Treatment of Moderate Alzheimer's Disease Subjects with Expanded Non- genetically Modified Natural Killer Cells (troculeucel; SNK01) With Enhanced Activity — Report of the Phase I results of the Phase I/IIa study

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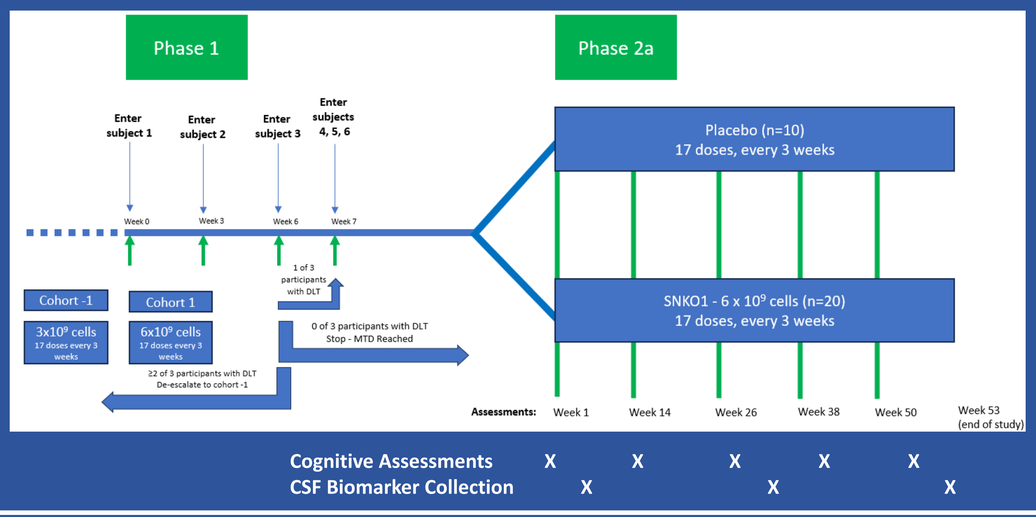
#LP020

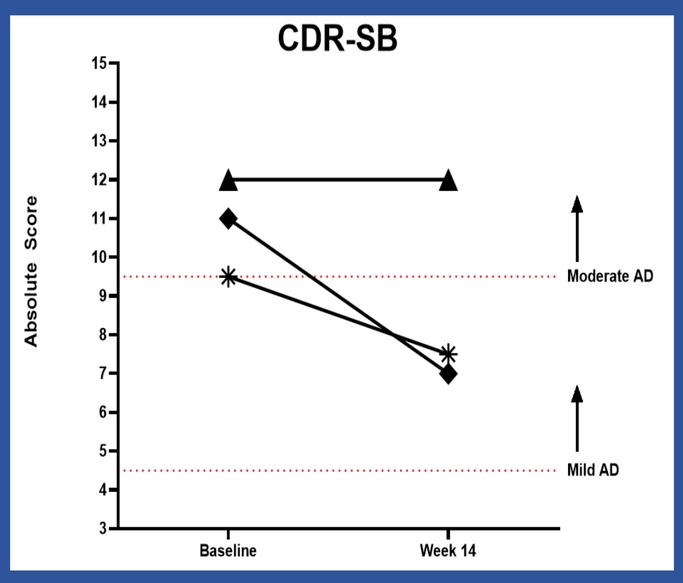
PURPOSE / OBJECTIVES

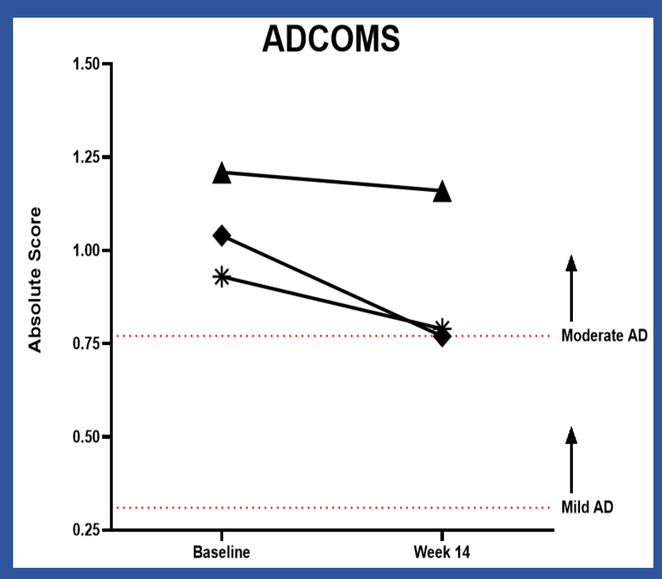
- Natural Killer (NK) cells play a profound role in the innate immune system and their importance in neurodegenerative disease has largely been overlooked despite preclinical studies demonstrating their ability to reduce neuroinflammation, which may be related to
  - their ability to identify and kill activated T cells,
  - their capability of balancing the ratio of protective to proinflammatory microglia,
  - their secretion of anti-inflammatory cytokines, and their ability to discard neurotoxic aggregates.
- SNK01 is an autologous non-genetically modified cryopreserved NK cell product with highly enhanced cytotoxicity and receptor expression.
- We have previously shown in a Phase I trial that 4 treatments with suboptimal doses of SNK01 in Alzheimer's Disease (AD) subjects was well tolerated and showed preliminary ability to impact cognition and improve protein aggregates and neuroinflammation biomarkers.
- We hypothesize that SNK01 at a higher dose can be safely infused in the Phase I part of this study and strive to confirm the positive impact on cognition and biomarkers in the double-blind randomized Phase IIa part of the study.

STUDY DESIGN



RESULTS





MATERIALS & METHODS

- In the Phase I part of the study, SNK01 was IV administered to 3 subjects with moderate AD (median age 80 years, median CDR-SB of 11) at a dose of 6 x 10^9 cells.
  - The primary endpoint was safety, monitored for 21 days after the first dose for each subject. These 3 subjects will continue to be treated every 3 weeks for 17 doses.
- In the Phase IIa part of the study (n=30), SNK01 or placebo (2:1) will be administered every 3 weeks for 17 doses, to subjects with moderate AD.
  - The primary endpoints will be safety and preliminary efficacy, with cognitive changes measured using CDR-SB, MMSE, NPI, ADCS-ADL-Severe and ADAS-Cog scales. The secondary endpoints will include changes in protein aggregate and neuroinflammation biomarker levels.

RESULTS

- Three (3) subjects were enrolled in the Phase I cohort.
- Early review of the data shows that after 3 months' treatment with a dose of 6 x 10^9 cells every 3 weeks
  - No treatment-related clinical or laboratory adverse reactions were seen
  - 2 of the 3 subjects went from a moderate to a mild AD rating on the CDR-SB scale
  - All 3 subjects had either a stable or improved ADCOMS score.
- These findings are similar to the SNK01-MX04 Phase I AD study (NCT04678453), where the product was well tolerated, and the one moderate AD subject who received the highest dose (a dose of 4B) also went from a moderate to a mild rating on the CDR-SB.

CONCLUSIONS

- SNK01 at the highest dose of 6 x 10^9 cells given to moderate AD subjects was well tolerated in this Phase I part of the study
- In 2/3 subjects SNK01 appeared to result in a clinical improvement from moderate AD to mild AD after only 3 months on therapy
- This study aims to confirm previous preliminary efficacy seen on both cognitive and biomarker changes in AD subjects.
- SNK01 will be evaluated for safety and efficacy in the randomized, placebo-controlled Phase IIa part of the study.

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