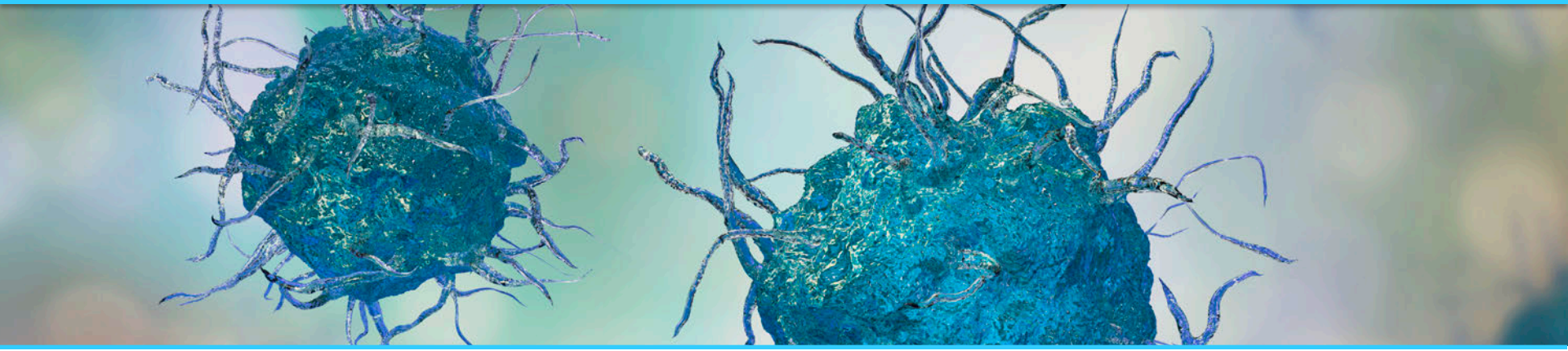
Author disclosure

- The presenting author, Dr. Bachier, discloses the following relevant conflicts of interest:
  - Honoraria from Celgene/Juno, CRISPR, and Allovir
  - Speakers Bureau participation for Sanofi



A Phase 1 Study of NKX101, an Allogeneic CAR Natural Killer (NK) Cell Therapy, in Subjects With Relapsed/Refractory (R/R) Acute Myeloid Leukemia (AML) or Higher Risk Myelodysplastic Syndrome (MDS)

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Abstract 1040 | Session: 616 Acute Myeloid Leukemia: Novel Therapy, excluding Transplantation: Poster I

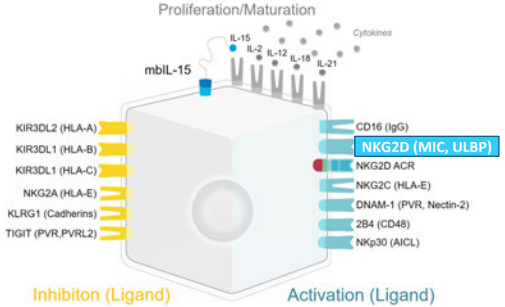
Allogeneic, non-engineered (NE) NK cells have clinical activity in AML, but significant limitations prohibit widespread use

A

- AML/high-risk MDS patients have poor prognosis[1, 2]
  - R/R AML: median OS 3.5-7.5 months
  - Intermediate to very high-risk MDS: median OS 0.8-3 years
- CAR-T success is limited by lack of AML-specific targets and a hostile microenvironment[3, 4]

B

NK cells cytotoxicity is driven by balance of activating and inhibitory receptors; NKG2D is a major activating receptor



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Systematic literature review of clinical use of allogeneic NE NK cells was undertaken by Nkarta between February and March 2019

- 586 patients (103 R/R AML) across 32 clinical trials
- 90.6% of patients were treated with haplo-matched, fresh non-engineered (NE) NK cells
- NK cells were well tolerated. Common AEs—fever, chills; higher grade AEs —cytopenias and infections
- No GVHD when given without bone marrow transplant, minimal CRS, neurotoxicity
- CRs observed in R/R AML supports use of NK cells and NKG2D ligands as a target in AML. However, major limitations in the manufacturing and cryopreservation of NK cells has restricted evaluation of higher doses and limited dosing largely to single academic centers

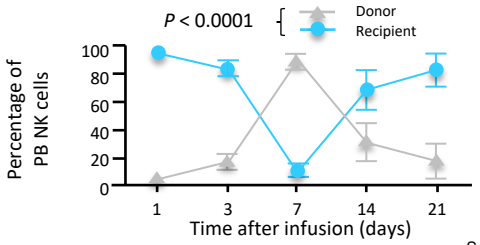
103 patients with R/R AML received single dose of haplo-matched fresh NK cells after LD

STUDY	RESPONSES*
Bachanova, 2014, A+B cohort	9 / 42 (21%)
Bachanova, C cohort	8 / 15 (53%)
Curti, 2011	1 / 5 (20%)
Kottaridis, 2015	1 / 1 (100%)
Miller, 2005	5 / 19 (26%)
Romee, 2016	5 / 9 (56%)
Rubnitz, 2015[LL]	6 / 12 (50%)
RESPONSE RATE	35 / 103 (34%)

**AML responses in patients with morphologic disease at baseline as reported in individual trials, patients with CR at study entry are excluded from summary. The 35 responses include 20 CR, 12 CRi, 2 CRp, and 1 MLFS.*

D

Transfused allogeneic NK cells are cleared commensurate with host immune recovery ~14-21 days after Cy/Flu LD



(PB = peripheral blood)

Source: Romee et al.[5]

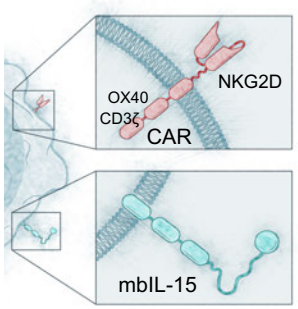
CRS = cytokine release syndrome; Cy/Flu = cyclophosphamide/fludarabine; GVHD = graft versus host disease; LD = lymphodepletion chemotherapy; MLFS = morphologic leukemia-free state; NK = natural killer; R/R = relapsed/refractory

NKX101 is an engineered NKG2D receptor CAR NK cell product that has 4- to 8-fold greater cytotoxicity and ~5X greater persistence than NE NK cells

A

NKX101: Engineered CAR NK cells with NKG2D-activating receptor, OX40 costimulatory domain, CD3ζ signaling moiety, membrane-bound IL-15

- NKG2D expression increased 10-fold compared to NE NK cells
- mbIL-15 serves as an autocrine growth factor for NK cells, potentially obviating the need for systemic cytokine support



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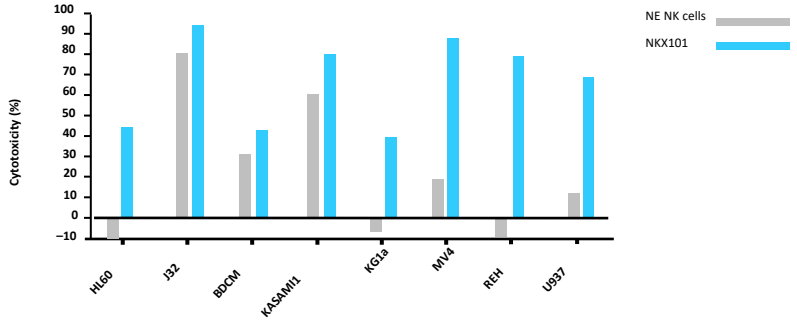
NKX101 is more cytotoxic toward AML cell lines compared to NE NK cells



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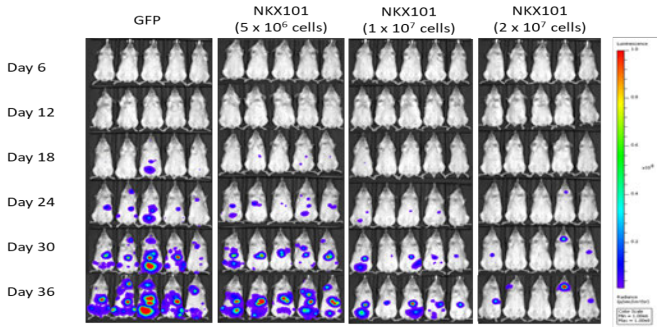
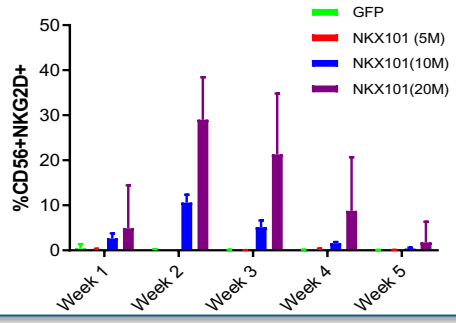
NKX101 demonstrates dose-dependent activity and persistence in immunodeficient AML mouse model



THP-1 xenograft model treated with a single dose of NK cells (i.v.) 2 days after tumor injection



NK = natural killer; NE = non-engineered

Nkarta's proprietary manufacturing technology has the potential to produce hundreds of cryopreserved NKX101 doses* from a single donor

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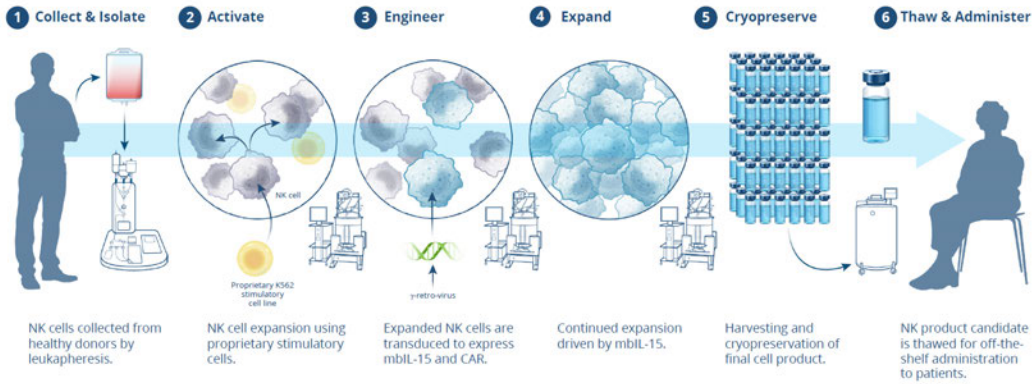

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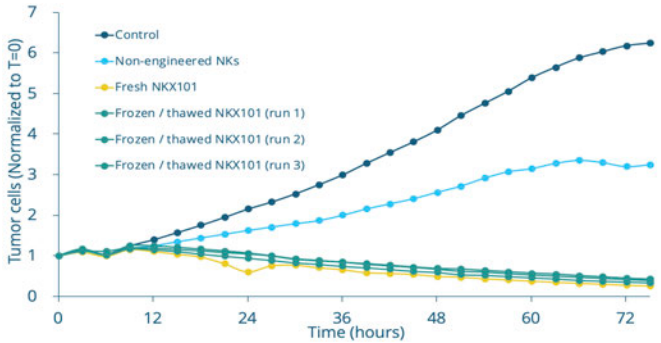
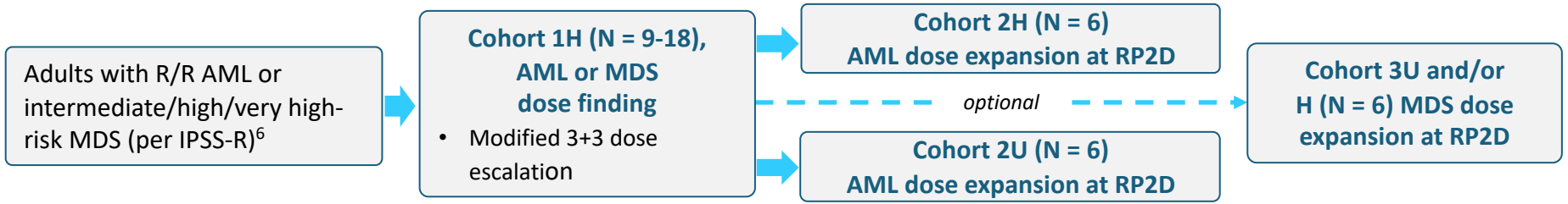
Cryopreserved and fresh NKX101 demonstrate comparable cytotoxicity in vitro



- Manufacturing process is scalable
- Cryopreserved, off-the-shelf NKX101 allows for clinical evaluation in a multicenter trial

*Assumes projected highest clinical trial dose of 1×10^9 cells/dose CAR^+ NK cells/dose

NKX101-101* is a phase 1 study evaluating the safety and activity of NKX101 monotherapy in patients with R/R AML or higher risk MDS



H = haploidentical, related donor-derived NKX101; U = unrelated donor-derived NKX101

Key Objectives

- Assess safety and tolerability, including dose-limiting toxicity (DLT)
- Identify MTD and/or RP2D
- Characterize PK, PDn, and immunogenicity
- Assess anti-tumor activity (efficacy)
- HLA, KIR and other immune regulatory ligand match/mismatch with safety and tolerability, PK, PDn, and anti-tumor activity

DLT definition

- ≥ NCI CTCAE Grade 3 non-hematological toxicity
- ≥ Grade 2 acute GVHD that is steroid refractory in non-transplant recipients

IPSS-R = International Prognosis Scoring System-Revised; MTD = maximum tolerated dose; PDn = pharmacodynamics; PK= pharmacokinetics; RP2D = recommended phase 2 dose

*ClinicalTrials.gov Identifier: NCT04623944

Study NKX101-101 enrolls a patient population with poor prognosis and limited treatment options

Key Inclusion Criteria	Key Exclusion Criteria
Adult ≥ 18 years of age	Acute promyelocytic leukemia with t(15;17) (q22;q12); or abnormal promyelocytic leukemia/retinoic acid receptor alpha (APML-RARA)
ECOG ≤ 2	Evidence of leukemic meningitis or known active CNS disease
Subjects in H cohorts: identification of suitable haplo-identical donor per BMT-CTN criteria[6]	Use of any anti-AML/MDS chemotherapeutic or targeted small molecule drug within 14 days prior or 5 half lives
AML: • R/R AML per standard ELN criteria[7] • Received at least 1 prior line of therapy. • WBC count ≤ 25 × 10^9/L • FLT3-mutated or IDH1/2-mutated disease, must have received prior appropriate targeted therapy	• Prior allogeneic transplant or donor lymphocyte infusion (DLI) for U cohorts • Any hematopoietic cell transplantation within 16 weeks prior to the first dose of NKX101
	Presence of residual non-hematologic toxicity from prior therapies that has not resolved to ≤ Grade 1
MDS: • Intermediate, high, or very high-risk MDS (per WHO and revised International Prognostic Scoring System[8]) • R/R MDS per standard IWG criteria, must have received 1 prior line of therapy[9]	Other comorbid conditions and concomitant medications prohibited as per study protocol
	Use of any prior CAR T or allogeneic adoptive NK cell therapy prior to the first dose of NKX101
Adequate organ function	Pregnant or lactating female

3 doses of NKX101 administered after lymphodepletion; 3 dose levels evaluated

	Cycle 1 *(Cycle 2 for patients with CR MRD+ with FDA concurrence)*																
	LD Chemotherapy					**NKX101 I.V. Administration; 28-day cycle**											
Study Day	–5	–4	–3	–2	–1	0	1	2-6	7	8	9-13	14	15	16-19	20	21-26	27	EOT
Study Treatment	✕	✕	✕			✕			✕			✕						
Safety	✕					✕	✕		✕	✕		✕	✕		✕			✕
PK	✕					✕	✕		✕	✕		✕	✕		✕		✕	✕
Efficacy	✕																✕	✕

- 3 doses of NKX101 per cycle after a single standard fludarabine/cyclophosphamide lymphodepletion chemotherapy
- 3 NKX101 dose levels planned: 1×10^8, 3×10^8, 1×10^9 viable CAR NK cells
- Dose finding with haplo-matched, donor-derived NKX101 builds on existing data with non-engineered NK cells
- Transitioning to unrelated donor-derived off-the-shelf NKX101 for dose expansion
  - As NKX101 is administered after host immune system conditioning, off-the-shelf NKX101 is expected to have similar persistence and anti-tumor activity as haplo-matched donor-derived cells
- Minimum 24-hour monitoring on NKX101 dosing days; proximity to (within 2-hour drive) study center for 1-week post-NKX101 infusion
  - Potential to decrease monitoring duration in later cohorts if protocol-specified safety criteria are met
- DLT observation period: Day 0-27 of treatment cycle
- Preliminary efficacy assessment: AML per updated ELN criteria[7], MDS using modified IWG criteria[9]

Summary

- High unmet need for patients with R/R AML and higher-risk MDS despite recent drug approvals
- CRs noted with use of non-engineered allogeneic NK cells in small academic studies but manufacturing limitations restrict widespread evaluation and dosing
  - Nkarta's proprietary manufacturing technology can produce cryopreserved NKX101, supporting multicenter evaluation
- NKX101 demonstrates increased potency against AML cells in vitro and in vivo preclinical studies and retains cytotoxicity after cryopreservation compared to fresh NE NK cells
- NKX101-101 is a first-in-human, multicenter trial of allogeneic NKX101 monotherapy in R/R AML/MDS patients with poor prognosis and limited treatment options
  - NKX101 monotherapy is administered after lymphodepletion; 3 dose levels of NKX101 are planned to evaluate safety, tolerability, PK, PD, and preliminary efficacy
  - Trial is designed to systematically evaluate activity of both haplo-related and unrelated off-the-shelf donor-derived NKX101
- **Trial is currently enrolling (NCT04623944)**

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