TPS9602 **Poster Session**

Phase I dose escalation and expansion study of PRAME T-cell receptor (TCR) engineered IL15-transduced cord blood–derived natural killer (NK) cells in patients with recurrent and/or refractory melanoma (PRAMETIME-Mel).

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Background: For patients with relapsed and/or refractory metastatic melanoma (RRFM), there is a critical need to test novel strategies with improved anti-tumor response and safety profile. Adoptive cell therapy (ACT) has been recognized as a promising avenue for addressing the unmet need for more potent anti-tumor approaches. Allogeneic cord blood (CB)-derived natural killer (NK) cell therapies have emerged as a therapeutic alternative to adoptive T-cell therapies given decreased toxicity and feasibility as an "off-the-shelf" therapy, bypassing the manufacturing time and treatment delays associated with autologous T-cell products. PRAME (PReferentially expressed Antigen in MElanoma), a cancer-testis antigen expressed on approximately 95% of cutaneous melanomas and not expressed outside of immune-privileged sites such as the testis, ovary, placenta, and endometrium, is a promising target for allogeneic NK cells engineered with a T cell receptor (TCR) to selectively target melanoma cells. In contrast to autologous T cell therapies that require exogenous systemic IL-2 as a supportive factor, NK cells engineered to express IL-15 have been observed to have minimal side effects while significantly enhancing the in vivo expansion and persistence of the transduced NK cells. PRAME TCR/IL-15 NK, an engineered TCR NK cell therapy, has demonstrated efficacy against melanoma cell lines in vitro and in vivo and safety against normal human cell lines. Building upon these preclinical findings, we propose this trial to explore the safety and efficacy of PRAME TCR/IL-15 NK cells in patients with RRFM. **Methods:** This phase I, single-center, open-label trial will assess the safety, tolerability, and efficacy of PRAME TCR/IL-15 cells in patients with HLA A*02:01 positive RRFM, with no prospective PRAME testing. The primary endpoints are to determine the safety, tolerability, maximum tolerated dose and recommended phase II dose. The secondary endpoints are to assess response and survival. The study will be comprised of dose escalation (4 dose levels, with a dose level -1 in case of excessive toxicities observed in dose level 1) and dose expansion. A maximum of 39 patients will be enrolled, including 24 patients in the dose escalation cohort and up to 15 patients in the dose expansion cohort. Enrolled patients will receive lymphodepletion chemotherapy (fludarabine 30 mg/m^2 and cyclophosphamide 500 mg/m^2) on days -6 to -3, followed by a single dose of PRAME TCR/IL-15 NK cells on day 0. Longitudinal blood and tissue samples will be collected for correlative immune analysis. Clinical trial information: NCT06660420. Research Sponsor: None.