New development Paradigm for Rare CNS cancers: Real World Data (RWD) Compared to Ongoing Safety and Feasibility Results from a Phase 1/2 Clinical Trial of 186RNL (Rhenium-186 Nanoliposome) (186Re) Obisbemeda in Recurrent Glioma: The ReSPECT-GBM Trial

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Aim/Introduction: 186RNL is a BMEDA-chelated 186Re encapsulated in nanoliposomes delivered via convection enhanced delivery (CED) with ongoing Phase 1 dose escalation and Phase 2 study. Unique 186Re properties (1-MeV β-decay and simultaneous γ-decay of 137 keV, allows therapy and imaging and has achieved durable, localized tumor retention, and high absorbed radiation doses[ARD]. We present updated results from ongoing trial ReSPECT-GBM (NCT01906385) with comparison to RWD in 186RNL in recurrent glioma patients. ***Materials and Methods:*** An analysis [data sourced from the Medidata Enterprise Data Store (MEDS)] was performed to determine if bevacizumab patients is an appropriate external control group for evaluating the treatment effect in current and upcoming CED trials. Deidentified patient-level historical clinical trial data, study and patient-level data from historical rGBM CED studies [D'Amico, J Neurooncol 2021] and an on-going Plus Therapeutics CED study were analyzed. Aggregate summary statistics were based on combined study- and patient-level data using weighted (by sample size) means, median of medians, incidence and OS rates (completed studies). Statistical analyses by log rank, proportional hazards and accelerated failure time (AFT) models were performed on the Phase 1 cohorts leading to the Phase 2 dose selection and trial initiation. ***Results:*** Twenty-one adult recurrent glioma patients across the first six dose-cohorts were analyzed. Single 186RNL dose ranged from 1.0-22.3 mCi in a volume of 0.6-8.8 mL, CED administration rate was 5-20 μl/min using 1-4 catheters and was well-tolerated. For the Phase 1 cohorts[6] leading to the ongoing Phase 2, three patients remain alive and 18 have died. The median overall survival (N=21) by log-rank analysis for patients receiving AARD of >100 Gy was 30 months. Proportional hazards and AFT modeling demonstrated AD and %tumor treated significantly correlated with OS. For RWD control analysis, all cohorts reported similar characteristics over a broad set of demographics, disease characteristics and medical history [age, race, gender, recurrence, grade and prior treatment]. While the baseline composition of rGBM study patients world-wide has changed over time to enroll healthier patients (ECOG=0) with smaller tumors, median OS has remained constant (bevacizumab:7.9 months; CED studies:8.4 months). **Conclusion:** Single-dose 186RNL by CED in adult patients with rGBM achieves high absorbed doses without significant toxicity, is well tolerated, with favorable overall survival compared to RWD controls. We are enrolling two studies in rGBM: larger tumors in the Phase 1 dose- escalation [>20 cm3]; Phase 2 [tumor ≤20 cm3]. Developing and Current results will be presented.