TPS7086 **Poster Session**

A phase 2 study to confirm safety and efficacy of MB-105, an autologous CD5-directed CAR T-cell therapy, in relapsed/refractory T-cell lymphoma (R/R TCL).

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Background: R/R TCL presents an unmet clinical need with limited treatment options and 3-year survival $< 20\%$. MB-105 is an autologous CD5-targeting CAR T-cell therapy developed at Baylor College of Medicine that has been designed to address the unique challenge of treating T-cell malignancies by overcoming CAR T-cell fratricide without additional engineering. In the phase 1 trial, 44% (4/9) patients experienced objective responses, including 2/3 complete responses with survival >5 years. Mid-trial manufacturing refinements enhanced MB-105 potency and persistence without compromising safety. We have developed an industrialized, 6-day process of manufacturing MB-105 and are conducting a phase 2, multicenter study in the USA to evaluate MB-105 in patients with R/R peripheral and cutaneous TCL (PTCL, CTCL). Durable responses and safety observed across all dose levels in phase 1 guided the dose selection for this trial. **Methods:** The study follows a Simon two-stage design with a safety run-in to confirm tolerability of the recommended phase 2 dose (RP2D) of 50 million cells in 6 patients. This is followed by an efficacy evaluation first in 15 patients then 46 total. Adaptive elements allow the independent data monitoring committee to adjust doses, monitoring schedules, or lymphodepletion regimens without formal protocol amendments Primary objectives are first to confirm tolerability of the recommended dose by CTCAE v5 and ASTCT for cytokine release syndrome and immune effector cell-associated neurotoxicity syndrome (CRS/ICANS) and then evaluate efficacy through central review. Secondary/other objectives include assessing response durability, overall survival, persistence, immune correlates and manufacturing success. Adults with R/R TCL who have failed ≥ 1 prior systemic therapy for PTCL or ≥ 2 for high-volume CTCL are eligible. Local pathology for CD5 expression is required, later confirmed by central lab. Patients must have adequate organ function, Karnofsky PS $\geq 70\%$, and no prior cell therapy/transplant within 60 days of leukapheresis. Key exclusions are Sezary syndrome (potential for high circulating tumor cells to affect manufacturing), active CNS involvement, infections, graft-versus-host disease > grade 2, or comorbidities that may interfere with study participation or endpoints. Patients are closely monitored for CRS/ICANS. Safety and efficacy are assessed intensively for the first 3 months and gradually less frequently over the subsequent 21 months. Imaging and post-infusion testing, including CAR-T persistence, immune profiling and biomarkers are conducted throughout. Patients are encouraged to participate in a separate long-term follow-up study. Recruitment is ongoing. Clinical trial information: NCT06534060. Research Sponsor: None.