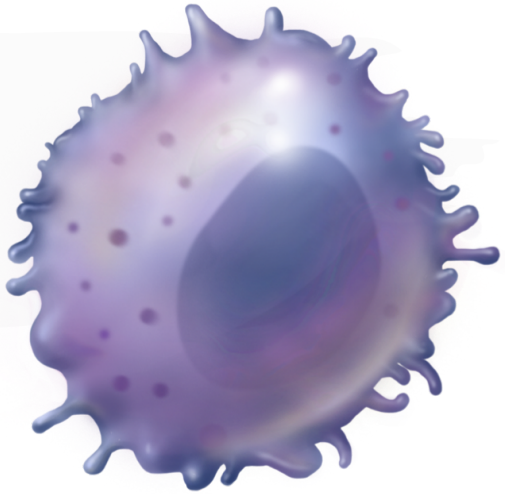
TAU 2024
Global Conference

SNK01 (Enhanced Natural Killer Cells) for Alzheimer's Disease

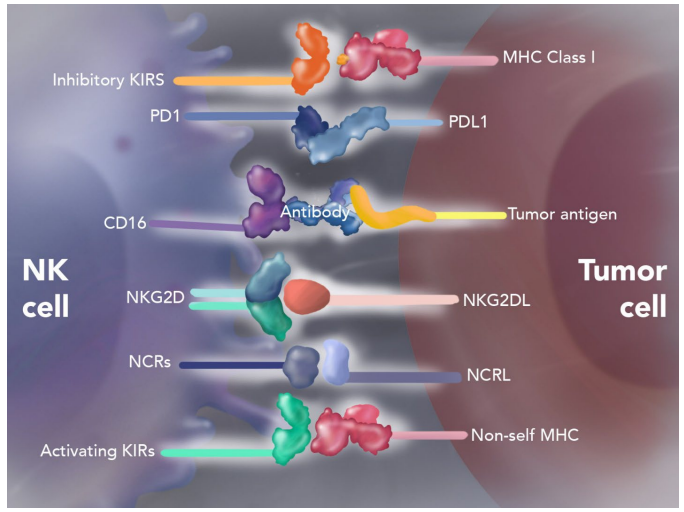
NKGEN BIOTECH

March 2024



Natural Killer Cells

Innate Immune System - 5-20% of circulating lymphocytes



Unlike T cells that have only one receptor, NK cells have 40+ receptors that allow them to distinguish Self (Healthy Cells/Tissue) from Non-Self (cancer, virally infected cells, autoreactive immune cells, etc.).

Immune regulatory capabilities

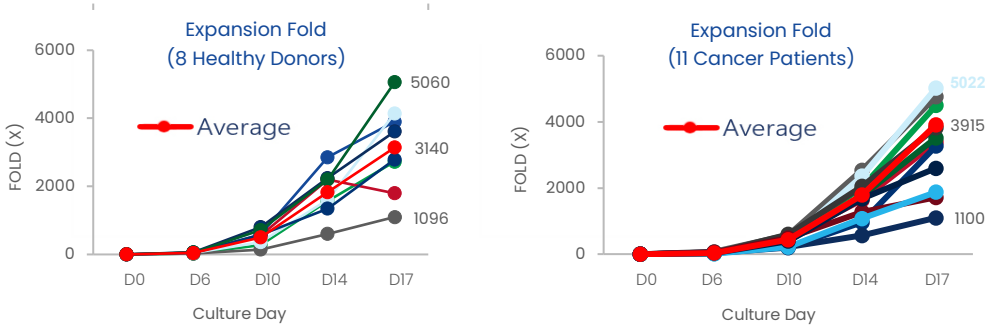
Weak and/or deficient NK cells have been shown to be correlated with various disease conditions.

Liu, S., Galat, V., Galat4, Y. et al. NK cell-based cancer immunotherapy: from basic biology to clinical development. J Hematol Oncol 14, 7 (2021).

NKGen's Manufacturing (CMC) Process

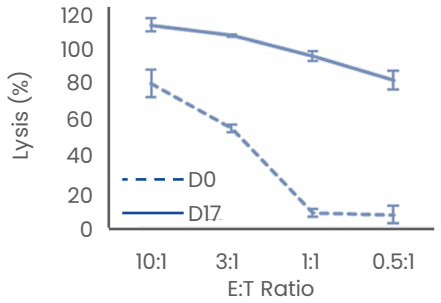
Expansion

NKGen can expand NK cells from any donor!



Cytotoxicity

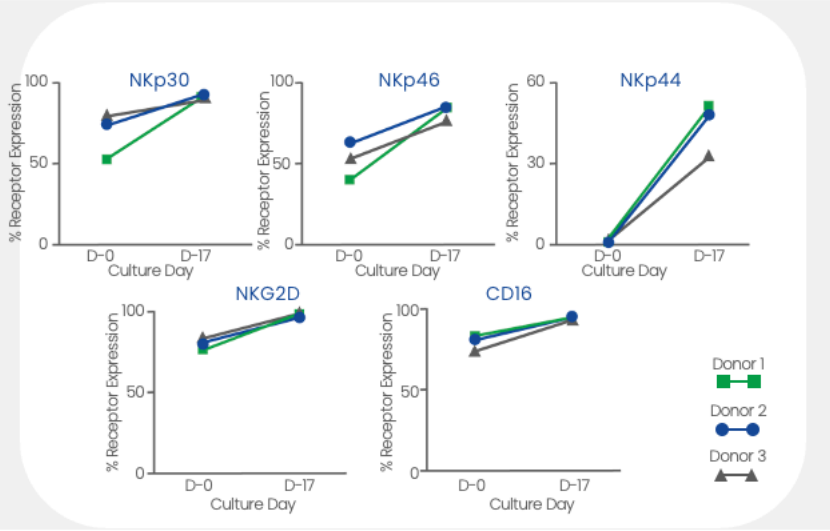
NKGen increases NK cell killing potential!



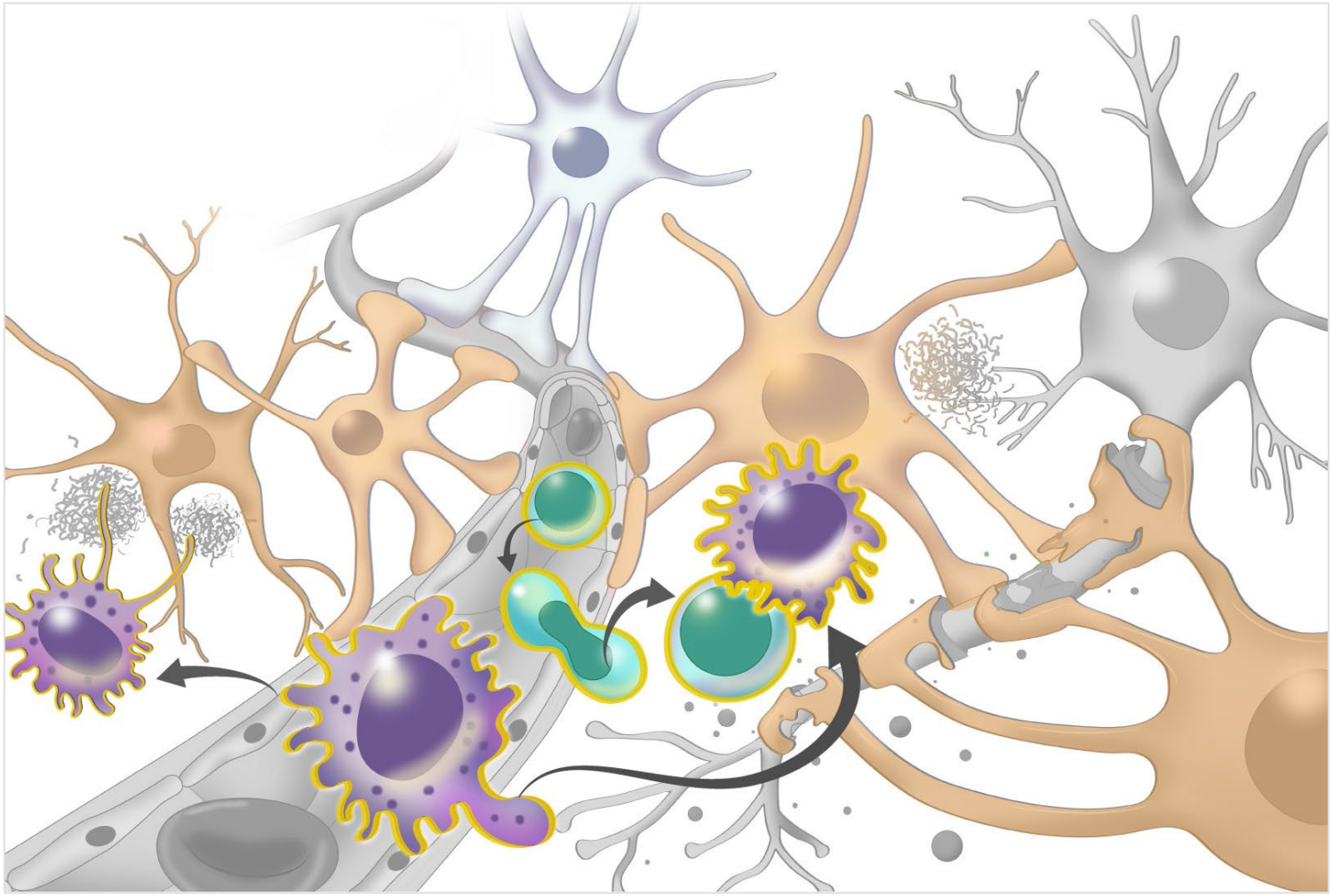
E:T Ratio = NK Cell : Cancer Cell Ratio
Target Cell = Myelogenous Leukemia

Receptor Expression Levels

NKGen increases receptor expression!



SNK01 Can Reduce Protein Accumulation and Clear Damaged Neurons



NK cells have been found to **prevent and reduce protein accumulation**[1,2] in alpha-synuclein and amyloid mouse models.

SNK01 has been found to phagocytose and digest proteins in vitro.

NK cells have also been found to **identify and eliminate damaged axons and neurons**[3]

1. Earls - PNAS - January 2020 117 (3) 1762-1771.
2. Marsh et al. PNAS February 2016 -E1317.
3. Davies et al., 2019, Cell 176, 716–728.

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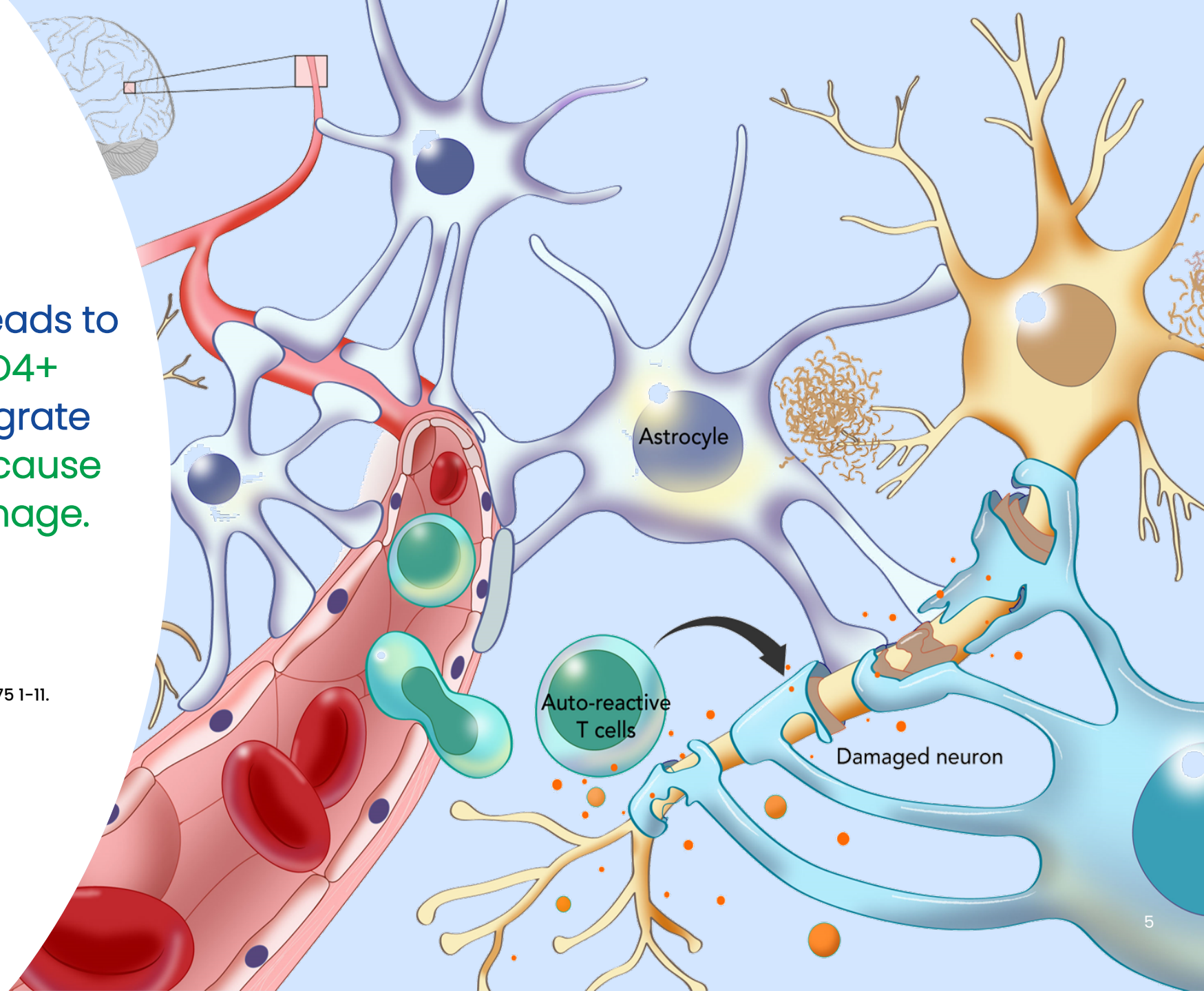
Chronic protein deposition leads to Activation of Autoreactive CD4+ and CD8+ T cells[1–5] which migrate to the brain via CXCR3[6] and cause neuroinflammation and damage.



1. Lindestam Arlehamn - NATURE Communications (2020) 11:1875 1-11.
2. Stojić-Vukanić Z - Front Immunol (2020) 11: 566225.
3. Monsonego - J. Clin. Invest. (2003) 112:415–422.
4. Machhi - Journal of Neuroinflammation (2021) 18:272.
5. Heneka - Lancet Neurol. (2015) 14(4): 388–405.
6. Zhou - Current Neuropharmacology, (2019) 17:142-150

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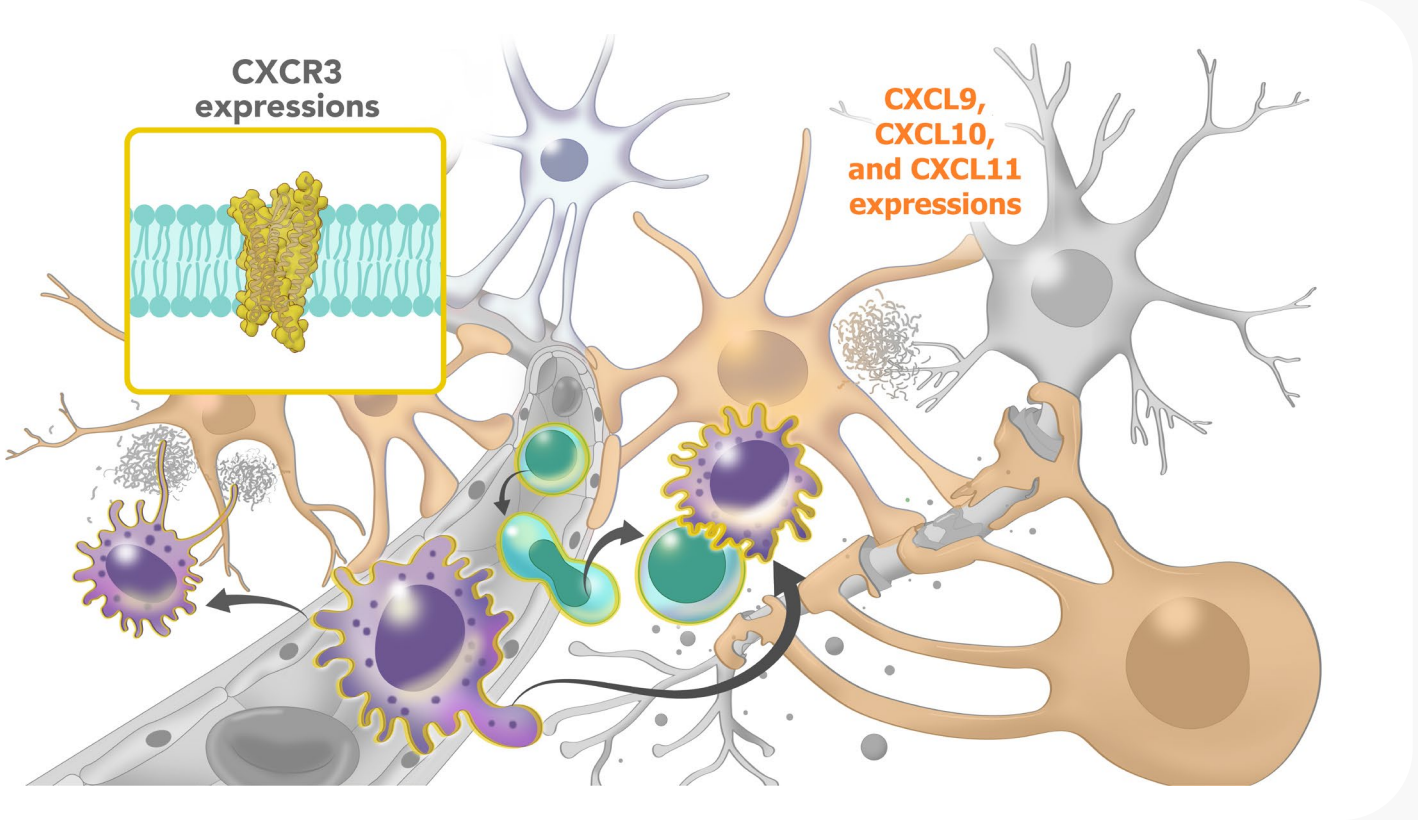
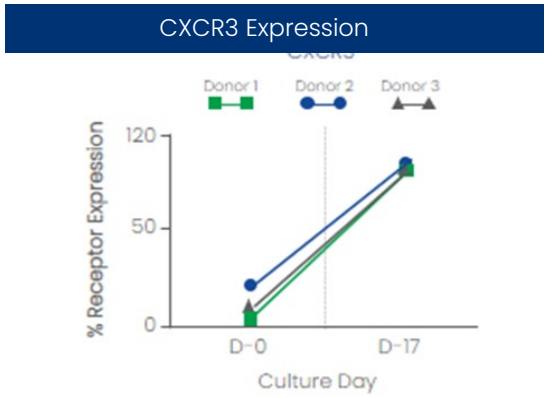
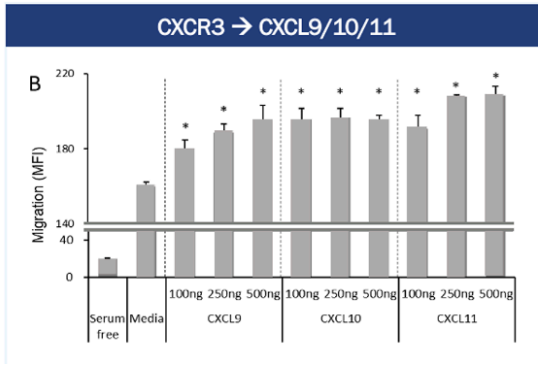
Autoreactive T cells And SNK01 Cross BBB Via CXCR3





MIGRATION POTENTIAL

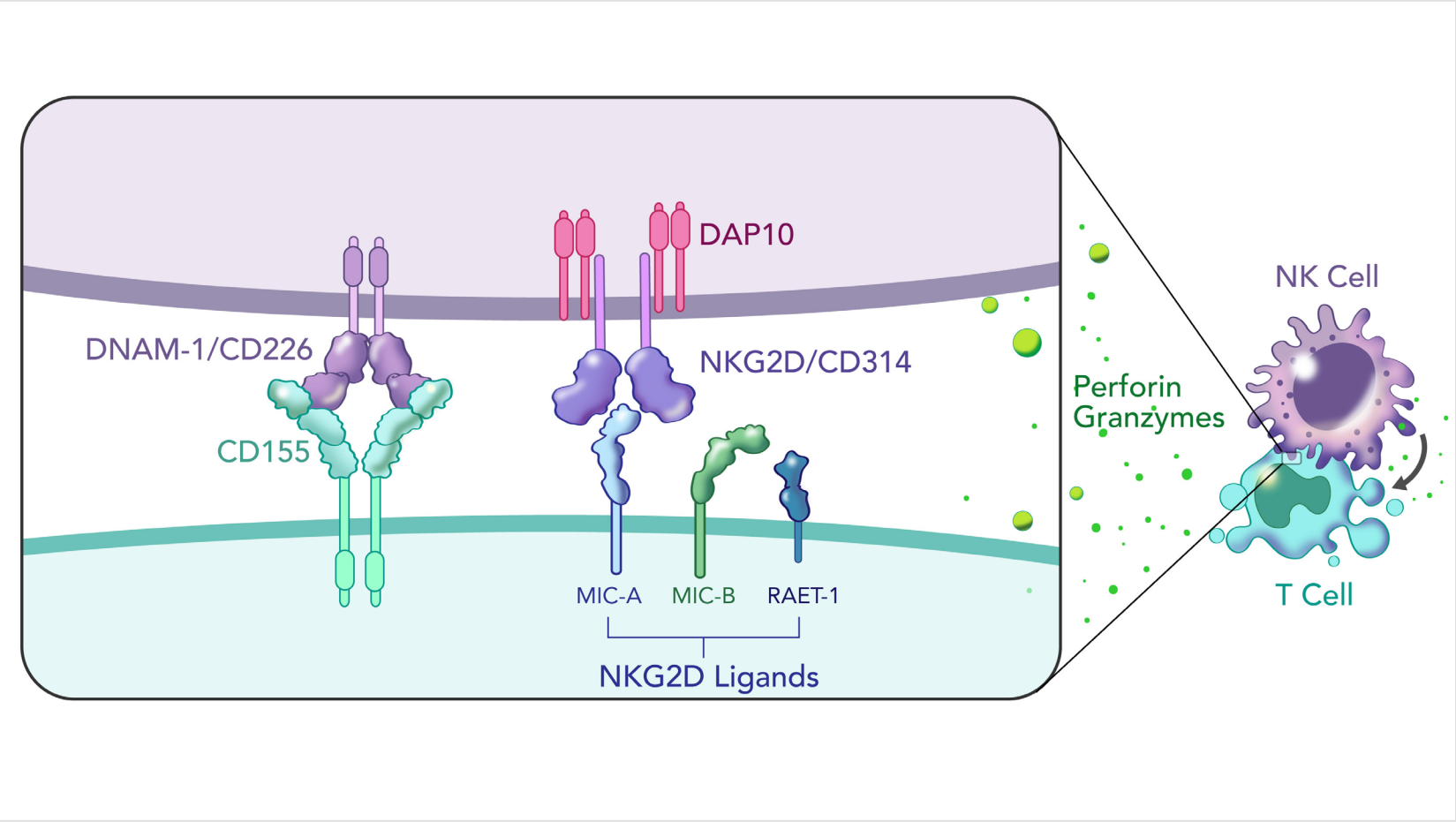


CXCR3+ T cells migrate to CXCL10 positive astrocytes that frequently are associated with amyloid deposits.[1]

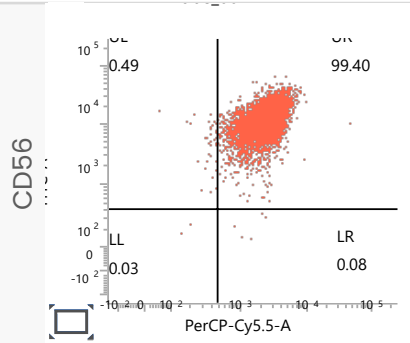
CXCR3 was highly expressed on a subpopulation of neurons and neuronal processes in the neocortex, hippocampus, striatum, cerebellum, and spinal cord.[1]

1. Xia - Neuroimmunol., 2000, 108(1-2), 227-235.

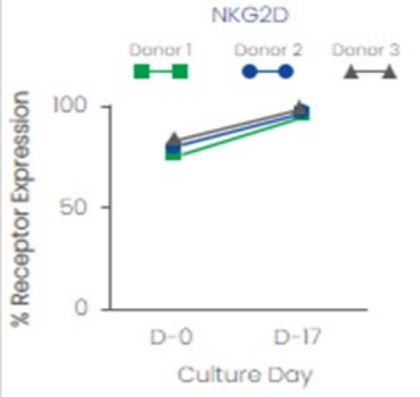
NK Cells Identify and Regulate Autoreactive T cells[1-4] (via NKG2D and DNAM-1)



DNAM-1



NKG2D



1. Rabinovich - J Immunol (2003) 170 (7): 3572–3576.
2. Lu - Immunity. 2007 May ; 26(5): 593–604.
3. Nielsen - PLoS ONE 7(2): e31959.
4. Ardolino - Blood (2011) 117 (18): 4778–4786.

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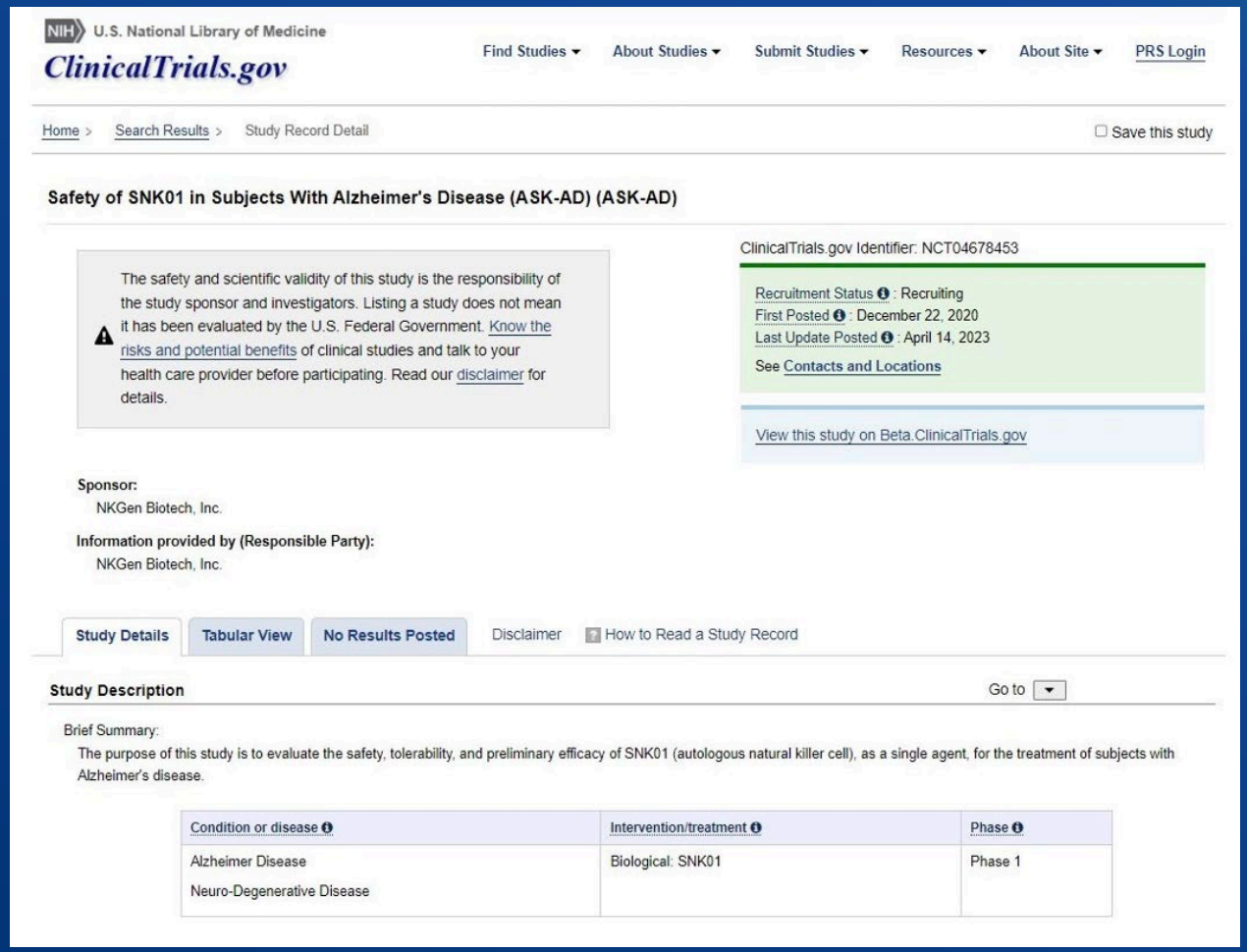
Phase I Study



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Save this study

Safety of SNK01 in Subjects With Alzheimer's Disease (ASK-AD) (ASK-AD)

The safety and scientific validity of this study is the responsibility of the study sponsor and investigators. Listing a study does not mean it has been evaluated by the U.S. Federal Government. Know the risks and potential benefits of clinical studies and talk to your health care provider before participating. Read our disclaimer for details.

ClinicalTrials.gov Identifier: NCT04678453

Recruitment Status : Recruiting
First Posted : December 22, 2020
Last Update Posted : April 14, 2023
See Contacts and Locations

View this study on Beta.ClinicalTrials.gov

Sponsor:
NKGen Biotech, Inc.

Information provided by (Responsible Party):
NKGen Biotech, Inc.

Study Details | Tabular View | No Results Posted | Disclaimer | How to Read a Study Record

Study Description Go to

Brief Summary:
The purpose of this study is to evaluate the safety, tolerability, and preliminary efficacy of SNK01 (autologous natural killer cell), as a single agent, for the treatment of subjects with Alzheimer's disease.

Condition or disease	Intervention/treatment	Phase
Alzheimer Disease Neuro-Degenerative Disease	Biological: SNK01	Phase 1

Proof of concept – safety study

3+3 dose escalation design - 1, 2, & $4x10^9$ cells.

SNK01 given via simple IV Q3W for 4 doses

Mild, moderate and severe AD patients (median MMSE score 14)

Cognitive Assessments and CSF & Plasma biomarkers collected:

Day 0
1 week post-tx
3 months post-tx

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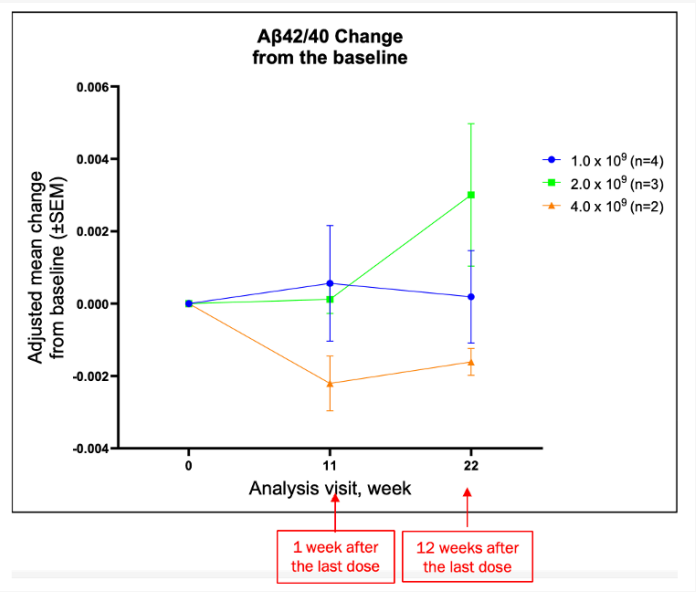
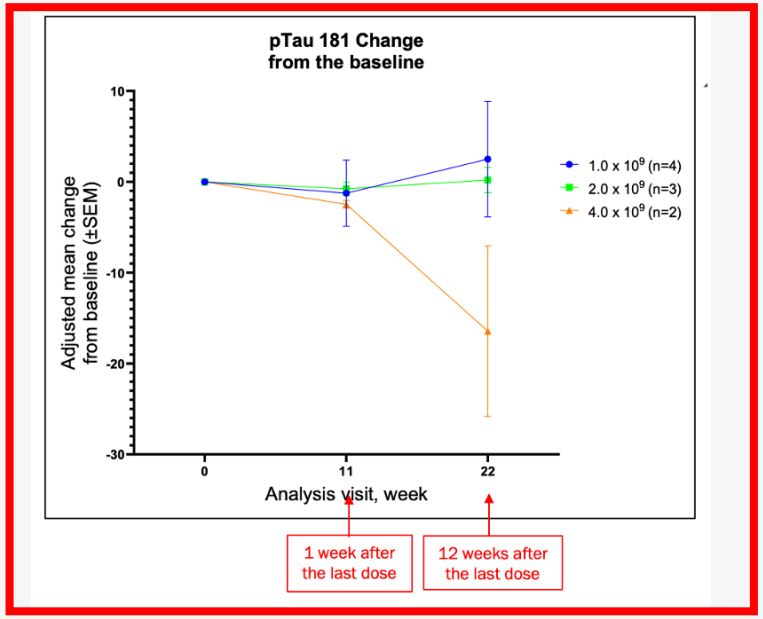
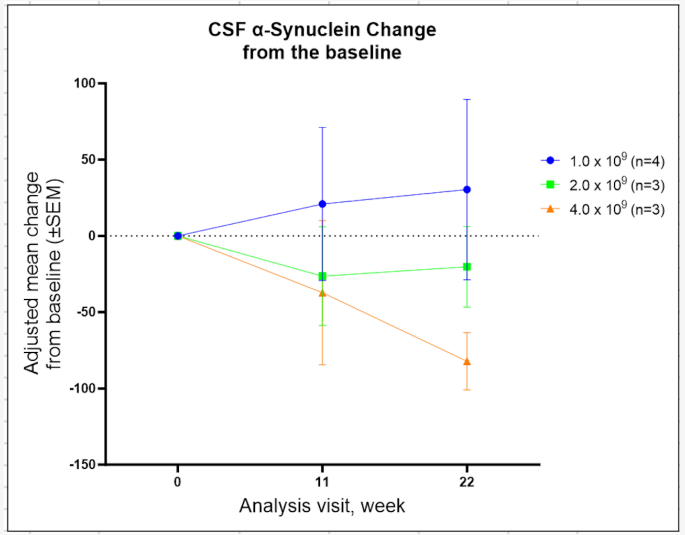
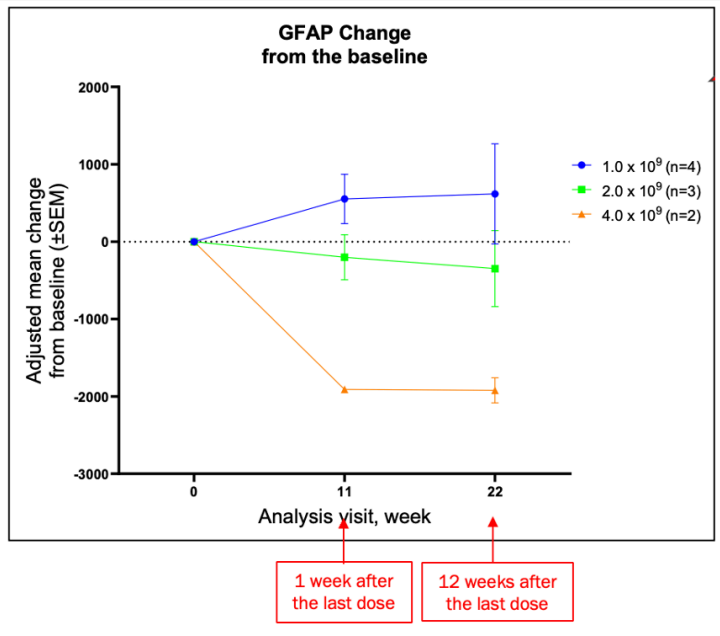
Data From MX04 Phase I Trial









No observed SAEs or dose limiting toxicity

Dose Response Observed for Several Biomarkers in CSF

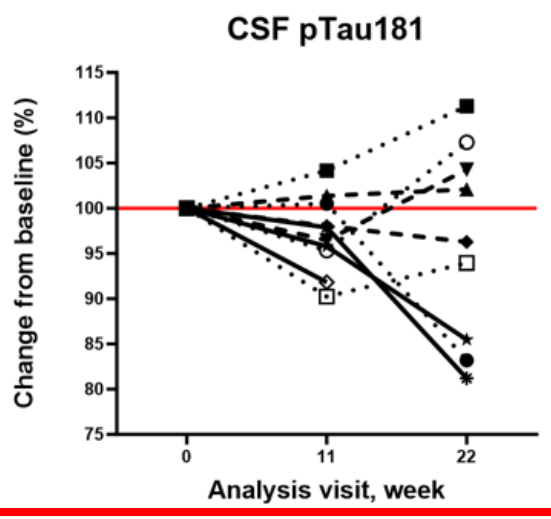
Improvements seen in AB42/40, p-Tau181, and alpha-synuclein protein levels

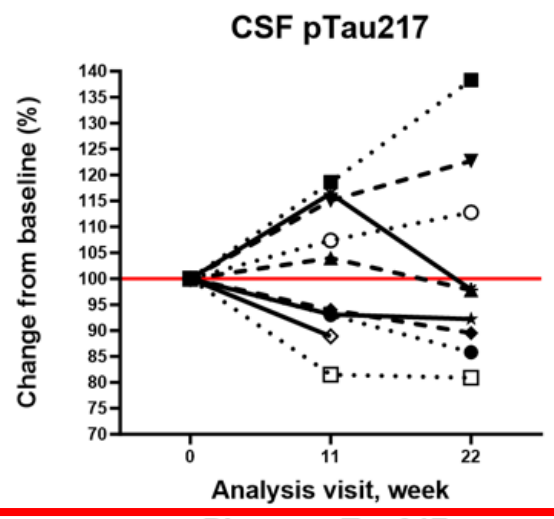
Reductions seen in neuroinflammation GFAP

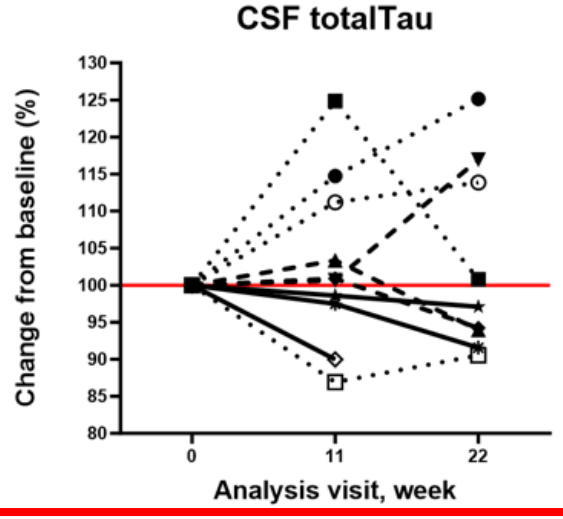
YKL-40, NF-L were reduced or stable in 50-60% of patients but not in a dose dependent manner.

Results

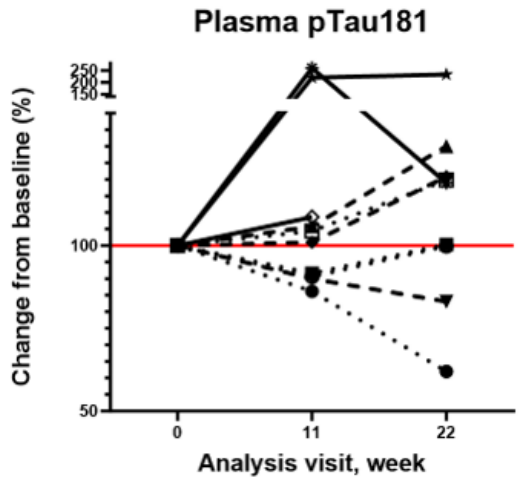
002 (moderate)
003 (moderate)
004 (mild)
005 (mild)
006 (severe)
007 (mild)
011 (mild)
012 (severe)
014 (moderate)
015 (mild)

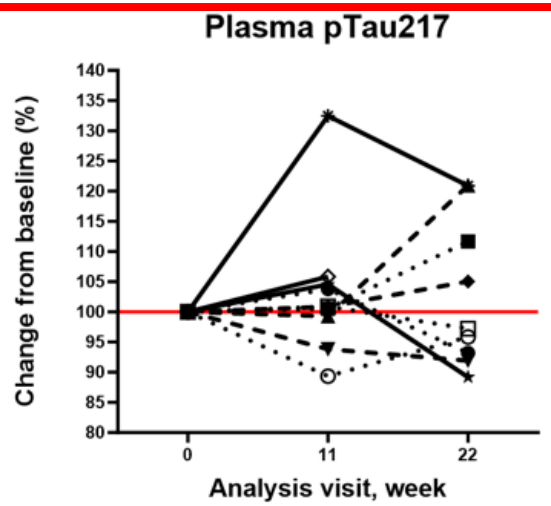


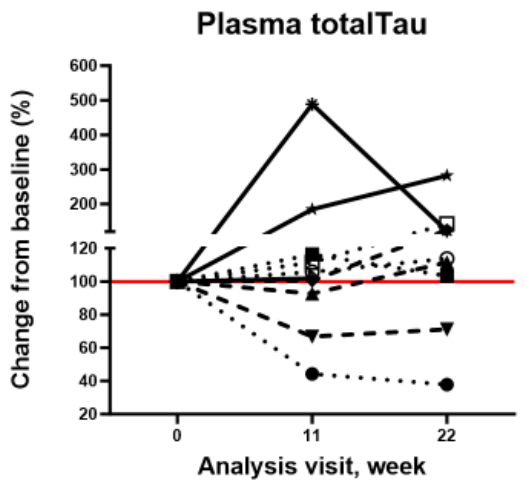




Week	11	22
Tau181	80%	56%
pTau217	50%	67%
Total Tau	40%	56%



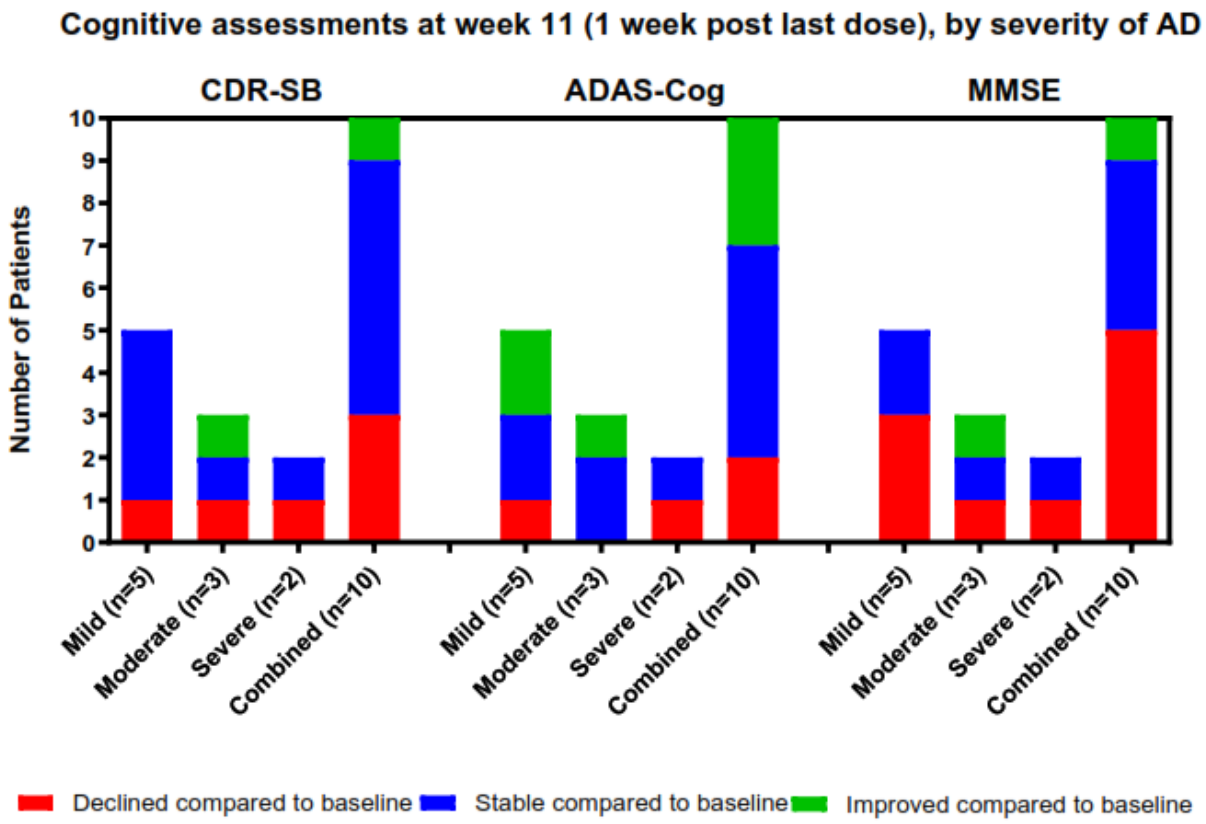


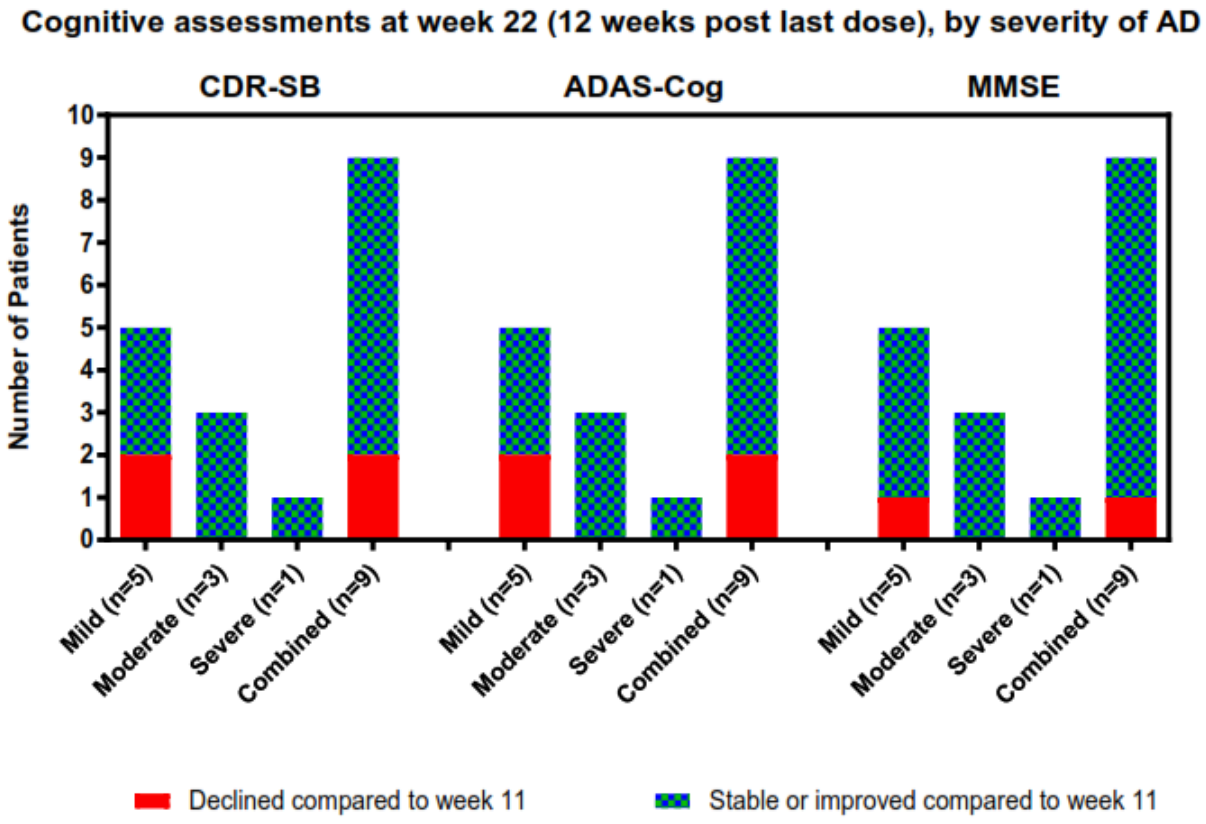


Week	11	22
Tau181	40%	33%
pTau217	30%	56%
Total Tau	30%	22%

Dotted lines are subjects in Cohort 1 ($1x10^9$ cells), dashed lines are subjects in Cohort 2 ($2x10^9$ cells) and solid lines are subjects in Cohort 3 ($4x10^9$ cells).

Results





Majority of patients showed stable or improved CDR-SB, ADAS-Cog, and MMSE at week 11 and week 22

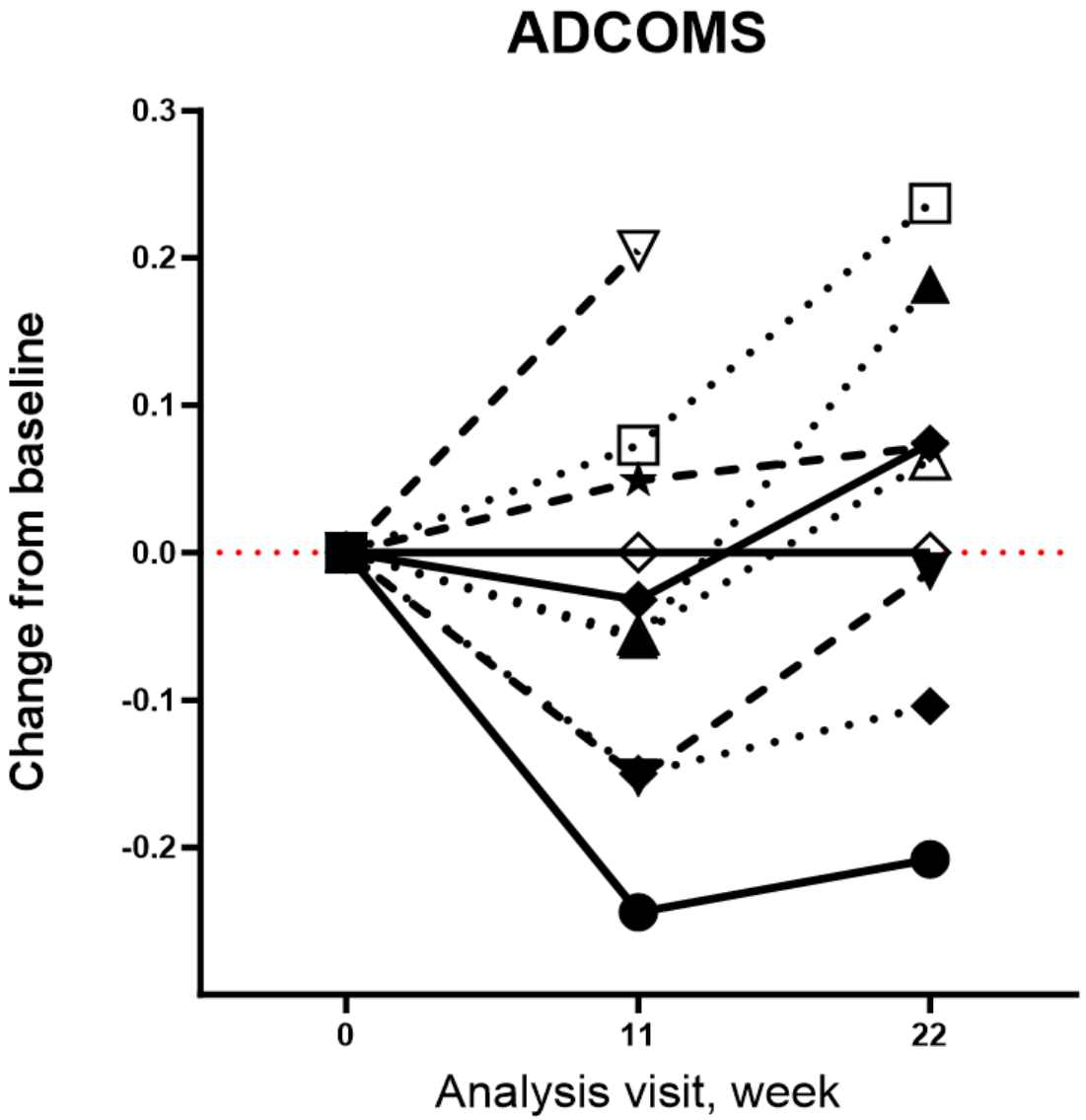
One patient improved from MMSE score of 14 to 22

Results

- 002 (moderate)
- 003 (moderate)
- 004 (mild)
- 005 (mild)
- 006 (severe)
- 007 (mild)
- 011 (mild)
- 012 (severe)
- 014 (moderate)
- 015 (mild)

*MCIDs used to determine stable or improved cognition: CDR-SB -2 (mild, moderate and severe); ADAS-Cog -3 (mild) or -4 (moderate and severe); MMSE +2 (mild) or +3 (moderate and severe); ADCOMS -0.1

Dotted lines are subjects in Cohort 1 ($1x10^9$ cells), Dashed lines are subjects in Cohort 2 ($2x10^9$ cells) Solid lines are subjects in Cohort 3 ($4x10^9$ cells)



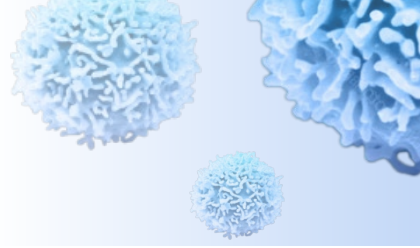
90% had either stable or improved ADCOMS scores, at one-week post-treatment (week 11).

78% had either stable or improved ADCOMS scores, at 6 months (week 22).

Week	11	22
Tau181	80% (78%)*	56% (67%)*
pTau217	50% (56%)*	67% (67%)*
Total Tau	40% (44%)*	56% (67%)*

* stable or improved ADCOMS

Conclusions



- SNK01 was very safe well tolerated.
- SNK01 was able to cross the BBB via a simple IV to reduce proteins and neuroinflammation.
- Results suggest that SNK01 may have clinical activity in AD.
- A randomized Phase II trial is now under way using higher doses (6 x 10^9 cells) and one year treatment duration.

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