Of the 7 patients receiving cytotoxic chemotherapy, no substantial response was observed. Of the 6 patients who received RT, one had disease progression. The median follow-up was 5.9 years. The 5-year event-free survival was 88.1%, while the 5-year overall survival was 96.3%. Two patients died, one of unclear cause and one of treatment-related acute myelogenous leukemia. Using log-rank tests, no difference in outcomes was observed based on molecular characteristics, degree of resection, metastatic status, or treatment modality. Conclusions: Although tumors with *MYB* and *MYBL1* alterations present with varying molecular and clinical features, they represent a group of tumors with favorable outcomes. Further characterization is required to identify the subgroup of tumors with a higher propensity for progression.

LGG-16. TO BE PRECISE - KNOW YOUR TARGETS: INSTITUTIONAL EXPERIENCE WITH TUMOR TARGETED THERAPY FOR RECURRENT/PROGRESSIVE PEDIATRIC LOW-GRADE GLIOMA AND PLEXIFORM NEUROFIBROMA

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Introduction: The oncogenic drivers of pediatric CNS tumors are rapidly being identified with the implementation of high throughput genetic screening. Precision medicine approaches to treatment have shown promising results, but data remains limited in the community oncology setting. We aim to describe our institutional experience using targeted therapies for plexiform neurofibroma and recurrent/progressive pediatric low-grade glioma (pLGG). Methods: We performed a retrospective chart review of all patients treated with tumor targeted therapies for recurrent/progressive pLGG and plexiform neurofibroma over the past 5 years. Results: Ten patients treated with tumor targeted therapies were identified. Regimens included combination Dabrafenib and Trametinib (n=3), Trametinib monotherapy (n=2), Selumetinib (n=3), Vemurafenib (n=1), and Larotrectinib (n=1). Median age at therapy initiation was 11.5 years (range 1.1 - 18 years). Tumor molecular status included BRAFV600E mutation (n=4), NF1 mutation (n=2), KIAA1549-BRAF fusion (n=1), NACC-NTRK fusion (n=1), and FGFR1 mutation (n=1). Patients trialed an average of 2 treatment regimens prior to targeted therapy initiation (range 0–5). Mean duration of therapy was 14.5 months (range .5–33 months) with 8 patients remaining on treatment. Based on modified RANO criteria, responses included partial (n=1), stable disease (n=8), and progressive disease (n=1). Progressive disease was noted after 4 months of treatment with Dabrafenib and Trametinib combination therapy, but rate of tumor growth was decreased. Subjective functional improvement was seen in 50% of patients. The most common toxicities included rash (n=5) and pyrexia (n=2). Trametinib was discontinued in one patient due to intra-tumoral hemorrhage of unclear etiology. Conclusion: Treatment of pediatric CNS tumors with targeted agents appears to be feasible and efficacious in the community oncology setting. Multi-institutional clinical trials are currently ongoing for each of these therapies. There remains a need for community oncology institutional data regarding their use.

LGG-17. CLINICAL OUTCOME OF PEDIATRIC LOW GRADE GLIOMA WITH POSITIVE BRAF-FUSION TREATED WITH MEK INHIBITOR

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Background: Low grade glioma (LGG) is the most common central nervous system (CNS) tumor in children. Some are treated with surgery alone, while chemotherapy is given for unresectable tumor with clinical symptoms or progression. Conventional chemotherapy is effective but 30–40% patients may have reactivation of disease requiring re-treatment throughout lifetime. MEK inhibitor for BRAF-fusion positive LGG is a new treatment option for refractory cases. Methods: Retrospective search in territory-wide pediatric oncology registry for children diagnosed with LGG from 2010–2020 in Hong Kong. To identify patients with molecular confirmed BRAF-fusion positive LGG and any treatment with MEK inhibitor. Results: Twelve patients (N=12) were identified with BRAF-fusion positive LGG, male:female was 1:2, age 0.3–15.1yr (median 5.0yr) at presentation. The median follow up duration was 1.8yr. Five patients (42%) had surgical resection only. Seven patients (58%) were given chemotherapy with Carboplatin / Vincristine. Five out of seven (n=7) treated patients (71%) have partial response at their initial treatment. Two patients (29%) had progressive disease during treatment and switched to second-line chemotherapy, vinblastine however without improvement. Three patients required re-treatment as disease reactivation. Total five patients had refractory diseases were treated with MEK inhibitor, Trametinib including one diagnosed NF-1. All of them have adverse skin reaction and raised transaminase with one required dose reduction. They have been taking the MEK inhibitor for 0.1–3.3 yr with sustainable partial response. Conclusion: Pediatric LGG has overall favourable prognosis. Some of them treated with surgery alone while conventional chemotherapy could also achieve satisfactory disease control. For refractory disease with BRAF-fusion positive, MEK inhibitor is a well tolerated treatment option showing sustainable partial response. However, prolonged medication and disturbing skin reaction are still a major concern for this group of patients. On-going clinical trials to compare conventional chemotherapy versus MEK inhibitor could give us more insight about the clinical benefit, patient selection and treatment duration.

MODELS

TMOD-01. A PROGNOSTIC NOMOGRAM MODEL AND ONLINE SOFTWARE FOR PATIENTS WITH NEWLY DIAGNOSED LOWER-GRADE GLIOMAS

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The nomogram represents a statistical model that incorporates multiple risk factors to estimate individualized survival probabilities. In this study, we developed a nomogram which provides an important tool for individulized survival predicition for newly diagnosed low-grade gliomas (LGG). A total number of 582 newly diagnosed LGG patients were included; the median age was 39.93 years and 42% were female. Cox regression analysis showed that younger age at diagnosis, WHO grade II vs. III, the IDHmut-codel vs. the IDHwt, and the IDHmut-non-codel vs. the IDHwt were significantly associated with better prognosis. The adjuvant treatment following surgery showed a trend towards improved survival. Subsequently, the nomogram to estimate 60-, 90-, and 120-month survival probabilities was established. Our data showed that the age at diagnosis was the largest contributor to patient survival, followed by molecular subtype, WHO grade, treatment and gender. The calibration plot showed that the observed and the nomogram predicted OS curves were well-aligned. In addition, we also validated our nomogram for LGG patients who received postsurgical adjuvant therapy through cross-validation and the calibration plot. Finally, we developed a free online tool for this nomogram (softwarewebsite:https://rrlnnomogram.shinyapps.io/LGG_Nom_Asian/). Overall, this model should be a useful tool for counseling patients in clinical practice including treatment decisions, follow-up, and prognosis.

TMOD-02. GEBTO: GENETICALLY ENGINEERED BRAIN TUMOR ORGANOIDS AS A NOVEL PRECLINICAL MODEL

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Background: One of the bottlenecks in basic and translational research on pediatric brain tumors, is the lack of suitable and representative preclinical models to study tumor biology and drug sensitivity. Over the last decades, extensive molecular characterization has uncovered many entities and subgroups with their unique oncodriving events. However, this heterogeneity is currently not reflected in the models available, especially not for *in vitro* models. Objectives: We aim to generate genetically engineered brain tumor organoids (GEBTO) to represent the molecular variety of embryonal brain tumors and ependymomas. Method: Human brain organoids derived from embryonic stem cells are generated to represent the region of tumor origin. To mimic oncodriving events, DNA plasmids are introduced via electroporation in the organoid cells to knockout tumor suppressor genes or overexpress oncogenes. Results: Cerebellar and cerebral forebrain organoids were generated as the tissue of origin for medulloblastoma and supratentorial ependymoma (ST-EPN), respectively. Based on the detection of GFP protein encoded by DNA plasmids, the organoid cells can be manipulated within a wide developmental window, which corresponds with the presence of the proposed cells of origin. Different oncodrivers and combinations thereof are now being tested to see whether they result in ectopic growth in cerebral or cerebellar organoids. When successful, the GEBTOs are histologically and molecularly characterized using (single cell) transcriptomic and epigenomic analyses to see how well they resemble human tumors. Discussion: Although further development is required, GEBTOs provide a novel avenue to model especially rare pediatric brain tumors, for which tissue and therefore patient-derived models are limited. It also allows for in-depth analyses of the potential cells of origin and the contribution of different mutations to tumor biology.