patients for confirmatory analysis: n=438). 438 patients from HIT-GBM-C/-D served as historical control. All pedHGG diagnoses had been confirmed by central neuroradiological and neuropathological review. Primary objective was achieved since non-inferiority of HIT-HGG-2007 in comparison to HIT-GBM-C/-D as indicated by 6 months event-free survival (EFS) was statistically confirmed (p=0.0125). Statistical survival analyses even revealed a better overall survival (OS) and EFS for HIT-HGG-2007 patients in comparison to their HIT-GBM-C/-D counterparts (EFS: p<0.0001; OS: p=0.0328). While EFS subgroup analyses for pontine and non-pontine pedHGG also showed a better survival of HIT-HGG-2007 patients (median EFS pontine pedHGG: 8.2 (n=152; confidence interval (CI): 7.6-9.4) versus 6.2 (n=170; CI: 5.5-6.9) months, p=0.0079; median EFS non-pontine pedHGG: 10.7 (n=276; CI: 9.6-12.4) versus 7.4 (n=267; CI: 6.4-9.2) months, p<0.0001), OS was only improved in HIT-HGG-2007 patients with non-pontine pedHGG (median OS non-pontine pedHGG: 19.3 (CI: 16.8-23.3) versus 16.2 (CI: 14.2-19.1) months; p=0.0181) but not with pontine pedHGG (median OS pontine pedHGG: 11.4 months versus 11.3 months, p=0.4021) Toxicity profile of HIT-HGG-2007 seemed very favorable with most CTCAE (common toxicity criteria adverse event) ≥ grade 3 as hematological toxicity, hepatotoxicity, and neurotoxicity. Less toxicity was observed during concomitant radiochemotherapy in comparison to HIT-GBM-C/-D. Further subgroup survival analyses as well as the assessment of the impact of MGMT promoter methylation are ongoing. In conclusion, our data show non-inferiority of the HIT-HGG-2007 trial with increased survival and less toxicity when compared with previous trials HIT-GBM-C/-D.

HGG-17. NOVEL FUSION IN CONGENITAL BRAINSTEM DIFFUSE HIGH-GRADE GLIOMA

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BACKGROUND: Infant-type hemispheric glioma, previously termed infantile glioblastoma multiforme, is a rare infantile neoplasm with improved survival and distinct molecular features when compared to other pediatric and adult-type high-grade glioma. Infant-type high-grade gliomas are typically located in the cerebral hemispheres and are characterized by ALK, ROS1, MET, and NTRK fusions. Typical brainstem gliomas (diffuse midline glioma, H3 K27-altered or diffuse intrinsic pontine glioma) are comparatively rare in this age group. As a result, the biology of brainstem congenital high-grade gliomas is poorly described. RESULTS: A 3 month old female who initially presented with failure to thrive had an apneic event and was found to have an infiltrative mass in the medulla with expansion into the pons and cervical spine on magnetic resonance imaging. She underwent surgical biopsy with pathology revealing diffuse high-grade glioma, WHO grade 4. Next generation sequencing showed no alterations to H3F3A, IDH, or fusions involving BRAF, ALK, ROS1, MET, or NTRK. Whole-transcriptome sequencing revealed a novel fusion of PDGFRB:APOBEC3C. She received chemotherapy with 2 cycles of carboplatin/etoposide and 2 cycles of carboplatin/etoposide/imatinib before having disease progression. She then underwent palliative radiation (35 Gy in 10 fractions) with near complete regression of her disease. Surprisingly, our patient has not had any progression of disease or new lesions now two years from her last therapy. CONCLUSION: Congenital high-grade glioma is a rare, unique entity that greatly differs from its adult and childhood counterparts. Here, we discuss a previously-unreported fusion of PDGFB:APOBEC3C in a patient with congenital brainstem diffuse high-grade glioma with a favorable clinical course. This highlights the importance of routine molecular characterization, both to better understand the complex biology of this rare disease and to guide prognosis and clinical decision making for individual patients and families.

HGG-18. LONG-TERM EFFICACY AND SAFETY OF LAROTRECTINIB IN PAEDIATRIC PATIENTS WITH TROPOMYOSIN RECEPTOR KINASE (TRK) FUSION-POSITIVE PRIMARY CENTRAL NERVOUS SYSTEM (CNS) TUMOURS

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INTRODUCTION: Neurotrophic tyrosine receptor kinase (*NTRK*) gene fusions are oncogenic drivers in various tumours. Larotrectinib, a highly selective TRK inhibitor, demonstrated an objective response rate (ORR) of 75% across 206 evaluable patients with various non-primary CNS cancers (Hong et al, ASCO 2021). We report long-term data on larotrectinib-treated paediatric patients with TRK fusion-positive primary CNS tumours. METHODS: Patients aged <18 years with TRK fusion-positive primary CNS tumours enrolled in two clinical trials (NCT02637687, NCT02576431) were included. Larotrectinib was administered at 100 mg/m^2 (maximum: 100 mg) twice-daily. Response was investigator-assessed per RECIST v1.1 and RANO. RESULTS: As of July 2021, 28 patients with TRK fusion-positive primary CNS tumours were enrolled, including 14 high-grade and eight low-grade gliomas. Median age at enrolment was 7.0 years (range 1.0–17.0). Twenty-three patients (82%) received prior systemic therapy and 12 (43%) received prior radiotherapy. The ORR was 39% (95% confidence interval [CI] 22–59): three complete responses, eight partial responses, 15 stable disease and two progressive disease. The 24-week disease control rate was 82% (95% CI 63–94). Median duration of response (DoR) was not reached; median follow-up was 25.6 months. Median progression-free survival was 21.9 months (95% CI 9.2–not estimable). Median overall survival (OS) was not reached; median follow-up was 27.6 months. DoR and OS 24-month rates were 53% and 71%, respectively. Treatment duration ranged from 1.0 to 39.0+ months. Treatment-related adverse events (TRAEs) were mostly Grade 1–2. Grade 3–4 events occurred in three patients (increased gamma-glutamyltransferase, hyperglycaemia, hypernatraemia, hyponatraemia and neutropaenia). No patients discontinued treatment due to TRAEs. Fourteen patients progressed on treatment; four continued treatment post-progression for ≥4 weeks. CONCLUSION: Larotrectinib demonstrated high disease control rate, durable responses and a manageable safety profile. These results support testing for *NTRK* gene fusions in paediatric patients with primary CNS tumours.

HGG-19. CO-OCCURRENCES OF A HIGH-GRADE GLIOMA WITH CAVERNOUS MALFORMATIONS AND PATHOGENIC VARIANTS IN *PDCD10* AND *SMARCA4*

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INTRODUCTION: The co-occurrence of multiple disease processes can make for more challenging diagnoses. Here we report an unusual case of a patient found to have an *IDH1*-mutant high-grade glioma along with multiple cerebral cavernous malformations and pathogenic germline variants in *PDCD10* and *SMARCA4*. CASE DESCRIPTION: A 17-year-old female presented with left arm paresthesia and weakness along with persistent headaches within the frontal and occipital regions that progressed in intensity to include nausea and emesis. A fast sequence magnetic resonance imaging (MRI) of her head was obtained that revealed the presence of multiple bilateral cystic lesions suspicious for cavernomas, with the most notable lesion in the right parietal lobe. Ophthalmology consultation revealed grade III papilledema bilaterally. A full brain MRI with and without contrast was obtained and demonstrated a right anterior parietal lobe lesion with associated mass effect, as well as multiple bilateral supratentorial and left cerebellar cavernous malformations. The patient underwent tumor debulking of her dominant lesion. Pathology revealed an *IDH1*-mutant diffuse astrocytoma, WHO grade III. Tumor genetic testing was done and identified a *SMARCA4* and two *TP53* variants. Germline genetic testing was then pursued which revealed a *PDCD10* pathogenic variant consistent with familial cerebral cavernous malformation syndrome and a likely pathogenic variant in *SMARCA4*. Treatment of her high-grade-glioma included radiation therapy followed by maintenance oral temozolomide. DISCUSSION: This case illustrates the unusual co-occurrences of a high-grade glioma with familial cavernous malformation syndrome and germline pathogenic variants in PDCD10 and *SMARCA4*. Our patient continues to do well clinically, but because of her risk of developing small cell carcinoma of the ovary she has elected to undergo a prophylactic bilateral salpingo-oophorectomy. Recognition of abnormal genetic results is critical in the setting of multiple disease processes and can play a crucial role in the on-going care for a patient.

HGG-20. PRMT5 PROMOTES THE FORMATION AND GROWTH OF PEDIATRIC HIGH-GRADE GLIOMA BY MAINTAINING TUMOR STEM CELL POPULATIONS

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BACKGROUND: Pediatric high-grade gliomas (PHGG) are aggressive, undifferentiated CNS tumors comprising two broad subtypes: diffuse mid-