]
Median DOR	NR	NR	NR	5.6 [5.6-NR]	NR	NR
1y-DOR	79% [65-97]	80% [65-97]	83 [69-100]	50 [13-100]	78 [62-97]	100

Conclusions: Our data confirm promising activity of P in first line treatment of CSCC with a manageable side effect profile. $CPS_{22C3} \geq 7\%$ appeared equivalent to $TPS_{E1L3N} \geq 1\%$ for predicting BOR and OS.

Clinical trial identification: NCT02883556.

Legal entity responsible for the study: AP-HP.

Funding: MSD.

Disclosure: E. Maubec: Financial Interests, Institutional, Funding: MSD; Financial Interests, Personal, Speaker, Consultant, Advisor: Sanofi, Pierre Fabre; Financial Interests, Personal, Other: Novartis. P. Petrow, I. Lopez: Other: GE Healthcare, Guerbet. F. Grange: Financial Interests, Institutional, Advisory Board: MSD, BMS. S. Dalac Rat: Financial Interests, Speaker, Consultant, Advisor: BMS, MSD, PFO, Novartis; Non-Financial Interests, Other: BMS, MSD, PFO, Novartis. All other authors have declared no conflicts of interest.

https://doi.org/10.1016/j.annonc.2023.09.2273

1140P Cemiplimab versus historical systemic treatments for locally advanced (la) or metastatic (m) cutaneous squamous cell carcinomas (CSCC): Results from the French study TOSCA

E. Gerard[1], C. Lebbe[2], E. Lanoy[3], G. Quereux[4], P. Bernard[5], M-A. Viguier[6], N. Meyer[7], L. Mortier[8], M. Dinulescu[9], D. Legoupil[10], E.M. Neidhardt[11], P. Saiag[12], S. Trabelsi-Messai[13], P. Celerier[14], C. Nardin[15], E. Maubec[16], E. Hainaut Wierzbicka[17], S. Perrier[18], S. Garnier[19], C. Robert[20]

[1]Department of Dermatology-Oncology, Hopital St. André, Bordeaux, France; [2]Department of Dermatology, Université Paris Cité APHP Hôpital Oncodermatologie Saint-Louis, INSERM U976, Paris, France; [3]AP-HP-Service d'Immunologie Clinique, Hôpital Européen Georges-Pompidou AP-HP, Paris, France; [4]Department of Dermatology, CHU Nantes, Nantes, France; [5]Department of Dermatology, CHU Dupuytren, Limoges, France; [6]Department of Dermatology-Venereology, Hôpital Robert Debré, Reims, France; [7]Department of Dermatology-Venereology, Clinique Médipôle Garonne, Toulouse, France; [8]Department of Dermatology, CHU de Lille, Lille, France; [9]Department of Melanomas and Skin Tumors, Centre Eugène Marquis, Rennes, France; [10]Department of Dermatology-Venereology, CHRU Brest - Hôpital Morvan, Brest, France; [11]Department of Medical Oncology, Centre Léon Bérard, Lyon, France; [12]Department of Dermatology and Oncology, Hôpital Ambroise Paré, Boulogne-Billancourt, France; [13]Department of Dermatology-Venereology, CHU Grenoble, La Tronche, France; [14]Department of Dermatology, CH La Rochelle, La Rochelle, France; [15]Department of Dermatology, Centre Hospitalier Universitaire and Université Franche Comté, Inserm 1098 RIGHT, Besancon, France; [16]Department of Dermatology, Hôpital Avicenne, Bobigny, France; [17]Department of Dermatology, CHU Jean Bernard, Poitiers, France; [18]HEOR, Sanofi, Paris, France; [19]Medical Oncology, Sanofi, Paris, France; [20]Department of Dermato-Oncology, Gustave Roussy et Université Paris Saclay, Villejuif, France

Background: The anti-PD1 antibody cemiplimab, is approved and recommended for patients with la/mCSCC based on a non-comparative pivotal study. In the absence of any prospective comparative study and to evaluate the extent of the benefit of cemiplimab versus previous therapies, the TOSCA study evaluated the effectiveness and safety of cemiplimab versus Historical Systemic Therapies (HST).

Methods: TOSCA is a large French retrospective, multicenter study in patients with laCSCC ineligible for curative surgery or radiation, or mCSCC, treated with cemiplimab via the Early Access Program (EAP) in 2018-2019, or with HST in 2013-2018 (NCT05302297). Primary endpoint was OS. Secondary endpoints were PFS, DOR, ORR, and safety. Only immunocompetent patients meeting the strict indication of the EAP were considered for effectiveness analysis using inverse probability weighting method (IPW). All patients were considered for safety analysis.

Results: A total of 280 patients were included in the study (cemiplimab, n=147 and HST, n=133) and 199 patients were considered for effectiveness analysis (cemiplimab, n=129 and HST, n=70). The median age was 81 (range 48—99) and 78 (52—93) years; males were 70% and 73% for cemiplimab and HST arms, respectively. 60% and 73% of patients had mCSCC, and 50% and 31% of patients received at least one previous systemic therapy in cemiplimab and HST arms. With a median follow-up of 20 and 10 months for cemiplimab and HST arms, and after controlling for confounding using IPW, the median OS was 21 and 10 months (hazard ratio [HR] [95%CI]: 0.57 [0.45-0.73]; *P*-value <0.0001), respectively. The median PFS was 14 and 5 months (HR [95% CI]: 0.57 [0.43-0.76]; *P*-value = 0.0001). The median DOR was 22 and 5 months (HR [95%CI]: 0.58 [0.30-1.12]; *P*-value = 0.1033). The ORR was 57% in cemiplimab group and 33% in HST group (*P*-value <0.001) including 30% and 15% of complete response, respectively. Adverse drug reactions of all grades were documented in 27% (cemiplimab) and 33% (HST) of patients.

Conclusions: TOSCA is the first comparative study in CSCC and showed significantly longer outcomes in patients treated with cemiplimab versus HST, confirming its benefits in patients with la/mCSCCs.

Clinical trial identification: NCT05302297.

Editorial acknowledgement: Padmanabham Salla, Sanofi Global Hub.

Legal entity responsible for the study: Sanofi.

Funding: Sanofi.

Disclosure: E. Gerard: Financial Interests, Personal, Speaker's Bureau: Pierre Fabre; Financial Interests, Personal, Other, Travel, Accommodations, Expenses: Pierre Fabre, BMS, Novartis, MSD Oncology. C. Lebbe: Financial Interests, Personal, Advisory Role, Consulting or advisory role: Bristol Myers Squibb, MSD, Novartis, Amgen, Roche, Merck Serono, Sanofi, Pierre Fabre; Financial Interests, Personal, Speaker's Bureau: Roche, Bristol Myers Squibb, Novartis, Amgen, MSD, Bristol Myers Squibb; Financial Interests, Personal, Other, Travel, Accommodations, Expenses: MSD, Novartis, Sanofi, Pierre Fabre; Other, Personal, Other, Other relationship: Avantis Medical Systems, InflaRx, Sanofi, Bristol Myers Squibb, MSD, Pierre Fabre, Novartis, Jazz Pharmaceuticals; Financial Interests, Personal, Other, Honoraria: Roche, Bristol Myers Squibb, Novartis, Amgen, MSD, Pierre Fabre, Pfizer, Incyte; Financial Interests, Personal and Institutional, Research Funding: Roche, Bristol Myers Squibb. E. Lanoy: Financial Interests, Personal, Advisory Role, Consulting or advisory role: Sanofi, Novartis. M. Viguier: Financial Interests, Personal, Advisory Role, Consulting or advisory role: AbbVie, Janssen, Bristol Myers Squibb, Lilly O., Boehringer Ingelheim. N. Meyer: Financial Interests, Personal, Advisory Role, Consulting or advisory role: Bristol Myers Squibb, MSD Oncology, Novartis, Pierre Fabre, Sun Pharma, Merckle GmbH; Financial Interests, Institutional, Research Funding: Bristol Myers Squibb, MSD Oncology. L. Mortier: Financial Interests, Personal, Other, Honoraria: Bristol Myers Squibb, MSD Oncology, Novartis, Sun Pharma; Financial Interests, Personal, Advisory Role, Consulting or advisory role: BMS GmbH & Co. KG, Sun Pharma, Novartis; Financial Interests, Institutional, Research Funding: MSD Oncology, Pierre Fabre; Financial Interests, Personal, Other, Travel, Accommodations, Expenses: Roche/Genentech, Novartis, Bristol Myers Squibb. M. Dinulescu: Financial Interests, Personal and Institutional, Other, Honoraria: AbbVie, Bristol Myers Squibb, Novartis, Sanofi; Financial Interests, Personal, Other, Travel, Accommodations, Expenses: AbbVie, Bristol Myers Squibb, Novartis, Sanofi. D. Legoupil: Financial Interests, Personal, Advisory Role, Consulting or advisory role: Bristol Myers Squibb, Pierre Fabre, MSD Oncology; Financial Interests, Personal, Other, Travel, Accommodations, Expenses: Pierre Fabre, Bristol Myers Squibb, MSD Oncology. E.M. Neidhardt: Financial Interests, Personal, Advisory Role, Consulting or advisory role: Novartis; Financial Interests, Personal, Other, Travel, Accommodations, Expenses: Pierre Fabre. P. Saiag: Financial Interests, Personal, Advisory Role, Consulting or advisory role: Bristol Myers Squibb, MSD, Pierre Fabre, Novartis, Roche/Genentech, Sanofi; Financial Interests, Personal, Other, Travel, Accommodations, Expenses: Pierre Fabre, Novartis, Roche, Bristol Myers Squibb, MSD; Financial Interests, Personal, Research Funding: Pierre Fabre. C. Nardin: Financial Interests, Personal, Advisory Role, Consulting or advisory role: Sanofi. E. Maubec: Financial Interests, Personal, Advisory Role, Consulting or advisory role: Pierre Fabre, Sanofi, Novartis; Financial Interests, Personal, Other, Travel, Accommodations, Expenses: MSD Oncology, Pierre Fabre, Novartis; Financial Interests, Institutional, Research Funding: MSD. E. Hainaut Wierzbicka: Financial Interests, Personal, Other, Honoraria: Bristol Myers Squibb, Sanofi, AbbVie, Novartis, Sun Pharma; Financial Interests, Personal, Advisory Role, Sanofi: Bristol Myers Squibb; Financial Interests, Personal, Advisory Role, Consulting or Advisory Role: Sanofi, AbbVie, Sun Pharma, Novartis; Financial Interests, Personal, Research Funding: AbbVie; Financial Interests, Personal, Other, Travel, Accommodations, Expenses: AbbVie, Novartis. S. Perrier, S. Garnier: Financial Interests, Personal, Full or part-time Employment, Sanofi employee may hold company stock/stock options: Sanofi. C. Robert: Financial Interests, Personal, Advisory Role, Consulting or advisory role: Bristol Myers Squibb, Roche, Novartis, Pierre Fabre, MSD, Sanofi, AstraZeneca, Pfizer; Financial Interests, Personal, Other, Stock and Other Ownership Interests: RiboNexus; Financial Interests, Institutional, Research Funding: Novartis, Phio Pharmaceuticals. All other authors have declared no conflicts of interest.

https://doi.org/10.1016/j.annonc.2023.09.2274

1141P Early discontinuation of cemiplimab in patients with advanced cutaneous squamous cell carcinoma

E. Croce[1], A. Boutros[2], E.T. Tanda[3], F. Cecchi[1], L. Arecco[4], C. Genova[5], I. Baldelli[6], M. Lambertini[7], E. Raposio[6], L. Del Mastro[8], F. Spagnolo[9]

[1]Medical Oncology 2 Unit, IRCCS Ospedale Policlinico San Martino, Genoa, Italy; [2]Dipartimento Oncologia Medica 2, IRCCS AOU San Martino - IST-Istituto Nazionale per la Ricerca sul Cancro, Genoa, Italy; [3]Dipartimento di Oncologia Medica, IRCCS Ospedale Policlinico San Martino, Genoa, Italy; [4]Clinica di Oncologia Medica, IRCCS Ospedale Policlinico San Martino, Genoa, Italy; [5]Lung Cancer Unit, Università degli Studi di Genova e Ospedale Policlinico San Martino IRCCS - DiMI, Genoa, Italy; [6]Department of Surgical Sciences and Integrated Diagnostics (DISC), Università degli Studi di Genova, Genoa, Italy; [7]Clinica di Oncologia Medica, IRCCS AOU San Martino - IST-Istituto Nazionale per la Ricerca sul Cancro, Genoa, Italy; [8]Internal Medicine Dept., IRCCS Ospedale Policlinico San Martino, Genoa, Italy; [9]Medical Oncology, IRCCS Ospedale Policlinico San Martino, Genoa, Italy

Background: Immunotherapy has drastically changed the treatment of advanced cutaneous squamous cell carcinoma. In three clinical trials, cemiplimab and pembrolizumab have been administered up to 24 months, although most objective responses have been observed within the first 3 months. To determine if a shorter exposure time to cemiplimab was associated with the long-term maintenance of clinical activity, we assessed the outcomes of patients with advanced cutaneous squamous cell carcinoma that had an early discontinuation of cemiplimab.

Methods: This is a single centre retrospective study including patients with histologically confirmed locally advanced or metastatic CSCC treated with cemiplimab at our Institution from August 19th, 2019, to August 8th, 2022. The objective response was assessed radiologically according to the RECIST 1.1 criteria or clinically according to the WHO criteria.

Results: A total of 48 patients receiving at least one dose of cemiplimab were included. Median time of treatment with cemiplimab was 6.8 (0 − 31.6) months, with an overall response rate (ORR) of 68%. Median time to response was 2.8 (0.6 - 19.1) months. Therapy was permanently discontinued in 20 patients due to adverse events (n=3) or patients' or physician's choice after achieving a stable disease, partial or complete response (n=17). At a median follow-up of 11.6 (1.4 − 45.0) months, the median PFS after treatment discontinuation was 15.8 months. No patient relapsed. Only one patient, after being treated for a haematological pathology, developed a new primary CSCC, while pre-existing lesions maintained complete clinical response.

Conclusions: Our findings suggest that early discontinuation of cemiplimab in patients with advanced CSCC upon achieving a tumour response does not appear to negatively impact on the duration of response.

Legal entity responsible for the study: The authors.

Funding: Italian Ministry of Health (Ricerca Corrente).

Disclosure: C. Genova: Financial Interests, Personal, Invited Speaker, Speaker's Bureau (scientific meeting): AstraZeneca, Bristol Myers Squibb, Merck Sharp & Dohme, Eli Lilly, Novartis; Financial Interests, Personal, Advisory Board, Advisory board: Amgen, Sanofi; Financial Interests, Personal, Advisory Board, Advisory Board: Roche, Takeda; Financial Interests, Institutional, Funding, Funding for support of translational study: Bristol Myers Squibb; Financial Interests, Institutional, Funding, Funding for support of translational study: AstraZeneca; Financial Interests, Institutional, Research Grant, Research Grant for translational study: Italian Ministry of Health; Non-Financial Interests, Principal Investigator, Local PI for clinical trials: AstraZeneca, Roche; Non-Financial Interests, Member, Scientific society membership: ASCO, AIOM, FONICAP, AIOT, IASLC, ISLB. M. Lambertini: Financial Interests, Personal, Advisory Board: Roche, AstraZeneca, Lilly, Novartis, Pfizer, Exact Sciences, MSD, Seagen, Gilead; Financial Interests, Personal, Invited Speaker: Takeda, Sandoz, Ipsen, Libbs, Knight, Daiichi Sankyo, Lilly, Pfizer, Novartis, Roche; Financial Interests, Personal, Other, Travel grant to attend ASCO 2022: Gilead; Financial Interests, Institutional, Coordinating PI, 2-year research grant paid to my Institution: Gilead. L. Del Mastro: Financial Interests, Personal, Invited Speaker, Educational meeting: Novartis, Symposia, Andromeda E20, Vyvamed srl; Financial Interests, Personal, Invited Speaker, Lecture: Ipsen; Financial Interests, Personal, Advisory Board, Her2+ and TN breast cancer: Roche; Financial Interests, Personal, Writing Engagement, Consultancy for TNBC text: Roche; Financial Interests, Personal, Advisory Board, denosumab: Amgen; Financial Interests, Personal, Advisory Board, Early and metastatic BC: Eli Lilly; Financial Interests, Personal, Invited Speaker, CDK4-6 inhibitors: Eli Lilly; Financial Interests, Personal, Advisory Board, tucatinib: Seagen Int; Financial Interests, Personal, Advisory Board, Oncotype dx: Exact sciences, Havas life; Financial Interests, Personal, Advisory Board, Neratinib: Pierre Fabre; Financial Interests, Personal, Invited Speaker, Internal training: MSD; Financial Interests, Personal, Invited Speaker, Educational meetings: Accademia Nazionale Medicina; Financial Interests, Personal, Writing Engagement, Author for BC text: Pensiero Scientifico Editore; Financial Interests, Personal, Advisory Board, Breast cancer: Uvet; Financial Interests, Personal, Other, Author slide kits and interviews: Think2it; Financial Interests, Personal, Advisory Board, Palbociclib: Pfizer; Financial Interests, Personal, Invited Speaker, Breast cancer: Aristea, Meeting srl; Financial Interests, Personal, Other, Author slide kits: Forum service; Financial Interests, Personal, Other, Author text about biosimilars: Edizioni Minerva Medica; Financial Interests, Personal, Other, consultant: Kardo srl; Financial Interests, Personal, Invited Speaker, Breast cancer meetings: Delphi international, Over srl; Financial Interests, Personal, Invited Speaker: Prex srl, Editree; Financial Interests, Personal, Advisory Board: Uvet, Collage S.p.A., Daiichi Sankyo, AstraZeneca, Agendia, Gilead; Financial Interests, Personal, Other, Interview: Infomedica srl; Financial Interests, Personal, Other, Consultant: Sharing progress in cancer care - Switzerland; Financial Interests, Personal, Other, Consultancy: Eli Lilly; Financial Interests, Institutional, Funding, National coordinating PI: Roche; Financial Interests, Institutional, Funding, Local PI: AstraZeneca, Roche, Eli Lilly, Daiichi Sankyo, Novella Clinical, Novartis; Non-Financial Interests, Institutional, Product Samples, Genomic Test: FoundationOne. F. Spagnolo: Financial Interests, Personal, Other: Roche, BMS, Merck, Pierre Fabre, Sanofi Genzyme; Financial Interests, Personal, Advisory Board: Novartis, Sun Pharma, MSD, Philogen. All other authors have declared no conflicts of interest.

https://doi.org/10.1016/j.annonc.2023.09.2275

1142P Personalized decision making in cutaneous squamous cell carcinoma: Integrating a clinico-pathological model for absolute metastatic risk into the staging systems

M. Wakkee[1], L. Pozza[2], H. van de Werken[3], A. Mooyaart[4], J. Dwarkasing[5], S. Alex[5], D. Bellomo[2], L. Zandwijk-Hollestein[1], B. Rentroia Pacheco[1]

[1]Dermatology, Erasmus MC Cancer Institute, Rotterdam, Netherlands; [2]Bioinformatics, SkylineDx BV, Rotterdam, Netherlands; [3]Computational Biology and Bioinformatics, Erasmus MC - Erasmus University Rotterdam, Rotterdam, Netherlands; [4]Pathology, Erasmus MC, Rotterdam, Netherlands; [5]Science, SkylineDx BV, Rotterdam, Netherlands

Background: Cutaneous squamous cell carcinoma (cSCC) is the second most common skin cancer, causing a staggering death toll comparable to that of melanoma, despite its low propensity to metastasize (2-5%). However, until recently, cSCC has been perceived as a non-life-threatening tumor, and current clinical practices are suboptimal: clinical staging systems cannot consistently and reliably identify patients at high risk of metastasis, and they do not provide absolute metastatic risk. Therefore, decisions about follow-up schedules and treatment cannot be personalized.

Methods: We sought to improve the risk stratification as defined by the American Joint Committee on Cancer (AJCC) and the Brigham and Women's Hospital (BWH), by integrating a recently developed clinico-pathological (CP) model for metastatic risk in cSCC patients. We tried to identify patients at increased risk within the low-risk group (AJCC: T1-T2, BWH: T1-T2a) and in the high-risk group (AJCC: T3-T4, BWH: T2b-T3), We performed our analysis in a Dutch nested case-control cohort (n=390); binarized the 5-year metastatic risk into CP High-Risk and CP Low-Risk, by selecting thresholds based on likelihood ratios.

Results: In the low-risk group, the metastatic risk is 1.1% (AJCC) and 1.2% (BWH). Within this group CP High-Risk patients (AJCC: 2.6%, BWH=1.9%) have an increased risk (AJCC: 10.3%, BWH: 16.2%) and would be offered follow-up; but not the CP Low-Risk patients (AJCC: 97.4%, BWH=98.1%) with a decreased risk (AJCC: 0.9%, BWH: 0.98%). In the high-risk group, the metastatic risk is 5.7% (AJCC) and 12.8% (BWH). Within this group, CP High-Risk (AJCC:7.9 %, BWH=21.8%) have an increased risk (AJCC: 40.5%, BWH: 43.4%) and could be offered more intensive follow-up and treatment (e.g., adjuvant treatment).

Conclusions: Our data show that our risk model can enhance the AJCC and BWH staging systems, by refining the risk stratification in both the low-risk and high-risk groups. This has the potential to help clinicians, dermatologists, radiotherapists, and clinical oncologists make more personalized decisions about more intense follow-up schedules and treatment of their cSCC patients.

Legal entity responsible for the study: Erasmus MC.

Funding: This study is funded by a PPP Allowance made available by Health ~ Holland, Top Sector Life Sciences & Health, to stimulate public-private partnerships. In this case a public-private partnership between Erasmus MC and SkylineDx BV.

Disclosure: M. Wakkee: Financial Interests, Institutional, Funding: Sanofi, Regeneron; Financial Interests, Personal, Speaker, Consultant, Advisor: Regeneron. L. Pozza, S. Alex: Financial Interests, Personal, Full or part-time Employment: SkylineDx BV. J. Dwarkasing: Financial Interests, Personal, Full or part-time Employment: SkylineDx BV; Financial Interests, Personal, Stocks/Shares: SkylineDx BV. D. Bellomo: Financial Interests, Personal, Full or part-time Employment: SkylineDx BV; Financial Interests, Personal, Stocks/Shares: SkylineDx. All other authors have declared no conflicts of interest.

https://doi.org/10.1016/j.annonc.2023.09.2276

1143P Changes in peripheral and local tumor immunity after cemiplimab treatment early describe clinical outcomes in patients with cutaneous squamous cell carcinoma

D. Esposito[1], A.R. Amato[2], C. Barraco[2], S. Belli[1], C.M. Ascione[1], A. Vallefuoco[1], F. Pepe[1], A. Servetto[1], R. Bianco[1], L. Formisano[1]

[1]Department of Clinical Medicine and Surgery, University of Naples Federico II, Naples, Italy; [2]Medical Oncology, Azienda Ospedaliera Universitaria Federico II, Naples, Italy

Background: Cutaneous squamous cell carcinoma (cSCC) − the second most common skin tumor - accounts for 20% of all deaths from skin cancer. Although the vast majority of patients can be managed with surgical excision, a small percentage of them have locally advanced or metastatic tumors for which programmed cell death 1 (PD-1) checkpoint inhibition was approved and demonstrated substantial antitumor activity. The absence of reliable markers of response and the lacking of a description of immune modulation upon treatment, highlight a clinical need to be addressed.

Methods: We collected tumor and liquid biopsies of 12 patients underwent to cemiplimab before and after 3-weeks of treatment. We profiled RNA of pre- and post-cemiplimab tumor biopsies using the PanCancer Immunoprofile Panel (Nanostring). We determined cytokines released in blood by multiplex ELISA, and lymphocytes abundance by flow cytometry.

Results: The analysis of transcriptional reprogramming in tumor biopsies showed that PD1 blockade induced the expression of PD1-regulated genes after treatment. Interestingly, cemiplimab treatment boosted immune cell activation only in responders patients (i.e. B- and T-cells), according to the host antitumor response expected upon PD-1 targeting. Focusing on peripheral markers, total regulatory T cells (Tregs) early increased in non-responders patients, but dissecting specific antigens of Treg populations, we identified the specific T-cell costimulator (ICOS) subpopulation with a different trend in responders and non-responders. ICOS-positive cells, indeed, increased their abundance in the peripheral blood only of responder patients, in line with recent data showing ICOS cells as positive markers of ICI efficacy in lung cancer. Finally, TNF-α *sera* levels decreased after treatment only in responder patients, in line with its role as a determinant of resistance to PD1 targeting.

Conclusions: Our results provided new key elements to monitor response to therapy, determining putative markers to early define responsiveness to ICI in cSCC patients and suggest how to improve their clinical management.

Legal entity responsible for the study: The authors.

Funding: Has not received any funding.

Disclosure: A. Servetto: Financial Interests, Personal, Other: Eli Lilly, MSD, Janssen; Financial Interests, Institutional, Funding: AIRC. R. Bianco: Financial Interests, Personal, Advisory Board: BMS, MSD, Pfizer, AstraZeneca, Eli Lilly, Novartis. All other authors have declared no conflicts of interest.

https://doi.org/10.1016/j.annonc.2023.09.2277

1144P High-plex spatial profiling of cutaneous squamous cell carcinoma to identify biomarkers associated with clinical outcomes: The cMIC study

R. Ladwa[1], J. Monkman[2], H. Sadeghirad[2], C. Cooper[3], G. Belz[2], J. Bowman[4], H. Schaider[5], H. Liu[6], A. Kulasinghe[2], S. Porceddu[7]

[1]Department of Cancer Services, Princess Alexandra Hospital & University of Queensland, Brisbane, QLD, Australia; [2]Translational Research Institute, The University of Queensland, St Lucia, QLD, Australia; [3]Pathology Queensland, Princess Alexandra Hospital - Metro South Health, Brisbane, QLD, Australia; [4]Surgical Oncology, Princess Alexandra Hospital - Metro South Health, Woolloongabba, QLD, Australia; [5]Dermatology, Princess Alexandra Hospital - Metro South Health, Woolloongabba, QLD, Australia; [6]Department of Cancer Services, Princess Alexandra Hospital - Metro South Health, Woolloongabba, QLD, Australia; [7]Radiation Oncology, Peter MacCallum Cancer Centre, Melbourne, VIC, Australia

Background: Cutaneous squamous cell carcinoma (cSCC) is the second most common non-melanoma skin cancer. Early stage cSCC is often cured with simple resection +/- radiotherapy, though some can recur, most commonly in immunosuppressed (IS) individuals. In advanced cSCC, approximately 50% of patients develop primary resistance to immune checkpoint inhibitors (ICI). There is a need to identify biomarkers by characterising the tumour microenvironment (TME) within different clinical groups.

Methods: Our retrospective study profiled whole tissue sections from n=50 patients from the Princess Alexandra Hospital. Study groups (G) included immunocompetent patients with (G1) de novo, localised cSCC (n=10), (G2) regional nodal metastasis (n=10), (G3) locoregional recurrent disease (n=10), (G4) recurrent/metastatic disease treated with ICI (n=10) and (G5) IS patients (n=10). In this exploratory study, we designed a high-dimensional Nanostring GeoMx Digital Spatial Profiling (DSP) experiment which enabled simultaneous readout of >80-plex proteins in the TME to profile immune cell content, immuno-oncology drug targets, cell lineage and architecture. These features within the TME were measured against the clinical groupings to identify differentially expressed proteins between the groups for future biomarker analysis.

Results: Our preliminary analysis has identified distinct cell phenotype compositions within the TME associated with the clinical groupings. Within the tumour there was a reduction in expression of VISTA and STING immune signaling markers in localized disease (G1/2 vs G4). This was most notable within the stomal compartments. G3/4 had a lower expression of IDO1/STING/VISTA immune signaling markers compared with G5 IS individuals. Moreover, we identified an increased metabolic activity in patients with resistant disease.

Conclusions: Our study highlights the utility of spatial proteomic profiling of the TME in cSCC for the identification of biomarkers associated with biologically distinct clinical groups. This study provides the foundation work for prospective validation of putative biomarkers associated with therapy response and resistance.

Legal entity responsible for the study: Metro South Hospital and Health Services.

Funding: Princess Alexandra Research Foundation.

Disclosure: R. Ladwa, S. Porceddu: Financial Interests, Personal, Advisory Board: MSD, Sanofi. All other authors have declared no conflicts of interest.

https://doi.org/10.1016/j.annonc.2023.09.2278

1145P Clinical characteristics and survival of patients with advanced Merkel cell carcinoma (MCC) treated with avelumab: Analysis of a prospective German MCC registry (MCC TRIM)

J.C. Becker[1], S. Mahmoudpour[2], D. Schadendorf[3], U. Leiter-Stoppke[4], F. Meier[5], R. Herbst[6], M. Sachse[7], S. Grabbe[8], C. Gebhardt[9], F. Ziller[10], C. Pfoehler[11], P. Mohr[12], L. Zimmer[13], E. Boutmy[2], S. Hoff[2], P. Verpillat[2], A. Fernandez Milano[14], M. Shlaen[15], C. Fu[16], S. Ugurel-Becker[17]

[1]Departments of Translational Skin Cancer Research and Dermatology, University Hospital Essen, Essen, Germany; German Cancer Consortium (DKTK), Partner Site Essen/Düsseldorf, German Cancer Research Center (DKFZ), Heidelberg, Germany; [2]Merck Healthcare KGaA, Darmstadt, Germany; [3]Department of Dermatology, University Hospital Essen Westdeutsches Tumorzentrum, Essen, Germany; [4]Dermatology, Center for Dermato-Oncology, Eberhard Karls University of Tübingen, Tuebingen, Germany; [5]Department of Dermatology, Faculty of Medicine and University Hospital Carl Gustav Carus, Technische Universität Dresden, Dresden, Germany; Skin Cancer Center at the University Cancer Centre Dresden and National Center for Tumor Diseases, Dresden, Germany; [6]Dermatology, Helios Klinikum Erfurt, Erfurt, Germany; [7]Dermatology, Allergology and Phlebology, Bremerhaven-Reinkenheide Hospital, Bremerhaven, Germany; [8]Dermatology, University Medical Center of the Johannes Gutenberg University, Mainz, Germany; [9]Dermatology and Venereology, University Medical Center Hamburg-Eppendorf, Hamburg, Germany; [10]Dermatology, DRK Krankenhaus Rabenstein, Chemnitz, Germany; [11]Dermatology, Saarland University Medical School, Homburg, Germany; [12]Dermatology, Elbe-Kliniken, Buxtehude, Germany; [13]Department of Dermatology, University Hospital Essen; German Cancer Consortium, Partner Site Essen; National Center for Tumor Diseases (NCT), NCT-West, Campus, Essen, Germany; [14]Epidemiology, IQVIA Commercial GmbH & Co., Frankfurt am Main, Germany; [15]Epidemiology, IQVIA Commercial GmbH & Co. OHG, Munich, Germany; [16]Biostatistics, IQVIA Solutions Enterprise Management Consulting (Shanghai) Co., Ltd., Beijing, China; [17]Department of Dermatology, University Hospital Essen, University of Duisburg-Essen & German Cancer Consortium Heidelberg, Heidelberg, Germany

Background: MCC is a rare and aggressive form of skin cancer. Avelumab was the first immunotherapy approved for adult patients with metastatic MCC in Europe. We investigated the clinical characteristics and survival outcomes of patients with MCC at the start of and after avelumab treatment.

Methods: Data from 684 patients in a prospective, noninterventional, multicenter, dynamic cohort of the MCC TRIM study who were enrolled after March 2019 were analyzed. Primary data from a study-specific electronic case report form and secondary data from the German national skin cancer registry ADOReg were combined. At data cutoff (Sept 30, 2022), patients diagnosed with unresectable stage III or IV MCC prior to avelumab treatment were included in this analysis. Survival outcomes were assessed by the Kaplan-Meier method.

Results: Of 116 patients with MCC receiving avelumab, 35.3% had stage III disease and 64.7% had stage IV. The mean (SD) age at initial diagnosis was 74.5 (10.4) y, and 62.1% of patients were male. Most patients had an Eastern Cooperative Oncology Group performance status $\leq$1 (76.7%); 21.6% had an immunosuppressive condition or took immunosuppressive medication. Diabetes was the most common comorbidity (23.3%). At a median follow-up of 28.75 mo (95% CI, 20.5-32.5 mo), median overall survival (OS) was not reached in stage III patients and was 52.0 mo (95% CI, 15.4 mo-not estimable [NE]) in stage IV patients. Median (95% CI) progression-free survival (PFS) was 11.8 mo (5.6 mo-NE) in stage III patients and 9.3 mo (3.5-13.7 mo) in stage IV patients. Most patients (86.2%) received avelumab as first-line (1L) therapy; of these, 37.0% had stage III disease and 63.0% had stage IV. Median OS with 1L avelumab was not reached in the stage III or IV group, but fewer events were observed in stage III vs stage IV patients (16.2% vs 36.5%); median PFS (95% CI) was 15.6 mo (5.6 mo-NE) and 7.3 mo (3.0-13.7 mo), respectively.

Conclusions: Demographics observed in MCC TRIM reflect those of the typical advanced MCC population. This nationwide study indicates that avelumab is effective in stage III and IV patients with advanced MCC in routine clinical practice.

Editorial acknowledgement: Editorial support was provided by Alana Reed on behalf of Clinical Thinking and was funded by Merck and Pfizer.

Legal entity responsible for the study: The authors.

Funding: This study was sponsored by Merck (CrossRef Funder ID: 10.13039/100009945), as part of an alliance between Merck and Pfizer.

Disclosure: J.C. Becker: Financial Interests, Personal, Speaker's Bureau: Amgen, Merck Serono, Pfizer, Recordati, Sanofi; Financial Interests, Personal, Advisory Board: Almirall, Boehringer Ingelheim, InProTher, ICON, Pfizer, 4SC, Sanofi/Regeneron; Financial Interests, Institutional, Research Grant: Bristol Myers Squibb, Merck Serono, HTG, IQVIA, Alcedis. S. Mahmoudpour: Financial Interests, Personal, Full or part-time Employment: Merck Healthcare KGaA, Darmstadt, Germany. D. Schadendorf: Financial Interests, Personal, Invited Speaker: BMS, Merck, Novartis, Roche, Sanofi; Financial Interests, Personal, Advisory Board: BMS, Immunocore, MSD, Neracare, Novartis, Pfizer, Philogen, Pierre Fabre, Sanofi/Regeneron; Financial Interests, Personal, Leadership Role: MSD; Financial Interests, Institutional, Research Grant: BMS, MSD; Financial Interests, Personal, Steering Committee Member: BMS, MSD, Novartis; Non-Financial Interests, Personal, Coordinating PI: BMS, Novartis; Financial Interests, Personal, Coordinating PI: MSD; Non-Financial Interests, Personal, Local PI: Philogen; Non-Financial Interests, Institutional, Coordinating PI: Pierre Fabre; Non-Financial Interests, Institutional, Local PI: Sanofi; Non-Financial Interests, Institutional, Member of Board of Directors: EORTC-MG. U. Leiter-Stoppke: Financial Interests, Institutional, Research Grant: MSD; Financial Interests, Personal and Institutional, Other, Lecturing: Roche, Novartis, Sanofi, MSD, Sun Pharma; Financial Interests, Personal, Speaker, Consultant, Advisor: Roche, Sanofi, MSD, Novartis, Sun Pharma, Allmiral Hermal. F. Meier: Financial Interests, Personal, Other, received travel support

or/and speaker's fees or/and advisor's honoraria: Novartis, Roche, Bristol Myers Squibb, MSD, Pierre Fabre, Sanofi, Immunocore; Financial Interests, Institutional, Research Funding: Novartis, Roche. R. Herbst: Financial Interests, Personal, Full or part-time Employment: Helios Klinikum Erfurt GmbH; Erfurt, Germany. M. Sachse: Financial Interests, Personal, Speaker, Consultant, Advisor: Novartis; Financial Interests, Personal, Advisory Board: Sanofi Genzyme. S. Grabbe: Financial Interests, Institutional, Research Grant: Novartis, Pierre Fabre; Financial Interests, Personal, Speaker's Bureau: Sun Pharma; Financial Interests, Personal, Speaker, Consultant, Advisor: Klinge Pharma, Novartis, Kyowa Kirin, BMS, MSD; Financial Interests, Personal, Other, Support for attending meetings and/or travel: UCB. C. Gebhardt: Financial Interests, Personal, Advisory Board: Almirall, Beiersdorf, Bristol Myers Squibb, Immunocore, Janssen, MSD, Novartis, Pierre Fabre Pharma, Sanofi Genzyme, Sun Pharma and Sysmex; Financial Interests, Institutional, Research Funding: Novartis, Sanofi Genzyme; Financial Interests, Personal, Other, travel support: Bristol Myers Squibb, Pierre Fabre Pharma, Sun Pharma; Financial Interests, Personal, Other, co-founder: Dermagnostix R&D. F. Ziller: Financial Interests, Personal, Advisory Board, Honoraria and/or travel support: Bristol Myers Squibb, MSD, Roche, Novartis, Pierre Fabre, Sanofi, Sun Pharma. P. Mohr: Financial Interests, Institutional, Research Grant: MSD, BMS, Novartis Pharmaceuticals, Amgen Inc., Beiersdorf, Pierre Fabre, Almirall Hermal, Immunocore LLC, Merck, Novartis Pharmaceuticals, Pfizer, Sun Pharma, Sanofi Genzyme, Regeneron Pharmaceuticals; Financial Interests, Personal, Advisory Board: BMS, MSD, Pierre Fabre, Sun Pharma, Sanofi Genzyme, Novartis, Amgen Inc.; Financial Interests, Personal, Other, travel support/accommodations: Pierre Fabre, BMS, MSD, Novartis, Sun Pharma; Financial Interests, Personal, Other, Leadership or fiduciary role in other board, society, committee or advocacy group: MID Melanom Info Deutschland. L. Zimmer: Financial Interests, Personal, Other, Honoraria: MSD, BMS, Pierre Fabre, Novartis; Financial Interests, Personal, Other, Support for attending meetings and/or travel: BMS, Novartis, Sun Pharma, Pierre Fabre; Financial Interests, Personal, Other, SuppoSupport for attending meetings and/or travel rt for attending meetings and/or travel from: MSD; Financial Interests, Personal, Advisory Board: BMS, MSD, Pierre Fabre, Novartis; Financial Interests, Personal, Leadership Role: Cancer Survivorship Committee; Non-Financial Interests, Personal, Leadership Role: DeCOG; Financial Interests, Other, Receipt of equipment, materials, drugs, medical writing, gifts or other services: Merck. E. Boutmy: Financial Interests, Personal, Full or part-time Employment: Merck. S. Hoff: Financial Interests, Personal, Full or part-time Employment: Merck Healthcare KGaA, Darmstadt, Germany. P. Verpillat: Financial Interests, Personal, Full or part-time Employment, at time of study: Merck. A. Fernandez Milano, C. Fu: Financial Interests, Personal, Full or part-time Employment: IQVIA Commercial GmbH & Co. OHG, Frankfurt am Main, Germany. M. Shlaen: Financial Interests, Personal, Financially compensated role: IQVIA Commercial GmbH & Co. OHG, Frankfurt am Main, Germany. S. Ugurel-Becker: Financial Interests, Institutional, Research Grant: BMS, Merck; Financial Interests, Personal, Advisory Board: BMS, MSD, Merck, Novartis; Financial Interests, Personal, Other, travel support: BMS, MSD, Pierre Fabre. All other authors have declared no conflicts of interest.

https://doi.org/10.1016/j.annonc.2023.09.2279

1146P Updated results from POD1UM-201: A phase II study of retifanlimab in patients with advanced or metastatic Merkel cell carcinoma (MCC)

G. Grignani[1], P. Rutkowski[2], C. Lebbe[3], M. Guida[4], C. Gaudy Marqueste[5], F.G.M. De Braud[6], F. Spagnolo[7], M. Burgess[8], H. Montaudie[9], R. Depenni[10], F. Spada[11], J. Pulini[12], M. Cornfeld[13], C. Tian[14], S. Bhatia[15]

[1]Oncologia Medica II, AOU Città della Salute e della Scienza di Torino, Turin, Italy; [2]Department of Soft Tissue/Bone Sarcoma and Melanoma, Maria Sklodowska-Curie National Research Institute of Oncology, Warsaw, Poland; [3]Department of Dermatology and CIC, Université de Paris, AP-HP Hôpital Saint-Louis, Paris, France; [4]Melanoma and Rare Tumors Unit, IRCCS Istituto Tumori Giovanni Paolo II, Bari, Italy; [5]Dermatology and Skin Cancer Department, Aix-Marseille University, AP-HM Timone, Marseille, France; [6]Medical Oncology and Hematology Department, Fondazione IRCCS Istituto Nazionale dei Tumori, Università di Milano, Milan, Italy; [7]Skin Cancer Unit, Medical Oncology 2, IRCCS Ospedale Policlinico San Martino and Department of Surgical Sciences and Integrated Diagnostics (DISC), University of Genoa, Genoa, Italy; [8]Hematology Oncology, Medical Oncology, UPMC Hillman Cancer Center, Pittsburgh, PA, USA; [9]Department of Dermatology, Centre Hospitalier Universitaire de Nice, Université Côte d'Azur, Nice, France; [10]Department of Oncology and Haematology, Division of Oncology, University Hospital of Modena, Modena, Italy; [11]Division of Gastrointestinal Medical Oncology and Neuroendocrine Tumors, European Institute of Oncology (IEO), IRCCS, Milan, Italy; [12]Clinical Development Department, Incyte Corporation, Wilmington, DE, USA; [13]Immuno-Oncology Department, Incyte Corporation, Wilmington, DE, USA; [14]Biostatistics, Incyte Corporation, Wilmington, DE, USA; [15]Department of Medicine, Division of Medical Oncology, University of Washington and Fred Hutchinson Cancer Center, Seattle, WA, USA

Background: Retifanlimab, a programmed death receptor-1 (PD-1)—blocking antibody, was recently approved in the United States for treatment of adult patients (pts) with metastatic or recurrent locally advanced MCC based on results from the open-label, single-arm POD1UM-201 study (NCT03599713). In the primary analysis including 65 chemotherapy-naive pts, responses were observed in 52% (95% CI: 40—65) of pts with 62% of responses exceeding 12 months by landmark analysis (ZYNYZ™ prescribing information). Safety was as expected for the PD-(L)1 inhibitor class. We present updated results on the full cohort of 101 pts.

Methods: Eligible pts were ≥18 years of age, had metastatic or recurrent unresectable loco-regional MCC, Eastern Cooperative Oncology Group (ECOG) performance status ≤1, measurable disease per Response Evaluation Criteria in Solid Tumors (RECIST) v1.1, and had not received prior MCC systemic treatment. Retifanlimab 500 mg was administered intravenously every 4 weeks (Q4W) for up to 2 years without premedication prophylaxis. The primary endpoint was overall response rate assessed by independent central review per RECIST v1.1. Secondary endpoints included duration of response, disease control rate, progression-free survival, overall survival, safety, and pharmacokinetics.

Results: The study enrolled 101 pts with chemotherapy-naive advanced/metastatic MCC, with the last pt initiating treatment on 24 June 2021. Pt and disease characteristics were representative of the typical MCC epidemiology. The median age was 71 (range, 38—90) years, 68 (67%) pts were male and predominantly white, 74 (73%) had an ECOG of 0, and one pt was HIV positive. A total of 91 (90%) pts had Stage IV disease, 69 (68%) had prior surgery, and 37 (37%) had prior radiotherapy. In evaluable tumour samples, Merkel cell polyomavirus was detectable in 73/96 (76%) and 83/95 (87%) had PD-L1 expression ≥1%. Efficacy and safety results for the full study population will be presented.

Conclusions: Retifanlimab has shown notable clinical activity with an acceptable safety in advanced/metastatic chemotherapy-naive MCC, and is a promising new treatment option for eligible pts.

Clinical trial identification: NCT03599713, EudraCT 2018-001627-39.

Editorial acknowledgement: Envision Pharma Group (Philadelphia, PA), funded by Incyte Corporation (Wilmington, DE).

Legal entity responsible for the study: Incyte Corporation (Wilmington, DE).

Funding: Incyte Corporation, Wilmington, DE.

Disclosure: G. Grignani: Financial Interests, Institutional, Other, Honoraria: Bayer, Eisai, Eli Lilly and Company, Merck, Novartis, Pfizer, PharmaMar; Financial Interests, Institutional, Advisory Role: Bayer, Eisai, Eli Lilly and Company, Novartis, Pfizer, PharmaMar; Financial Interests, Institutional, Research Grant: Bayer, Novartis, PharmaMar. P. Rutkowski: Financial Interests, Institutional, Advisory Board, Honoraria: AstraZeneca Blueprint Medicines, Bristol Meyers Squibb, Merck Serono, MSD, Novartis, Philogen, Pierre Fabre, Sanofi; Financial Interests, Institutional, Other, Institutional support: Pfizer. C. Lebbe: Financial Interests, Personal, Advisory Board: Bristol Myers Squibb, MSD, Novartis, Amgen, Roche, Merck Serono, Sanofi, Pierre Fabre; Financial Interests, Personal, Funding: Roche, Bristol Myers Squibb; Non-Financial Interests, Advisory Role: Bristol Myers Squibb, MSD, Novartis, Amgen, Roche, Merck Serono, Sanofi, Pierre Fabre; Other, Honoraria, Speaker's Bureau, Research funding: Roche; Other, Honoraria, Speaker's bureau, Travel, Accommodation, Expenses, Research funding, Board: Bristol Myers Squibb; Other, Honoraria, Speaker's bureau, Travel, Accommodations, Expenses, Board: Novartis, MSD; Other, Honoraria, Speaker's bureau: Amgen; Other, Honoraria, Travel, Accommodations, Expenses, Board: Pierre Fabre; Other, Honoraria: Pfizer; Other, Honoraria: Incyte; Other, Travel, accommodations, Expenses, Board: Sanofi; Other, Board: Avantis Medical Systems, Jazz Pharmaceuticals; Other, Participation on a Data Safety Monitoring Board or Advisory Board: InflaRx. M. Guida: Financial Interests, Institutional, Advisory Role: Bristol Myers Squibb, MSD, Novartis, Pierre Fabre. C. Gaudy Marqueste: Financial Interests, Institutional, Advisory Board, Honoraria: Bristol Myers Squibb, MSD, Pierre Fabre; Financial Interests, Institutional, Other, Participated in clinical trials and Travel grants: Bristol Myers Squibb, MSD, Pierre Fabre; Financial Interests, Institutional, Other, Participated in clinical trials: GSK, Huyabioscience, Incyte, Merck Serono, Novartis, Regeneron, Replimune, Kartos. F.G.M. De Braud: Financial Interests, Institutional, Advisory Role: Roche, EMD Serono, NMS Nerviano Medical Science, Sanofi, MSD, Incyte, Bristol Myers Squibb, Menarini, AstraZeneca, Pierre Fabre, Mattiolo 1885 , MCCann Health, Taiho; Financial Interests, Institutional, Speaker's Bureau: Bristol Myers Squibb, Healthcare Research & Pharmacoepidemiology, Merck, MSD, Pfizer, Servier, Sanofi, Roche, Amgen, Incyte, Dephaforum, Seagen, Nadirex, Ambrosetti, Itanet; Financial Interests, Funding, Research: Novartis, Hoffmann LaRoche Ltd., Bristol Myers Squibb, Ignyta Operating INC, Kymab, Pfizer, Tesaro, MSD, MedImmune LCC, Exelixis Inc., Loxo Oncology Incorporated, Daiichi Sankyo Dev. Limited, Basilea Pharmaceutica International AG, Janssen Cilag International NV, Merck KGaA, IQVIA. F. Spagnolo: Financial Interests, Institutional, Advisory Board: Bristol Myers Squibb, Merck, MSD, Novartis, Pierre Fabre, Philogen, Sanofi, Sun Pharma. M. Burgess: Financial Interests, Institutional, Funding, Research: Merck; Financial Interests, Institutional, Advisory Board: EMD Serono, Immune Design, SpringWorks Therapeutics. H. Montaudie: Financial Interests, Institutional, Other, Honoraria: Bristol Myers Squibb, Merck Serono, MSD, Novartis, Pierre Fabre; Financial Interests, Institutional, Other, Institutional support: Bristol Myers Squibb, Leo Pharma; Financial Interests, Institutional, Other, Participated in clinical trials: Bristol Myers Squibb, Checkpoint Therapeutics, Huyabioscience, Incyte, Merck Serono, MSD, Nektar Pharmaceuticals, Novartis, Pierre Fabre, Regeneron, Replimune; Financial Interests, Institutional, Other, Travel grant: Bristol Myers Squibb, Pierre Fabre, Novartis. R. Depenni: Financial Interests, Institutional, Advisory Board: Bristol Myers Squibb, MSD, Novartis, Pierre Fabre, Sanofi. F. Spada: Financial Interests, Institutional, Other, Honoraria for lectures and/or advisory boards and/or manuscript writing: Advanced Accelerator Application, Ipsen, Merck/MSD, Novartis, Pfizer; Financial Interests, Institutional, Invited Speaker, Institutional support: GETNE, Hutchmed, Incyte Corporation. J. Pulini, M. Cornfeld, C. Tian: Financial Interests, Institutional, Full or part-time Employment: Incyte; Financial Interests, Institutional, Stocks/Shares: Incyte. S. Bhatia: Financial Interests, Institutional, Advisory Board: Bristol Myers Squibb, Castle Biosciences, EMD Serono, Exicure, Genentech, Incyte, Sanofi-Genzyme; Financial Interests, Institutional, Research Grant: 4SC, Amphivena Therapeutics, Bristol Myers Squibb, Checkmate, EMD Serono, Immune Design, Incyte Biosciences, Merck, NantKwest, Nektar, Novartis, OncoSec, Regeneron, Xencor; Financial Interests, Institutional, Stocks/Shares: Moderna.

https://doi.org/10.1016/j.annonc.2023.09.2280

1147P First-line treatment (tx) patterns and overall survival (OS) of patients (pts) with advanced Merkel cell carcinoma (aMCC) in England from 2013-2022: Results of a nationwide observational cohort study

C. Knott[1], S. Mahmoudpour[2], M. Kearney[2], E. Boutmy[2], P. Verpillat[2]

[1]Health Data Insight CIC, NHS England, Cambridge, UK; [2]Merck Healthcare KGaA, Darmstadt, Germany

Background: MCC is a rare, aggressive cutaneous neoplasm. In September 2017, the European Commission approved avelumab (Ave) for the tx of metastatic MCC based on demonstrated meaningful survival benefit. This study sought to investigate tx patterns and OS of pts with aMCC (stage III/IV) in the National Cancer Registration Dataset (NCRD) in England.

Methods: This cohort included pts ≥18 years and newly diagnosed with stage III/IV MCC (ICD-O: C44, 8247 morphology) between January 2013 and December 2020 in

the NCRD in England and followed up until May 2022. Summary and descriptive statistics were calculated for categorical and continuous variables. The Kaplan-Meier method was used to estimate median OS from diagnosis date (overall) and OS from initiation of 1L tx stratified by regimens received and by stage at baseline.

Results: A total of 667 pts with aMCC were included. Mean age (SD) was 77.4 years (10.3), most pts were male (61.0%), and 14.1% were immunocompromised. At diagnosis, 66.3% and 33.7% had stage III and IV disease, respectively. The mean (SD) baseline modified Deyo-Charlson Comorbidity Index was 4.0 (1.8). Overall, 478 pts (71.7%) died during follow-up; median OS from diagnosis was 18.4 months (95% CI, 15.6-20.9). In total, 199 pts (29.8%) received 1L tx (39.2% Ave, 60.8% non-Ave). When stratified by stage, 26.9% of stage III pts received systemic tx (39.5% Ave, 60.5% non-Ave); the corresponding numbers for stage IV pts were 35.6% (38.7% Ave, 61.3% non-Ave). OS from 1L initiation is presented in the table.

Table: 1147P

OS from 1L initiation	Stage III		Stage IV	
	Ave	Non-Ave	Ave	Non-Ave
n	47	72	31	49
Deaths during follow-up, n (%)	20 (42.6)	54 (75.0)	16 (51.6)	40 (81.6)
Median OS months (95% CI)	37.8 (12.9-NE)	13.0 (8.3-19.6)	19.9 (5.0-NE)	7.2 (5.9-9.1)
12-months survival rate, % (95% CI)	67 (51-79)	52 (40-63)	55 (36-70)	31 (18-44)
18-months survival rate, % (95% CI)	56 (39-69)	41 (29-52)	52 (33-67)	24 (14-37)
24-months survival rate, % (95% CI)	56 (39-69)	35 (24-46)	48 (29-64)	NE

NE, not estimable.
*Non-Ave includes 95.5% chemotherapy and 4.5% other treatment.

Conclusions: This nationwide real-world study of pts with aMCC demonstrates the effectiveness of Ave with considerably prolonged survival in pts with both stage III and stage IV disease. The study findings validate results from the JAVELIN Merkel 200 clinical trial and other observational studies.

Editorial acknowledgement: Editorial support was provided by Eleanor Bishop on behalf of Clinical Thinking and was funded by Merck and Pfizer.

Legal entity responsible for the study: The authors.

Funding: This study was sponsored by Merck (CrossRef Funder ID: 10.13039/100009945), as part of an alliance between Merck and Pfizer.

Disclosure: C. Knott: Financial Interests, Personal, Full or part-time Employment: Health Data Insight CIC; NHS England. S. Mahmoudpour, M. Kearney: Financial Interests, Personal, Full or part-time Employment: Merck. E. Boutmy: Financial Interests, Personal, Full or part-time Employment: Merck; Financial Interests, Personal, Stocks/Shares: Merck. P. Verpillat: Financial Interests, Personal, Full or part-time Employment, at the time of the study: Merck.

https://doi.org/10.1016/j.annonc.2023.09.2281

1148P Avelumab as second-line or later (2L+) treatment (tx) in patients (pts) with metastatic Merkel cell carcinoma (mMCC): Real-world tx patterns in France

A. Blom Fily[1], L. Mortier[2], B. Van Hille[3], M. Samimi[4], L. Luciani[3], C. Cahuzac[3], C. Robert[5], G. Quereux[6], E. Maubec[7], C. Maillard[8], H. Miotti[8], F. Aubin[9], C. Lenormand[10], M-N. Solbes[3], A.B. Duval Modeste[11], I. Kachaner[12], C. Lebbe[13], C. Dutriaux[14], P. Saiag[1]

[1]CHU Ambroise-Paré, Boulogne-Billancourt, France; [2]Service de Dermatologie, Hôpital Claude Huriez, CHU de Lille, Lille, France; [3]Merck Santé S.A.S., Lyon, France, an affiliate of Merck KGaA, Lyon, France; [4]CHU de Tours, Hôpital Trousseau, Chambray-lès-Tours, France; [5]Institut Gustave Roussy, Villejuif, France; [6]CHU de Nantes, Hôpital Hôtel-Dieu, Nantes, France; [7]Hôpital Avicenne - APHP, Bobigny, France; [8]IQVIA Opérations France, La Défense, France; [9]Dermatologie, CHU et Inserm 1098, Besançon, France; [10]Mcu-ph, Service de Dermatologie, Hôpitaux Universitaires de Strasbourg, Strasbourg, France; [11]Hopital Charles-Nicolle - CHU de Rouen, Rouen, France; [12]Pfizer, Paris, France; [13]Université Paris Cité, Dermato-Oncology, CIC AP-HP Hôpital Saint-Louis, Paris, France; [14]CHU de Bordeaux, Hôpital Saint-André, Bordeaux, France

Background: Avelumab has been approved worldwide for the tx of mMCC based on results from the JAVELIN Merkel 200 trial. The French Health Technology Assessment Agency requested the collection of real-world data from pts with mMCC from a comprehensive registry; data for overall survival (OS), tx patterns, and time to tx failure (TTF) with 2L+ avelumab are reported here.

Methods: This retrospective noninterventional study evaluated pts with mMCC in France using 2 databases: CARADERM (French national database of rare dermatologic cancers) and Système National des Données de Santé (SNDS; national healthcare database). Pts with mMCC who initiated 2L+ avelumab outside a clinical trial between Aug 2016 and Dec 2019 were eligible. Pts were followed up for 24 months from start of avelumab. TTF was defined as time from avelumab initiation to discontinuation for any reason, including progression, toxicity, or death.

Results: 180 pts received 2L+ avelumab, including 112 pts in the CARADERM database and 68 additional pts after SNDS linkage. Median age at diagnosis was 74.0 years; 66.7% of pts were male, and 98.3% had received first-line (1L) chemotherapy alone. The most common 1L tx in evaluable pts (CARADERM database) were cisplatin or carboplatin + etoposide (59.6%) and etoposide alone (12.8%). Median follow-up was 13.1 months. Median OS from start of 2L+ avelumab was 14.6 months (95% CI, 9.9-21.3 months). Of the evaluable pts (n=175) at the last follow-up, 9.1% were receiving avelumab, 31.4% had discontinued tx, and 57.1% had died; 2.3% were lost to follow-up. Median TTF was 8.5 months (95% CI, 6.2-10.5 months) overall; in CARADERM and non-CARADERM database pts, median TTF was 9.9 months (95% CI, 6.5-14.3 months) and 6.5 months (96% CI, 4.4-9.5 months), respectively. 12- and 24-month rates of pts without tx failure were 38.9% (95% CI, 31.6%-46.1%) and 15.5% (95% CI, 10.4%-21.4%), respectively. In evaluable pts who discontinued avelumab (CARADERM only), 30.3% received no subsequent tx, 50.6% received chemotherapy alone, and 19.1% received other tx.

Conclusions: These data provide insights into tx patterns among pts with mMCC receiving 2L+ avelumab in routine clinical practice in France.

Editorial acknowledgement: Medical writing support was provided by Eleanor Bishop on behalf of Clinical Thinking and was funded by Merck and Pfizer.

Legal entity responsible for the study: The authors.

Funding: This study was sponsored by Merck Santé S.A.S., Lyon, France, an affiliate of Merck KGaA (CrossRef Funder ID: 10.13039/100009945), as part of an alliance between Merck and Pfizer.

Disclosure: A. Blom Fily: Financial Interests, Personal, Other, travel and accommodation expenses: Merck; Financial Interests, Personal, Advisory Role: Merck. L. Mortier: Financial Interests, Personal, Other, travel and accommodation expenses: Bristol Myers Squibb; Novartis, Roche/Genentech. B. van Hille: Financial Interests, Personal, Full or part-time Employment: Merck Santé S.A.S., Lyon, France, an affiliate of Merck KGaA. M. Samimi: Financial Interests, Personal, Invited Speaker, received fees for speaking at educational meetings: Amgen; Financial Interests, Personal, Invited Speaker, received fees for speaking at educational meetings: Novartis; Financial Interests, Personal, Advisory Board: Merck, Pfizer; Financial Interests, Personal, Other, travel and accommodation expenses: AbbVie, Amgen SAS, Bristol Myers Squibb, Celgene SAS, Galderma International, Janssen Cilag, Lilly France SAS, MSD, Pierre Fabre Médicaments France, Sanofi-Aventis. L. Luciani, C. Cahuzac: Financial Interests, Personal, Full or part-time Employment: Merck Santé S.A.S., Lyon, France, an affiliate of Merck KGaA. C. Robert: Financial Interests, Personal, Advisory Role: Roche, Novartis, Bristol Myers Squibb, MSD, Pierre Fabre, Sanofi, AstraZeneca, Sun Pharma; Financial Interests, Personal, Other, Co-founder: Ribonexus. E. Maubec: Financial Interests, Personal, Advisory Board: Pierre Fabre, Sanofi, Novartis; Financial Interests, Personal, Other, Travel and Accommodation Expenses: MSD, Pierre Fabre, Novartis; Financial Interests, Personal, Funding: MSD. F. Aubin: Financial Interests, Personal, Advisory Board: Bristol Myers Squibb, Novartis, Sanofi, MSD, AbbVie, Janssen-Cilag, Leo Pharma, Amgen, Celgene. M. Solbes: Financial Interests, Personal, Full or part-time Employment: Merck Santé S.A.S., Lyon, France, an affiliate of Merck KGaA. I. Kachaner: Financial Interests, Personal, Full or part-time Employment: Pfizer. C. Lebbe: Financial Interests, Personal, Other, Honoraria: Amgen, Bristol Myers Squibb, Incyte, MSD, Novartis, Pfizer, Pierre Fabre, Roche; Financial Interests, Personal, Advisory Role: Amgen, Bristol Myers Squibb, MSD, Novartis, Roche; Financial Interests, Personal, Speaker's Bureau: Amgen, Bristol Myers Squibb, Novartis, Roche; Financial Interests, Personal, Research Grant: Bristol Myers Squibb, Roche; Financial Interests, Personal, Other, Travel and Accommodation Expenses: Bristol Myers Squibb; Financial Interests, Personal, Other: Avantis Medical Systems. C. Dutriaux: Financial Interests, Personal, Advisory Board, Honoraria: MSD, Bristol Myers Squibb, Novartis, Pierre Fabre, Sun Pharma. P. Saiag: Financial Interests, Personal, Advisory Board: Bristol Myers Squibb, MSD, Pierre Fabre, Novartis, Roche/Genentech, Sanofi; Financial Interests, Personal, Other, Travel and accommodation expenses: Pierre Fabre, Novartis, Bristol Myers Squibb, MSD; Financial Interests, Personal, Research Funding: Pierre Fabre. All other authors have declared no conflicts of interest.

https://doi.org/10.1016/j.annonc.2023.09.2282

1149P Prognosis for patients with metastatic Merkel cell carcinoma with a complete response on avelumab treatment

L. Zijlker[1], S. Levy[2], W. Wolters[2], H.V. van Thienen[3], A.C.J. van Akkooi[4], M. Tesselaar[5]

[1]Surgical Oncology, NKI-AVL - Netherlands Cancer Institute/Antoni van Leeuwenhoek Hospital, Amsterdam, Netherlands; [2]Department of Medical Oncology, NKI-AVL - Netherlands Cancer Institute/Antoni van Leeuwenhoek Hospital, Amsterdam, Netherlands; [3]Department of Medical Oncology, Netherlands Cancer Institute, Amsterdam, Netherlands; [4]Surgical Oncology Dept., Melanoma Institute Australia, Wollstonecraft, NSW, Australia; [5]Medical Oncology, NKI-AVL - Netherlands Cancer Institute/Antoni van Leeuwenhoek Hospital, Amsterdam, Netherlands

Background: Immune checkpoint inhibitor (ICI) treatment of patients with metastatic Merkel cell carcinoma (mMCC) has shown high response rates, ranging from 33%-73%. The ideal duration of treatment is however currently unknown. We aimed to evaluate if avelumab treatment for mMCC can be safely stopped after 1 year of treatment and confirmed complete response (CR) by FDG-PET/CT.

Methods: Patients who received >one dose of avelumab treatment for mMCC between November 2017 and February 2022 were included in this study. Treatment was discontinued in case of a FDG-PET/CT confirmed CR after 1 year (26 cycles) of avelumab, or a CR and unacceptable toxicity earlier on. Primary endpoint was recurrence free survival (RFS).

Results: Sixty-five patients were included: 25 (38%) had a FDG-PET/CT confirmed CR at discontinuation of avelumab. In those 25 patients, reasons for discontinuation of treatment were completion of 1 year of treatment in 13 patients (52%), toxicity in 5

patients (20%) and patient preference in 7 patients (28%). Median duration of treatment in this group was 11 months (IQR 6.1-11.7). Median follow-up was 27 months (IQR 15.8-33.8). The 12 months RFS was 88% (95% CI 0.74-1) and median RFS was not reached. Two patients (9,5%) had a recurrence, at 4 and 7 months after discontinuation of treatment.

Conclusions: Avelumab treatment for patients with mMCC can be safely discontinued after one year of treatment and a PET/CT confirmed CR, as responses appear to be durable, with a 12 months RFS of 88%.

Legal entity responsible for the study: The authors.

Funding: Has not received any funding.

Disclosure: A.C.J. van Akkooi: Financial Interests, Institutional, Advisory Board: Amgen, Bristol Myers Squibb, Novartis, MSD - Merck, Merck-Pfizer, Pierre Fabre, Sanofi, Sirius Medical, 4SC, Provectus; Financial Interests, Institutional, Research Grant, NIVEC study: Amgen; Financial Interests, Institutional, Research Grant: Merck-Pfizer. All other authors have declared no conflicts of interest.

https://doi.org/10.1016/j.annonc.2023.09.2283

1150P Transforming growth factor-beta-1 and soluble co-inhibitory immune checkpoints as putative drivers of immune suppression in advanced basal cell carcinoma

B.L. Rapoport[1], R. Anderson[2], S. Siwele[3], H. Steel[2], L. Kwofie[2], M. Kgokolo[3], T. Smit[4], P. Meyer[2], N. Malinga[3]

[1]Medical Oncology Department, The Medical Oncology Centre of Rosebank, Johannesburg, South Africa; [2]Department of Health, University of Pretoria, Pretoria, South Africa; [3]Dermatology, University of Pretoria, Pretoria, South Africa; [4]Research, The Medical Oncology Centre of Rosebank, Johannesburg, South Africa

Background: Basal cell carcinoma's (BCC) mortality rate is low; however, it is associated with substantial morbidity. Transforming growth factor-b1 (TGF-b1) is a key player in cell proliferation, differentiation, apoptosis, and immune regulation. TGF-b1 is associated with immunosuppression and resistance to immunotherapeutic drugs. The current study compared levels and possible associations between systemic soluble ICMs (sICMs) and a group of humoral modulators of immune suppressor cells in a cohort of patients with advanced BCC, (n=40) and a group of healthy control subjects (n=20).

Methods: We measured sICMs and immunosuppressive humoral modulators by using multiplex bead array or ELISA procedures. The sICMs comprised seven co-inhibitory (CTLA-4, BTLA, LAG-3, PD-1, PDL-1, PDL-2, and TIM-3) and eight co-stimulatory (CD27, CD28, CD40, CD80, CD86, GITR, GITRL, and ICOS) proteins, as well as the two dual-active sICPs, HVEM and TLR2. The 7 humoral modulators of immunosuppressor cells included arginase 1, fibroblast activation protein (FAP), RANTES (CCL5), interleukin-10, TGF-b1, and the M2-type macrophage biomarkers, soluble CD163 (sCD163) and sCD206.

Results: Plasma levels of six co-inhibitory sICPs, sCTLA-4, sLAG-3, sPD-1, sPD-L1, and sTIM-3 and sPD-L2 were significantly elevated in the cohort of BCC patients ($p<0.001$-$p<0.00001$), while that of sBTLA was significantly decreased ($p<0.006$). Of the co-stimulatory sICPs, sCD27 was significantly increased ($p<0.0002$) in the cohort of BCC patients, with the levels of the others essentially comparable with those of the control patients; of the dual active sICPs, sHVEM, sTLR2 was elevated ($p<0.00001$) and TLR2 comparable with the control group. Correlation heat maps revealed selective, strong associations of TGF-b1 with seven co-stimulatory (z=0.618468-0.768131) and 4 co-inhibitory (z=0.674040-0.808365) sICPs, as well as with sTLR2 (z=0.696431).

Conclusions: Notwithstanding the association of BCC with selective elevations in the levels of a large group of co-inhibitory sICPs, our novel findings also imply the probable involvement of TGF-b1 in driving immunosuppression in this malignancy, possibly via activation of regulatory T cells.

Legal entity responsible for the study: The authors.

Funding: University of Pretoria and The Medical Oncology Centre of Rosebank.

Disclosure: All authors have declared no conflicts of interest.

https://doi.org/10.1016/j.annonc.2023.09.2284

1151P Characteristics and treatment outcomes in cutaneous adnexal carcinomas

A. Rock[1], R. Nelson[2], J. Yeh[3], M. Onyshchenko[1]

[1]Medical Oncology, City of Hope, Duarte, CA, USA; [2]Division of Biostatistics, City of Hope Comprehensive Cancer Center, Duarte, CA, USA; [3]Hematology/Oncology, Harbor - UCLA Medical Center, Torrance, CA, USA

Background: Cutaneous adnexal tumors comprise a heterogenous group of both benign and malignant tumors evolving from the four primary adnexal structures. Malignant adnexal tumors encompass a variety of histologic subtypes with varying clinical presentation. Due to the rarity of these conditions, incidence and prevalence is not well understood. In a retrospective analysis, estimated five-year Overall Survival (OS) and Disease-Free Survival (DFS) were estimated at 73% and 98%, respectively. There is a paucity of data surrounding the preferred clinical management of cutaneous adnexal tumors due to the rarity of these entities.

Methods: Patients with malignant adnexal tumors were identified using the National Cancer Database (NCDB). We examined demographic, clinicopathologic, and treatment information. Excluded from our cohort were patients with metastatic or unknown disease stage, positive or unknown margin status, unknown radiation and/or chemotherapy status, and unknown vital status. Chi-square analyses were used to assess differences across sebaceous versus non-sebaceous histologies. Multivariable Cox proportional hazard models were used to evaluate the effects of treatment modalities on overall survival after controlling for relevant covariates (age, race, and stage).

Results: 3,694 patients were included in the final analysis. The most prevalent malignant cutaneous adnexal tumor included sebaceous carcinoma (n=1699, 46%), eccrine porocarcinoma (n = 568, 15.4%), and skin appendage carcinoma (n =415, 11.2%). In patients with fully resected cutaneous adnexal tumors with negative surgical margins, multivariable results showed that receipt of adjuvant radiation was associated with statistically significantly longer survival compared to not receiving radiation (HR .76 (95%CI 0.61 — 0.96)). Non-sebaceous histology was also associated with longer survival than sebaceous histology (HR 0.78 (95% CI 0.69 — 0.88)). After stratifying by histologic groups, adjuvant radiation was associated with longer overall survival in sebaceous carcinoma (HR 0.62 (95% CI 0.42 — 0.92)), while receipt of adjuvant radiation in non-sebaceous histology groups was not associated with overall survival (HR 0.85 (95% CI 0.65 — 1.13)). Use of adjuvant chemotherapy following R0 resection was not associated with overall survival in the sebaceous group, while in the non-sebaceous group, chemotherapy was associated with shorter overall survival (HR 3.92 (95% CI 1.94 — 7.92)).

Conclusions: Acknowledging the limitations of a retrospective evaluation of real-world data, there does not appear to be a benefit for adjuvant chemotherapy after R0 resection in cutaneous adnexal carcinomas. Alternatively, omission of adjuvant radiotherapy was associated with an increased risk of mortality.

Legal entity responsible for the study: The authors.

Funding: Has not received any funding.

Disclosure: All authors have declared no conflicts of interest.

https://doi.org/10.1016/j.annonc.2023.09.2285

1152P Association of immune-related adverse events (irAE) requiring glucocorticoids (GCs) with outcome and biomarkers in advanced cutaneous malignant melanoma (CMM) treated with immune checkpoint inhibitors (ICI)

F. Costa Svedman[1], M. Liapi[2], A. Chatzidionysiou[2], A. Månsson-Broberg[3], S. Egyhazi Brage[4]

[1]Department of Oncology, Karolinska University Hospital-Solna, Stockholm, Sweden; [2]Department of Medicine, Karolinska Institutet, Stockholm, Sweden; [3]Department of Medicine, Karolinska Institutet, Huddinge, Sweden; [4]Oncology-Pathology Department, Karolinska Institutet - Bioclinicum, Solna, Sweden

Background: Therapy with ICIs have been successful with long-term survival benefits for some CMM patients. However, ICIs may also cause irAEs which could be serious and demand the prescription of GC. The combination of ICIs improves treatment efficacy but increases the risk for irAEs. The impact of GC treated irAE (GC-irAE) on efficacy of ICIs is not fully understood and biomarkers assessing the risk for irAE requiring GC treatment are not available. We studied a cohort of patients with metastatic CMM treated with ICI to evaluate if GC-irAE impact clinical outcome. We also investigated whether inflammation proteins in baseline plasma samples may predict the development of GC-irAE.

Methods: This is a cohort study performed at Karolinska University Hospital in Sweden including 98 subjects with advanced CMM (M1a-d), who received anti-PD1 alone (n=88), anti-PD1+ epacadostat (clinical trial, n=3) or ipilimumab + nivolumab (n=8) as 1st line therapy in most cases (85%). Clinical data regarding the use of GC to treat irAE were collected retrospectively. If GC-irAE occurred, the type of irAE was assembled. Baseline plasma samples from 58 of the 98 patients were analyzed utilizing the OLINK inflammation protein panel platform.

Results: In the whole cohort 65% were male and median age was 70 years. The median PFS and OS for the whole cohort were 12 and 38 months, respectively. Of 98 patients 44% developed GC-irAE. The most common GC-irAE were hypophysitis (11%), dematitis (7%), colitis (7%) and pneumonitis (6%). The median time to GC treatment start after ICI therapy was 146 days. The median PFS and OS for GC-irAE vs patients without GC-irAE were 24 and 73 months vs 5 and 18 months, respectively. Patients developing hypophysitis had a longer OS compared to other patients. High baseline levels of IL8 and S100A12 were associated with worse OS and high levels of DNER was associated with better OS and with risk of developing hypophysitis.

Conclusions: Patients developing a GC-irAE had significantly increased PFS and OS compared to the other patients. Further studies on potential biomarkers for risk of developing hypophysitis are warranted to timely avoid serious complications.

Legal entity responsible for the study: Karolinska University Hospital, Region Stockholm.

Funding: Cancerfonden, Radiumhemmets Forskningsfond and Region Stockholm (ALF).

Disclosure: F. Costa Svedman: Financial Interests, Institutional, Speaker, Consultant, Advisor, participated in an expert panel, honorary payment to the clinic: Pfizer; Financial Interests, Institutional, Speaker, Consultant, Advisor, Travel financing for participating in a preceptorship and reporting. Payment went to the clinic: Merck; Financial Interests, Institutional, Speaker, Consultant, Advisor, I do not receive any payment personally: BMS; Other, Institutional, Local PI, I do not receive any payment personally: Eisai, Merck, Idera; Other, Institutional, Coordinating PI, I do not receive any payment personally: Merck. A. Chatzidionysiou: Financial Interests, Institutional, Financially compensated role, Consultant fees went to Institutional Research: Eli Lilly, AbbVie, Pfizer; Other, Institutional, Coordinating PI: Janssen, Pfizer. A. Månsson-Broberg: Financial Interests, Institutional, Funding, Research funding: Amgen; Financial Interests, Institutional, Speaker, Consultant, Advisor: Orion Pharma, BMS; Other, Institutional, Local PI: Cardio3BioSciences. All other authors have declared no conflicts of interest.

https://doi.org/10.1016/j.annonc.2023.09.2286

1153P Incidence and characteristics of immunotherapy related adrenal insufficiency in a monocenter, pan-cancer cohort of 4314 patients

M.W. Lucas[1], N.C. Helderman[2], A.O. van de Velde[3], E. Kapiteijn[4], R.S. van Leeuwaarde[5], C.U. Blank[1]

[1]Medical Oncology Department, NKI-AVL - Netherlands Cancer Institute/Antoni van Leeuwenhoek Hospital, Amsterdam, Netherlands; [2]Medical Oncology, LUMC-Leiden University Medical Center, Leiden, Netherlands; [3]Scientific Administration, Netherlands Cancer Institute, Amsterdam, Netherlands; [4]Medical Oncology Dept., Leiden University Medical Center (LUMC), Leiden, Netherlands; [5]Internal Medicine, NKI-AVL - Netherlands Cancer Institute/Antoni van Leeuwenhoek Hospital, Amsterdam, Netherlands

Background: The rapidly developing field of immune checkpoint inhibitors (ICI) necessitates insights in long-term adverse events (AE), like ICI related adrenal insufficiency (irAI). In meta-analyses of clinical trials, primary AI (PAI) incidence is likely overestimated (4-7% for combination ICI), as PAI and secondary AI (SAI) are rarely distinguished.

Methods: In this monocenter, pan-cancer retrospective analysis, patients with a single malignancy who received anti-PD-(L)1 and/or anti-CTLA-4 therapy before September 10th 2021 and received (hydro/fludro)cortisone were identified. irAI was considered when AI was diagnosed in the absence of adrenal metastases, -surgery, -radiotherapy and long-term corticosteroid use. Diagnosis of PAI was based on cortisol <13 µmol/l and ACTH >60 ng/l, synacthen test and/or presence of mineral-corticoid dysfunction. SAI was diagnosed when ACTH <60 ng/l with low cortisol or in case of confirmed hypophysitis. Other irAI cases were labeled as unknown origin.

Results: Of 4314 patients with ICI, 160 (3.7%) developed irAI, consisting almost exclusively of SAI (3.1%) rather than PAI (0.05%, P<.001). irAI incidence was significantly higher for combination treatment versus anti-PD-(L)1 monotherapy (OR 4.95, 95% CI 3.55-6.97, p<.001). SAI presented as hypophysitis in 38% and as isolated adrenal deficiency in 62% of cases. Age, gender, metastatic status of the malignancy, history of endocrine or autoimmune disorder and other grade 3-4 AEs did not differ between PAI and SAI, or hypophysitis and IAD cases.

Table: 1153P Incidence of immunotherapy related adrenal insufficiency

	Anti-PD-(L)1	Anti-CTLA-4	Combination anti-PD-1 + anti-CTLA-4	Total
Melanoma	3.8% 29/768	3.1% 10/326	11.1% 59/533	6.7% 98/1466
Lung cancer	1.0% 12/1199	0	4.5% 2/44	1.1% 14/1243
Urethral and renal cancer	1.2% 3/246	0% 0/1	10.6% 15/142	4.6% 18/395
Breast cancer	2.0% 5/254	0	14.3% 2/14	2.6% 7/268
Colorectal cancer	2.4% 2/85	0	3.7% 4/108	3.1% 6/193
Bladder cancer	3.6% 4/111	0% 0/10	10.0% 5/50	5.4% 9/168
Other	0.6% 3/484	0% 0/2	5.0% 5/101	1.4% 8/581
Total	1.8% 58/3147	2.9% 10/339	9.3% 92/992	3.7% 160/4314

Conclusions: In contrast to what is suggested in trials, ICI-induced primary adrenal insufficiency was extremely rare in this real-world analysis, while secondary adrenal insufficiency was dominantly prevalent. Combination therapy leads more frequently to irAI. In conclusion, an improved understanding of irAI is needed, which may lead to improved diagnosis, and is essential for the development of predictive biomarkers.

Legal entity responsible for the study: The authors.

Funding: Has not received any funding.

Disclosure: E. Kapiteijn: Financial Interests, Institutional, Advisory Board: BMS, Novartis, Pierre Fabre, Merck, Delcath, Bayer, Lilly; Financial Interests, Institutional, Coordinating PI: BMS, Pierre Fabre, Delcath. C.U. Blank: Financial Interests, Institutional, Advisory Board: BMS, MSD, Roche, Novartis, GSK, AZ, Pfizer, Lilly, GenMab, Pierre Fabre; Financial Interests, Personal, Advisory Board: Third Rock Ventures; Financial Interests, Personal, Stocks/Shares: Immagene; Financial Interests, Institutional, Coordinating PI: NanoString, BMS, Novartis, 4SC; Financial Interests, Personal, Stocks/Shares, intention to develop IFN signature algorithm: NewCo, no name yet; Other, pending patent: WO 2021/177822 A1. All other authors have declared no conflicts of interest.

https://doi.org/10.1016/j.annonc.2023.09.2287

1154P Thromboembolic events in patients with melanoma receiving immune checkpoint inhibitors: Incidence and risk factors

D. van Dorst[1], M.M. Hofman[1], R.M. de Waal[1], E. Oomen-de Hoop[1], K.D. Joode[1], S. Bins[1], S.L. Koolen[1], A. Joosse[1], J. Versmissen[2], A.A.M. Van der Veldt[1], R.H. Mathijssen[1]

[1]Medical Oncology Department, Erasmus MC Cancer Institute, Rotterdam, Netherlands; [2]Department of Internal Medicine, Erasmus MC - Erasmus University Rotterdam, Rotterdam, Netherlands

Background: Immune checkpoint inhibitors (ICI) improve survival for multiple tumor types, but are possibly associated with thromboembolism (TE). Nonetheless, for patients with melanoma specifically, the risk of TE and its association with treatment setting remain largely unknown. Therefore, we investigated the incidence of TE and associated risk factors in two groups of patients with melanoma who received either palliative or adjuvant ICI therapy between April 2016 and September 2021.

Methods: In this cohort study, baseline characteristics and TE incidences (combined incidence of venous (VTE) and arterial (ATE) thromboembolism) were retrospectively collected from patients with stage III and IV melanoma included in the MULTOMAB trial (NL55840.078.15) until 2 years after the first ICI dose or censoring (switch to alternative anticancer treatment or loss to follow-up). The association between patient characteristics and TE occurrence was analyzed by the Fine-Gray model with backward selection using all-cause death as competing risk.

Results: Out of the 458 included patients, 28 (6%) patients developed a TE during a median follow-up of 17 months, consisting of 18 (4%) VTEs and 10 (2%) ATEs. Median time to TE occurrence was 5.2 months. In the advanced disease (N=315) and adjuvant (N=143) cohort, 23 (7%) and 5 (3%) patients developed TE, respectively. The incidence rates of TE per 100 person years was 4.9 in the total cohort, and 6.4 and 2.4 in respectively the advanced disease and adjuvant cohort. In the advanced disease cohort, BMI (sHR: 1.1 per point BMI increase [95% CI, 1.02 − 1.1, P=0.007]) and nivolumab + ipilimumab combination therapy (sHR 2.5 versus monotherapy [95% CI, 1.08 − 5.6, P = 0.03]) were risk factors for TE occurrence.

Conclusions: In patients with melanoma receiving ICI therapy, TE seems to occur predominantly in patients with advanced disease. In this treatment setting, ICI combination therapy and higher BMI are risk factors for TE. Although this suggests that particularly increased tumor load is a main predisposing factor, possible prothrombotic effects of particularly ICI combination therapy cannot be ruled out. Future research should further study the etiology of TE during ICI therapy while taking disease burden into account.

Clinical trial identification: NL55840.078.15.

Legal entity responsible for the study: The authors.

Funding: Has not received any funding.

Disclosure: K.D. Joode: Financial Interests, Institutional, Other, Travel expenses by Ipsen - all paid to Institution: Ipsen; Financial Interests, Institutional, Other, Travel expenses by Pamgene - all paid to Institution: Pamgene. A.A.M. Van der Veldt: Financial Interests, Institutional, Other, Consultancy all paid to institute: MSD, Merck, BMS, Pfizer, Eisai, Roche, Sanofi, Novartis, Pierre Fabre, Ipsen. R.H. Mathijssen: Financial Interests, Institutional, Research Grant, Investigator-initiated research: Astellas, Bayer, Cristal Therapeutics, Pfizer, Roche, Sanofi, Servier, Boehringer Ingelheim, Novartis; Financial Interests, Institutional, Coordinating PI: Pamgene. All other authors have declared no conflicts of interest.

https://doi.org/10.1016/j.annonc.2023.09.2288

1155P Application of novel machine learning to predict immunotherapy related toxicities for metastatic melanoma patients from baseline 18F-FDG PET/CT scans

R.J. Francis[1], M. Dell'Oro[1], E.S. Gray[2], D. Huff[3], T.G. Perk[3], R. Munian-Govindan[3], M.A. Ebert[4], M. Millward[5]

[1]Australian Centre for Quantitative Imaging, School of Medicine, University of Western Australia, Perth, WA, Australia; [2]School of Medical and Health Sciences, Edith Cowan University, Perth, WA, Australia; [3]Science, AIQ Solutions, Madison, WI, USA; [4]Department of Radiation Oncology, Sir Charles Gairdner Hospital, Nedlands, WA, Australia; [5]School of Medicine, University of Western Australia, Perth, WA, Australia

Background: Immunotherapy (I/O) has been shown to provide durable responses in metastatic melanoma (MM) patients, however, I/O related adverse events (irAE) are frequently experienced and can be challenging. ^{18}F-FDG PET/CT medical imaging, has the potential to predict both tumor response and irAE non-invasively. Developing machine learning (ML) models to quantify features derived from medical images represents an opportunity to predict toxicity and influence clinical patient care. This study implements automated organ segmentation and ML methods using ^{18}F-FDG PET/CT images to predict irAE for patients with MM.

Methods: ^{18}F-FDG PET/CT scans from 128 patients with MM were retrospectively collected between 2009 and 2021 (IRB approved protocol). Patients received $\geq$ 1 course of I/O. Organs were segmented automatically using AIQ Solutions technology. Segmented regions were used to quantify FDG organ uptake and correlate with toxicities including adrenal insufficiency, alanine aminotransferase increase, colitis/diarrhea, pancreatitis, and thyroid dysfunction. Imaging features were extracted from organs at baseline (BL) and early follow-up. Organ uptake and changes across time were evaluated for predicting irAE. A random forest model was trained using BL organ uptake to predict occurrence of an irAE. Performance was evaluated using area under the receiver operating characteristic curve (AUC).

Results: The patients (89 male and 39 female) average age was 63 (range 23-88). Overall, there were 105 irAE grouped per organ for univariate analysis, with the high frequency of hypothyroidism, raised alanine aminotransferase and colitis/diarrhea. The overall AUC for prediction of any irAE based on the BL scan was 0.76. Change in 95th percentile between pre-I/O work up and subsequent scans of SUVs was predictive of irAE in thyroid (AUC=0.95) and bowel (AUC=0.94).

Conclusions: Our results indicate that ML using quantitative features from ^{18}F-FDG PET/CT imaging has the potential to identify irAE early. Importantly, there may be imaging features on the BL scan that indicate MM patient's likelihood of developing an irAE before starting I/O. This warrants further investigation in a prospective setting.

Legal entity responsible for the study: The authors.

Funding: Has not received any funding.

Disclosure: All authors have declared no conflicts of interest.

https://doi.org/10.1016/j.annonc.2023.09.2289

1156P Immune-related adverse events in a nationwide cohort of melanoma patients treated with adjuvant anti-PD1: Seasonal variation and association with outcome

E. Ellebæk[1], R.S. Jurlander[2], L.M. Guldbrandt[3], R.B. Holmstroem[4], M. Donia[5], C.A. Haslund[6], H. Schmidt[7], L. Bastholt[8], C.H. Ruhlmann[8], I-M. Svane[4]

[1]Oncology Department, Herlev and Gentofte Hospital, Herlev, Denmark; [2]Oncological Department, Herlev Hospital - National Center for Cancer Immune Therapy (CCIT-DK), Herlev, Denmark; [3]Clinical Oncology, Institute of Clinical Medicine, Aarhus University Hospital Skejby, Aarhus, Denmark; [4]Department of Oncology, Herlev Hospital - National Center for Cancer Immune Therapy (CCIT-DK), Herlev, Denmark; [5]Oncology Department, Herlev Hospital - National Center for Cancer Immune Therapy (CCIT-DK), Herlev, Denmark; [6]Oncology Department, Aalborg University Hospital, Aalborg, Denmark; [7]Department of Oncology, Aarhus University Hospital, Aarhus, Denmark; [8]Dept. of Oncology, OUH - Odense University Hospital, Odense, Denmark

Background: The introduction of immune checkpoint inhibitors (ICIs) has transformed the treatment of advanced melanoma. However, treatment comes with the risk of immune-related adverse events (irAEs). Especially now that immunotherapy has moved to the adjuvant setting, doctors and patients must weigh potential benefits versus risks based on as much available information as possible. Real-world data are essential for decision-making.

Methods: A nationwide study on irAEs in Danish real-world patients treated with adjuvant anti-PD1 therapy for resected stage III-IV melanoma from 2018-2022. Data were retrieved from two national databases, the IMMUNOTOX database and the Danish Metastatic Melanoma Database (DAMMED).

Results: Data from 792 patients were included. The majority of patients were male (55%) with a median age of 62 (range 16-88) at time of first treatment. In total, 697 patients (88%) experienced an irAE, the most common being fatigue (44%). Low-grade irAEs (grades 1-2) were very common, whereas different subtypes of severe irAEs (grades 3-5) were observed in 0.3-4%. In total, 121 patients (15.3%) experienced severe irAEs out of which five patients (0.6%) died due to irAE. Having at least one irAE was associated with a lower risk of melanoma relapse. Seasonal variation was observed with more frequent debut of organ-specific (gastrointestinal, ocular, musculoskeletal, and thyroid) irAEs during summer, while mild skin toxicities were more frequent in the winter period.

Conclusions: In this nationwide cohort of real-world adjuvant melanoma patients, we observe that having any grade of irAEs, as well as a severe irAE, is slightly more frequent compared to clinical phase III trials and comparable to previously published real-world studies. Further, the risk of relapse from melanoma is lower among patients experiencing an irAE. Finally, significant seasonal variation in irAE incidence was observed.

Legal entity responsible for the study: The authors.

Funding: Has not received any funding.

Disclosure: E. Ellebæk: Financial Interests, Personal, Invited Speaker: Pierre Fabre, BMS, Novartis, MSD, Pfizer; Other, Travel and conference expenses: MSD, Pierre Fabre. R.B. Holmstroem: Non-Financial Interests, Personal, Invited Speaker, Talk on Immune-related adverse events: Best Practice Nordic. M. Donia: Financial Interests, Personal, Invited Speaker, Teaching: Novartis, Roche; Financial Interests, Personal, Other, Advisor: Achilles Therapeutics; Non-Financial Interests, Other, Sub-investigator of clinical trial with connected translational research: Bristol Myers Squibb; Non-Financial Interests, Personal, Proprietary Information, Proprietary data access: Bristol Myers Squibb; Non-Financial Interests, Personal, Proprietary Information, Proprietary Data Access: Genentech; Other, Chairman of the Melanoma and Non-melanoma Skin Cancer Scientific Committee: Danish Medicines Council (Medicinrådet). C.A. Haslund: Financial Interests, Personal, Invited Speaker: MSD, GSK, BMS; Financial Interests, Institutional, Local PI: BMS, Tesaro, MSD, IO Biotech, Chimerix, Incyte; Financial Interests, Institutional, Coordinating PI: GSK, Celgene Aps. L. Bastholt: Non-Financial Interests, Advisory Role, Scientific Committee under Danish Medicines Agency regarding new Treatments of Melanoma, Skin Cancer and Thyroid Cancer: Danish Medicines Agency. I. Svane: Financial Interests, Personal, Advisory Board: BMS, Pierre Fabre, Novartis; Financial Interests, Personal, Invited Speaker: MSD, Pierre Fabre, Novartis, Roche, BMS; Financial Interests, Personal, Writing Engagement: MSD; Financial Interests, Personal, Stocks/Shares, Cofounder and Founder warrants: IO Biotech; Financial Interests, Institutional, Research Grant: Adaptimmune, Enara Bio, Lytix Biopharma, TILT Biotherapeutics; Financial Interests, Institutional, Funding: Evaxion; Non-Financial Interests, Principal Investigator: BMS, Novartis, Roche, TILT Biotherapeutics, Lytix Biopharma. All other authors have declared no conflicts of interest.

https://doi.org/10.1016/j.annonc.2023.09.2290

1157P Corticosteroids and second-line immunosuppressants for immune-related adverse events and melanoma survival

R.J. Verheijden[1], J.C. Janssen[2], A.E. Putker[3], S.P.G.R. Veenstra[4], G.A.P. Hospers[5], M.J.B. Aarts[6], K.W. Hehenkamp[7], V.L.E. Doornebosch[8], M. Verhaert[9], F.W.P.J. Van den Berkmortel[10], F.H. Burgers[11], J.B.A.G. Haanen[11], D. Piersma[8], E. Kapiteijn[7], M. Labots[4], M.J. Boers-Sonderen[3], A.A.M. Van der Veldt[2], S. Aspeslagh[9], A.M. May[12], K.P.M. Suijkerbuijk[1]

[1]Department of Medical Oncology, University Medical Center Utrecht, Utrecht, Netherlands; [2]Department of Medical Oncology, Erasmus Medical Center, Rotterdam, Netherlands; [3]Department of Medical Oncology, Radboud University Medical Center, Nijmegen, Netherlands; [4]Department of Medical Oncology, Amsterdam UMC, location VUmc, Amsterdam, Netherlands; [5]Department of Medical Oncology, University Medical Center Groningen, Groningen, Netherlands; [6]Department of Medical Oncology, Maastricht University Medical Center+, Maastricht, Netherlands; [7]Department of Medical Oncology, Leiden University Medical Center, Leiden, Netherlands; [8]Department of Internal Medicine, Medisch Spectrum Twente, Enschede, Netherlands; [9]Department of Medical Oncology, Universitair Ziekenhuis Brussel, Jette, Belgium; [10]Department of Medical Oncology, Zuyderland Medical Center, Sittard-Geleen, Netherlands; [11]Department of Medical Oncology, NKI-AVL - Netherlands Cancer Institute/Antoni van Leeuwenhoek Hospital, Amsterdam, Netherlands; [12]Julius Center for Health Sciences and Primary Care, University Medical Center Utrecht, Utrecht, Netherlands

Background: Recent studies indicate an association between immunosuppressive medication for immune-related adverse events (irAEs) and impaired survival. Whether this is related to corticosteroids or second-line immunosuppressants (IS) is unknown. We assessed the association of immunosuppressive regimens with survival in patients with melanoma.

Methods: Patients with advanced melanoma who received IS for irAEs induced by first-line anti-PD-1+/-anti-CTLA-4 were included from 11 Dutch and Belgian hospitals. Associations of cumulative and peak doses of corticosteroids and use of second-line IS with progression free survival (PFS) from start of IS and overall survival (OS) since immune checkpoint inhibitor (ICI) initiation were assessed using multivariable Cox regression. Analyses were adjusted for sex, age, stage, performance status, LDH, ICI type and irAE type.

Results: Among 382 patients with irAEs, 255 had IPI+NIVO-induced irAEs and 127 had anti-PD-1-monotherapy-induced irAEs. 268 patients received only corticosteroids; 113 patients additionally received second-line IS. High peak corticosteroid dose was associated with worse PFS (HR 1.47 95%CI 1.00-2.16) and OS (HR 2.17 95%CI 1.49-3.16). Cumulative corticosteroid dose was not associated with PFS or OS (Table). Use of second-line IS was associated with worse PFS (HR 1.57 95%CI 1.04-2.38); for OS, this was the case when correction for cumulative corticosteroid dose (HR 1.57 95%CI 1.06-2.33), but not when correcting for peak corticosteroid dose (HR 1.25 95%CI 0.84-1.85). Subgroup analyses will be presented.

Table: 1157P Association of immunosuppressive irAE management with survival

	PFS HR (95%CI) since immunosuppression	OS HR (95%CI) since ICI
Univariable		
Steroid peak dose (per 100mg)	**1.90 (1.39-2.61)**	**1.89 (1.39-2.57)**
Steroid cumulative dose (per 1000mg)	1.06 (1.00-1.12)	0.95 (0.90-1.01)
2nd-line IS	**1.83 (1.32-2.52)**	**1.43 (1.04-1.97)**
Multivariable including steroid peak dose and 2nd-line IS		
Steroid peak dose (per 100mg)	1.47 (1.00-2.16)	**2.17 (1.49-3.16)**
2nd-line IS	**1.57 (1.04-2.38)**	1.25 (0.84-1.85)
Multivariable including steroid cumulative dose and 2nd-line IS		
Steroid cumulative dose (per 1000mg)	1.01 (0.94-1.08)	0.95 (0.89-1.02)
2nd-line IS	**1.64 (1.09-2.47)**	**1.57 (1.06-2.33)**

Conclusions: Our data suggest that use of second-line immunosuppressants and high peak corticosteroid dose are associated with impaired survival among patients requiring IS for irAEs, while there is no association between cumulative corticosteroid dose and survival.

Legal entity responsible for the study: University Medical Center Utrecht.

Funding: Has not received any funding.

Disclosure: G.A.P. Hospers: Financial Interests, Institutional, Advisory Board: Amgen, Bristol Myers Squibb, Roche, Merck Sharp & Dohme, Pfizer, Novartis, Sanofi, Pierre Fabre; Financial Interests, Institutional, Research Funding: Bristol Myers Squibb, Seerave. M.J.B. Aarts: Financial Interests, Institutional, Advisory Board: Amgen, Bristol Myers Squibb, Novartis, Merck Sharp & Dohme, Merck-Pfizer, Pierre Fabre, Sanofi, Astellas, Bayer; Financial Interests, Institutional, Research Funding: Merck-Pfizer. J.B.A.G. Haanen: Financial Interests, Institutional, Advisory Board: Bristol Myers Squibb, Achilles Therapeutics, Ipsen, Merck Sharp & Dohme, Merck Serono, Pfizer, Molecular Partners, Novartis, Roche, Sanofi, Third Rock Venture, Iovance Biotherapeutics; Financial Interests, Institutional, Advisory Board, SAB member: BioNTech, Immunocore, Gadeta, Instil Bio, PokeAcel, T-Knife; Financial Interests, Personal, Advisory Board, SAB member: Neogene Therapeutics, Scenic; Financial Interests, Personal, Stocks/Shares: Neogene Therapeutics; Financial Interests, Institutional, Research Grant: Bristol Myers Squibb, BioNTech US, Merck Sharp & Dohme, Amgen, Novartis, Asher Bio; Non-Financial Interests, Member: ASCO, AACR, SITC; Other, Editorial Board ESMO Open: ESMO; Other, Editor-in-Chief IOTECH: ESMO; Other, Editorial Board: Kidney Cancer. E. Kapiteijn: Financial Interests, Institutional, Advisory Board: BMS, Novartis, Pierre Fabre, Merck, Delcath, Bayer, Lilly; Financial Interests, Institutional, Coordinating PI: BMS, Pierre Fabre, Delcath. M. Labots: Financial Interests, Institutional, Advisory Board: Bristol Myers Squibb, Janssen-Cilag BV. A.A.M. Van der Veldt: Financial Interests, Institutional, Advisory Board: Bristol Myers Squibb, Merck Sharp & Dohme, Sanofi, Pfizer, Novartis, Roche, Eisai, Merck, Pierre Fabre, Ipsen. S. Aspeslagh: Financial Interests, Institutional, Advisory Board: Merck Sharp & Dohme, Sanofi, Roche, Bristol Myers Squibb, Pfizer, Ipsen, Galapagos. K.P.M. Suijkerbuijk: Financial Interests, Institutional, Advisory Board: Novartis, BMS, AbbVie, Pierre Fabre, MSD; Financial Interests, Institutional, Invited Speaker: Roche; Financial Interests, Institutional, Research Grant: Novartis, TigaTx. All other authors have declared no conflicts of interest.

https://doi.org/10.1016/j.annonc.2023.09.2291

1158P Association of corticosteroid (CS) exposure with treatment failure in patients (pts) with advanced melanoma treated with immune checkpoint inhibitors (ICIs)

H.M.L. Le[1], J. Pozas Perez[2], M.V. San Roman Gil[2], J.J. Serrano Domingo[2], J. Larkin[1]

[1]Medicine Department, The Royal Marsden Hospital - NHS Foundation Trust, London, UK; [2]Medical Oncology Department, Ramón y Cajal University Hospital, Madrid, Spain

Background: Around 25% of pts with advanced melanoma lose established responses to ICIs. Recent studies suggest that systemic CS, predominantly used for managing immune-related adverse events (IRAEs), could be a cause of acquired resistance to ICIs, with a detrimental effect on survival. The impact of systemic CS on pts with initial response to ICIs remains unknown.

Methods: This is a retrospective study of 113 pts with advanced melanoma treated with ipilimumab and nivolumab (I/N) at The Royal Marsden Hospital between 2013 and 2021 who achieved initial disease stability or disease response. Pts were divided into cohort A (sustained response to I/N, N = 72) and cohort B (loss of response to I/N, N = 41). The daily CS exposure was evaluated from cycle 1 of I/N (prednisolone equivalent doses). STATA was used for statistical analysis.

Results: Most pts had cutaneous melanoma (73.6% in cohort A vs 75.6% in cohort B), stage IV disease (91.7% vs 95.1%) and were treatment-naïve (86.1% vs 85.4%). More pts in cohort B had a BRAF mutation (46.3% vs 38.9% in cohort A), high LDH (29.3% vs 19.4%), brain (24.4% vs 20.8%) and liver metastases (26.8% vs 18.1%) at baseline. The median number of I/N cycles was 4 in cohort A and 3 in cohort B. Up to 27 pts in cohort A (38%) and 24 in cohort B (59%) discontinued treatment during the induction phase due to toxicity. All pts in our study were given CS for IRAEs management. Up to 97.6% of pts in cohort B received CS, compared to 69.4% in cohort A. Pts who were treated with CS had a significantly higher rate of treatment failure (44.4% vs 4.4%, $p < 0.001$). The average cumulative CS dose per patient in cohort A was 4830 mg compared to 4201 mg in cohort B ($p = 0.897$). The average daily CS dose in cohort A was 32 mg/day compared to 30 mg/day in cohort B ($p = 0.889$). Pts unexposed to CS have a trend for longer overall survival (NR vs NR, HR 0.25 [0.03-1.92]).

Conclusions: Our study suggests a correlation between systemic CS use and higher rates of treatment failure, as well as a trend for shorter survival in pts with advanced melanoma treated with I/N. The dose of CS was similar in both cohorts. However, as this is a single centre retrospective experience, these findings should be confirmed in larger studies.

Legal entity responsible for the study: The authors.

Funding: Has not received any funding.

Disclosure: H.M.L. Le: Financial Interests, Personal, Sponsor/Funding, Meeting attendance: Pfizer, Novartis. J. Larkin: Financial Interests, Personal, Invited Speaker: BMS, Pfizer, Roche, Pierre Fabre, AstraZeneca, Novartis, EUSA Pharma, MSD, Merck, GSK, Ipsen, Aptitude, Eisai, Calithera, Ultimovacs, Seagen, Goldman Sachs, eCancer, Inselgruppe, Agence Unik; Financial Interests, Personal, Other, Consultancy: Incyte, iOnctura, Apple Tree, Merck, BMS, Eisai, Debiopharm; Financial Interests, Personal, Other, Honorarium: touchIME, touchEXPERTS, VJOncology, RGCP, Cambridge Healthcare Research, Royal College of Physicians; Financial Interests, Institutional, Funding: BMS, MSD, Novartis, Pfizer, Achilles, Roche, Nektar, Covance, Immunocore, Pharmacyclics, Aveo. All other authors have declared no conflicts of interest.

https://doi.org/10.1016/j.annonc.2023.09.2292

1159P Characterization of melanoma of unknown primary in the era of immunotherapy and targeted therapy in Spain: Results from the prospective real-world study GEM 1801

P. Cerezuela-Fuentes[1], A. Piñero-Madrona[2], E. Muñoz-Couselo[3], J.L. Manzano[4], M-Á. Berciano-Guerrero[5], M. Majem[6], E. Espinosa[7], A. Soria[8], P. Ayala de Miguel[9], A. García Castaño[10], G. Crespo[11], L. Gutiérrez Sanz[12], C. Aguado de la Rosa[13], L.A. Fernández-Morales[14], T. Puértolas[15], J. Fra[16], M. Rodríguez de la Borbolla[17], L. Bellido[18], S. Martín Algarra[19], I. Márquez-Rodas[20]

[1]Medical Oncology Department, Hospital Clínico Universitario Virgen de la Arrixaca, Murcia, Spain; [2]Department of Surgery, Hospital Clínico Universitario Virgen de la Arrixaca, Murcia, Spain; IMIB-Arrixaca, Murcia, Spain; [3]Medical Oncology Department, Hospital Universitari Vall d'Hebron y Vall d'Hebron Institute of Oncology (VHIO), Barcelona, Spain; [4]Medical Oncology Department, Instituto Catalán de Oncología, ICO-Badalona, H. Germans Trias i Pujol, Badalona, Spain; [5]Unidad Intercentros de Oncología, Hospitales Universitarios Regional y Virgen de la Victoria (HURyVV), Instituto de Investigaciones Biomédicas de Málaga (IBIMA), Malaga, Spain; [6]Medical Oncology Department, Hospital de la Santa Creu i Sant Pau, Barcelona, Spain; [7]Medical Oncology Department, Hospital Universitario La Paz, CIBERONC, Madrid, Spain; [8]Medical Oncology Department, Hospital Universitario Ramón y Cajal, Madrid, Spain; [9]Medical Oncology Department, Hospital Universitario San Pedro de Alcántara, Cáceres, Spain; [10]Medical Oncology Department, Hospital Universitario Marqués de Valdecilla, Santander, Spain; [11]Medical Oncology Department, Hospital Universitario de Burgos, Burgos, Spain; [12]Medical Oncology Department, Hospital Universitario Puerta de Hierro, Madrid, Spain; [13]Medical Oncology Department, Hospital Universitario Clínico San Carlos, Madrid, Spain; [14]Medical Oncology Department, Hospital Universitari Parc Taulí, Sabadell, Spain; [15]Medical Oncology Department, Hospital Universitario Miguel Servet, Zaragoza, Spain; [16]Medical Oncology Department, Hospital Universitario Río Hortega, Valladolid, Spain; [17]Medical Oncology Department, Hospital Universitario de Valme, Seville, Spain; [18]Medical Oncology Department, Complejo Asistencial Universitario de Salamanca, Salamanca, Spain; [19]Medical Oncology Department, Clinica Universidad de Navarra, Pamplona, Spain; [20]Medical Oncology Department, Hospital General Universitario Gregorio Marañon, Madrid, Spain

Background: The clinical presentation of patients (pts) diagnosed with melanoma of unknown primary (MUP) is not clearly known, like their therapeutic assignment and their evolution in terms of responses obtained, toxicity, and relapse profile in the actuality.

Methods: GEM1801 is a prospective observational study including pts with melanoma that analyzes the clinical and pathological disease presentation patterns, the different lines of treatment choices and the health outcomes derived from treatments. Here we focus on the clinical and evolution characterization of pts diagnosed with MUP.

Results: From Aug 2018 to Dec 2022, 893 evaluable pts were enrolled, 133 (14.9%) being MUP. Median age was 63 years (range 24-93), 81 (60.9%) male. Distal metastases were present in 117 (88%) pts with most (50.4%) having $\geq$ 3 affected organs, including ganglia (53.4%), lung (41.4%) or brain (30.1%). LDH was elevated in 50 (37.6%) pts. BRAF was mutated in 79 (54.9%) pts. Adjuvant therapy was administered to 28 (21.1%) pts with MUP, being immunotherapy less frequently prescribed than in pts with known primary (17.3% vs 27.1%; p=0.017). Immunotherapy was also less frequent for the 1st line in the metastatic/locally advanced setting (53.6% vs 64%; p=0.039). Conversely, more pts with MUP were enrolled in clinical trials exploring combo of immunotherapy and targeted therapy (9.1% vs 4.8%; p=0.074).

Table: 1159P

	N, (%)	Median PFS (95% CI), months	Median OS (95% CI), months
BRAF + IT	17 (12.8)	18.9 (4.4-NR)	24.9 (24.1-NR)
BRAF + TT	40 (30.1)	13.3 (7.1-27.5)	13.9 (8.3-NR)
BRAF - IT	41 (30.8)	6.7 (3.5-NR)	17.9 (9.6-NR)

IT = Immunotherapy; TT = Targeted therapy.

Conclusions: MUP in Spain comprises a population with a multiorgan presentation and frequent brain metastasis, which was followed by worse outcomes than the general melanoma population. Having MUP diagnosis seems to influence the therapeutic assignment, specially for immunotherapy schemes.

Clinical trial identification: NCT03605771.

Editorial acknowledgement: We acknowledge MFAR Clinical Research staff for their assistance in the development of this abstract.

Legal entity responsible for the study: Grupo Español Multidisciplinar de Melanoma (GEM).

Funding: GEM through industry partners Novartis, Pierre Fabre, Incyte, BMS, Roche y MSD.

Disclosure: E. Muñoz-Couselo: Financial Interests, Personal, Speaker, Consultant, Advisor: BMS, MSD, Novartis, Pierre Fabre, Sanofi, Roche; Other, Personal, Advisory Board: Amgen, BMS, MSD, Novartis, Pierre Fabre, Roche, Sanofi; Other, Personal, Other, Honoraria: Amgen, BMS, Novartis, Pierre Fabre, Roche; Other, Personal, Principal Investigator: Amgen, BMS, GSK, MSD, Novartis, Pierre Fabre, Roche, Sanofi. E. Espinosa: Financial Interests, Personal, Speaker, Consultant, Advisor: BMS,

Novartis, Pierre Fabre; Financial Interests, Personal, Advisory Role: MSD. L.A. Fernández-Morales: Financial Interests, Personal, Speaker, Consultant, Advisor: BMS, MSD, Pierre Fabre, Roche, Novartis, Pfizer. T. Puértolas: Financial Interests, Personal, Advisory Role: Bristol Myers Squibb, Immunocore, Novartis, Seagen; Other, Personal, Other, Travel, Accommodation, Expenses: Novartis, MSD, Pierre Fabre. I. Márquez-Rodas: Financial Interests, Personal, Advisory Board: BMS, MSD, Novartis, Pierre Fabre, Roche, GSK, AstraZeneca, Celgene, Regeneron, Sanofi, Merck Serono, Highlight Therapeutics, Bioline Rx, Sun Pharma, Immunocore; Financial Interests, Personal and Institutional, Coordinating PI: Pierre Fabre; Financial Interests, Institutional, Coordinating PI, GEM1802 clinical trial: Novartis; Financial Interests, Institutional, Coordinating PI, GEM1801 clinical study: BMS, Roche, Pierre Fabre, Incyte, MSD; Financial Interests, Institutional, Coordinating PI, National coordinator of Spotlight 203 clinical trial: Highlight Therapeutics; Non-Financial Interests, Advisory Board: Spanish Melanoma group. All other authors have declared no conflicts of interest.

https://doi.org/10.1016/j.annonc.2023.09.2293

1160P Methods of nivolumab administration in advanced melanoma: A comparison of patients' clinical outcomes treated with flat dose or weight-adjusted dose, FLATIMEL study

I. Campo le Brun[1], S. Dalle[2], L. Mortier[3], O. Dereure[4], S. Dalac Rat[5], C. Dutriaux[6], M-T. Leccia[7], D. Legoupil[8], H. Montaudie[9], J. De Quatrebarbes[10], C. Gaudy Marqueste[11], E. Maubec[12], P. Saiag[13], C. Pages[14], F. Brunet Possenti[15], F. Granel Brocard[16], R. Porcher[17], W. Lefevre[18], C. Lebbe[19], E. Kempf[1]

[1]Department of Medical Oncology, Université Paris Est Créteil, Assistance Publique - Hôpitaux de Paris, Creteil, France; [2]Oncology Department, Lyon Sud Hospital Center, Pierre Benite, France; [3]Oncology Department, CHRU de Lille - Hôpital Roger Salengro, Lille, France; [4]Dermatology Dept., University of Montpellier, Montpellier, France; [5]Dermatology, CHU Dijon, Dijon, France; [6]Medical Oncology Department, CHU Bordeaux - Hopital St. André, Bordeaux, France; [7]Dermatoloy, CHU Grenoble Alpes - Site Nord (La Tronche), La Tronche, France; [8]Department of Dermatology-Venereology, CHRU Brest - Hôpital Morvan, Brest, France; [9]Department of Dermatology, Centre Hospitalier Universitaire de Nice, Université Côte d'Azur, Nice, France; [10]Dermatology, Le Centre Hospitalier Annecy Genevois, Metz-Tessy, France; [11]Dermatology, AP-HM - CHU La Timone Enfants, Marseille, France; [12]Dermatology, Hôpital Avicenne - APHP, Bobigny, France; [13]Department of Dermatology and Oncology, Hôpital Ambroise Paré, Boulogne-Billancourt, France; [14]Dermatology, Institut Claudius Regaud - IUCT Oncopole, Toulouse, France; [15]Oncodermatology, Hopital Bichat - Claude-Bernard AP-HP, Paris, France; [16]Onco Dermatology, CHRU Nancy, Nancy, France; [17]Epidemiology, Université de Paris - Faculté de Médecine, Paris, France; [18]Dermato-Oncology, Assistance Publique - Hopitaux de Paris, Paris, France; [19]Department of Dermatology, Université Paris Cité APHP Hôpital Oncodermatologie Saint-Louis, INSERM U976, Paris, France

Background: Nivolumab obtained marketing authorization in advanced melanoma (AM) with weight-adjusted (WA) dose administration (3 mg/kg/2 weeks) [1]. Based on modeling studies (no clinical data), EMA advised in 2018 that nivolumab should be administered in flat dose regimen (240 mg/2 weeks or 480 mg/4 weeks) [2 3]. The aim of the FLATIMEL study was to compare clinical outcomes of AM patients treated with both nivolumab dose calculation methods.

Methods: AM patients were prospectively included in the national multicenter MelBase database since 2013 (NCT02828202). Patients treated by nivolumab monotherapy in first line enrolled in MelBase were included in our study. We compared safety and efficacy of nivolumab in 2 groups of patients treated by flat or WA dose. The primary endpoint was the incidence of immune-related adverse events (irAEs) of grade $\geq$ 3. Secondary endpoints were incidence of irAEs of any grade, overall survival (OS) and progression free survival (PFS). Inverse probability of treatment weighting was used to balance groups on their baseline characteristics.

Results: Between June 2015 and January 2022, 546 patients followed in MelBase were included in this study: 252 in the flat dose group and 294 in the WA group. Patients with metastatic organs $\geq$ 3 ($p<0.0001$), brain metastasis ($p=0.0005$) or M1c AJCC (7th edition) tumor stage ($p=0.001$) were more frequent in the WA group. After weighting, no difference between both groups was observed for irAEs grade $\geq$ 3 (n=65, 12%), ($p= 0.51$), whereas irAEs of any grade (n=314, 57.5%) were more frequent in the flat dose group ($p=0.044$), especially muco-cutaneous and endocrine toxicities. Median OS was 32.3 and 20.6 months in flat dose and WA group respectively ($p= 0.004$), and median PFS was 3.5 and 2.8 months, respectively ($p= 0.003$).

Conclusions: There was no difference in the incidence of severe irAEs between AM patients treated by WA or flat dose of Nivolumab. Survival results were superior in the flat dose group, which may be explained by a temporal bias. Cost effectiveness studies are necessary.

Legal entity responsible for the study: MELBASE database.

Funding: INCa, Roche, BMS, Novartis, MSD, Amgen.

Disclosure: L. Mortier: Financial Interests, Personal, Advisory Board: BMS, MSD, Pierre Fabre, Novartis, Sanofi. H. Montaudie: Financial Interests, Personal, Research Funding: BMS, Merck, MSD, Novartis, Pierre Fabre, Leo pharma, Checkpoint Therapeutic, Huyaboiscience, Incyte, Nektar Pharmaceutical, Regeneron, Replimune; Financial Interests, Personal, Funding: BMS, Merck Serono, MSD Novartis, Pierre Fabre; Financial Interests, Institutional, Advisory Board: BMS, Leo Pharma. C. Pages: Financial Interests, Personal, Advisory Board: BMS. C. Lebbe: Financial Interests, Personal, Funding: Roche, BMS, Novartis, Amgen, MSD, Pierre Fabre, Pfizer, Incyte; Financial Interests, Personal, Advisory Role: BMS, MSD, Novartis, Amgen, Roche, Merck Serono, Sanofi, Pierre Fabre; Financial Interests, Personal, Invited Speaker: Roche, BMS, Novartis, Amgen, MSD; Financial Interests, Institutional, Research Funding: Roche, BMS, Novartis, Amgen, MSD; Financial Interests, Personal, Advisory Board: Avantis Medical Systems, InflaRx, Sanofi, BMS, MSD, Pierre Fabre, Novartis, Jazz Pharmaceuticals; Financial Interests, Personal, Other: BMS, MSD, Novartis, Sanofi, Pierre Fabre. All other authors have declared no conflicts of interest.

https://doi.org/10.1016/j.annonc.2023.09.2294

1161P Therapeutic outcome of molecular profiling of melanoma patients resistant to standard treatment: Real-world data

M. Sakkal[1], M. Aldea[2], A. Bayle[3], D. Vasseur[4], E. Routier[2], D. Belkadi-Sadou[5], A. Marchand[5], A. Gazzah[2], C. Smolenschi[6], R. Bahleda[7], C. Baldini[8], S. Champiat[9], Y. Loriot[10], L. Lacroix[11], E. Rouleau[12], A. Hollebecque[13], A. Italiano[13], S. Ponce Aix[1], C. Robert[14]

[1]Drug Development Department (DITEP), Gustave Roussy - Cancer Campus, Villejuif, France; [2]Medical Oncology Department, Institut Gustave Roussy, Villejuif, France; [3]Digestive Oncology Department, Institut Gustave Roussy, Villejuif, France; [4]Molecular Biology, Gustave Roussy - Cancer Campus, Villejuif, France; [5]Medical Oncology Department, Gustave Roussy - Cancer Campus, Villejuif, France; [6]Digestive Oncology Department, Gustave Roussy, Villejuif, France; [7]Drug Development Department, Gustave Roussy - Cancer Campus, Villejuif, France; [8]Drug Development Department, Institut Gustave Roussy, Villejuif, France; [9]Drug Development Department (DITEP), Institut Gustave Roussy, Villejuif, France; [10]Cancer Medicine Department, Institut Gustave Roussy, Villejuif, France; [11]Medical Biology and Pathology Department, Gustave Roussy - Cancer Campus, Villejuif, France; [12]Tumor Genetics, Gustave Roussy - Cancer Campus, Villejuif, France; [13]DITEP, Institut Gustave Roussy, Villejuif, France; [14]Dermatology Department, Institut Gustave Roussy, Villejuif, France

Background: Therapeutic options for advanced melanoma patients (pts) resistant to standard treatment (Tx): immunotherapy & anti-BRAF-based targeted therapy represent a high medical need. Objective: Our aim was to evaluate the applicability of precision medicine in melanoma pts who failed standard tx based on molecular profiling (MP) of their tumors & the resulting clinical outcome.

Methods: All pts with advanced melanoma resistant to standard tx who had a MP at Gustave Roussy between April 2021 & March 2023 were included in this retrospective study. MP was performed by using Next Generation sequencing by using Foundation one CDX/liquidCDX & it was based on 3 protocols: STING (NCT04932525), MCLA-128 (NCT03321981) & STARTRK (NCT02568267) which allowed liquid & tissue biopsies studies. Molecular actionability was based on ESMO Scale for Clinical Actionability of Molecular Targets (ESCAT) classification.

Results: We performed MP for 184 pts: 174 had melanoma, 2 pts with EWSR1-ATF1 fusion & 1 with EWSR1-CREB1, which allowed a diagnosis correction to clear cell sarcoma & the initiation of the appropriate sarcoma tx, 3 BCC, 3 cSCC & 1 Merkel cell cancer. For the 174 melanoma pts, apart from the BRAF V600 mutation (50% of the pts), a putative actionable molecular orientation was found in 51.6% of the pts. The most frequent molecular alterations were: NRAS (23.2%), PTEN (12.6%), ATM (8.4%), CDKN2A (7.4%), BRAF class II (6.3%), BRAF class III (5.3%), KIT (4.2%) PIK3CA (3.2%), MAP2K1 (3.2%), NF1 (2.1%), AKT (1.1%), HRAS (1.1%), MET (1.1%), ALK (1.1%), ARID1A (1.1%), CDK4 (1.1%), CCND1 (1.1%). Molecularly matched tx was administered to 15 pts: anti-MEK ($n = 11$) & imatinib ($n = 2$). Among the 11 pts on anti-MEK, 1 partial response was seen after 9 months of tx & the remaining 10 pts rapidly progressed after 1-3 months of anti-MEK tx as for the 2 pts on imatinib. Unfortunately, no precision medicine tx was available to target the other potentially actionable mutations at the time they were needed.

Conclusions: Potentially actionable mutations can be found in more than 50% of pts with resistant melanoma. Tumor agnostic trials based on molecular alterations should be more broadly available to evaluate the potential benefit of innovative precision medicine in this population.

Legal entity responsible for the study: The authors.

Funding: Has not received any funding.

Disclosure: All authors have declared no conflicts of interest.

https://doi.org/10.1016/j.annonc.2023.09.2295

1162P Prolonged exposure to proton pump inhibitors (PPI) at the time of initiation of immune checkpoint blockade (ICB) mediates better clinical outcomes in patients with metastatic melanoma

K.S. Shohdy[1], Y. Hatahet[2], T. Gillham[2], E.T.T. Yacoub[3], A. Gupta[4], F. Gomes[4], F. Thistlethwaite[1], F. Blackhall[1], P. Lorigan[1], N. Cook[5]

[1]Division of Cancer Sciences, The Christie NHS Foundation Trust and The University of Manchester, Manchester, UK; [2]Experimental Cancer Medicine Team, The Christie NHS Foundation Trust, Manchester, UK; [3]Department of Surgery, Cairo University, Giza, Egypt; [4]Department of Medical Oncology, The Christie NHS Foundation Trust, Manchester, UK; [5]Division of Cancer Sciences, The Christie NHS Foundation Trust and The University of Manchester, Manchester, UK

Background: Tumor acidity negatively regulates tumor-specific effector T cells in the tumor microenvironment. Conflicting results emerged on the impact of PPI on the efficacy of ICB.

Methods: A retrospective analysis was conducted on patients (pts) with metastatic melanoma treated with ICB between 2019 and 2020 at the Christie NHS Foundation Trust. Data on demographics, sites of disease, performance status (PS), comorbidities, types of therapy, progression-free (PFS), and overall survival (OS) were collected. Statistical analyses were performed with univariable and multivariable Cox regression models. The aim was to define the association between PPI exposure (defined as 30 days before or after the initiation of ICB and for at least 21 days concomitant with ICB) and PFS, and OS.

Results: Data was collected on 189 pts with a median age of 60 years; 57.14% were male, 88% had ECOG PS 0/1, 17% were BRAF mutant, 28% had elevated serum LDH, and 28.5% had brain metastases. 162 (86%) pts received ICB as their first line of treatment for advanced disease. The majority of pts (92%) received ipilimumab and nivolumab, and 8% received pembrolizumab. 83 (44%) of pts were identified as PPI users with a median duration of PPI use concomitantly with ICB of 365 days (range 21-1976 days). PPI use was significantly associated with longer median PFS (not reached vs. 7.3 months, Hazard ratio (HR):0.53, 95%CI:0.35-0.79, p=0.002) and longer median OS (not reached vs. 17.2 months, HR:0.47, 95%CI:0.30-0.73, p=0.001). In a multivariable regression analysis accounting for age, gender, PS, Charlson comorbidity score, BRAF status, elevated LDH, brain and liver metastases, and line of treatment, the favorable impact of PPI use on PFS (HR:0.53, 95%CI:0.35-0.81, p=0.003) and OS (HR: 0.43, 95%CI:0.27-0.69, p<0.0001) was maintained.

Conclusions: Exposure to PPI for more than 21 days at the initiation of ICB mediates better clinical outcomes. Our findings suggest that the duration and timing of PPI use should be considered when investigating the impact on ICB outcomes. Prospective studies are required to test the priming effect of PPI on tumors with acidic microenvironments.

Legal entity responsible for the study: The Christie NHS Foundation Trust.

Funding: Has not received any funding.

Disclosure: All authors have declared no conflicts of interest.

https://doi.org/10.1016/j.annonc.2023.09.2978

1163P CD39 affect the prognostic role of NLR via N2 neutrophils in metastatic melanoma patients treated with immunotherapy

D. Mallardo[1], M. Fordellone[2], A. White[3], M. Ottaviano[1], F. Sparano[1], M. Bailey[4], B.A. Facchini[1], S. Ong[3], P. Maiolino[5], C. Caracò1[6], S.E. Church[7], E. Cavalcanti[8], S. Warren[4], A. Budillon[9], A. Cesano[4], E. Simeone[1], P. Chiodini[2], P.A. Ascierto[1]

[1]Melanoma, Cancer Immunotherapy and Development Therapeutics Department, Istituto Nazionale Tumori - IRCCS - Fondazione Pascale, Naples, Italy; [2]Medical Statistics Unit, Università degli Studi della Campania Luigi Vanvitelli, Naples, Italy; [3]Research and Development, NanoString Technologies, Seattle, WA, USA; [4]Research and Development, NanoString Technologies, Inc., Seattle, WA, USA; [5]Hospital Pharmacy, Istituto Nazionale Tumori - IRCCS - Fondazione Pascale, Naples, Italy; [6]Division of Surgery of Melanoma and Skin Cancer, Istituto Nazionale Tumori IRCCS - Fondazione G. Pascale, Naples, Italy; [7]R&D, NanoString Technologies, Seattle, WA, USA; [8]Division of Laboratory Medicine, Istituto Nazionale Tumori IRCCS - Fondazione G. Pascale, Naples, Italy; [9]Translational Research, Istituto Nazionale Tumori - IRCCS — Fondazione G. Pascale, Naples, Italy

Background: The immune checkpoint inhibitors (ICIs) revolutionized cancer therapeutic landscape and substantially improved the survival of patients (pts) with advanced malignancies. Several predictive biomarkers are under evaluation, in order to identify patients who can benefit from ICI. Recently, elevated NLR, calculated from absolute neutrophil count and white cell count, were found to be independent predictors of reduced survival and increased risk of progression in melanoma patients receiving ICI. The purpose of this study is to retrospectively investigate relationship of NLR with inflammation-immune mediators.

Methods: Gene profiling analysis was performed from 78 basal PBMCs of metastatic melanoma pts treated in first line with anti-PD1 using NanoString IO360 panel. Patient's characteristics are listed in table. To identify the best genes signature the Sparse Partial Least Squares Discriminant Analysis (sPLS-DA) was applied.

Results: Overall, 78 patients were included in the analysis. Pts with high NLR at baseline (ratio >5.57) had a poorer PFS (HR=7.27, 95% CI = 3.5-14.8; p < 0.0001) and OS (HR=3.98; 95% CI = 2.0-7.9) than the pts with low NLR. Brain metastases were present in a higher proportion of pts with high NLR compared to those with low NLR (p=0.01). In the trascriptomic analysis, NLR was associated with SH2D1A, CD3, ZAP70, CD45RA genes, while a high NLR with CCNA1, LDHA, IL18R1, CD39, PTEN, MYD88 and MMP9 genes (ROC curve, AUC=0.97, p<0001). The signatures are also associated to response. In addition, CD39 expression is higher in NLR high and is associate with increase of N2 neutrophils. NLR increase on treatment is also associated to worse outcome and a specific genetic signature.

Table: 1163P

Patient characteristics	N = 78
Median age	61 (range 27-91)
Gender: female/male, n (%)	41 (53)/37 (47)
Melanoma AJCC VII Stage	
Stage IV, n (%)	74 (94)
Stage IIIC	4 (5)
Stage IIIB	1 (1)
CNS metastases at baseline, n (%)	18 (23)
BRAF Status	
Wilde type, n (%)	59 (76)
Mutation, n (%)	16 (21)
NA, n (%)	3 (3)
Response rate at 1st assessment	
Complete response, n (%)	9 (11)
Partial response, n (%)	16 (21)
Stable disease, n (%)	17 (22)
Progression disease, n (%)	36 (46)
ORR, n (%)	39 (50)
DCR, n (%)	25 (32)
LDH	
High	26 (33)
Normal	34 (44)
NA	18 (23)

Conclusions: NLR high is related with immunosuppressive, inflammatory and tumor related genes; in particular with N2 neutrophils associate to adenosine pathway activation. This could explain the prognostic role of NLR. Further investigations are needed to get additional information.

Legal entity responsible for the study: Paolo Antonio Ascierto.

Funding: Italian Ministry of Health (IT-MOH).

Disclosure: A. White, M. Bailey, S. Ong, S.E. Church, S. Warren, A. Cesano: Financial Interests, Personal, Stocks or ownership: NanoString. P.A. Ascierto: Financial Interests, Personal, Advisory Board: Bristol Myers Squibb, Roche-Genentech, Merck Sharp & Dohme, Novartis, Merck Serono, Pierre Fabre, AstraZeneca, Sun Pharma, Sanofi, Idera, Sandoz, Immunocore, 4SC, Italfarmaco, Nektar, Boehringer Ingelheim, Eisai, Regeneron, Daiichi Sankyo, Pfizer, OncoSec, Nouscom, Lunaphore, Seagen, iTeos, Medicenna, Bio-Al Health. All other authors have declared no conflicts of interest.

https://doi.org/10.1016/j.annonc.2023.09.2979

1164P Changes of TCR repertoire in metastatic melanoma and renal cell carcinoma patients treated with nivolumab correlate with overall survival

M. Klabusay[1], R. Lemstrova[2], J. Skácel[3]

[1]Oncology Department, University Hospital Olomouc, Olomouc, Czech Republic; [2]Clinical Oncology Department, FN Olomouc/University Hospital Olomouc, Olomouc, Czech Republic; [3]Oncology, Palacky University Olomouc - Faculty of Medicine and Dentistry, Olomouc, Czech Republic

Background: Melanoma and renal cell carcinoma are common cancers with growing incidence rates. Nivolumab, anti-programmed-death 1 protein (PD1) antibody selectively blocks the interaction between PD-1 and its ligand PD-L1 and enables a restart of the immune response against cancer cells, significantly improving survival in patients with metastatic melanoma and metastatic renal cell carcinoma (mRCC). It was hypothesized that proliferation of specific T cell clones may be associated with response to anti-PD1 therapy. The aim of this study was to analyze T cell repertoire in metastatic melanoma and mRCC patients treated with nivolumab and to correlate in with disease progression and overall survival.

Methods: Blood samples of 35 patients with metastatic melanoma and 21 patients with mRCC were evaluated and compared to 14 healthy controls. All melanoma patients were treated in 1st or 2nd line with nivolumab, all mRCC patients were treated with nivolumab in 2nd to 5th line after prior interferon α, sunitinib, pazopanib, everolimus or axitinib. Mononuclear cells were isolated from the peripheral blood on Histopaque. Cells were stained with directly labeled anti-CD3 PerCP-Cy5.5, anti-CD4 APC, anti-CD8 APC-Cy7 and anti-TCR FITC and PE antibodies. In total, 24 Vβ TCR families were evaluated. Measurement was performed by multicolor flow cytometry.

Data were analyzed with Wilcoxon non-parametric test and principal component analysis.

Results: Significant changes in several TCR families ($p<0.001$) were confirmed: an increase of $CD4^+$ cells or an increase of $CD8^+$ cells were observed. In several patients, highly enriched individual populations of $CD4^+V\beta$ or $CD8^+V\beta$ cells were observed (>10% of $CD3^+$). In these patients, median overall survival (OS) in 5 year observation was not reached, while in patients who did not show enriched $V\beta$ cells, median OS was 3.15 years.

Conclusions: Significant changes in TCR repertoire were observed in melanoma and mRCC patients treated with nivolumab compared to healthy controls. Very high levels of CD4 and CD8 lymphocytes with defined TCR $V\beta$ families were identified in approximately 40% of patients. Clonal expansion of $CD4^+$ and $CD8^+$ cells correlates with the response to treatment and overall survival.

Legal entity responsible for the study: The authors.

Funding: Palacky University in Olomouc.

Disclosure: All authors have declared no conflicts of interest.

https://doi.org/10.1016/j.annonc.2023.09.2980

1165P Single cell spatial features of in-transit melanoma associated with patient outcome to immunotherapy

X. Bai[1], C. Quek[2], G. Al-Eryani[3], K. Harvey[3], I. Silva[4], A.M. Menzies[5], A. Swarbrick[3], G.V. Long[4], R. Scolyer[6], J. Wilmott[7]

[1]Translational Research Group, Melanoma Institute Australia, Wollstonecraft, NSW, Australia; [2]Melanoma Translational Research, Melanoma Institute Australia, Wollstonecraft, NSW, Australia; [3]Garvan Institute of Medical Research, Darlinghurst, NSW, Australia; [4]Melanoma Institute Australia, Wollstonecraft, NSW, Australia; [5]Medical Oncology Department-Suite 5/6, Melanoma Institute Australia, Wollstonecraft, NSW, Australia; [6]Pathology, Royal Prince Alfred Hospital, Camperdown, NSW, Australia; [7]Melanoma Institute Australia, University of Sydney, Sydney, NSW, Australia

Background: Melanoma in-transit metastasis (ITM) occurs in up to 20% of patients with cutaneous melanoma. The 10-year melanoma-specific survival for patients with ITM varies from 75% to 43%. Anti-PD-1-based immunotherapy is used when patients develop unresectable stage III disease or distant metastasis (stage IV). The tumour microenvironment (TME) of ITM melanoma remains poorly understood, where distinct cellular and spatial features can influence patients' outcome to therapy. This study aims to characterise the spatial TME in ITM melanoma patients.

Methods: We performed 40-plex PhenoCycler imaging on FFPE whole-tissue sections and CITE-Seq using tumour dissociates from 20 ITM patients treated with immunotherapy, 10 biopsied at baseline and 10 biopsied at the time of progression. Using bioinformatic analysis including spatial neighbourhood characterisation and receptor-ligand analyses, we investigated the TME features in ITM melanoma.

Results: Spatial neighbourhood analysis identified tertiary lymphoid structures (TLSs) consisting of B cells, $CD8^+$ T cells and dendritic cells, and these immune cells are interfacing HLA-A^{high} melanoma at the tumour margin. An enrichment for TLSs in pre-treatment ITM was associated with good immunotherapy outcome. Distinct subtypes of macrophages were stratified by phenotypic marker expression and spatial location, and intratumoural enrichment of M1-like macrophages ($CD68^+$HLA-$DR^+CD107a^+CD163^-$) was associated with immunotherapy response. Intra-tumoural melanoma heterogeneity was demonstrated in ITMs from patients with primary resistance to treatment and at progression. The resistant TME subtypes displayed a multitude of immune evasive phenotypes, including the upregulation of immune checkpoint receptors (LAG3, VISTA, IDO1), high proliferation, collagen deposition, and low immune recruitment. Single cell sequencing analysis demonstrates cellular programs correlated with response and resistance features in ITM patients.

Conclusions: Taken together, these findings provide insights into the spatial TME interactions associated with immunotherapy response, facilitating the development of biomarkers and therapeutic targets.

Legal entity responsible for the study: The authors.

Funding: Melanoma Institute Australia.

Disclosure: All authors have declared no conflicts of interest.

https://doi.org/10.1016/j.annonc.2023.09.2981

1166P Multi-modal and longitudinal characterization of the tumor and immune microenvironment from primary melanoma to in-transit and distant metastasis

G. Tarantino[1], A. Zaremba[2], T. Vallius[3], F. Rambow[4], L. Zimmer[2], A. Sucker[5], E. Livingstone[6], R. Pelletier[7], S. Makhzami[4], G. Murphy[8], C. Lian[8], P. Sorger[7], D. Liu[1], D. Schadendorf[9]

[1]Medical Oncology, Dana-Farber Cancer Institute, Harvard Medical School, Boston, MA, USA; [2]Dermatology, Universitätsklinikum Essen, Essen, Germany; [3]Department of Oncology, Turku University Hospital (Tyks), Boston, MA, USA; [4]Applied Computational Cancer Research, University Hospital Essen, Essen, Germany; [5]Dermatology, University Hospital Essen, Essen, Germany; [6]Dermatology Department, University Hospital Essen Westdeutsches Tumorzentrum, Essen, Germany; [7]Laboratory of Systems Pharmacology, Harvard Medical School, Boston, MA, USA; [8]Dermatology, Brigham and Women's Hospital, Boston, MA, USA; [9]Department of Dermatology - Hautklinik, University Hospital Essen Westdeutsches Tumorzentrum, Essen, Germany

Background: In-transit metastases (ITM) in melanoma represent a clinical entity where tumor lesions are found between the primary tumor and the draining lymph node. ITM is associated with worse prognosis. However, a significant subset of patients have discordance with high burden of locoregional relapses, but durable distant progression free survival. We studied two such patients to profile the dynamics and evolution of longitudinal tumor samples and identify mechanisms underlying these heterogeneous phenotypes.

Methods: We used whole exome sequencing (WES), bulk RNAseq, snRNAseq, and high-plex Cyclic Immunofluorescence (CyCIF) imaging to profile 28 biopsies over 7 years from pt1 (acral lentiginous melanoma, with progressive disease) and 22 biopsies over 11 years from pt2 (cutaneous melanoma, with durable remission).

Results: Pt1 (progressive disease) tumors had low to absent levels of immune infiltrate, low tumor mutational burden (TMB) and 5-hmC loss. Phylogenetic analysis revealed co-evolution of seven genetic lineages with multiple independent resistance-associated alterations; the majority of distant metastases emerged from a single lineage characterized by high aneuploidy and TMB, and a likely pathogenic missense mutation in TET2. The brain metastasis diverging early in molecular evolution but emerging late in disease had the highest TMB and aneuploidy. In another lineage, we identified WNT-beta catenin transcriptional signature contributing to TIL exclusion. In contrast, phylogenetic analysis of pt2 (durable remission) revealed six co-evolved genetic lineages with acquisition of mutational signature 11 and high TMB (53 mut/MB) after dacarbazine chemotherapy. In line with this, several tumor samples contained abundant Ki67+ CD8+ TILs and regression-like stromal changes, reflective of an autonomous effective host-immune response leading to a complete remission independent of any systemic therapy.

Conclusions: This study identifies genomic and phenotypic features linked to aggressive phenotypes and distant metastasis, including high aneuploidy, TET2 mutation, and 5hmC loss. Additional spatial analysis (GeoMx) is currently ongoing.

Legal entity responsible for the study: The authors.

Funding: Doris Duke foundation.

Disclosure: All authors have declared no conflicts of interest.

https://doi.org/10.1016/j.annonc.2023.09.2982

1167P Spatial and single cell landscaping of immune microenvironment and melanoma subpopulations of metastasizing and non-metastasizing early-stage melanomas

M. Andhari[1], A. Antoranz[2], D. Massi[3], A. Szumera-Cieckiewicz[4], F. Bosisio[2]

[1]Biomedical Science, KU Leuven, Leuven, Belgium; [2]Imaging and Pathology, KU Leuven, Leuven, Belgium; [3]Department of Health Sciences, Università di Firenze, Florence, Italy; [4]Department of Pathology and Laboratory Medicine, Maria Sklodowska-Curie National Research Institute of Oncology, Warsaw, Poland

Background: Patients with thin melanoma (Breslow thickness <1) at early stages are not intensively followed up due to the very low risk of developing metastatic disease. However, 3-8% of thin melanoma cases do metastasize, and recognizing them could potentially candidate them to a more intensive follow-up and even to neoadjuvant therapy. However, due to the small size of early-stage lesions and the unavailability of fresh samples for single-cell dissociation, before the development of spatial single-cell technologies a thorough landscaping of these tumours was not possible. In this study, we have applied a state-of-the-art single-cell and spatial technology to deeply characterize the immune microenvironment of metastasizing (M+) and non-metastasizing (M-) thin melanoma samples and pose the basis for biomarker discovery in this group of patients.

Methods: In collaboration with the Pathology subcommittee of the Melanoma group of the EORTC, we collected 37 M+ and 40 M- thin melanoma patient samples matched for the most prognostically relevant clinical factors, including Breslow thickness, age, gender, location of occurrence, ulceration, and mitosis. We investigate their cellular and functional landscape using 39 protein markers measured spatially at

single-cell level applying the MILAN (Multiple iterative labeling by antibody neo-deposition) method.

Results: There were no significant differences in the percentage of cell types present in M+ and M- samples. However, the analysis of recurrent cellular communities revealed that PD1+ T cells and PDL1+ macrophages were located at the tumor-stroma interface in M+ patients, whereas cellular communities with a high percentage of macrophages but no significant contact with cytotoxic T cells were present at the border of the tumor in M- patients.

Conclusions: This study gives the first spatial single cell landscape of thin melanoma and finds relevant communities in metastasizing patients that could be exploited in the future to adjust combinatorial therapies and drive better personalized medicine for thin melanoma patients.

Legal entity responsible for the study: The authors.

Funding: Flanders Research Foundation (FWO), KU Leuven.

Disclosure: All authors have declared no conflicts of interest.

https://doi.org/10.1016/j.annonc.2023.09.2983

1168P Tumor PD-L1 predicts the outcome of PD-1-based immunotherapy in metastatic melanoma depending on the type of tissue examined

J-M. Placke[1], M. Kimmig[1], K. Griewank[1], E. Hadaschik[1], R. Herbst[2], P. Terheyden[3], J. Utikal[4], C. Pfoehler[5], J. Ulrich[6], A. Kreuter[7], P. Mohr[8], R. Gutzmer[9], F. Meier[10], E. Dippel[11], J. Welzel[12], J.C. Becker[13], M. Weichenthal[14], A. Tasdogan[1], D. Schadendorf[15], S. Ugurel-Becker[1]

[1]Dermatology, University Hospital Essen, Essen, Germany; [2]Dermatology, Helios Klinikum Erfurt, Erfurt, Germany; [3]Dermatology, UKSH - Universitätsklinikum Schleswig-Holstein - Campus Lübeck, Lübeck, Germany; [4]Skin Cancer Unit, UMM - Universitaetsklinikum Mannheim, Mannheim, Germany; [5]Dermatology, UKS - Universitaetsklinikum des Saarlandes, Homburg, Germany; [6]Dept. of Dermatology and Skin Cancer Center, Harzklinikum Dorothea Christiane Erxleben GmbH-Wernigerode, Wernigerode, Germany; [7]Dermatology, Helios Klinikum Oberhausen, Oberhausen, Germany; [8]Dermato-Oncology Department, Dermatologic Center Buxtehude, Buxtehude, Germany; [9]Department of Dermatology, Skin Cancer Center Minden, Minden, Germany; [10]Skin Cancer Center, National Center for Tumor Diseases, Dept. of Dermatology, Universitaetsklinikum Carl Gustav Carus Dresden, Dresden, Germany; [11]Dermatology, Klinikum der Stadt Ludwigshafen am Rhein gGmbH, Ludwigshafen, Germany; [12]Dermatology, Universitätsklinikum Augsburg, Augsburg, Germany; [13]Translational Skin Cancer Research, DKFZ - German Cancer Research Center, Heidelberg, Germany; [14]Dermatology Department, Christian-Albrechts-University Kiel, Kiel, Germany; [15]Department of Dermatology - Hautklinik, University Hospital Essen Westdeutsches Tumorzentrum, Essen, Germany

Background: PD-1-based immune checkpoint inhibition (ICI) is the major backbone of current melanoma therapy. Tumor PD-L1 expression represents one of few biomarkers predicting ICI therapy outcome. Here, we systematically investigated whether the type of tumor tissue examined for PD-L1 expression has an impact on ICI therapy outcome prediction.

Methods: Pre-treatment tumor tissue obtained before 1st ICI therapy for non-resectable stage III/IV metastatic melanoma was prospectively collected within the DeCOG multicenter study Tissue Registry in Melanoma. Stratified by tissue type, best overall response (BOR), progression-free survival (PFS), and overall survival (OS) were correlated with tumor PD-L1 expression (cutoff $\geq$5%).

Results: Of 448 patients, tumor PD-L1 was determined on 95 primary tumors (PT; 36.8% positivity), 153 skin (34.0% positivity), 115 lymph node (LN; 50.4% positivity), and 85 organ (40.8% positivity) metastases. Skin metastases were significantly more often classified as PD-L1 negative than LN metastases (OR=0.751; 95%CI=0.599-0.956; P=0.007). PD-L1 positivity was predictive for BOR if determined on LN (CR/PR 37.5% versus 16.1%; OR=0.319; 95%CI=0.138-0.76; P=0.010), but not on skin metastases (CR/PR 36.0% versus 28.0%; OR=0.778; 95%CI=0.379-1.554; P=0.49), translating into favorable survival for PD-L1 positivity determined on LN metastases (median PFS 22.0 versus 3.5 months, HR=0.490; 95%CI=0.310-0.775; P=0.002; median OS 68.9 versus 16.6 months, HR=0.519; 95%CI=0.307-0.880P=0.014). PD-L1 positivity determined on PT (PFS= HR=0.757; 95%CI=0.467-1.226; P=0.27; OS= HR=0.528; 95%CI=0.305-0.913; P=0.032) was predictive to a lesser extent. No relevant survival differences were detected by PD-L1 determined on skin metastases. Multivariate analysis revealed tumor PD-L1 determined on LN metastases as independent predictive factor for PFS (HR=0.43; 95%CI=0.24-0.75; P=0.003) and OS (HR=0.51; 95%CI=0.27-0.96; P=0.037).

Conclusions: For outcome prediction of PD-1-based immunotherapy in melanoma, tumor PD-L1 determined on LN metastases was more reliable than that assessed on PT. PD-L1 determined on skin metastases showed no predictive value and cannot be recommended for clinical use.

Clinical trial identification: CA209-578.

Legal entity responsible for the study: Dirk Schadendorf.

Funding: BMS.

Disclosure: J. Placke: Financial Interests, Personal, Funding: BMS; Financial Interests, Personal, Advisory Board: Novartis, Sanofi, Pierre Fabre, Therakos. P. Terheyden: Financial Interests, Personal, Advisory Board: Bristol Myers Squibb, Novartis, Merck Sharp & Dohme, Pierre Fabre, CureVac, Sanofi, Roche, Kyowa Kirin, Biofrontera. J. Utikal: Financial Interests, Personal, Advisory Board: Amgen, Bristol Myers Squibb, Immunocore, Merck Sharp & Dohme, Novartis, Pierre Fabre, Roche, Sanofi. C. Pfoehler: Financial Interests, Personal, Advisory Board: Novartis, Bristol Myers Squibb, MSD, Merck, Celgene, AbbVie, Sun Pharma, Pierre Fabre, UCB, Nutricia Milupa, Janssen, Leo. P. Mohr: Financial Interests, Personal, Advisory Board: Bristol Myers Squibb, Beiersdorf, Merck Sharp & Dohme, Pierre Fabre, Sun Pharma, Immunocore, Novartis. R. Gutzmer: Financial Interests, Personal, Advisory Board: Roche, BMS, MSD, Novartis, Amgen, Merck, Sun Pharma, Sanofi, Pierre Fabre, 4SC, Immunocore. F. Meier: Financial Interests, Personal, Advisory Board: Novartis, Roche, BMS, MSD, Pierre Fabre, Sanofi, Immunocore. J.C. Becker: Financial Interests, Personal, Advisory Board: Amgen, Merck, Recordati, Sanofi, Boehringer Ingelheim, InProTher, Almirall; Financial Interests, Personal, Other, Member of a DMSB: 4SC; Financial Interests, Institutional, Research Grant: IQVIA, Alcedis, Merck; Non-Financial Interests, Institutional, Product Samples: 4SC. D. Schadendorf: Financial Interests, Personal, Invited Speaker: BMS, Novartis, MSD, Roche, Merck Serono, Sanofi; Financial Interests, Personal, Advisory Board: BMS, Novartis, MSD, Immunocore, Pierre Fabre, Sanofi/Regeneron, Pfizer, Philogen, Neracare; Financial Interests, Personal, Steering Committee Member: Novartis, BMS, MSD; Financial Interests, Institutional, Coordinating PI: Novartis, BMS, MSD, Pierre Fabre; Financial Interests, Institutional, Research Grant: BMS, MSD; Financial Interests, Institutional, Local PI: Sanofi, Philogen; Non-Financial Interests, Member of Board of Directors: EORTC-MG. S. Ugurel-Becker: Financial Interests, Personal, Advisory Board: Bristol Myers Squibb, Merck Serono, Merck Sharp & Dohme, Novartis. All other authors have declared no conflicts of interest.

https://doi.org/10.1016/j.annonc.2023.09.2984

1169P Tumour transcriptional and spatial protein profiling in Mexican patients reveals that acral lentiginous melanoma is characterized by an immunosuppressive microenvironment

M.E. Vázquez-Cruz[1], C. Molina-Aguilar[1], P. Basurto-Lozada[1], H. Martinez Said[2], A. Álvarez Cano[3], D.Y. Garcia-Ortega[4], L.A. Tavares-de la Paz[5], D. Hinojosa-Ugarte[5], A. Hidalgo Miranda[6], P. Abrao Possik[7], I. Ferreira[8], J.M. Martinez[9], M.P. Levesque[10], D. Adams[8], C.D. Robles-Espinoza[1]

[1]Laboratorio de Genética y Bioinformática del Cáncer - LIIGH UNAM, Universidad Nacional Autónoma de México, Queretaro, Mexico; [2]Melanoma Clinic and Soft Tissue Tumour Dept., The National Cancer Institute, Mexico City, Mexico; [3]Cirugia Oncologica, Christus Muguerza Alta Especialidad, Monterrey, Mexico; [4]Skin, Soft Tissue and Bone Tumors Department, INCAN - Instituto Nacional de Cancerologia, Mexico City, Mexico; [5]Hematology Oncology, Hospital Regional de Alta Especialidad del Bajio, León, Mexico; [6]Laboratorio Genómica del Cáncer, INMEGEN - Instituto Nacional de Medicina Genomica, Mexico City, Mexico; [7]Division of Cellular Biology, Brazilian National Cancer Institute, Rio de Janeiro, Brazil; [8]Experimental Cancer Genetics, Wellcome Trust Sanger Institute, Cambridge, UK; [9]Dermatology, USZ - University Hospital Zürich, Zurich, Switzerland; [10]Translational Dermato - Oncology, USZ - University Hospital Zürich, Zurich, Switzerland

Background: Acral lentiginous melanoma (ALM), although overall a rare type of melanoma, is the most common form of the disease in a number of countries in Latin America, Africa, and Asia; it is associated with a poor prognosis and recurrence. In this study, we seek to gain a better understanding of the tumor-immune components of ALM and their relationship to transcriptional programs.

Methods: Tumour samples were collected from patients undergoing treatment at the National Cancer Institute of Mexico, and have been annotated with vast clinical information. We performed transcriptome sequencing through exome-capture bulk RNA-sequencing on 65 primary tumors from 64 Mexican patients, and did spatial protein profiling using a tissue microarray on 110 tumor segments from 45 patients. Samples were collected at the National Cancer Institute of Mexico and have been annotated with vast clinical information.

Results: We identified differentially expressed genes such as *CXCL8*, *MMP1*, and T*ERT* in ulcerated lesions. RNA deconvolution showed a high abundance of cancer-associated fibroblasts (CAFs) and the absence of NK cells. Consensus clustering identified three ALM subgroups based on global gene expression. Integration of spatial protein information confirmed the high abundance of CAFs- associated markers and the absence of CD56. Fibronectin, SMA, and the cancer stem cell marker CD44 were markedly elevated. We investigated expression patterns within particular regions of interest and found that fibronectin, VISTA, SMA, IDO1, CD34, CD45, CD3, HLA-DR, and CD45RO were differentially expressed in non-tumor regions, while tumor ROIs expressed B7-H3, CD127, GAPDH, and Ki-67 significantly at higher levels. Comparisons between RNA and protein for 35 targets are being conducted.

Conclusions: So far, our analyses point to genes that could drive important prognostic characteristics. We confirmed that ALM is characterized by an immunosuppressive tumor microenvironment. The role of CAFs and the mechanisms affecting NK cells require further research. The present project will enhance our understanding of the TME components and the antitumor response in an understudied disease.

Legal entity responsible for the study: Carla Daniela Robles Espinoza.

Funding: CONACyT A3-S-31603, UNAM PAPIIT IN209422, Welcome Sanger Institute International Fellowship, Melanoma Research Alliance Pilot Award #825924, William Guy Forbeck Research Foundation.

Disclosure: D. Adams: Other, Institutional, Other, DJA is supported by AstraZeneca, OpenTargets and is a paid consultant for Microbiotica: AstraZeneca. All other authors have declared no conflicts of interest.

https://doi.org/10.1016/j.annonc.2023.09.2985

1170P Survival outcome prediction of primary melanoma tumours from histology images using deep learning

C. Bossard[1], Y. Salhi[2], G. Quereux[3], A. Khammari[3], S. Salhi[2], C. Jérôme[1]

[1]Pathology, IHP Group, Nantes, France; [2]Research, DiaDeep, Lyon, France; [3]Dermatology, CHU du Nantes - Hôtel-Dieu, Nantes, France

Background: Predictive and prognostic biomarkers represent the cornerstone of clinical oncology. Improving the prognostication of melanoma is needed to select patients for effective adjuvant therapies. Taking into account that tumor tissue contains a large amount of clinically relevant hidden information that is not fully exploited, we propose a weakly-supervised deep-learning approach on H&E-stained whole-slide image (WSI) to directly predict survival outcomes in melanoma patients.

Methods: We designed a deep neural (DL) network that extracts features from no-padding patches of WSI (tiles of size 512x512 pixels) using a self-supervised learning framework, which are then fed along with survival information into the DL network assigning a survival risk score to each WSI/patient. The model was trained and validated on 195 cases of primary melanoma diagnosed between 2015 and 2017 originating from the IHP Group and the French RicMel network. Performance was evaluated using cross-validations as well as an external set of 238 cases from the TCGA database. Concordance index (c-index) was used as a metric to assess the performance of the proposed approach.

Results: For the prediction of survival outcomes, the proposed pipeline yielded a c-index of 0.75 and 0.66 for the IHP Group cohort and TCGA dataset respectively. Furthermore, we were able to significantly discriminate the 2 groups of patients, with a good and a poor prognosis in terms of survival with $p<0.001$ for IHP and $p=0.01$ for the TCGA based on Kaplan-Meier survival analysis. Our prediction model outperforms the reported scores for the other types of tumours based on deep learning frameworks.

Conclusions: This innovative weakly-supervised deep-learning approach to HE image analysis allows the deep-network to choose its own morphological features, and thus highlights new morphological prognostic biomarkers. Based on this prognostic risk score, we aim to accelerate and improve the clinical decision-making process in the field of melanoma. Due to this exiting result, the performance of our algorithm is challenge on a third independent dataset.

Legal entity responsible for the study: The authors.

Funding: Has not received any funding.

Disclosure: All authors have declared no conflicts of interest.

https://doi.org/10.1016/j.annonc.2023.09.2986

1171P Evaluation of the transcriptomic presence of tumor associated antigens (TAAs) from antibody drug conjugates (ADCs) and PD-L1 in melanoma: Options for new clinical opportunities

J. Bartolome, C. Nieto-Jimenez, A. López de Sá, C. Diaz-Tejeiro, M. Antonanzas Basa, C. Aguado, A. Manzano Fernández, P. Pérez Segura, A. Ocana Fernandez

Medical Oncology Dept., Hospital Clinico Universitario San Carlos, Madrid, Spain

Background: Identification of tumor associated antigens (TAAs) is a main goal in order to design antibodies against tumoral cells. These antibodies can be the base for the construction of antibody drug conjugates (ADCs). It is necessary to identify indications to develop combinations of ADCs with immunotherapies including check point inhibitors (CPIs). We evaluate the transcriptional co-expression of TAAs with PD-L1 (CD274) in melanoma, to identify the best ADC to be combined with anti-PD-(L)1 therapies.

Methods: Information on all ADC TAAs in clinical development was extracted from ClinicalTrials.gov and Federal Drug Administration (FDA) website. Data from TCGA was downloaded to evaluate the expression of identified TAAs in melanoma. Correlation of every pair of genes with CD274 (PD-L1) was performed with Pearson correlation coefficients. Survival outcomes were studied with Kaplan Meier curves and hazard ratios. Tumor Immune Estimation Resource (TIMER) platform was used to investigate the association between the selected TAA and immune cell populations.

Results: 32 TAAs from 123 ADCs were identified. 6 genes that coded for TAAs were upregulated in primary and metastatic melanoma compared with normal tissue, including CD22 (4.55 TMP vs 0.44 TPM), CD74 (1653.72 TPM vs 514.44 TPM), MET (13.13 TPM vs 4.44 TPM), ERBB3 (143.8 TPM vs 70.33 TPM), LIV-1 (66.01 TPM vs 32.37 TPM) and SLAMF7 (10.06 TPM vs 1.09 TPM). A positive correlation for CD74 (Rho: 0.647) and SLAMF7 (Rho: 0.65) with PD-(L)1 was observed. Expression of CD74 correlated with favorable overall survival in melanoma patients treated with any CPI (N: 397, HR: 0.52 CI 0.39-0.69, Log-rank P=3.3e-06), and for those only treated with anti-PD-1 agents (N: 325, HR: 0.52 CI 0.38-0.73, Log-rank P=7.8e-05). Similar findings were observed for SLAMF7 for any CPI (N: 397, HR: 0.5 CI 0.38-0.66, Log-rank P=3.9e-07) and anti-PD-1 (N: 325, HR: 0.53 CI 0.39-0.72, Log-rank P=4.3e-05).

Conclusions: CD74 and SLAMF7 is highly present in melanoma, correlates with PD-L1 expression and predict response to anti-PD-(L)1 therapies. This finding suggests to explore potential combinations between ADCs against these targets and anti-PD-(L)1 therapies.

Legal entity responsible for the study: The authors.

Funding: Has not received any funding.

Disclosure: All authors have declared no conflicts of interest.

https://doi.org/10.1016/j.annonc.2023.09.2987

1172P Analysis of the microbiome of metastatic melanoma patients with complete response to immunotherapy

M. Golcic[1], L. Simetic[2], D. Herceg[3], K. Blazicevic[4], G. Kenđel-Jovanović[5], I. Dražić[6], A. Belančić[7], N. Skočibušić[8], D. Palčevski[9], I. Rubinić[8], V. Vlahović-Palčevski[8], T. Majnarić[10], R. Dobrila-Dintinjana[11], S. Plestina[12]

[1]Department for Radiotherapy and Oncology, Clinical Hospital Center Rijeka, Rijeka, Croatia; [2]Oncology, KBC - University Hospital Centre Zagreb, Zagreb, Croatia; [3]Department of Oncology, KBC - University Hospital Centre Zagreb, Zagreb, Croatia; [4]Oncology Department, KBC - University Hospital Centre Zagreb, Zagreb, Croatia; [5]Nutrition, ZZJZ PGŽ, Rijeka, Croatia; [6]Mathematics, University of Rijeka - Faculty of Engineering, Rijeka, Croatia; [7]Pharmacology, University of Rijeka - Faculty of Medicine, Rijeka, Croatia; [8]Pharmacology, University Hospital KBC Rijeka, Rijeka, Croatia; [9]Allergology, University Hospital KBC Rijeka, Rijeka, Croatia; [10]Family Medicine, Community Health Center of Primorsko-goranska County, Rijeka, Croatia; [11]Radiotherapy and Oncology Department, University Hospital KBC Rijeka, Rijeka, Croatia; [12]Oncology Dept., KBC - University Hospital Centre Zagreb, Zagreb, Croatia

Background: While immunotherapy has improved the prognosis of metastatic melanoma patients, a minority of patients will have prolonged remission. Recent data have emphasized the role of the gut microbiome in response to immunotherapy; however, there is a discrepancy in defining the optimal microbiome. Although recent fecal microbial transplantation (FMT) trials only included patients with sustained response to immunotherapy, a mixed response was registered, with scarce data on the antimicrobial resistance of the donors. A thorough evaluation of the gut microbiome of potential FMT donors is warranted before future trials.

Methods: A shotgun metagenomic sequencing was performed on Illumina NextSeq 2000 platform on stool samples of metastatic melanoma patients with complete and sustained response to immunotherapy (N=15).

Results: The average age of patients was 61.0 ($\pm$12.2) years. Patients usually received immunotherapy in the first line (N=14, 93.3%), with an average time to complete response of 7.6 ($\pm$ 4.6) months. Firmicutes were the most common phylum with a relative abundance of 62.1% $\pm$ 13.2, followed by the Bacteroidetes (31.7% $\pm$ 13.8). Protobacteria were present in all patients, ranging from 0.06-3.4%. On Class level, Clostridia were the most abundant (53.9% $\pm$ 10.4), followed by Bacteroidia (31.7% $\pm$ 13.8). Similar results were seen for the order level, while Lachnospiraceae were the most common family (30.2% $\pm$ 8.6) but ranged from 8.1 $-$ 43.8%, followed by Ruminococcaceae (6.7% $\pm$ 14.0), and Bacteroidaceae (6.2% $\pm$ 11.6). Only 14 bacterial families were present in all patients (25.4%). On the genus level, *Bacteroides* had the highest relative abundance (11.6% $\pm$ 6.2), followed by *Lachnospiraceae* (10.1% $\pm$ 5.9), and *Phocaeicola* (6.2% $\pm$ 4.4). 377 different species were found, with six patients (40%) reporting no traces of the *Akkermansia municiphila*. Antimicrobial resistance was most commonly found for tetracyclines (63.3% $\pm$ 6.9), macrolide-lincosamine-streptogramin B (14.5% $\pm$ 7.9), and sulfonamide trimethoprim (4.4% $\pm$ 2.4).

Conclusions: Patients with complete and sustained response to immunotherapy exhibit a heterogeneous gut microbiome with common resistance to Tetracycline antibiotics.

Legal entity responsible for the study: The authors.

Funding: Croatian Society of Medical Oncology.

Disclosure: All authors have declared no conflicts of interest.

https://doi.org/10.1016/j.annonc.2023.09.2988

1173P NRAS mutation as an independent prognostic factor for resectable Chinese acral melanoma

Y. Xu[1], X. Lin[1], X. Liu[2], W. Sun[1], T. Hu[1], W. Yan[1], C. Wang[3], X. Zhang[4], Z. Luo[4], Y. Chen[3]

[1]Department of Musculoskeletal Oncology, Fudan University Affiliated Cancer Hospital, Shanghai, China; [2]Department of Head & Neck Tumors and Neuroendocrine Tumors, Fudan University Shanghai Cancer Center, Shanghai, China; [3]Department of Musculoskeletal Surgery, Fudan University Shanghai Cancer Center, Shanghai, China; [4]Department of Gastrointestinal Medical Oncology, Fudan University Shanghai Cancer Center, Shanghai, China

Background: Acral melanoma (AM) is the most common subtype of Chinese melanoma population, taking up over 50%-60%. Compared to cutaneous melanoma, AM is lack of frequent driven mutation like BRAF alternation which only occurs around 10%. Meanwhile, 10%-15% of AM can harbor NRAS mutation. This single-center retrospective study aims to investigate the survival impact of NRAS mutant status on Chinese AM after receiving radical surgery.

Methods: We retrospectively collected AM patients who received radical surgery in Fudan University Shanghai Center with confirmative genomic information from 2017 to 2021. Information of clinicopathologic factors and recurrence and survival outcomes was retrieved from patients document database of our hospital.

Results: Totally 317 patients were recruited in our study.170 (53.6%) were males and median age was 62 years old (range 26-89). 281 (88.6%) cases had primary lesion at lower extremity. The mean Breslow thickness were 3.9mm and ulceration rate was 65.9%. According to AJCC 8th staging system, there were 12% Stage I, 32.2% Stage II and 55.8% Stage III. Genomic alternation occured included 71(22.4%) NRAS, 36 (11.4%) BRAF, 33 (10.4%) KIT and the other 177 (55.8%) widetype of these three genes. No statistical difference was observed in most of clinicopathologic factors between NRAS-mut and NRAS-wt patients. However, NRAS-mut group had higher risk of nodal metastasis beyond 1st tier basin (42.3% vs 27.2, P<0.002).With median follow-up of 22 months, NRAS-mut patients had significantly worse relapse-free survival (RFS, P<0.0001) and overall survival (OS, P=0.010). Distant metastasis-free survival (DMFS) was also numerically reduced but not reached significance (P=0.074). Multivariate analysis showed NRAS mutation was an independent prognostic factors for both RFS (P=0.008) and OS (P=0.025).Among patients receiving adjuvant anti-PD1 monotherapy, median RFS time was significantly worse for NRAS-mut patients (9 months vs 26 months, P<0.0001).

Conclusions: In conclusion, AM harboring NRAS mutation had higher risk of relapse and death as well as reduced efficacy of adjuvant anti-PD1 monotherapy compared to NRAS-wt after radical surgery. NRAS mutation was an independent prognostic factor for resectable Chinese AM population.

Legal entity responsible for the study: The authors.

Funding: This research was funded by Shanghai Science and Technology Development Funds, grant number 9411951700; LinGang laboratory "Seeking Distinguished Young Scholars" project, grant number LG-QS-202205-11; National Natural Science Foundation of China, grant number 81802636.

Disclosure: All authors have declared no conflicts of interest.

https://doi.org/10.1016/j.annonc.2023.09.2989

1174P Sex differences in advanced melanoma in Spain: Results from the prospective real-world study GEM 1801

E. Muñoz Couselo[1], M-Á. Berciano-Guerrero[2], J.L. Manzano[3], A. Soria[4], P. Cerezuela-Fuentes[5], G. Crespo[6], M. Antoñanzas[7], T. Puértolas[8], A. García Castaño[9], L. Gutiérrez Sanz[10], E. Espinosa[11], P. Ayala de Miguel[12], M. Majem[13], R. López Castro[14], L.A. Fernández-Morales[15], B. Rivas[16], J. Medina[17], A. Berrocal[18], S. Martín Algarra[19], I. Márquez-Rodas[20]

[1]Medical Oncology Department, Hospital Universitari Vall d'Hebron y Vall d'Hebron Institute of Oncology (VHIO), Barcelona, Spain; [2]Unidad Intercentros de Oncología, Hospitales Universitarios Regional y Virgen de la Victoria (HURyVV). Instituto de Investigaciones Biomédicas de Málaga (IBIMA), Malaga, Spain; [3]Medical Oncology Department, Instituto Catalán de Oncología, ICO-Badalona, H. Germans Trias i Pujol, Badalona, Spain; [4]Medical Oncology Department, Hospital Universitario Ramón y Cajal, Madrid, Spain; [5]Medical Oncology Department, Hospital Clínico Universitario Virgen de la Arrixaca, Murcia, Spain; [6]Medical Oncology Department, Hospital Universitario de Burgos, Burgos, Spain; [7]Medical Oncology Department, Hospital Universitario Clínico San Carlos, Madrid, Spain; [8]Medical Oncology Department, Hospital Universitario Miguel Servet, Zaragoza, Spain; [9]Medical Oncology Department, Hospital Universitario Marqués de Valdecilla, Santander, Spain; [10]Medical Oncology Department, Hospital Universitario Puerta de Hierro, Madrid, Spain; [11]Medical Oncology Department, Hospital Universitario La Paz, CIBERONC, Madrid, Spain; [12]Medical Oncology Department, Hospital Universitario San Pedro de Alcántara, Cáceres, Spain; [13]Medical Oncology Department, Hospital de la Santa Creu i Sant Pau, Barcelona, Spain; [14]Medical Oncology Department, Hospital Clínico Universitario de Valladolid, Valladolid, Spain; [15]Medical Oncology Department, Hospital Universitari Parc Taulí, Sabadell, Spain; [16]Medical Oncology Department, Complejo Asistencial Universitario de Salamanca, Salamanca, Spain; [17]Medical Oncology Department, Hospital Universitario Toledo, Toledo, Spain; [18]Medical Oncology Department, Hospital General Universitario Valencia, Valencia, Spain; [19]Medical Oncology Department, Clínica Universidad de Navarra, Pamplona, Spain; [20]Medical Oncology Department, Hospital General Universitario Gregorio Marañón, Madrid, Spain

Background: The incidence of melanoma is increasing in patients (pts) of both sexes, with female pts generally living longer than their male counterparts. This study assessed the sex-based difference in survival of pts with melanoma and the relationship of this difference with pathological features and response to different treatment options in Spain.

Methods: GEM1801 is a prospective observational study that analyzes the clinical and pathological disease presentation patterns, the different lines of treatment choices and the health outcomes derived from treatments. Here we focus on the sex of pts diagnosed with locally advanced unresectable or metastatic melanoma and their first line (1L) treatment assigned.

Results: From Aug 2018 to Dec 2022, 712 evaluable pts were enrolled, 430 males (60.4%) and 282 (39.6%) females. Median age was 67 years (range: 22-95). Most were superficial spreading (42.6% vs 30.5%; p<0.001), being more frequent than other types in females. Primary tumors were more frequently located in the trunk and head in males and in extremities in females (p<0.001). Chronic sun exposure was more frequent among males (12.3% vs 4.6%; p=0.002). Sex led to no statistically significant differences in therapeutic assignment. At data cutoff, the median follow-up was 14.4 m (95% CI: 13.3-16.2). Efficacy is shown in the table.

Table: 1174P

	N, (%)	Median PFS (95% CI), months	p-value Cox	Median OS (95% CI), months	p-value Cox
BRAF + IT Male	61 (58.7)	20.6 (7.9-NR)	0.381	35.8 (24.1-NR)	0.766
BRAF + IT Female	43 (41.3)	15.3 (6.5-NR)		NR (22.9-NR)	
BRAF + TT Male	109 (57.4)	9.7 (7.5-12.2)	0.001	13.9 (11.7-26.2)	0.026
BRAF + TT Female	81 (42.6)	16.8 (10.2-27.5)		26.1 (21.1-NR)	
BRAF - IT Male	158 (64.6)	9.6 (6.6-24.9)	0.827	29.6 (17.9-47.9)	0.865
BRAF - IT Female	89 (35.4)	8.8 (6.5-16.8)		23 (18.4-NR)	

IT = Immunotherapy; TT = Targeted therapy.

Conclusions: Melanoma in Spain showed sex-based differences in prevalence, histology type, primary location and risk factors exposure. Therapies are not assigned based on sex. TT in 1L showed significantly better outcomes in females, which may suggest a potential prognostic role of sex useful for therapeutic assignment.

Clinical trial identification: NCT03605771.

Editorial acknowledgement: We acknowledge MFAR Clinical Research staff for their assistance in the development of this abstract.

Legal entity responsible for the study: Grupo Español Multidisciplinar de Melanoma (GEM).

Funding: Grupo Español Multidisciplinar de Melanoma (GEM).

Disclosure: E. Muñoz Couselo: Financial Interests, Personal, Speaker, Consultant, Advisor: BMS, MSD, Novartis, Pierre Fabre, Sanofi, Roche; Financial Interests, Personal, Advisory Board: Amgen, BMS, MSD, Roche, Sanofi, Novartis, Pierre Fabre; Financial Interests, Personal, Principal Investigator, Clinical trial participation: Amgen, BMS, GSK, MSD, Pierre Fabre, Roche, Sanofi, Novartis; Financial Interests, Personal, Other, Honoraria: Amgen, BMS, Pierre Fabre, MSD, Novartis, Roche. M. Berciano-Guerrero: Financial Interests, Personal, Speaker, Consultant, Advisor: BMS, MSD, Eisai, Pierre Fabre, Roche, Novartis; Financial Interests, Personal and Institutional, Research Grant, Research project. Recipient: My Institution: Novartis. T. Puértolas: Financial Interests, Personal, Advisory Role: Bristol Myers Squibb, Immunocore, Novartis, Seagen; Financial Interests, Personal, Other, Travel, Accommodation, Expenses: Novartis, MSD, Pierre Fabre. E. Espinosa: Financial Interests, Personal, Invited Speaker: BMS, Novartis, Pierre Fabre; Financial Interests, Personal, Advisory Board: MSD; Non-Financial Interests, Personal, Leadership Role, Grupo Español Multidisciplinario de Melanoma (GEM): Vice president: GEM. L.A. Fernández-Morales: Financial Interests, Personal, Speaker, Consultant, Advisor, Speak at sponsored meeting: BMS, MSD, Pierre Fabre, Roche, Novartis, Pfizer; Financial Interests, Personal, Advisory Role: Novartis, Pfizer. J. Medina: Financial Interests, Personal, Speaker, Consultant, Advisor: Novartis, Roche, Pierre Fabre, BSM, MSD, Sanofi. I. Márquez-Rodas: Financial Interests, Personal, Advisory Board: BMS, MSD, Novartis, Pierre Fabre, Roche, GSK, AstraZeneca, Celgene, Regeneron, Sanofi, Merck Serono, Highlight Therapeutics, Bioline Rx, Sun Pharma, Immunocore; Financial Interests, Personal and Institutional, Coordinating PI, GEM1802 clinical trial: Pierre Fabre; Financial Interests, Institutional, Coordinating PI, GEM1801 Clinical Study: Novartis, BSM, Roche, Pierre Fabre, Incyte, MSD; Financial Interests, Institutional, Coordinating PI, National coordinator of Spotlight 203 clinical trial: Highlight Therapeutics; Non-Financial Interests, Member of Board of Directors: Spanish Melanoma Group. All other authors have declared no conflicts of interest.

https://doi.org/10.1016/j.annonc.2023.09.2990

1175P Return to work after neoadjuvant versus adjuvant immunotherapy in stage III melanoma patients

J. Lijnsvelt[1], Z. Lievense[2], E. Albers[3], M. Lopez-Yurda[1], L.V. Van De Poll-franse[4], C.U. Blank[2]

[1]Mod Department, NKI-AVL - Netherlands Cancer Institute/Antoni van Leeuwenhoek Hospital, Amsterdam, Netherlands; [2]Medical Oncology, NKI-AVL - Netherlands Cancer Institute/Antoni van Leeuwenhoek Hospital, Amsterdam, Netherlands; [3]QoL, NKI-AVL - Netherlands Cancer Institute/Antoni van Leeuwenhoek Hospital, Amsterdam, Netherlands; [4]Psychosocial Research and Epidemiology Department, NKI-AVL - Netherlands Cancer Institute/Antoni van Leeuwenhoek Hospital, Amsterdam, Netherlands

Background: Neoadjuvant immunotherapy in stage III melanoma improved event-free survival compared to 1 year adjuvant therapy. Six weeks of neoadjuvant combination immunotherapy, currently tested in phase III, induces even higher response rates, allowing frequently the omission of extensive surgery and adjuvant therapy. These developments and the rising incidence of melanoma will lead to an exponential increase of melanoma long-term survivors. However, immunotherapy can cause somatic and psychological adverse effects impairing patients' daily life including their return to work (RTW), which has also a strong societal impact. Therefore, we analyzed RTW after neoadjuvant versus adjuvant immunotherapy.

Methods: 88 patients (44 neoadjuvant, 44 adjuvant), 18-66 years old, working (including voluntary work) at start therapy were included to be retrospectively telephone-interviewed concerning their RTW. Partial RTW was defined as RTW after initial discontinuation of work; full RTW was the timepoint that patients worked the same capacity, hours as prior to therapy. Database lock was date January, 3rd 2023.

Results: Patient characteristics were balanced, except for extent of surgery (index or sentinel lymph node procedure only vs therapeutic lymph node dissection) which was more frequently less extensive in the neoadjuvant cohort (64% vs 36%). Patients returned to work more quickly in the neoadjuvant group compared to the adjuvant cohort, with a 6-month partial RTW cumulative incidence of 80% vs 58% and 84% versus 73% at 12 months. At 24 months the adjuvant group catched up and partial RTW was almost the same with 91% and 92%. Incidence of full RTW was higher at all timepoints for the neoadjuvant cohort compared to the adjuvant cohort with 55% vs 38%, 70% vs 50% and 82% vs 62% at 6, 12 and 24 months, respectively. Aside neoadjuvant therapy, lower level of education, and larger extent of surgery were independent parameters associated with reduced RTW.

Conclusions: Our study suggests that treatment duration, the extent of surgery, and educational level might be factors influencing return to work in patients with stage III melanoma.

Legal entity responsible for the study: The authors.

Funding: Has not received any funding.

Disclosure: C.U. Blank: Financial Interests, Institutional, Advisory Board: BMS, MSD, Roche, Novartis, GSK, AZ, Pfizer, Lilly, GenMab, Pierre Fabre; Financial Interests, Personal, Advisory Board: Third Rock Ventures; Financial Interests, Personal, Stocks/Shares: Immagene; Financial Interests, Institutional, Coordinating PI: NanoString, BMS, Novartis, 4SC; Financial Interests, Personal, Stocks/Shares, intention to develop IFN signature algorithm: NewCo, no name yet; Other, pending patent: WO 2021/177822 A1. All other authors have declared no conflicts of interest.

https://doi.org/10.1016/j.annonc.2023.09.2991

1176P Planned drug holidays during immunotherapy in advanced and metastatic melanoma patients: A nation-wide study

A.M. Czarnecka[1], P. Teterycz[1], K. Ostaszewski[1], P. Blonski[1], M.K. Zielińska[1], L. Galus[2], R. Dziura[3], N. Kempa-Kamińska[4], B. Cybulska-Stopa[5], J. Mackiewicz[2], M. Ziętek[6], P. Rutkowski[1]

[1]Department of Soft Tissue/Bone Sarcoma and Melanoma, Maria Sklodowska-Curie National Research Institute of Oncology, Warsaw, Poland; [2]Department of Medical and Experimental Oncology, Institute of Oncology, Poznan University of Medical Sciences, Poznan, Poland; [3]Deparment of Clinical Oncology, Holy Cross Cancer Center, Kielce, Poland; [4]Department of Clinical Oncology, Lower Silesian Oncology, Pulmonology and Hematology Center, Wroclaw, Poland; [5]Department of Clinical Oncology, Maria Sklodowska-Curie National Research Institute of Oncology, Cracow Branch, Kraków, Poland; [6]Department of Oncology, Wroclaw Medical University, Wroclaw, Poland

Background: The optimal duration of immunotherapy (ITH) for patients(pts) with unresectable/metastatic melanoma has not been defined and de-escalation strategies are under debate. Drug holidays are defined as intentional cessation of immunotherapy for period of time, in pts with therapy benefits, till potential progression (PD). While avails of drug holidays include reduction of toxicity and treatment cost as well as increased quality of pts' life, there are also potential risks including PD. Our study aimed to describe disease control upon drug holidays in melanoma pts treated with palliative ITH.

Methods: Pts with advanced unresectable/metastatic melanoma were treated with anti-PD1-based ITH. Patients were referred for drug holidays after $\geq$12 months of ITH. Pts who stopped the treatment due to toxicity were excluded from analysis. During study patients had imaging every 3 months. Primary endpoint was overall survival (OS), and secondary endpoints were median duration of drug holiday, 2nd progression-free survival (PFS2) after PD on drug holidays.

Results: 175 patients (80F/95M) treated for advanced unresectable/metastatic melanoma were referred for drug holidays. 116(67.4%) were *BRAF*-negative melanoma patients. 84 pts were treated with nivolumab, 6 with nivolumab+ipilimumab, 85 with pembrolizumab; and 152(86.9%) were treated in first line. Patients treated for $\geq$24 months(m) before drug holidays had significantly longer OS (p=0.003) and longer PFS till disease PD on drug holidays(p=0.00053) in multivariate analysis. PFS was dependent on best response before drug holidays with the longest in CR group (p=0.011). The median duration of drug holidays was 17 m (IQR: 8-24). At the median follow-up of 48 m (95%CI: 45-51), median OS was not reached, and 5-year OS rate was 89% (95%CI: 83-96). At ITH retreatment objective response was 64% and PFS2 rate at 1-year was 69% (95%CI: 48-99). At the time of analysis 141 pts were still on drug holidays and 11 died due to melanoma PD.

Conclusions: For melanoma pts drug holidays may be offered to ITH responders. The majority of melanoma patients on drug holidays are progression-free at 24m after ITH discontinuation. ITH rechallenge allows achieving disease control after initial progression on drug holidays.

Legal entity responsible for the study: The authors.

Funding: Has not received any funding.

Disclosure: A.M. Czarnecka: Financial Interests, Personal, Invited Speaker: BMS, MSD, Novartis, Pierre Fabre. P. Teterycz: Financial Interests, Personal, Other, travel grant: Sanofi. L. GalusR. Dziura, B. Cybulska-Stopa: Financial Interests, Personal, Speaker's Bureau: BMS, Roche, MSD, Novartis, Pierre Fabre. J. Mackiewicz: Financial Interests, Personal, Speaker's Bureau: BMS, GSK, Roche, MSD, Novartis, Pierre Fabre. M. Ziętek: Financial Interests, Personal, Speaker's Bureau: BMS, MSD, Novartis. P. Rutkowski: Financial Interests, Personal, Invited Speaker, Honoraria for Lectures: MSD, BMS, Pierre Fabre; Financial Interests, Personal, Advisory Board: MSD, BMS, Pierre Fabre, Merck, Sanofi, Blueprint Medicines, Philogen; Financial Interests, Personal, Invited Speaker: Merck, Sanofi, Novartis, AstraZeneca; Financial Interests, Institutional, Research Grant, research grant for ISS: Pfizer; Financial Interests, Institutional, Funding, research grant for institution: BMS; Non-Financial Interests, Member of Board of Directors: Polish Society of Surgical Oncology; Non-Financial Interests, Member of Board of Directors, President: Polish Oncological Society. All other authors have declared no conflicts of interest.

https://doi.org/10.1016/j.annonc.2023.09.2992

1177P Assessment of tumour burden reduction per photography vs magnetic resonance imaging in patients with locally advanced basal cell carcinoma receiving sonidegib 200 mg

R. Gutzmer[1], F. Kiecker[2], C. Loquai[3], R. Dummer[4], A. Hauschild[5], N. Squittieri[6], R. Arntz[7], S. Martelli[7], J. Dierlamm[7], C. Robert[8]

[1]Dermatology, Skin Cancer Center, Ruhr University Bochum Medizinische Universitätsklinik, Bochum, Germany; [2]Dermatology, Vivantes Klinikum Neukoelln, Berlin, Germany; [3]Dermatology, Universitätsmedizin der Johannes Gutenberg-Universität Mainz, Mainz, Germany; [4]Dermatology Department, Universitätsspital Zürich - Klinik für Dermatologie, Zurich, Switzerland; [5]Department of Dermatology, UK-SH, Campus Kiel, Kiel, Germany; [6]Oncology and Dermatology, Sun Pharma, Princeton, NJ, USA; [7]Medical Affairs, Sun Pharmaceutical Industries (Europe) B.V., Hoofddorp, Netherlands; [8]Dermatology Department, Institut Gustave Roussy, Villejuif, France

Background: Sonidegib is a Hedgehog pathway inhibitor approved for the treatment of locally advanced basal cell carcinoma (laBCC) in the US, EU, Switzerland, and Australia, and metastatic BCC (mBCC) in Switzerland and Australia not amenable to curative surgery or radiotherapy. This analysis compared tumour burden reduction using photography or magnetic resonance imaging (MRI) in patients with laBCC that had a time to first tumour response (TFTR) within 6 months of starting treatment.

Methods: The double-blind, multicentre, phase II BOLT study assessed the efficacy and safety of sonidegib 200 mg with laBCC. Tumour burden reduction was assessed using both colour photography and MRI by central review. Tumour response was defined as a >10 mm unidimensional decrease in tumour size. Safety assessments included adverse event (AE) monitoring.

Results: Overall, among 66 patients with laBCC receiving sonidegib 200 mg, TFTR <3 months was achieved by 31 patients per photography and 11 patients per MRI assessment; TFTR from 3 to <6 months was achieved by 8 patients per photography and 12 per MRI. For patients with a TFTR of <3 months, the median (minimum, maximum) percent change from baseline in tumour size was −18.5 (−100.0, 35.9) vs −23.8 (−100.0, −11.9) at 9 weeks, −33.4 (−100.0, 38.5) vs −54.0 (−100.0, −27.1) at 25 weeks, −30.7 (−100.0, 12.0) vs −82.1 (−100.0, −52.9) at 41 weeks, and −29.0 (−100.0, 57.8) vs −82.1 (−100.0, −58.8) at 61 weeks per photography vs MRI, respectively. For patients with a TFTR from 3 to <6 months, the median (minimum, maximum) percent change from baseline in tumour size was not available at 9 weeks, −16.0 (−100.0, 18.1) vs −37.0 (−77.3, −12.5) at 25 weeks, −32.9 (−54.7, 22.3) vs −79.2 (−100.0, −41.5) at 41 weeks, and −35.1 (−46.8, −23.4) vs −77.3 (−100.0, −31.6) at 61 weeks per photography vs MRI, respectively. Sonidegib was well tolerated, and most AEs were Grade 1/2 in severity.

Conclusions: In patients with a TFTR within 6 months of starting treatment with sonidegib, an overall greater reduction in tumour size was reported per MRI assessment vs photography, with photography underestimating the extent of tumour response.

Clinical trial identification: NCT01327053.

Editorial acknowledgement: Writing and editorial support were provided by Duncan McCloskey, PhD, of AlphaBioCom, a Red Nucleus company, and funded by Sun Pharma.

Legal entity responsible for the study: Sun Pharma.

Funding: Sun Pharma.

Disclosure: R. Gutzmer: Non-Financial Interests, Personal, Speaker, Consultant, Advisor: Almirall, Amgen, Bristol Myers Squibb, Immunocore, Merck Serono, Merck Sharp & Dohme, Novartis, Pfizer, Pierre Fabre, Roche, Sanofi Genzyme, Sun Pharmaceutical Industries, Inc., 4SC, Bayer; Non-Financial Interests, Personal, Research Funding: Amgen, Johnson & Johnson, Merck Serono, Novartis; Financial Interests, Advisory Board: Sun Pharmaceutical Industries, Inc. F. Kiecker: Financial Interests, Personal, Research Grant: Amgen, Bristol Myers Squibb, Merck Sharp & Dohme, Novartis, Pierre Fabre, Roche, Sanofi. C. Loquai: Non-Financial Interests, Personal, Advisory Board: Bristol Myers Squibb, Roche, Novartis, Merck Sharp & Dohme. R. Dummer: Non-Financial Interests, Personal, Advisory Board: Amgen, Bristol Myers Squibb, CatalYm, Merck Sharp & Dohme, Novartis, Pierre Fabre, Roche, Sanofi, Second Genome, Sun Pharmaceutical Industries, Inc., Takeda. A. Hauschild: Non-Financial Interests, Personal, Speaker, Consultant, Advisor: Roche, Novartis, Amgen, Celgene, GSK, MedImmune, MelaSciences, Merck Serono, OncoSec, Eisai; Non-Financial Interests, Personal, Research Funding: Roche, Novartis, Amgen, Celgene, GSK, MedImmune, MelaSciences, Merck Serono, OncoSec, Eisai. N. Squittieri, R. Arntz, S. Martelli, J. Dierlamm: Financial Interests, Personal, Full or part-time Employment: Sun Pharmaceutical Industries Inc. C. Robert: Non-Financial Interests, Personal, Speaker, Consultant, Advisor: Amgen, Array BioPharma, Bristol Myers Squibb, Merck, Merck Serono, Novartis, Pierre Fabre, Roche.

https://doi.org/10.1016/j.annonc.2023.09.2993

1178P Melanoma incidence rises for pediatrics: 15-year nationwide retrospective cohort study in Korea (2004-2019)

J. Oh[1], S-H. Beom[2]

[1]Hemato-Oncology Department, Yongin Severance Hospital, Yonsei University College of Medicine, Yongin-si, Republic of Korea; [2]Internal Medicine, Yonsei University, Seoul, Republic of Korea

Background: Melanoma is the fifth most common cancer and, although rare, is the most common skin malignancy in those under 20 years old in the United States (US), with an average annual incidence rate (IR) of 5.5-6.0 cases per million. Since the 1970s, the incidence of pediatric melanoma has increased with an average annual percent change of 2−2.9% in the US. Epidemiological knowledge and predictors of melanoma among children and adolescents (age < 20 years) in Korea are limited.

Methods: Using data from National Health Insurance (NHI) database, we identified incident melanoma cases diagnosed at 0-19 years old during 2004-2019 in Korea, respectively. Using a joinpoint regression model, associations between demographic factors and melanoma incidence rates (IR) were evaluated by calculating incidence rate ratios and 95% confidence intervals (CI).

Results: We identified a total of 1160 patients (age < 20 years) with cutaneous malignant melanoma from 2004-2019. The overall average annual melanoma incidence was 0.22 per million (95% CI, 0.21-0.23) in Korea. It increased with age (age 0-4: 0.3, age 5-9: 0.6, age 10-14: 0.6, age 15-19: 07 per 100,000 persons) but there was no difference in IR according to sex. The age-adjusted incidence of melanoma decreased 4.5% yearly from 2004 to 2012 (95% CI, -8.9%—0.1%) but increased 12.6% yearly from 2012 to 2019 (95% CI, 5.9%—19.6%). A strong correlation between melanoma IR and nevi was confirmed (OR 85.4, 95% CI 67.97 - 106.40, P < 0.001) and this was also linked to the survival rate (5-year survival rate: 97.7% vs 91.9%, P = 0.044).

Conclusions: Although the incidence of melanoma in children and adolescent is very low, it is clear that it increases in Korea. To our knowledge, this is the first report to suggest that melanoma IR trends in children and adolescent are annually increasing in Korea. Most importantly, we must increase awareness and education amongst pediatricians, internists and the general population with regard to prevention and early diagnosis of melanoma for both children and adults. In addition, the physicians should include a complete skin examination for children with congenital nevi.

Legal entity responsible for the study: Jisu Oh.

Funding: Has not received any funding.

Disclosure: All authors have declared no conflicts of interest.

https://doi.org/10.1016/j.annonc.2023.09.2994

1179P The underestimated skin cancer risk after liver transplantation: A meta-analysis of 147154 patients

A.E. El-Qushayri[1], A.R. Mahmoud[1], A.G. Tawfik[2], A. Yasmine Benmelouka[3], B. Nardone[4]

[1]Minia University - Faculty of Medicine, Al-Minya, Egypt; [2]Pharmacotherapy, University of Utah, Salt Lake City, UT, USA; [3]University of Algiers, Algiers, Algeria; [4]Dermatology, Northwestern University Feinberg School of Medicine, Chicago, IL, USA

Background: Recent reports have been shown an increased risk of de-novo malignancies in liver transplant recipients (LTRs) which is reported to be a leading cause of mortality in these patients. The aim of this systematic review and meta-analysis was to assess the prevalence of skin cancer in LTRs.

Methods: We systematically searched in five databases till 20th April 2023 through the search term ("liver transplantation" OR "liver transplant") AND ("skin cancer" OR "melanoma" OR "squamous cell carcinoma" OR "non-melanoma skin cancer" OR "post-transplant cancer" OR "post transplant cancer"). We used random effect model to overcome the significant heterogeneity we observed.

Results: A total of 34 studies, with 147154 LTRs were included. The pooled prevalence of skin cancer (all types) was 4.8% (95%confidence interval (CI): 3.6-6.5). Subgroup analysis based upon the follow up duration of each study, indicated that skin cancer prevalence increased with long duration of follow up: 0-4 years, 2.4% (95%CI: 0.5-9.9), 4-8 years, 4.2% (95%CI 2.9-6.2), and >8 years, 7.6% (95%CI: 4.7-12). Australia followed by South America had the highest prevalence of skin cancer, 20.6% (95%CI: 12.9-31.3), and 9.4% (95%CI: 5.8-14.8), in order; while Asia had the lowest prevalence 0.4% (95%CI: 0-3.8). The most common type of skin cancers was non-melanoma skin cancer reported as a combined type with a prevalence of 2.9% (95%CI: 1.1-6.9), followed by squamous cell carcinoma, basal cell carcinoma and Bowen's cancer, 2.5% (95%CI: 1.4-4.4), 2.5% (95%CI: 1.5-4.1) and 0.8% (95%CI: 0.2-3.2), in order.

Conclusions: Consistent with what it has been reported for other organ transplants, the results from this study showed that skin cancer following liver transplantation is not rare. LTRs in Australia should receive annual dermatologic examination due to their high prevalence of skin cancers. Moreover, non-melanoma skin cancers may be the prevalent type if skin cancer is suspected in LTRs. Substantial dermatological surveillance programs are recommended in LTRs to improve quality of life as well as the associated mortality; especially with the increased prevalence after long follow up durations.

Legal entity responsible for the study: The authors.

Funding: Has not received any funding.

Disclosure: All authors have declared no conflicts of interest.

https://doi.org/10.1016/j.annonc.2023.09.2995

1180TiP Randomized phase II trial (PORTSIDE) evaluating encorafenib (enco) and binimetinib (bini) plus pembrolizumab (pembro) versus nivolumab (nivo) and ipilimumab (ipi) for the treatment of advanced BRAF-mutant melanoma

D. Schadendorf[1], R. Dummer[2], A. Ribas[3], C. Robert[4], R.J. Sullivan[5], A. King[6], A. Polli[7], A. di Pietro[8], P.A. Ascierto[9]

[1]Department of Dermatology - Hautklinik, University Hospital Essen Westdeutsches Tumorzentrum, Essen, Germany; [2]Dermatology Department, Universitätsspital Zürich - Klinik für Dermatologie, Zurich, Switzerland; [3]Department of Medicine, Jonsson Comprehensive Cancer Center at UCLA, Los Angeles, CA, USA; [4]Dermatology Department, Institut Gustave Roussy, Villejuif, France; [5]Cancer Center, MGH - Massachusetts General Hospital, Boston, MA, USA; [6]R&D UK, Pfizer, Inc., Tadworth, UK; [7]Oncology Statistics Department, Pfizer Italy, Milan, Italy; [8]GPD Immuno-Oncology Department, Pfizer Italia S.r.l., Milan, Italy; [9]Melanoma, Cancer Immunotherapy & Developmental Therapeutics, Istituto Nazionale Tumori - IRCCS - Fondazione Pascale, Naples, Italy

Background: Anti—PD-1 therapy (eg, pembro, nivo) in the adjuvant setting is one of the standard-of-care regimens for patients with BRAF-mutant metastatic melanoma. However, a significant proportion of patients have a limited or no response to anti—PD-1 therapy. Therefore, there is an unmet need to determine the optimal treatment sequence in patients resistant to anti—PD-1 therapy. BRAF + MEK inhibitors (eg, enco + bini) are also treatment options for BRAF-mutant metastatic melanoma. This phase II trial will evaluate the combination of enco + bini + pembro vs nivo + ipi in participants (pts) with advanced BRAF-mutant melanoma who progressed during or after anti—PD-1 therapy.

Trial design: PORTSIDE is an international open-label trial recruiting approximately 150 pts. Pts will be randomized 1:1 to receive either enco 450 mg (QD, PO), bini 45 mg (BID, PO), and pembro 200 mg (Q3W, IV) in 21-day cycles or 4 cycles of induction with nivo 1 mg/kg (Q3W, IV) and ipi 3 mg/kg (Q3W, IV) followed by maintenance with nivo 480 mg (Q4W, IV). Pts will be stratified by type of PD-1 resistance (primary vs secondary) and baseline lactate dehydrogenase level (above vs below the upper limit of normal). Pts must be $\geq$18 years old with histologically confirmed unresectable locally advanced or metastatic cutaneous BRAF V600E/K-mutant melanoma (per AJCC 8th edition) with $\geq$1 measurable lesion per RECIST v1.1. Pts must have received only 1 prior line of systemic therapy for melanoma and have confirmed disease progression per RECIST v1.1, either during or after receipt of an anti-PD1 therapy. Pts must have an ECOG PS of 0 or 1 and adequate organ function. Pts who discontinued prior anti—PD-1 therapy due to toxicity or who may not tolerate combination therapy are not eligible. Pts must not have previously participated in the STARBOARD study (NCT04657991) or received prior treatment with BRAF and/or MEK inhibitors, ipi, combined immunotherapy with anti-PD1/L1 treatment, or any other anticancer agents. The primary endpoint is objective response rate; key secondary endpoints are progression-free and overall survival.

Editorial acknowledgement: Editorial/medical writing support was provided by Darren Chow, MSc, of Meditech Media and was funded by Pfizer.

Legal entity responsible for the study: Pfizer, Inc.

Funding: This trial was sponsored by Pfizer in collaboration with Merck Sharp & Dohme LLC, a subsidiary of Merck & Co., Inc., Rahway, NJ, USA.

Disclosure: D. Schadendorf: Financial Interests, Personal, Invited Speaker: BMS, Novartis, MSD, Roche, Merck Serono, Sanofi, Novartis, BMS, MSD; Financial Interests, Personal, Advisory Board: BMS, Novartis, MSD, Immunocore, Pierre Fabre, Sanofi-Regeneron, Pfizer, Philogen, Neracare; Financial Interests, Institutional, Invited Speaker: Novartis, BMS, MSD, Pierre Fabre, Sanofi, Philogen; Financial Interests, Institutional, Research Grant: BMS, MSD; Non-Financial Interests, Member of Board of Directors: EORTC-MG. R. Dummer: Financial Interests, Personal, Other, Consulting and/or advisory role: Novartis, Merck Sharp & Dohme (MSD), Bristol Myers Squibb (BMS), Roche, Amgen, Takeda, Pierre Fabre, Sun Pharma, Sanofi, CatalYm, Second Genome, Regeneron, Alligator, MaviVAX SA, touchIME, T3 Pharma, Pfizer, Simcere. A. Ribas: Financial Interests, Personal, Advisory Board, Honoraria for consulting: Amgen, AstraZeneca, Merck, Novartis, Jazz; Financial Interests, Personal, Advisory Board, Member of the Scientific Advisory Board: Apricity, Appia, Arcus, Compugen, Immpact, Lutris, MapKure, Merus, PACT Pharma, Synthekine, Tango; Financial Interests, Personal, Member of Board of Directors, Member of the Board of Directors: Arcus, Lutris, PACT Pharma; Financial Interests, Personal, Stocks/Shares, Stock ownership: 4C Biomed, Apricity, Appia, Arcus, Compugen, Highlight, ImaginAb, Immpact, ImmuneSensor, Inspirna, Isoplexis, Lutris, MapKure, Merus, Pluto, Synthekine, PACT Pharma, Tango, Advaxis, CytomX, RAPT, Kite-Gilead; Financial Interests, Personal, Invited Speaker: Arsenal Bio; Financial Interests, Institutional, Funding: Agilent, Bristol Myers Squibb; Non-Financial Interests, Advisory Role, Member of the scientific advisory board: Highlight, ImmuneSensor, Inspirna, Pluto. C. Robert: Financial Interests, Personal, Other, Consultancy fees: BMS, Roche, Pierre Fabre, Novartis, Sanofi, MSD, AstraZeneca, Pfizer. R.J. Sullivan: Financial Interests, Personal, Advisory Board: Merck, Novartis, Bristol Myers Squibb, Eisai, Iovance, OncoSec, Pfizer, Replimune, Marengo; Financial Interests, Personal, Royalties: Up-To-Date; Financial Interests, Institutional, Research Grant: Merck; Financial Interests, Institutional, Invited Speaker: GSK, Pfizer, Sanofi, Moderna, Roche-Genentech, BioMed Valley Discoveries, Astex, Compugen, Beigene, Novartis, Rubius, Alkermes, Simcha Therapeutics, OnKure, Marengo, Synthekine. A. King: Other, Institutional, Full or part-time Employment: Pfizer, Inc. A. Polli: Financial Interests, Institutional, Full or part-time Employment: Pfizer, Inc. A. di Pietro: Other, Institutional, Full or part-time Employment: Pfizer, Inc. P.A. Ascierto: Financial Interests, Personal, Other, Consultant and Advisory Role: BMS, Roche Genentech, MSD, Novartis, Merck Serono, Pierre Fabre, AstraZeneca, Sun Pharma, Sanofi, Idera, Sandoz, Immunocore, 4SC, Nektar, Boehringer Ingelheim, Regeneron; Financial Interests, Personal, Other, Consultant and Advisory Role, Travel support: Pfizer/Array; Financial Interests, Personal, Other, Consultant Role: Italfarmaco; Financial Interests, Personal, Other, Advisory Role: Eisai, Seagen; Financial Interests, Personal, Other, Consultant Role: Daiichi Sankyo, Pfizer, OncoSec, Nouscom, Lunaphore; Financial Interests, Personal, Other, Consultant role and travel support: Bio-AI Health; Financial Interests, Personal, Other, Consultant role: Medicenna; Financial Interests, Personal, Advisory Board, Consultant and Advisory Role: iTeos; Financial Interests, Personal, Advisory Board, Consultant and Advisory role: ValoTx; Financial Interests, Personal, Advisory Board, Consultant and Advisor role. Travel support: Replimune; Financial Interests, Personal, Advisory Board, Advisor role: Bayer; Financial Interests, Institutional, Funding, Clinical Trial: Pfizer/Array, Roche Genentech, Sanofi; Financial Interests, Personal, Advisory Board: Erasca; Financial Interests, Institutional, Funding, Clinical trial and translational research: BMS; Non-Financial Interests, Leadership Role, President since 2010: Fondazione Melanoma Onlus Italy; Non-Financial Interests, Leadership Role, President since 2014: Campania Society of ImmunoTherapy of Cancer (SCITO) Italy; Non-Financial Interests, Other, Member of Steering Committee since 2016: Society for Melanoma Research (SMR); Non-Financial Interests, Member of Board of Directors, November 2017 - December 2021: Society for Immunotherapy of Cancer (SITC); Non-Financial Interests, Member: ASCO, SITC, EORTC Melanoma Cooperative Group, SMR, AIOM.

https://doi.org/10.1016/j.annonc.2023.09.2996

1181TiP BEPCOME-MB: Treatment of BRAFV600 mutated melanoma brain metastases with encorafenib + binimetinb + pembrolizumab with or without stereotactic radiosurgery

P. Saiag[1], S. Gourgou[2], J. Régis[3], T.M.S. Amaral[4], U. Leiter-Stoppke[5], F.C. Bidard[6], C. Garbe[7], J.J. Grob[8], T. Lacornerie[9], A. Lamrani-Ghaouti[10], D. Couch[10], M. Charissoux[11]

[1]Dermatology and Oncology Department, Hopital Ambroise Pare AP-HP, Boulogne-Billancourt, France; [2]Biostatistics, ICM - Institut régional du Cancer de Montpellier, Val d'Aurelle, Montpellier, France; [3]Dept. of Functional Neurosurgery & Radiosurgery, CHU de Marseille - Hôpital de la Timone, Marseille, France; [4]Dermato-Oncology Department, Skin Cancer Clinical Trials Center, University of Tuebingen, Tuebingen, Germany; [5]Dermatology, Universitaetsklinik Tuebingen, Tuebingen, Germany; [6]Medical Oncology Department, Institut Curie, Paris, France; [7]Dermatologische Onkologie, Universitaets-Hautklinik Tuebingen, Tuebingen, Germany; [8]Service de Dermatologie et Cancérologie Cutanée, Hopital St. Marguerite Assistance Publique Hopitaux de Marseille, Marseille, France; [9]Service de Physique Médicale, Centre Oscar Lambret, Lille, France; [10]Research & Development Department, Unicancer, Paris, France; [11]Département Radiothérapie Oncologique, ICM - Institut du Cancer de Montpellier, Montpellier, France

Background: Melanoma is an aggressive disease with a high propensity to metastasize to the central nervous system. Melanoma brain metastases (MBM) were associated with poor overall survival (OS), with a median OS of 4—5 months before the era of immune checkpoint inhibition (ICI). Nowadays, first-line treatment with BRAF/MEK inhibitors in patients (pts) with BRAFV600 mutated melanoma and MBM induces ~60% intracranial response, which are unfortunately short-lived. Combined ICI with ipilimumab + nivolumab demonstrated longer-lasting efficacy, but is associated with high rates of toxicity and very limited efficacy in patients with symptomatic MBM. Stereotactic radiosurgery (SRS) for single or multiple lesions is an effective modality to achieve MBM control. Its place upfront or later has not been established. A triplet therapy with BRAF/MEK inhibitors encorafenib (E) + binimetinib (B) and anti-PD-1 monoclonal antibody pembrolizumab (P) is an attractive strategy in BRAFV600 mutated MBM, with a rapid disease response (attributed to E+B) and durable disease control (attributed to P), even in symptomatic MBM, with potentially better tolerability than ipilimumab + nivolumab. This trial aims to test the feasibility of this regimen with or without upfront SRS.

Trial design: This phase II, randomised, controlled, open-label trial assesses the efficacy and safety of adding upfront SRS to E+B+P in the treatment of pts with BRAFV600 mutated melanoma and MBM. Patients are randomly assigned (1:1) to receive (a) E+B+P, or (b) upfront SRS of all cerebral metastases $\geq$5 mm in diameter, followed by E+B+P. Patients will be treated until disease progression. An amendment to allow previous treatment with anti-PD-1 is ongoing. Using intracranial progression-free survival (IC-PFS) assessed by central review as the primary endpoint, 150 patients will be needed to detect an increase in the median IC-PFS in the SRS + E+B+P arm (HR of 0.60 with 80% power and 2-sided 5% significance level). Secondary endpoints include response rate, disease control, OS, toxicity and quality of life. Exploratory endpoints include predictive factors of response and mechanisms of primary and acquired resistance.

Clinical trial identification: EudraCT n°: 2021-006331-26; NCT04074096.

Legal entity responsible for the study: Unicancer.

Funding: Pierre Fabre Médicament.

Disclosure: All authors have declared no conflicts of interest.

https://doi.org/10.1016/j.annonc.2023.09.2997