BENEFICIAL EFFECT ON CSF AND PLASMA TAU PROTEINS AND COGNITIVE FUNCTION IN ALZHEIMER'S DISEASE SUBJECTS TREATED WITH EXPANDED NON- GENETICALLY MODIFIED AUTOLOGOUS NATURAL KILLER CELLS (SNK01)

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Abstract:

Background: The importance of Natural Killer (NK) cells of the innate immune system in neurodegenerative disease has largely been overlooked despite studies demonstrating their ability to reduce neuroinflammation (by eliminating activated T cells, degrading protein aggregates and secreting anti-inflammatory cytokines). SNK01 is an autologous non-genetically modified NK cell product which has shown increased activity.

Methods: In this Phase 1 study, SNK01 was administered IV every three weeks for a total of 4 treatments using a 3+3 dose escalation design (1, 2 and 4 x 10^9 cells) in subjects with either mild, moderate, or severe AD (Median MMSE was 14). Cognitive assessments and CSF/plasma pTau217 and pTau181 analyses were performed at baseline and at 1 and 12 weeks after the final dose. The primary endpoint was safety and secondary endpoints included changes in cognitive assessments and biomarker levels.

Results: Eleven subjects (5 males, 6 females) were enrolled (10 were evaluable). No treatment related adverse events were observed. Despite 70% of subjects being treated at relatively low doses of SNK01, 50-70% of all enrolled subjects in the trial had either stable or improved CDR-SB, ADAS-Cog and/or MMSE scores at one-week post-treatment (week 11). 50% of subjects (5/10) had a decrease in CSF pTau217 and 80% (8/10) had stable/decreased CSF pTau181 compared to baseline values, 30% (3/10) had a decrease in plasma pTau217 and 40% (4/10) had a decrease in plasma pTau181. Where data was available, this decrease continued through week 22 (12 weeks after the last dose) for CSF pTau217 for all subjects (4), for CSF pTau181 for 5/7 subjects, for plasma pTau217 for 2/3 subjects and for plasma pTau181, for 3/4 subjects. At week 11, the changes corresponded to stable or decreased CDR-SB for CSF pTau217 in 2/5 subjects, for CSF pTau181, in 5/8 subjects, for plasma pTau217, in 1/2 subjects (where data was available), and for plasma pTau181, in 3/4 subjects.

Conclusions: SNK01 was safe and well tolerated. SNK01 appears to have clinical activity in AD while also reducing CSF and plasma Tau protein levels. A larger trial with a higher dosing/duration has been initiated in the US in 2023.

Keywords: natural killer cells, neuroinflammation, pTau

Clinical Trial Registry: NCT04678453;
https://classic.clinicaltrials.gov/ct2/show/NCT04678453

Disclosures: Authors Song, Betito, Chang, Mata, Lee, Hui, and Hong are all employees and shareholders of NKGen Biotech who is the sponsor of this trial.