in 6 of 7 the samples (RYR1, SNX25, DSC2). Strikingly, there was one gene, ADGRL3, which was found to be consistently mutated in the entire disease progression process. Our findings therefore suggest that ADGRL3 might play roles in the disease progression of ependymoma patient.

EPEN-06. CHEMOTHERAPY OF RECURRENT EPENDYMOMA: LONG-TERM RESPONSE ONLY IN FEW CASES

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INTRODUCTION: The efficacy of chemotherapy in recurrent ependymoma is unclear. We present results from the German HIT-REZ-studies. METHODS: 137 patients were analyzed regarding the treatment with chemotherapy at first recurrence, the time from first relapse to progression (PFS) and to either time-point of death or last follow-up (OS). Tumor response evaluation was based on MRI and clinically; molecular data was available in 80. RESULTS: In our cohort, 96 patients (20 supratentorial, 73 infratentorial, 3 spinal) received chemotherapy during first recurrence: 49 (51.0%) temozolomide (TMZ) monotherapy, 12 (12.5%) HIT-SKK regime, 9 (9.4%) carboplatin/etoposide (CE) and 26 (27.1%) other combinations. In 19.8% (26.5% in TMZ), chemotherapy was administered prior to surgery (neoadjuvant), which resulted in tumor progression in 78% (85% in TMZ). Gross-total resection was achieved in 86% without neoadjuvant chemotherapy and in 74% (69% in TMZ) with neoadjuvant treatment. Switching to trofosfamide/etoposide (TE) after surgery and unresponsiveness to TMZ showed further progression in all cases of tumor-residuum after surgery. Regarding 1-year-PFS, treatment with HIT-SKK (50.0%±14.4%) or CE (55.6%±16.6%) was advantageous over TMZ (30.2%±6.7%). However, 5-y-OS was lower in CE (19.0% ±16.8%) than in TMZ (39.8%±7.7%) and HIT-SKK (42.9%±8.7%). Long-term control was seen in individual cases of TMZ, HIT-SKK and CE, with TMZ providing longest response of 72 months. CONCLUSION: Neoadjuvant TMZ has no significant advantage regarding PFS. However, in few cases chemotherapy prevented progression after incomplete resection. Difficulties in response evaluation and variability in therapies hinder conclusions. Supported by the German Children's Cancer Foundation

EPEN-07. PATTERNS OF EXTRANEURAL METASTASES IN PEDIATRIC SUPRATENTORIAL EPENDYMOMA: CASE SERIES AND REVIEW OF THE LITERATURE

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BACKGROUND: Ependymomas account for 10% of all malignant pediatric intracranial tumors. Standard therapy includes maximal safe surgical resection followed by involved-field radiation. Up to 50% of localized pediatric ependymomas recur. Extraneural metastases at time of recurrence are rarely reported. OBJECTIVE: To describe extraneural metastases of pediatric ependymomas. METHODS: Retrospective review of patients' medical records and literature review. RESULTS: Three patients with history of locally recurrent, supratentorial ependymoma developed extraneural metastases: one in a cervical lymph node, one with a scalp nodule, and one with a dural lesion. Each extraneural recurrence had similar histologic and molecular features as the initial diagnosis. The cervical lymph node recurrence was treated with multimodal therapy; she is without disease four years later. The isolated scalp nodule occurred at the exit site of a subgaleal drain placed during prior resection. Following nodule resection, he developed additional scalp and lymph node disease and is receiving palliative care. The isolated dural recurrence occurred at the exit site of a ventriculoperitoneal shunt placed following a previous resection. She died of progressive disease 18 months after dural lesion resection. Reports of lymph node, scalp, and dural metastases of ependymomas are exceedingly rare, and outcomes are poor. CONCLUSIONS: Extraneural manifestations of ependymoma are rare. Regional seeding from prior surgical procedures may play a role in metastatic spread. Extraneural metastases should be considered in children previously treated for ependymoma who develop local findings even in the absence of CNS relapse. Salvage therapy with curative intent should be considered using a multimodal approach.

EPEN-09. IMPACT OF MOLECULAR SUBGROUP ON OUTCOME FOR INFANTS <12 MONTHS WITH INTRACRANIAL EPENDYMOMA - GERMAN EXPERIENCE FROM HIT2000, INTERIM-2000-REGISTRY AND I-HIT-MED REGISTRY

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BACKGROUND: For infant ependymoma (EP), decision for radiotherapy during first-line therapy is a dilemma. We analyzed therapy outcomes of EP patients younger than 12 months at diagnosis according to molecular subgroup. PATIENTS AND METHODS: Between 2001 and 2017, 30 patients with histological diagnosis of intracranial EP <12 months at diagnosis with DNA-methylation profiling available were registered in HIT-MED-studies/-registries. RESULTS: In 3/30, DNA methylation-based CNS tumor classification suggested a diagnosis other than EP or could not be assigned to a reference class. Of the remaining 27 tumors, 16 were classified as PF-A, 8 as *RELA*-fusion positive and 3 as *YAP*-fusion positive. Median age at diagnosis was 0.73 (0.30–0.99) years. After a median follow-up time of 5.36 (0.20–12.90) years, 59.3% experienced progressive disease (PD). 5y-PFS and -OS for the whole cohort were 38.2% and 73.1%. *RELA*- and *YAP*-fusion positive EP had significantly better OS than PF-A (5y-OS for PF-A: 55.9%; *RELA* 100%; *YAP* 100%; p=0.023). PFS was not significantly different. All but one patient with relapsed PF-A died despite multimodal salvage strategies. In contrast, patients with relapsing *RELA*- and *YAP*-fusion positive EP (n=5), survived with a combination of re-surgery and first or second local radiotherapy. CONCLUSION: In this cohort of infants <12 months, patients with PF-A had a significantly inferior OS compared to patients with *RELA*- and *YAP*-fusion positive EP. Salvage therapy was ineffective for patients with PF-A, whereas patients with can *RELA*- and *YAP*-fusion positive EP can be long-term survivors after PD. Therefore, subgroups-specific therapy should be discussed.

EPEN-10. SPINAL MYXOPAPILLARY EPENDYMOMA AND METHYLATION-PROFILING: THE MD ANDERSON CANCER CENTER (MDACC) EXPERIENCE

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INTRODUCTION: Spinal myxopapillary ependymoma (MPE) is a rare histological variant of ependymoma, classified as WHO grade I tumor. Further interrogation of the molecular and clinical profile is warranted,

to better understand the biology and clinical phenotype. We summarize our institutional experience with spinal MPE including methylation-profiling. METHODS: A retrospective analysis of charts during the period of 2001 to 2019 of histologically proven MPE was done. We performed methylation profiling for 12 patients by Infinium MethylationEPIC Kit. RESULTS: 26 patients with spinal MPE were identified, median age of diagnosis was 34.2 years with a range of 11 to 59.9 years. Ten patients were below 30 years of age, lumbar spine location was commonest and 6 had leptomeningeal spread at diagnosis. All the patients underwent surgery and 11 received radiation following surgery. Eight patients below the age of 30 received radiation due to residual disease or metastases. Methylation profiling revealed 11,752 CpGs differentially methylated between the younger and older patients ($p < 0.05$), however only one CpG cg22496254 associated with gene NCAPG/DCAF16 (role in promoting mitosis) was detectable with FDR < 0.25 that overly methylated in the younger age group. This is a new finding in MPE. CONCLUSIONS: Spinal MPE is a rare spinal tumor. Our study though limited by numbers, showed younger patients had aggressive phenotype, most requiring radiation. Methylation profiling reaffirmed this finding and trend in the younger patients. Prospective studies in a larger cohort of patients with methylation profiling are needed to identify prognostic variables and new targets for treatment.

EPEN-11. ONGOING RESPONSE IN A MULTIPLY RELAPSED METASTATIC POSTERIOR FOSSA EPENDYMOMA A AFTER VORINOSTAT AND CONCOMITANT IRRADIATION

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BACKGROUND: Among the nine molecular subgroups of ependymoma identified, posterior fossa ependymoma A (PF-EPN-A) confers the worst prognosis. These tumors often relapse despite aggressive resection and irradiation, resulting in limited therapeutic options. Although the genomic profile of PF-EPN-A does not typically show any recurrent alterations; they demonstrate distinct epigenetic changes which can be targeted with modulators such as histone deacetylase (HDAC) inhibitors. These inhibitors have shown efficacy in pre-clinical studies in both their anticancer and radiosensitizing properties. CASE: We describe a male diagnosed with a posterior fossa ependymoma at 3 years of age. After initial therapy with resection and focal irradiation, he went on to have a number of recurrences requiring multimodal therapy. Most recently, he developed diffuse intraventricular and leptomeningeal disease not amenable to surgical intervention. Genetic evaluation demonstrated a BCOR mutation and methylation profile was consistent with PF-EPN-A. He received 23.4 Gray craniospinal irradiation with a 30.6 Gray boost to the nodular lesions. Vorinostat was given concomitantly for radio-sensitization in 2 week intervals for a total of 6 weeks. Serial imaging after irradiation revealed decreased tumor burden with almost complete resolution of disease at 15 months. Unfortunately, MRI at 18 months exhibited mild interval growth of 2 lesions. CONCLUSIONS: To our knowledge, this is the first report of a clinical response in a pediatric patient with PF-EPN-A following irradiation administered concomitantly with vorinostat therapy. This response highlights the importance of further studies evaluating this combination therapy and its potential use in this population.

EPEN-13. PRIMARY EXTRADURAL SACROCOCCYGEAL SUBCUTANEOUS MYXOPAPILAR EPENDYMOMA MISDIAGNOSED AS PILONIDAL CYST IN A 7 YEAR-OLD BOY: A CASE REPORT

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BACKGROUND: Ependymomas occur in the brain or spinal cord and rarely as an extraspinal variety at the sacrococcygeal region, separated from the spinal cord. This rare presentation is thought to originate from a group of heterotopic ependymal cells called the coccygeal medullary vestige. There are few reports of this occurrence in children. CLINICAL CASE: A 7-year-old male presented with a history of a soft mass arising in the sacrococcygeal area 3 years earlier, diagnosed as pilonidal cyst at primary level and treated with surgery twice, as this mass recurred the boy was sent to our hospital, a 3rd surgery was performed, all tumoral tissue was removed, no attachment with dural space was founded, pathology revealed myxopapilar ependymoma with positivity for PS100, EMA and Vimentin. After surgery a Follow up MRI of cranium and spine showed absence of disease, no radiotherapy neither chemotherapy was implemented. He has been on surveillance from 3 years now without recurrence. CONCLUSION: This report highlights the fact that pediatric ependymoma can have an extradural presentation and can be confounded with pilonidal cyst, total resection is needed to control the disease. Potential for recurrence or metastatic disease can continue 20 years from the time of primary tumor, so prolonged surveillance is important.

EPEN-14. GENERATION OF A C11ORF95-RELA FUSION TARGETING ANTIBODY AS A DIAGNOSTIC TOOL FOR SUPRATENTORIAL EPENDYMOMA

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Ependymomas account for 10% of paediatric brain tumours and arise in the ventricular walls of the central nervous system. Ependymomas were previously classified as one tumour type and all patients received similar treatment. However, recent genomic studies have identified nine different molecular subgroups of the disease, including one supratentorial subtype characterized by a novel fusion gene C11ORF95-RELA. When introduced into neural stem cells, this fusion is a potent driver of tumorigenesis and its presence in patient samples has previously also been shown to negatively correlate with overall survival. Accurate diagnosis of this subgroup is currently limited to sophisticated approaches such as break-apart FISH or RNA sequencing. Here, we report the generation of a C11ORF95-RELA Fusion-specific antibody that can be used for routine immunohistochemistry (IHC). Candidate antibodies were first selected using phage display and favourable leads were subjected to affinity maturation using ribosome display after a screening process involving immunoblotting and IHC. Further IHC-based screening of affinity-matured candidates using fusion-positive and -negative mouse tissue as well as human fusion-negative ependymoma tumour tissue produced one lead antibody. The antibody detects fusion-specific nuclear staining pattern on fusion-positive tissue and does not react with fusion-negative tissues. This candidate antibody is currently being tested on human fusion-positive ependymoma tissue. This accurate diagnostic tool holds great promise to transform the management of patients with supratentorial ependymoma.

EPEN-16. TRANSCRIPTIONAL REGULATORY CIRCUITRIES AS MOLECULAR TARGETS IN EPENDYMOMA

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Genomic sequencing has driven precision-based oncology therapy; however, genetic drivers remain unknown or non-targetable for many malignancies, demanding alternative approaches to identify therapeutic leads. Ependymomas comprise histologically similar tumor entities driven by distinct molecular mechanisms, such as fusion oncoproteins, genome-wide chromosomal instability, or disruption of DNA methylation patterns. Despite these differences, ependymomas resist chemotherapy and lack available targeted agents for clinical trial development. Based on our previous findings, we hypothesized that mapping chromatin landscapes and super enhancers (SE) could uncover transcriptional dependencies as targets for therapy (Mack, Pajtler, Chavez et al., Nature, 2018). To functionally test the requirement of these SE genes for ependymoma cellular growth, we designed a pooled RNA interference screen against 267 SE associated genes. Our screen was performed in one *C11ORF95-RELA*-fusion model and two PF-EPN-A models as controls in biological triplicates. As an indication that our screen was successful, positive controls scored among lead hits including *KIF11, BUB1B, PHF5A and MYC*. Importantly, we identified many subtype specific dependencies in both *C11ORF95-RELA*-fusion and PF-EPN-A models, thus revealing novel pathways that potentially govern subgroup-specific ependymoma cell growth. Further, several candidates detected across all ependymoma lines were also identified as pan-cancer dependencies or glioma/glioblastoma specific essential genes from the DepMap Cancer Dependency Gene Resource. Our findings reveal novel targets and pathways that are essential for ependymoma cell growth, which may provide new insight into therapeutic strategies against these aggressive brain tumors.

EPEN-17. FAVORABLE OUTCOME TO INTENSIVE CHEMOTHERAPY WITHOUT IRRADIATION IN INFANTILE METASTATIC EPENDYMOMA WITH A NOVEL MOLECULAR PROFILE: A CASE REPORT

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