



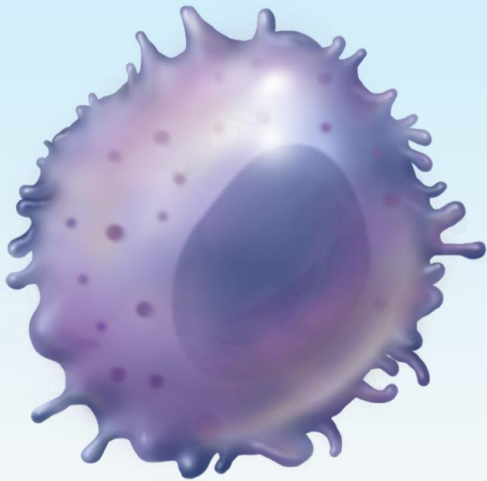
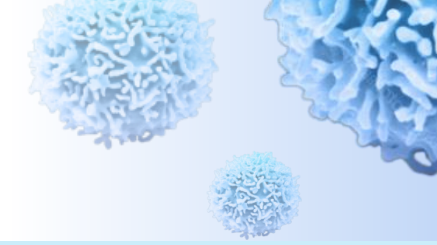
SNK02 : Cryopreserved Allogeneic Enhanced Natural Killer Cells



June 2024

For Investor Use Only

Natural Killer Cells



Innate Lymphoid Cells:

- 5-20% of circulating lymphocytes

Surface Phenotype:

- CD3- CD56+

Can Distinguish Non-Self/Dangerous Cells From Healthy Cells:

- Ability to kill a broad range of “dangerous” cells
- Mediate antibody-dependent cellular cytotoxicity (ADCC)
- Additional regulatory capabilities, mediated by secreted cytokines

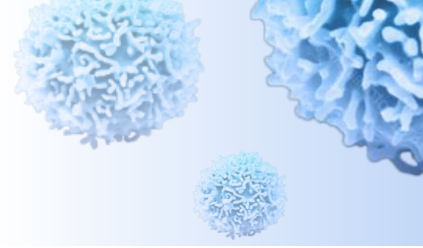
Arundhati Mandal & Chandra Viswanathan

Disease	NK Cell Activity and/or Number
Viral infection	↓ Activity & number
Cancer	↓ Activity
Rheumatoid Arthritis	↓ Activity & number (blood), ↑ number in synovium
Systemic Lupus Erythematosus	↓ Activity & number
Asthma	↓ Number (blood), ↑ number in lungs
Type I Diabetes	↓ Activity and number?

Hematology/Oncology and Stem Cell Therapy – June 2015, Vol. 8, Issue 2, pp: 47-55 (Adapted)

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

NKGen's Differentiated CMC Platform



Autologous, Allogeneic, and CAR-NK products

Expansion capability demonstrates the potential to produce commercially viable quantities of allogeneic NK cells from a single blood collection –over 100K doses

Cryopreservation process that can maintain high viability, cytotoxicity, and activating receptor expression

Allogeneic NK cell product that **does not require lymphodepletion**

State-Of-The-Art GMP Manufacturing Facility

Licensed cell therapy manufacturing facility

- 25,000 sq ft facility (12,000 sq ft for GMP) completed in 2019
- CAP/CLIA Laboratory
- Facility owned and operated by NKGen Biotech

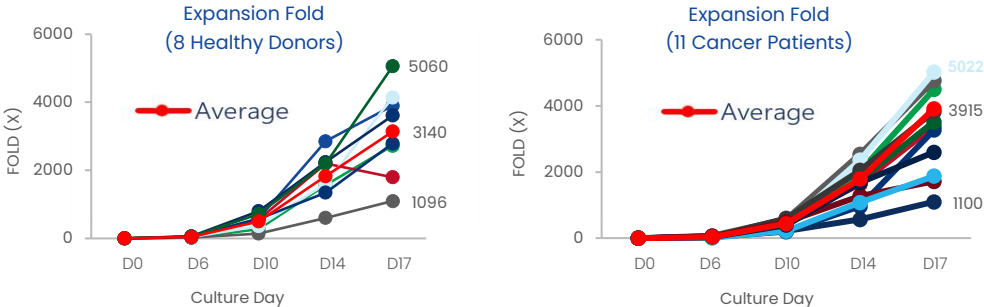


NKGen's Manufacturing (CMC) Process results in Superior Cell Expansion, Increased Cytotoxicity, and Increased Activating Receptor Expression

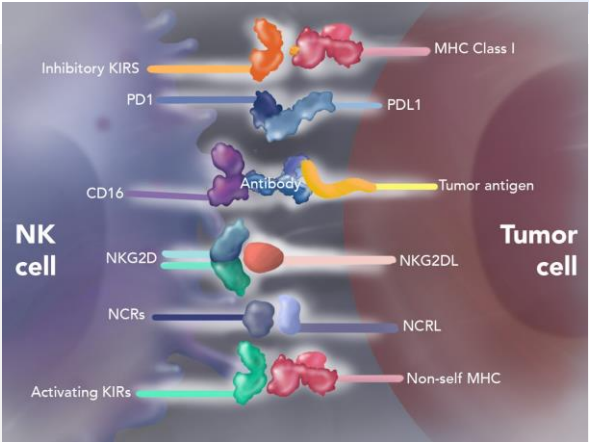


Expansion

NKGen can expand NK cells from any donor!

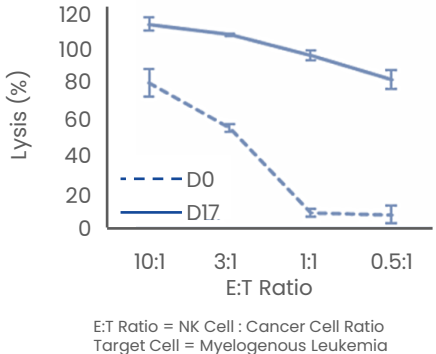


NK cell activating receptors and ligands



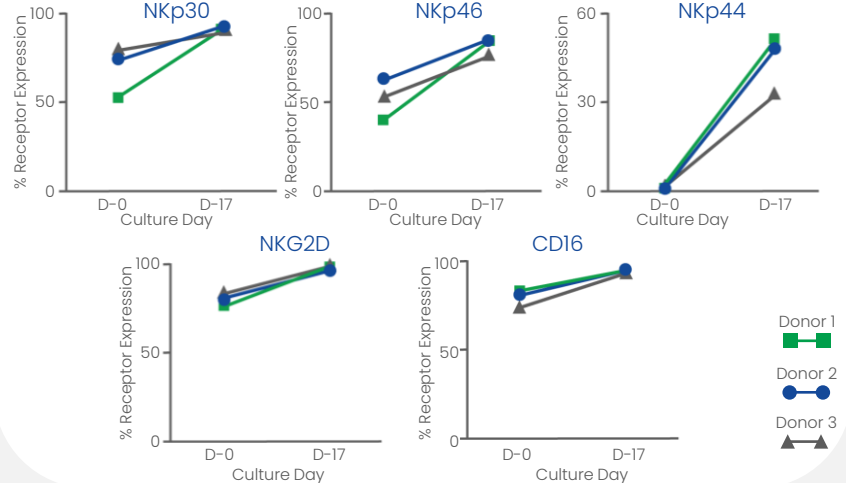
Cytotoxicity

NKGen increases NK cell killing potential!

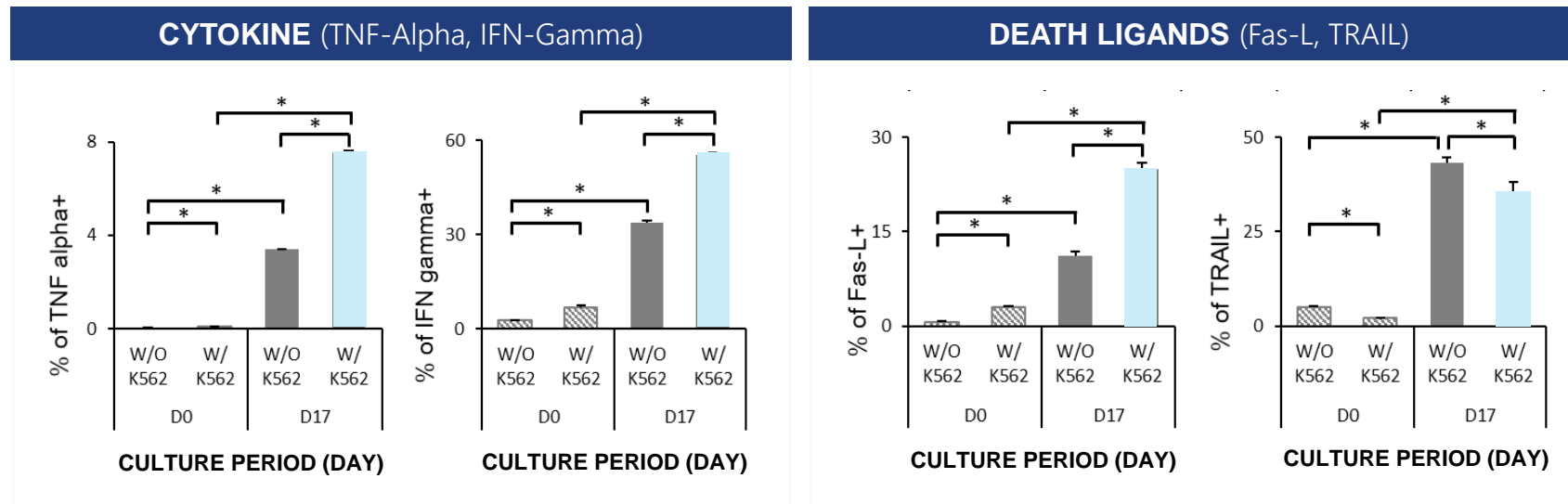


Receptor Expression Levels

NKGen increases receptor expression!



Increased Cytokine and Death Receptor Expression



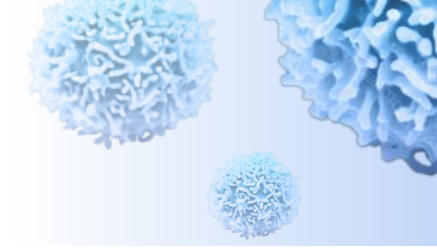
INCREASED EXPRESSION OF CYTOKINES AND DEATH RECEPTORS THAT ARE RELATED TO TUMOR CELL KILLING



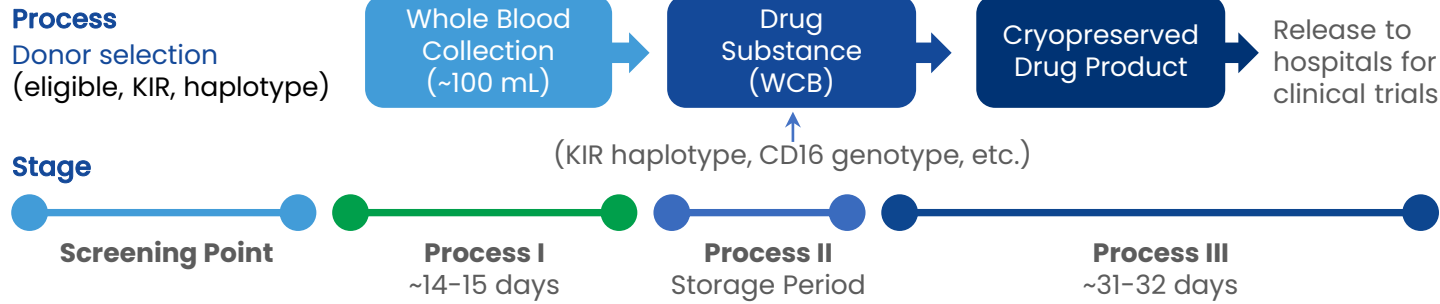
ADDITIONAL ABILITY TO KILL CANCER CELLS

Test		Method	Specification
Appearance		Macrographic Observation	Injection of white suspension fluid filled inside a transparent bag
Identity	Specific Surface Antigen	Flow Cytometry	≥ 80% positive for CD56+/CD3-
Purity	Negative Surface Antigen	Flow Cytometry	< 5% positive for each CD3, CD14 and CD20
Endotoxin		USP <85> Bacterial Endotoxins Test	≤ 0.5 EU/mL
Cell Viability		Trypan Blue Staining Method (EP <2.7.29>)	≥ 70%
Total Cell Number		Trypan Blue Staining Method (EP <2.7.29>)	0.8 - 1.2 x 10 ⁹ cells/50 mL, 1.8 - 2.2 x 10 ⁹ cells/100 mL or 3.6 - 4.4 x 10 ⁹ cells/200 mL
Mycoplasma		MycoAlert / qPCR method	No mycoplasma contamination
		Agar and Broth Media Culture Method	No mycoplasma contamination
Sterility		USP <71> Sterility Tests	No microorganism contamination
		USP <71> Sterility Tests	No microorganism contamination
		Gram Staining	No microorganism contamination
Potency	Cytotoxicity Assay (against K562 cells)	Calcein AM	Cytotoxicity against K562: ≥ 50% (E:T ratio of 10:1)

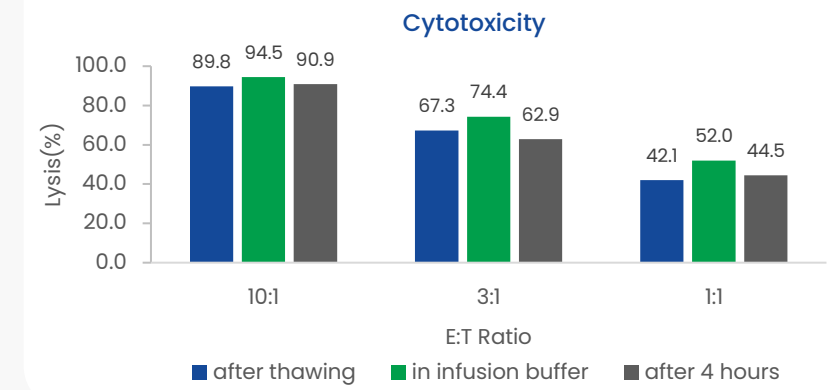
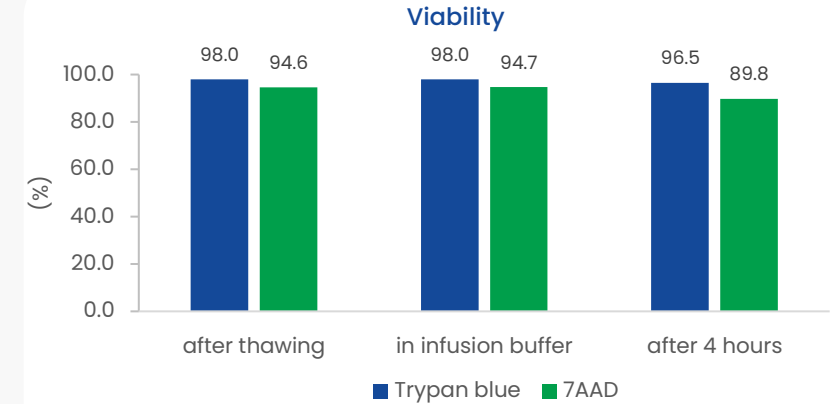
NKGen Can Produce Over 100,000 Doses And Maintain High Viability And Cytotoxicity



Not All Companies Can Produce Large Numbers of Doses And Preserve Viability and Cytotoxicity With Their Cryopreservation

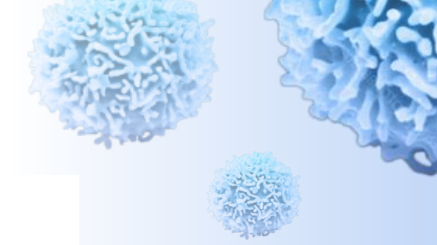


Starting Material	Drug Substance Process I & II (1-1.5 x 10 ⁷ cells/vial)	Drug Product (3x10 ⁹ cells/dose)		Note (Actual Production Scale)
		Process III / Batch	Total Doses (Drug Substance X Process III)	
Whole Blood (~100 mL)	~400 vials	270 - 340	108,000 - 136,000	Estimated Dose
		35 - 70	14,000 - 28,000	Stage I (Preclinical - Phase I)
		135 - 200	54,000 - 80,000	Stage II (Phase II)
		> 270	108,000	Stage III (Phase III - NDA)

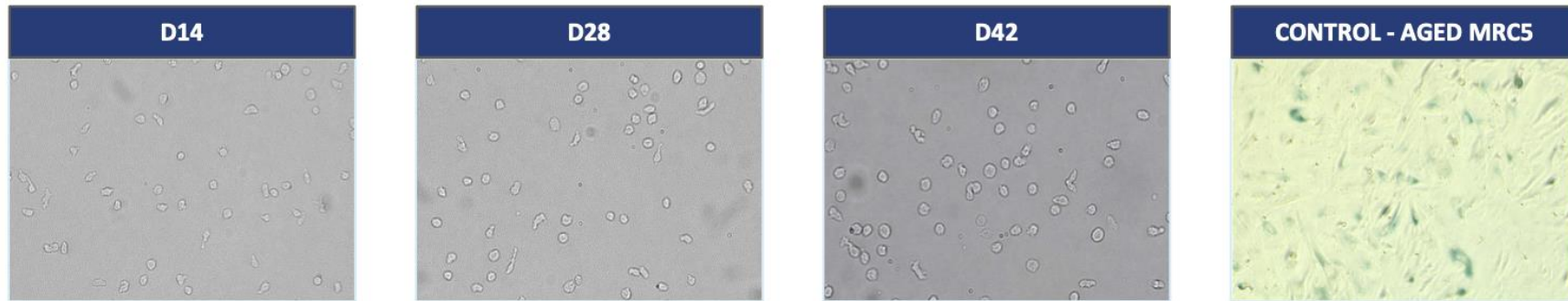


1. After thawing of cryopreserved SNK.
2. After dilution of thawed SNK with infusion buffer
3. After 4 hours storing of diluted SNK

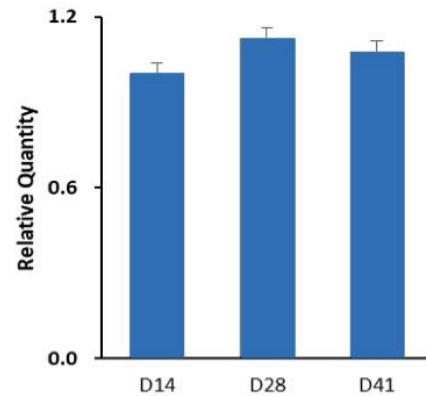
Allogenic Senescence



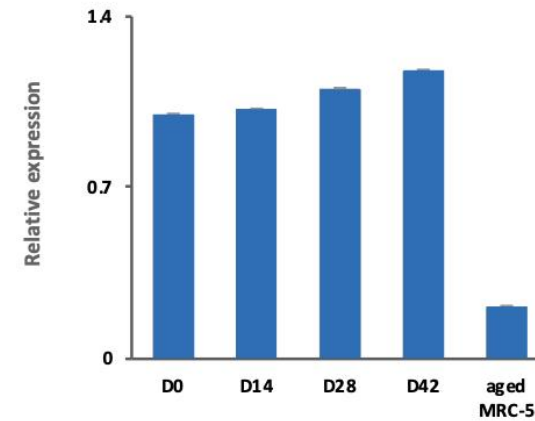
1. SENESENCE-ASSOCIATED B-GALACTOSIDASE (SA-B-GAL) STAINING



2. P16 (CYCLIN-DEPENDENT KINASE INHIBITOR 2A)

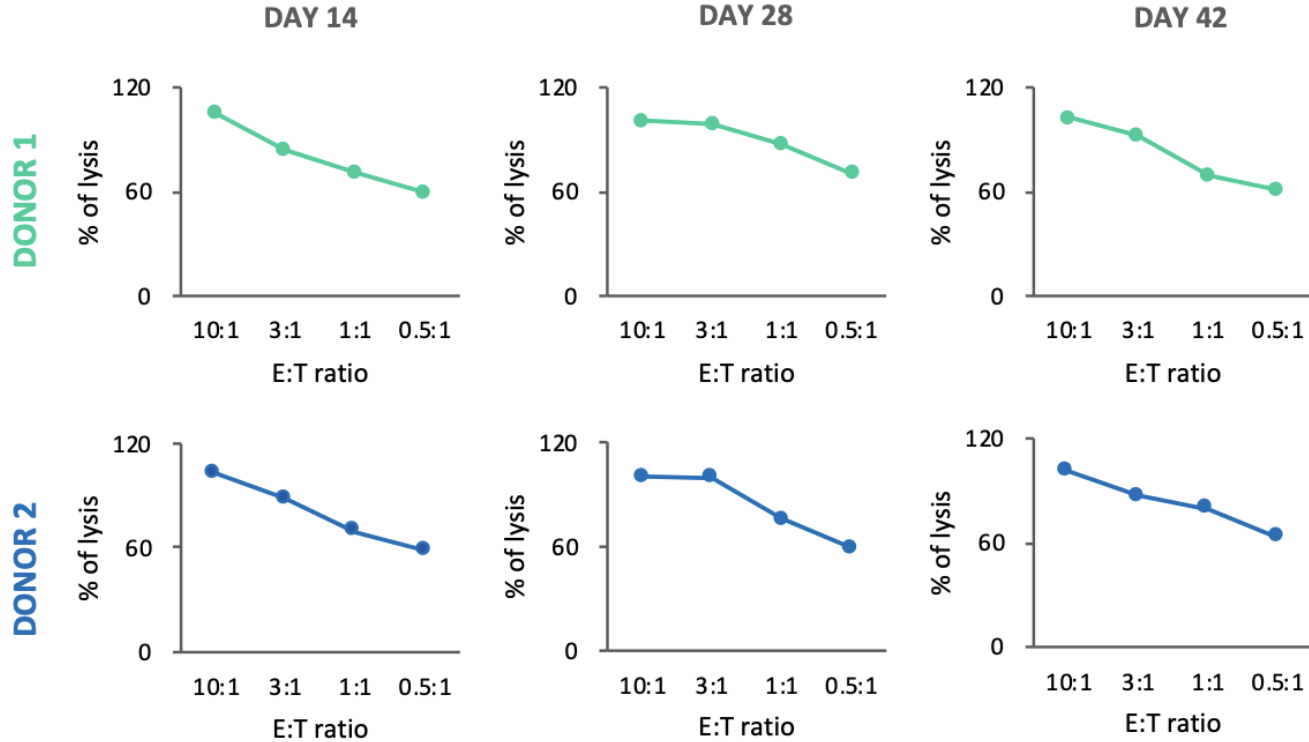
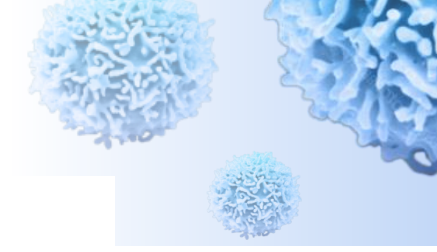


3. TELOMERASE ACTIVITY



LONG-TERM CULTURE OF NK CELLS DOES NOT INDUCE NK CELLS' SENESENCE

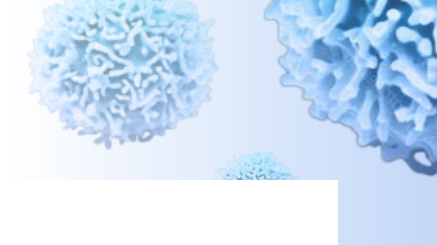
Allogeneic Cytotoxicity



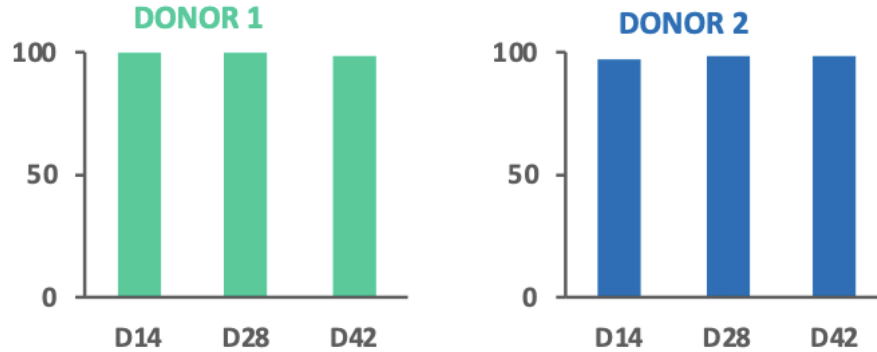
	DAY	10:1	3:1	1:1	0.5:1
DONOR 1	D14	105.1	84.3	70.8	59.5
	D28	101.0	98.7	87.4	70.3
	D42	102.9	92.6	69.9	61.0
DONOR 2	D14	102.9	88.6	69.5	58.5
	D28	100.3	99.3	75.7	59.2
	D42	101.1	86.7	79.3	62.9

**LONG-TERM CULTURE OF NK CELLS (DAY 28, 42)
DOES NOT CHANGE NK CELLS' CYTOTOXICITY AGAINST CANCER CELLS**

Allogenic Receptor Expression



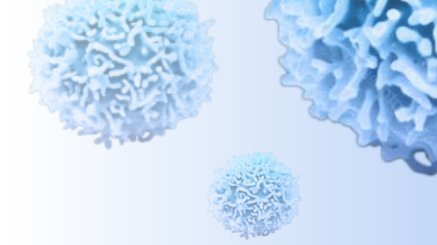
PURITY (CD56+/CD3- NK CELLS)



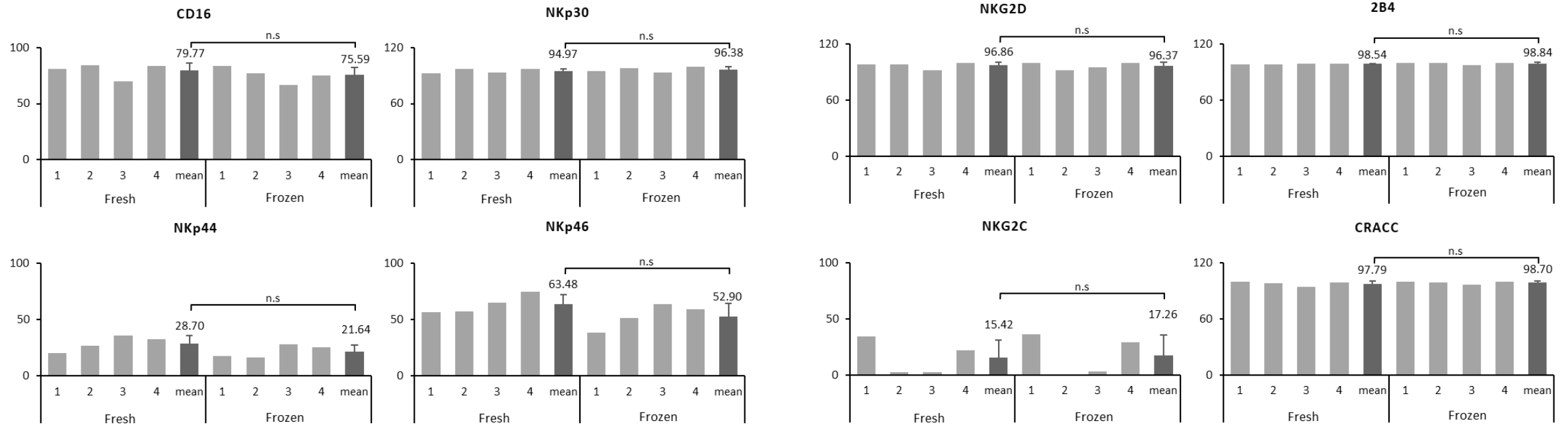
(%)	DONOR 1	DONOR 2
D14	99.35	97.21
D28	99.48	98.51
D42	98.02	98.71

SURFACE MARKER EXPRESSION

(%)	DAY	NKp44	NKp30	NKp46	CD16	NKG2D	CXCR3	CD62L	PD-1
DONOR 1	D14	17.98	81.04	85.79	95.37	99.44	99.42	56.19	0.25
	D28	19.56	80.51	75.03	94.78	99.21	99.21	44.75	0.19
	D42	20.63	81.23	78.24	94.16	95.82	97.14	48.33	0.10
DONOR 2	D14	19.49	95.08	86.20	87.12	95.19	94.19	27.73	0.15
	D28	21.47	97.36	91.27	91.83	94.21	97.55	30.63	0.32
	D42	24.46	97.79	95.39	95.27	98.20	98.00	36.67	0.29

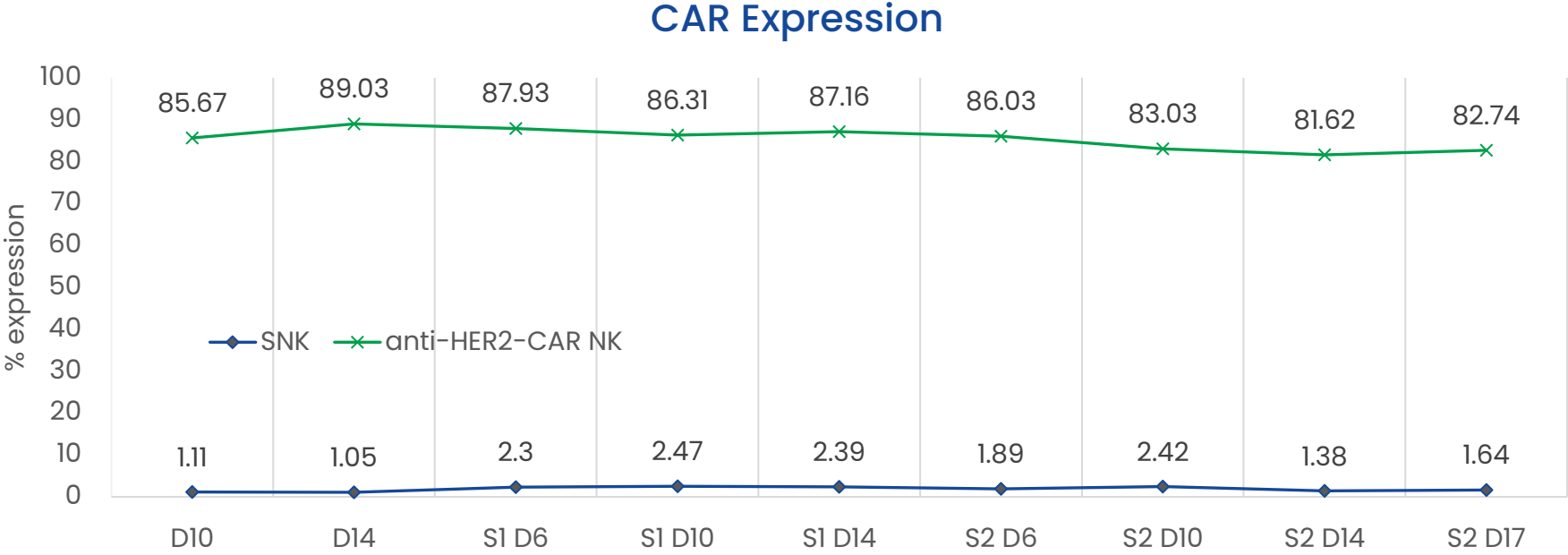
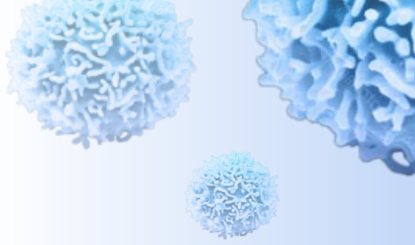


- **Surface maker expression levels of SNK02**



Surface expression levels (%) of activating receptors on each pre-cryopreserved (Fresh) and post-cryopreserved (Frozen) CD56⁺ NK cells in SNK01 derived from each donor were analyzed flow cytometrically and depicted with bright gray-colored bars on left side of each graph. Average values (mean ± SD) from 4 different donor-derived SNK01s were presented as a dark gray-colored bar on right side of each graph.

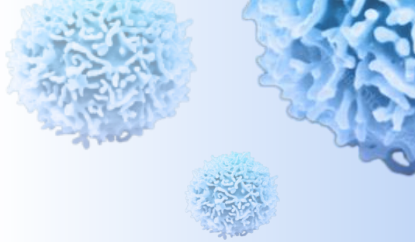
Expression Level Of Anti-HER2-CAR on NK Cell



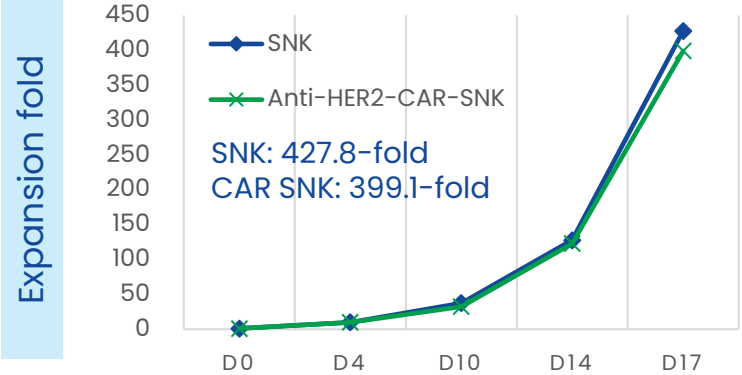
Promoter



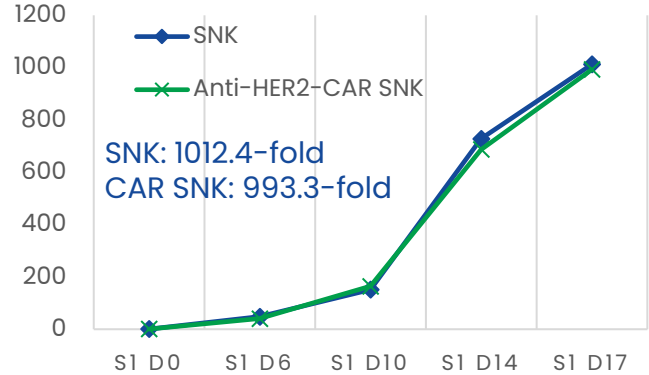
NK Cell Expansion Rate



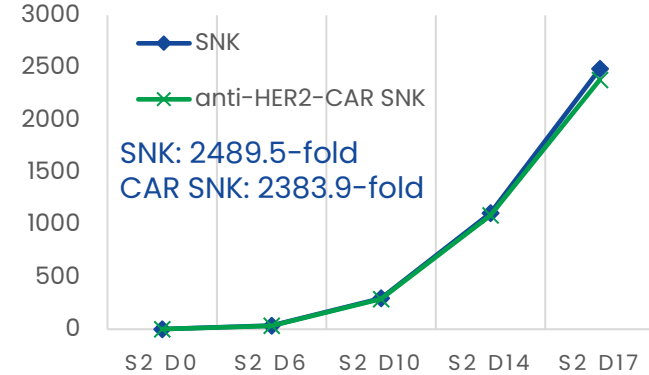
Expansion Rate (P1)



Expansion Rate (S1)

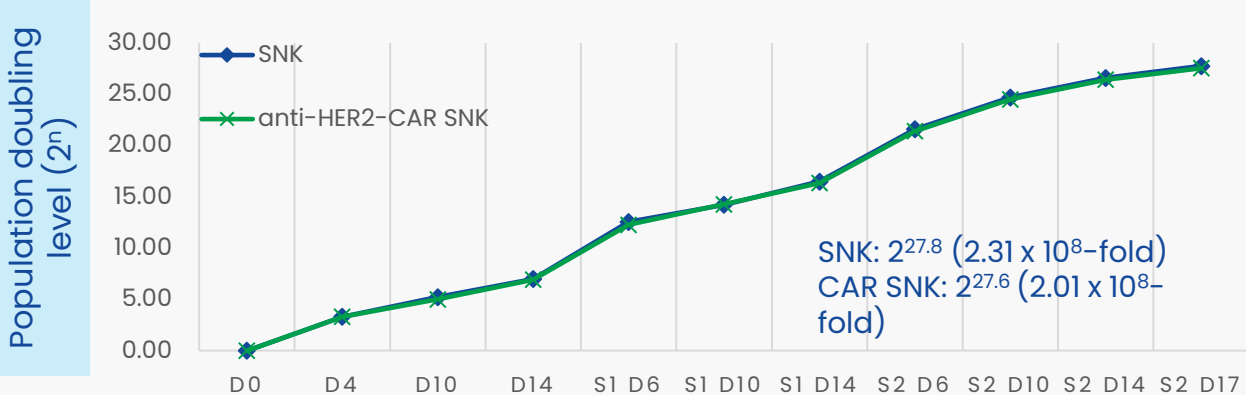


Expansion Rate (S2)



SNK: non-transduced NK cells

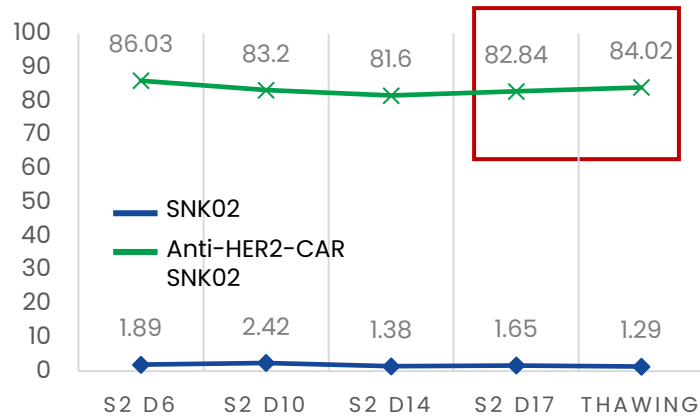
PDL



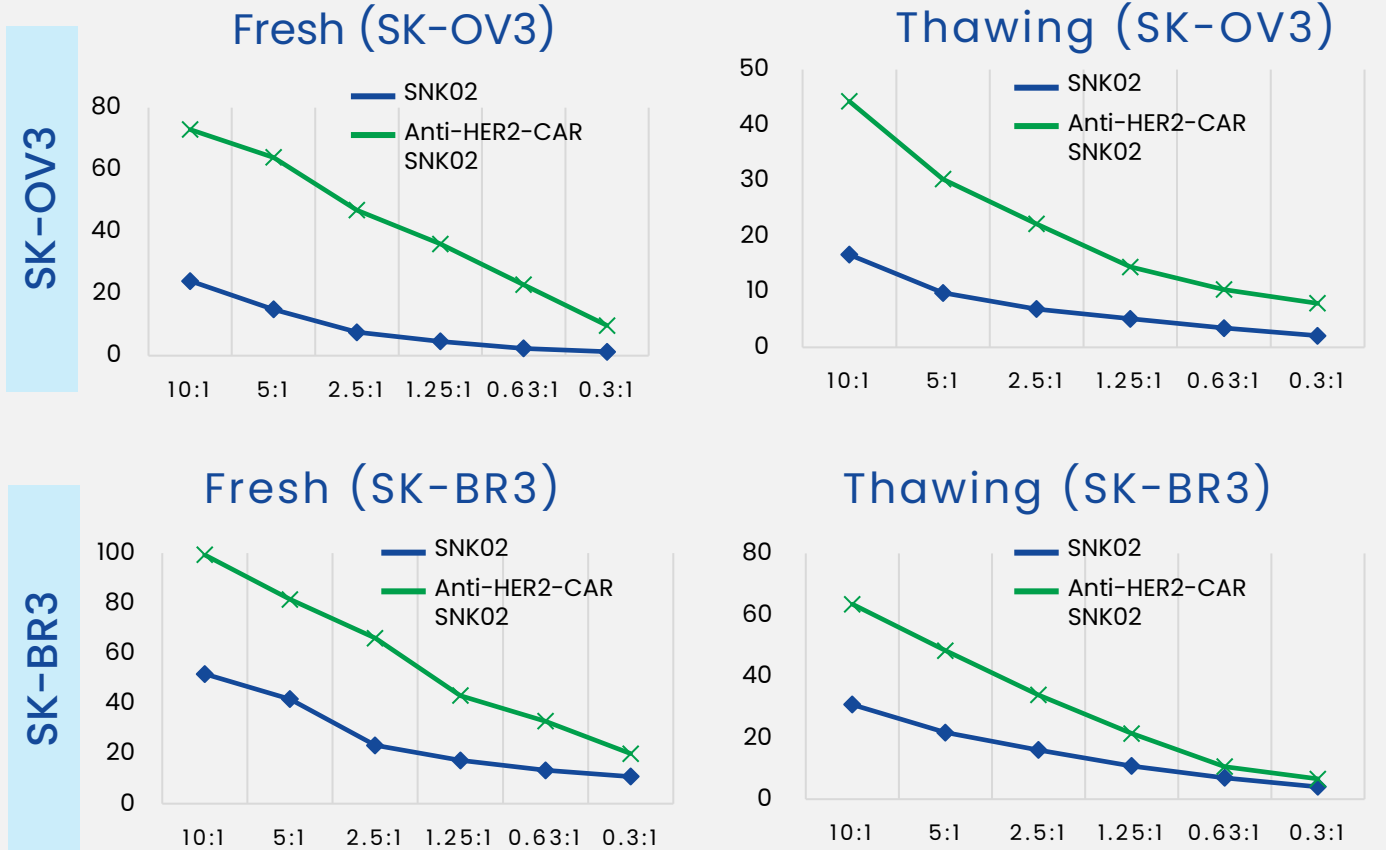
The Effect Of Freezing/Thawing On CAR Expression & Cytotoxicity

CAR Expression

Persistence

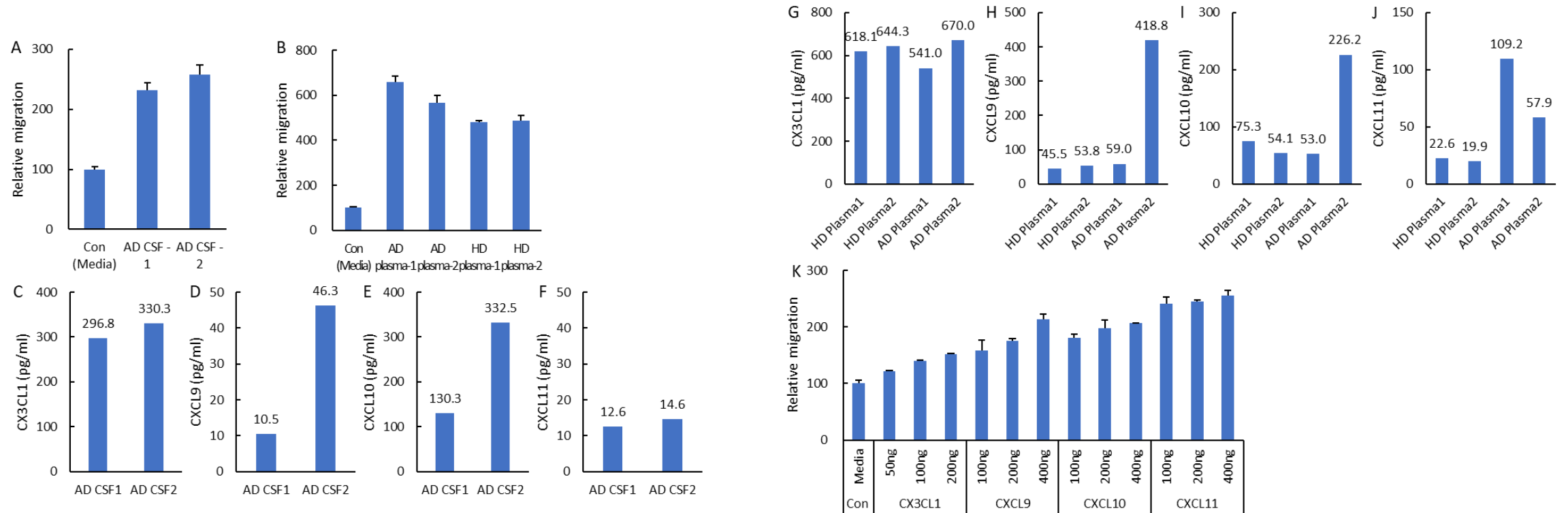


Cytotoxicity (2 hours)



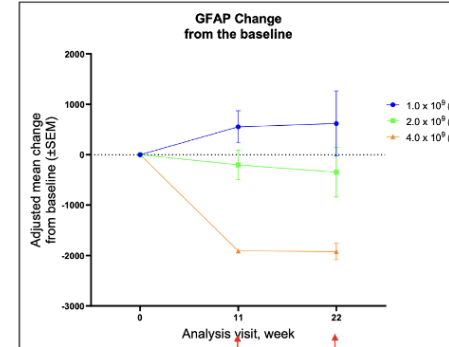
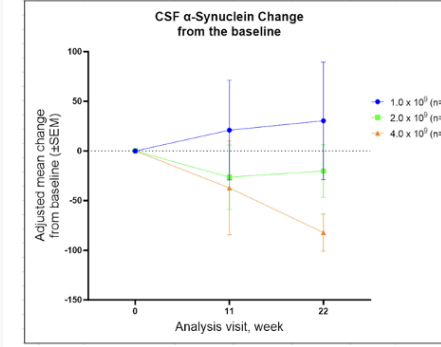
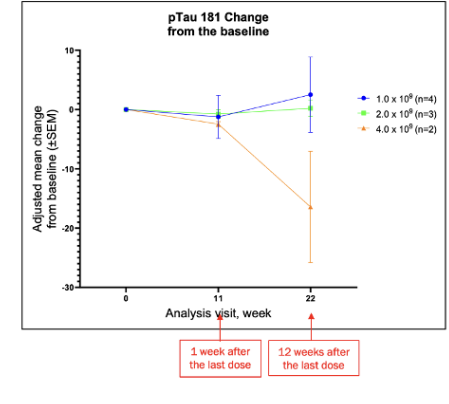
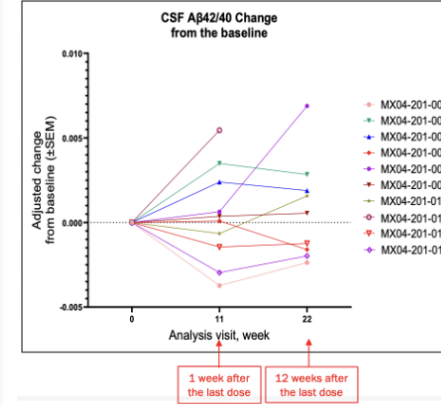
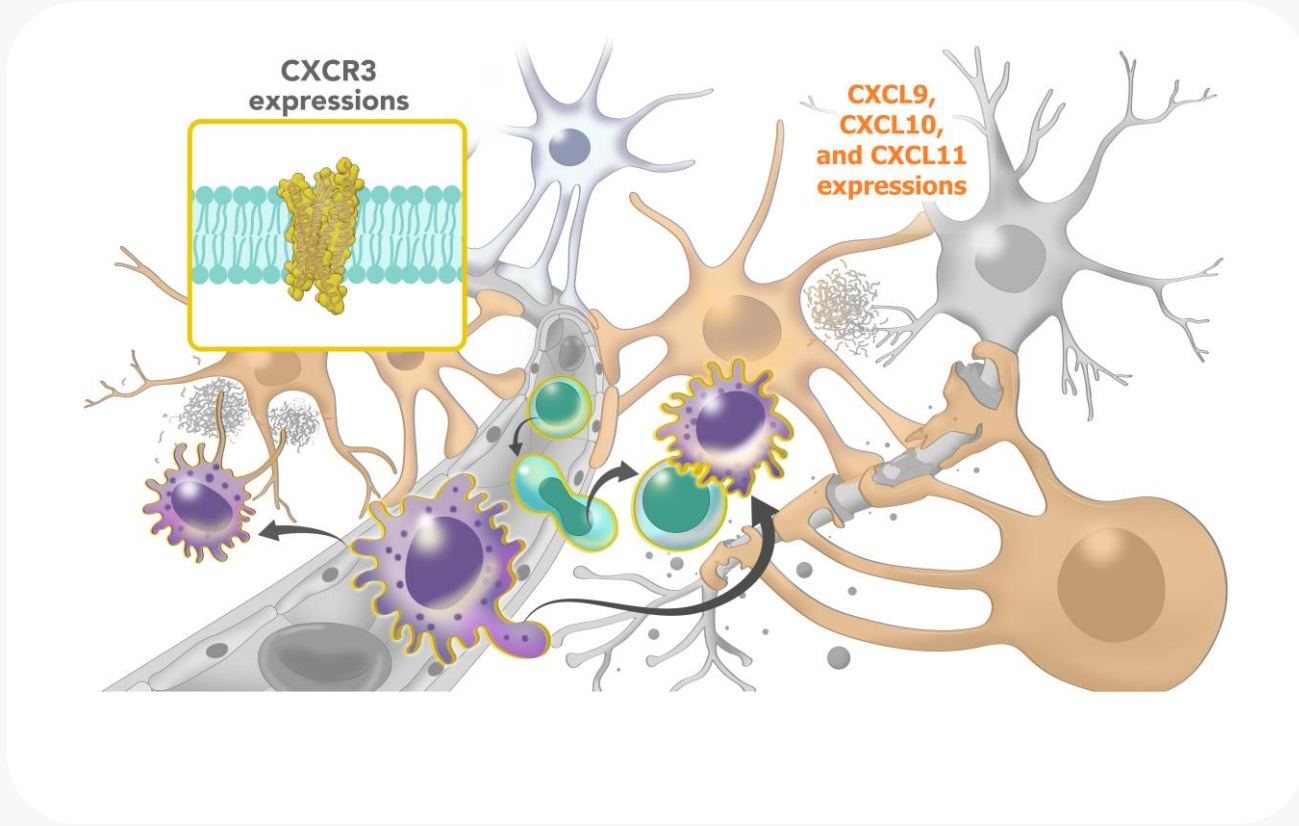
SNK01 Has High CXCR3 Expression And Strong Migration Potential to cross the BBB

- **Migratory Potential of SNK01 toward cerebrospinal fluid (CSF) and plasma from Alzheimer disease (AD) patients.**



(A) The migration of SNK01 cells toward control medium (Con) and medium containing CSF from AD patients (AD CSF-1 and AD CSF-2) was measured by trans-well migration assay. Relative migration to average value of control (Media) sample was presented in percentage on graphs. (B) The migration of SNK01 cells toward control medium (Media) and medium containing plasma from AD patients (AD plasma-1 and AD plasma-2) and healthy donors (HD plasma-1 and HD-plasma 2) was measured by trans-well migration assay. Relative migration to average value of control (Media) sample was presented in percentage on graphs. (C-F) Concentration of chemokine ligands, CX3CL1 (Fractalkine) and CXCL9, CXCL10, CXCL11, for CX3CR1 and CXCR3 receptors was measured in CSF from AD patients (AD CSF-1 and AD CSF-2). (G-J) Concentration of chemokine ligands for the CX3CR1 and CXCR3 was measured in plasma from AD patients (AD plasma-1 and AD plasma-2) and healthy donors (HD plasma-1 and HD-plasma 2). (K) Migratory potential of SNK01 toward the chemokine ligand. The migration of SNK01 cells toward control medium (Con) and the indicated concentrations of CX3CR and CXCR3 ligands was measured by trans-well migration assay. Relative migration to average value of control (Media) sample was presented in percentage on graphs.

Autoreactive T cells And SNK01 Cross BBB (Blood Brain Barrier) Via CXCR3



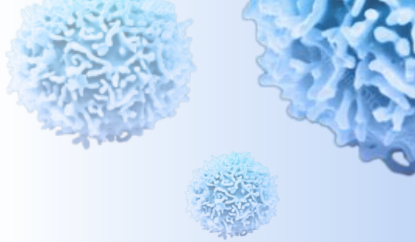
CXCR3+ T cells migrate to CXCL10 positive astrocytes that frequently are associated with amyloid deposits.¹

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

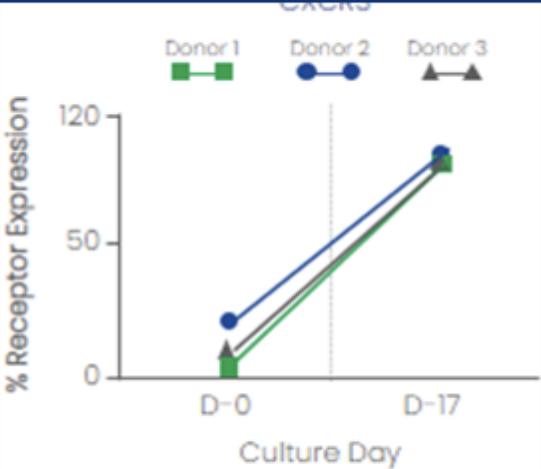


1. Xia - Neuroimmunol, 2000, 108(1-2), 227-235.

SNK02 Has High CXCR3 Expression And Strong Migration Potential to cross the BBB

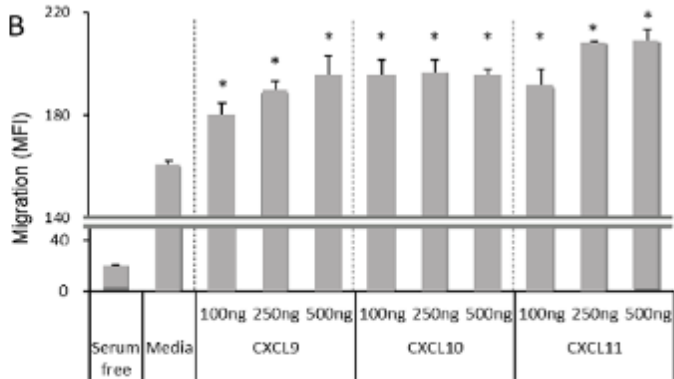


CXCR3 Expression



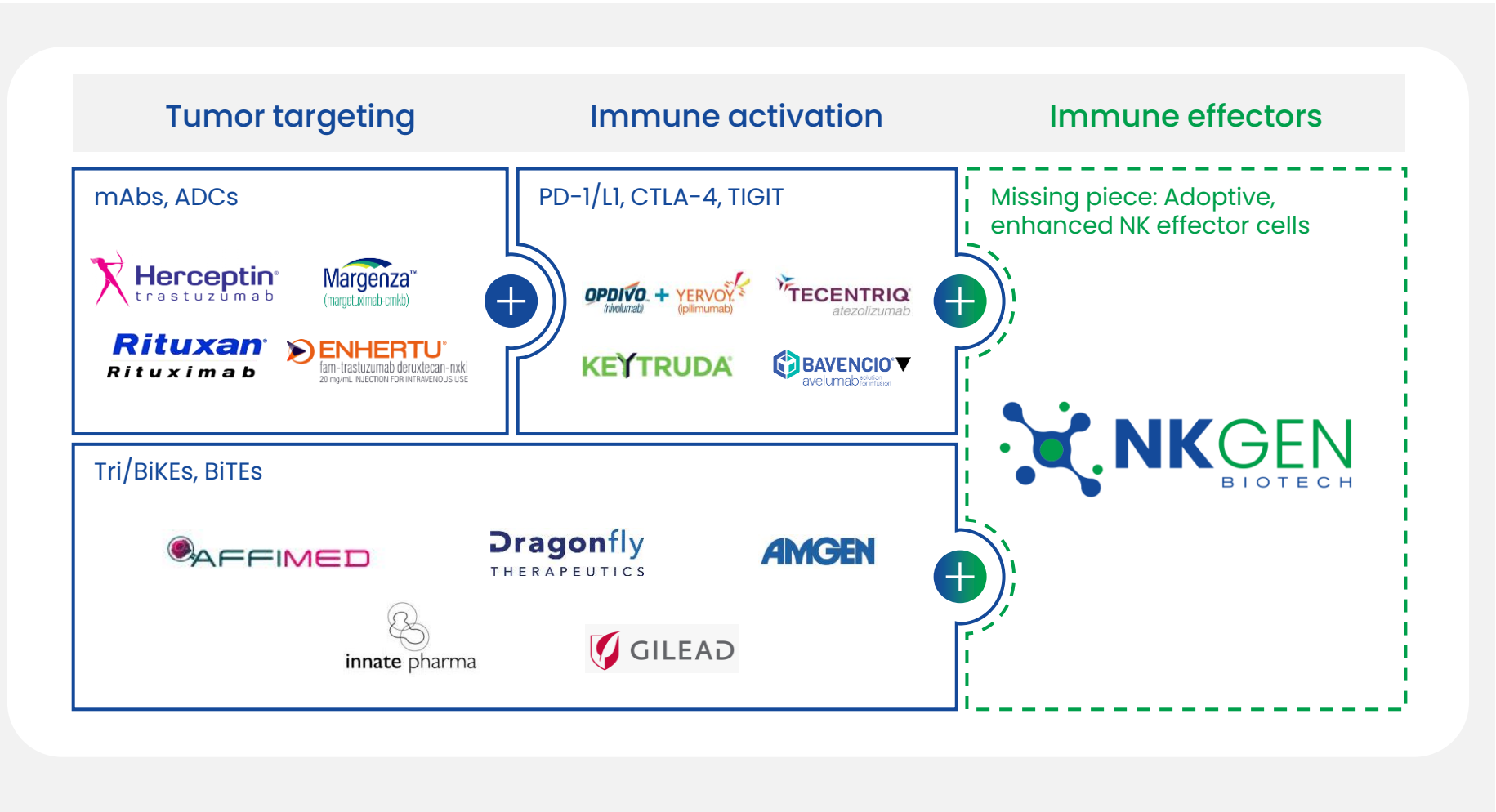
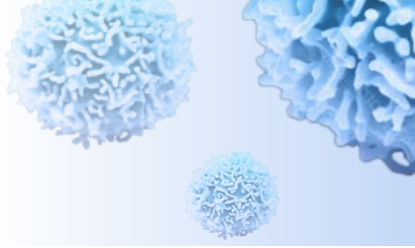
MIGRATION POTENTIAL

CXCR3 → CXCL9/10/11



Oncology Program

NK Cells: The Missing Piece In Cancer Therapeutics?

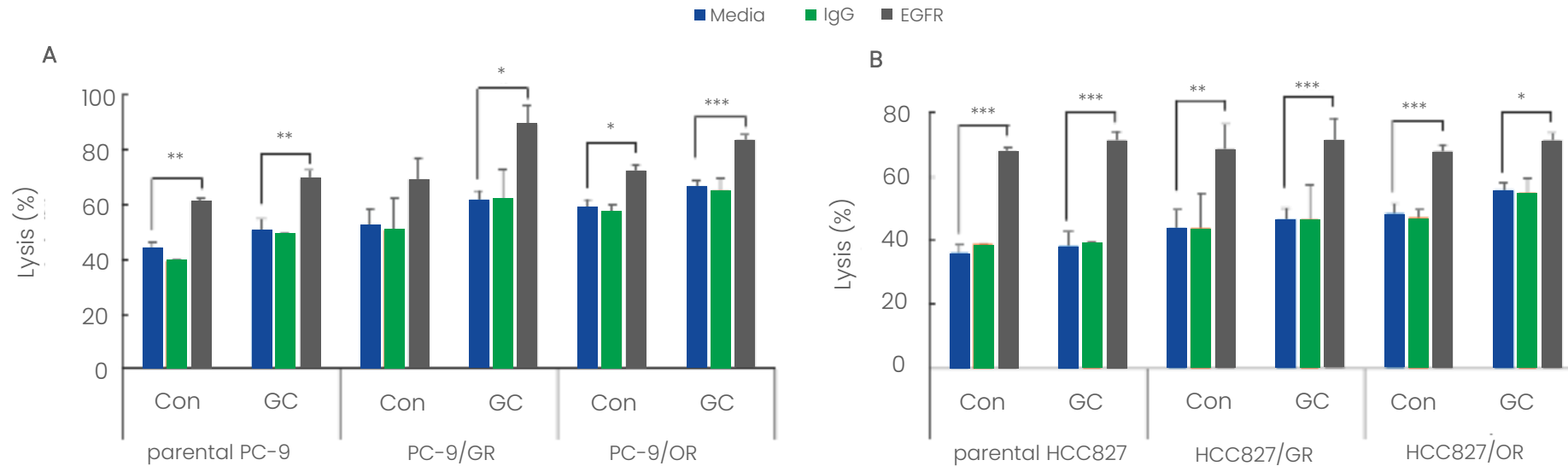
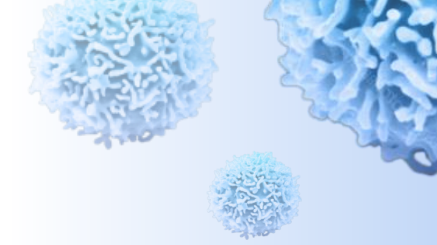


We believe that the future of cancer therapies will be in **combination therapies** that enable precision targeting, immune activation and immune effector response simultaneously.

SNK cells may provide the “missing” piece for modular treatment approach – regimens that can be easily adapted to include new agents as data become available.

Effect Of NK Cells On Cetuximab-mediated ADCC

Preliminary Phase I data Presented at ASCO 2023



Cetuximab-mediated ADCC activity of NK cells in EGFR-TKI-resistant NSCLC cells. Parental PC-9, PC-9/GR, and PC-9/OR cells (A) as well as parental HCC827, HCC827/GR and HCC827/OR NSCLC cells (B) were treated with (GC) or without (Con) gemcitabine plus carboplatin for 24 hours and then co-cultured with NK cells for 2 hours at the E:T ratio of 3:1 in the presence of media alone (Media), isotype control IgG antibody (IgG) or cetuximab (EGFR). The cytotoxic activity of NK cells against NSCLC cells was shown as mean \pm SD. One-way ANOVA with Tukey's post hoc analysis was applied for statistical analysis. * $p < 0.05$, ** $p < 0.01$, and *** $p < 0.005$, relative to untreated cells (Media).



NKMax and Merck KGaA, Darmstadt, Germany Expand Clinical Collaboration to Include Phase I/IIa Trial Investigating the Combination of SNK01 with ERBITUX® (cetuximab) in Metastatic NSCLC

April 13, 2021 09:30 ET | Source: [NKGen Biotech, Inc.](#)

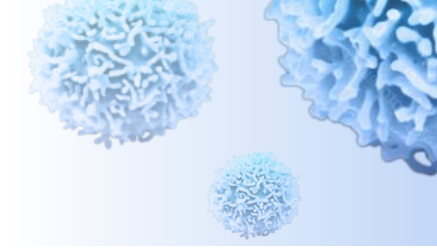
Cetuximab: anti-EGFR antibody.

A Study on the Anti-Tumor Activity of SNK01 in EGFR-TKI-Resistant Non-small Cell Lung Cancer, NKMax Co., Ltd., *Internal In Vitro Test Report, NKMAX-R20-04*, October 30, 2020 [page 30].



ASCO 2023 Poster Presentation

SNK01 Phase I/IIa Clinical Trial Results



ClinicalTrials.gov Identifier: NCT04872634

12 patients with TKI resistant metastatic NSCLC were evaluated

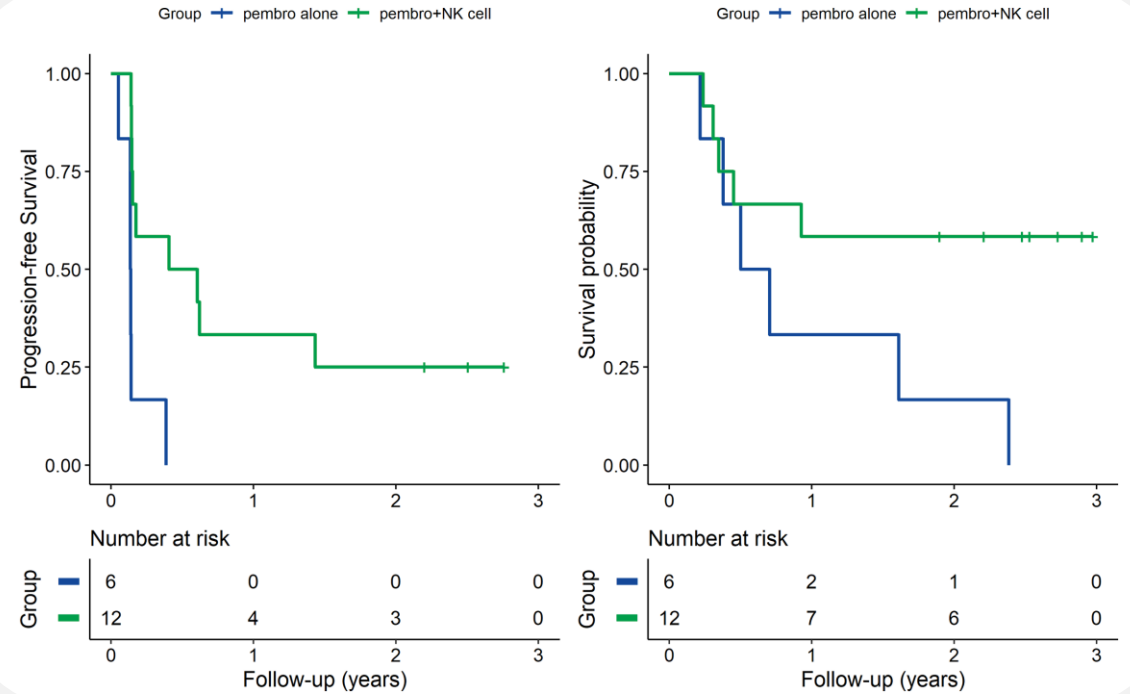
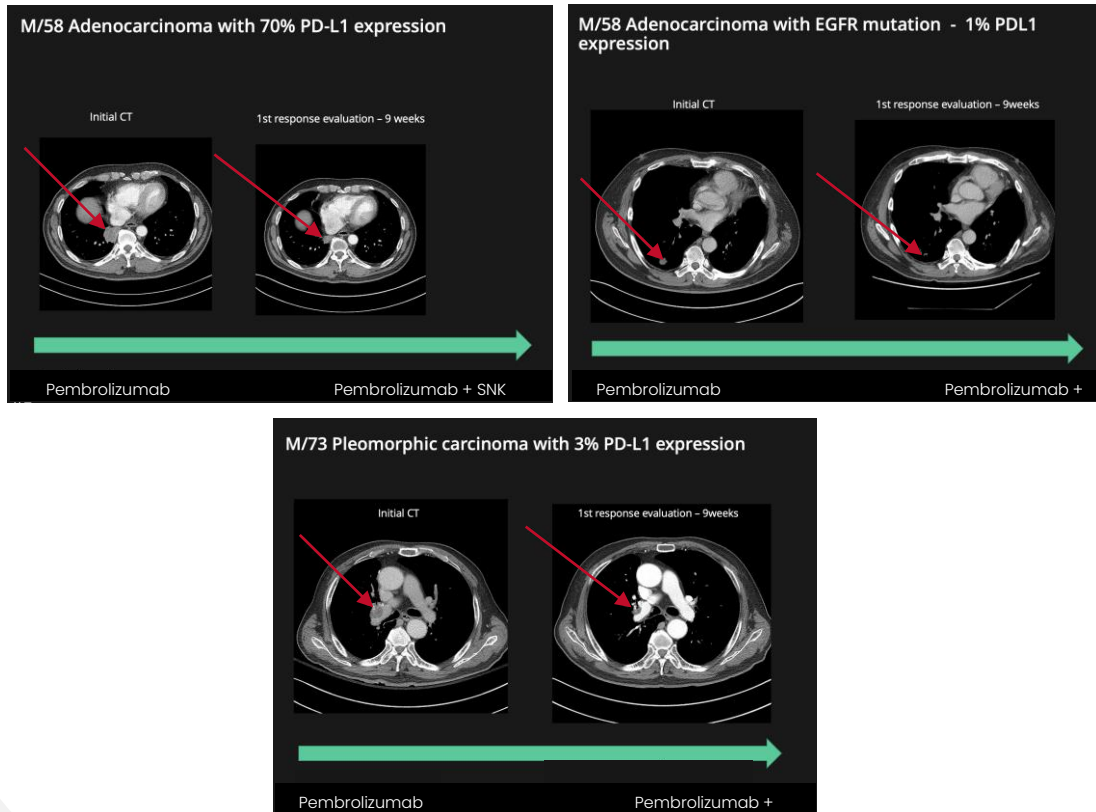
Dose-limiting toxicity was not observed, therefore the maximum tolerated dose of SNK01 was determined to be 6×10^9 cells/dose

No SNK01-related adverse events of Grade 3 or higher were observed

The objective response rate was 25% (3/12), disease control rate (DCR) was 100%, with 3/12 patients experiencing a partial response (25%) and 9/12 with stable disease (75%) for the total of the 12 patients

Median progression free survival (PFS) was 163 days. Some patients are still being followed and an updated PFS will be provided at a later date

Improved Survival Rates Following SNK01 Combination Treatment with a PD-1 Inhibitor



SNK01 + pembrolizumab
Pembrolizumab monotherapy

	2-Year PFS	2-Year Survival
SNK01 + pembrolizumab	25%	58.3%
Pembrolizumab monotherapy	0%	16.7%

Synergistic improvement in 2-year survival rates following SNK01 combination with pembrolizumab in NSCLC

Two-year efficacy of SNK01 plus pembrolizumab for non-small cell lung cancer: Expanded observations from a phase I/IIa randomized controlled trial. This trial included 20 patients with advanced NSCLC with a PD-L1 tumor proportion score of 1% or greater who failed prior to front-line platinum-based therapy.

Hyung Jun Park, Yong Man Kim, Jae Seob Jung, Wonjun Ji, Jae Cheol Lee, Chang-Min Choi. Thorac Cancer. 2022; 1-7.

Can SNK Change The TME For PD-L1- Tumors?

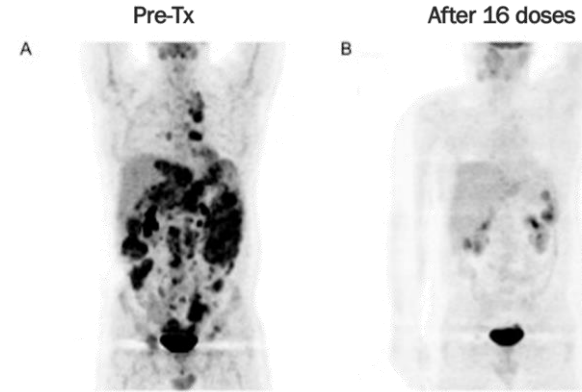
NK cells can positively affect the TME to help make PD-L1 negative tumors respond to ICIs*

Patient Age: 32¹

- Stage IVB Desmoplastic Small Round Cell Sarcoma
- Diagnosed 2017
- Disease included lung, abdomen and pelvis with extensive disease in abdominal/ pelvic lymph nodes and liver
- **PD-L1 Negative Tumor**

Failed Therapies

1. doxorubicin, cytoxan, and vincristine
2. etoposide and ifosfamide
3. adoxorubicin and ifosfamide
4. irinotecan, vincristine, and Temodar*
5. Yondelis* and Keytruda*



Patient Age: 58²

- Stage IV Chondrosarcoma
- Diagnosed 2019
- Disease included lung, abdomen and pelvis with extensive liver disease. Non-healing large pelvic wound due to tumor progression.
- <10% PD-L1+, Microsatellite stable

Failed Therapies

1. Opdivo*
2. Ibrance*
3. panzopanib



1. Erlinda M. Gordon, et al. (2022). Durable Responses Using SNK01 Autologous Enhanced Natural Killer Cells and Pembrolizumab for Chemotherapy-Resistant Advanced Sarcoma: Case Reports, Literature Review and Future Perspectives. *J. Cancer Research and Cellular Therapeutics*. 6(5).

2. Victoria S. Chua, Poster Presentation: USFDA Authorized Compassionate Use of SNK01 (Autologous Non-Genetically Modified Natural Killer Cells With Enhanced Cytotoxicity) and Immune Checkpoint Inhibitors in Advanced Heavily Pre-treated Sarcoma. A Promising Regimen. ESMO Annual Meeting 2022.

ACTIVE, NOT RECRUITING ⓘ

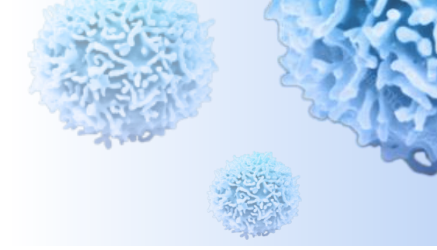
Study of Allogeneic Blood-derived Natural Killer Cells to Evaluate Safety and Tolerability in Cancer Refractory to Conventional Therapy

ClinicalTrials.gov ID ⓘ NCT05990920

Sponsor ⓘ NKGen Biotech, Inc.

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

Last Update Posted ⓘ 2024-03-01



Study Overview

Brief Summary

The goal of this clinical trial is to test SNK02 in participants with pathologically confirmed cancer that is refractory to conventional therapy. The main questions it aims to answer are:

- Is SNK02 safety and tolerable when administered weekly as an intravenous infusion
- What is the maximum dose that is tolerated of SNK02 Participants will be administered SNK02 weekly for 8 weeks and undergo medical evaluation to provide initial clinical safety data for the treatment of cancer with allogeneic NK cells as a monotherapy treatment.

[+ Show more](#)

Official Title

A Phase 1, Open-Label, Dose Escalation Study of Allogeneic Blood-derived Natural Killer Cells to Evaluate Safety and Tolerability in Participants With Pathologically Confirmed Cancer Refractory to Conventional Therapy

Conditions ⓘ

Pathologically Confirmed Cancer Refractory to Conventional Therapy Refractory Cancer
Metastatic Cancer Recurrent Cancer [Show 4 more conditions](#)

Intervention / Treatment ⓘ

- Biological: SNK02

Study Start (Actual) ⓘ

2023-08-23

Primary Completion (Estimated) ⓘ

2024-08

Study Completion (Estimated) ⓘ

2024-12

Enrollment (Actual) ⓘ

6

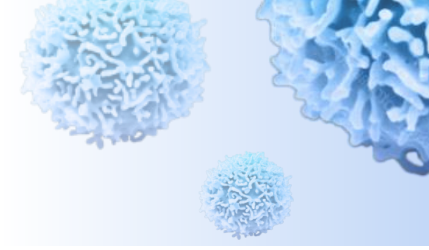
Study Type ⓘ

Interventional

Phase ⓘ

Phase 1

US01 – SNK02



	Stage	Dx	Dose	# Prior Tx	Toxicity		Total doses	Comments
001	IV	Angiosarcoma	6 B	4	2	SD	18	Stable 4 mos.
003	IV	Leiomyosarcoma	6 B	7	3	SD	12	Stable for 3 mos.
004	IV	Endometrial Adenocarcinoma	6 B	1	1	SD	8	Stable for 2 mos.
005	IV	Pleomorphic sarcoma	6 B	5	5	PD	4	Patient died of respiratory failure due to lung disease progression
007	IV	Colorectal CA	6 B	4	1	SD	10	Stable for 3 mos.
008	IV	Colorectal CA	6 B	4	1	PD	4	Progressive liver mets

Lab Panels and collection timepoint

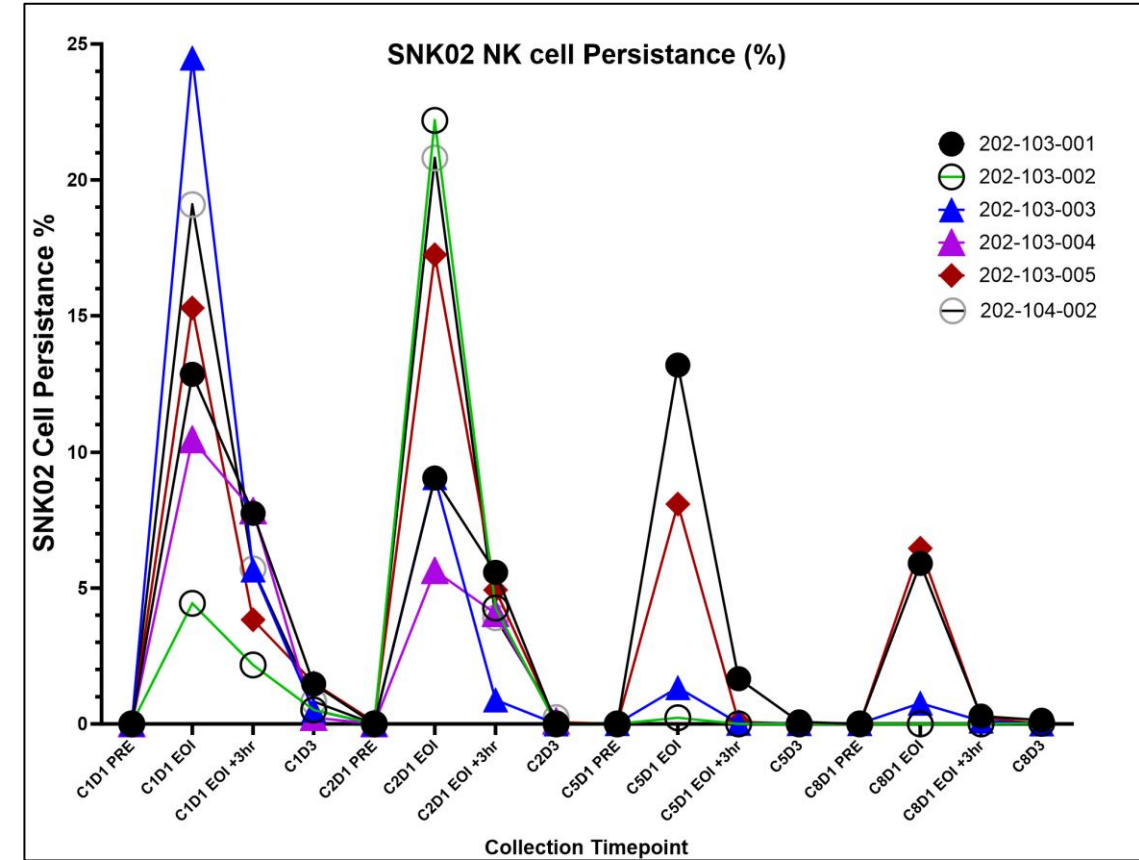


	Screening	Cycle 1				Cycle 2				Cycle 5				Cycle 8				Subsequence collection once every four cycles (e.g. cycle 12, 16, 20, 24...)	EOT
	Day -42 to Day -1	Day 1			Day 3	Day 1			Day 3	Day 1			Day 3	Day 1			Day 3		
		Pre	EOI	+3h EOI		Pre	EOI	+3h EOI		Pre	EOI	+3h EOI		Pre	EOI	+3h EOI			
		-2h max	+15 mins max	± 15 mins		-2h max	+15 mins max	± 15 mins		-2h max	+15 mins max	± 15 mins		-2h max	+15 mins max	± 15 mins			
Tumor Markers		X				X				X				X				X	X
Immunophenotyping		X				X				X				X				X	X
Cytokine/Chemokine Profile		X				X				X				X				X	X
NK Cell Activity		X				X				X				X				X	X
Donor Specific Antibody Assay		X				X				X				X					X
SNK02 Chimerism Assay		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X		X
MHC Class 1	X																		
KIR haplotyping	X																		

SNK02 Persistence - Chimerism by NGS on total NK Cells (%)



Time Points/Subjects	SNK02 Persistence - Chimerism by NGS on total NK Cells (%)					
	202-103-001	202-103-002	202-103-003	202-103-004	202-103-005	202-104-002
C1D1-PRE	0	0	0	0	0	0
C1D1-EOI	12.85	4.44	24.49	10.46	15.29	19.09
C1D1-3hEOI	7.75	2.17	5.67	7.84	3.84	5.71
C1D3	1.47	0.52	0.51	0.24	1.51	0.83
C2D1-PRE	0	0	0	0	0.08	0
C2D1-EOI	9.05	22.19	9.07	5.64	17.25	20.81
C2D1-3hEOI	5.58	4.27	0.89	4.06	4.93	3.91
C2D3	0	0	0	0.1	0.07	0.24
C5D1-PRE	0	0	0.02		0	
C5D1-EOI	13.19	0.23	1.34		8.09	
C5D1-3hEOI	1.67	0	0.03		0.08	
C5D3	0.08	0	0.02		0.01	
C8D1-PRE	0	0	0.02		0	
C8D1-EOI	5.91	0	0.77		6.47	
C8D1-3hEOI	0.29	0	0.11		0.24	
C8D3	0.14	0.03	0		0	
EOT	0	0	0			0



- All subjects increased donor cells % at End of Infusion
- Decreased donor cells % at End of Infusion in subsequence doses
- Most subjects have undetected donor cells one week after dosing prior to the next dose.
- **Donor cells likely to reside in secondary lymphoid organ after infusion and no circulating in peripheral blood.**

Subject ID	HLA	Autoantibodies - HLA Class I, II %CPRA*				
		C1D1**	C2D1	C5D1	C8D1	EOT
202-103-001	Class I	NEG	NEG	NEG	POS	
	Class II	NEG	NEG	NEG	POS	
202-103-002	Class I	NEG	NEG	POS-99 %CPRA	POS-100 %CPRA	POS-100 %CPRA
	Class II	NEG	NEG	POS-89 %CPRA	POS-100 %CPRA	POS-99 %CPRA
202-103-003	Class I	NEG	NEG	POS-35 %CPRA	POS-77 %CPRA	
	Class II	POS-54 %CPRA	POS 91-%CPRA	POS-99 %CPRA	POS-99 %CPRA	
202-103-004	Class I	NEG	POS			
	Class II	NEG	NEG			
202-103-005	Class I	NEG	NEG	POS-74 %CPRA	POS-93 %CPRA	
	Class II	NEG	NEG	NEG	POS-83 %CPRA	
202-104-002	Class I	POS 7%CPRA	POS 7%CPRA			POS 98%CPRA
	Class II	NEG	NEG			POS 88%CPRA

*A Calculated Panel Reactive Antibody (CPRA) score estimates the percentage of donors whose organs would be incompatible with the transplant candidate. Patients with high CPRA scores have fewer potentially compatible donors.

The CPRA is calculated based on the percentage of potential donors against whom a transplant candidate has developed antibodies. A higher CPRA indicates a higher level of sensitization.

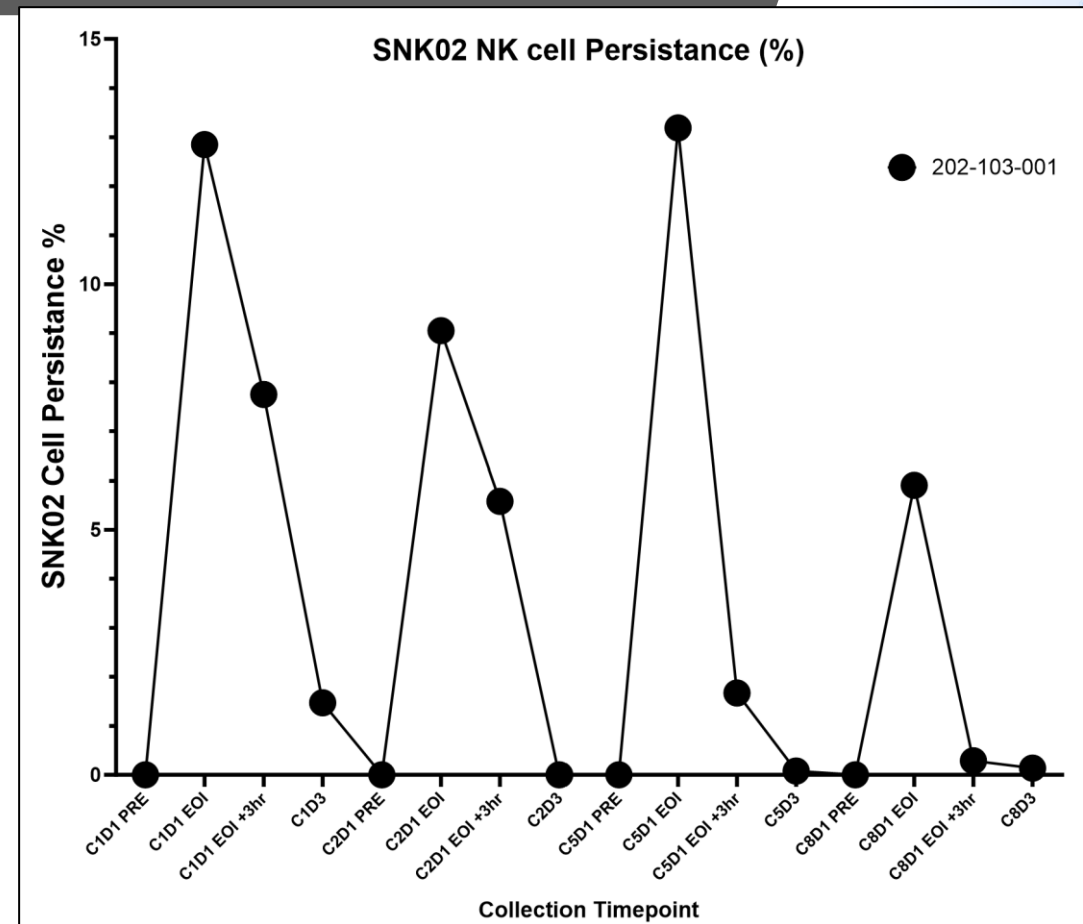
- For example, a CPRA of 0% means the patient has no antibodies against potential donors, while a CPRA of 100% means the patient has antibodies against all potential donors.

** C1D1 Baseline pre-treatment detected pre-existing HLA class I or class II Antibodies from studied subjects

202-103-001 – 18 total doses



Subject ID	Cycle #	Timepoint	Percentage of total NK Cell in peripheral blood (%)	
			Patient's NK Cell	Donor SNK02
202-103-001	C1	Pre	100	0
		EOI	87.15	12.85
		+3 hrs EOI	92.25	7.75
		Day 3	98.53	1.47
	C2	Pre	100	0
		EOI	90.95	9.05
		+3 hrs EOI	94.42	5.58
		Day 3	100	0
	C5	Pre	100	0
		EOI	86.81	13.19
		+3 hrs EOI	98.33	1.67
		Day 3	99.92	0.08
C8	Pre	100	0	
	EOI	94.09	5.91	
	+3 hrs EOI	99.71	0.29	
	Day 3	99.86	0.14	



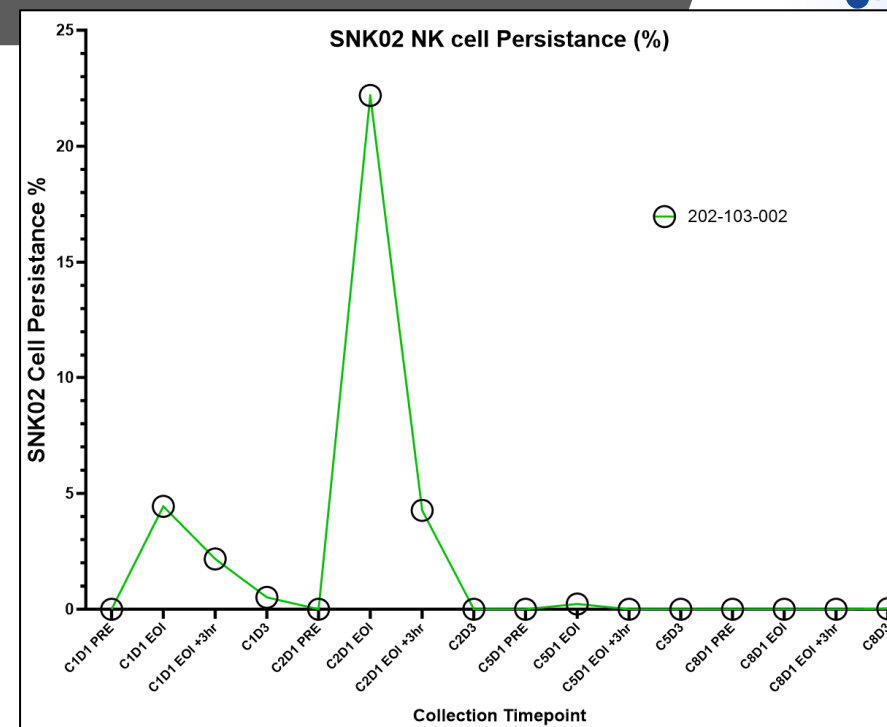
Subject ID	HLA	Donor Specific Antibodies -HLA Class I, II - %CPRA*			
		C1D1	C2D1	C5D1	C8D1
202-103-001	Class I	NEG	NEG	NEG	POS
	Class 2	NEG	NEG	NEG	POS

Cycle	AETERM	AESEV	AEOU
C2D1	Scrotal wound	Grade 2	Resolved
C12D1	scrotal pain	Grade 1	Ongoing



202-103-002 – 12 total doses

Subject ID	Cycle #	Timepoint	Percentage of total NK Cell in peripheral blood (%)	
			Patient's NK Cell	Donor SNK02
202-103-002	C1	Pre	100	0
		EOI	95.56	4.44
		+3 hrs EOI	97.83	2.17
		Day 3	99.48	0.52
	C2	Pre	100	0
		EOI	77.81	22.19
		+3 hrs EOI	95.73	4.27
		Day 3	100	0
	C5	Pre	100	0
		EOI	99.78	0.23
		+3 hrs EOI	100	0
		Day 3	100	0
	C8	Pre	100	0
		EOI	100	0
		+3 hrs EOI	100	0
		Day 3	99.97	0.03

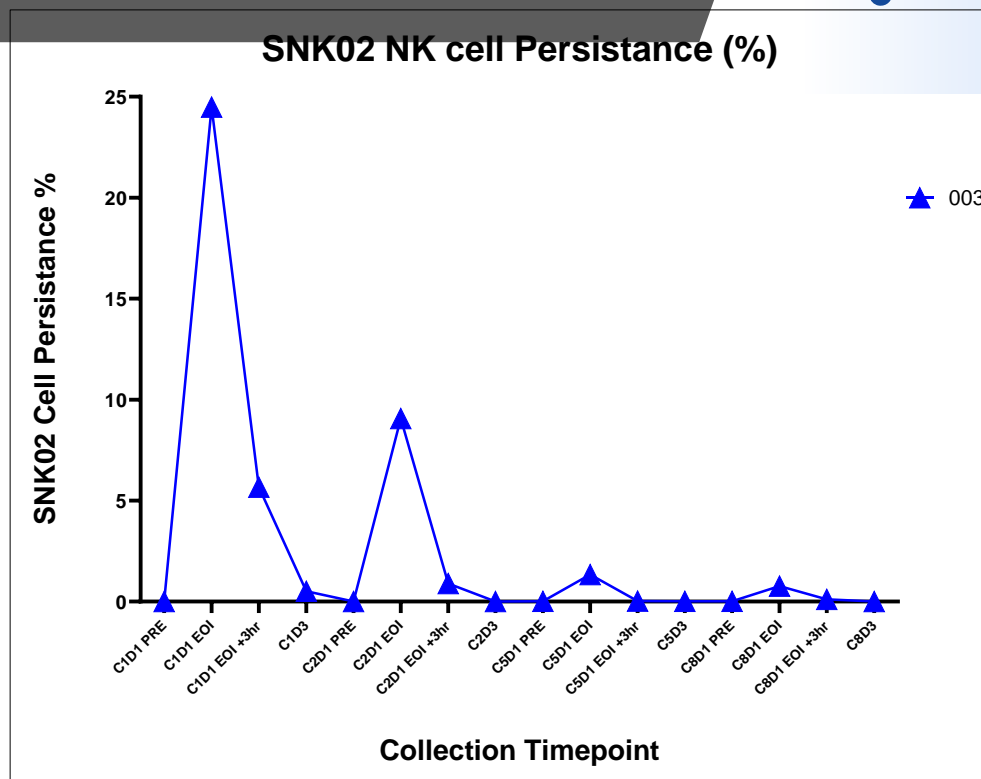


Cycle	AETERM	AESEV	AEOUT
C1D1	Fever	Grade 2	Resolved
C1D1 + 1 Day	Headaches	Grade 1	Resolved
C1D1 + 1 Day	Uppershoulder/neck stiffness	Grade 1	Resolved
C2D1 + 1 Day	Fever	Grade 1	Resolved
C2D1 + 1 Day	Chills	Grade 1	Resolved
C2D1 + 1 Day	Increased fatigue	Grade 3	Resolved
C4D1 + 4 Days	Nausea, intermittent	Grade 1	Ongoing
C4D1 + 3 Days	Fever, intermittent	Grade 2	Ongoing
C4D1 + 4 Days	Nausea, intermittent	Grade 1	Ongoing
C4D1 + 4 Days	Vomiting, intermittent	Grade 1	Ongoing
C4D1 + 4 Days	Abdominal pain, intermittent	Grade 1	Ongoing
C4D1 + 5 Days	Fatigue, intermittent	Grade 1	Ongoing
C6D1 + 6 Days	Left chest wall pain	Grade 1	Ongoing
C10D1	Partial bowel obstruction	Grade 2	Resolved

Subject ID	HLA	Donor Specific Antibodies -HLA Class I, II %CPRA*			
		C1D1	C2D1	C5D1	C8D1
202-103-002	Class I	NEG	NEG	POS-99 %CPRA	POS-100 %CPRA
	Class 2	NEG	NEG	POS-89 %CPRA	POS-100 %CPRA

202-103-003 – 10 total doses

Subject ID	Cycle #	Timepoint	Percentage of total NK Cell in peripheral blood (%)	
			Patient's NK Cell	Donor SNK02
202-103-003	C1	Pre	100	0
		EOI	75.51	24.49
		+3 hrs EOI	94.33	5.67
		Day 3	99.49	0.51
	C2	Pre	100	0
		EOI	90.93	9.07
		+3 hrs EOI	99.09	0.89
		Day 3	100	0
	C5	Pre	99.98	0.02
		EOI	98.64	1.34
		+3 hrs EOI	99.97	0.03
		Day 3	99.98	0.02
	C8	Pre	99.98	0.02
		EOI	99.23	0.77
		+3 hrs EOI	99.89	0.11
		Day 3	100	0



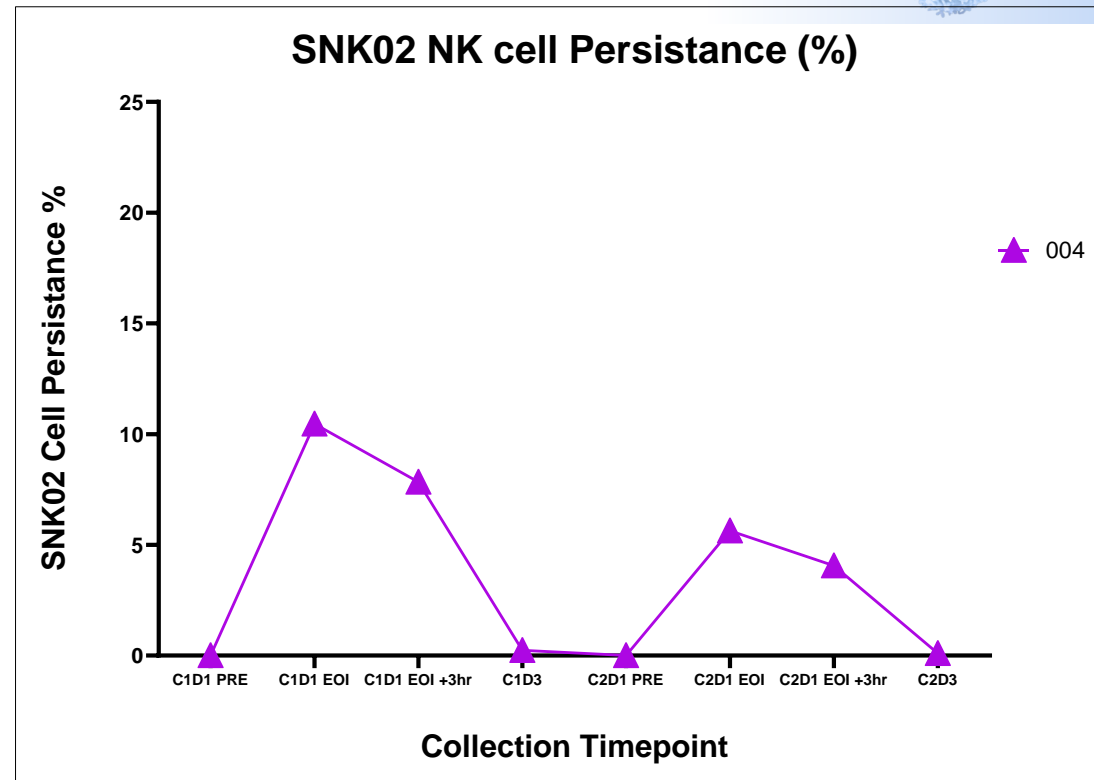
Cycle	AETERM	AESEV	AEOU
C2D1	Chills	Grade 1	Resolved
C2D1 + 1 Day	Diarrhea	Grade 1	Resolved
C3D1	Chills	Grade 1	Resolved
C2D1 + 2 Days	Dysuria	Grade 1	Resolved
C3D1	Nausea, intermittent	Grade 1	Ongoing
C3D1	Urinary tract infection	Grade 2	Resolved
C5D1	Diarrhea, intermittent	Grade 1	Ongoing
C2D1 + 1 Day	Intermittent rigors	Grade 1	Ongoing
C4D1	Fatigue, intermittent	Grade 2	Ongoing
C6D1+ 6 Days	Increased cough	Grade 2	Ongoing
C7D1	Left shoulder pain with radiation to fingertips	Grade 1	Ongoing
C9D1+ 6 Days	Increased dyspnea	Grade 2	Ongoing

Subject ID	HLA	Donor Specific Antibodies -HLA Class I, II %CPRA*			
		C1D1	C2D1	C5D1	C8D1
202-103-003	Class I	NEG	NEG	POS-35 %CPRA	POS-77 %CPRA
	Class 2	POS-54 %CPRA	POS 91-%CPRA	POS-99 %CPRA	POS-99 %CPRA

202-103-004 – 4 total doses



Subject ID	Cycle #	Timepoint	Percentage of total NK Cell in peripheral blood (%)	
			Patient's NK Cell	Donor SNK02
202-103-004	C1	Pre	100	0
		EOI	89.54	10.46
		+3 hrs EOI	92.16	7.84
		Day 3	99.77	0.24
	C2	Pre	100	0
		EOI	94.36	5.64
		+3 hrs EOI	95.94	4.06
		Day 3	99.9	0.1



Subject ID	HLA	Donor Specific Antibodies -HLA Class I, II %CPRA*	
		C1D1	C2D1
202-103-004	Class I	NEG	POS
	Class 2	NEG	NEG

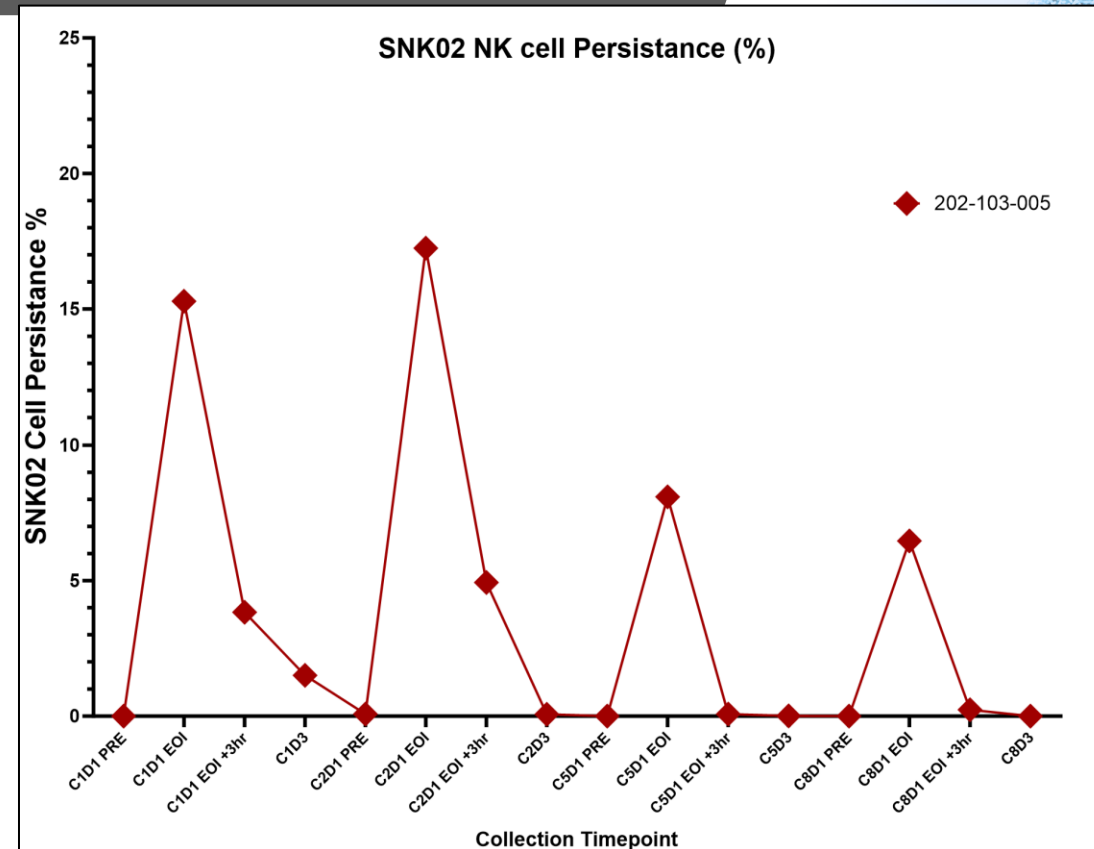
Cycle	AETERM	AESEV	AEOUT
C3D1	Anxiety	Grade 1	Ongoing
C3D1	Memory loss	Grade 1	Ongoing
C6D1 + 5 Days	Respiratory Failure (symptomatic disease progression)	Grade 5	Death



202-103-005 – 8 total doses



Subject ID	Cycle #	Timepoint	Percentage of total NK Cell in peripheral blood (%)	
			Patient's NK Cell	Donor SNK02
202-103-005	C1	Pre	100	0
		EOI	84.71	15.29
		+3 hrs EOI	96.14	3.84
		Day 3	98.49	1.51
	C2	Pre	99.92	0.08
		EOI	82.61	17.25
		+3 hrs EOI	95.07	4.93
		Day 3	99.93	0.07
	C5	Pre	100	0
		EOI	92.17	8.09
		+3 hrs EOI	99.92	0.08
		Day 3	99.99	0.01
	C8	Pre	100	0
		EOI	93.53	6.47
		+3 hrs EOI	99.76	0.24
		Day 3	100	0



Subject ID	HLA	Donor Specific Antibodies -HLA Class I, II %CPRA*			
		C1D1	C2D1	C5D1	C8D1
202-103-005	Class I	NEG	NEG	POS-74 %CPRA	POS-93 %CPRA
	Class 2	NEG	NEG	NEG	POS-83 %CPRA

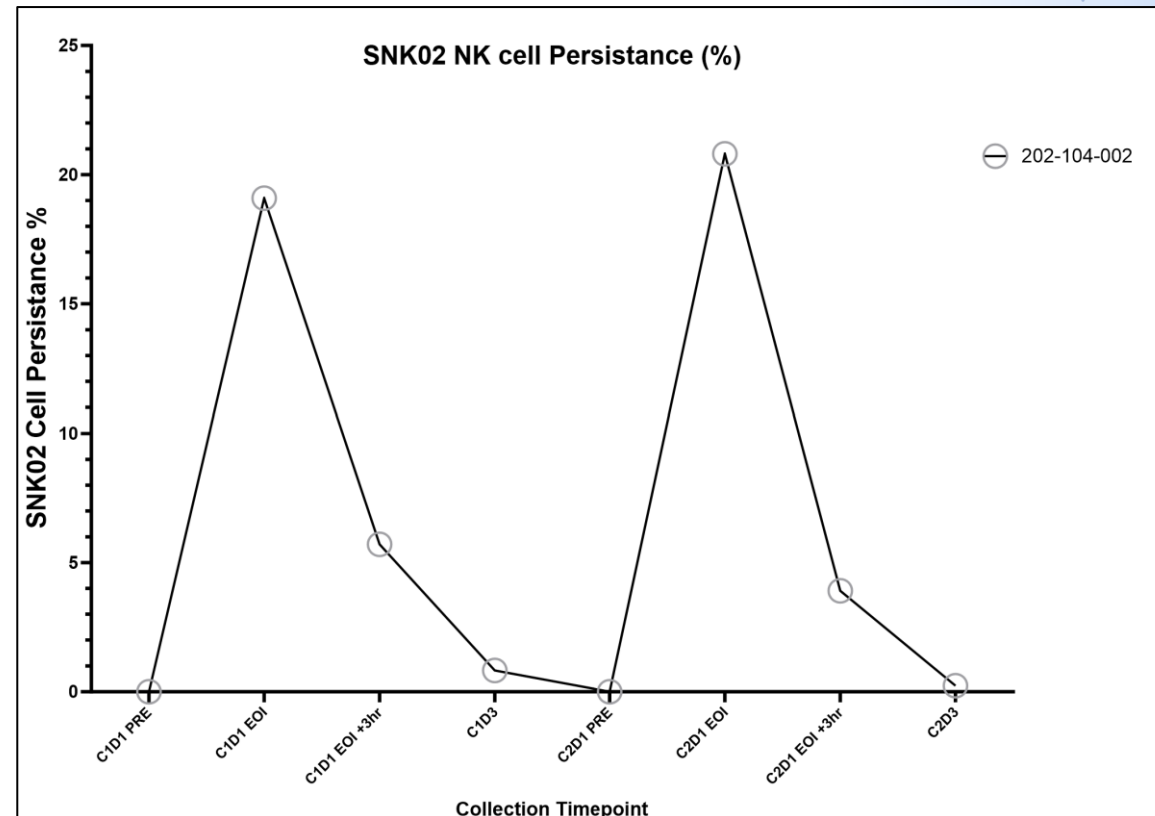
Cycle	AETERM	AESEV	AEOU
C2D1	Rigors	Grade 1	Resolved
C2D1	Fatigue	Grade 1	Ongoing
C4D1 + 1 Day	Vomiting	Grade 1	Ongoing
C4D1 + 1 Day	Rigors	Grade 1	Resolved
C6D1	Rigors, intermittent	Grade 1	Resolved
C6D1	Nausea, intermittent	Grade 1	Ongoing
C9D1	Rigors intermittent	Grade 2	Ongoing



202-104-002 – 4 total doses



Subject ID	Cycle #	Timepoint	Percentage of total NK Cell in peripheral blood (%)	
			Patient's NK Cell	Donor SNK02
202-104-002	C1	Pre	100	0
		EOI	80.91	19.09
		+3 hrs EOI	94.29	5.71
		Day 3	99.17	0.83
	C2	Pre	100	0
		EOI	79.19	20.81
		+3 hrs EOI	96.09	3.91
		Day 3	99.76	0.24



Subject ID	HLA	Donor Specific Antibodies -HLA Class I, II %CPRA*		
		C1D1	C2D1	EOT
202-104-002	Class 1	POS 7%CPRA	POS 7%CPRA	POS 98%CPRA
	Class 2	NEG	NEG	POS 88%CPRA

Cycle	AETERM	AESEV	AEOU
C1D1	Chill	Grade 1	Resolved
C2D1	Abdominal pain	Grade 1	Resolved
C2D1	Fever	Grade 1	Resolved
C3D1	Fever	Grade 1	Resolved
C3D1	Chills	Grade 1	Resolved
C2D1	Transaminitis	Grade 1	Ongoing



HLA Matching



HLA	AL22-SNK02-D0005	SNK02-202-103-001	SNK02-202-103-002	SNK02-202-103-003	SNK02-202-103-004	SNK02-202-103-005	SNK02-202-104-002
A	A*02:06:01	A*02:01:01	A*02:06:01	A*02:01:01	A*03:01:01	A*01:01:01	A*02:01:01
	A*33:03:01	A*68:02:01	A*68:02:01	A*32:01:01	A*68:02:01	A*29:02:01	A*24:02:01
B	B*44:03:01	B*14:02:01	B*15:16:01	B*07:02:01	B*14:02:01	B*44:03:01	B*35:02:01
	B*46:01:01	B*49:01:01	B*46:01:01	B*51:01:01	B*15:01:01	B*08:01:01	B*35:03:01
C	C*01:02:01	C*07:01:01	C*01:02:01	C*01:02:01	C*03:04:01	C*07:01:01	C*04:01:01
	C*14:03:01	C*08:02:01	C*14:02:01	C*07:02:01	C*08:02:01	C*16:01:01	C*04:01:01
DQB1	DQB1*06:01:01	DQB1*03:19:01	DQB1*02:02:01	DQB1*05:01:01	DQB1*03:01:01	DQB1*02:02:01	DQB1*03:01:01
	DQB1*06:04:01	DQB1*05:01:01	DQB1*05:01:24	DQB1*05:02:01	DQB1*03:02:01	DQB1*05:03:01	DQB1*03:01:01
DRB1	DRB1*08:03:02	DRB1*01:02:01	DRB1*13:03:01	DRB1*01:01:01	DRB1*04:01:01	DRB1*07:01:01	DRB1*11:04:01
	DRB1*13:02:01	DRB1*11:02:01	DRB1*15:02:01	DRB1*16:01:01	DRB1*13:03:01	DRB1*14:54:01	DRB1*12:01:01
Number of matched at allelic level		0/10	3/10	1/10	0/10	1/10	0/10

Red-Mismatch
Green-Match

KIR-Ligand Matching



- KIR-Ligand Mismatch:**

This occurs when the KIRs on the donor NK cells do not recognize the HLA ligands present on the recipient's cells.

A KIR mismatch in GvH direction can enhance the GvH effect. The absence of inhibitory signals allows the donor NK cells to remain active and attack tumor cells in the recipient, contributing to the anti-tumor cells effect.

The mismatched KIRs on the donor NK cells are not inhibited by the recipient's HLA molecules, leading to increased NK cell activity against the recipient's tumor cells.

Donor/Subject ID	Typing	Ligand	Match/Mismatching in GvH direction
SNK02-AL22	HLA-B*44:03	Bw4-80T	
	HLA-B*46:01	Bw6	
	HLA-C*01:02	C1	
	HLA-C*14:03	C1	
202-103-001	HLA-B*14:02	Bw6	Match
	HLA-B*49:01	Bw4-80I	
	HLA-C*07:01	C1	
	HLA-C*08:02	C1	
202-103-002	HLA-B*15:16	Bw4 - 80I	Match
	HLA-B*46:01	Bw6	
	HLA-C*01:02	C1	
	HLA-C*14:02	C1	
202-103-003	HLA-B*07:02	Bw6	Match
	HLA-B*51:01	Bw4 - 80I	
	HLA-C*01:02	C1	
	HLA-C*07:02	C1	
202-103-004	HLA-B*14:02	Bw6	Mismatch
	HLA-B*15:01	Bw6	
	HLA-C*03:04	C1	
	HLA-C*08:02	C1	
202-103-005	HLA-B*44:03	Bw4 - 80T	Match
	HLA-B*08:01	Bw6	
	HLA-C*08:01	C1	
	HLA-C*07:01	C1	
202-104-002	HLA-B*35:02	Bw6	Mismatch
	HLA-B*35:03	Bw6	
	HLA-C*04:01	C2	
	HLA-C*04:01	C2	





- **SNK02 was given weekly repeatedly for up to 18 consecutive weeks appears to be safe and to have some anti-tumor effects in heavily pretreated solid tumors.**
- **Donor specific antibodies were developed in all subjects after multiple doses (b/w 2 to 8 weeks)**
- **SNK02 persistence decreased after repeat dosing and when auto-antibodies were detected.**
- **Donor specific antibodies were developed specific to the major and cross reactivity groups. Further study is needed to investigate the occurrence of AE to the generation of DSA.**
- **Due to the small number of subjects in this phase I study, further study is needed to investigate the correlation of alloreactivity of the donor NK Cells from the HLA and KIR match and mismatch effects.**
- **SNK02 treatment from numerous donors rather than one donor will be investigated.**
- **SNK02 will be explored in combination with immune checkpoint inhibitors and antibody therapy.**



Thank you

