munoglobulin and mucin domain protein family. It is expressed on multiple immune cell types, including T cells, NK cells, myeloid populations, and microglia, regulating adaptive and innate immunity. In silico assessment of TIM-3 expression in DIPG datasets showed a robust expression of this gene. Single-cell sequencing analyses of DIPG biopsies uncover TIM-3 expression, especially in microglia. In vivo efficacy studies showed that treatment with AbTIM-3 significantly increased overall survival in two DIPG immunocompetent orthotopic models, led to long-term survivors (50%), and showed immune memory. TIM-3 treatment led to a significant increase in the tumor microenvironment of microglia, granulocytes, NK, and CD8+ cells and higher levels of IFNγ, GrzB and TNFα corresponding with an NK and T-cell activate phenotypes. Interestingly, there was a decrease in the Treg population which causes an increase in the pro-inflammatory CD8/Treg ratio. CD4, CD8 or NK cell depletion leads to a significant but not a total loss of treatment efficacy. CD4+ and CD8+ cells were aumented in treated draining lymph nodes and expressed higher amounts of pro-inflamattory cytokines than control-mice. Population analysis and depletion experiments demonstrated the relevance of NK, CD4, CD8 and myeloid populations in the response to anti-TIM-3 therapy. Interestingly, the depletion of the different immune populations combined or using immunodeficient Rag2 mice, did not completely abrogate the treatment efficacy. These results suggest the concurrence of an additional mechanism of action that together with the immune response leads to a robust anti-DIPG effect. In conclusion, these data demonstrate that TIM-3 is a potential target for the treatment of DIPG.

DIPG-23. ARTIFICIAL INTELLIGENCE FOR DETECTING ACVR1 MUTATIONS IN PATIENTS WITH DIPG USING MRI AND CLINICAL DATA

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INTRODUCTION: ACVR1 mutations are found in about 25% of patients with diffuse intrinsic pontine glioma (DIPG). Recent work has identified the combination of vandetanib and everolimus as a promising therapeutic approach for these patients. We investigate the predictive power of an AI model integrating clinical and radiomic information to predict ACVR1 mutation. METHODS: This retrospective monocentric study includes 65 patients with known ACVR1 status. Patients were scanned at the diagnosis time with at least one of the four structural MRI modalities (pre- and post-contrast T1, T2, FLAIR) and basic clinical information (age and sex) was collected. Radiomic features were extracted within the tumor region from each modality. For each modality, a recursive feature elimination method was used to select the most relevant features. Inside a leave-one-out framework, up to five logistic regression models were built: one per MRI modality and one for the clinical information. The final prediction for each patient was computed as the mean of the probabilities of ACVR1 mutation for the up to 5 different models. Assigning a different weight to clinical data according to age, (more or less than 10 years old) was also tested. RESULTS: Out of the 65 patients (mean age 7.9±3.7, 15 patients older then 10 years), ACVR1 mutations were identified with a 78% accuracy (sensitivity = 92% and specificity = 75%) in the leave-out-out process. Accounting for the clinical data in the model increase the accuracy to 82% (resp. sensitivity = 86% and specificity = 80%). CONCLUSION: The proposed multi model approach compensates for missing MR modalities while taking advantage of all the available information. Our first results suggest that a dedicated model could be developed for younger patients to improve the prediction. The different models will now be tested using additional data coming from the ongoing multicentric BIOMEDE trials.

DIPG-24. NEUROLOGICAL SYMPTOM IMPROVEMENT AFTER RE-IRRADIATION IN PATIENTS WITH DIFFUSE INTRINSIC PONTINE GLIOMA (DIPG): A RETROSPECTIVE ANALYSIS OF THE SIOP-E-HGG/DIPG PROJECT.

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PURPOSE: To investigate the spectrum of neurological triad improvement in patients with diffuse intrinsic pontine glioma (DIPG) treated by re-irradiation (re-RT) at first progression. METHODS: Re-analysis of the SIOP-E retrospective DIPG cohort by investigating clinical benefits after re-RT with focus on the neurological triad. Patients were divided as "responding" or "non-responding" to re-RT. To assess the interdependence between patients' characteristics and clinical benefits we used a Chi-Square or Fisher's Exact test. Survival according to clinical response to re-RT was calculated by the Kaplan-Meier method. RESULTS: As earlier reported, 77% (n = 24/31) of patients had any clinical benefit after re-RT. Among 25/31 well documented patients, 44% (n=11/25) had improvement in cranial nerve palsies, 40% (n=10/25) in long-tract signs, 44% (11/25) in cerebellar signs. Clinical benefits were observed in at least 1, 2 or 3 out of 3 symptoms of the DIPG triad, in 64%, 40% and 24% respectively. Patients irradiated with a dose ≥ 20 Gy versus < 20 Gy may improve slightly better with regards of ataxia (67% *versus* 23%; *P*-value = 0.028). The survival from the start of re-RT to death was not different between responding and non-responding DIPG patients (*P*-value = 0.871). CONCLUSION: A median re-irradiation dose of 20 Gy provides a neurological benefit in two-third of patients with an improvement of at least one symptom of the triad. DIPG patients receiving ≥20 Gy appear to improve slightly better with regards of ataxia, however we need more data to determine whether dose escalation up to 30 Gy provides additional benefit.

DIPG-25. PATTERNS OF CEREBROSPINAL FLUID DIVERSION AND SURVIVAL IN CHILDREN WITH DIFFUSE INTRINSIC PONTINE GLIOMA: A REPORT FROM THE INTERNATIONAL DIFFUSE INTRINSIC PONTINE GLIOMA REGISTRY

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BACKGROUND: There are no standard practice guidelines for cerebrospinal (CSF) diversion for diffuse intrinsic pontine glioma (DIPG), nor clear understanding of potential for palliation and life-prolongation. We evaluated CSF diversion characteristics in children with DIPG to determine incidence, indications, symptom effects, and survival. METHODS: Data

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