Peripheral and tissue persistence of agenT-797, an allogeneic INKT cell-based therapy for the treatment of cancer

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Background

Intravascular natural killer T (INKT) cells are a unique subset of T cells that exhibit both direct and indirect anti-tumor activities. INKT cells can recognize and kill tumor cells directly and release cytokines including interferon-γ (IFN-γ), IL-2 and TNF-α, leading to tumor cell destruction. INKT cells also play a key role in regulating the immune response by producing cytokines, such as interferon-gamma and interleukin-4, that promote the activation and differentiation of other immune cells. We have developed an allogeneic INKT cell product (agentT-797) for use in mismatched patients, and without lymphodepletion, agentT-797 is ex vivo expanded, highly scalable, and under evaluation in a broad spectrum of diseases, including a Phase I clinical trial to assess safety and efficacy of agentT-797 monotherapy or in combination with pembrolizumab and nivolumab (PD-1) in patients with solid tumors (NCT01528663). We present data on the biomarker signatures and persistence of our allogeneic cell therapy which underlie the observed efficacy of agentT-797.

Methods

We describe the results of a Phase I clinical trial evaluating the safety and efficacy of agentT-797 monotherapy or in combination with pembrolizumab and nivolumab in patients with solid tumors. The trial is registered with ClinicalTrials.gov, identifier NCT01528663. The study included patients with metastatic solid tumors who were not candidates for standard of care therapy. The agentT-797 cells were administered as an intravenous infusion, and the safety and efficacy of the treatment were assessed.

Results

Well Tolerated in Patients across Multiple Tumor Types

Evidence of Clinical Benefit in Extensively Pre-treated Patients

No Lymphodepletion - 6 Months Persistence

Duplex Sequencing - Maximal Sensitivity SNP Analysis

Phase 1/2 of agentT-797 Patients with Advanced Solid Tumors (NCT01508623)

Table 1. Patient demographics and summary of AEs. Patients (N=19) with solid tumors treated with agentT-797 at two dose levels (SD/PR) were treated with pembrolizumab and nivolumab. Dose escalation was performed on a 3+3 design. a) Phase 1 (SD/PR): Pts were treated with a combination of agentT-797 and pembrolizumab (PD-L1); b) Phase 2 (PR): Pts were treated with a combination of agentT-797 and nivolumab (PD-1).

Table 1. Patient demographics and summary of AEs. Patients (N=19) with solid tumors treated with agentT-797 at two dose levels (SD/PR) were treated with pembrolizumab and nivolumab. Dose escalation was performed on a 3+3 design.

- In Phase 1, patients were treated with pembrolizumab (PD-L1) or nivolumab (PD-1) and agentT-797 at dose levels of 0.1x10^6 to 1x10^6 cells/kg.
- In Phase 2, patients were treated with pembrolizumab (PD-L1) or nivolumab (PD-1) and agentT-797 at dose levels of 1x10^6 to 3x10^6 cells/kg.

- All patients received pembrolizumab (PD-L1) or nivolumab (PD-1) at a dose of 200 mg/kg every 3 weeks, followed by a maintenance dose of 100 mg/kg every 6 weeks.

- The primary endpoint was safety and tolerability, and the secondary endpoints included objective response rate, clinical benefit rate, and duration of response.

Conclusions

- Single administration of agentT-797 (allo-INKT) cells showed clinical benefit in patients with heavily pre-treated solid tumors (n=34); including a partial response in 3L gastric cancer (n=1) and disease stabilization (n=10).
- agentT-797 was administered without lymphodepletion or HLA-matching and demonstrated a tolerable safety profile with no DLTs reported.
- agentT-797 induced a systemic IFNγ-based pro-inflammatory signature which likely initiated increased expression of pro-inflammatory and lymphoid-attracting mediators within tumors, leading to increased tumor infiltration by cytokotoxic lymphocytes (NK cells and CTLL) and clonal T cell expansion in cancers with high neoantigen burden.
- agentT-797 demonstrated unprecedented persistence for an allogeneic, unmatched immune cell therapy in the absence of lymphodepletion, and may thus exhibit an increased duration of action compared to allogeneic immune cell therapies with shorter persistence.
- agentT-797 may act as a potent mediator of tumor immune infiltration, thus overcoming one of the key barriers facing immunotherapy, and underscoring its potential use as an universal adjuvant in immunotherapy.
- MiNK Therapeutics plans to evaluate agentT-797 in combination with SOC (pembrolizumab/nivolumab) +/- botulinsilimab (CTLA-4) in nHL NSCLC (Tan et al., AACR 2020), testicular cancer (Ph1/2 expansion NCT01088623) and in 2/3L gastric (Ph1/2 IST Janjigian et al.)

Endnotes

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