<0.0001). Diffusion restriction (qualitatively) was uncommon but only seen in *BRAF* V600E (p=0.0042) with lower ADC ratio (quantitatively) (p=0.003). Additionally, *BRAF* V600E mutant tumors appeared more infiltrative than *BRAF* fusion and wild-type (p=0.0002). **CONCLUSION:** *BRAF* fusion and *BRAF* V600E mutant pLGG have unique imaging features that can be used to differentiate from each other and wild-type pLGG using standard radiology review with high inter-reader agreement. In the era of targeted therapy, these features can be useful for therapeutic planning prior to surgery.

LGG-09. A NATIONWIDE SERVICE EVALUATION OF SAFETY, RADIOLOGIC AND VISUAL OUTCOME REFINING BEVACIZUMAB-BASED TREATMENTS IN CHILDREN WITH PROGRESSIVE LOW-GRADE GLIOMA

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INTRODUCTION: Bevacizumab/Irinotecan is currently 3rd-line treatment in the UK for progressive Paediatric Low-Grade Glioma (PLGG) based on limited evidence. A nationwide service evaluation was conducted to review its safety and efficacy amongst a larger cohort. METHODS: Data from children with PLGG receiving Bevacizumab-based Treatments (BBT) from 11 UK Centres (2009-2020) were reviewed. Radiological and visual outcomes were based on standardized measurements. Clinical-radiological correlation was investigated. Time to progression from BBT stop, progression free-survival (PFS) curves and multivariate analysis of prognostic factors (p 0.05) were performed. RESULTS: 88 children with PLGG (88% OPG, 24% NF1) had BBT for radiological (43%), visual (20%) or combined (27%) progression, after 40 months (median) from diagnosis. Amongst OPG cases, visual acuity (VA) per eye (better/worse) before BBT was logMAR 0.0-0.3 (23/7) 0.3 - 1.0 (27/20), > 1.0 (14/18) and LP/NLP (8/27), with 19/8 children respectively blind (LP/NLP) in one or both eyes. Bevacizumab 10 mg/kg every 14 days (median 24 doses) was given as 3rd line+ with Irinotecan (85%) or alongside 1st/2nd line chemo (15%) leading to remarkable radiological (88%) and visual (74%) responses (stable or improved) within 3-6 months, with limited toxicity. 12% progressed on treatment, and 8% died unrelated to BBT. After initial response 65% progressed at a median of 8 months (4 - 23) after BBT, resulting in 3-year-all-causes-PFS of 16% and 3-yr-visual-PFS of 45% from start of BBT. Visual concordance with MRI was poor (36%) but increases (47%) when better-eye determines visual outcome. Lack of NF1 and diencephalic syndrome (DS) at presentation were independent negative prognostic factors for PFS. CONCLUSIONS: A remarkable but transient effect of BBT has been confirmed. Visual > radiological responses can be sustained after BBT. Variations in current BBT strategies justifies further research, including the potential upfront use alongside conventional first-line chemotherapy as sight-saving strategy.

LGG-10. EVALUATION OF THE CHEMOTHERAPY EFFICACY OF CHILDREN WITH OPTIC PATHWAY GLIOMA IN A TERTIARY HOSPITAL IN CHINA

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OBJECTIVE: In order to analyze the chemotherapy efficacy of children with optic pathway glioma (OPG), the clinical, treatment and prognosis factors of children with OPG who received the German International Society of Pediatric Oncology (SIOP) low-grade glioma (LGG) 2004 regimen chemotherapy, were retrospectively analyzed. METHOD: From September 2014 to October 2019, a total of 60 patients with OPG were enrolled and accept LGG 2004 chemotherapy in the Department of Pediatrics, Beijing Shijitan Hospital, Capital Medical University, China. The progression-free survival (PFS) rates and overall survival (OS) rates were analyzed by the Kaplan-Meier method. Both univariate and multivariate analyses were performed using the Cox-proportional hazards model. The test standard α=0.05. RESULTS: Until January 1st, 2022, all children were alive, and the clinical symptoms were improved at any degree, and well tolerated during the whole treatment. The median follow-up time was 3.7 years (range 2.3-7.1 years), the average time of objective response was 6.8 months (range from 2 to 21 months), and the 5 year PFS rates were 73.0 ± 7.24 %. However, about 3 to 8 months later, 8 cases (age <4 years) relapsed which attained partial remission (PR) at the end of the whole therapy. These relapsed cases were performed the LGG 2004 regimen again, and all had an objective response after 4~6 courses of treatment. In addition, two children (age>8 years old) progressed rapidly during treatment, and had to be performed local radiotherapy and reached complete remission (CR). Another two cases with BRAF V600E mutation, reached a significant remission after 3 months of targeted therapy with selumetinib. Furthermore, the COX multivariate analysis shows that spinal metastasis is an independent risk factor of prognosis of children with OPG. CONLUSIONS: Chemotherapy can improve the clinical efficacy of children with OPG, which is better when combining with bevacizumab and/or targeted therapy.

LGG-11. ANALYSIS OF NEUROSURGICAL COMPLICATIONS IN PEDIATRIC SUPRATENTORIAL MIDLINE LOW-GRADE GLIOMA – RESULTS FROM THE GERMAN LGG STUDIES

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OBJECTIVE: Around 80% of all pediatric low-grade glioma (LGG) patients undergo at least one tumor surgery. Interventions in the supratentorial midline (SML) are particularly challenging due to the proximity of eloquent areas, yet associated complications are scarcely reported. We investigated the frequency of neurosurgical complications and related impairments and aimed at identifying risk factors for their appearance related to patient characteristics or the procedure. PATIENTS AND METHOD: Records were retrospectively analyzed from 321 patients with SML-LGG from the successive multicenter German LGG studies, who underwent neurosurgery at 63 hospitals between May 12th,1998 and June 27th, 2020. RESULTS: 543 operations (235 resections, 168 biopsies, 140 non-tumor interventions) were performed on 321 patients (54% male, median age 9 years, 11% NF1 positive, 43% visual pathway glioma). Surgical mortality rate was 0,93% (n=3). Applying the Drake classification postoperative surgical morbidity was observed in 259 cases (47,7%), medical morbidity in 103 cases (19%). 30-day persistence rate of newly developed neurological deficits was 44,8% (65/165 cases); neuroendocrine impairment affected 57 patients (17,8%), visual deterioration 34 (10,6%). Complications/impairments following resections were associated with patient age below 3 years at operation, tumor volume above 80 cm^3, presence of hydrocephalus prior to surgery, complete resection, intervention in centers with fewer reported resections and surgery performed between 1998-2006 by univariate analysis. In contrast, the neurosurgical approach, tumor location, NF1 status as well as previous antineoplastic treatment were not associated with the frequency of complications. Regarding biopsies, open biopsies showed significantly more surgery-associated complications/impairments compared with stereotactic procedures. CONCLUSIONS: Neurosurgery-associated complications and impairments were frequent in pediatric patients with supratentorial midline LGG undergoing open surgery in the German LGG-studies. We identified six patient- and institution-associated factors that may increase the risk for surgical complications. Skills at the treating center and extent of resection should be considered appropriately prior to intervention.

LGG-13. THE CLINICAL AND MOLECULAR CHARACTERISTICS OF PROGRESSIVE HYPOTHALAMIC/OPTIC PATHWAY PILOCYTIC ASTROCYTOMA

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Unresectable hypothalamic/optic pathway pilocytic astrocytoma (PA) can be challenging to manage due to repeated progressions despite mul-

tiple lines of therapy. To identify clinical and biologic factors associated with tumor progression, we retrospectively identified 72 unresectable non-NF1-associated hypothalamic/optic pathway PA. Tumors were classified as high-risk (50%) if they progressed after three or more lines of chemotherapy/targeted therapy, progressed after radiation, developed metastatic disease, or died of disease. DNA methylation profiling and transcriptome analysis (RNA sequencing) were performed on treatment-naïve tumors with available tissue (n=40), and the findings were validated by immunohistochemistry (IHC) on additional tumor tissue. The median follow-up of the entire cohort was 12.3 years. High-risk tumors were associated with male sex (M:F = 2.6:1), younger age at diagnosis (median 3.2 years vs. 6.7 years, P = 0.005), and high incidence of KIAA1549-BRAF fusion (81.5% vs. 38.5%, P = 0.0032). High-risk tumors demonstrated decreased CpG methylation and increased RNA expression in many mitochondrial genes and genes downstream of E2F and NKX2.3 transcription factors. Transcriptome analysis identified transcription factor TBX3 and proto-oncogene serine/threonine protein kinase PIM1 as common downstream targets of both E2F and NKX2.3 and potential drivers of tumor progression. IHC confirmed increased expression of TBX3 and PIM1 in high-risk tumors. PIM1 is known to increase the stability and transcriptional activity of MYC, and gene enrichment analysis identified enrichment of MYC targets. Signaling pathways known to be implicated in PA, such as MAPK and PI3K/AKT/mTOR, were also enriched, in addition to pathways related to mitochondrial biogenesis and oxidative phosphorylation. Our results support the model in which the p53-PIM1-MYC axis and TBX3 act alongside MAPK and PI3K/AKT/mTOR pathways to promote tumor progression, highlighting potential new targets for combination therapy and refining disease prognosis.

LGG-14. LOGGIC (LOW GRADE GLIOMA IN CHILDREN) CORE BIOCLINICAL DATA BANK: ESTABLISHMENT AND ADDED CLINICAL VALUE OF AN INTERNATIONAL MOLECULAR DIAGNOSTIC REGISTRY FOR PEDIATRIC LOW-GRADE GLIOMA PATIENTS

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BACKGROUND: The international, multicenter registry LOGGIC Core BioClinical Data Bank aims to enhance the understanding of tumor biology in pediatric low-grade glioma (pLGG) and provide clinical and molecular data. In addition to routine histopathological and molecular analyses, LOGGIC Core determines the driver alteration as precisely as possible to support treatment decisions and participation in interventional trials. Hence, the question arises whether comprehensive implementation of RNA sequencing using Fresh Frozen (FF) tumor tissue to identify underlying gene fusions improves diagnostic accuracy and provides a clinical benefit. METHODS: Establishment of an international molecular and clinical registry including the logistical and analytical pipeline. First analysis of all patients age 0 to 18, which were included in Germany as part of the German HIT-LOGGIC-program between April 2019 and February 2021, and for whom FF tissue was available. This included histopathological evaluation, immunohistochemistry, 850k methylation analysis, gene panel sequencing, RNA sequencing using FF tissue. RESULTS: FF tissue was available in 178/379 included cases. RNA sequencing was performed on 125 samples. In this prospective, population based cohort, we confirmed KIAA1549:BRAF-fusion (57%), BRAFV600E-mutation (9%) and FGFR1-changes (10%) as most frequent alterations. 12% of cases presented rare gene fusions (e.g. TPM3:NTRK1, EWSR1:VGLL1, GOPC:ROS1, SH3PXD2A:HTRA1, PDGFB:LRP1). In 19% of cases, RNA sequencing detected an actionable target not identified by conventional methods. CONCLUSION: The addition of RNA sequencing reveals clinically relevant alterations including rare gene fusions. By demonstrating improvement of diagnostic accuracy and making precision oncology studies (MEKi/RAFi/ERKi/NTRKi/FGFRi/ROSi) more accessible, the added value for pLGG patients becomes apparent. LOGGIC Core is currently being rolled out internationally and aims to define the new state of the art standard molecular diagnostics. We propose to include RNA sequencing as part of routine diagnostic procedures for all pLGG patients, especially in tumors where no common MAPK alteration was identified.

LGG-15. LATE MORTALITY AND MORBIDITY OF ADULT SURVIVORS OF CHILDHOOD GLIOMA TREATED ACROSS THREE DECADES: A REPORT FROM THE CHILDHOOD CANCER SURVIVOR STUDY

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PURPOSE: Pediatric low-grade glioma therapy has evolved to delay or eliminate radiation. The impact of therapy changes on long-term outcomes remains unknown. METHODS: Cumulative incidence of late mortality (death >5 years from diagnosis), subsequent neoplasms (SNs), and chronic health conditions (CHCs, CTCAE grading criteria) were evaluated in the Childhood Cancer Survivor Study among 5-year survivors of glioma diagnosed 1970-1999. Outcomes were evaluated by diagnosis decade and by treatment exposures received ≤5 years following diagnosis (surgery-only, chemotherapy ± surgery, and cranial radiation ± surgery or chemotherapy). Relative risk (RRs) with 95%CIs estimated long-term outcomes using multivariable piecewise exponential models. RESULTS: Among 2,684 eligible survivors (age at diagnosis (median [range]), 7 years [0-20 years]; time from diagnosis, 24 years [5-48 years]), exposure to cranial radiation decreased [51% (1970s), 45% (1980s), 25% (1990s)] along with late tumor recurrence (>5 & ≤15 years from diagnosis) [9.8% (1970s), 8.8% (1980s), 5.0% (1990s)]. The 15-year cumulative incidence of late mortality was 10.3% (1970s), 6.5% (1980s), and 6.0% (1990s) (p<0.001, comparison of cumulative incidence curves). The 15-year cumulative incidence of grade 3-5 CHCs was 19.7% (1970s), 17.8% (1980s), and 14.2% (1990s) (p<0.0001). A reduction in SN incidence was not observed. In multivariable analyses excluding treatment exposure, later diagnosis (1990s vs. 1970s) was associated with lower risk of late mortality, grade 3-5 CHCs and SNs. Inclusion of treatment exposure in the model attenuated the effect of diagnosis decade. Radiation or chemotherapy exposure increased risk compared to surgery alone for late mortality (radiation RR 4.95, 95%CI 3.79-6.47; chemotherapy RR 2.88, 95%CI 1.85-4.48), CHCs (radiation RR 4.02, 95%CI 3.28-4.94; chemotherapy RR 1.66, 95%CI 1.13-2.45), and SNs (radiation RR 4.02, 95%CI 3.06-6.13, chemotherapy RR 2.08, 95%CI 1.03-4.23)). CONCLUSION: Late mortality and CHCs decreased in childhood glioma survivors diagnosed from 1970-1999 largely due to therapy changes, particularly avoidance of cranial radiation, without increased late recurrence.