Background FT516 is an allogeneic, off-the-shelf natural killer (NK) cell cancer immunotherapy derived from a clonally master induced pluripotent stem cell (iPSC) line expressing hnCD16 to optimize antibody-dependent cellular cytotoxicity (ADCC) when combined with monoclonal antibodies (mAbs). A Phase I dose-escalation study of FT516 in combination with rituximab for patients with B-cell lymphomas has shown favorable safety and anti-tumor activity. We report results from a Phase I dose-escalation study of FT516 in combination with avelumab for patients with advanced solid tumors.

Methods Patients initially received 2 treatment cycles, with the option for 2 additional cycles, each cycle consisting of 3 days of outpatient conditioning chemotherapy (cyclophosphamide 500 mg/m² and fludarabine 30 mg/m²) followed by 3 once-weekly doses of FT516 with subcutaneous IL-2 (6 MIU). Avelumab 800 mg was administered every 2 weeks until progression. FT516 dose escalation was based on 3+3 design. Endpoints included safety, tolerability, and anti-tumor activity.

Results As of a data cutoff of 16 May 2022, 12 patients (non-cutaneous melanoma [6], cutaneous melanomas [4], non-small cell lung cancer and triple-negative breast cancer [1 each]) with a median of 3 prior therapies were treated, including 11 patients who received prior anti-PD-(L)1 therapy. Doses of 90 million (n=3), 300 million (n=3), or 900 million (n=6) FT516 cells/dose were administered. No dose-limiting toxicities, graft vs. host disease, neurotoxicity, FT516-related Grade ≥3 adverse events (AEs), or FT516-related serious AEs were reported. Grade 1 cytokine release syndrome was reported in 1 patient. Tumor burden reduction was observed in 6 patients, with a median peak reduction of 12.9% (range 3.5, 50); 1 patient with cutaneous melanoma refractory to 2 prior anti-PD-1 containing regimens achieved and maintained partial response per iRECIST through 6.2 months after initiation of treatment, and 6 patients had stable disease per iRECIST with median duration of disease control of 4.9 (range 3.8, 10.9) months.

Conclusions Up to 900 million FT516 cells administered with IL-2 in multiple doses and multiple cycles in combination with avelumab are safe and tolerable, with evidence of anti-tumor activity following failure of prior anti-PD-(L)1 therapy. These data support the development of next-generation iPSC-derived NK cells engineered with additional synthetic functional elements designed to enhance anti-tumor activity in solid tumors.

REFERENCE

Ethics Approval This study is being conducted in accordance with the Declaration of Helsinki and was approved by all Institutional Review Boards from each clinical site participating in the study. Specific approval numbers can be provided upon request.