suppresses in the later stage (virus-releasing stage). Inhibition of the Ras signaling pathway at the early stage of viral infection prevents vaccinia virus from replicating, while viral oncolysis appears to be accelerated when the pathway was blocked after sufficient viral reproduction.

THER-08. SGT53 – A NOVEL P53 NANOMEDICINE INDUCES SIGNIFICANT RESPONSES IN CHILDREN WITH RECURRENT MEDULLOBLASTOMA AND CHOROID PLEXUS CARCINOMA: A REPORT OF TWO CASES

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BACKGROUND: Abnormal p53 function commonly defines high-risk CNS tumors, but functional restoration has eluded investigators. SGT-53 is a targeted nanomedicine encapsulating a plasmid DNA encoding wild-type human p53 with a transferrin receptor-targeting scFv on the nanocomplex surface resulting in efficient delivery across the BBB and robust tumor binding/uptake. Data generated by collaborators demonstrated synergy with irradiation and chemotherapy. REPORT: Two children with recurrent CNS malignancies have been treated with SGT-53, each receiving greater than 50 infusions in combination with irradiation and chemotherapy with no grade 3/4 AEs positively attributed to SGT-53. The first was an 11yo male with recurrent disseminated p53+ SHH medulloblastoma, with bulky intracranial/thoracolumbar disease. He received irradiation followed by biweekly doses of SGT-53 and temozolomide, bevacizumab and irinotecan given one week out of four. This patient exhibited a complete response of all disease on his first follow-up scan 8 weeks after therapy initiation and remained in remission for 8 months. The second patient was a 3yo male with disseminated recurrent choroid plexus carcinoma. He received CSI with SGT-53, followed by SGT-53, temozolomide and irinotecan as described above, again with no related grade 3/4 AEs. He experienced a partial response to all sites of disease and completed therapy after six months, progressing 7.8 months after initiating treatment. CONCLUSIONS: SGT-53 was well tolerated in two heavily-pretreated patients despite aggressive combinatorial strategies. The majority of the AEs experienced were mild and manageable. Each patient had significant responses, suggesting that SGT-53 should be evaluated in a clinical trial for similar patients.

THER-09. ONCOLYTIC ADENOVIRUS, DNX-2401, FOR NAIVE DIFFUSE INTRINSIC PONTINE GLIOMAS: A PHASE I CLINICAL TRIAL

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The objective of this trial is to determine the safety, tolerability, and toxicity of DNX-2401 in newly diagnosed DIPG patients (NCT03178032) followed by radiotherapy. Secondary endpoints are overall survival at 12 months, percentage of responses and induced immune response against tumor. Tumor biopsy was performed through the cerebellar peduncle, followed by intratumoral injection of DNX-2401 (N=12). Three patients were treated with $1x10^{10}$vp and given the lack of toxicity we escalated to $5x10^{10}$vp. The procedure was well tolerated and reduced tumor volume was demonstrated in all patients after combined treatment (virus + radiotherapy). We performed molecular studies (RNAseq and the Oncomine Childhood Research Panel from Thermo Fisher). The immune cell composition of the biopsies pre-virus injection was assessed using multiplexed quantitative immunofluorescence. T cells were hardly detectable in these tumors while macrophages were abundant. Using a multiplexed TCR-sequencing mRNA-based assay to analyze 18 available paired pre- and post-treatment samples from the trial, we detected increased clonal T cell diversity following treatment with the virus. We also measured pre and post treatment neutralizing antibodies and their relationship with survival. Finally, we performed functional studies using 2 cell lines isolated from patients included in this trial to assess the response to the virus (infectivity, viability, T-cell recognition). In summary, the virus has shown safety and efficacy in some patients. The information obtained in this clinical study would aid understanding the response of DIPG patients to viral therapies and, therefore, to better tailor this strategy to improve the survival of these patients.