characterized, potential paracrine effects influencing antitumor immunity remain enigmatic. However, they are important to decipher, as immunotherapies targeting IDH1-mutant gliomas are emerging. AIM: This study aimed at characterizing a potential cell-specific modulatory role of the oncometabolite R-2-HG in shaping the immune microenvironment of IDH1-mutant gliomas. METHODS AND RESULTS: By means of expression dataset analyses, syngeneic murine tumor models and human glioma tissue, as well as a novel astrocyte-specific IDH1R132H-knock in model, we demonstrate that R-2-HG impairs endogenous and IDH1(R132H)-specific antitumor T cell immunity. This is underlined by functional and transcriptomic analyses of myeloid cells indicating a R-2-HG-driven induction of tolerogenicity and compromised antigen presentation. Metabolomic profiling was complemented by mitochondrial respiration assays, calcium measurements and pathway analyses in primary human and mouse immune cells to delineate key molecular mechanisms by which tumor-derived R-2-HG corrupts the glioma immunoenvironment. The functional relevance of R-2-HG-mediated impairment of antitumor immunity was demonstrated in vivo and potential pharmacological strategies abrogating its effects were assessed. CONCLUSION: Glioma-derived R-2-HG impairs antitumor immunity by affecting both infiltrating T-cells and the associated myeloid compartment, thus contributing to tumorigenesis and resistance to therapy. Immunotherapeutic strategies against IDH-mutant gliomas may benefit from approaches to prevent excess R-2-HG production or its uptake by immune cells.

OS10.3 RANDOMIZED PHASE 3 STUDY EVALUATING THE EFFICACY AND SAFETY OF NIVOLUMAB VS BEVACIZUMAB IN PATIENTS WITH RECURRENT GLIOBLASTOMA: CHECKMATE 143

D. A. Reardon[1a], A. Omuro[2a], A. A. Brandes[3], J. Rieger[4,5], A. Wick[6], J. Sepulveda[7], S. Phuphanich[8], P. de Souza[9], M. S. Ahluwalia[10], M. Lim[11], G. Vlahovic[12b], J. Sampson[12b]; [1]Dana-Farber Cancer Institute and Harvard University School of Medicine, Boston, MA, United States, [2]Memorial Sloan-Kettering Cancer Center, New York, NY, United States, [3]AUSL-IRCCS Institute of Neurological Sciences, Bologna, Italy, [4]Klinikum der Goethe-Universität, Frankfurt, Germany, [5]University of Tübingen, Tübingen, Germany, [6]Neurology Clinic, University of Heidelberg, National Center for Tumor Diseases, Heidelberg, Germany, [7]Hospital Universitario 12 De Octubre, Madrid, Spain, [8]Cedars-Sinai Medical Center, Los Angeles, CA, United States, [9]University of Western Sydney School of Medicine, Liverpool, Australia, [10]Cleveland Clinic, Cleveland, OH, United States, [11]The Johns Hopkins Hospital, Baltimore, MD, United States, [12]Duke University Medical Center, Durham, NC, United States.

BACKGROUND: Despite available treatment options for patients (pts) with recurrent glioblastoma (GBM), < 5% of pts survive 5 years beyond initial diagnosis, and no single-agent therapy has demonstrated a survival benefit in the second-line setting, including bevacizumab (bev), which is approved for the treatment of recurrent disease. Nivolumab (nivo), a fully human IgG4 monoclonal antibody that inhibits the programmed death 1 receptor, has provided clinical benefit in multiple cancer types. In cohort 2 of the open-label, phase 3 CheckMate 143 study (NCT02017717), the efficacy and safety of nivo was compared with that of bev in pts with GBM experiencing their first recurrence after prior radiotherapy (RT) and temozolomide (TMZ). METHODS: Pts with no prior VEGF therapy were randomized 1:1 to receive nivo 3 mg/kg Q2W or bev 10 mg/kg Q2W until confirmed disease progression; pts were stratified by the presence/absence of measurable disease. The primary endpoint was overall survival (OS); secondary endpoints were 12-mo OS rate and investigator-assessed progression-free survival (PFS) and objective response rate (ORR) per Response Assessment in Neuro-Oncology criteria. RESULTS: At the time of final analyses (Jan 20, 2017), 369 pts were randomized to the nivo (n = 184) or bev (n = 185) treatment arms; of these pts, 182 received nivo and 165 received bev. At baseline, most pts in the nivo (83%) and bev (84%) arms had measurable disease, and 40% (nivo) and 43% (bev) of pts required corticosteroids, with 14% (nivo) and 15% (bev) receiving ≥ 4 mg/day. Deaths were reported in 154 (nivo) and 147 (bev) pts; median OS was 9.8 mo with nivo and 10.0 mo with bev, and the 12-mo OS rate was 42% in both arms. PFS medians were 1.5 mo (nivo) and 3.5 mo (bev). Among evaluable pts treated with nivo (n = 153) or bev (n = 156), ORRs were 8% (nivo) and 23% (bev); duration of response medians were 11.1 mo (nivo) and 5.3 mo (bev). Treatment-related AEs (TRAEs) occurred in 57% (nivo) and 58% (bev) of pts; the most common TRAEs (≥ 10% of pts in either arm; nivo vs bev) were fatigue (21% vs 14%) and hypertension (1% vs 22%). Grade 3–4 TRAEs were reported in 18% (nivo) and 15% (bev) of pts. Serious AEs (all causality) were reported in 46% (nivo) and 35% (bev) of pts; seizure (8% vs 6%) and malignant neoplasm progression (11% vs 7%) were the only serious AEs reported in ≥ 5% of pts in either arm. AEs leading to discontinuation occurred in 10% (nivo) and 15% (bev) of pts. **CONCLUSIONS:** Nivo did not demonstrate an improved OS compared with bev in pts with recurrent GBM. The ORR was lower with nivo than bev; however, responses with nivo were more durable. The safety profile of nivo was consistent with that observed in other tumor types. Studies of nivo in combination with RT ± TMZ in pts with newly diagnosed GBM are ongoing.

OS11 GLIOMAS

OS11.1 TEMOZOLOMIDE (TMZ) 1 WEEK ON/1 WEEK OFF AS INITIAL TREATMENT FOR HIGH RISK LOW GRADE OLIGODENDROGLIAL TUMORS: A PHASE II AINO (ITALIAN ASSOCIATION FOR NEURO-ONCOLOGY) STUDY

A. Pellerino, F. Franchino, A. Pace, C. Carapella, C. Dealis, M. Caroli, M. Faedi, C. Bomprezzi, R. Rudà, R. Soffietti; Department of Neuro-Oncology, University and City of Health and Science Hospital on behalf the AINO, Turin, Italy.

INTRODUCTION: The efficacy of dose-dense temozolomide (TMZ, 1 week on/1 week off) in grade II gliomas is not well known, and the impact could depend on the molecular subtype. In this regard prospective data are still missing. PATIENTS AND METHODS: Between 2006 and 2010 a single arm phase II study on 60 evaluable patients with grade II oligodendroglial tumors (WHO 2007) was performed. Inclusion criteria were as follows: 1) age ≥ 18 years; 2) KPS ≥ 70; 3) biopsy-proven grade II oligodendroglioma or oligoastrocytoma according to WHO 2007; 4) presence of a measurable residual tumor after surgery. The primary endpoint of the study was tumor response on MRI according to RANO criteria, while the secondary endpoints were progression-free survival (PFS), overall survival (OS), and seizure control according to Engel classification. Most patients (65%) had an active epilepsy at the time of start of chemotherapy. Molecular factors were available in 49/60 patients (81.7%): 21/60 (35%) patients were IDH1-2 mutated/1p19q codeleted, 4/60 (6.7%) were IDH1-2 mutated/1p19q non-codeleted and 24/60 (40%) were IDH1-2 wild-type. The median number of cycles of dose-dense TMZ was 11 (range 2–18). Median follow up was 64 months (range 7–112). RESULTS: Overall, response rate following dose-dense TMZ was as follows: PR in 21/60 (35%) patients, minor PR (mPR) in 14/60 (23%), SD in 21/60 (35%) and PD in 4/60 (7%). Most patients achieved the best tumor response within 6 months after the start of TMZ. Among patients with mPR and PR, 15/49 (30.6%) were IDH1-2 mutated/1p19q codeleted and 11/49 (22.4%) were IDH1-2 wild-type. PFS was 71.4% at 36 months and 28.6% at 60 months with a median value of 46 months in the IDH1-2 mutated/1p19q codeleted subgroup, while PFS was 45.8% at 36 months and 25% at 60 months with a median value of 34 months in the IDH1-2 wild-type subgroup. OS was 90.5% at 36 months and 66.7% at 60 months with a median value of 76 months in the IDH1-2 mutated/1p19q codeleted subgroup, while OS was 66.7% at 36 months and 50% at 60 months with a median value of 60 months in the IDH1-2 wild-type subgroup. The number of patients with IDH1-2 mutated but not 1p/19q codeleted tumors was too small to allow meaningful correlations with response and survival. Seizure improvement was achieved in 29/34 patients (85%) following TMZ: 17/33 (52%) patients at 12 months and 18/29 (62.1%) at 24 months were seizure-free (Engel class I). The time of maximal seizure response was earlier than that observed on MRI (3 months vs 6 months). CONCLUSIONS: Dose-dense TMZ has shown a significant activity in terms of tumor and seizure control, especially in IDH1-2 mutated/1p19q codeleted patients. Seizure reduction could represent an early indicator of response to chemotherapy and maybe predict the duration of response.

OS11.2 RISK-ADJUSTED SURVIVAL OUTCOMES FOR AND FEATURES OF 1P/19Q CODELETION OLIGODENDROGLIOMAS

B. Iorgulescu, C. Zogg, W. Gormley, E. Chiocca, D. Reardon, P. Wen, D. Haas-Kogan, B. Alexander, K. Ligon, T. Smith; Brigham and Women's Hospital, Boston, MA, United States.

BACKGROUND: Oligodendrogliomas (OGs) are diffuse gliomas defined by IDH mutation and 1p/19q codeletion, in which response to treatment and survival are dictated not by histology, but by molecular subtypes. METHODS: The US NCDB was queried for OG patients newly-diagnosed from 2004–2014. Patient and tumor factors were compared by Chi2 or t test. Overall survival (OS) was assessed by Cox proportional hazards and Kaplan-Meier methods, stratified by histology, grade, and codeletion status, and risk adjusted for age, sex, race, Charlson's comorbidity index, insurance, facility location, chemoradiotherapy, and tumor location, laterality, and size. RESULTS: 14,948 patients with gliomas with OG histology remained after exclusion, 67% (n=10,075) were WHO gr2, 33% were WHO gr3 (i.e. anaplastic), and 36% displayed mixed oligoastrocytoma histology. Complete 1p/19q data were available in 20% (n=2,920). Compared to gr2 non-codeleted cases, codeleted OGs presented at an older median age of 43 yrs (IQR: 25–52; vs. 38 yrs, IQR: 25–51, p<0.0001). Notably, 67% were MGMT methylated (vs. 38%, p<0.001) and 75% arose in the frontal lobe (vs. 56%, p<0.001), and 12% in the temporal lobe (vs. 30%). For treatment, 41% of gr2 codeleted OGs received chemotherapy (vs. 36%, p<0.01), 28% received radiotherapy (vs. 41%, p<0.001), 86% underwent surgery, 55% of which were GTR. In risk-adjusted analysis of gr2 OGs, codeletion was associated with significantly improved OS (HR 0.44, 95%CI: 0.27–0.72, p=0.001), with 2-yr and 5-yr OS rates of 96% (95%CI; 94–97) and 87% (95%CI: 84–90), respectively; vs. 87% (95%CI: 84–90) and 70% (95%CI:

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