tions are described in DMG. This is the first case report of targeting ATM mutation with a PARP inhibitor which resulted in prolonged remission of metastatic DMG. Olaparib was well tolerated.

DIPG-20. DETERMINATION AND MANAGEMENT OF HYDROCEPHALUS IN PATIENTS WITH DIPG, AN INSTITUTIONAL EXPERIENCE

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BACKGROUND: The is no consensus in best practices for the management of hydrocephalus in patients with Diffuse Intrinsic Pontine Glioma (DIPG). To date, the impact on survival of hydrocephalus and Cerebro-Spinal Fluid (CSF) diversion in this population remains to be elucidated. Herein, we describe our institutional experience. METHODS: Patients with a clinical and radiological diagnosis of DIPG were identified at the Hospital for Sick Children between 2000–2019. Images at diagnosis and at disease progression were assessed for hydrocephalus using the frontal-occipital ratio (FOR) method. Proportional hazard analyses were used to identify factors correlated with survival. RESULTS: Eighty-nine consecutive patients diagnosed with DIPGs were treated at our institution. At diagnosis, 29% (n=26) of patients presented with hydrocephalus, seven patients underwent CSF diversion. Out of the remaining nineteen patients, n=6 had stable or improved hydrocephalus in follow-up scans, n=6 had persistent hydro and n=2 required CSF diversion at the time of disease progression. Seven did not undergo a follow-up scan. Out of sixty-five patients with imaging at the time of progression, fifty-five percent of patients (n=36) presented with hydrocephalus and ten of them required CSF diversion. On univariate analysis, the presence of hydrocephalus or CSF diversion at diagnosis and/or did not correlate with a survival advantage. CONCLUSIONS: CSF diversion for the management of hydrocephalus in patients with DIPG does not impact survival and in some cases resolves spontaneously after the initiation of radiotherapy and steroids. This observation needs to be validated in a prospective cohort.

DIPG-21. INDUCTION OF MITOTIC ABNORMALITIES AND BMI-1 MODULATION TO TREAT DIFFUSE INTRINSIC PONTINE GLIOMA

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Diffuse intrinsic pontine glioma (DIPG) is a poor-prognosis pediatric brain tumor with a median survival of less than one year. No effective therapy is currently available, and no therapeutic advances have been made in several decades. BMI-1 is a member of the multimeric protein complex Polycomb repressor complex 1 (PRC1). It has been implicated in self-renewal of normal and cancer cells, and in DNA damage signaling. We have previously identified BMI-1 as a potential therapeutic target in DIPG and have shown that BMI-1 is highly expressed in DIPG tumors regardless of histone 3 subtype. In the present study, we show that the modulation of BMI-1 leads to DNA damage, M phase cell cycle arrest, chromosome abnormalities and cell death. Furthermore, modulation of BMI-1 sensitizes DIPG patient-derived stem-like cells to ionizing radiation (IR). Treatment of DIPG stem-like cells with PTC596, a BMI-1 modulator, and IR, impairs the kinetics of DNA damage response (DDR). Both DDR foci formation and resolution were delayed, resulting in further reduction in cell viability compared with either treatment alone. *In vivo*, treatment of mice bearing DIPG xenografts with PTC596 leads to decreased tumor volume and growth kinetics, increased in-tumor apoptosis and sustained animal survival benefit. Gene expression analysis indicates that *BMI-1* expression correlates positively with DIPG stemness and BMI-1 signature. Together our findings indicate that BMI-1 modulation is associated with mitotic abnormalities, impaired DDR and cell death, supporting the combination of BMI-1 modulation and radiation as a promising novel therapy to treat children with DIPG.

DIPG-22. DISSECTING THE ONCOGENIC ROLE OF *FOXR2* IN DIFFUSE INTRINSIC PONTINE GLIOMA

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BACKGROUND: Diffuse intrinsic pontine gliomas (DIPGs) pose particular challenges for treatment. We recently completed a genomic analysis of close to 200 DIPGs and high-grade gliomas. We identified that nearly 10% of all DIPGs have increased expression of the fork head domain transcription factor *FOXR2*. We hypothesize that *FOXR2* accelerates gliomagenesis in histone mutant DIPGs and represents a previously unexplored therapeutic target. METHODS: To determine whether *FOXR2* is sufficient to mediate gliomagenesis, we applied an integrative genomics approach using both *in vitro* and *in vivo* DIPG models: mouse neural stem cell models expressing *FOXR2*, *in vivo* mouse models using *in utero* brainstem electroporation, patient-derived DIPG cell lines, and RNA sequencing analysis of human and mouse tumors expressing *FOXR2*. RESULTS: Our data shows that *FOXR2* indeed is an oncogene that rapidly accelerates gliomagenesis using an *in vivo* brainstem *in utero* electroporation model of DIPG. In human tumors, increased *FOXR2* expression is mutually exclusive with *MYC* amplification suggesting functional redundancy. *In vivo*, *FOXR2* results in large brainstem gliomas and rapid neurologic decline of animals. Transcriptional profiling of these tumors demonstrates activation of *MYC* signaling pathways. *In vitro*, we have further identified patient-derived cell lines with increased expression of *FOXR2*. CONCLUSION: *FOXR2* is sufficient to enhance gliomagenesis and represents a previously understudied therapeutic target for patients with the devastating disease DIPG.

DIPG-23. SINGLE CASE REPORT OF LOW DOSE RADIOTHERAPY AND CHEMOTHERAPY IN THE TREATMENT OF DIPG

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A 3 year-old girl, was noted to have progressive gait problem since Nov. 2017 and brought to hospital for checkup. Brain MRI on Jan. 2018 showed T2 hyperintensity infiltrative pontine lesion, favoring diffuse infiltrative pontine glioma and mild obstructive hydrocephalus, received VP-shunting on Jan. 15, 2018. Due to the refusal of surgical biopsy for tissue proof, we started the radiotherapy from Jan. 24, 2018, using Rapidarc technique with 6MV photon energy to treat the brain stem lesion, ended on Feb. 24, 2018 with total dose of 25.5Gy in 17 fractions as our usual practice. Following the completion of radiotherapy, we started the adjuvant chemotherapy using 1-week on, 1-week off regimen of temozolomide using dosage of 75 mg/sq-m/day, and this patient's general condition returned back to nearly normal. Serial follow-up images of brain MRI on 04/30/2018, 08/01/2018, 11/30/2018, 02/26/2019, 05/30/2019, 08/28/2019 showed slow progression of the pontine lesion, without the development of contrast enhanced new lesion. She maintained the functional independent until Sep. 2019, she was noted to have symptoms of ataxic gait, esotropia and choking on drinking liquid. We started the retreatment of radiotherapy from Oct.7, 2019, using same technique, ended on Nov. 5, 2019 with total dose of 30Gy in 20 fractions. The symptoms improved partially after the treatment, with residual weakness over left extremity. We are still treating the patient with adjuvant temozolomide, and she has survived most of time functionally independent in these 2 years.

DIPG-25. KETOGENIC DIET IN DIFFUSE INTRINSIC PONTINE GLIOMA IN CHILDREN: A RETROSPECTIVE STUDY INVESTIGATING THE FEASIBILITY

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PURPOSE: Diffuse Intrinsic Pontine Glioma (DIPG) is one of the most devastating diseases amongst children with cancer, thus novel strategies are urgently needed. We aimed to retrospectively evaluate the feasibility of the carbohydrate restricted ketogenic diet (KD) in DIPG patients. METHODS: Searches of MEDLINE and Embase identified four publications meeting the inclusion criteria (diagnosis of DIPG and exposition to a KD ≥ 3 months). One additional case was identified by contact with experts. The minimal feasibility criteria were defined as the ability to use the KD for ≥ 3 months. Individual patient data were extracted from the publications or obtained from investigators. RESULTS: Five patients (males, n=3; median age 4.4 years; range, 2.5–17 years) met the inclusion criteria (one