Neuro-Oncology 24:i191–i192, 2022.
10.1093/neuonc/noac079

LATE BREAKING ABSTRACTS

LTBK-02. SAFETY OF GROWTH HORMONE REPLACEMENT THERAPY IN CHILDHOOD CRANIOPHARYNGIOMA

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INTRODUCTION: Treatment for childhood-onset craniopharyngioma (cCP) has shifted from complete to limited resection aiming to avoid additional hypothalamic morbidity. Up to 90% of cCP patients develop growth hormone deficiency (GHD). GH replacement therapy (GHRT) is of high importance for linear growth and metabolic state. Hardly any studies evaluated the optimal time to start GHRT in relation to tumor progression or recurrence. Our aim was to assess the effect of GHRT in cCP on tumor progression/recurrence. METHODS: Patients with cCP diagnosed between 2001 and 2022, with at least one year of follow-up were included. Tumor progression/recurrence was defined as tumor progression/recurrence requiring intervention. Kaplan Meier and multivariable cox regression analyses were estimated for tumor progression/recurrence. Comparison was made between cCP patients with GHRT and without GHRT. Of the cCP patients receiving GHRT, those given GHRT ≤ 1 year of cCP diagnosis were compared to those given GHRT >1 year after cCP diagnosis. RESULTS: Of 59 cCP patients, 52 were diagnosed with GHD and 51 (86.4%) received GHRT. Sixteen cCP patients (31.4%) developed tumor progression/recurrence during GHRT compared to four cCP patients (50.0%) without GHRT. Mean progression free survival (PFS) did not differ between cCP patients with or without GHRT (GHRT: 5.55 years 95% CI 3.74 - 7.36 vs. no GHRT: 3.69 years 95% CI 1.44 - 5.93). Of cCP patients who started GHRT ≤1 year after cCP diagnosis, 36.4% developed tumor progression/recurrence compared to 27.6% of cCP patients who received GHRT > 1 year after diagnosis (PFS: 8.45 years CI 95% 5.54 – 11.36 vs. 7.99 years CI 95% 6.03 – 9.94). Limited surgery was associated to tumor progression/recurrence (HR 6.99 CI 95% 2.10 – 23.25). CONCLUSION: GHRT does not seem to influence tumor progression/recurrence in cCP. These results support early initiation of GHRT in cCP patients to optimize linear growth and metabolic outcome.

LTBK-03. TARGETED MASS SPECTROMETRY OF SERIAL CSF AND SERUM SPECIMENS FROM CHILDREN WITH DIFFUSE INTRINSIC PONTINE GLIOMA TREATED WITH INTRACRANIAL B7-H3 CAR T CELLS

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Considering the high expression of B7-H3 (CD276) on diffuse intrinsic pontine glioma (DIPG) and preliminary evidence that repeated locoregional delivery of CAR T cells to patients with CNS tumors was feasible and tolerable, we open the phase 1 trial BrainChild-03 (NCT04185038). Children with DIPG in Dose Regimen 1 received 40 intraventricular B7H3CAR doses, with the two patients enrolling post-progression surviving >400 days from initial CAR T infusion. To evaluate for immune and tumor responses that may correlate with clinical and radiographic evaluations, we performed targeted proteomic analysis on serial CSF and serum biospecimens.

MRM-MS is a targeted mass spectrometry that provides sensitive measurement of proteins in cancer tissues and fluids. In 2 patients with longitudinal biospecimens, we identified 50 CSF and 59 serum proteins above level of detection. In general, there were fewer serum fluctuations compared to the CSF, supporting that intracranial delivery provides local immune activation. Sharp fluctuations of several immunoregulatory peptides were measured in the CSF at pre and post infusion timepoints, including BCL10, CXCL13, TIM-3, ICOSLG, and PD-L2. Notably, several analytes tracked consistently in the CSF of both patients, including markers of macrophage maturation and immune cell recruitment, including CD14, CD163, CD44, CSF-1, CXCL13 and VCAM-1. B7-H3 was detected in the CSF and serum of both patients. S005, who progressed on protocol therapy, had a sharp increase in B7-H3 in the CSF during Course 2, while S008, who had clinical improvement on protocol therapy, had consistently lower B7-H3 present. Notably, serum B7-H3 steadily declined in both patients over time, with the exception of a transient increase in S005 between Courses 4 and 5. Future work for all enrolled patients with DIPG will explore the correlation of these targeted proteomic measurements with clinical end points for potential use as markers of efficacy of therapy or adverse events.

LTBK-04. LATE BREAKING ABSTRACT: MEK162 (BINIMETINIB) IN CHILDREN WITH PROGRESSIVE OR RECURRENT LOW-GRADE GLIOMA: A MULTI-INSTITUTIONAL PHASE II AND TARGET VALIDATION STUDY

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BACKGROUND: RAS/RAF/MEK/ERK pathway activation is the primary driver for most pediatric low-grade gliomas (pLGG). MEK162 (binimetinib) is an orally bioavailable MEK1/2 inhibitor with superior brain penetration in a preclinical model. The primary objective of this multi-institutional phase II and target validation study was to assess stratum-specific efficacy of binimetinib in progressive pLGG. METHODS: Eligible children aged 1-18 years with previously treated radiographically progressive pLGG were enrolled and treated with binimetinib, starting dose 32mg/m^2/dose twice daily. Stratum 1 included patients with pLGG with documented BRAF fusion; stratum 2, neurofibromatosis 1 (NF1)-associated pLGG; stratum 3, sporadic pLGG without documented BRAF fusion; and stratum 4, patients undergoing planned tumor biopsy who began binimetinib preoperatively. Partial and minor responses (PR and MR) were defined as ≥50% and ≥25% decrease in maximal two-dimensional measurements. RESULTS: Of 86 patients enrolled, 85 were evaluable for response. Of these, 48 (56%) showed a radiographic response (30 PR and 18 MR) in the first year of treatment. Response rate for stratum 1 (n=28) was 50% (12 PR and 2 MR); 12 (43%) had stable disease (SD) and 2 (7%) progressive disease (PD). Stratum 2 (n=21) response rate was 43% (5 PR, 4 MR), with 12 (57%) SD and no PD. Stratum 3 (n=29) response rate was 69% (10 PR, 10 MR), 4 (14%) SD and 5 (17%) PD. Stratum 4 (n=7) include 3 PR, 2 MR, 2 SD. Nineteen (22%) discontinued treatment for toxicity (most commonly dermatologic), and an additional 42 (49%) required dose reduction. Median dose at the time of PR/MR was 28mg/m^2; responses were seen at doses as low 16mg/m^2. CONCLUSION: Binimetinib is highly effective in the treatment of both NF1-associated and sporadic pLGG, with or without documented BRAF fusion. Modified dosing strategies to improve tolerability may be considered in future trials.