NKX019, an Allogeneic, Off-the-Shelf, CD19-Targeting, CAR NK-Cell Therapy, Induces Deep CD19+ B-Cell Depletion in Haematological Malignancy and Models of Autoimmune Disease

POS1184

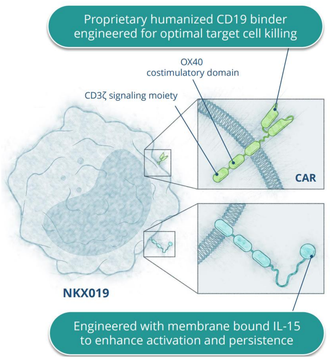
Mira Tohmé, Meriam Vejiga, Wendy Yu, Emily Kang*, Katharine Yu, Jessica Wei, Jessica Sood, Max Zhang, Nikki Kimura*, Damie J Juat*, Ivan H Chan, Kyle Hansen, James B Trager*, Sandeep S Hora, Shawn Rose, Ann M Kapoun, David Shook*, Phung Gip

Nkarta, Inc., South San Francisco, CA, USA. *Affiliation at the time of the studies.

Introduction

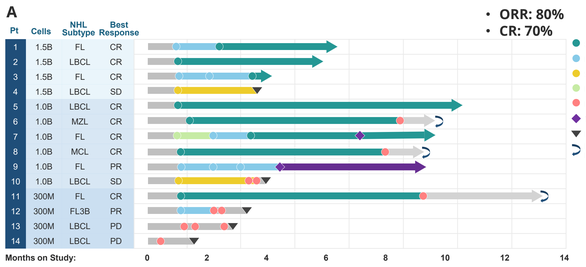
- Autologous chimeric antigen receptor (CAR) T-cell therapies have shown remarkable clinical activity in autoimmune (AI) disease via B-cell targeting, with many patients achieving durable, drug-free remission[1-3]
- However, safety concerns persist, including toxicities such as cytokine release syndrome (CRS), immune effector cell–associated neurotoxicity syndrome (ICANS), and graft-versus-host disease (GVHD)[4,5]
- Long manufacturing times, complex logistics, and the cost burden of lengthy hospital stays associated with CAR T-cell therapy limit patient access and impact broader adoption[6-8]
- Allogeneic natural killer (NK)-cell therapy may help address these challenges
- NKX019 is an investigational, allogeneic, CD19-targeted, CAR NK-cell therapy derived from healthy donor peripheral blood mononuclear cells (PMBCs) and cryopreserved for off-the-shelf use[9]
- NKX019 expresses a humanized anti-CD19 scFv CAR fused to costimulatory (OX40) and signaling (CD3ζ) domains to enhance killing, along with membrane-bound interleukin (IL)-15 to support persistence (**Figure 1**)[9]
- In a phase 1 clinical trial for relapsed or refractory B-cell malignancies (NCT05020678), NKX019 demonstrated robust antitumor activity and a favorable safety profile, including no ICANS or grade >3 CRS (**Figure 2**)[9]
- We evaluated the activity of NKX019 in samples collected from participants with B-cell–mediated AI diseases

Figure 1. NKX019 schematic



CAR, chimeric antigen receptor; IL, interleukin.

Figure 2. NKX019 demonstrated durable responses with a favorable safety profile in NHL



B

Safety profile	All participants (N = 34)
Grade ≥3 CRS	1 (2.9)
ICANS	0
GVHD	0
NKX019-related deaths	0

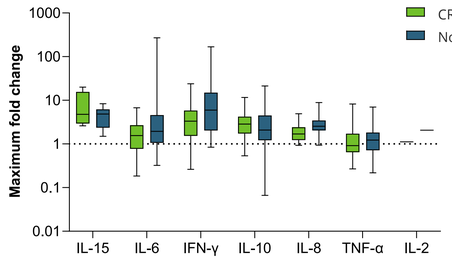
A Swimmer plot showing treatment duration, clinical response, and outcomes for 14 participants with relapsed/refractory NHL treated with NKX019. All participants received ≥2 prior lines of therapy and underwent lymphodepletion with fludarabine and cyclophosphamide before NKX019 infusion (dose range: 300M–1.5B cells). Reported ORR and CR rates are at the 2 highest dose cohorts depicted (n = 10 treated with 1.0B and 1.5B cells). Each bar represents an individual participant, stratified by infused NKX019 cell dose and NHL subtype. Adapted from Dickinson M, et al. *HemaSphere*. 2023;7(S3):e37234fb.
B Summary of TRAEs of special interest in N = 34 participants.
B, billion; CR, complete response; CRS, cytokine release syndrome; FL, follicular lymphoma; FL3B, follicular lymphoma grade 3B; GVHD, graft-versus-host disease; ICANS, immune effector cell–associated neurotoxicity syndrome; LBCL, large B-cell lymphoma; M, million; MCL, mantle cell lymphoma; MZL, marginal zone lymphoma; NHL, non-Hodgkin lymphoma; ORR, overall response rate; PD, progressive disease; PR, partial response; pt, participant; SD, stable disease; TRAE, treatment-related adverse event.

Methods

- Samples from participants with non-Hodgkin lymphoma (NHL) dosed with NKX019 and PBMCs from participants with various B-cell–mediated AI diseases (systemic sclerosis [SSc], systemic lupus erythematosus [SLE], idiopathic inflammatory myopathies [IIM], myasthenia gravis [MG], rheumatoid arthritis [RA], and multiple sclerosis [MS]) were obtained
- Samples were evaluated to assess depletion of CD19+ B cells, B-cell reconstitution, and immune repertoire using flow cytometry and genomic analyses (10X Genomics 5′ Single Cell Gene Expression profiling paired with B-cell receptor [BCR] sequencing)
- In vivo studies were performed in NOD *scid* gamma (NSG) mice, naïve and inoculated with human CD19+ B-cell lymphoma cell lines treated with NKX019, to evaluate the activity and biodistribution of NKX019 in tissue samples by bioluminescence imaging (IVIS Spectrum) and qPCR, respectively

Results

Figure 3. NKX019 clinical responses in participants with NHL occurred without elevations in proinflammatory cytokines commonly reported with CAR T-cell therapies in oncology

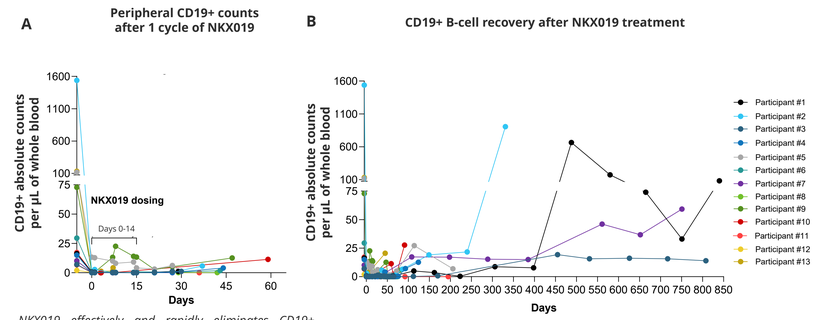


The indicated cytokines were measured in the serum of participants with NHL treated with NKX019 monotherapy (n = 27) across dose levels using MSD technology. Data are shown as the maximum fold change from baseline per treatment cycle on a $\log_{10}$ scale. The dotted line represents a fold change of 1 (no change from baseline).

[a]Non-CR includes participants with partial response, stable disease, or progressive disease.

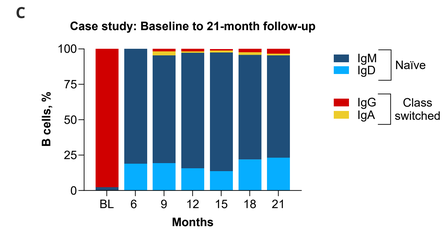
CR, complete response; IFN, interferon; IL, interleukin; MSD, Meso Scale Discovery®; NHL, non-Hodgkin lymphoma; TNF, tumor necrosis factor.

Figure 4. NKX019 depletes and resets the B-cell compartment in participants with NHL



NKX019 effectively and rapidly eliminates CD19+ B cells from the circulation in participants with NHL after a single cycle of treatment (LD + 3 doses NKX019)

B cells recover by approximately day 50 following NKX019 treatment

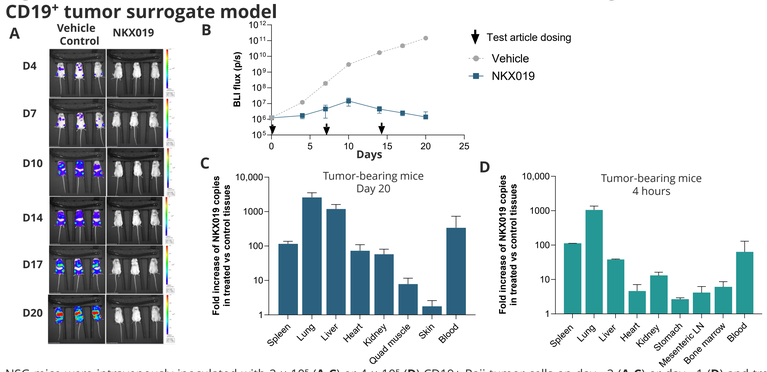


Emergent CD19+ B cells following NKX019 treatment show a significant increase in the proportion of naïve and non–class-switched B cells, suggesting immune reset of the B-cell compartment

A-B Peripheral CD19+ B-cell absolute counts were quantified by flow cytometry following a single cycle of NKX019 treatment (shown in **A**) and at end-of-treatment and long-term follow-up time points (shown in **B**) in 13 participants with NHL. Only participants with baseline counts above the LOQ (>0.2 cells/µL) are shown. Each line represents an individual participant. **C** Representative case study demonstrating a shift in the B-cell compartment from class-switched dominance (IgG/IgA) to a naïve, non–class-switched profile (IgM/IgD) after NKX019 treatment, as determined by BCR sequencing of PBMCs. This shift was maintained for up to 21 months post-treatment.

BCR, B-cell receptor; BL, baseline; Ig, immunoglobulin; LD, lymphodepletion; LOQ, limit of quantification; NHL, non-Hodgkin lymphoma; PBMC, peripheral blood mononuclear cell.

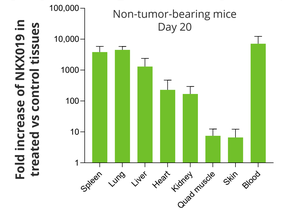
Figure 5. NKX019 eliminates CD19+B cells and traffics to several organs in an in vivo CD19+ tumor surrogate model



NSG mice were intravenously inoculated with 2 × 10^5 (**A-C**) or 4 × 10^5 (**D**) CD19+ Raji tumor cells on day −2 (**A-C**) or day −1 (**D**) and treated with 7M (**A-C**) or 7.5M (**D**) NKX019 cells or 5% FLEXBUMIN® vehicle control (n = 3 per group) on days 0, 7, and 14 (**A-C**) or day 0 (**D**). (**A**) Representative BLI images illustrating tumor burden over time. (**B**) BLI flux (p/s) was quantified per group. (**C-D**) NKX019 tissue infiltration was evaluated on day 20 (**C**) or at 4 hours (**D**) post-treatment using transgene-specific qPCR (copies per 100 ng gDNA) and expressed as fold increase in treated vs control tissues. (**B-D**) Data are shown on a $\log_{10}$ scale and represent mean ± SD.

BLI, bioluminescence imaging; D, day; gDNA, genomic DNA; LN, lymph node; M, million; NSG, NOD *scid* gamma; p/s, photons/second; qPCR, quantitative polymerase chain reaction; SD, standard deviation.

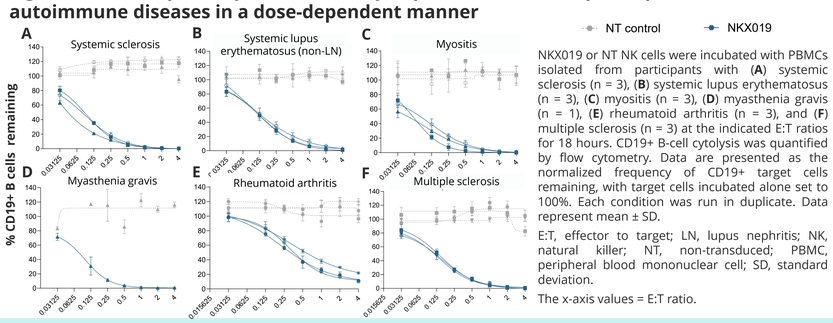
Figure 6. NKX019 demonstrates inherent trafficking to multiple tissues, including lymphoid organs, kidneys, lungs, muscles, and skin, in a naïve mouse model



NSG mice were treated with 7M NKX019 cells or 5% FLEXBUMIN® vehicle control (n = 3 per group) on days 0, 7, and 14. NKX019 tissue infiltration was evaluated on day 20 after NKX019 infusion using transgene-specific qPCR (NKX019 copies per 100 ng gDNA) and expressed as fold increase in treated vs control tissues. Data are shown on a $\log_{10}$ scale and represent mean ± SD.

gDNA, genomic DNA; M, million; NSG, NOD *scid* gamma; qPCR, quantitative polymerase chain reaction; SD, standard deviation.

Figure 7. NKX019 potently and selectively depletes B cells from participants with autoimmune diseases in a dose-dependent manner



NKX019 or NT NK cells were incubated with PBMCs isolated from participants with (**A**) systemic sclerosis (n = 3), (**B**) systemic lupus erythematosus (n = 3), (**C**) myositis (n = 3), (**D**) myasthenia gravis (n = 1), (**E**) rheumatoid arthritis (n = 3), and (**F**) multiple sclerosis (n = 3) at the indicated E:T ratios for 18 hours. CD19+ B-cell cytolysis was quantified by flow cytometry. Data are presented as the normalized frequency of CD19+ target cells remaining, with target cells incubated alone set to 100%. Each condition was run in duplicate. Data represent mean ± SD.

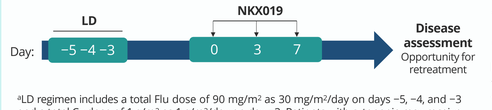
E:T, effector to target; LN, lupus nephritis; NK, natural killer; NT, non-transduced; PBMC, peripheral blood mononuclear cell; SD, standard deviation.

The x-axis values = E:T ratio.

Conclusions

- NKX019 induced **robust B-cell depletion** followed by reconstitution of the B-cell compartment in participants with NHL, consistent with an **immune reset**
- Nonclinical in vitro and in vivo data demonstrated that **NKX019 effectively depletes CD19+ cells** derived from **participants with AI diseases** and in CD19+ lymphoma models, respectively
- **NKX019** demonstrated an inherent capacity **to traffic to lymphoid organs** and **disseminate across multiple tissues**
- Collectively, these data provide compelling support for **NKX019 as a novel therapeutic approach for the treatment of B-cell–mediated AI diseases**
- The safety and tolerability of **NKX019 is currently being evaluated in 2 ongoing phase 1/2 basket studies** in participants with **B-cell–mediated AI diseases**, including **lupus nephritis** and **primary membranous nephropathy** (NCT06557265, NTRUST-1) and **SSc, IIM, refractory RA, and ANCA–associated vasculitis** (NCT06733935, NTRUST-2), as well as investigator-sponsored trials for **SLE** (NCT06518668) and **generalized MG**

NKX019 Treatment Schema for Autoimmune Indications



[a]LD regimen includes a total Flu dose of 90 mg/m² as 30 mg/m²/day on days −5, −4, and −3 and a total Cy dose of 1 g/m² as 1 g/m²/day on day −3. Patients with cytopenia may receive Cy alone at a total dose of 1 g/m² as 1 g/m²/day on day −3.

B, billion; CAR, chimeric antigen receptor; Cy, cyclophosphamide; Flu, fludarabine; LD, lymphodepletion; NK, natural killer.

LD (Flu + Cy)
- Established standard dosing[a]
- Dose option for Cy alone for patients with cytopenia
- Outpatient administration

NKX019
- Currently dosing at 4B CAR NK cells
- No geographic restrictions for patients following dosing
- May be given in an outpatient setting
- Only a 2-hour observation period post-administration

References

1. Müller F, et al. *N Engl J Med*. 2024;390(8):687-700.
2. Ohno R, et al. *Semin Arthritis Rheum*. 2024;67:152479.
3. Schett G, et al. *Immunity*. 2024;57(12):2705-9.
4. Xie G, et al. *EBioMedicine*. 2020;59:102975.
5. Michaelson JS, et al. *J Exp Med*. 2024;221(5):e20240499.
6. Lin H, et al. *Front Immunol*. 2021;12:744823.
7. Keating SJ, et al. *Transplant Cell Ther*. 2022;28(7):404.e1-e6.
8. Veomett N, et al. Poster presented at Transplantation & Cellular Therapy Annual Meeting; February 4-7, 2026.
9. Dickinson M, et al. *HemaSphere*. 2023;7(S3):e37234fb.

Acknowledgements

These studies were funded by Nkarta, Inc. Writing and editorial support were provided by Claire Strothman, PhD, of Red Nucleus and funded by Nkarta, Inc.

Presenter disclosure

MT is an employee of, may own stock in, and received travel support and other services from Nkarta, Inc.

This poster was previously presented at the American College of Rheumatology (ACR) Convergence 2025 Annual Meeting; October 24-29, 2025; Chicago, IL, USA.

Contact

Mira Tohmé: mtohme@nkartatx.com
Phung Gip: pgip@nkartatx.com

Please scan QR code for a copy of the poster.

Presented at the European Alliance of Associations for Rheumatology (EULAR) Annual Meeting; June 3-6, 2026; London, UK