ASCO Annual Meeting May 31 – June 4, 2024

Abstract #e14515

Interim Analysis of a Phase I Study using Cryopreserved Non-genetically Modified Allogeneic Natural Killer Cells With Enhanced Cytotoxicity (SNK02) in Patients with Advanced Solid Tumors without Lymphodepletion.

Victoria Chua, Sant P. Chawla, Erlinda Maria Gordon, William Feske, Lucia Hui, Hank Lee, Yoonmi Kang, Juan Mata, Katia Betito, Paul Y Chang, Paul Y. Song; Sarcoma Oncology Research Center, Santa Monica, CA; Sarcoma Oncology Center, Santa Monica, CA; Medical Imaging Center of Southern California, Santa Monica, CA; NKGen Biotech Inc., Santa Ana, CA.

Background: Natural killer (NK) cells play a key role as the main effector cells toward cancer in innate immunity. A leading approach to boost NKcell-mediated anti-tumor activity is via the adoptive transfer of ex vivo activated NK cells. Current allogeneic donor-derived products require lymphodepletion to prevent immunologic rejection of donor cells by the recipient and ensure adequate cell delivery of the product cells to the target. However, lymphodepletion can negatively impact combination therapies where a robust T cell response is desired. SNK02 is a first-in-kind, cryopreserved allogeneic non-genetically modified NK cell product with significant anti-tumor cytotoxicity and over 90% expression of CD16, NKG2D, NKp46, and DNAM-1, that can be consistently produced on a large commercial scale. We hypothesized that higher doses of SNK02 (to overcome autodigestion) could be delivered frequently without the need for lymphodepletion and that it might demonstrate activity against solid tumors that have failed multiple prior standard-of care treatment options.

Methods: In this Phase 1 dose escalation study (NCT05990920), SNK02 was administered intravenously (IV) weekly for 8 consecutive weeks in patients with advanced solid tumors. The starting dose was 6 x 10^9 SNK02 cells. The primary endpoint was safety based on adverse events (AEs), vitals, laboratory tests, and physical exams.

Results: As of Feb 1, 2023, 5 patients with advanced refractory solid tumors have been enrolled. Median age was 64 (range 44 – 71) and 3 were male. The subtypes were 1 leiomyosarcoma, 1 angiosarcoma, 1 endometrial adenocarcinoma, 1 undifferentiated pleomorphic sarcoma, and 1 colorectal adenocarcinoma. Four of five patients completed 8 cycles of SNK02. There was 1 death on study, which was deemed unrelated to the investigational product (IP). Out of the 36 doses administered through Cycle 8, there were 17 Grade 1, 3 Grade 2, and 1 Grade 3 adverse AEs related to IP. The Grade 3 AE of increased fatigue resolved after 1 day with no intervention required. Auto-antibodies appeared to develop around cycle 5 and appeared to correlate with AEs. The best objective response of SD was demonstrated in 100% of patients that completed the 8 cycles.

Conclusions: SNK02 was well tolerated as a monotherapy and appears to have some clinical activity against pretreated solid tumors despite the lack of lymphodepletion. SNK02 will continue to be studied as a monotherapy and in potential combination treatment regimens with monoclonal antibodies and immune checkpoint inhibitors.