type LMD is associated with worse prognosis compared to nodular-type LMD. Absence of extracranial disease at the time of surgery was the most consistent factor associated with LMD on follow-up.

LOCL-07

LOCO-REGIONAL INFUSION OF GB-13 (IL13.E13K-PE4E) AS A POTENTIALLY PROMISING TREATMENT FOR RECURRENT HIGH-GRADE GLIOMA

Julian Rechberger[1], Soumen Khatua[1], Jian Campian[1], Jann Sarkaria[1], Jonathan Schwartz[1], David Daniels[1], Randy Schrecengost[2]; [1]Mayo Clinic, Rochester, MN, USA. [2]Targepeutics, Inc., Hershey, PA, USA

INTRODUCTION: High grade gliomas (HGG) are devastating diseases with largely unchanged survival outcomes despite decades of research. Recent studies suggest the interleukin 13 receptor subunit alpha 2 (IL-13Rα2) is selectively upregulated in up to 80% of HGG, including glioblastoma (GBM) and diffuse midline gliomas (DMG) harboring H3K27 alterations. Immunotoxins targeting IL-13Rα2 have been demonstrated as safe and have shown some benefit for patients with HGG in previous phase I/II and III clinical trials. We hypothesized that by using GB-13 (IL13.E13K-PE4E), a novel peptide-toxin that binds IL-13Rα2 with high specificity and possesses a Pseudomonas exotoxin moiety, we would enhance the anti-tumor effects of this immunotherapy for HGG *in vitro* and *in vivo* while decreasing off-target toxicity. METHODS: We examined the pharmacological effects of GB-13 in multiple patient-derived cell lines and rodent models of HGG. GBM and DMG lines were used to confirm IL-13Rα2 expression and sensitivity towards GB-13. Tumor naïve rats were evaluated for toxicity, and orthotopic PDX mice were used to monitor tumor size and survival following loco-regional infusion of GB-13. RESULTS: GB-13 induced a potent cytotoxic response strongly predicated on IL-13Rα2 expression in vitro. No treatment-related adverse effects were noted after 7-day continuous intracranial infusion of GB-13 in tumor naïve rats. Further, in IL-13Rα2-upregulated orthotopic PDX mice, direct intratumoral administration of GB-13 via convection-enhanced delivery abrogated tumor growth and prolonged survival. CONCLUSIONS: Given these promising results as well as the critical need for novel therapies in CNS malignancies, we are progressing to human trials using GB-13 targeting recurrent HGG. Ongoing safety studies in tumor-bearing animals will be able to define dose levels for the initial adult study-arm and the following pediatric study-arm. In this Phase 1 clinical trial, we hypothesize that loco-regional infusion of GB-13 will safely enhance tumor clearance by causing selective killing of IL-13Rα2-upregulated HGG cells.

LOCL-08

SAFETY AND FEASIBILITY OF RHENIUM-186 NANOLIPOSOME (186RNL) IN RECURRENT GLIOMA: THE RESPECT™ PHASE 1 TRIAL

Andrew Brenner[1], Marc Hedrick[2], Norman LaFrance[2], Ande Bao[3], William Ohillips[4], Torel Patel[5], Jeffrey Weinberg[6], John Floyd[4]; [1]University of Texas, San Antonio, TX, USA. [2]PLUS Therapeutics, San Antonio, TX, USA. [3]Case Western Reserve University, Cleveland, OH, USA. [4]University of Texas, San Antonio, TX, USA. [5]University of Texas, Dallas, TX, USA. [6]University of Texas, MD Anderson, Houston, TX, USA

BACKGROUND: Liposomal rhenium-186 (186RNL) is a potent source of electrons with short path length, low dose rate, high radiation density and gamma emission. Preclinically, 186RNL via convection enhanced delivery (CED) achieves very high doses of targeted radiation and a wide therapeutic index. We report the updated results of ReSPECT, the first in man, dose escalation phase 1 trial of 186RNL in recurrent glioma. METHODS: Following computer assisted treatment planning and placement of intracranial catheter(s), we performed a single administration of 186RNL by CED. Whole body planar and SPECT/CT imaging was obtained on days 1-8 following treatment for dosimetry and distribution. Patients were followed for safety, progression and survival. RESULTS: Twenty-one patients across 7 cohorts received 1.0-22.3mCi in a tumor volume of 0.6-8.80mL. Mean tumor volume was 8.3mL (0.9-22.8mL). Patients had a mean of 1.7 recurrences, 5 with prior bevacizumab. 19 (91%) were grade 4 gliomas, and 100% were after cohort 4. We used a CED rate of 5-20µl/min per catheter, with 1-4 catheters per patient. Tumor mean absorbed radiation dose was 255Gy (8.9-740Gy) while exposure outside the brain was negligible. The mean percentage tumor in the treated volume (Tu/Tv) was 60.3% (19.8%-100%). Thus far, we have observed no dose limiting toxicities, one grade 3 treatment related adverse event (AEs), and the majority of AEs were mild in intensity. The incidence and severity of AEs did not correlate with increasing dose. Mean Tu/Tv in patients not receiving prior bevacizumab was 75% vs. 48% in those that had. Thus far, overall survival (OS) in 16 bevacizumab naïve patient is 49 weeks with 7 patients still alive and a positive correlation of OS to Tu/Tv. CONCLUSIONS: 186RNL achieves high absorbed doses without significant toxicity with favorable overall survival. Updated delivery feasibility, safety and overall survival will be presented.

LOCL-09

SHORT-TERM SEIZURE OUTCOMES IN PATIENTS WITH TREATED WITH LASER INTERSTITIAL THERMAL THERAPY

Ethan Srinivasan[1], Ryan Edwards[1], Emily Lerner[1], Aden Haskell-Mendoza[1], Peter Fecci[2]; [1]Duke University School of Medicine, Durham, NC, USA. [2]Duke University Hospital, Department of Neurosurgery, Durham, NC, USA

Laser interstitial thermal therapy (LITT) is a minimally invasive treatment modality for intracranial tumor and radiation necrosis (RN). A transient increase in edema following LITT typically resolves within three months post-procedure. We sought to characterize the short-term seizure outcomes during this period for patients undergoing LITT for tumor or RN. A retrospective analysis of 86 consecutive patients treated with LITT from 2015-2019 at a single institution was conducted. Data on baseline demographics, treatment details, and clinical course were collected. Thirty-one (36%) had a seizure within one year following LITT, 19 (22%) of which occurred within the first 90 days post-LITT (71% of all seizures). Forty-three (50%) patients had documented pre-LITT seizures, with 27 (63% of all seizures) of those occurring within 90 days pre-LITT. Between patients with and without post-LITT seizures within the first 90 days, there were no significant differences in gender, age, pre-LITT KPS, pre-LITT volume, pre-LITT resection, pre-LITT stereotactic radiotherapy, pre-LITT chemo- or immuno-therapy, use of AEDs or steroids before or after LITT, location, or pathology at the time of treatment. Patients with seizures in the first 90 days post-treatment were significantly more likely to have received pre-LITT whole brain radiotherapy (WBRT) (32% vs. 9%, p=0.02). Of the 18 patients with pre-LITT seizures within 90 days, 9 (50%) were entirely seizure free in the 90-day post-LITT period. In summary, seizure is a known complication of LITT for intracranial lesions, with the majority occurring in the first 90 days post-procedure. WBRT was significantly associated with 90-day post-LITT seizure, which may represent a diminished neurologic reserve in these patients. These findings may help guide clinicians in determining patients appropriate for LITT and those who may require closer monitoring and longer AED tapers in the short-term period following ablation.

LOCL-10

EVOLUTION OF FUNCTIONAL OUTCOMES AFTER LASER INTERSTITIAL THERMAL THERAPY (LITT) VERSUS RESECTION IN THE TREATMENT OF LESIONS IN OR NEAR THE PRIMARY MOTOR CORTEX

Ethan Srinivasan[1], Emily Lerner[1], Ryan Edwards[1], Aden Haskell-Mendoza[1], Joshua Jackson[2], David Huie[2], Peter Fecci[2]; [1]Duke University School of Medicine, Durham, NC, USA. [2]Department of Neurosurgery, Duke University Hospital, Durham, NC, USA

Laser interstitial thermal therapy (LITT) has become increasingly common, particularly in the treatment of progressive lesions after stereotactic radiosurgery for brain metastases. Previous work has illustrated the sensitivity to its use near critical structures, including the corticospinal white matter tracts. A single-surgeon retrospective study was performed of patients who underwent LITT or open resection for lesions located in or near the primary motor cortex, with functional outcomes graded relative to pre-treatment symptoms at 30, 90, and 180 days. Forty patients met inclusion criteria, with median age 64 years (57-72), and estimated baseline KPS 80 (80-90). Nineteen (47.5%) received LITT and 21 (42.5%) resections with intra-operative motor mapping. LITT patients trended towards smaller maximum diameters (2.1 cm vs 2.8 cm, p<0.01), with shorter ICU (0 vs 1 day, p<0.01) and hospital stays (1 vs. 2 days, p<0.01). At 30 days after treatment, 88.9% of resected patients had stable or improved symptoms compared to 35.3% of the LITT cohort (p<0.01). At 90 days, the difference was 87.5% to 50% (p=0.04), and at 180 days 100% to 85.7% (p=0.3684). When separated by new vs. progressive lesions, steroid responsiveness, and lesion histology, similar though not statistically significant trends were identified. In summary, LITT and resection provided similar functional outcomes in the treatment of lesions in or near the primary motor cortex for patients who survived at least 180 days post-treatment. Patients who received resection tended to have better functional outcomes in the nearer term. These differences are likely due to transient, expected post-LITT edema that subsides with time.

LOCL-11

EGFR-MUTATED NON-SMALL CELL LUNG CANCER (NSCLC) LEPTOMENINGEAL DISEASE (LMD) IN A LARGE STEREOTACTIC RADIOSURGERY PATIENT COHORT: INCIDENCE AND OUTCOME

Reed Mullen, Bernadine Donahue, Juan Alzate, Joshua Silverman, Assaf Berger, Kenneth Bernstein, Douglas Kondziolka; NYU Langone Health, New York City, NY, USA

AIM: Patients with EGFR-mutated NSCLC brain metastases (BM) treated with targeted agents +/- radiosurgery (SRS) have increasing life expectancies. Systemic treatment may become less effective in preventing CNS progression