

geries. Results: On average, patients were 11.5 [standard deviation (SD)=4.0] years old and predominantly treatment naïve (97.6%). Most were white/Caucasian (85.4%), and 53.7% were female. Most patients had been diagnosed with NF1 and PN for >5 years (80.5% and 68.3%, respectively). A majority of patients (58.5%) had >20 café-au-lait spots. Most patients (59.8%) had >1 PN, with 11.0% reporting >5 PNs, frequently located on the back (40.2%) and head (32.9%). Common symptoms included pain (64.6%), disfigurement (32.9%), and motor dysfunction (28.0%). Common comorbidities included attention-deficit disorder (56.1%) and headaches (47.6%). Few patients had received complete resections of their tumors (12.2%), and 39.0% reported ≥1 debulking surgery. Among the 32 patients with debulking surgeries, 5 patients (15.6%) reported complications, including acute complications (60.0%) and post-operative symptoms (40.0%). Debulking surgery-related emergency room visits and hospitalizations were common (25.0% and 53.1%, respectively); mean length of stay per hospitalization was 5.9 (SD=6.2) days. Conclusion: The clinical disease burden of NF1 PN among this pediatric patient population is substantial. While debulking surgeries are used for symptom management, they were related to considerable clinical sequelae.

RARE-07. EFFICACY AND SAFETY OF LAROTRECTINIB IN PEDIATRIC PATIENTS WITH TROPOMYOSIN RECEPTOR KINASE (TRK) FUSION-POSITIVE PRIMARY CENTRAL NERVOUS SYSTEM (CNS) TUMORS

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Background: NTRK gene fusions are oncogenic drivers in various CNS and non-CNS tumors. Larotrectinib is a highly selective TRK inhibitor approved to treat patients with TRK fusion cancer, with an objective response rate (ORR) of 78% across multiple non-CNS cancers (McDermott et al, ESMO 2020). We report updated data on pediatric patients with TRK fusion-positive primary CNS tumors. Methods: Patients aged <18 years with primary CNS tumors harboring an NTRK gene fusion enrolled in two clinical trials (NCT02637687, NCT02576431) were identified. Larotrectinib was administered until disease progression, withdrawal, or unacceptable toxicity. Response was investigator assessed. Results: By July 2020, 26 pediatric patients with TRK fusion-positive CNS tumors were treated. Tumor histologic subtypes included high-grade glioma (n=13), low-grade glioma (n=7), glioneuronal tumor (n=2), neuroepithelial tumor (n=2), CNS neuroblastoma (n=1), and small round blue cell tumor (n=1). Median age was 7.0 years (range 1.3–16.7). The ORR was 38% (95% CI 20–59%): 3 complete responses, 7 partial responses (including 2 pending confirmation), 14 stable disease, and 2 progressive disease. The ORR in patients with high-grade glioma was 38% (95% CI 14–68%). Nineteen of 21 patients (90%) with measurable disease had tumor shrinkage. The 24-week disease control rate was 77% (95% CI 56–91%). Median duration of response (DoR), PFS and overall survival (OS) were not reached. The 12-month rates for DoR, PFS and OS were 75%, 65%, and 86%, respectively. Duration of treatment

ranged from 1.2 to 31.3+ months. Treatment-related adverse events were reported for 15 patients (58%) and were Grade 3–4 in 3 patients (12%), with no discontinuations related to larotrectinib. Conclusions: In pediatric patients with TRK fusion-positive CNS tumors, larotrectinib demonstrated durable responses, high disease control rate, and good tolerability. These results support testing for NTRK gene fusions in pediatric patients with CNS tumors.

RARE-08. POTENTIAL NEW THERAPIES FOR DIFFUSE INTRINSIC PONTINE GLIOMAS IDENTIFIED THROUGH HIGH THROUGHPUT DRUG SCREENING

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Diffuse Intrinsic Pontine Gliomas (DIPGs) are the most devastating of all brain tumors. There are no effective treatments, hence almost all children will die of their tumor within 12-months. There is an urgent need for novel effective therapies for this aggressive tumor. We performed a high-throughput drug screen with over 3,570 biologically active, clinically approved compounds against a panel of neurosphere-forming DIPG cells. We identified 7 compounds - auranofin, fenretinide, ivermectin, lanatoside, parthenolide, SAHA and mefloquine - that were confirmed to have potent anti-tumor activity against a panel of DIPG-neurospheres, with minimal effect on normal cells. Using cytotoxicity and clonogenic assays, we found that these drugs were able to inhibit DIPG-neurosphere proliferation and colony formation *in vitro*. To determine whether the *in vitro* efficacy could be replicated *in vivo*, we tested the activity of each of these compounds in an orthotopic DIPG model. Of the agents tested, fenretinide, auranofin and SAHA were the most active anti-tumor agents, significantly enhancing the survival of tumor bearing animals. Mechanistic studies showed fenretinide enhancing apoptotic cell death of DIPG cells via inhibition of PDGFRα transcription and downregulation of the PI3K/AKT/MTOR pathway. We therefore examined the therapeutic efficacy of fenretinide using a second orthotopic model with PDGFRα amplification. We used two different fenretinide formulations which were found to enhance survival. Fenretinide is clinically available with safety data in children. Validation of the activity of Fenretinide in PDGFRα-amplified or overexpressed DIPGs will lead to the development of a clinical trial, allowing the advancement of fenretinide as potentially the first active therapy for DIPG.

RARE-09. POORLY DIFFERENTIATED CLIVAL CHORDOMA IN EXTREME YOUNG AGE; CASE ILLUSTRATION AND REVIEW OF LITERATURE

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Chordomas are rare tumors believed to be originated from notochordal remnants. Of all intracranial neoplasms, the incidence of cranial chordomas is less than 1%¹. The youngest patient with an intracranial chordoma reported in the literature was a newborn in the first few days after birth⁹. Intracranial chordoma are more predominant in males compared to females¹. The clinical features of intracranial chordoma in the pediatric age group commonly include increased Intracranial pressure, lower cranial nerves palsy, and torticollis². There is no optimum treatment, however, surgical resection of the tumor followed by radiation therapy reported successful outcome³. This is a case of a poorly differentiated clival chordoma of a 23-month old boy. The clinical features, pathological, radiological findings, and surgical technique are discussed with an elaboration of the current review of the literature of clival chordoma in the extreme young age group. To the best of our knowledge, this is the youngest age of clivus chordoma reported in Saudi Arabia.

RARE-10. PRIMARY INTRACRANIAL EWING SARCOMA IN A 12 MONTH OLD MALE

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Background: Ewing sarcoma (EWS) is a rare type of pediatric bone and soft tissue tumor that accounts for approximately 1% of all pediatric ma-