NEW PATHWAYS TO SMARTER MEDICINE™

Role of IL-15 within the Cell Therapy Landscape

Investor and Analyst Event

December 2022

This presentation includes forward-looking statements regarding Nektar's proprietary drug candidates, the timing of the start of and plans for ongoing or planned clinical trials with partners, the therapeutic potential of our drug candidates, the timing and outcome of regulatory decisions, and future availability of clinical trial data. Actual results could differ materially, and these statements are subject to important risks detailed in Nektar's filings with the SEC including the Form 10-Q filed on November 4, 2022. Nektar undertakes no obligation to update forward-looking statements as a result of new information or otherwise.

Today’s Speakers

Mary Tagliaferri, MD

Chief Development Officer
at Nektar Therapeutics

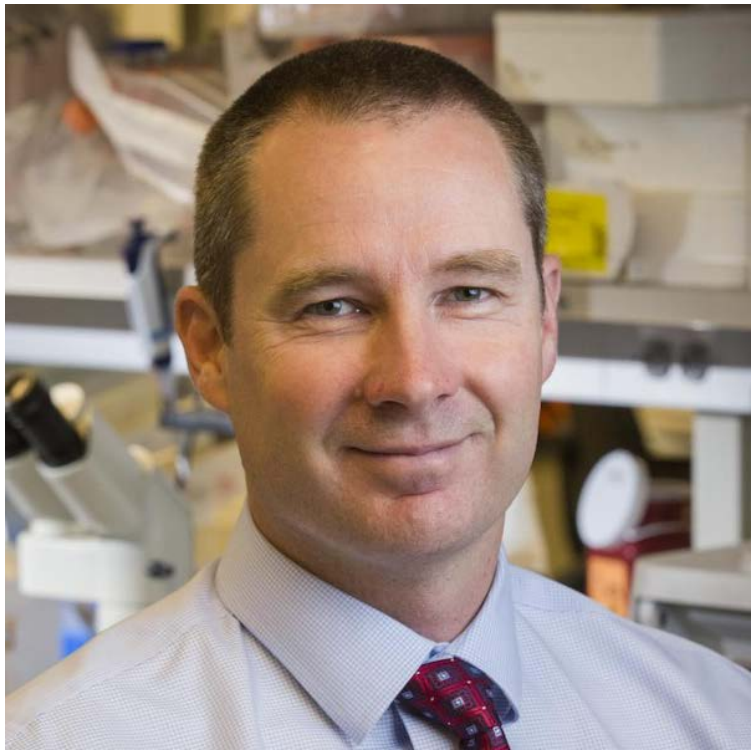
Mario Marcondes, MD, PhD

VP, Head of Clinical Development
at Nektar Therapeutics

Cameron Turtle, MBBS, PhD

Chair of Cancer Immunotherapy
at University of Sydney and
Fred Hutchinson Cancer Center
affiliate

Cameron Turtle, MBBS, PhD – University of Sydney



Cameron Turtle, MBBS, PhD, spent 16 years at Fred Hutchinson Cancer Research Center, the University of Washington, and Seattle Cancer Care Alliance (SCCA). He served as Professor of Medicine and as an attending physician, specializing in treating blood diseases with cellular immunotherapies and hematopoietic stem cell transplantation. He is now the Chair of Cancer Immunotherapy at Sydney Medical School at the University of Sydney, Australia. He is a leader in the field of immuno-oncology and novel T cell therapies and has led many clinical trials evaluating chimeric antigen receptor T (CAR-T) cell therapies in non-Hodgkin's lymphoma, acute lymphoblastic leukemia, and chronic lymphocytic leukemia. Dr. Turtle designed the investigator-sponsored, Phase 1 trial at Fred Hutchinson Cancer Research Center of NKTR-255 in combination with Breyanzi, an approved CAR-T cell therapy, in patients with relapsed or refractory large B cell lymphoma.

Agenda

Role of IL-15 within the Cell Therapy Landscape

- ***ASH 2022: "Safety, Tolerability, PK/PD, and Preliminary Efficacy of NKTR-255, a Novel IL-15 Receptor Agonist, in Patients with Relapsed/Refractory Hematologic Malignancies"***
  - *Mary Tagliaferri, MD, Nektar Therapeutics*
- ***Overview of Cell Therapy Landscape and Rationale for NKTR-255 Combination with CAR-T***
  - *Cameron Turtle, MBBS, PhD, University of Sydney and Fred Hutchinson Cancer Center (Turtle Lab)*
- ***Ongoing and Planned Studies***
  - *Mary Tagliaferri, MD, Nektar Therapeutics*
- ***Q&A Session***

3 Pillars of Development Strategy for NKTR-255

Potentiate Cellular Therapies

- Phase 2/3 study combining NKTR-255 with commercially approved CD-19 targeted CAR T cell therapies in 2L+ relapsed/refractory DLBCL
- Phase 1/2 IST with Stanford (Dr. Crystal Mackall) combining NKTR-255 with CD19/CD22 CAR T cell therapies in B-cell ALL
- Phase 1/2 IST with Fred Hutchinson (Dr. Cameron Turtle) combining NKTR-255 with Breyanzi in LBCL

Augment ADCC

- Phase 1/2 study combining NKTR-255 with NKTR-255 + Daratumumab in Multiple Myeloma
- Phase 1/2 study combining NKTR-255 with Cetuximab in HNSCC

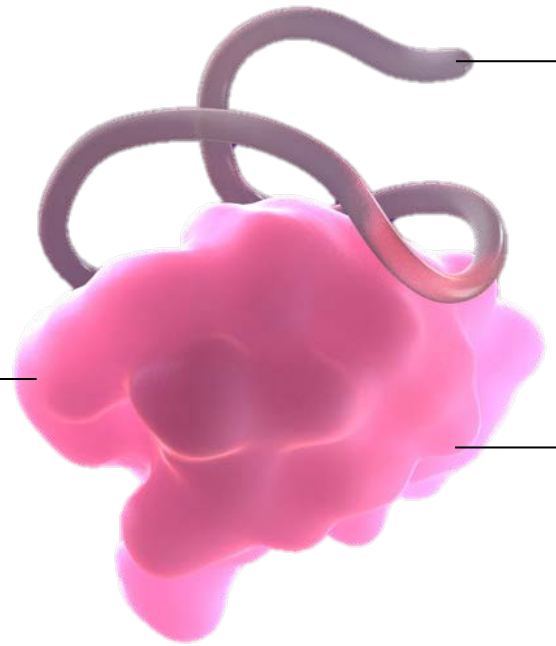
Synergize with Checkpoint Inhibitors

- Phase 2 study with Merck KGaA combining NKTR-255 plus avelumab in patients with mUC in the maintenance setting (Bladder Javelin Medley Trial)
- Phase 1/2 IST with MDACC (Dr. Steven Lin) combining NKTR-255 plus durvalumab in patients with Stage 3 NSCLC and lymphopenia

NKTR-255: IL-15 Agonist Designed to Capture Full Receptor Binding

Nektar leveraged polymer conjugation technology used in approved PEGylation products to create NKTR-255

Native IL-15 amino acid sequence with no mutagenesis retains IL-15Rα binding specificity and maintains IL-15 biological context

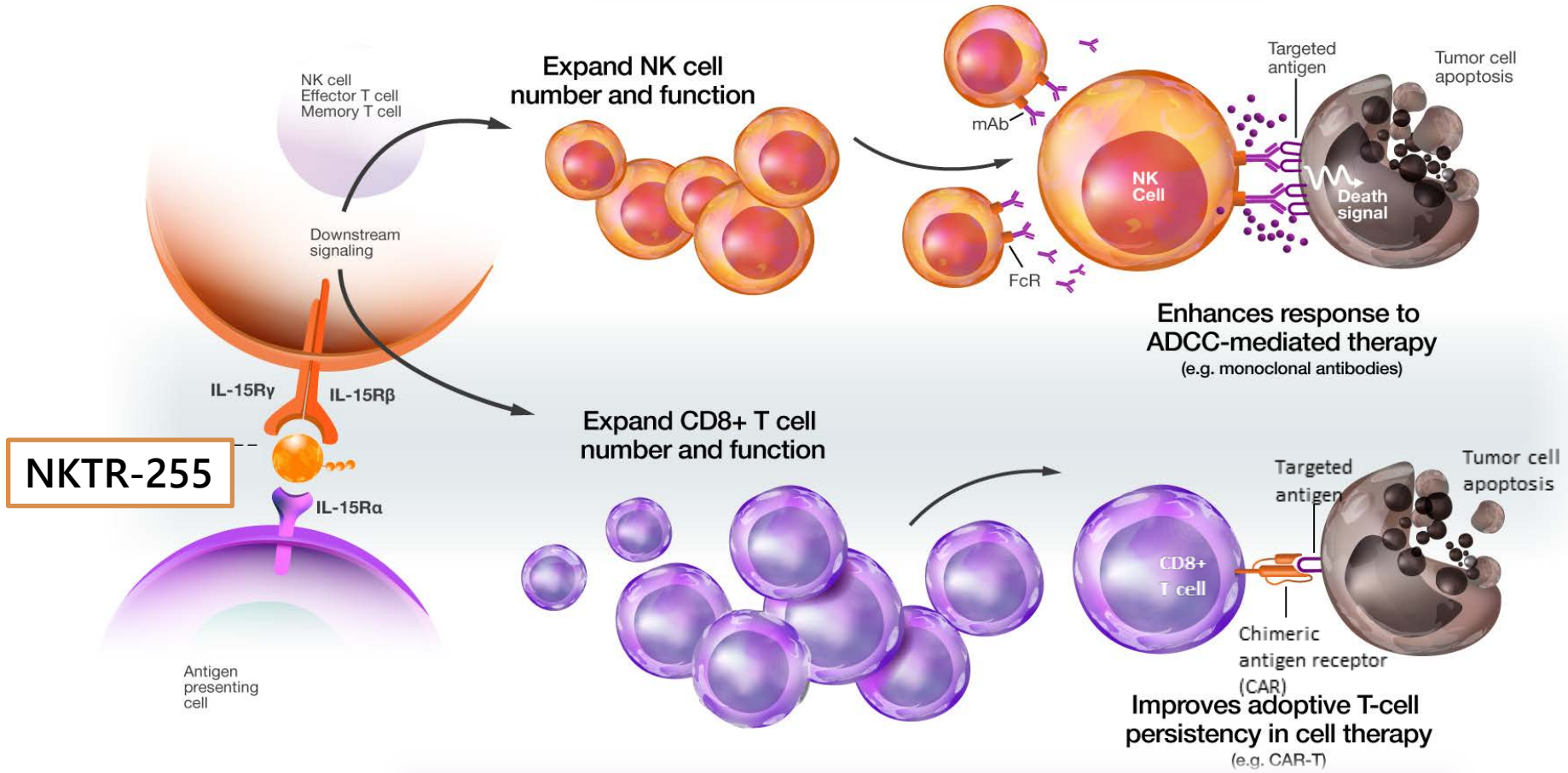


PEG moiety improves PK and PD of native IL-15 (Q3W/Q4W dosing) to increase CD8+ T cell and NK cell number and function in patients

Streamlined and scalable manufacturing process

NKTR-255 is Designed to Boost NK Cells and Expand CD8+ Effector and Memory T-cells

Boost NK cell numbers and function



Enhancement of ADCC Antibodies

Daratumumab
Rituximab
Cetuximab

Potential to combine with any targeted antibody that utilizes an ADCC MOA

Enhancement of CAR-T Regimens

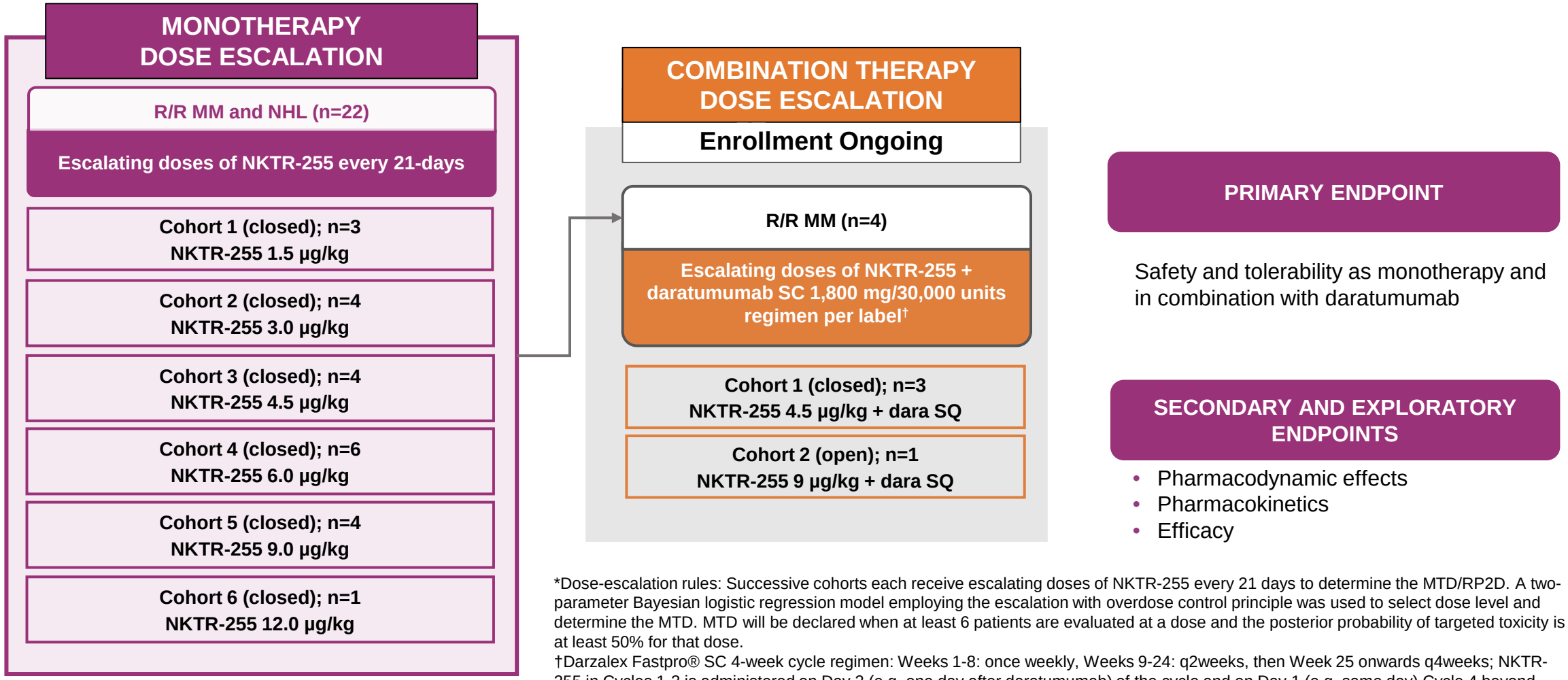
CD19 CAR-T
BCMA CAR-T
CD38 CAR-T

Potential to expand into other hematological and solid tumor CAR-T and cellular therapies

Increase duration of response for CAR-T and cellular therapies

ADCC: Antibody-dependent cellular cytotoxicity; IL-15, interleukin-15

ASH 2022: Study Design and Patients



PRIMARY ENDPOINT

Safety and tolerability as monotherapy and in combination with daratumumab

SECONDARY AND EXPLORATORY ENDPOINTS

- Pharmacodynamic effects
- Pharmacokinetics
- Efficacy

*Dose-escalation rules: Successive cohorts each receive escalating doses of NKTR-255 every 21 days to determine the MTD/RP2D. A two-parameter Bayesian logistic regression model employing the escalation with overdose control principle was used to select dose level and determine the MTD. MTD will be declared when at least 6 patients are evaluated at a dose and the posterior probability of targeted toxicity is at least 50% for that dose.

†Darzalex Fastpro® SC 4-week cycle regimen: Weeks 1-8: once weekly, Weeks 9-24: q2weeks, then Week 25 onwards q4weeks; NKTR-255 in Cycles 1-3 is administered on Day 2 (e.g. one day after daratumumab) of the cycle and on Day 1 (e.g. same day) Cycle 4 beyond

ASH 2022: Heavily Pre-treated Population Enrolled in NKTR-255 Dose-Escalation Phase (n=26)

Patient Demographics and Disease Characteristics

Patients with NHL (n=8)		
Median age (range), years		65.5 (59–80)
Sex, n (%)	Female Male	4 (50) 4 (50)
Median (range) time since diagnosis, months		53.6 (12.9–226.0)
Median (range) number of prior therapies		4 (1–12)
Disease subtype, n (%)	Large B-cell lymphoma Diffuse large B-cell Lymphoma Follicular lymphoma Other/missing	1 (13) 4 (50) 2 (25) 1 (13)
Bulky disease, n (%)	Yes No Unknown	1 (13) 6 (75) 1 (13)
Prior therapies of interest, n (%)	Autologous stem cell transplants Allogeneic stem cell transplants CAR-T	2 (25) 1 (13) 4 (50)
CD20 containing regimens, n (%)	Rituximab	8 (100)
International Prognostic Index score, n (%)	0–1 2–3 4–5 Unknown	1 (13) 3 (38) 3 (38) 1 (13)

Patients with MM (n=18)			
	NKTR-255 monotherapy (n=14)		NKTR-255 + Dara (n=4)
Median age (range), years		64.0 (49–78)	61.5 (52–70)
Sex, n (%)	Female Male	4 (29) 10 (71)	2 (50) 2 (50)
Median (range) time since diagnosis, months		86.0 (25.2–231.7)	122.4 (90.9–174.3)
Median (range) number of prior therapies		6 (3–16)	5.5 (5–10)
Cytogenetic risk, n (%)	Standard Intermediate High Not Available	7 (50) 0 5 (38) 2 (14)	2 (50) 1 (25) 1 (25) 0
Paraprotein type, n (%)	IgG IgA Light chain myeloma Unknown	7 (50) 3 (21) 2 (14) 2 (14)	1 (25) 1 (25) 2 (50) 0
Prior therapies of interest, n (%)	Autologous stem cell transplants Allogeneic stem cell transplants CAR-T	9 (64) 1 (7) 6 (43)	3 (75) 1 (25) 3 (75)
	IMiD Lenalidomide Proteasome inhibitor	14 (100) 13 (93) 14 (100)	4 (100) 4 (100) 4 (100)
CD38 experience, n (%)	Yes	14 (100)	4 (100)
ISS stage at screening, n (%)	I II III IV Not Available	7 (50) 4 (28) 1 (7) 0 2 (14)	2 (50) 1 (25) 0 0 1 (25)

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Clinical cutoff: October 20, 2022. CAR-T, chimeric antigen receptor T-cell therapy; CD, cluster of differentiation; IgA/G, immunoglobulin A/G; IMiD, Immunomodulatory imide drugs; ISS, International Staging System; MM, multiple myeloma; NHL, non-Hodgkin lymphoma.

ASH 2022: Most TRAEs were Transient and Resolved Spontaneously or Using Standard Treatment Protocols

Select TRAEs; n (%)	1.5 µg/kg (n=3)	3 µg/kg (n=4)	4.5 µg/kg (n=4)	6 µg/kg (n=6)	9 µg/kg (n=4)	12 µg/kg (n=1)	4.5 µg/kg + dara (n=3)	9 µg/kg + dara (n=1)	Total (N=26)
Grade 1 or 2 (≥25% of safety population)									
Flu-like symptoms[a]	2 (67)	4 (100)	4 (100)	5 (100)	2 (50)	1 (100)	2 (67)	0	20 (77)
Infusion-related reaction	0	0	3 (75)	3 (50)	2 (50)	1 (100)	1 (33)	1 (100)	11 (42)
Fatigue	0	2 (50)	1 (25)	3 (50)	2 (50)	1 (100)	2 (66)	0	11 (42)
Grade 3 (≥5% of safety population)									
Neutropenia[b]	0	1 (25)	1 (25)	0	1 (25)	1 (100)	0	0	4 (18)
Anemia	0	0	0	1 (17)	1 (25)	0	0	0	2 (8)
Thrombocytopenia	0	0	0	1 (17)	1 (25)	0	0	0	2 (8)
Lymphopenia[c]	0	1 (25)	0	0	0	1 (100)	0	0	2 (8)
Grade 4 (all)									
Lymphopenia[c]	0	0	2 (50)	2 (33)	1 (25)	0	0	0	5 (19)

- 12 (46%) patients experienced serious TEAEs, of which 8 (31%) were NKTR-255 related. Serious TEAEs that occurred in 2 or more patients are IRR (Grade 1-2, n=5), CRS (Grade 1, n=2)
- Grade ≥3 lymphopenia occurred in 27% (7/26) of patients receiving NKTR-255. The median time to baseline recovery for these lymphopenia events was 3 days (range: 2 to 9 days)
- No ADAs detected in 54 samples collected from 17 subjects treated with NKTR-255 monotherapy for up to 8 cycles over the dose range of 1.5 to 9 µg/kg.

Clinical cutoff: October 20, 2022. During the first cycle, patients were not allowed to receive pre-medications (e.g. antipyretic/antihistamines). Patients counted only once within each preferred or grouped term, using highest reported toxicity grade.

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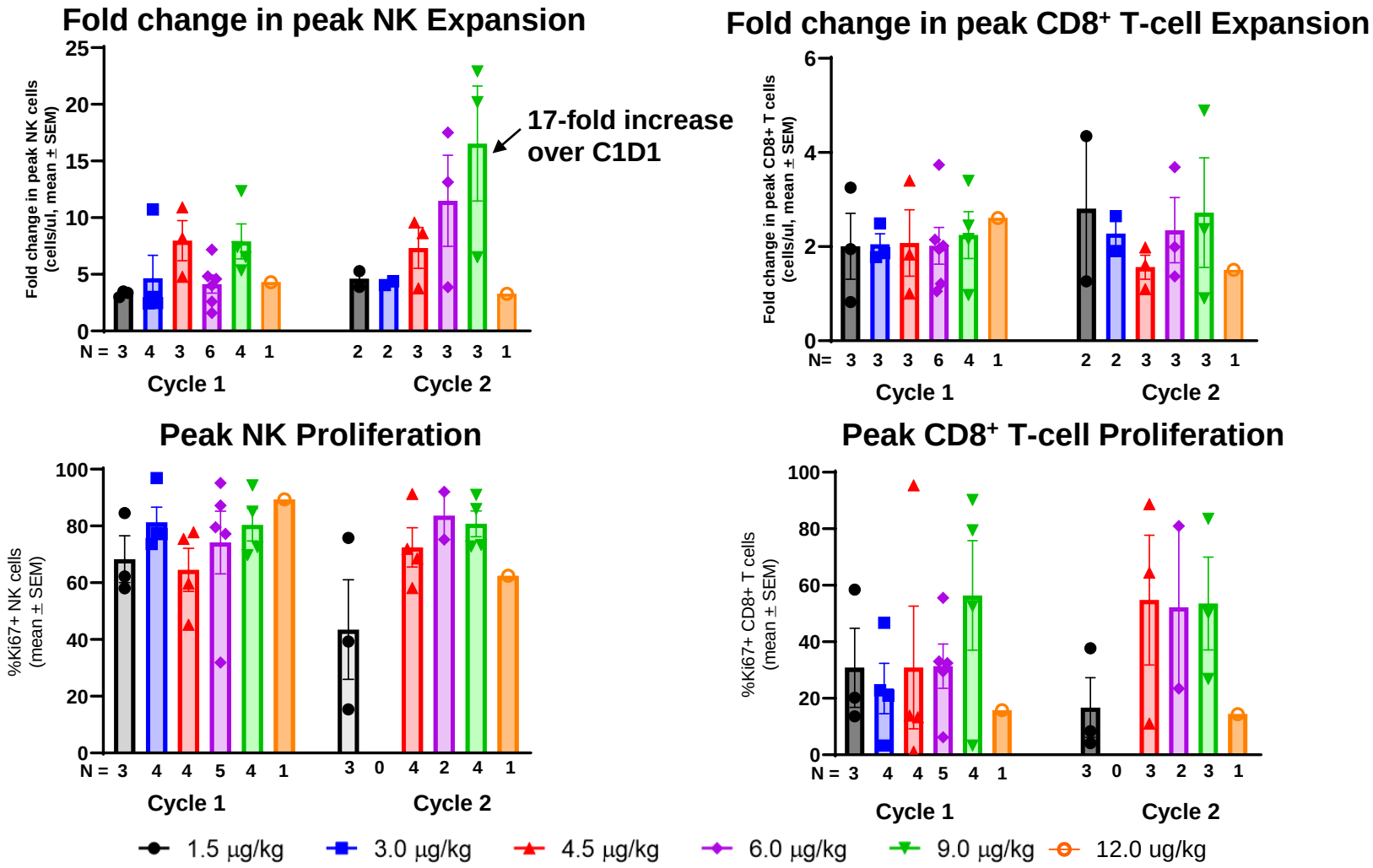
[a]Group term includes body temperature increased, chills, headache, myalgia, hyperhidrosis, hyperpyrexia, influenza like illness, nausea, pyrexia, [b]Group term includes neutropenia, leukopenia and white blood cell count decreased, [C]Group term includes lymphopenia and lymphocyte count decreased

ASH 2022: NKTR-255 Monotherapy Led to Expansion and Increased Proliferative Capacity of NK and CD8+ T cells

Peak expansion and proliferation in Cycles 1 and 2



Fold change in cell numbers calculated from C1D1/predose; peak response of cellular expansion at D8-D10 of each cycle

Peak proliferative response at D4 for most patients; no Ki67 data available for 3.0 µg/kg patients in C2

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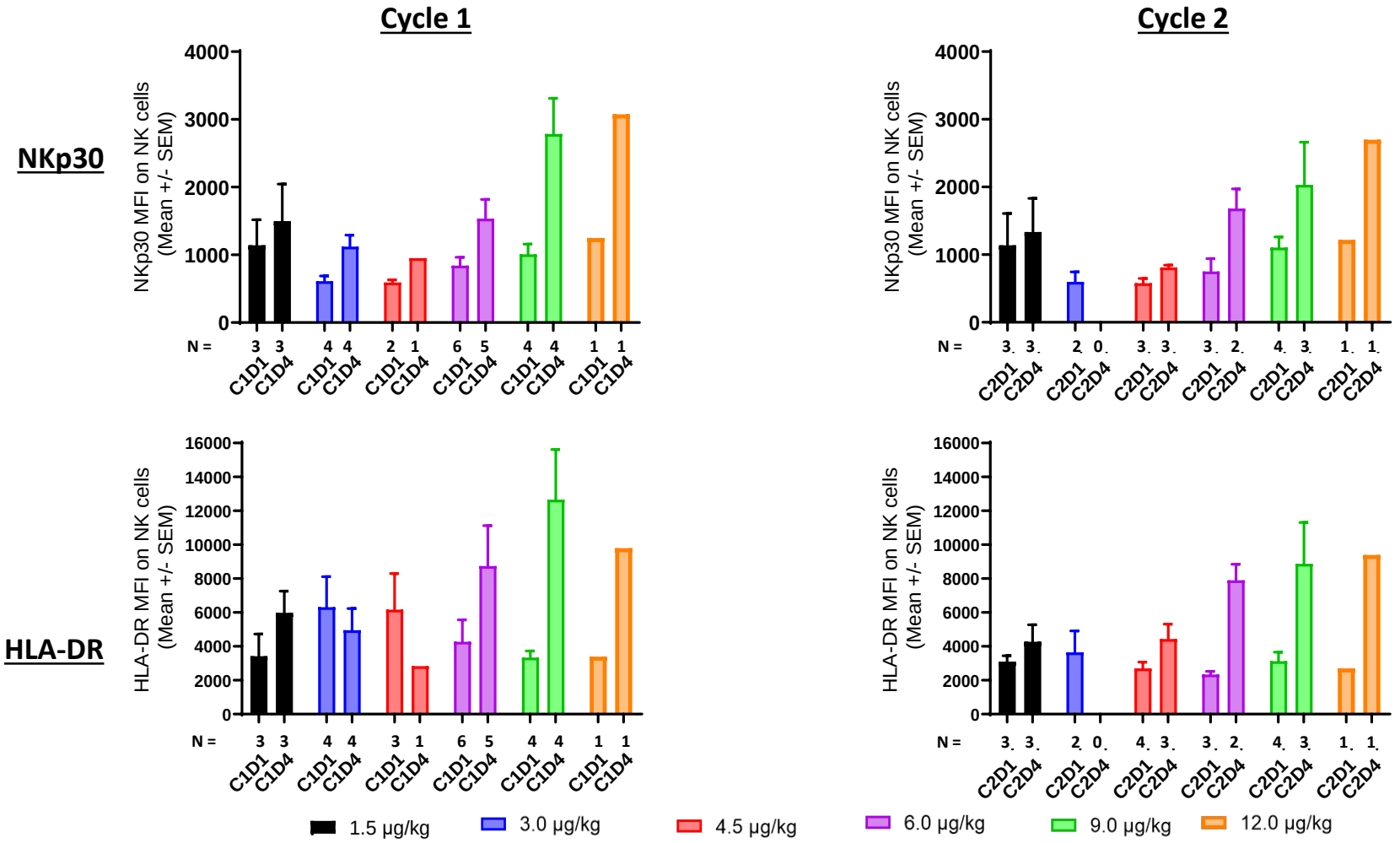
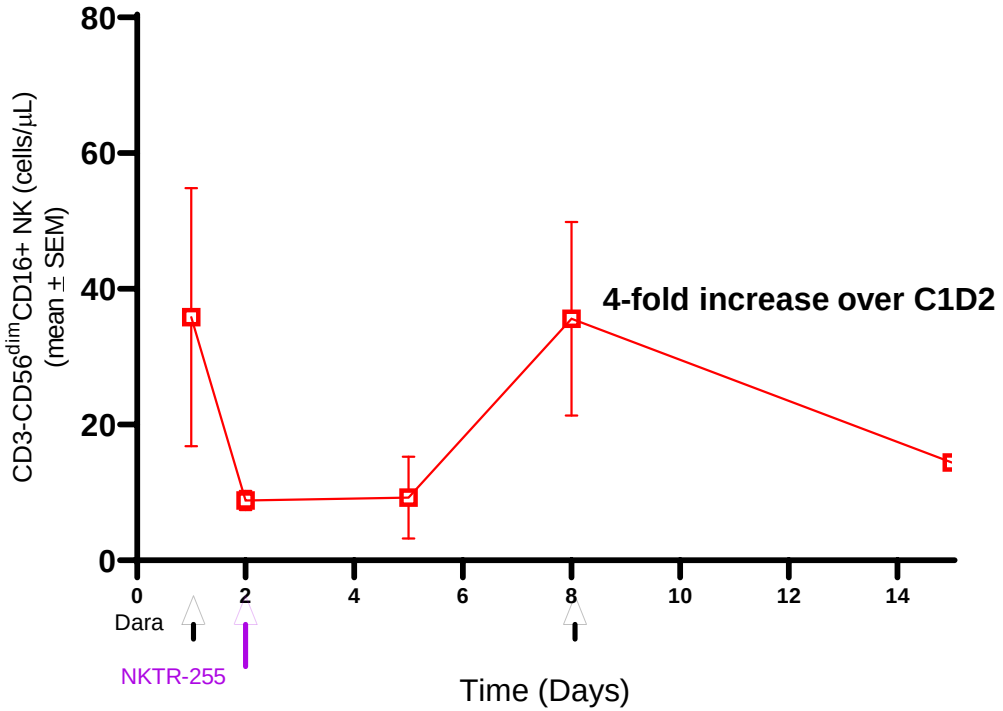
ASH 2022: NKTR-255 Monotherapy Increased Activation Markers on NK cells



NKp30 is key activation marker linked to enhancement of NK cell cytotoxicity and cytokine secretion
HLA-DR is functional marker and increases lead to greater functional activity (enhanced degranulation and cytokine secretion) in NK cells

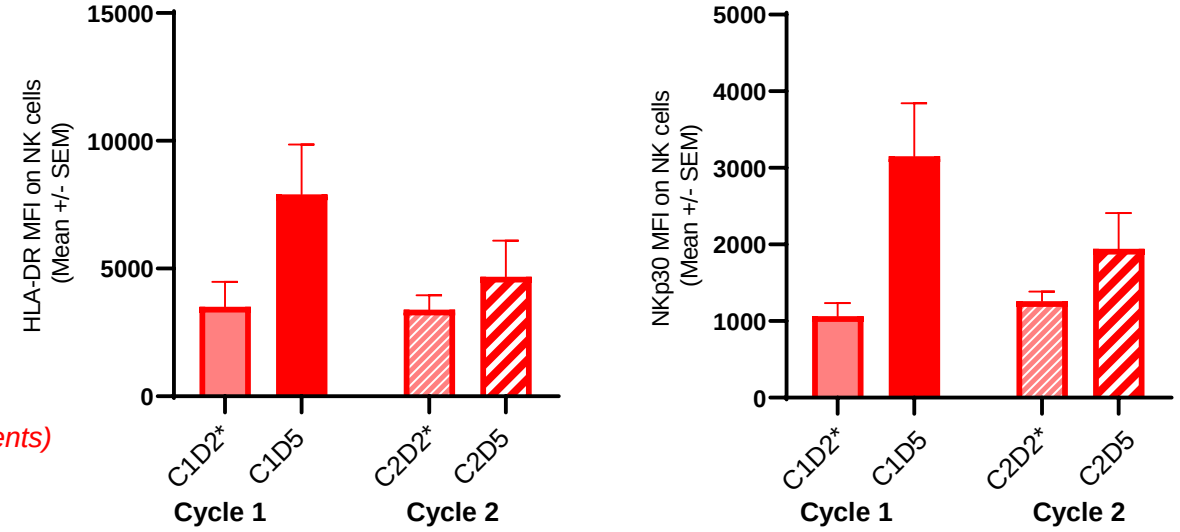
ASH 2022: Absolute Number of CD16+ NK cells and NK Activation Markers Increased in Response to 4.5 µg/kg NKTR-255 After Administration of Daratumumab

Absolute Number of CD56^{dim}CD16+ NK Cells



(N=3 patients)

Activation Marker Expression on Total NK Cells

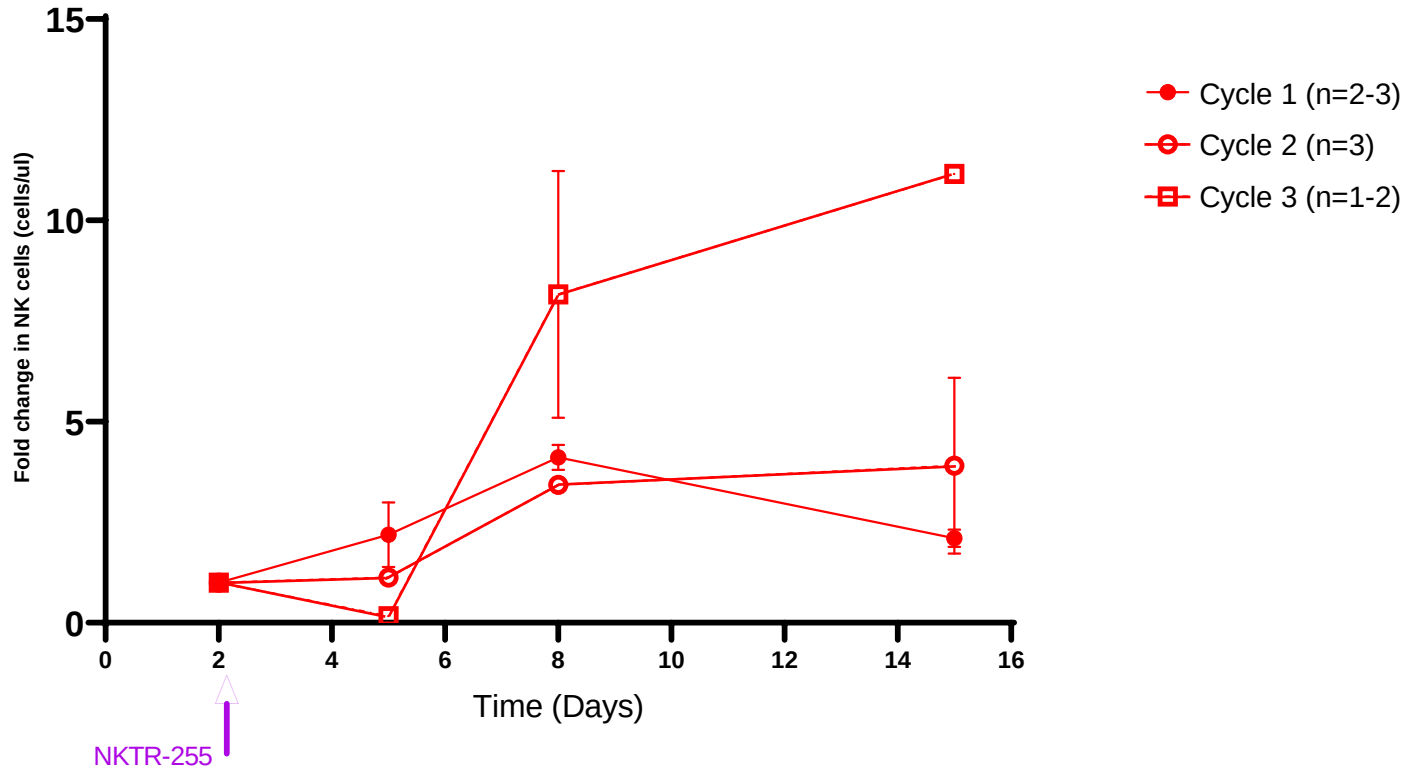


**day of NKTR-255 administration*

Daratumumab administered weekly (Weeks 1-8), q2w (Weeks 9-24): q4w (Week 25+); NKTR-255 in Cycles 1-3 is administered on Day 2 of the cycle and on Day 1 Cycle 4+

ASH 2022: Absolute Number of NK Cells Rescued with NKTR-255 After Daratumumab Administration Over Multiple Cycles in Patients with ≥3 Prior Lines of Treatment

Fold change in NK cell Increase Across Cycles

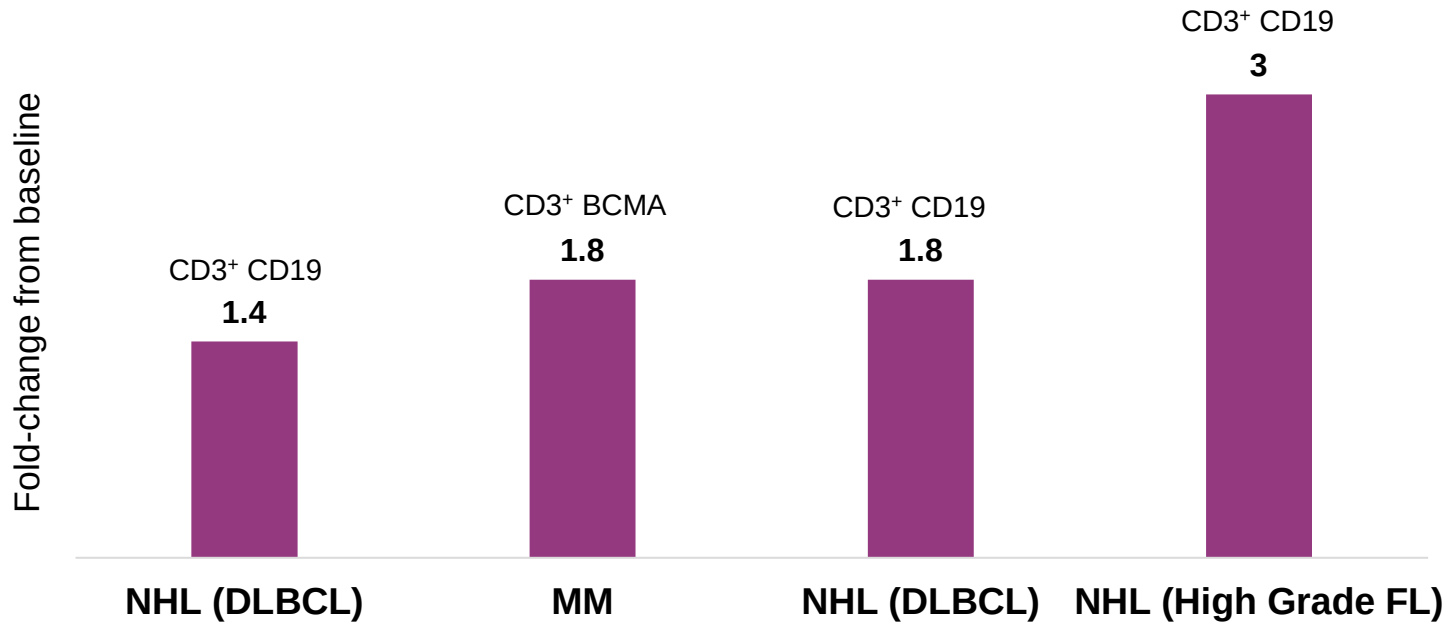


- NK cell expansion was maintained in subsequent cycles of treatment with NKTR-255.
- All of the patients receiving combination therapy showed disease stabilization.

Fold change calculated from day of NKTR-255 administration for each cycle (CxD2)

ASH 2021: NKTR-255 Monotherapy Increased CAR-T Cell Levels in Patients Greater than 1 Year Past CAR-T Infusion

Clinical Characteristics and Pharmacodynamic Effects Following NKTR-255 Treatment in Patients with Detectable* CAR-T/CAR-NK Cell Counts at Baseline



Product	Axicabtagene ciloleucel	Idecabtagene vicleucel	Axicabtagene ciloleucel	Tisagenlecleucel
Days since infusion	111	440	532	483
# of cycles of NKTR-255	2	2	5	3

All patients had achieved a partial or complete response to prior CAR-T therapy. Pharmacodynamic data were analyzed for patients with measurable CAR-T cells at baseline; fold change was calculated as treatment with NKTR-255 over baseline (baseline=1); CAR-T, chimeric antigen receptor T-cell therapy; CD, cluster of differentiation; DLBCL, diffuse large B-cell lymphoma; FL, follicular lymphoma; MM, multiple myeloma; NHL, non-Hodgkin lymphoma.

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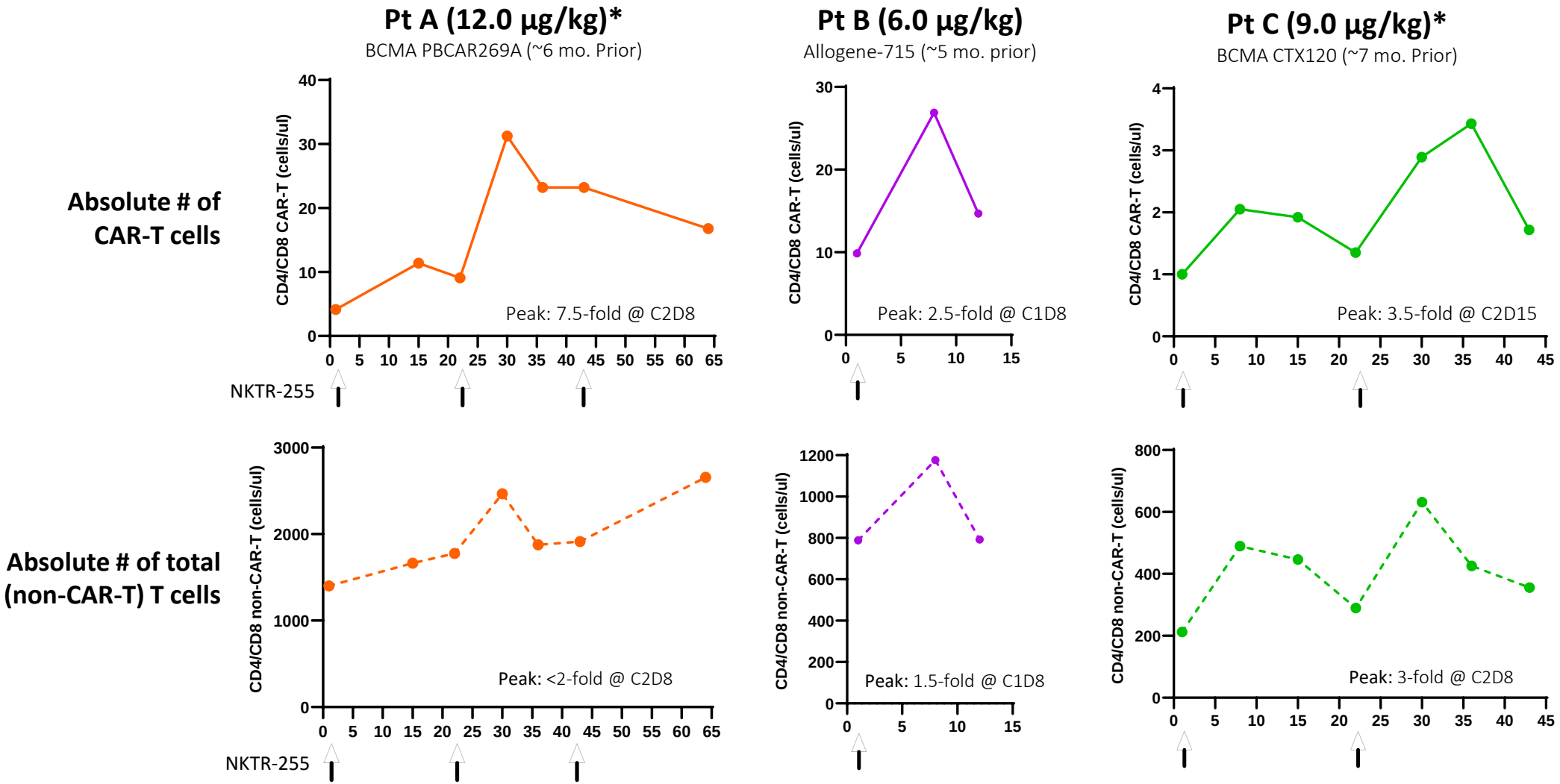
Source: Turtle, et al., *Blood*, Vol 138, Supplement 1, 2021, Page 2815.

ASH 2022: Allo-Reactivity to CAR-T Cells was Not Induced With NKTR-255 Monotherapy Treatment Amongst Patients Previously Treated with Off-the-Shelf Allogeneic CAR-T Cells



*Continued expansion of CAR-T cell numbers with repeat administration of NKTR-255 (Pts A & C)

Clinical Data Demonstrate that NKTR-255 Provides IL-15 Pathway Activation in Liquid and Solid Tumors

NKTR-255 is designed to capture the full IL-15 pathway to increase NK cells and cytotoxic function

Parameter	Liquid Tumor *(NKTR-255-02)*	Solid Tumor *(NKTR-255-03)*
Route of Administration*	IV, q3wk	IV, q3wk
Antibody-Like Dosing Pharmacokinetics: IV $t_{1/2}$ (hr)	27-87 hr	27.8 hr
NK cell expansion	Yes, 7-17-fold	Yes, 3-9-fold
NK cell proliferation	Yes	Yes
CD8 T cell expansion	Yes, 2-3-fold	Yes, 2-3-fold
CD8 T cell proliferation	Yes	Yes
Upregulation of activation markers (HLA-DR, CD107a, NKp30, and Granzyme B) on NK cells	Yes	Yes

Additional Messages:

- Consistent level of NK and CD8+ T cell expansion and proliferation in multiple tumor types (NHL, MM, CRC, SCCHN)
- NK and CD8+ T cell elevations observed in MM patients with compromised bone marrow, even in presence of doublet with Dara
- Optimized PK/PD profile for both monotherapy and in combination with targeted antibodies

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Agenda

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- ***Overview of Cell Therapy Landscape and Rationale for NKTR-255 Combination with CAR-T***
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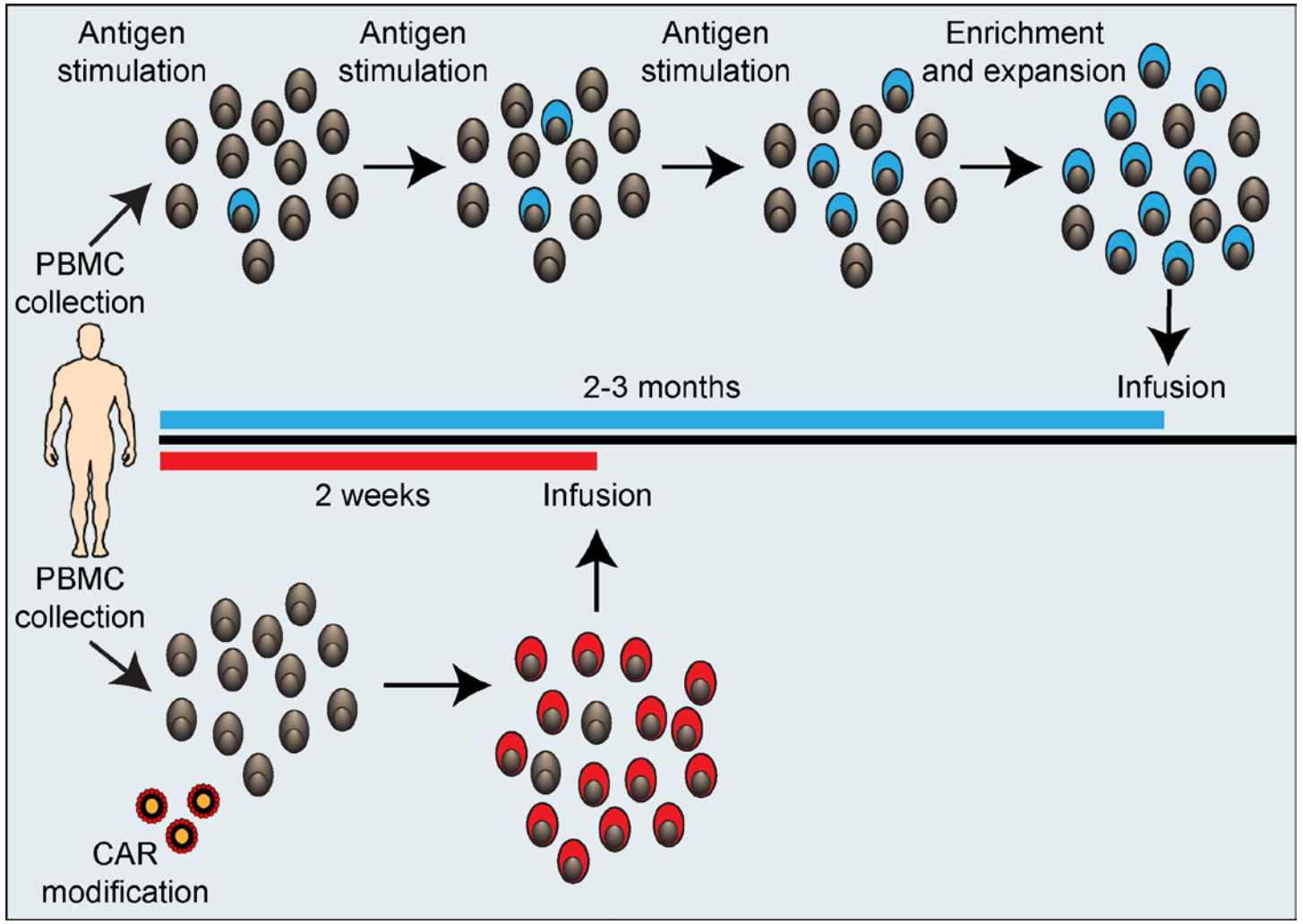
- ***Q&A Session***

Redirection of T Cell Specificity by Genetic Modification

Repetitive antigen stimulation

Genetic redirection of the specificity of competent T cells to tumors

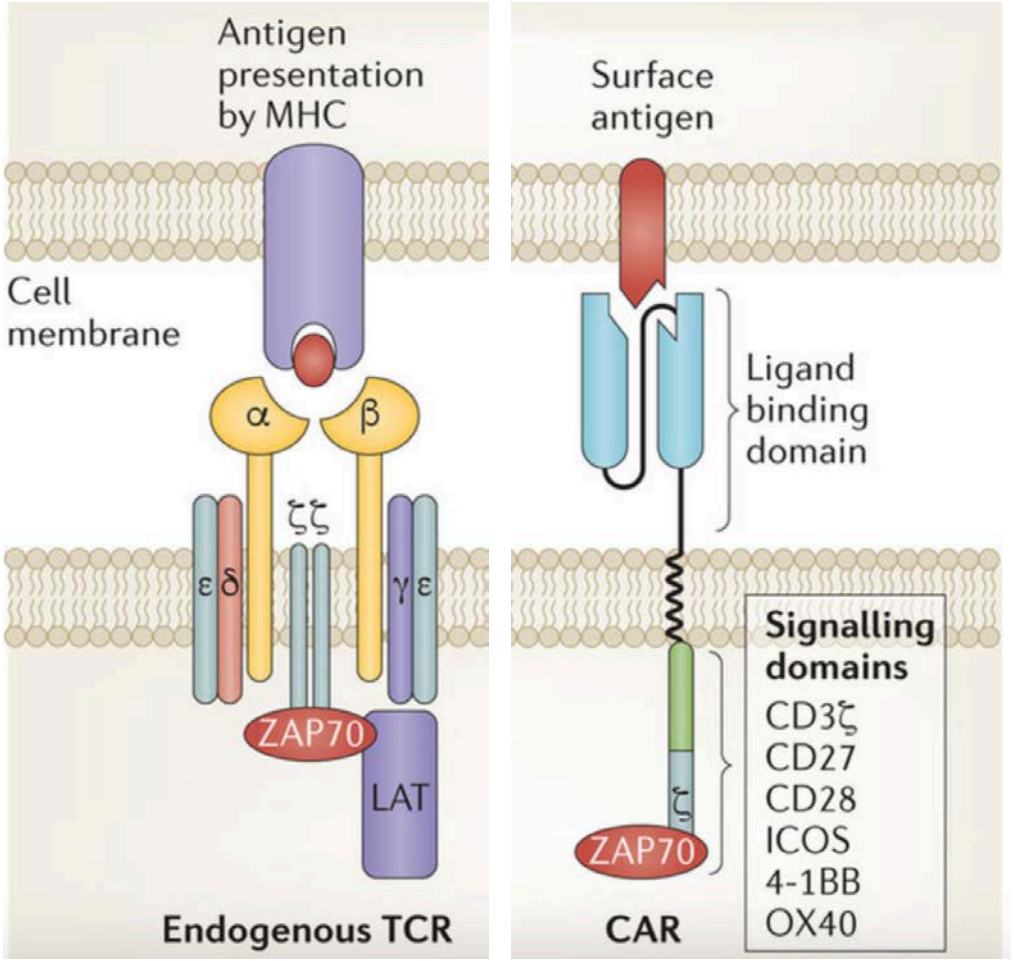


Turtle. Int J Heme, 2013

Structure of Native T Cell Receptors and Recombinant Chimeric Antigen Receptors

Tumor cell

T cell



CARs

- Target surface molecules
- No HLA restriction
- ‘In-line’ costimulation
- Engineered T cell subsets can be redirected to an appropriate target antigen

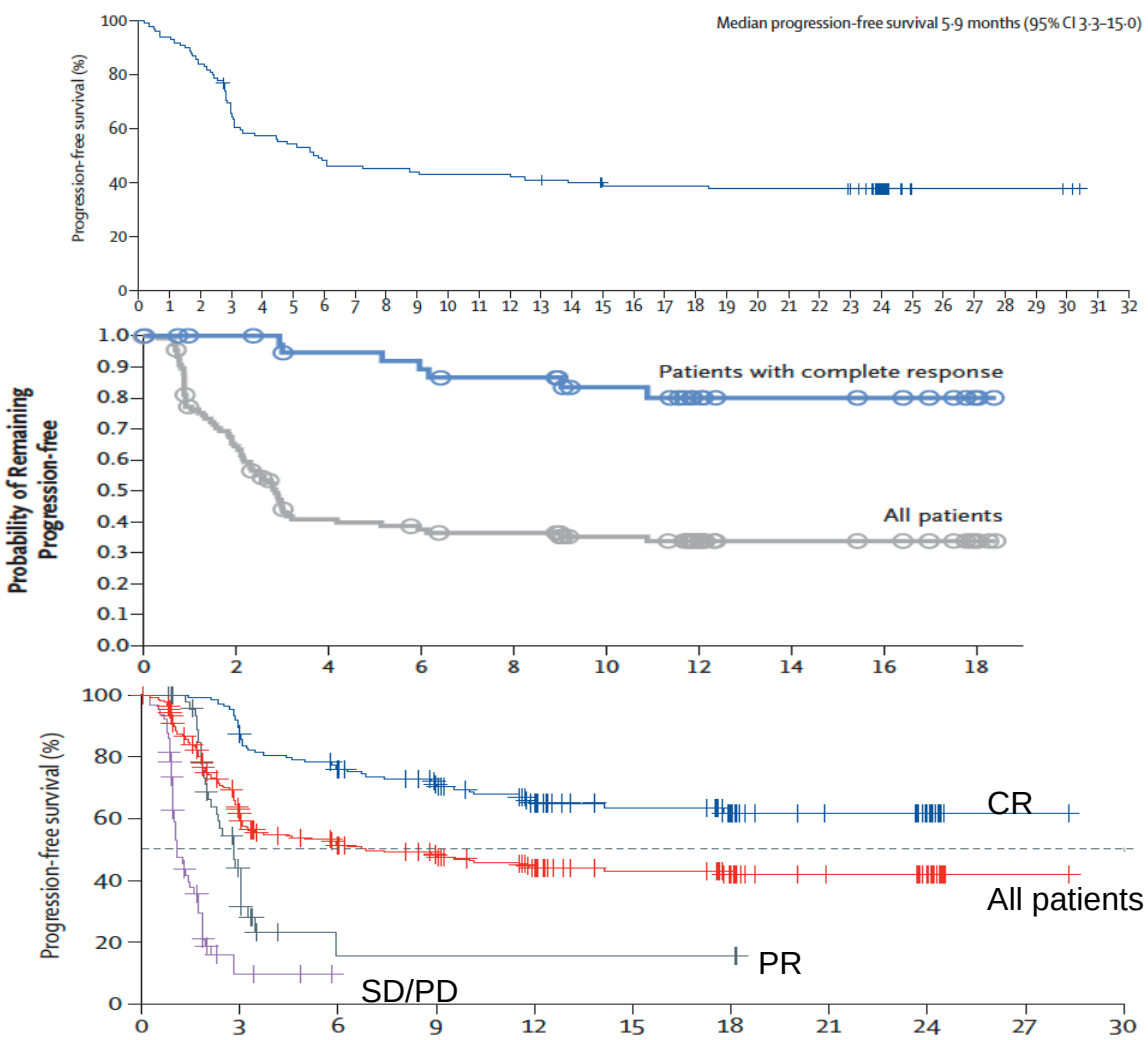
Fesnak, Nat Rev Cancer, 2016

Durable Responses Achieved in Patients with R/R LBCL After Treatment with Different CD19 CAR-T Cell Products

ZUMA-1 – axicabtagene ciloleucel
Follow-up, median (interquartile range), months: 27.1 (25.7-28.8)
Locke FL, *et al*. *Lancet Oncol*. 2018

JULIET – tisagenlecleucel
Follow-up, median (range), months: 14.0 (0.1-26)
Schuster SJ, *et al*. *N Engl J Med*. 2018

TRANSCEND NHL 001 – lisocabtagene maraleucel
Follow-up, median (95% CI), months: 12.3 (12.0-17.5)
Abramson JS, *el al*. *The Lancet*. 2020

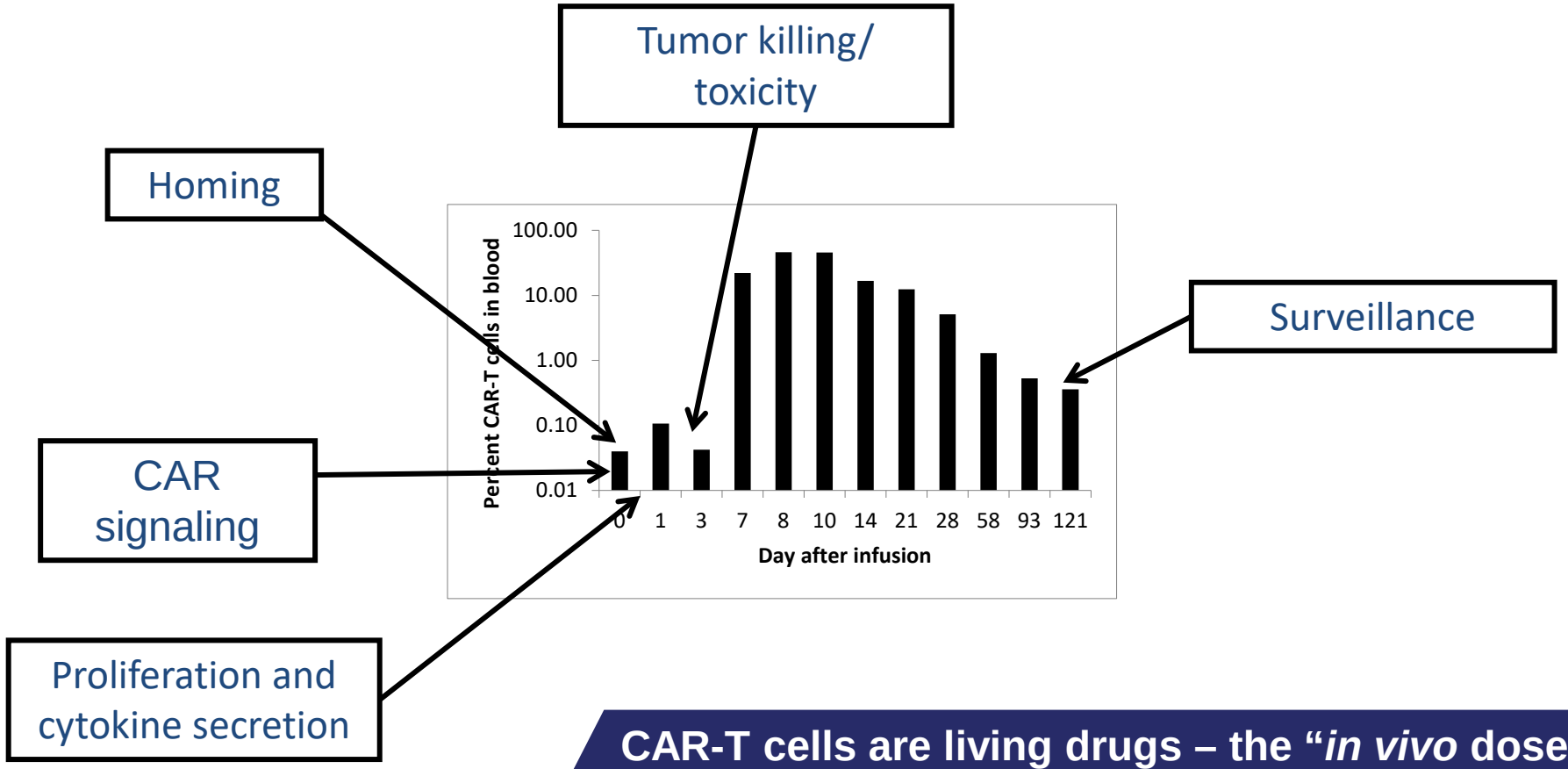


Despite paradigm-changing outcomes for R/R LBCL, ~60% of patients failed to achieve durable CR after CD19 CAR-T cells

SCHOLAR-1: CRR 7% with standard of care https://pubmed.ncbi.nlm.nih.gov/28774879/

Novel Strategies are Needed to Improve CR Rates and Enhance Duration of Responses of CAR-T Therapies

CAR-T Cells: A Living Drug

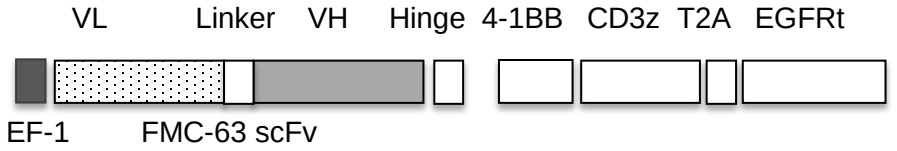


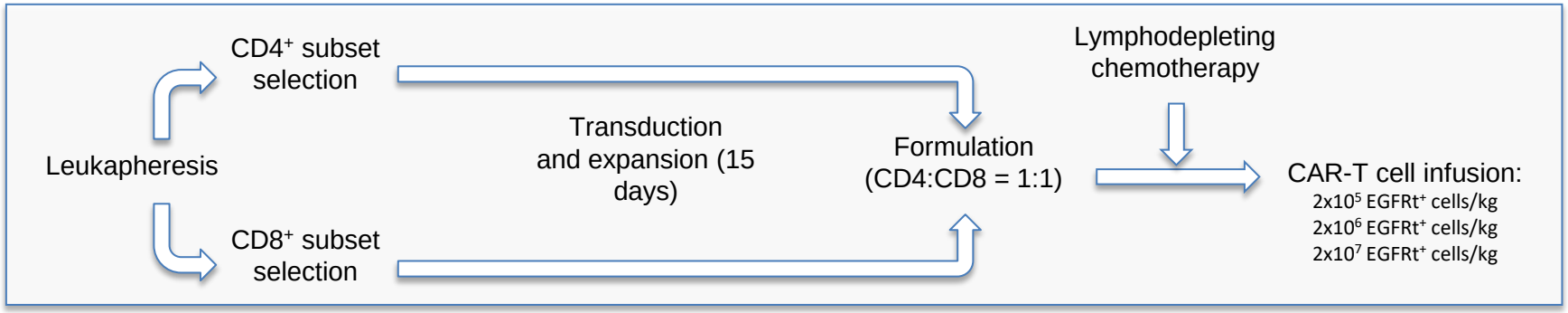
CAR-T cells are living drugs – the "*in vivo* dose" depends on the cell dose, the antigen burden, lymphodepletion regimen, and other patient/treatment/tumor characteristics

Fesnak, Nat Rev Cancer, 2016;
Heiblig M, et al. World J Stem Cells. 2015 Aug 26; 7(7):1022-38.

Clinical Trial of Defined Composition CD19 CAR-T Cells for B Cell Malignancies (NCT01865617)

Lentiviral vector:





Eligibility

- R/R CD19+ B cell malignancy (B-ALL, NHL, CLL)
- ≥ 18 years

197 treated

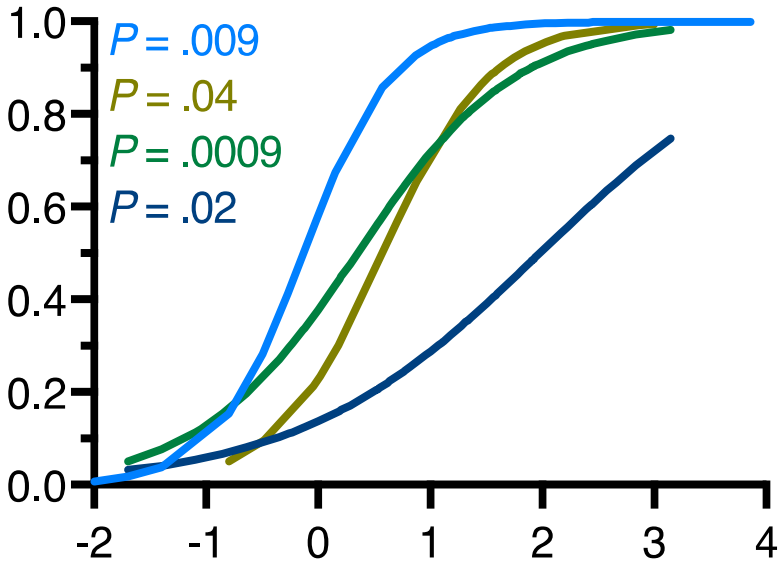
- 197 treated
- ALL, n=65
- NHL, n=82
- CLL/Richter's, n=50

Responses

B-ALL: 85% MRD-neg CR
NHL: Aggressive (n=47): 40% CR
NHL: Indolent (n=10): 89% CR
CLL/Richter's (n=24): 21% CR

Turtle et al, J Clin Invest, 2016; Gardner et al, Blood, 2016; Turtle et al, Sci Trans Med, 2016; Turtle et al, J Clin Oncol, 2017; Gust et al, Cancer Discovery, 2017; Hay et al, Blood, 2017; Hill et al, Blood, 2018; Hay et al, Blood, 2019; Hirayama et al, Blood (1), 2019; Hirayama et al, Blood (2), 2019; Hill et al, Blood Adv, 2019; Shadman et al, Blood Adv, 2019; Gauthier et al, Blood, 2020; Sheih et al, Nat Comm, 2020; Gauthier et al, Blood, 2021; Juluri, Blood Adv, 2021; Hirayama et al, Blood Adv, 2022

In Vivo CAR-T Cell Counts are Associated with Response

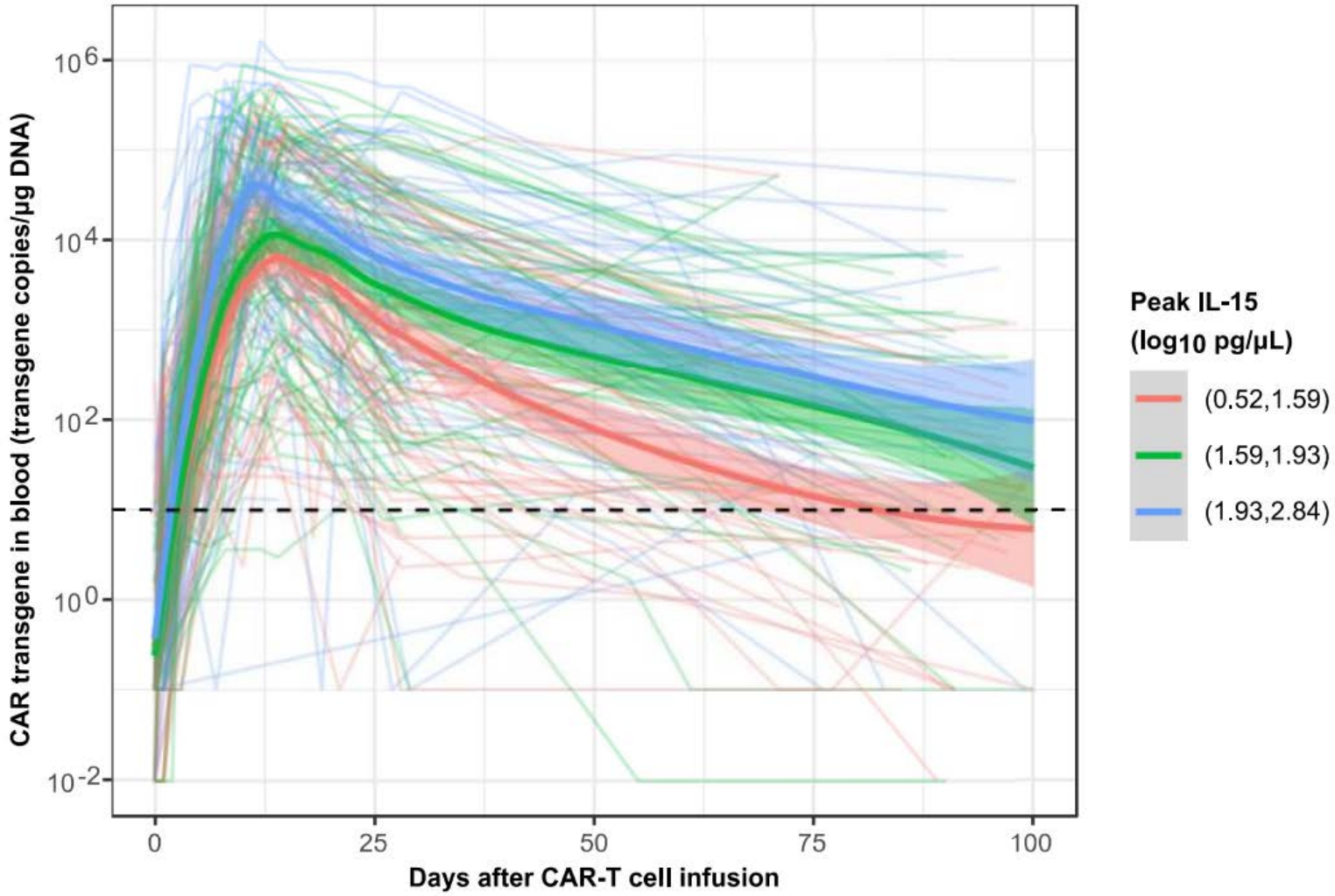


BM CR: ALL

CR: NHL

Hay et al. Blood, 2017

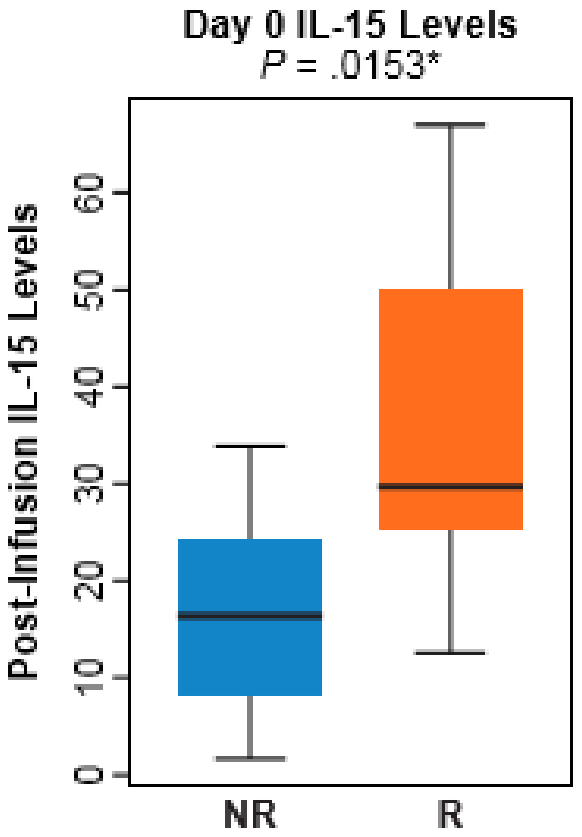
Higher Peak of IL-15 is Associated with Higher CD19 CAR-T Cell $AUC_{0\text{-}90}$ in Humans



Hirayama et al. *Blood Adv.* 2022 Nov 4: bloodadvances.2022008697

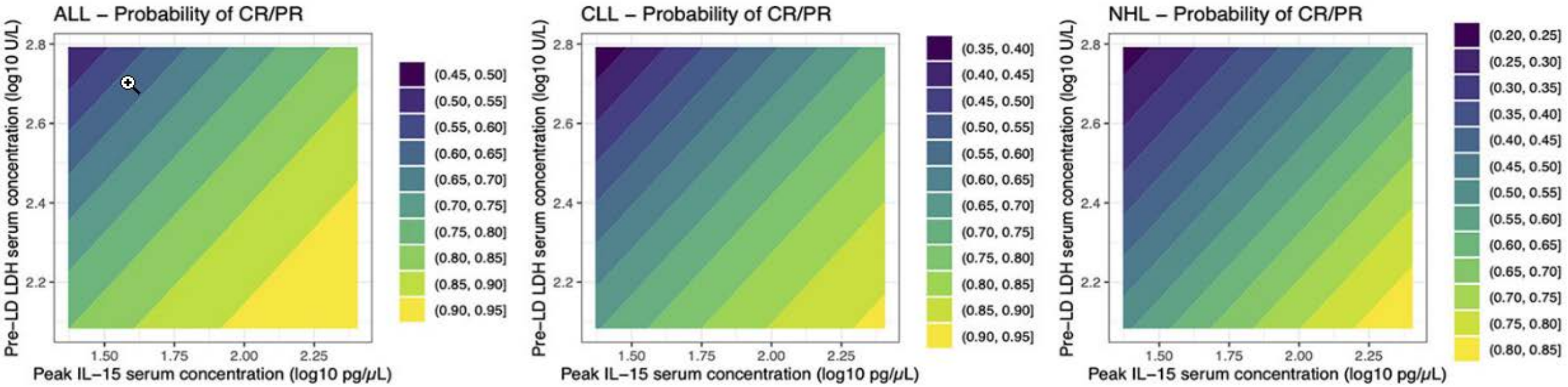
IL-15 Levels Associate with CAR-T Cell Counts and Response to CD19 CAR-T Cell Immunotherapy in LBCL

Kochenderfer et at, JCO, March 2017



Rossi et at, Blood, June 2018

High IL-15 is Associated with Response to CD19 CAR-T Cell Therapy in High- and Low-risk B-ALL, CLL and NHL



Probabilities of CR/PR were adjusted to Cy/Flu lymphodepletion and are shown in color-coded contours.
Responses defined by 2019 NCCN guidelines for ALL, 2018 iWCLL for CLL, and 2014 Lugano criteria for NHL. Abbreviations: LD, lymphodepletion; ALL, acute lymphoblastic leukemia; CLL, chronic lymphocytic leukemia; NHL, non-Hodgkin lymphoma; CR, complete response; PR, partial response; LDH, lactate dehydrogenase.

Association of IL-15 with response is evident in both *high- and low-risk disease*

Gauthier et al, Blood, (2020), 136 (Supplement 1), 2020, Pages 37-38.

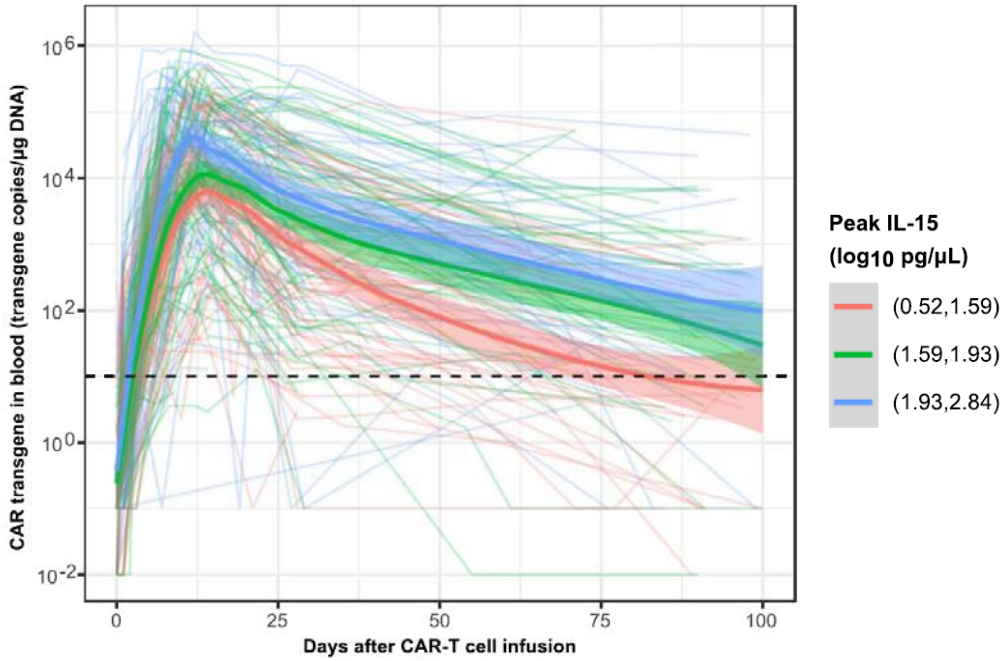
Rationale for Combining NKTR-255 with CD19 CAR-T Cell Therapy

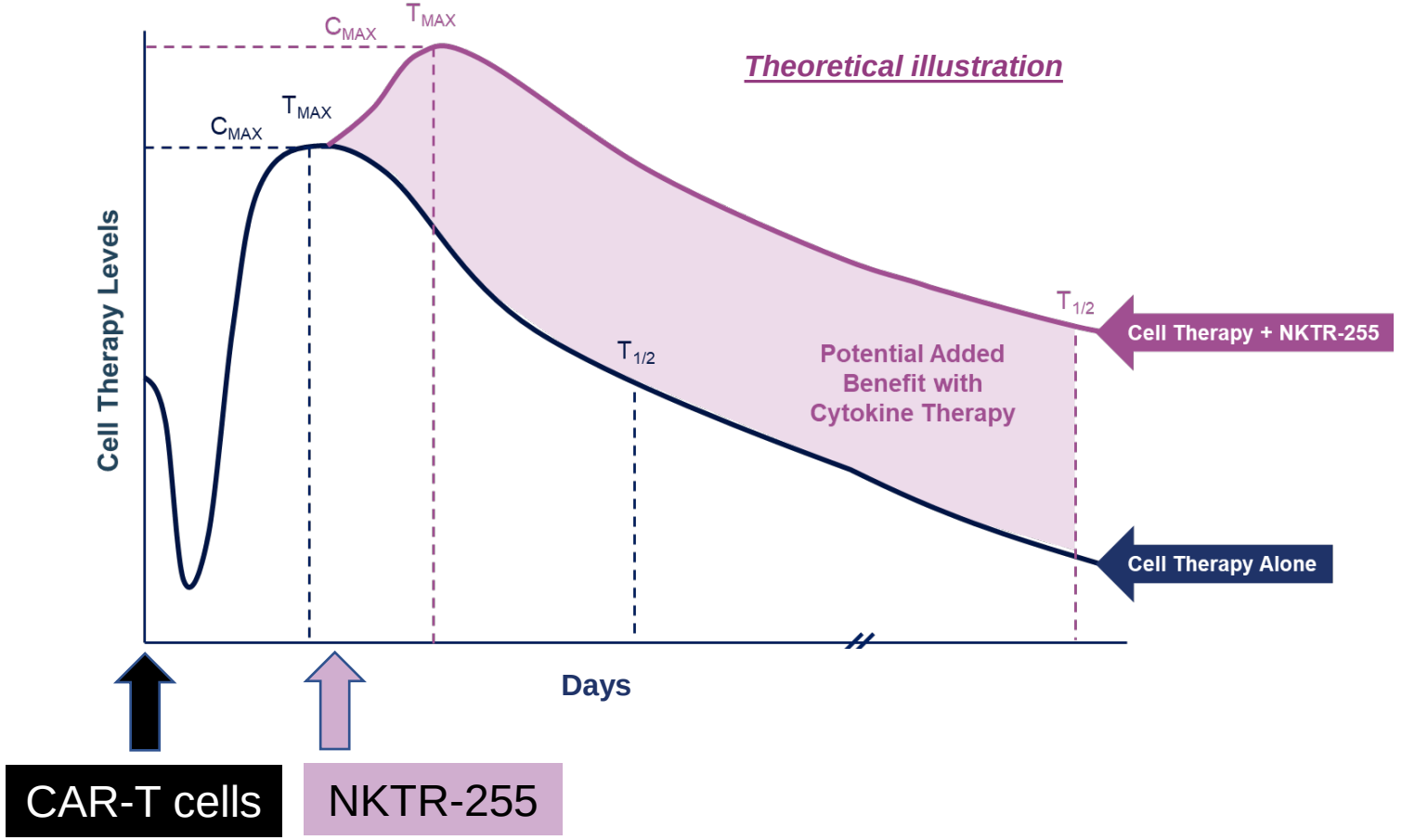
- Approximately 60% of LBCL patients treated with CD19 CAR-T cells fail to achieve durable CR
- Poor *in vivo* CAR-T cell counts are a key reason for failure of CAR-T cell therapy
- High IL-15 levels promote higher *in vivo* counts and higher AUC of CAR-T cells
- High IL-15 levels associate with better response rates to CD19 CAR-T cell therapy

Exogenous IL-15 supplementation is the logical way forward

Combining Cell Therapy with Exogenous Cytokine May Increase Cmax and Extend CAR-T Cell Persistence in LBCL

Higher peak IL-15 levels correlate with higher CD19 CAR-T cell AUC0-90





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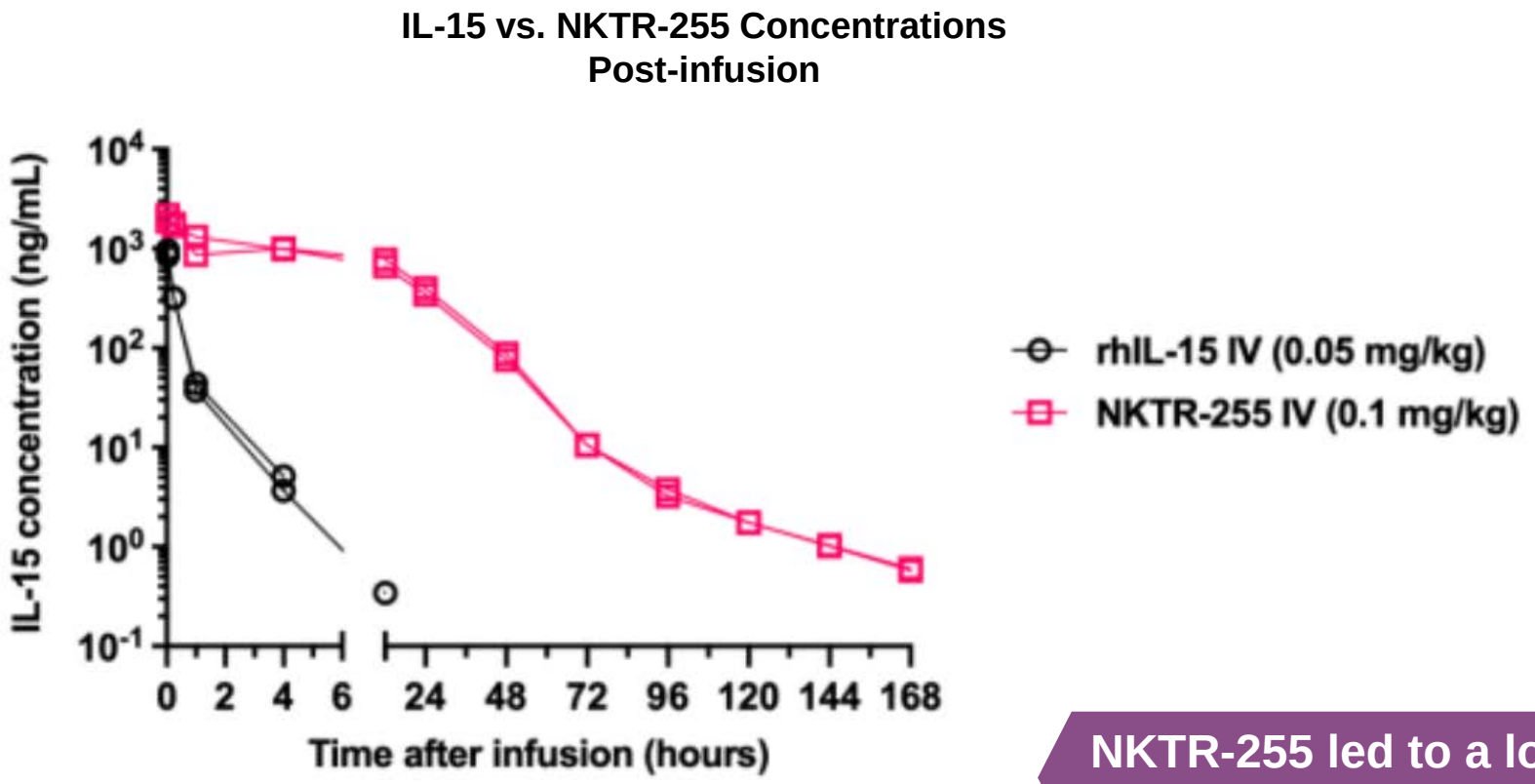
Higher AUC of NKTR-255 Compared to Native rhIL-15 in Non-human Primates



NKTR-255 led to a longer IL-15 half-life (30.5 vs. 1.2 hours)

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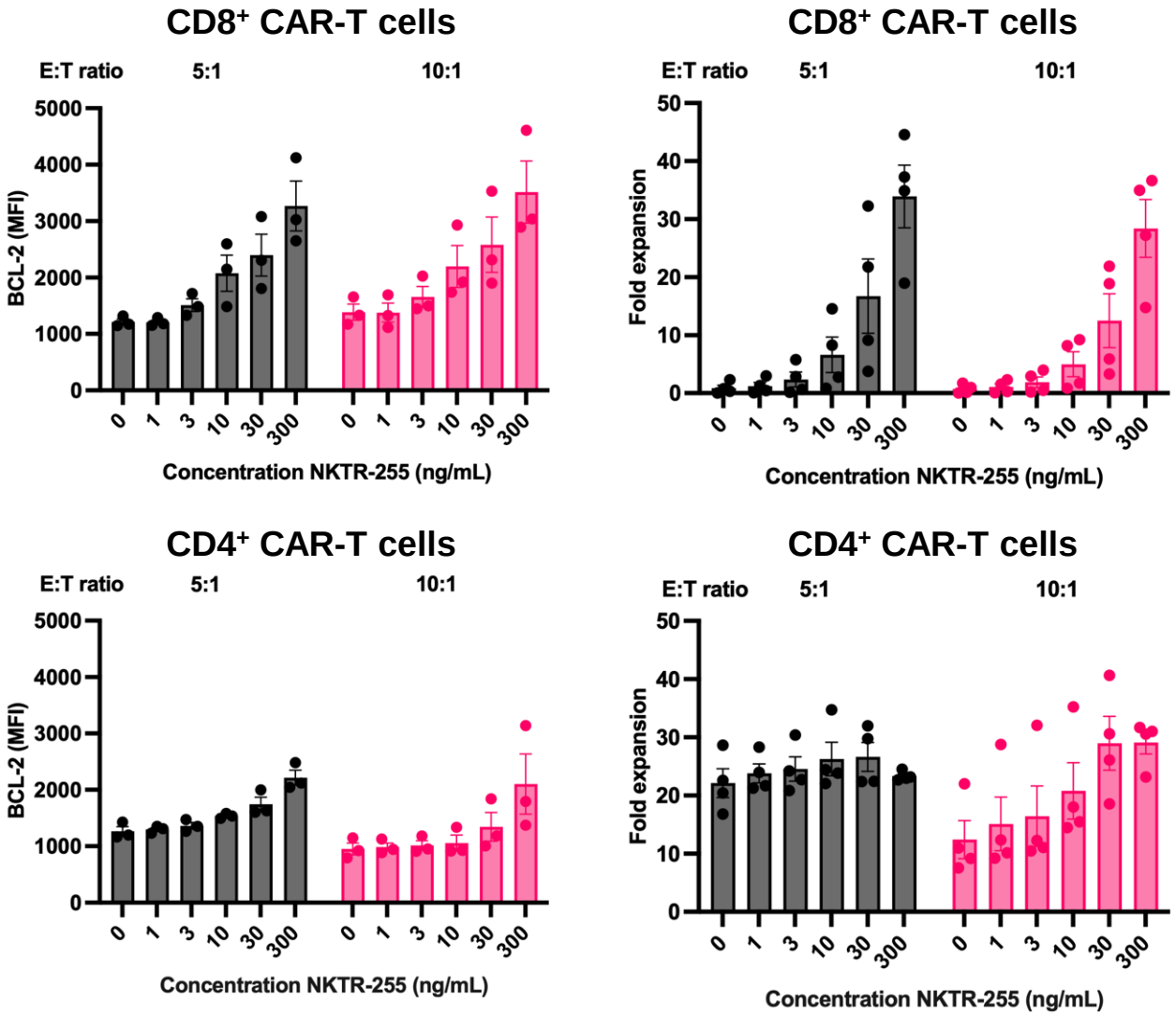
Human CD19 CAR-T Cells Exhibit a Dose-dependent Response to NKTR-255 at High and Low Antigen Burden

CD19 CAR-T cells + K562-CD19



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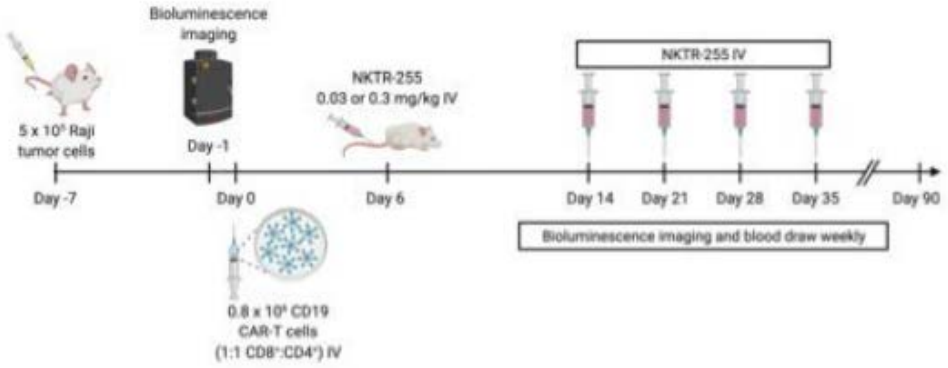
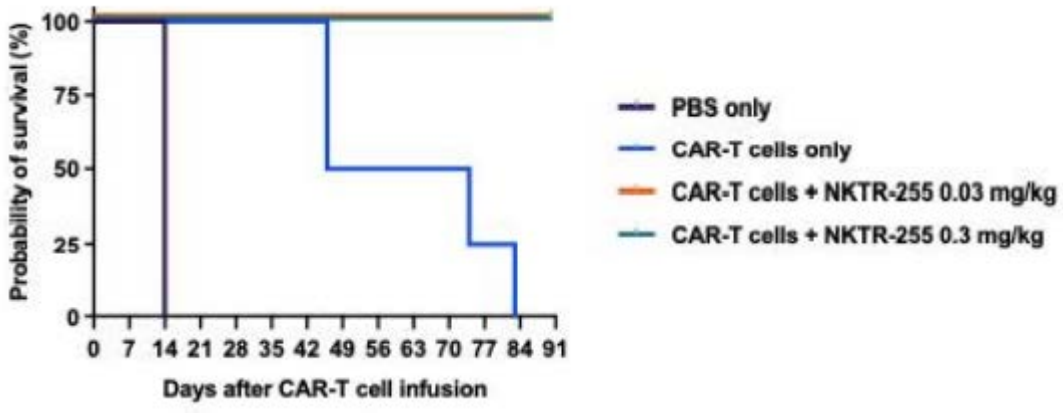
E:T – effector:target ratio

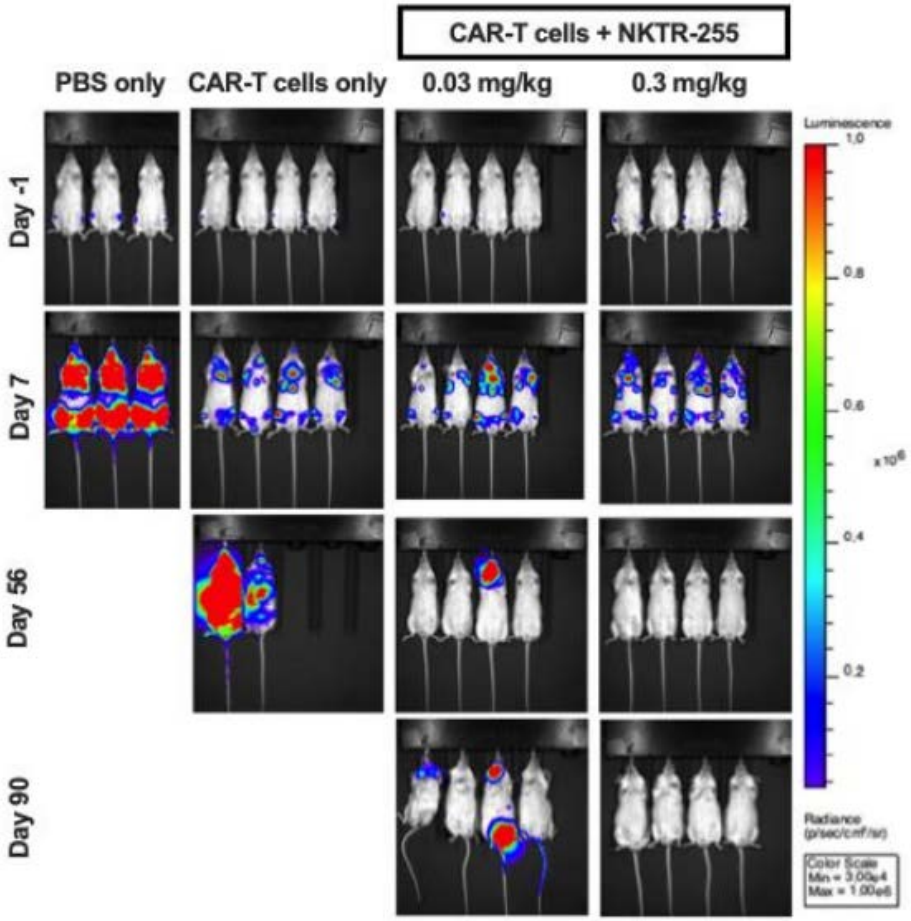
NKTR-255 Induces Dose-dependent Increased *In Vivo* Anti-tumor Efficacy of Human CD19 CAR-T Cells



Kaplan-Meier Survival Curve



Bioluminescence Imaging of Raji Tumor Burden at Indicated Timepoints



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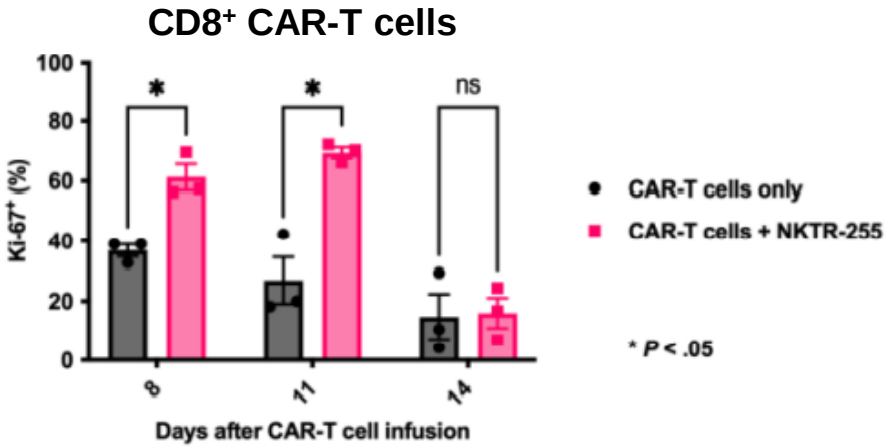
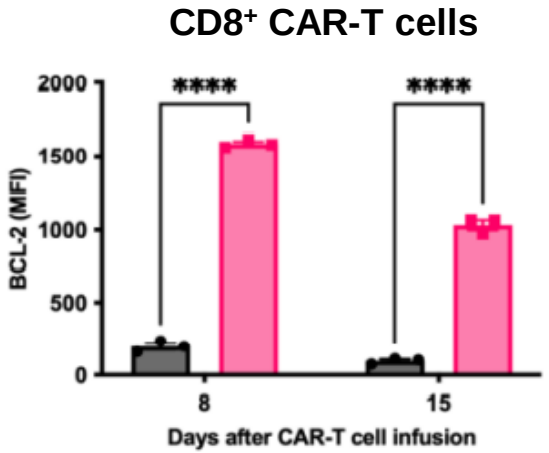
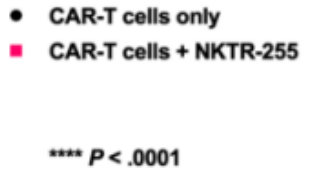
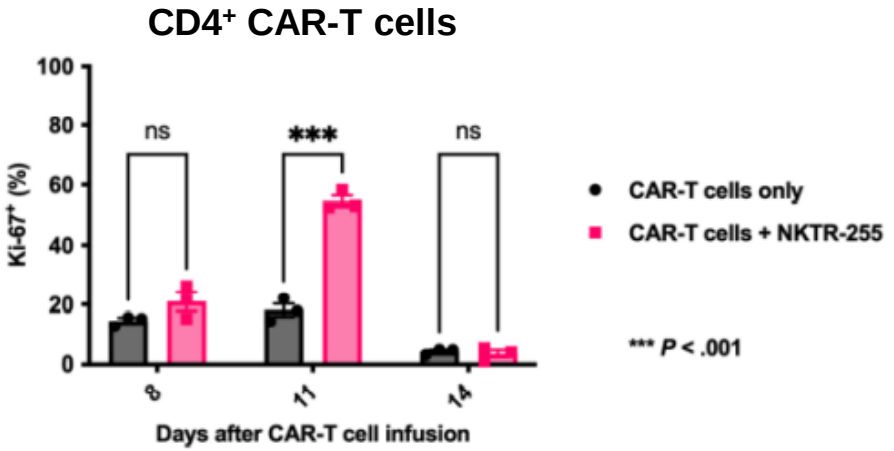
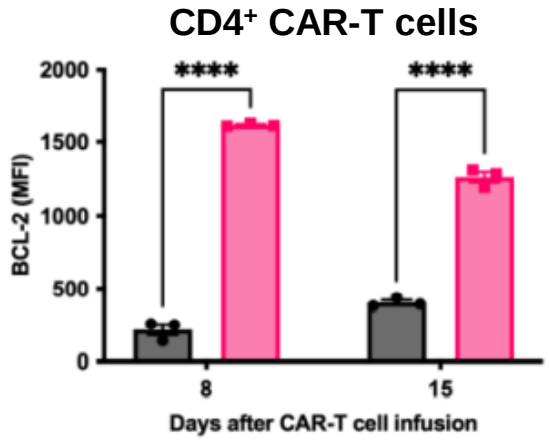
NKTR-255 Increases Proliferation and Anti-apoptotic Bcl-2 in Human CAR-T Cells in Marrow of Lymphoma Bearing Mice

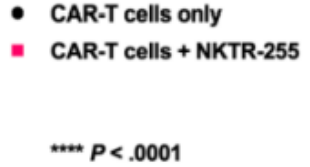












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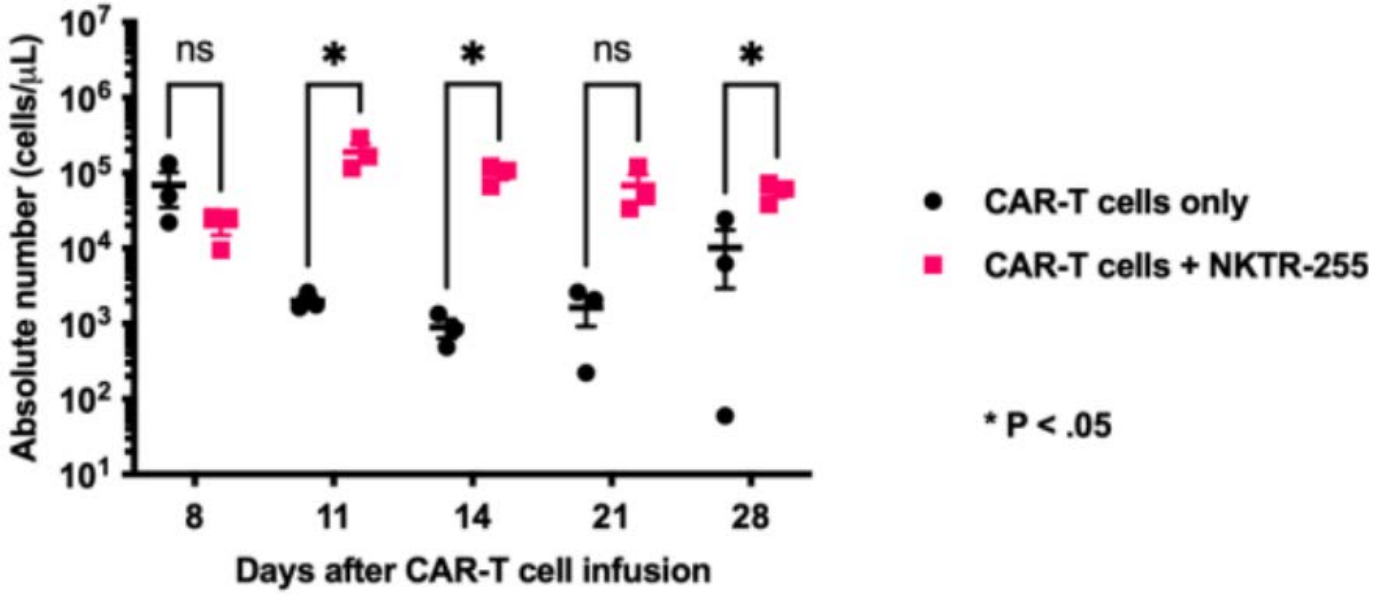
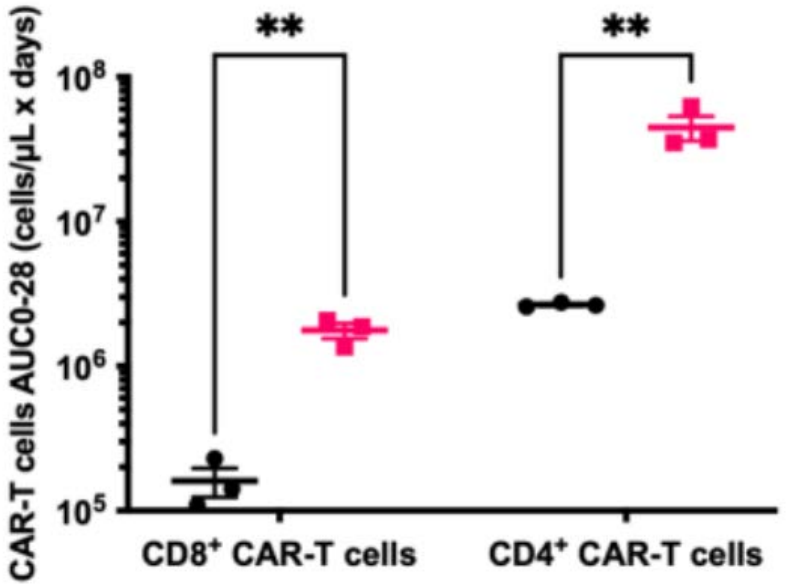
NKTR-255 Increases Accumulation of Human CAR-T Cells in Marrow of Lymphoma Bearing Mice

CD8+ CAR-T Cells



CD8+ and CD4+ CAR-T cell AUC0-28



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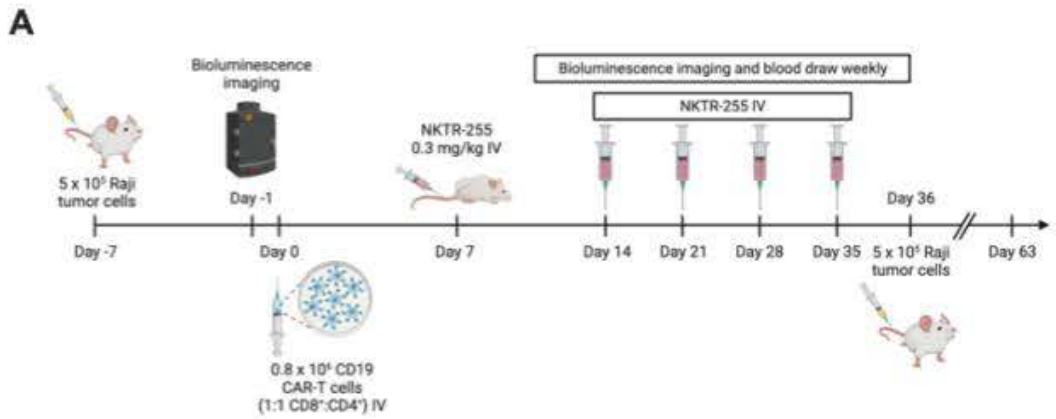
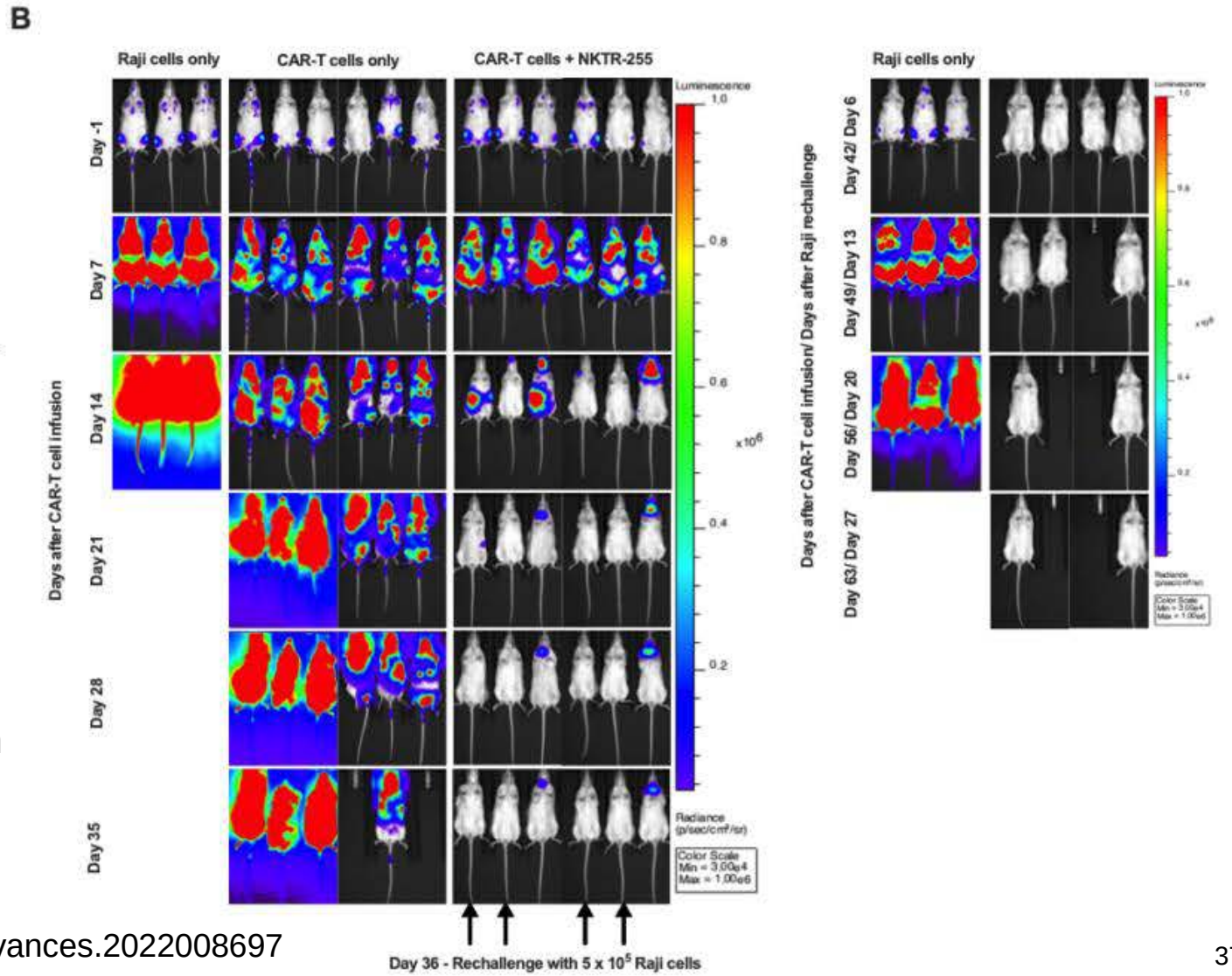
Robust and Durable CAR-T cell Function after NKTR-255 Supplementation is Demonstrated by Rejection of Tumor Rechallenge





Mice received CAR-T cells on Day 0. On day 35, tumor-free mice (arrows) were rechallenged with Raji tumor cells and imaged weekly to assess tumor burden

Hirayama et al. *Blood Adv*. 2022 Nov 4: bloodadvances.2022008697

Summary

- Although CAR-T cell therapy is a paradigm-changing cancer treatment, 60% of LBCL patients still fail to achieve durable CR after CD19 CAR-T cell immunotherapy
- In LBCL patients high IL-15 is associated with better *in vivo* CAR-T cell counts and better efficacy of CD19 CAR-T cells in both high- and low-risk disease
- NKTR-255 is a novel IL-15 agonist that demonstrates favorable pharmacokinetics compared to rhIL-15 in non-human primates
- NKTR-255 enhanced the proliferation and survival of competent human CD19 CAR-T cells, enabling better anti-tumor efficacy in immunodeficient mice bearing human lymphoma treated with human CAR-T cells
- The data provide strong rationale to support studies of NKTR-255 supplementation in adoptive T cell therapies

Agenda

Role of IL-15 within the Cell Therapy Landscape

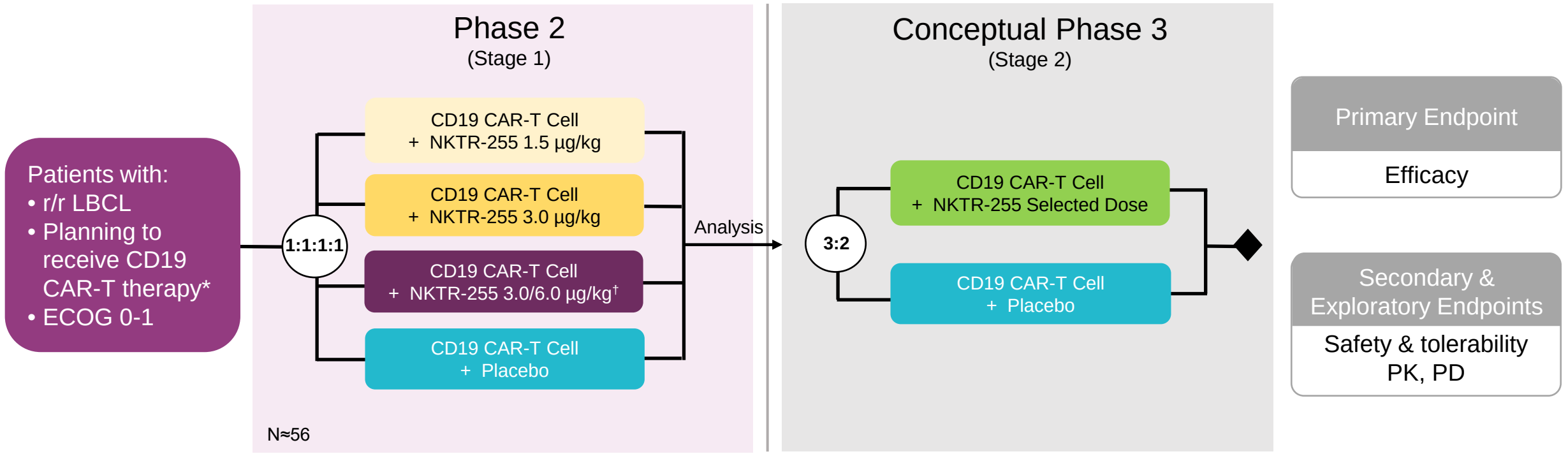
- ***ASH 2022: "Safety, Tolerability, PK/PD, and Preliminary Efficacy of NKTR-255, a Novel IL-15 Receptor Agonist, in Patients with Relapsed/Refractory Hematologic Malignancies"***
  - *Mary Tagliaferri, MD, Nektar Therapeutics*
- ***Overview of Cell Therapy Landscape and Rationale for NKTR-255 Combination with CAR-T***
  - *Cameron Turtle, MBBS, PhD, University of Sydney and Fred Hutchinson Cancer Center (Turtle Lab)*
- ***Ongoing and Planned Studies***
  - *Mary Tagliaferri, MD, Nektar Therapeutics*
- ***Q&A Session***

NKTR-255 Clinical Program Focus

	Program	Phase	Indication	Partner
Liquid Tumors	NKTR-255 + Breyanzi® YESCARTA®	Phase 2/3	Diffuse Large B-Cell Lymphoma	
Liquid Tumors	NKTR-255 + Rituxan® Rituximab	Phase 1/2 Dose Escalation	R/R Non-Hodgkin's Lymphoma *NCT04136756*	
Liquid Tumors	NKTR-255 + DARZALEX Faspro® (daratumumab and hyaluronidase-fihj) Injection for subcutaneous use | 1,800mg/30,000units	Phase 1/2 Dose Escalation	R/R Multiple Myeloma *NCT04136756*	janssen Drug Supply
Liquid Tumors	NKTR-255 + Breyanzi®	P1/2 IST in approved indication	Non-Hodgkin's Lymphoma Diffuse Large B-Cell Lymphoma *NCT05359211*	FRED HUTCH CURES START HERE™
Liquid Tumors	NKTR-255 + *Proprietary CD19/22 (unapproved)*	P1/2 IST	Relapsed/Refractory (r/r) B-ALL *NCT03233854*	Stanford MEDICINE
Solid Tumors	NKTR-255 + BAVENCIO® avelumab Injection 20 mg/mL	Phase 2 Ongoing	Maintenance Treatment Bladder Cancer *NCT05327530 (Comparative Study)*	Merck Pfizer Clinical Collaboration 50/50 Sponsored by Merck KGaA
Solid Tumors	NKTR-255 + ERBITUX® CETUXIMAB	Phase 1/2 Dose Escalation	R/R Colorectal Cancer R/R Head and Neck Squamous Cell Carcinoma *NCT04616196*	
Solid Tumors	NKTR-255 + IMFINZI® durvalumab Injection for Intravenous Use 50 mg/mL	P1/2 IST in approved indication	Stage 2 NSCLC Post Chemoradiation	THE UNIVERSITY OF TEXAS MD Anderson Cancer Center Making Cancer History®

NEKTAR

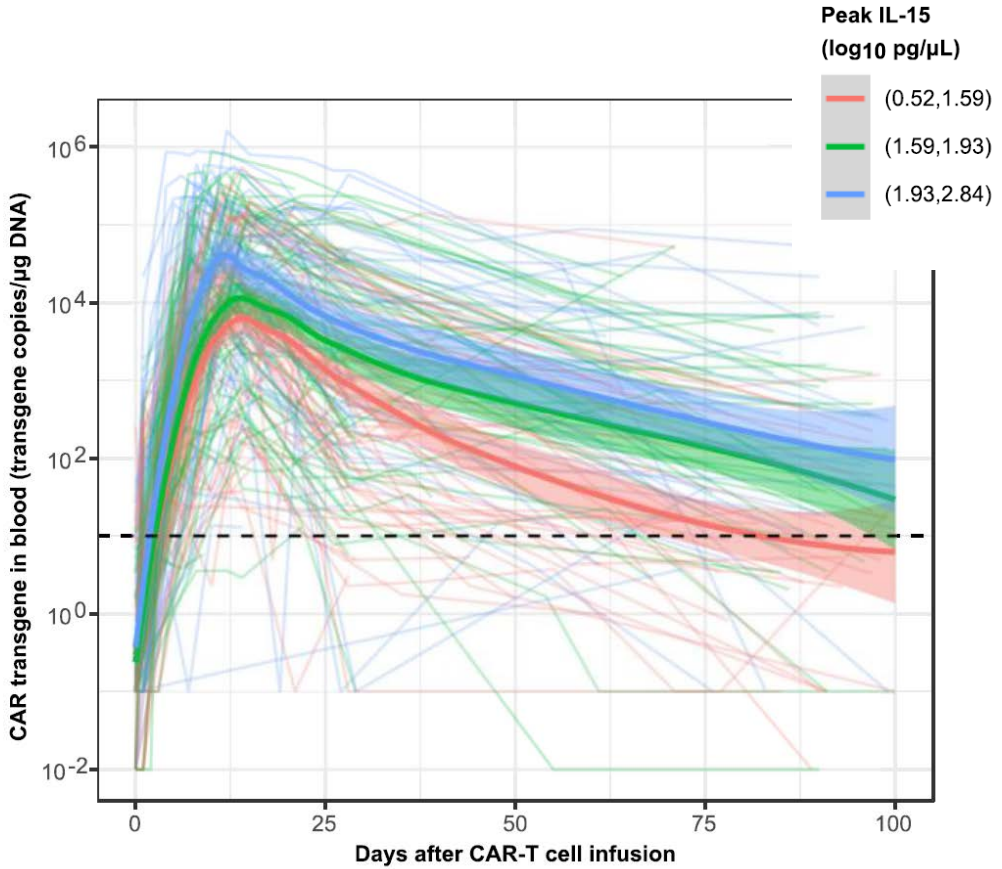
Phase 2/3 Randomized Double-Blind, Placebo-Controlled Study of NKTR-255 vs Placebo Following CD19-Directed CAR-T Cell Therapy in LBCL

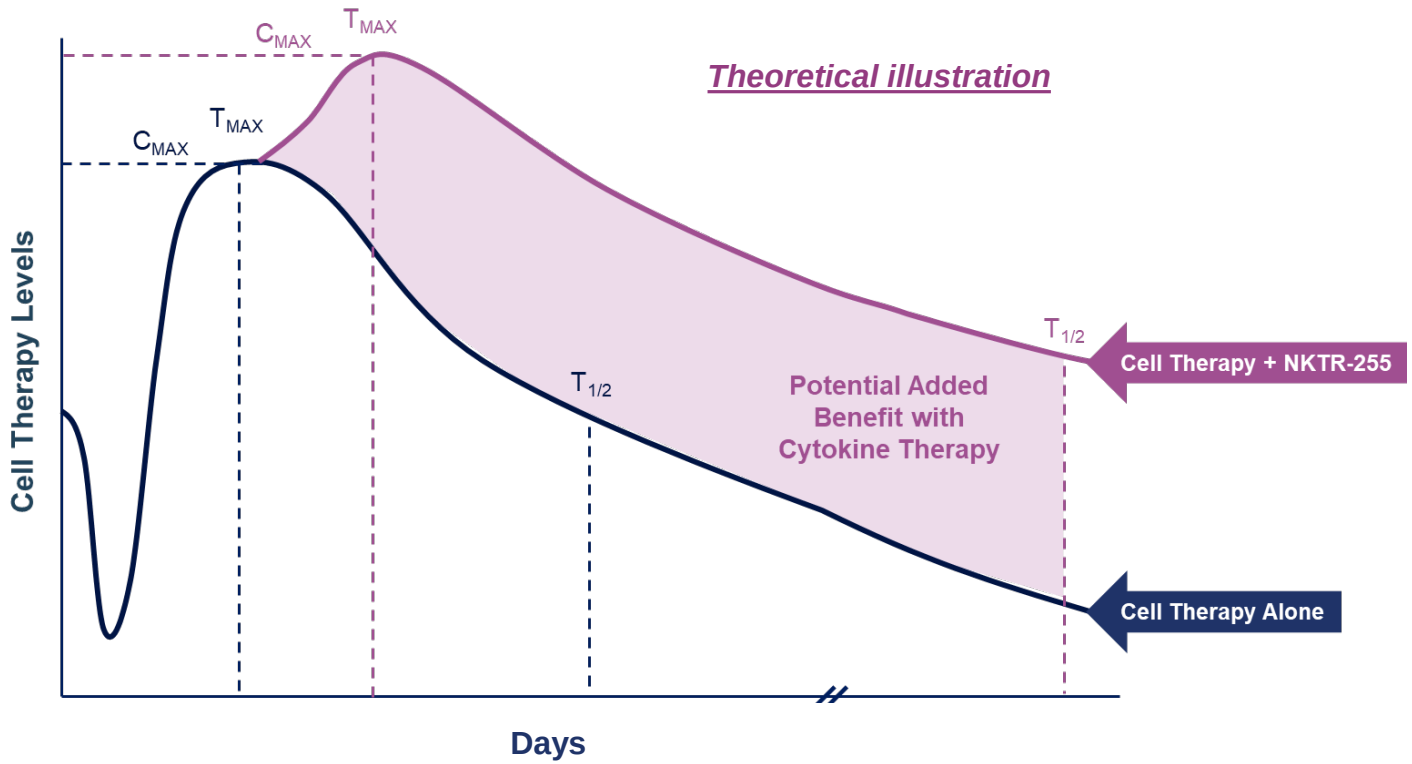


Based upon results of the Phase 2 portion of the study, final design of the Phase 3 portion of the study will be determined, including NKTR-255 dose, sample size and endpoints of the study

LBCL=large B-cell lymphoma; CAR-T=chimeric antigen receptor T-cell therapy; DL=dose level; PK=pharmacokinetics; PD=pharmacodynamics; r/r=relapse and refractory
*CD19 CAR-T cell therapy includes axi-cel or liso-cel (or tisa-cel in Stage 2).
† Step-up dose regimen initiating with 3.0 µg/kg NKTR-255 in Cycle 1 and continuing in Cycle 2 and beyond with 6.0 µg/kg NKTR-255
Randomization will be stratified according to the cellular product that the patient receives (ie, axi-cel or liso-cel [or tisa-cel in Stage 2]) and baseline LDH, and should take place no more than 1 day prior to the first study drug administration.

Combining Cell Therapy with Exogenous Cytokine May Increase Cmax and Extend CAR-T Cell Persistence in LBCL





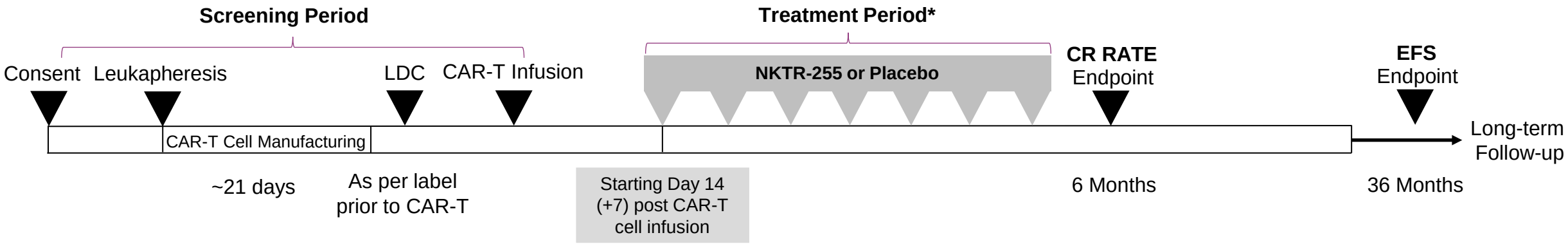
Higher peak IL-15 levels correlate with higher CD19 CAR-T cell AUC0-90 in humans.

CAR transgene (FlapEF1α copies/µg DNA) is shown as polynomial regression lines for three distinct tertiles of serum IL-15 peak concentration. Shaded areas represent 95% CI of the LOESS estimates. [11]

NEKTAR

Source: Hirayama et al. *Blood Adv*. 2022 Nov 4: bloodadvances.2022008697; Epub ahead of print. PMID: 36332004.

NKTR-255 or Placebo Dosed Following Commercially Approved CD19-Directed CAR-T Cell Therapy



*Study drug (NKTR-255 or placebo) infusion will be administered every 3 weeks (q3w) for up to 7 cycles or 5 months, whichever is earlier.

Q&A session

Mary Tagliaferri, MD

Chief Development Officer
at Nektar Therapeutics

Mario Marcondes, MD, PhD

VP, Head of Clinical Development
at Nektar Therapeutics

Cameron Turtle, MBBS, PhD

Chair of Cancer Immunotherapy
at University of Sydney and
Fred Hutchinson Cancer Center
affiliate

Poster 3335: A Phase 2/3, Randomized, Double Blind, Placebo-Controlled, Multicenter Study of NKTR-255 Vs Placebo Following CD-19 Directed CAR-T Therapy in Patients with Relapsed/Refractory Large B-Cell Lymphoma

Poster 4652: Safety, Tolerability, PK/PD, and Preliminary Efficacy of NKTR-255, a Novel IL-15 Receptor Agonist, in Patients with Relapsed/Refractory Hematologic Malignancies