FIRST IN HUMAN DATA OF NKX019, AN ALLOGENEIC CAR NK FOR THE TREATMENT OF RELAPSED/REFRACTORY (R/R) B-CELL MALIGNANCIES

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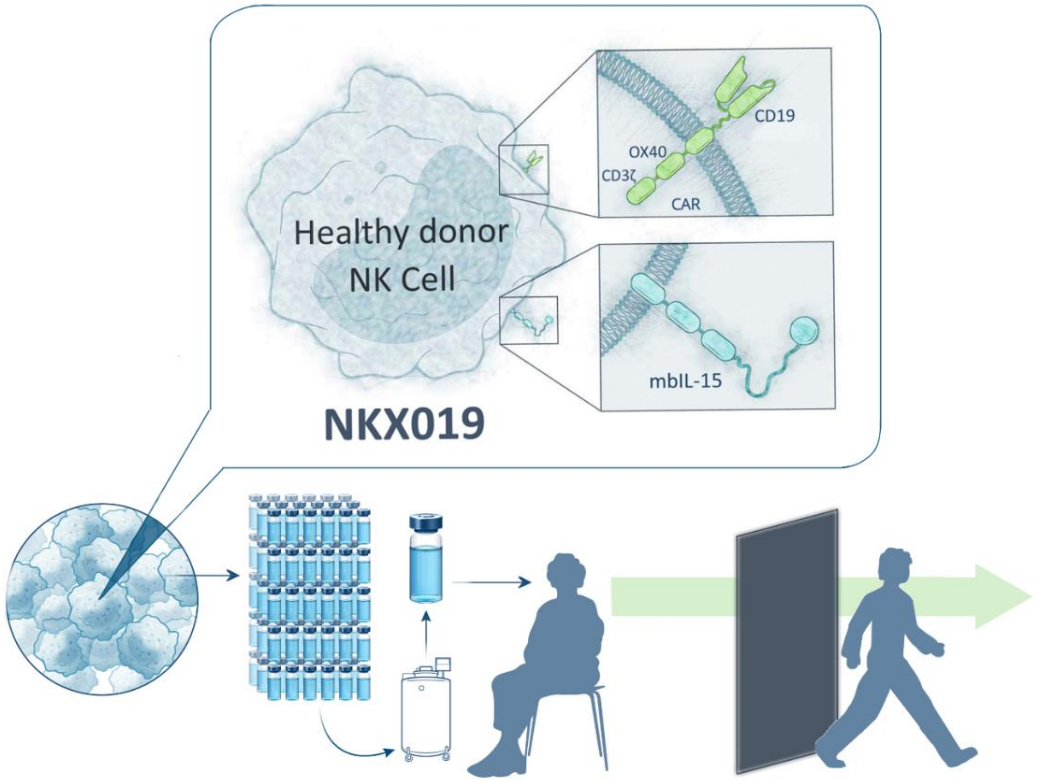
Autologous CAR T-cell Therapy Transformative but with Limitations

- Custom manufacturing of auto CAR T-cell therapy precludes precludes prompt treatment and can result in manufacturing failure
- T-cell mediated toxicities are common and can be severe, thereby limiting the population of eligible patients
- Administration of CAR T-cell therapy is limited to certified treatment centers, further restricting patient access

CAR: chimeric antigen receptor; CR: complete response; CRS: cytokine release syndrome; ICANS: immune cell associated neurotoxicity syndrome; ICU: intensive care unit; LBCL: large B-cell lymphoma; NHL: non- lymphoma; USPI: U.S. Prescribing Information.

NKX019: On Demand Allogeneic NK Based Cellular Therapy



- NK cells provide important antigen independent tumor surveillance and kill tumor cells via a balance of activating and inhibitory signals
- NKX019 is a cryopreserved, allogeneic CD19-targeting CAR NK-cell therapy, derived from healthy donors
- NKX019 contains an OX40 costimulatory domain as well as mbIL-15 for activation

A Multicenter, Open-Label, Phase 1 Study of NKX019

Key Inclusion Criteria

- r/r CD19+ B-cell malignancies
- Received ≥2 prior lines of therapy
- ECOG PS 0 or 1
- CAR T-cell therapy naïve (dose-finding phase)

Endpoints:

- Safety and tolerability
- Anti-tumor activity
- Pharmacokinetics

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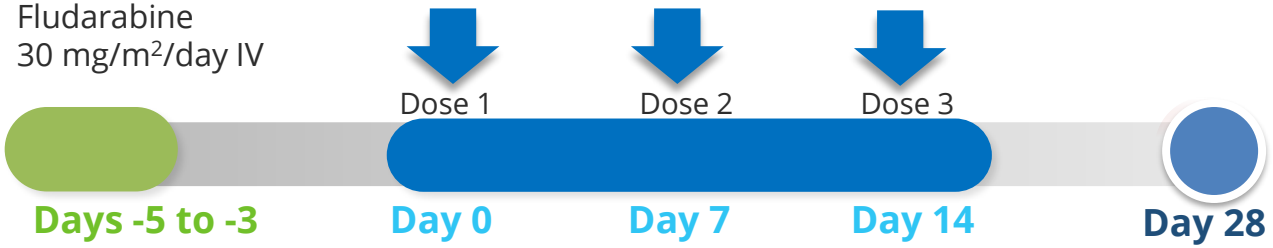
Lymphodepletion

- Cyclophosphamide 300 mg/m^2/day IV (dose-finding phase)
- Fludarabine 30 mg/m^2/day IV

NKX019

3 doses per 28-day cycle



- Multiple cycles allowed to **deepen response** for subjects tolerating and benefiting from treatment
- Subjects in **CR** may receive additional cycle as **consolidation**

Efficacy assessment*

Post-treatment follow-up

Subjects with initial clinical benefit and subsequent progression may receive **retreatment**

**Efficacy based on: Lugano criteria for NHL; 2018 iwCLL guidelines for CLL; NCCN v1.2020 for B-ALL*
CAR: chimeric antigen receptor; CR: complete response; ECOG PS: Eastern Cooperative Oncology Group performance status; EOT: end of therapy; r/r: relapsed/refractory; iwCLL: International Workshop on Chronic Lymphocytic Leukemia; NCCN: National Comprehensive Cancer Network.

Baseline Characteristics

	Total (N=19)
Age, median (range)	**59 (21-82)**
Baseline ECOG PS 1	**13**
Australia/US	**13/6**
Diagnosis	
Large B cell lymphoma (LBCL)[#] IPI 3+	**7** 3 (43%)
Follicular lymphoma (FL) FLIPI high risk	**5** 3 (60%)
Marginal zone lymphoma (MZL)	**1**
Mantle cell lymphoma (MCL)	**1**
Chronic lymphocytic leukemia (CLL)	**2**
B-cell acute lymphoblastic leukemia (B-ALL)	**3**
Prior lines of therapy, median (range)	**4 (2 - 10)**

[#]LBCL includes 6 DLBCL and 1 FL3b.

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DLBCL: diffuse large B-cell lymphoma; ECOG PS: Eastern Cooperative Oncology Group performance status; FL3b: follicular lymphoma grade 3b; FLIPI: Follicular Lymphoma International Prognostic Index; LBCL: large B-cell lymphoma; NHL: non-Hodgkin lymphoma.

NKX019 Toxicity Profile

- No ICANS / neurotoxicity, GVHD, Grade 5
- No dose-limiting toxicities
- One (5%) Grade ≥ 3 infection
- Myelosuppression, consistent with standard lymphodepletion, was the most common Grade ≥ 3 toxicity and manageable

Grade 3/4 AEs in >1 subject	Total N=19
Subjects with any ≥ Grade 3 AEs	16 (84%)
Neutrophil count decreased	12 (63%)
Platelet count decreased	8 (42%)
Febrile neutropenia	5 (26%)
Anemia	4 (21%)
WBC count decreased	3 (16%)
Lymphocyte count decreased	2 (11%)

Treatment-emergent AEs regardless of relationship.

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AE: adverse event; GVHD: graft versus host disease; ICANS: immune effector cell-associated neurotoxicity syndrome. WBC: white blood cell count.

Transient and Manageable Infusion-Related Effects

5/19 patients (26%) developed fever within 8 hours that resolved within 24 hours

Patient	Grade	Investigator assessment	Anti-IL-6 therapy	Steroids	Description of event
#1	G1	IRR	N	N	Fever within 8 hours; resolved with antipyretics and did not recur
#2	G1	IRR	N	N	Fever within 5 hours; resolved with antipyretics and did not recur
#3	G2	CRS	N	N	Fever and hypotension within 8 hours; resolved with antipyretics and did not recur
	G1	CRS	N	N	Fever within 6 hours; resolved with antipyretics and did not recur
#4	G3	CRS	Y	Y	Fever and hypoxia within 5 hours; fever resolved within 24 hours and did not recur
#5	G1	IRR	N	N	Tachycardia (no fever) within 3 hours; resolved within 24 hours without intervention
	G2	CRS	Y	N	Fever with hypotension and hypoxia within 6 hours; symptoms resolved within 24 hours after treatment and did not recur

No apparent association between symptoms and response

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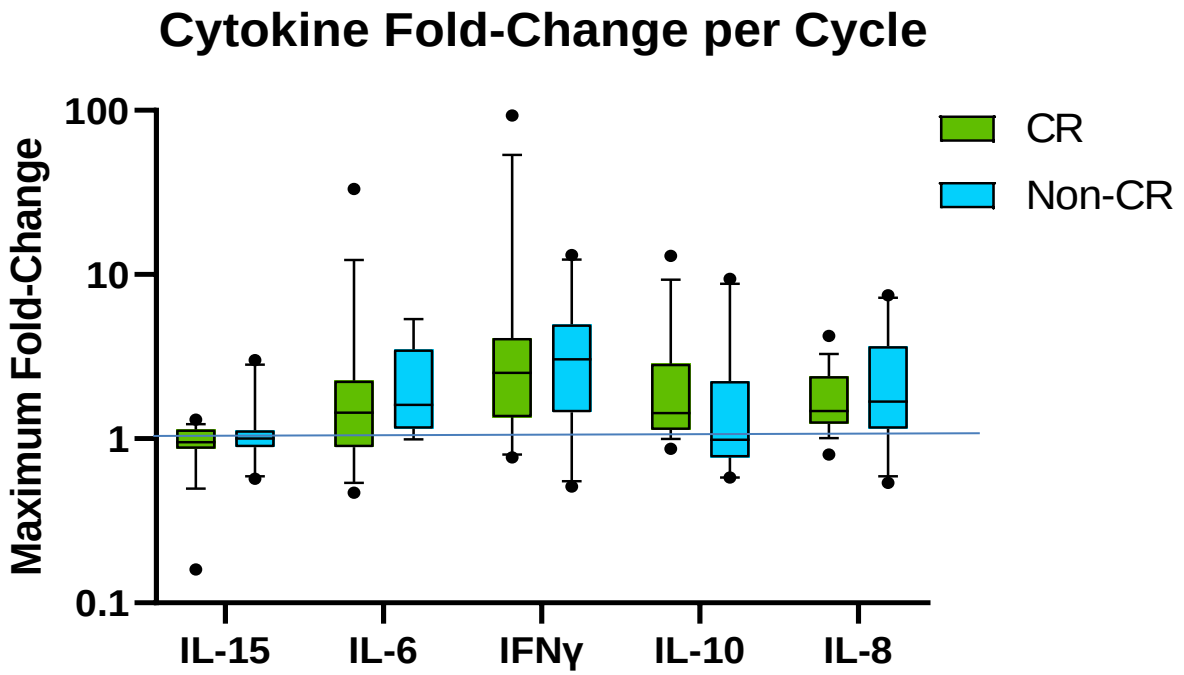
CAR: chimeric antigen receptor; CRS: cytokine release syndrome; G: grade.

Modest Cytokine Change from Baseline

- IL-6, IFNγ, IL-10, and IL-8 levels were measured at baseline and several timepoints during the 28 day treatment cycle
- Minimal elevations above baseline
- No association between elevated serum cytokines and clinical response



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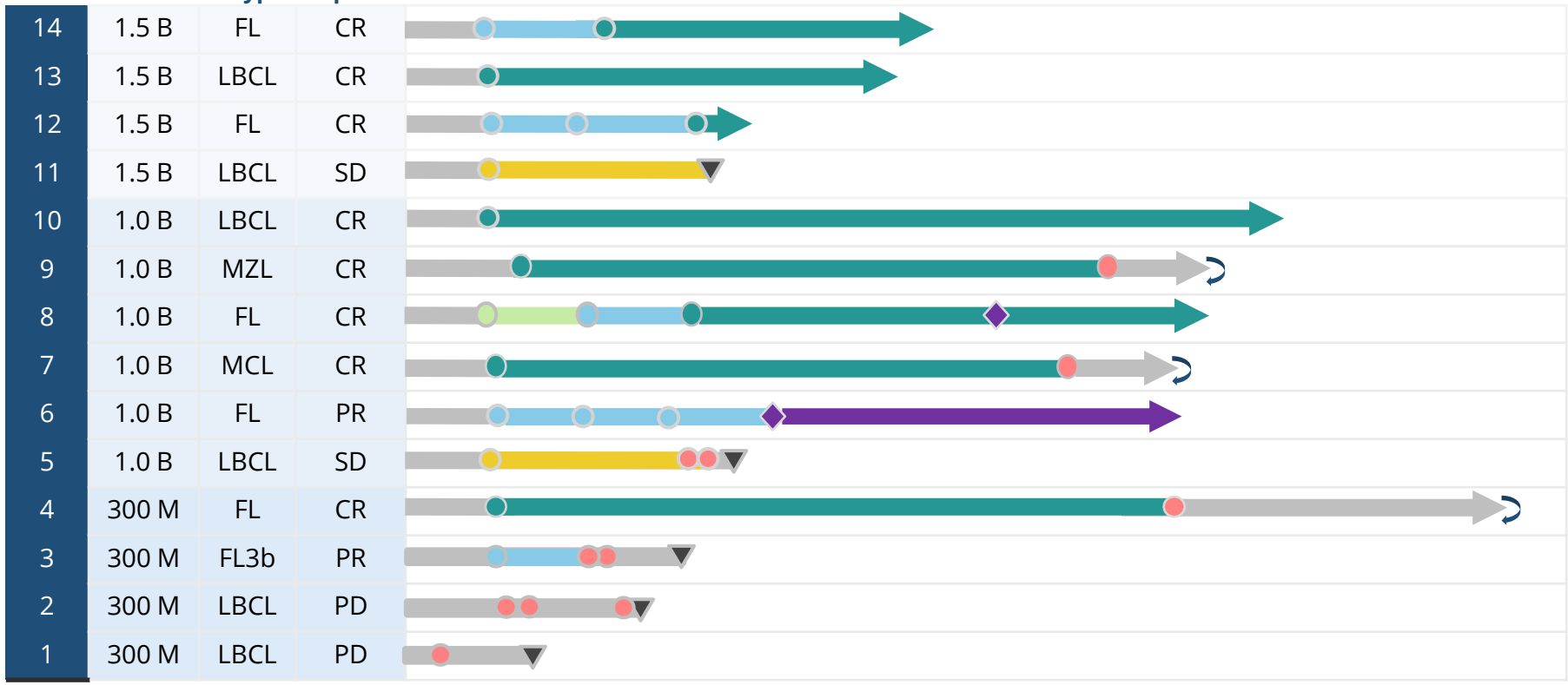
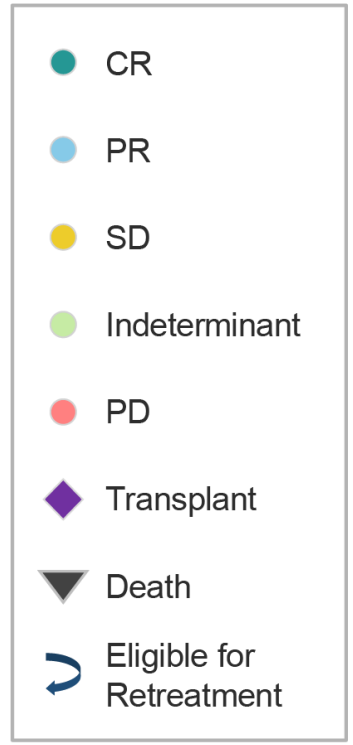
M. Davila et al., *Sci Transl Med*. 2014; Hay et al., *Blood*, 2017.

CAR: chimeric antigen receptor; CR: complete response; CRS: cytokine release syndrome.

Efficacy Across Histologies

Patient	Cells	NHL Subtype	Best Response
14	1.5 B	FL	CR
13	1.5 B	LBCL	CR
12	1.5 B	FL	CR
11	1.5 B	LBCL	SD
10	1.0 B	LBCL	CR
9	1.0 B	MZL	CR
8	1.0 B	FL	CR
7	1.0 B	MCL	CR
6	1.0 B	FL	PR
5	1.0 B	LBCL	SD
4	300 M	FL	CR
3	300 M	FL3b	PR
2	300 M	LBCL	PD
1	300 M	LBCL	PD





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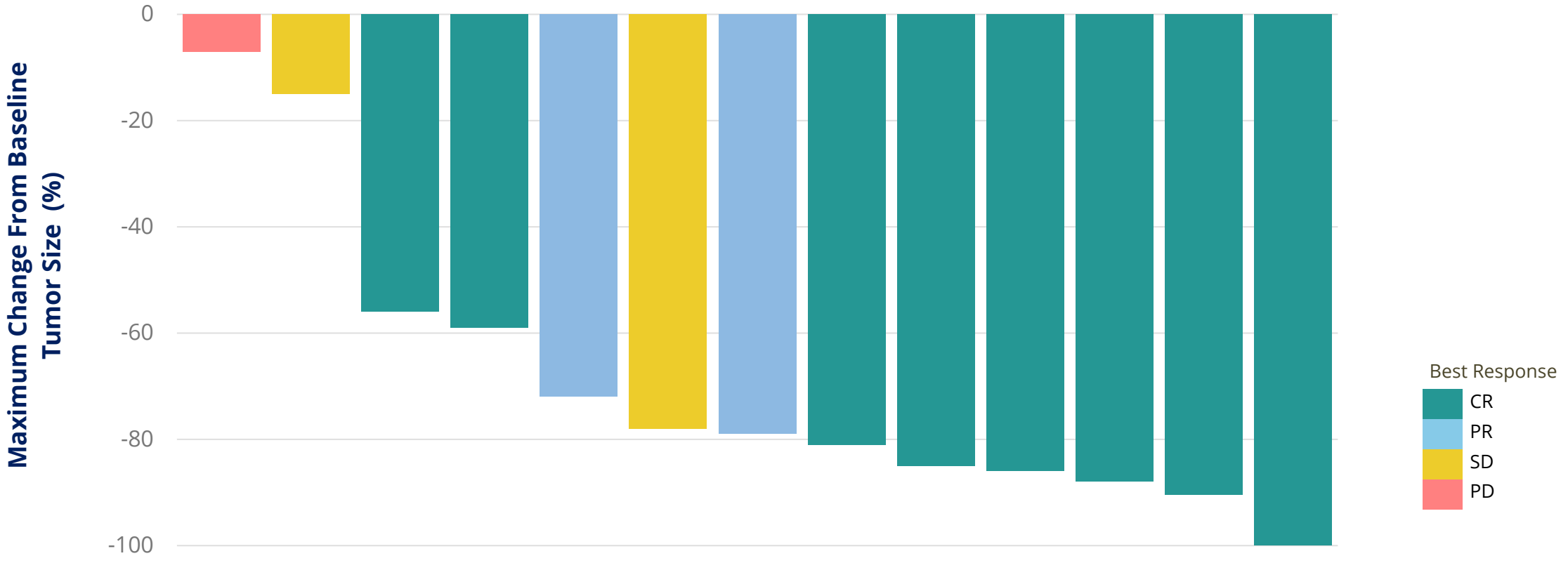
CR: complete response; FL: follicular lymphoma; FL3b: follicular lymphoma grade 3b; LBCL: large B-cell lymphoma; MCL: mantle cell lymphoma; MZL: marginal zone lymphoma; PD: progressive disease; PR: partial response; SD: stable disease.

Tumor Reduction with NKX019



One patient discontinued therapy after a single dose and did not have follow up evaluation

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NKX019 at Higher Doses Correlated with Higher C_{max}

Dose Level	C_{max}	All subjects	CR	Non-CR
300 M cells	**n**	5	1	4
	Median (range)	***< 6.7*** (< *6.7*-393)	**393** (393)	***< 6.7*** (< *6.7*-234)
1 B/1.5 B cells	**n**	14	7	7
	Median (range)	**156.9** (< *6.7*-567.0)	**298** (< *6.7*-567.0)	***< 6.7*** (< *6.7*-481)

6.7 = Lower limit of quantification
C_{max}, given as transgene copies/µg of DNA.

Peak concentration trended higher in patients achieving CR

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C_{MAX}, peak detected concentration; CR: complete response.

Conclusions

- NKX019 had no DLTs, ICANS, GVHD, or Grade > 3 CRS
- At highest dose levels, 8 of 10 patients with NHL responded (80% ORR), and 7 of 10 patients achieved complete responses (70% CR), including 50% CR in LBCL
- Deep responses with durability > 6 months in multiple patients with potential for retreatment should tumor recur
- On demand availability and manageable safety profile make outpatient administration possible

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Acknowledgements

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