

PHASE I STUDIES OF AGENT-797, A NOVEL ALLOGENEIC INVARIANT NATURAL KILLER T (iNKT) CELL THERAPY, FOR THE TREATMENT OF PATIENTS WITH SOLID TUMORS OR MULTIPLE MYELOMA

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Background AgenT-797, is an allogeneic CD1d-restricted T cell population (iNKT) that responds to lipid antigenic stimulation with potent cytokine secretion. iNKTs promote innate and adaptive immunity, home to critical organs (e.g., liver/lung/bone marrow), suppress myeloid-derived suppressor cells, and recondition the tumor microenvironment. AgenT-797 is a scalable, off-the-shelf therapy that retains potent cytotoxicity after cryopreservation and can be administered without lymphodepletion. This analysis represents data from 2 ongoing phase 1 studies of agenT-797 in patients with relapsed/refractory (r/r) multiple myeloma (MM) (NCT04754100) and agenT-797 alone or combined with pembrolizumab or nivolumab in r/r solid tumors (NCT05108623).

Methods Patients with r/r solid tumors and measurable disease per RECIST 1.1 received either agenT-797 monotherapy at 4.3×10^6 cells/kg or 1.4×10^7 cells/kg or in combination with pembrolizumab or nivolumab. Patients with r/r multiple myeloma received agenT-797 at 1.4 or 4.3×10^6 cells/kg or 1.4×10^7 cells/kg after having failed at least three prior treatments (proteasome inhibitor, immunomodulatory agent and anti-CD38 antibody). Dose-escalation followed a 3+3 scheme and endpoints included safety, persistence of agenT-797, anti-tumor activity measured as duration of response, progression-free survival, and time to response. Adverse events (AEs) were reported per CTCAE v5.0 and dose limiting toxicities (DLTs) were evaluated.

Results Enrollment commenced May 2022; as of July, thirteen patients with r/r solid tumors (median age 62y, range 46-92) were treated with a single dose of agenT-797 as a monotherapy (cervical, gastric, breast, pancreas, thymoma, GU, others) or in combination with approved anti-PD-1 (NSCLC, RCC, SCC). In r/r multiple myeloma, four patients (median age 55y, range 50-72) with ECOG 0 and median 5 prior lines of therapy were treated with a single dose of agenT-797, without lymphodepletion in two escalating cohorts. No DLTs were observed. Tolerability was favorable with no cytokine release syndrome (CRS), neurotoxicity, or severe immune-related AEs. No patients experienced treatment-related serious adverse events nor AEs \geq grade 3. Enrollment is ongoing with early observations including reduction of liver mets and SD>3 (Rectal) and >50% reduction of tumor cells in bone marrow with SD>10 (multiple myeloma).

Conclusions AgenT-797 is a novel iNKT cell potential therapy for patients with solid tumor cancers and hematologic malignancies. Updated data on safety, efficacy, and translational analyses, including persistence, serum biomarkers, and alloimmunity, will be presented.

Trial Registration NCT04754100; NCT05108623

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