RESULTS OF A PHASE I TRIAL OF FT500, A FIRST-IN-CLASS, OFF-THE-SHELF, IPSC-DERIVED NK CELL THERAPY COMBINED WITH PD-1/PD-L1 CHECKPOINT BLOCKADE THERAPY AND IL-2 IN PATIENTS WITH ADVANCED SOLID TUMORS

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Background FT500, an allogeneic natural killer (NK) cell cancer immunotherapy derived from a clonal induced pluripotent stem cell (iPSC) line, is available off-the-shelf for on-demand administration to patients in multi-dose regimens. In preclinical studies, FT500 has been shown to recruit and activate T cells, increasing response to checkpoint inhibition for enhanced inflammatory cytokine production and tumor elimination. We report results from a Phase I clinical trial of patients with classical Hodgkin lymphoma (cHL) or non-small cell lung cancer (NSCLC) who were relapsed/refractory to prior anti-PD-1/L1 immune-checkpoint inhibitor (ICI) therapy and received FT500 combined with ICI therapy and IL-2.

Methods Treatment consisted of 2 days of outpatient conditioning chemotherapy (cyclophosphamide 300 mg/m² and fludarabine 25 mg/m²), followed by two 29-day cycles of 3 once-weekly doses of 300 million FT500 cells/dose with subcutaneous IL-2 (6 MIU), and nivolumab, pembrolizumab, or atezolizumab administered at standard dose and schedule. Key endpoints included safety, tolerability, and anti-tumor activity.

Results As of 09 May 2022 data cutoff, 5 patients with cHL and 7 patients with NSCLC, with a median of 10 and 3 prior therapies, respectively, were treated. No events of cytokine release syndrome, neurotoxicity, or graft-versus-host disease were observed. Most common treatment-emergent adverse events (AEs) included lymphopenia and anemia. No FT500-related serious AEs were reported; only 1 Grade 3 FT500-related AE of lymphopenia was reported. For cHL, objective response by RECIL was reported in 4 patients (1 complete, 1 partial, 2 minor), with median peak tumor burden reduction of 24.9% (range 10.2, 72.4) and median response through 7.9 months (range 4.1, 12.0) from initiation of treatment, including an ongoing complete response subsequently lost to follow-up at 8.7 months. For NSCLC, tumor burden reduction was observed in 3 patients, with median peak reduction of 9.8% (range 6.3, 40); 1 patient refractory to 2 prior ICI-containing regimens had an ongoing partial response by iRECIST through 12.6 months from initiation of treatment, and 3 had stable disease with median duration of disease control of 7.7 months (range 3.4, 8.6).

Conclusions Six doses of 300 million FT500 cells with IL-2 and concurrent ICI therapy is safe and tolerable, with evidence of durable anti-tumor activity observed in heavily pretreated patients resistant to anti-PD1/L1 therapy. These results support the development of next-generation iPSC-derived NK cells engineered with synthetic functional elements designed to synergize with ICI therapy and enhance anti-tumor activity in solid tumors.

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.