NEKTAR®

NEW PATHWAYS TO SMARTER MEDICINE™

Society for Immunotherapy of Cancer 2020 Annual Meeting

Investor & Analyst Call

November 11, 2020

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 6, 2020. Nektar undertakes no obligation to update forward-looking statements as a result of new information or otherwise.

Today’s Speakers

Dr. Adi Diab

Associate Professor of Melanoma Medical Oncology at MD Anderson

Dr. Brendan D. Curti

Director of the Melanoma Program, Cytokine and Adoptive Immunotherapy and Genitourinary Oncology Research at Providence Cancer Institute

Dr. Nina Shah

Associate Professor, Department of Medicine at University of California San Francisco

Dr. Alan Tan

Assistant Professor Department of Internal Medicine, Division of Hematology, Oncology and Cell Therapy at Rush Medical College

Dr. Jonathan Zalevsky

Chief Research & Development Officer at Nektar Therapeutics

Dr. Wei Lin

Senior Vice President and Head of Development at Nektar Therapeutics

Dr. Adi Diab – MD Anderson

Adi Diab, M.D., serves as Associate Professor of Melanoma Medical Oncology at The University of Texas MD Anderson Cancer Center. Dr. Diab is one of the lead investigators in PIVOT-02, the Phase 1/2 study of BEMPEG plus nivolumab, and in REVEAL, the Phase 1/2 study of NKTR-262 and BEMPEG. He is also on the steering committee for the BMS-sponsored Phase 3 registrational study, PIVOT IO 001, which is ongoing, in patients with previously untreated metastatic melanoma. His research is focused on developing new immunotherapeutic strategies that will improve clinical outcomes in patients. He has authored or co-authored over thirty scientific publications and abstracts and serves as a reviewer for *Cancer Discovery*, *Journal of Clinical Oncology*, *Nature Reviews Journal of Immunotherapy* and *Journal of the American Society of Hematology*.

Dr. Brendan D. Curti – Providence Cancer Institute

Brendan D. Curti, M.D., is the Robert W. Franz Chair for Clinic Research and Member in the Earle A. Chiles Research Institute at Providence Cancer Institute. He serves as the Director of Cytokine and Adoptive Immunotherapy, Melanoma Program and Genitourinary Oncology Research. His clinical research focuses on developing new immunotherapies for melanoma, renal cell carcinoma, prostate cancer and bladder cancer. He previously served as a Senior Investigator in the Biological Response Modifiers Program at the National Cancer Institute and was an Associate Professor at the Penn State College of Medicine before joining the Earle A. Chiles Research Institute at Providence Cancer Institute.

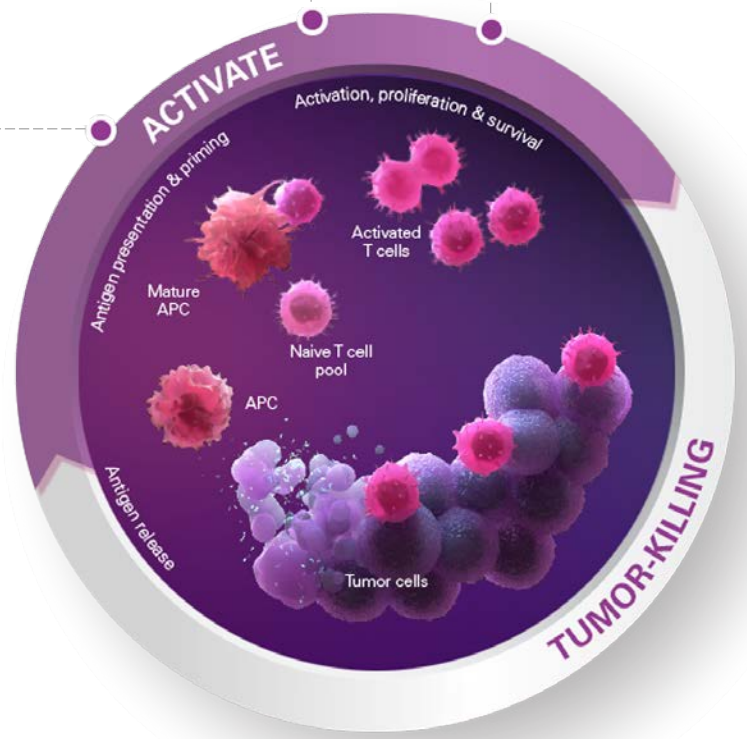
Dr. Nina Shah – University of California San Francisco

Nina Shah, M.D., is an Associate Professor in the Department of Medicine at the University of California San Francisco and a specialist in blood diseases who focuses on treating multiple myeloma, a type of cancer affecting certain cells in the bone marrow. Her areas of professional interest include the intersection of immunology and oncology as well as helping patients fight multiple myeloma by boosting their immune systems. She is an investigator in the NKTR-255 Phase 1/2 study in hematological malignancies. She belongs to the American Society of Clinical Oncology, American Society of Hematology and American Society for Transplantation and Cellular Therapy.

Dr. Alan Tan – Rush Medical College

Alan Tan, MD, is an Assistant Professor in the Division of Hematology, Oncology and Cell Therapy at Rush Medical College. He specializes in kidney cancer, bladder cancer, prostate cancer and melanoma. He also has an extensive background in hematologic malignancies. Dr. Tan has clinical research interest in designing and implementing clinical trials to test novel immunotherapies and targeted therapies for renal cell carcinoma and GU malignancies. He is an investigator in the NKTR-255 Phase 1/2 study in hematological malignancies. He also has interest in precision genomic cancer medicine, identifying molecular alterations that will serve as targets for individualized treatment strategies.

Today's Agenda



IL-2

"Progression-free Survival and Biomarker Correlates of Response With BEMPEG Plus NIVO in Previously Untreated Patients With Metastatic Melanoma: Results From The PIVOT-02 Study"

- *Wei Lin, M.D., Nektar Therapeutics*

TLR 7/8

"REVEAL: Phase 1 Dose-Escalation Study of NKTR-262, a Novel TLR7/8 Agonist, Plus Bempegaldesleukin: Local Innate Immune Activation and Systemic Adaptive Immune Expansion for Treating Solid Tumors"

- *Jonathan Zalevsky, Ph.D., Nektar Therapeutics*

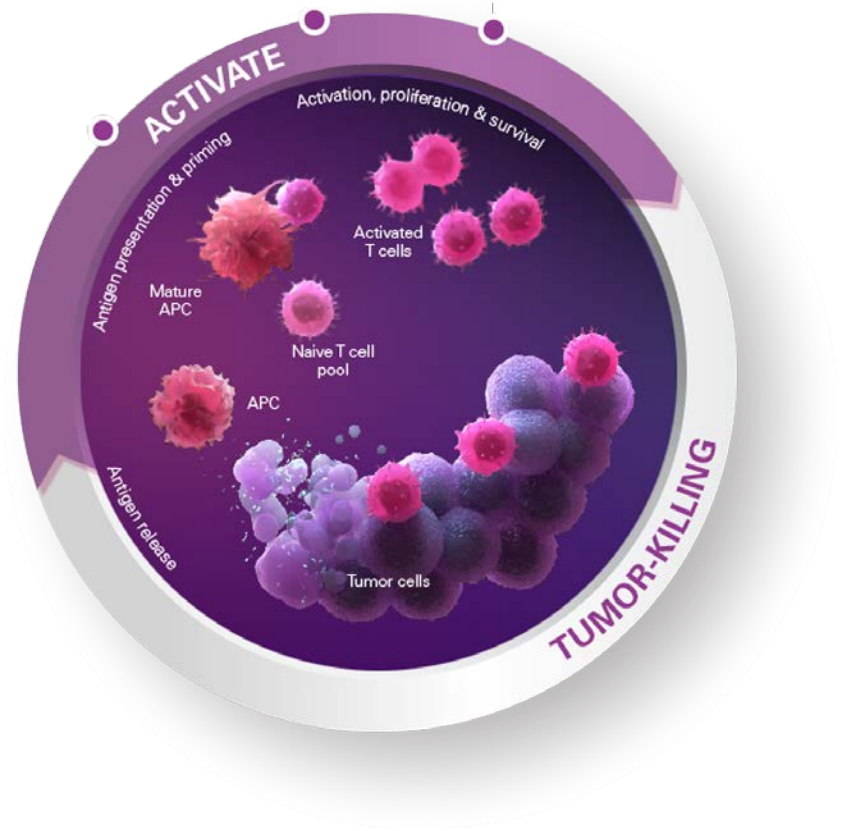
IL-15

"First-in-human Phase I Study of NKTR-255 in Patients With Relapsed/Refractory Hematologic Malignancies"

- *Nina Shah, M.D., UCSF*
- *Alan Tan, M.D., Rush University*

Q&A Expert Panel

BEMPEG: CD-122 Preferential IL-2 Pathway Agonist



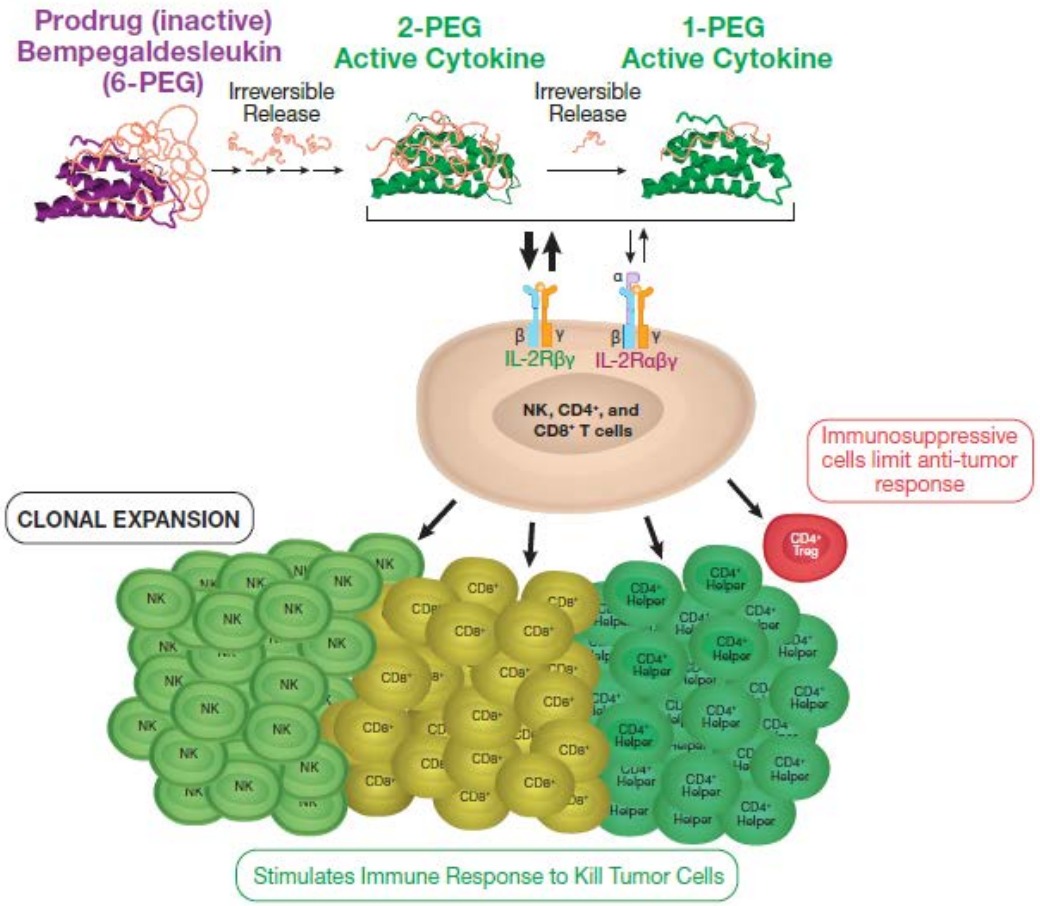
IL-2

Progression-free Survival and Biomarker Correlates of Response With BEMPEG Plus NIVO in Previously Untreated Patients With Metastatic Melanoma: Results From The PIVOT-02 Study

Adi Diab[1], Scott S. Tykodi[2], Gregory A. Daniels[3], Michele Maio[4], Brendan D. Curti[5], Karl D. Lewis[6]; Sekwon Jang[7], Ewa Kalinka[8], Igor Puzanov[9], Alexander I. Spira[10], Daniel C. Cho[11], Shanhong Guan[12], Erika Puente[12], Ute Hoch[12], Sue L. Currie[12], Tuan Nguyen[12], Wei Lin[12], Mary A.Tagliaferri[12], Jonathan Zalevsky[12], Mario Sznol[13], Michael E. Hurwitz[13]

[1]The University of Texas MD Anderson Cancer Center, Houston, TX, USA; [2]Seattle Cancer Care Alliance, Seattle, WA, USA; [3]University of California, La Jolla, CA, USA; [4]Azienda Ospedaliera Universitaria Senese, Siena, Italy; [5]Providence Cancer Institute and Earle A. Chiles Research Institute, Portland, OR, USA; [6]University of Colorado, Aurora, CO, USA; [7]Inova Schar Cancer Institute, Fairfax, VA, USA; [8]Polish Mother's Memorial Hospital – Research Institute, Lodz, Poland; [9]Roswell Park Comprehensive Cancer Center, Buffalo, NY, USA; [10]Virginia Cancer Specialists, Fairfax, VA, USA; [11]NYU Medical Oncology Associates, New York, NY, USA; [12]Nektar Therapeutics, San Francisco, CA, USA; [13]Yale School of Medicine, New Haven, CT, USA

BEMPEG Signals Preferentially Through The Interleukin-2 Receptor Pathway



- Bempegaldesleukin (BEMPEG; NKTR-214) is a CD122-preferential IL-2 pathway agonist shown to increase tumor-infiltrating lymphocytes, T-cell clonality and PD-1 expression[1,2]
- BEMPEG plus the CPI nivolumab (NIVO) has been shown to convert tumors from PD-L1(-) at baseline to PD-L1(+) on-treatment[3]
- Low levels of baseline tumor-infiltrating lymphocytes[4–6] and T-cell inflammation[7] is predictive of a poor response to CPIs

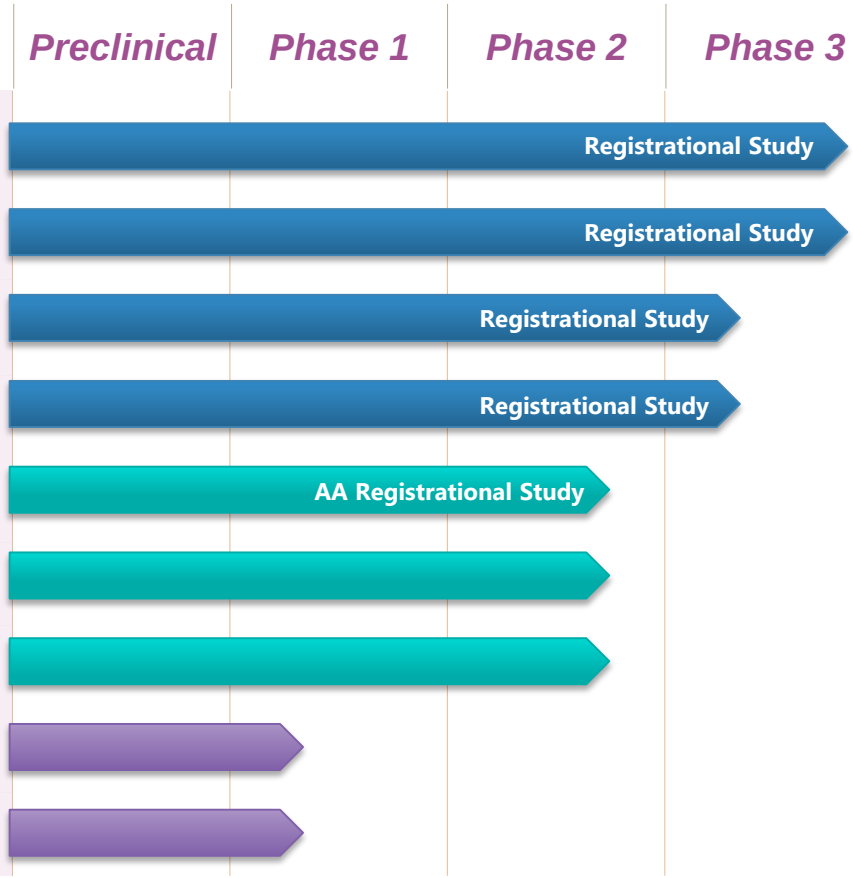
CPI, checkpoint inhibitor; IL, interleukin; NK, natural killer; PD-(L)1, programmed death-(ligand) 1; Treg, regulatory T cell.

1. Charych D, et al. *PLoS One* 2017; 12: e0179431; 2. Bentebibel SE, et al. *Cancer Discov* 2019;9:711–21; 3. Diab A, et al. *Cancer Discov* 2020;10:1158–73; 4. Daud AI, et al. *J Clin Oncol* 2016;34:4102–09;
5. Daud AI, et al. *J Clin Invest* 2016;126:3447–52; 6. Tumeh PC, et al. *Nature* 2014;515:568–71; 7. Ayers M, et al. *J Clin Invest* 2017;127:2930–40.

BEMPEG Development Program in Solid Tumors

Pipeline

Partner	Indication	Program
Bristol Myers Squibb™	Metastatic Melanoma	Bempegadesleukin (bempeg) + OPDIVO®
Bristol Myers Squibb™	Renal Cell Carcinoma	Bempeg + OPDIVO®
Bristol Myers Squibb™	Muscle-invasive Bladder Cancer	Bempeg + OPDIVO®
Bristol Myers Squibb™	Adjuvant Melanoma	Bempeg + OPDIVO®
Bristol Myers Squibb™	Bladder Cancer	Bempeg + OPDIVO®
Bristol Myers Squibb™	Renal Cell Carcinoma	Bempeg + OPDIVO® + TKI
	1L NSCLC	Bempeg + KEYTRUDA®
vaccibody	Head & Neck SCC	Bempeg + VB10.NEO
	Multiple Solid Tumors	NKTR-262 + Bempeg



BEMPEG Plus NIVO in Metastatic Melanoma

- Despite CPI therapy as an effective treatment option, there is an unmet need for therapies to produce durable and deeper responses in more patients with metastatic melanoma
- Safety and clinical activity of BEMPEG plus NIVO was evaluated in PIVOT-02, a multicenter phase 1/2 study in multiple solid tumors[1]
  - Encouraging preliminary clinical activity and safety data were seen in metastatic melanoma, including durable responses that deepened over time[1,2]
- BEMPEG plus NIVO received FDA Breakthrough Therapy Designation in July 2019 for patients with previously untreated, unresectable or metastatic melanoma
- **Here, we report the updated results from PIVOT-02 (NCT02983045) in previously untreated patients with metastatic melanoma, including median PFS and biomarker correlates of response**

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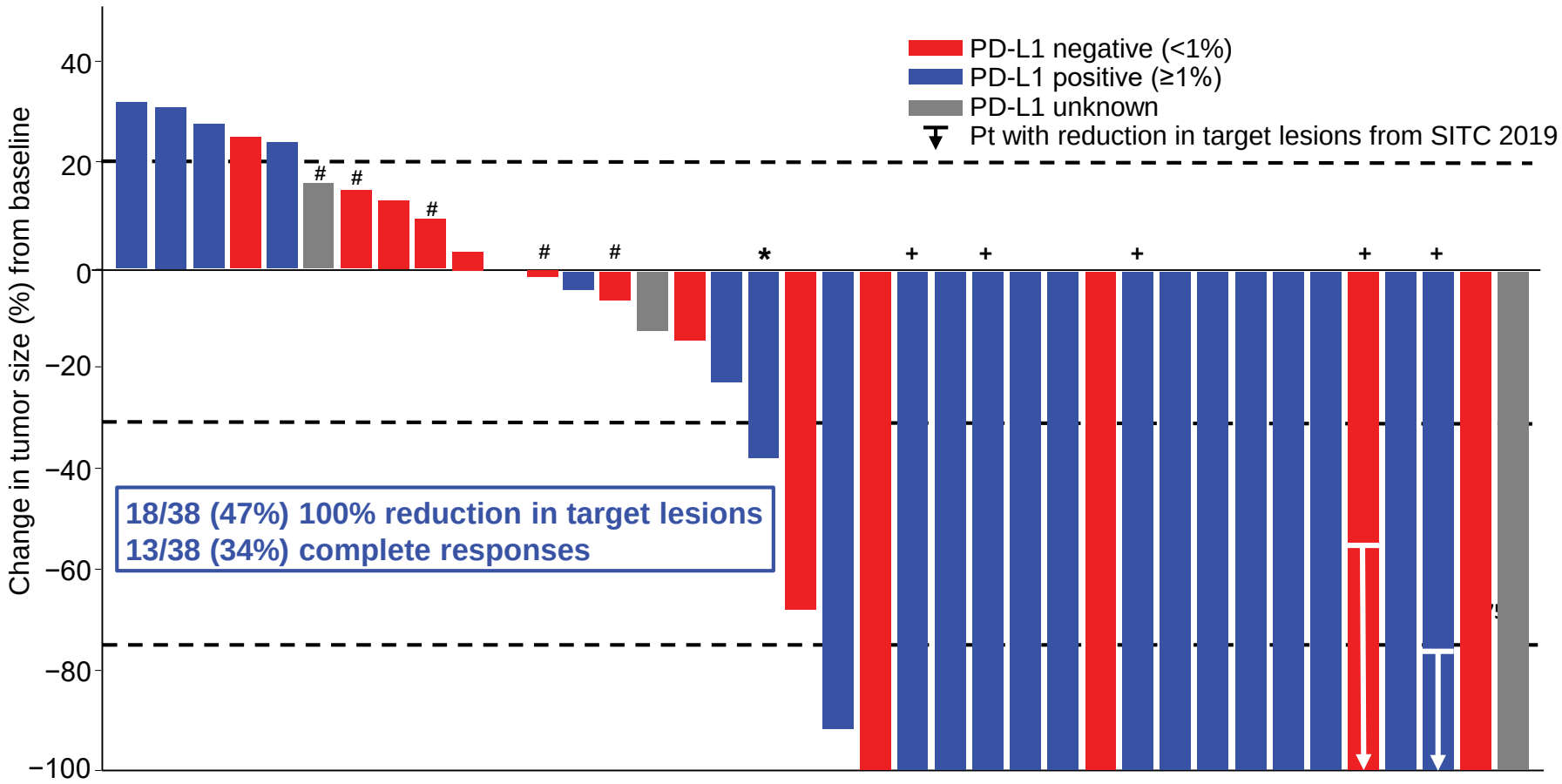
CPI, checkpoint inhibitor; FDA, U.S. Food and Drug Administration; PFS, progression-free survival.

1. Diab A, et al. *Cancer Discov* 2020;10:1158–73; 2. Diab A, et al. Oral presentation at SITC 2019:O35.

Stage IV 1L Melanoma: Best Overall Response by Independent Radiology



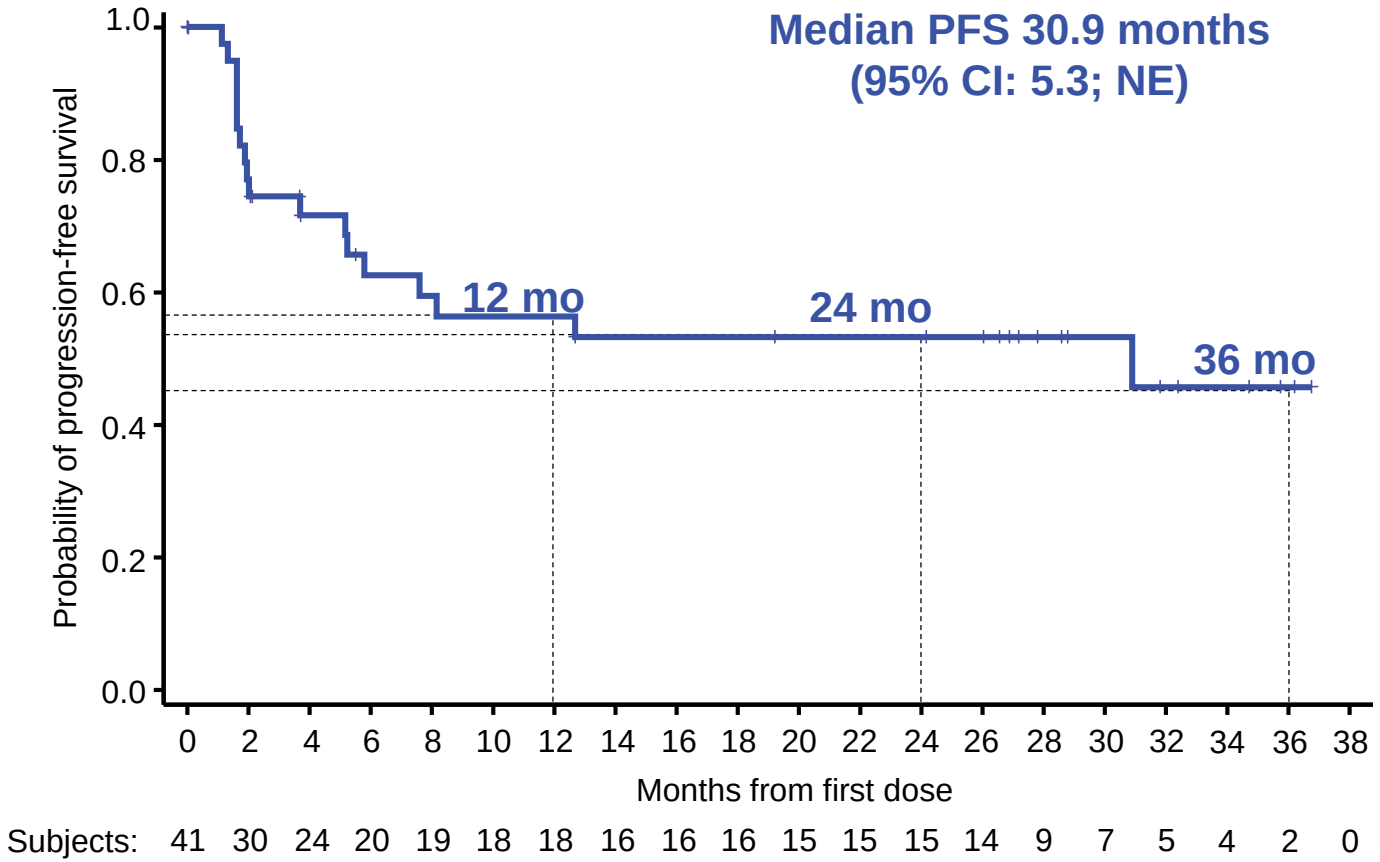
1L Melanoma (n=38 Efficacy Evaluable) Median 29.0 Months of Follow-up	ORR
Confirmed ORR (CR+PR)	**20 (53)**
CR	**13 (34)**
PD-L1 negative (n=13)	**5 (39)**
PD-L1 positive (n=22)	**14 (64)**
PD-L1 unknown (n=3)	**1 (33)**
LDH >ULN (n=11)	**5 (46)**
Liver metastases (n=10)	**5 (50)**
Median % reduction from baseline	**−78.5**
Median time to response (months)	**2.0**
Median time to CR (months)	**7.9**

All 5 responses in patients with liver metastases were CRs

1L Melanoma (n=38 Efficacy Evaluable)	
Median duration of follow-up (months)	**29.0**
Median number of cycles (range)	**9 (1–35)**
Number of cycles ≥6, n (%)	**29 (70.7)**
Pts with ongoing responses, n (%)	**16 (80.0)**
Median duration of response (months)	**NE**

Data cutoff: 1SEPT2020. Response evaluable population includes eligible patients with measurable disease (per RECIST 1.1) at baseline and have ≥1 post-baseline tumor assessment. All objective responses are confirmed. #Best overall response is progressive disease due to non-target lesion progression or presence of new lesion; *Best overall response is SD; +Best overall response is PR. CR for target lesion, non-target lesion still present. CR complete response; LDH, lactate dehydrogenase; ORR, objective response rate; PD-L1, programmed death-ligand 1; PR, partial response; SD, stable disease; ULN, upper limit of normal.

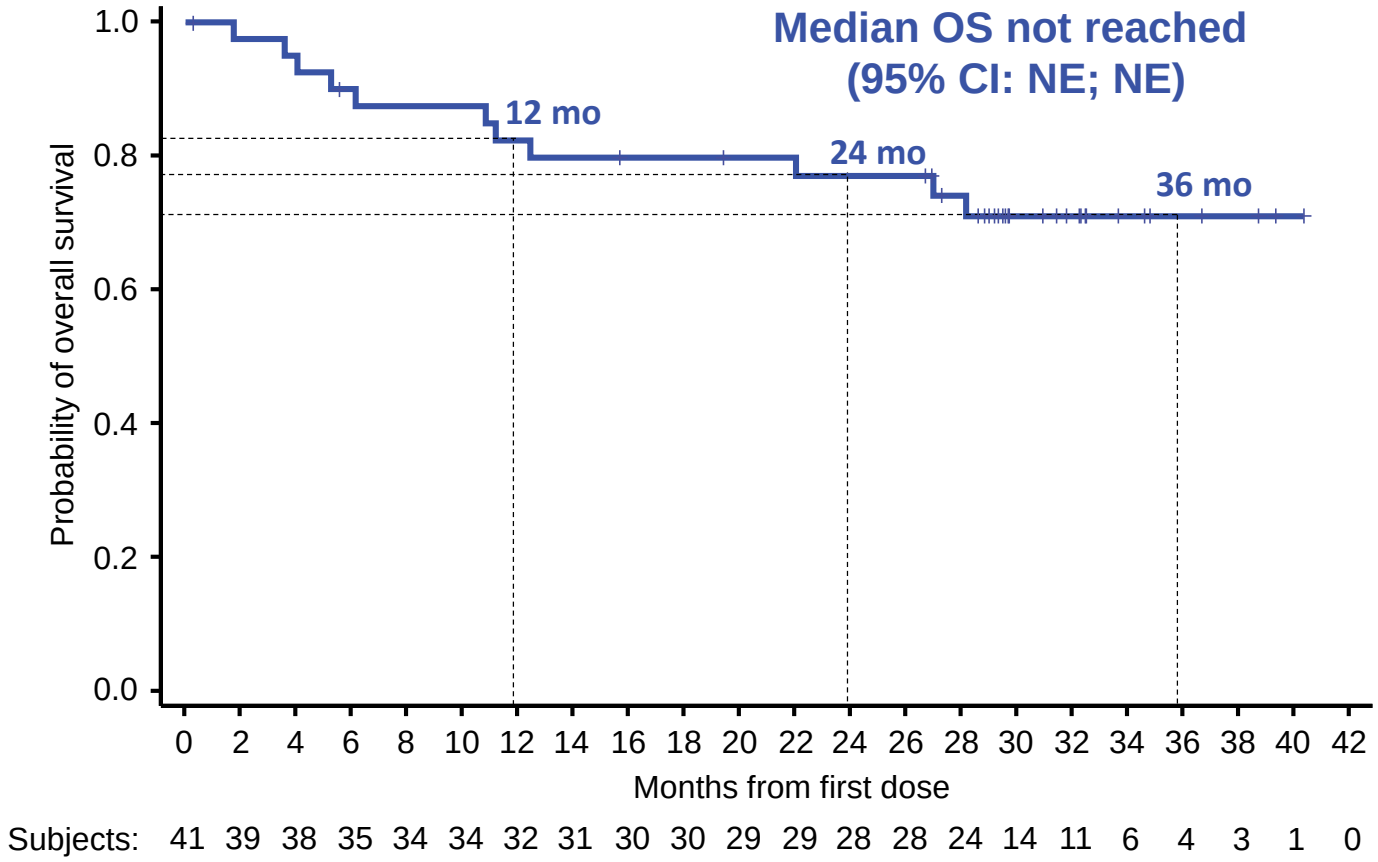
mPFS 30.9 Months (95% CI: 5.3; NE) at Median Follow-up of 29.0 Months



Kaplan–Meier Estimate of PFS by BICR (RECIST v1.1)	Total (N=41)
Rate at 12 months, % (95% CI)	56.2 (38.4; 70.6)
Rate at 24 months, % (95% CI)	53.1 (35.4; 67.9)
Rate at 36 months, % (95% CI)	45.5 (25.5; 63.5)

Data cutoff: 1SEPT2020.
BICR, blinded independent central radiology; NE, not estimable; mPFS, median progression-free survival.

mOS Not Reached (95% CI: NE, NE) at Median Follow-up of 29.0 Months



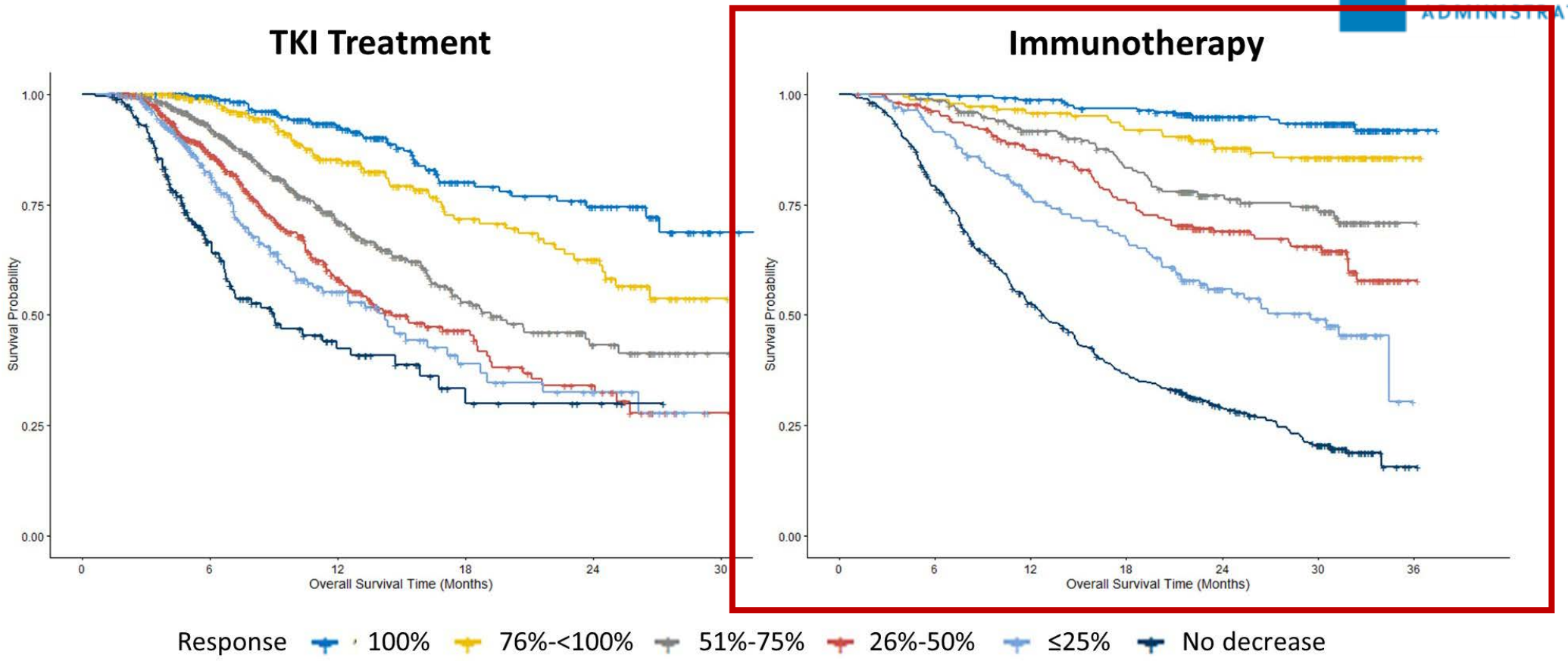
Kaplan–Meier Estimate of Overall Survival	Total (N=41)
Rate at 12 months, % (95% CI)	82.3 (66.4; 91.1)
Rate at 24 months, % (95% CI)	77.0 (60.4; 87.3)
Rate at 36 months, % (95% CI)	70.9 (53.5; 82.8)

Data cutoff: 1SEPT2020.
NE, not estimable; mOS, median overall survival.

ASCO 2019 Osgood et. al., Retrospective Analysis of Untreated Metastatic Melanoma Patients: Depth of Response (DpR) Correlates with Longer OS

4,826 patients across 10 randomized controlled trials with previously untreated unresectable or metastatic melanoma

Overall Survival by Reduction Category



Source: 2019 ASCO FDA presentation J Clin Oncol 37, 2019 (suppl; abstr 9508).
"Depth of Response and Survival in Advanced or Metastatic Melanoma", Osgood, C., et al.

Historical Comparisons in 1L Metastatic Melanoma

	BEMPEG PLUS NIVO			NIVO ONLY			NIVO PLUS IPI		
	PIVOT-02 ≈7 months*	PIVOT-02 ≈1.6 year*	PIVOT-02 ≈2.4 year*	CM067 1 year[1]	CM067 2 year[2]	CM067 3 year[3]	CM067 1 year[1]	CM067 2 year[2]	CM067 3 year[3]
Median Time of Follow-Up (months)	**7.2**	**18.6**	**29.0**	12.2-12.5	20.7	38.0	12.2-12.5	20.7	38.0
Complete Response (CR)	**24%**	**34%**	**34%**	9%	NA	16%	12%	NA	19%
Overall Response Rate (ORR)	**53%**	**53%**	**53%**	44%	44%	44%	58%	NA	58%
Median Progression-Free Survival (mPFS)	**NR**	**NR**	**30.9 months**	6.9 months	6.9 months[3]	6.9 months	11.5 months	11.5 months	11.5 months

	BEMPEG PLUS NIVO			NIVO ONLY			NIVO PLUS IPI		
	PIVOT-02 1 year	PIVOT-02 2 year	PIVOT-02 3 year	CM067 1 year[1]	CM067 2 year[2]	CM067 3 year[3]	CM067 1 year[1]	CM067 2 year[2]	CM067 3 year[3]
Landmark Overall Survival (OS)	**82%**	**77%**	**71%**	NA	59%[3]	52%	NA	64%	58%

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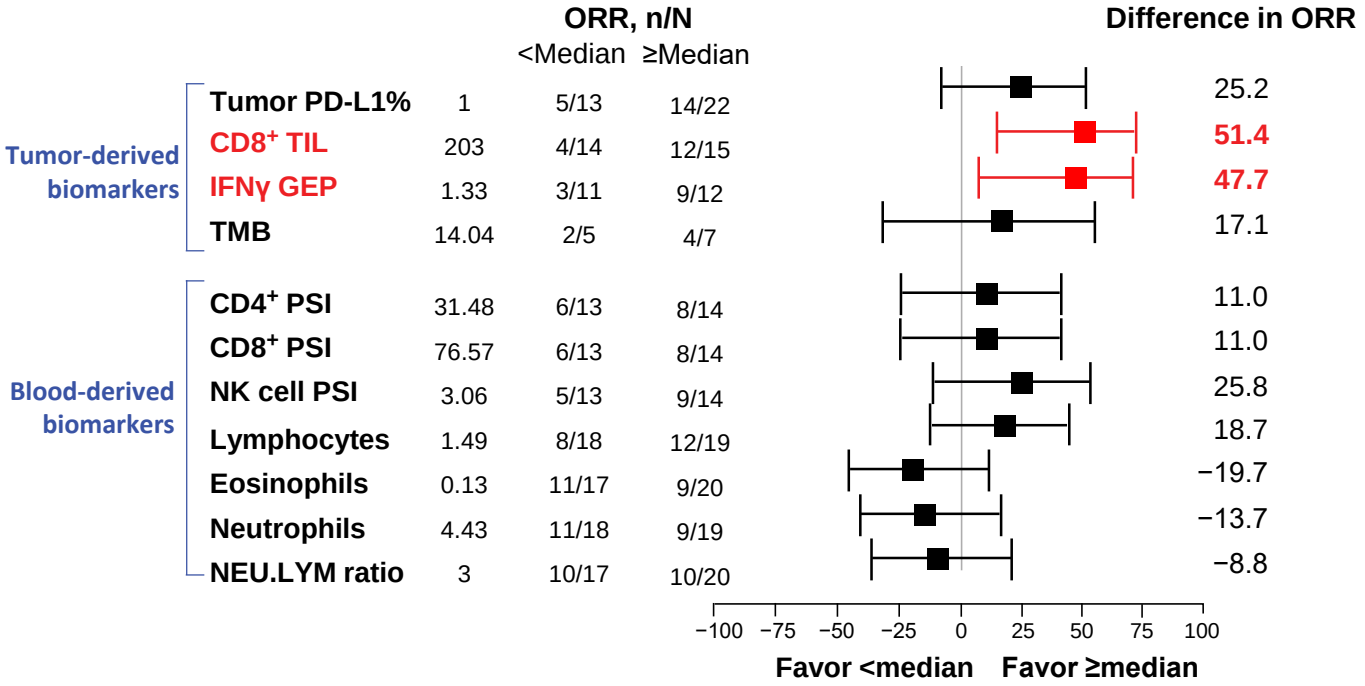
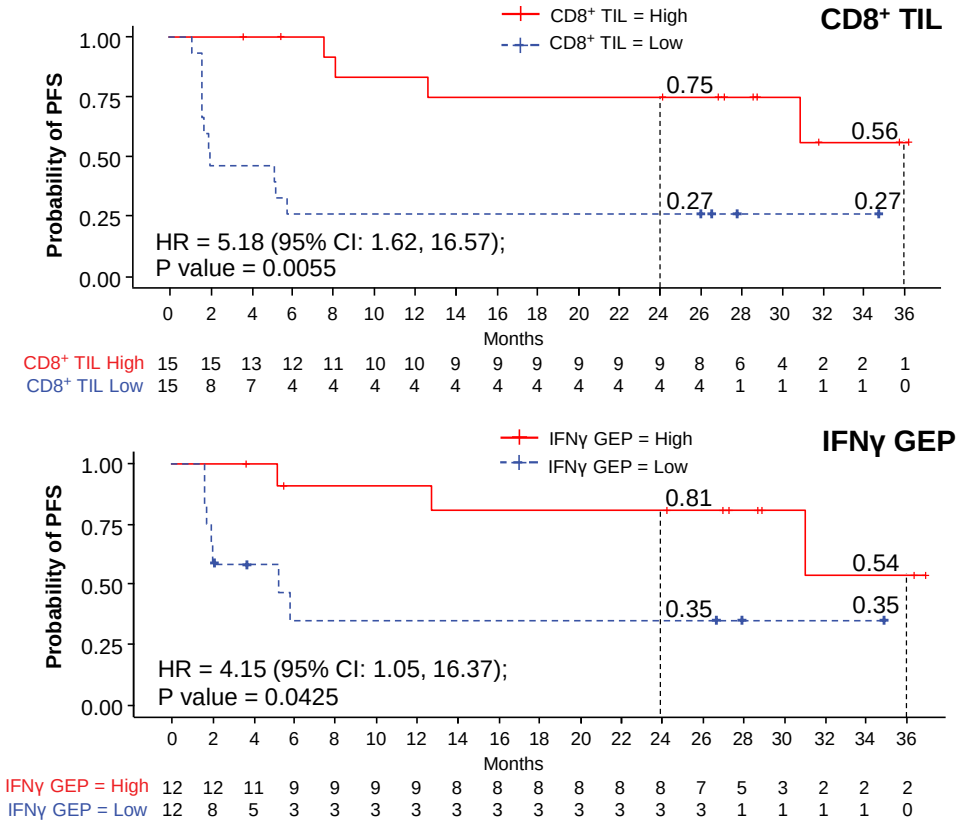
NR – not reached; NA – not available or not reported; PEMBRO – pembrolizumab; NIVO – nivolumab; IPI – ipilimumab;
1. Larkin J, et al. N Engl J Med 2015;373:23-34; 2. Wolchok et al. ASCO 2016: Abstract 9505; 3. Wolchok et al. N Engl J Med 2017; 377:1345-1356

Relationship Between Baseline Biomarkers and Response

High CD8+ TIL and IFNγ GEP at baseline associated with higher ORR[a]



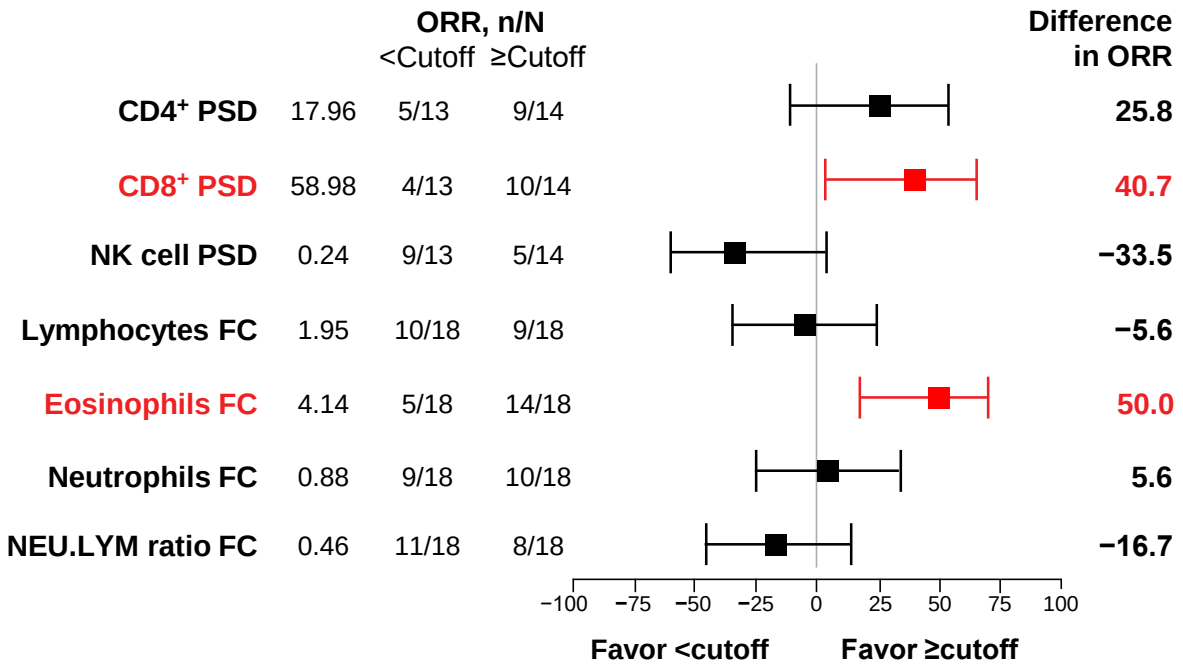
Increased CD8+ TIL and IFNγ GEP associated with longer PFS[b]



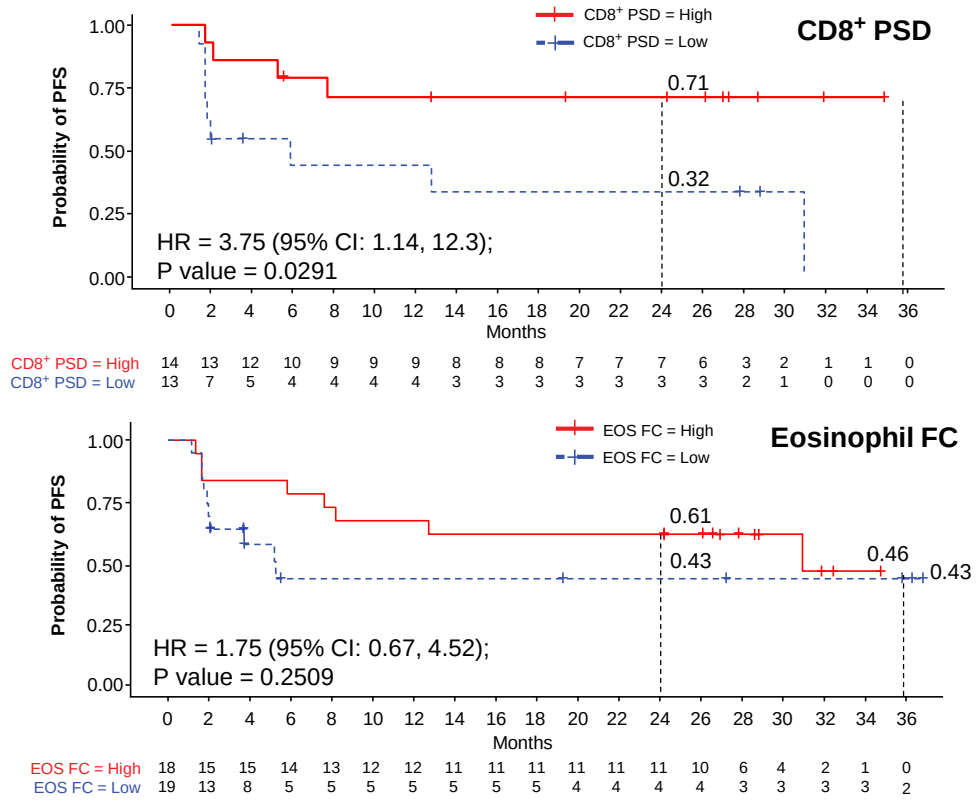
Data cutoff: 1SEPT2020. [a]Best overall response (RECIST 1.1) by BICR; median (≥median vs <median) cutoff for markers; efficacy-evaluable population, n=38. [b]CD8+ TIL and IFNγ GEP (high vs low by median cutoff); safety population (N=41). GEP, gene expression profile; NEU.LYM ratio, neutrophil to lymphocyte ratio; NK, natural killer; ORR, objective response rate; PFS, progression-free survival; PSI, polyfunctional strength index, using IsoPlexis technology; TIL, tumor-infiltrating lymphocyte; TMB, tumor mutational burden.

Relationship Between On-treatment (Day 8) Blood Biomarkers in Matched Samples and Response

Increased CD8+ PSD and eosinophils associated with higher ORR[a]

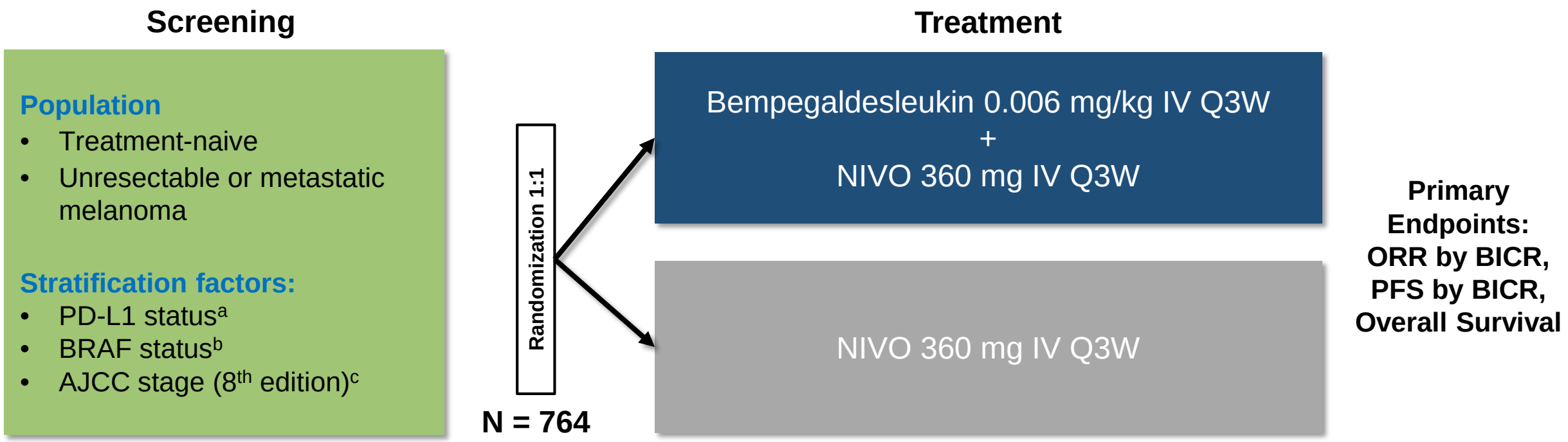


Increased CD8+ PSD, but not eosinophils associated with longer PFS[b]



Data cutoff: 1SEPT2020. [a]Best overall response (RECIST 1.1) by BICR; median (≥median vs < median) cutoff for markers; efficacy-evaluable population, n=38. [b]CD8+ PSD (high vs low by median cutoff); PFS, by BICR; safety population (N=41). EOS, eosinophils; FC, fold change at C1D8 vs C1D1; NEU.LYM ratio, neutrophil to lymphocyte ratio; NK, natural killer; ORR, objective response rate; PFS, progression-free survival; PSD, difference in PSI between C1D1 and C1D8; PSI, polyfunctional strength index, using IsoPlexis technology.

PIVOT IO 001 Study Design in Patients with Previously Untreated, Unresectable or Metastatic Melanoma

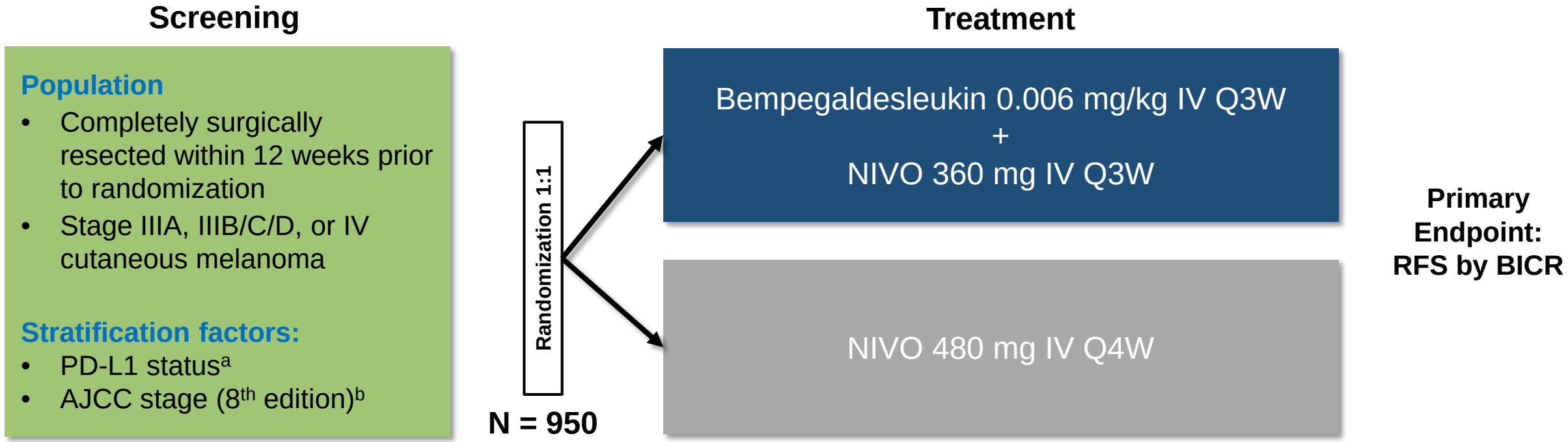


[a]Tumor cell PD-L1 expression (≥1% or <1%/Indeterminate) determined using 28-8 pharmDx (Dako, an Agilent Technologies, Inc. company, Santa Clara, CA). [b]V600-mutant vs wild-type. [c]M0/M1 any [0] vs M1 any [1], based on the screening imaging and laboratory test results (lactate dehydrogenase level).

AJCC, American Joint Committee on Cancer; BICR, blinded independent central review; IV, intravenous; NIVO, nivolumab; ORR, overall response rate; OS, overall survival; PD-L1, programmed death ligand 1; PFS, progression-free survival;Q3W, every 3 weeks; RECIST, Response Evaluation Criteria In Solid Tumors.

PIVOT 12 Study Design in Adjuvant Melanoma Setting

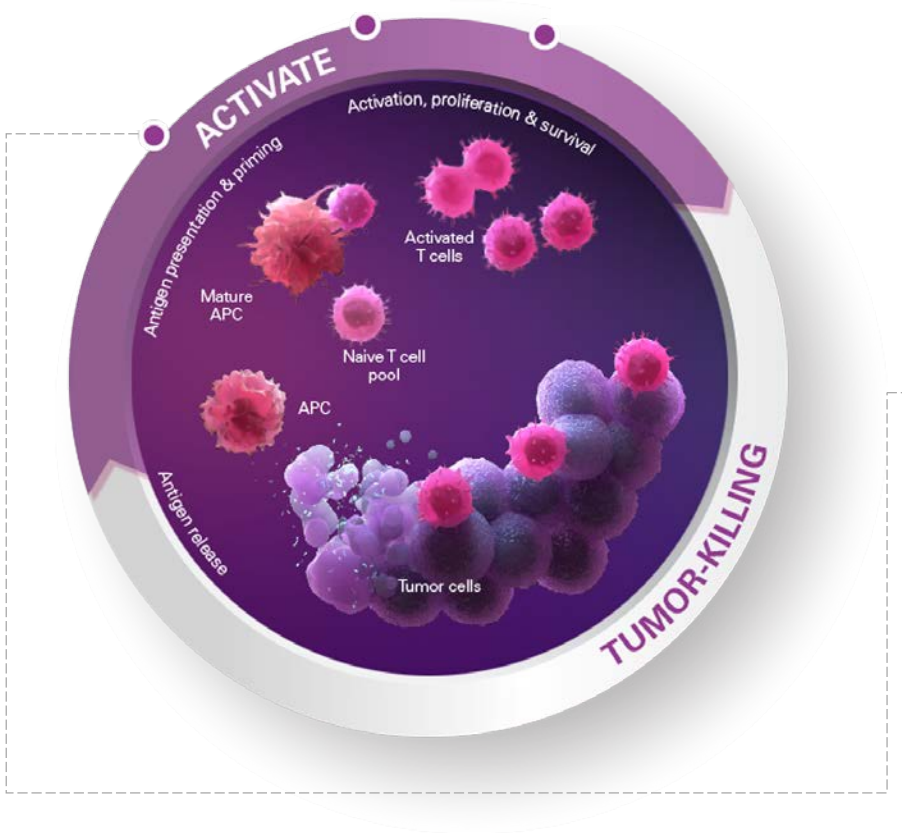
A Phase 3, Randomized, Open-label Study to Compare Adjuvant Immunotherapy of Bempegaldesleukin (BEMPEG) Combined With Nivolumab (NIVO) Versus NIVO After Complete Resection of Melanoma in Patients at High Risk for Recurrence



[a]Tumor cell PD-L1 expression (≥1% or <1%/Indeterminate) determined using 28-8 pharmDx (Dako, an Agilent Technologies, Inc. company, Santa Clara, CA). [b]M0/M1 any [0] vs M1 any [1], based on the screening imaging and laboratory test results (lactate dehydrogenase level).

AJCC, American Joint Committee on Cancer; BICR, blinded independent central review; IV, intravenous; NIVO, nivolumab; RFS, relapse-free survival; PD-L1, programmed death ligand 1; Q3W, every 3 weeks; Q4W, every 4 weeks

NKTR-262: TLR 7/8 Agonist



TLR 7/8

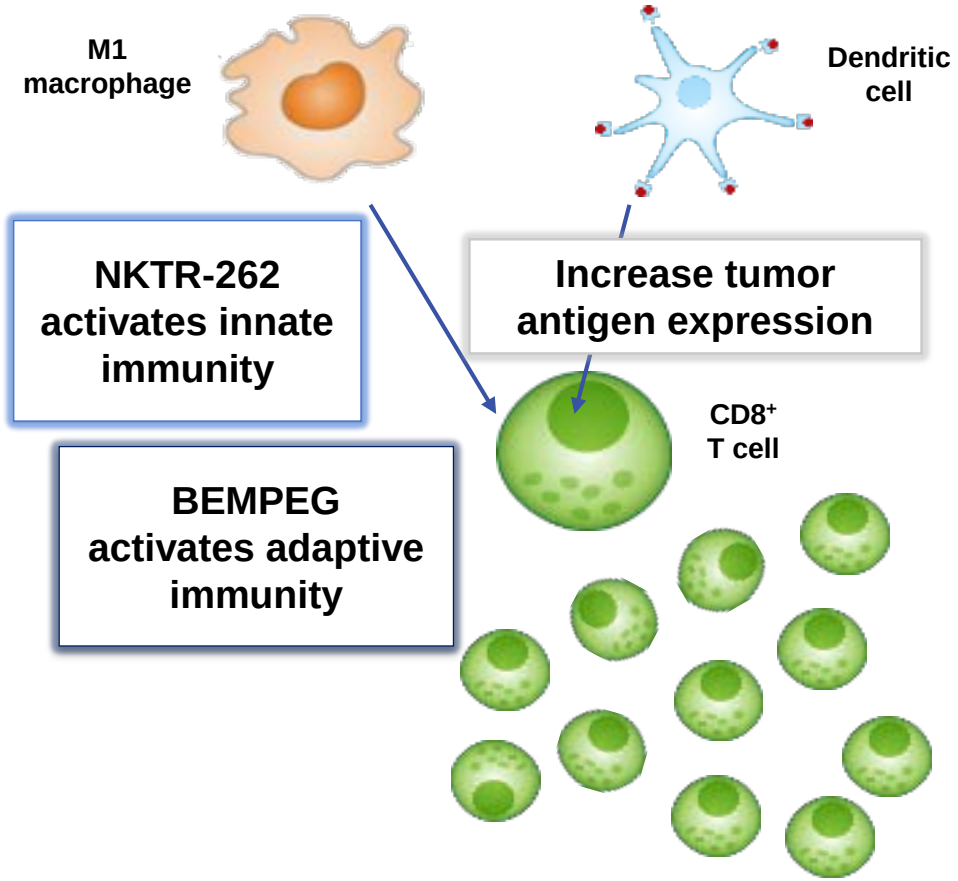
REVEAL: Phase 1 Dose-Escalation Study of NKTR-262, a Novel TLR7/8 Agonist, Plus Bempegaldesleukin: Local Innate Immune Activation and Systemic Adaptive Immune Expansion for Treating Solid Tumors

Adi Diab[1], Brendan D. Curti[2], Mehmet A. Bilen[3], Andrew S. Brohl[4], Evidio Domingo-Musibay[5], Erkut H. Borazanci[6], Christie Fanton[7], Cat Haglund[7], Mona Vimal[7], Danni Yu[7], Mann Muhsin[7], Mario Q. Marcondes[7], Anh Nguyen[7], Mary A. Tagliaferri[7], Wei Lin[7], Jonathan Zalevsky[7], Sandra P. D'Angelo[8]

[1]The University of Texas MD Anderson Cancer Center, Houston, TX, USA; [2]Providence Cancer Institute and Earle A. Chiles Research Institute, Portland, OR, USA; [3]Winship Cancer Institute of Emory University, Atlanta, GA, USA; [4]H. Lee Moffitt Cancer Center and Research Institute, Tampa, FL, USA; [5]University of Minnesota Medical Center, Minneapolis, MN, USA; [6]HonorHealth Research Institute, Scottsdale, AZ, USA; [7]Nektar Therapeutics, San Francisco, CA, USA; [8]Memorial Sloan Kettering Cancer Center and Weill Cornell Medical College, New York, NY, USA

MoA: Targeting the Innate and Adaptive Immune Response With NKTR-262 Plus BEMPEG

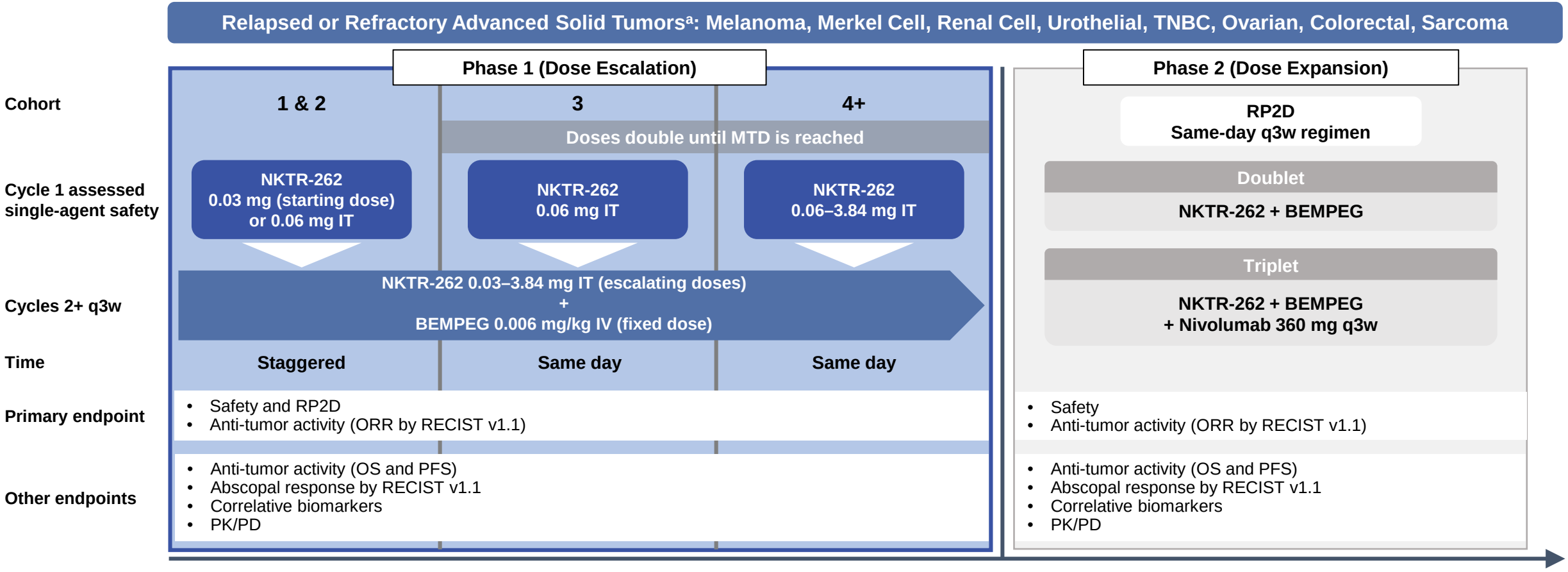
- NKTR-262 is an intratumorally delivered TLR7/8 agonist that activates APCs to prime new antigen-specific cytotoxic T cells
- Bempegaldesleukin (BEMPEG or NKTR-214) is an investigational, first-in-class, CD122-preferential, IL-2–pathway agonist
- In preclinical models, NKTR-262 plus BEMPEG combined innate immune signaling and enhanced antigen presentation with sustained T-cell activation, resulting in tumor growth inhibition of treated and abscopal lesions[1]
- High levels of TLR activation in the TME after NKTR-262 dose[1] allow us to understand PK/PD, and subsequently characterize the safety of NKTR-262



APC, antigen-presenting cell; IL, interleukin; MoA, mechanism of action; PD, pharmacodynamics; PK, pharmacokinetics; TLR, toll-like receptor; TME, tumor microenvironment.

1. Kivimae S, et al. *J Immunother Cancer* 2017;5(Suppl 2):P275.

REVEAL: Phase 1/2 Study Schema



[a]Injected lesions 20–90 mm in diameter.
Cohorts 1 and 2 explored staggered administration of NKTR-262 and BEMPEG; cohort 3 onwards explored same-day administration of NKTR-262 and BEMPEG.
IT, intratumoral; MTD, maximum tolerated dose; ORR, objective response rate; OS, overall survival; PD, pharmacodynamics; PFS, progression-free survival; PK, pharmacokinetics; q3w, every 3 weeks; RP2D, recommended Phase 2 dose; TNBC, triple-negative breast cancer.

Dose-Escalation Cohorts and the Clinical Activity of NKTR-262 Combined With BEMPEG

Dose Escalation	N=36	NKTR-262 (mg IT)	BEMPEG (mg/kg q3w IV)	Tumor Type
Cohort 1	3	0.03 (starting dose)	0.006	Melanoma, sarcoma
Cohort 2	7	0.06	0.006	Melanoma, sarcoma, CRC
Cohort 3				
Cohort 4	3	0.12	0.006	TNBC, RCC
Cohort 5	4	0.24	0.006	TNBC, RCC, CRC, Merkel cell
Cohort 6	4	0.48	0.006	Melanoma
Cohort 7	4	0.96	0.006	Melanoma
Cohort 8	3	1.92	0.006	Melanoma
Cohort 9 (RP2D)	**8**	**3.84**	**0.006**	**Melanoma**

- As of 1 Sept 2020, 36 patients with R/R metastatic solid tumors were enrolled across nine cohorts
  - Of the 28 patients in the efficacy-evaluable population, eight (29%) had regression in the injected lesions
- 2 of 22 efficacy-evaluable, heavily pretreated melanoma patients (9%) experienced an objective response
  - 1 had a 50% reduction in tumor burden and 1 had a 100% reduction in sum of diameters in the non-injected target lesions

Initial results of clinical activity; further assessments are ongoing.
CRC, colorectal cancer; IT, intratumoral; IV, intravenous; q3w, every 3 weeks; RCC, renal cell carcinoma; RP2D, recommended Phase 2 dose; R/R, relapsed or refractory; SD, stable disease; TNBC, triple-negative breast cancer.

Treatment-Related Adverse Events

Preferred Term, n (%)	Total (N=36)
Patients reporting ≥1 TRAE (NKTR-262 monotherapy) (≥10% listed below)	**17 (47.2)**
Flu-like symptoms[a]	8 (22.2)
Fatigue	4 (11.1)
Nausea	4 (11.1)
Patients reporting ≥1 TRAE (NKTR-262 + BEMPEG) (≥20% listed below)	**35 (97.2)**
Flu-like symptoms[a]	28 (77.8)
Fatigue	16 (44.4)
Nausea	15 (41.7)
Pruritus[b]	15 (41.7)
Rash[c]	13 (36.1)
Vomiting	9 (25.0)
Grade ≥3 TRAEs (NKTR-262 + BEMPEG) (≥5% listed below)	**11 (30.6)**
Elevated ALT	2 (5.6)
Hypotension	2 (5.6)
Leukocytosis	2 (5.6)
Rash[c]	2 (5.6)
Syncope	2 (5.6)

*One DLT of transient grade 3 elevated ALT and grade 4 elevated AST in the highest dose cohort

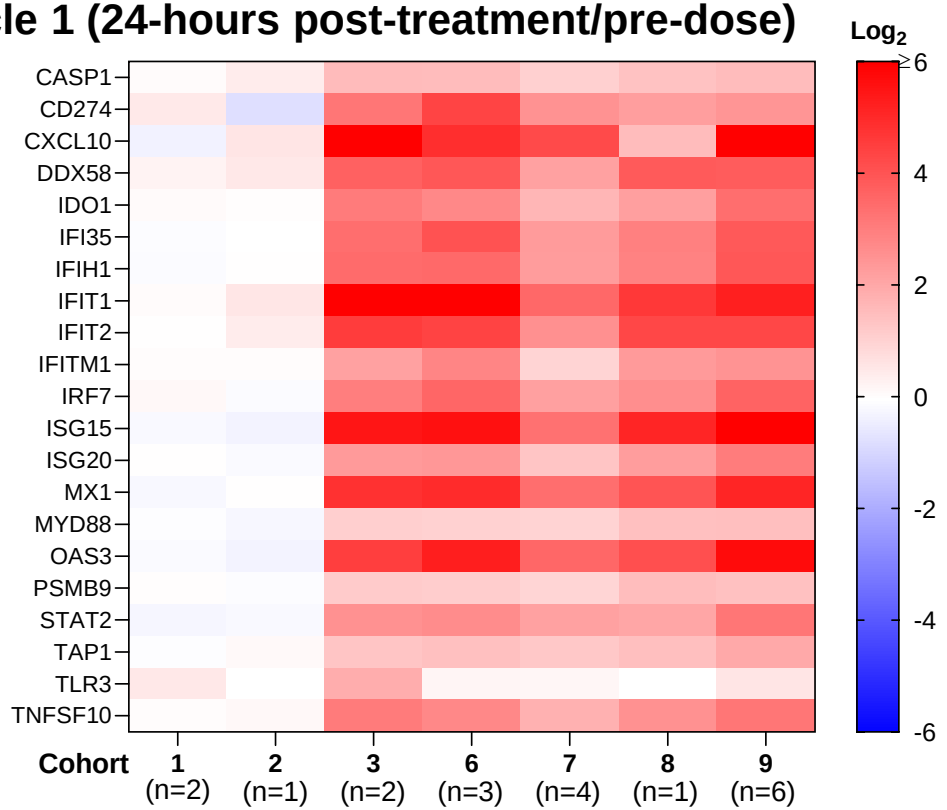
The safety profile of NKTR-262 + BEMPEG was favorable and tolerable, with few treatment discontinuations due to adverse events[d]

The MTD was not reached*

[a]Flu-like symptoms included the following preferred terms: influenza-like illness, influenza, pyrexia, chills. [b]Pruritus included the following preferred terms: pruritus, pruritus generalized. [c]Rash included the following preferred terms: erythema, rash, rash erythematous, rash maculo-papular, rash papular, rash pruritic, rash pustular, rash vesicular, rash generalized, rash macular. [d]Four patients discontinued treatment due to an adverse event. ALT, alanine aminotransferase; AST, aspartate aminotransferase; DLT; dose-limiting toxicity; MTD, maximum tolerated dose; TRAE, treatment-related adverse event.

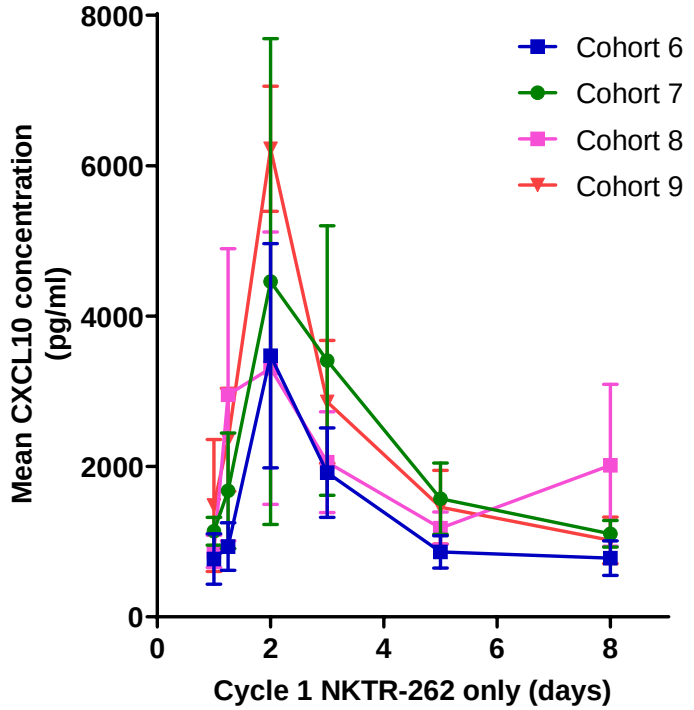
Dose-dependent Induction of Type 1 IFN Genes and CXCL10 Chemokine in Blood Consistent With TLR7/8 Target Engagement

Gene expression changes in peripheral blood, Cycle 1 (24-hours post-treatment/pre-dose)



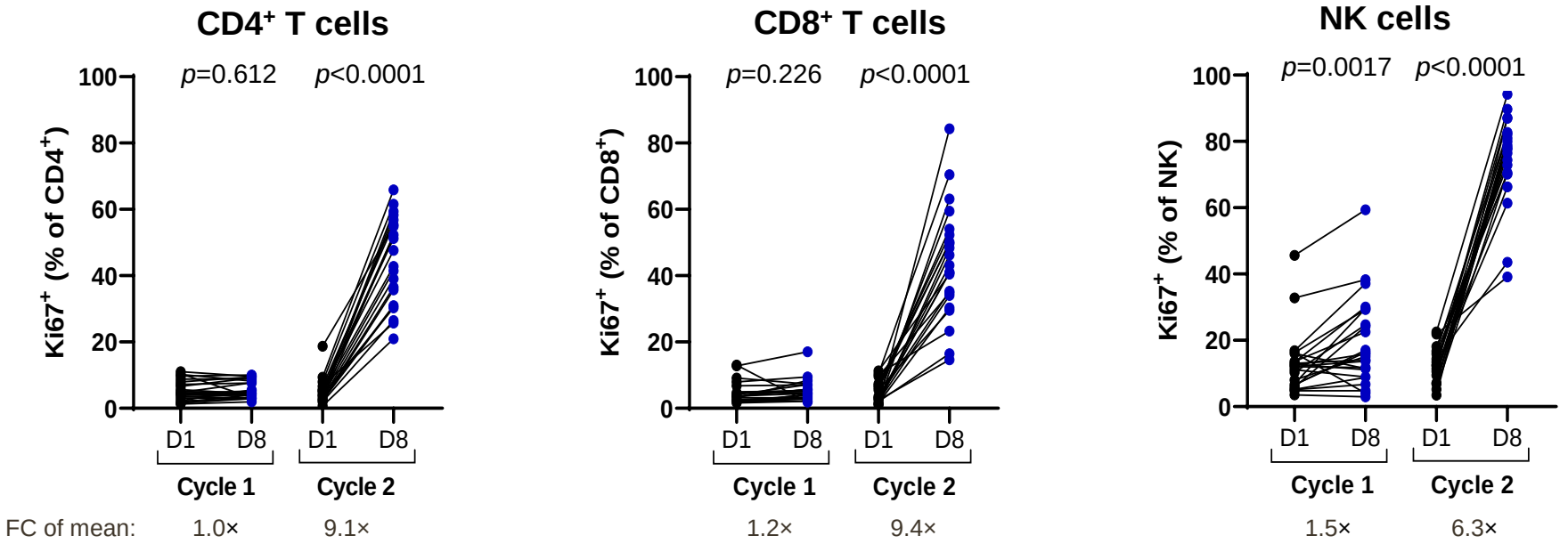
Median log_2 fold change at 24-hours post-cycle 1 NKTR-262 monotherapy for each cohort

Induction of plasma CXCL10/IP10 in Cycle 1



Data shown are for patients with melanoma.

Increased Proliferation (%Ki67$^+$) of CD4$^+$, CD8$^+$, and NK Cells in Blood in Cycle 2 is Consistent With the MoA of BEMPEG*

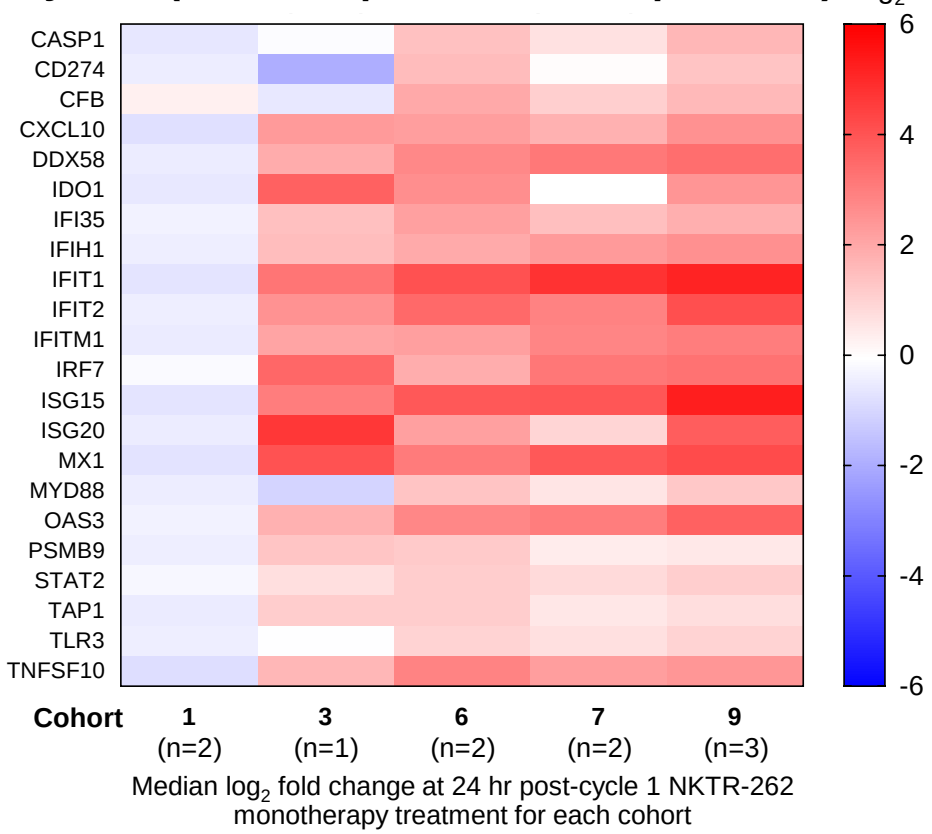


Minimal induction of proliferative immune cell subsets in Cycle 1 reflects retention of NKTR-262 in the TME following local delivery

*Matched pairs only; n=24 in Cycle 1, n=22 in Cycle 2.
Cycle 1: NKTR-262 monotherapy; **Cycle 2:** first exposure to NKTR-262 + BEMPEG.
D, day; FC, fold change; MoA, mechanism of action; NK, natural killer; TME, tumor microenvironment.

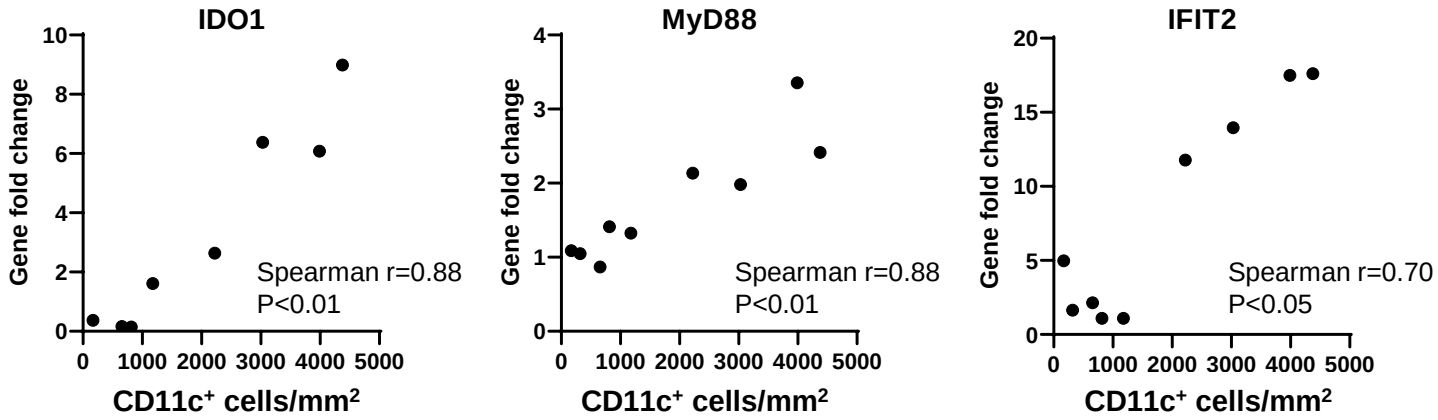
Induction of Type 1 IFN Genes in Biopsies Correlates With Density of CD11c$^+$ NKTR-262–Targeted Cells

Gene expression changes in melanoma biopsies, Cycle 1 (24-hours post-treatment/pre-dose)



Median log_2 fold change at 24 hr post-cycle 1 NKTR-262 monotherapy treatment for each cohort

Representative correlations between select genes and CD11c$^+$ density[a]

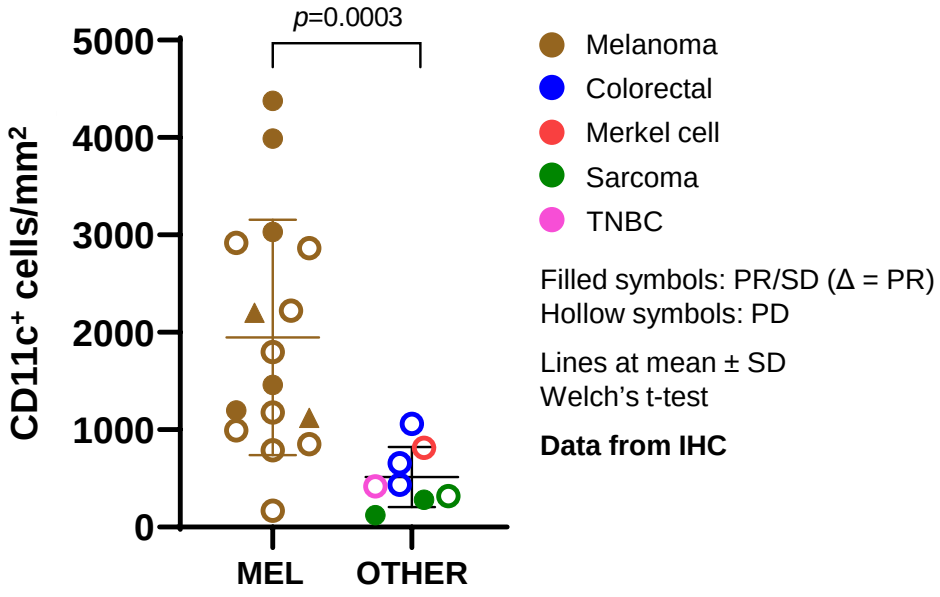


Dose- and CD11c$^+$-dependent induction of Type 1 IFN genes in melanoma biopsies consistent with TLR7/8 target engagement

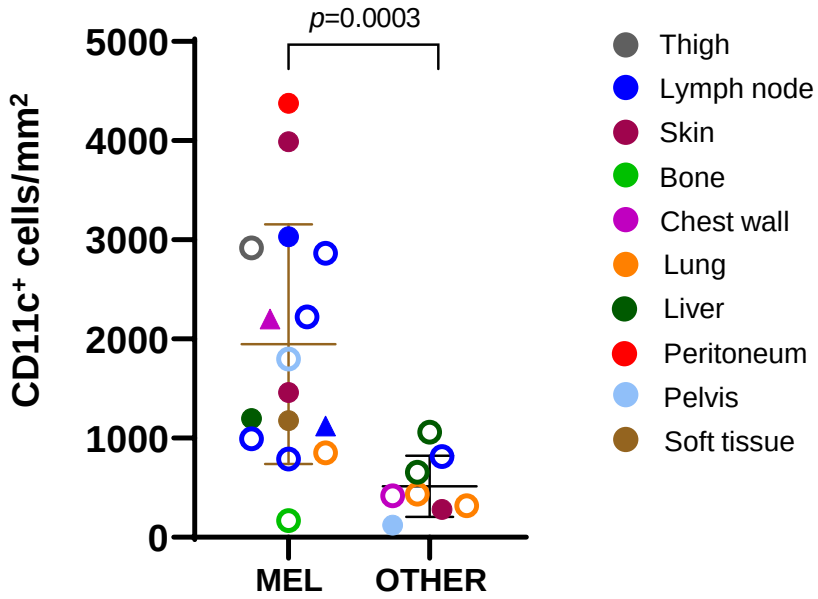
[a]Correlation between fold change of induction for each gene (at Day 2) and CD11c$^+$ density (by IHC) at baseline across samples where both datasets available (melanoma [6], sarcoma [1], Merkel cell [1], CRC [1]).
IFN, interferon; TLR, toll-like receptor.

Higher Density of CD11c$^+$ Target Cells in Melanoma Baseline Biopsies vs Other Tumor Types

Melanoma vs other indications



Location of biopsy



Preliminary data show a potential trend for a higher density of CD11c$^+$ cells with an anti-tumor effect in melanoma

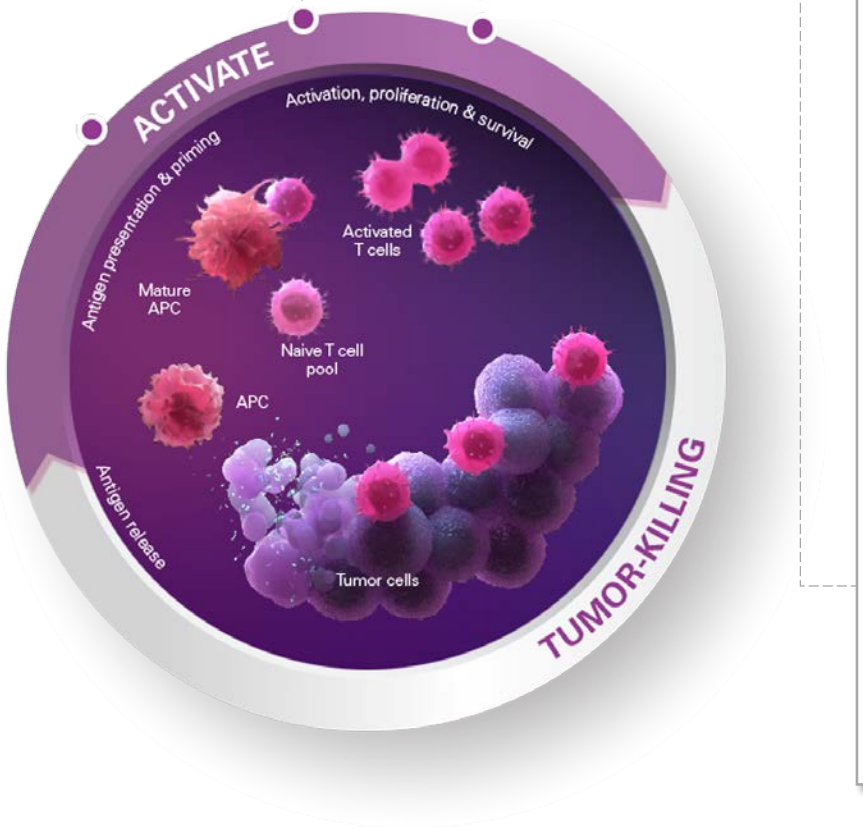
Biopsies taken at 24 hours post-cycle 1 NKTR-262 monotherapy for each cohort.
IHC, immunohistochemistry; MEL, melanoma; PD, progressive disease; PR, partial response; SD, stable disease; TNBC, triple-negative breast cancer.

REVEAL: Conclusions

- NKTR-262 IT, as monotherapy or in combination, showed early signs of clinical activity and an acceptable safety profile in this highly relapsed/refractory melanoma patient population
- MTD was not reached; the totality of the safety, PK/PD, and biomarker data supported selection of NKTR-262 3.84 mg IT plus BEMPEG 0.006 mg IV q3w as the RP2D
  - For NKTR-262, robust TLR7/8 engagement supported the MoA, and the minimal toxicity profile underscored the benefit of local delivery
  - NKTR-262 plus BEMPEG induced systemic activation of T and NK cells demonstrating engagement of the entire immune activation cascade required for systemic tumor clearance
  - CD11c+ target cells were significantly more abundant in baseline melanoma biopsies vs other tumor types; induction of TLR7/8-responsive genes significantly correlated with $CD11c^{+}$ baseline density
- Our findings support the ongoing Phase 1b dose expansion of NKTR-262 plus BEMPEG, with or without nivolumab, in patients with relapsed/refractory melanoma

IT, intratumoral; IV, intravenous; MoA, mechanism of action; MTD, maximum tolerated dose; NK, natural killer; PD, pharmacodynamics; PK, pharmacokinetics; q3w, every 3 weeks; RP2D, recommended Phase 2 dose; TLR, toll-like receptor.

NKTR-255: IL-15 Agonist



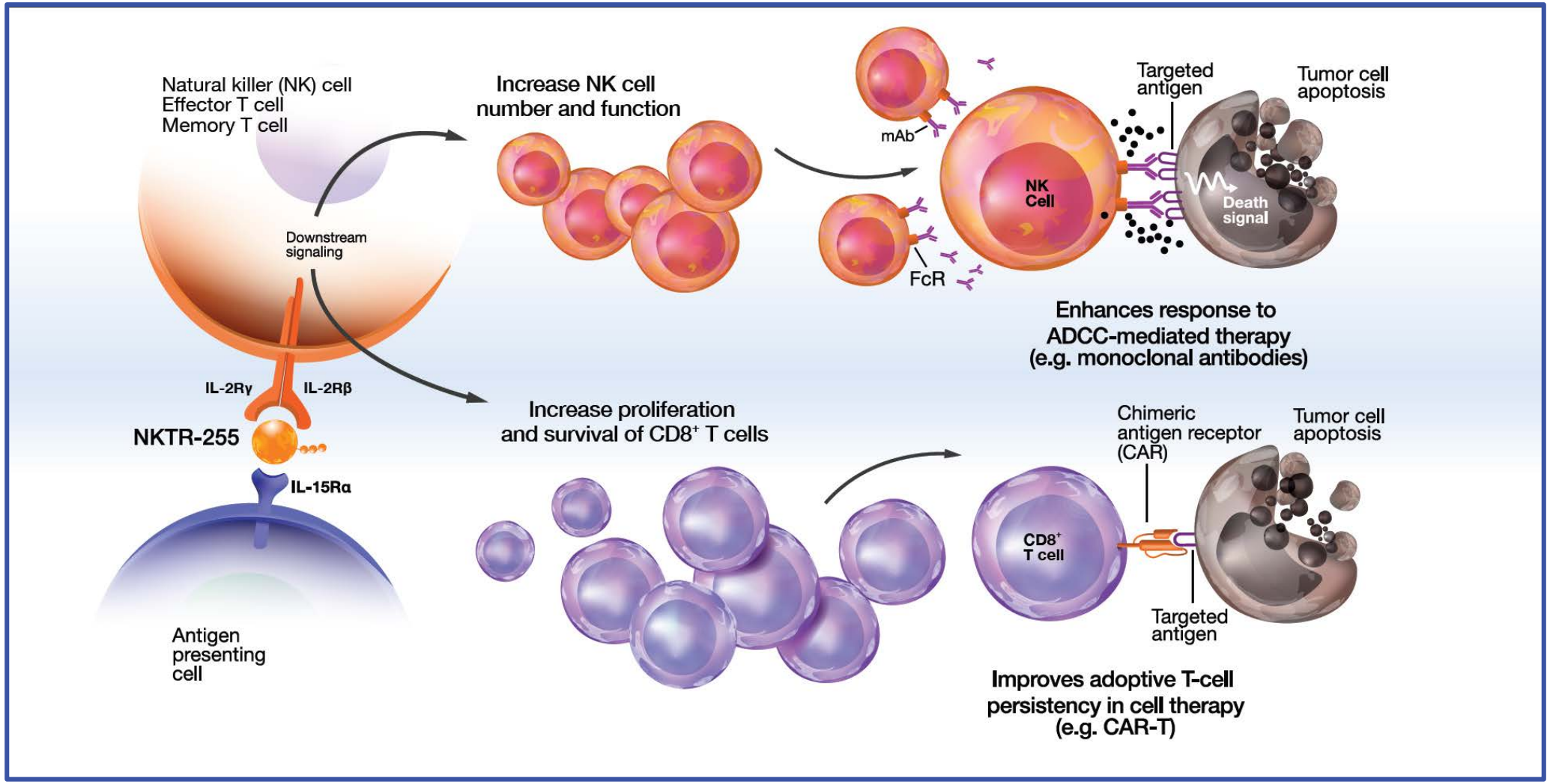
IL-15

First-in-human Phase I Study of NKTR-255 in Patients With Relapsed/Refractory Hematologic Malignancies

Nina Shah[1], Alan Tan[2], Lihua E. Budde[3], Craig C. Hofmeister[4], Andrew J. Cowan[5], Hayder Saeed[6], Jing C. Ye[7], Mitchell S. Cairo[8], David A. Rizzieri[9], Gregory J. Orloff[10], Xue Snow Ge[11], Zachary Lee[11], Neha Dixit[11], Wildaliz Nieves[11], Mona Vimal[11], Haijun Ma[11], Takahiro Miyazaki[11], Loui Madakamutil[11], Mario Q. Marcondes[11], Wei Lin[11], Mary A. Tagliaferri[11], Jonathan Zalevsky[11], Krina K. Patel[12]

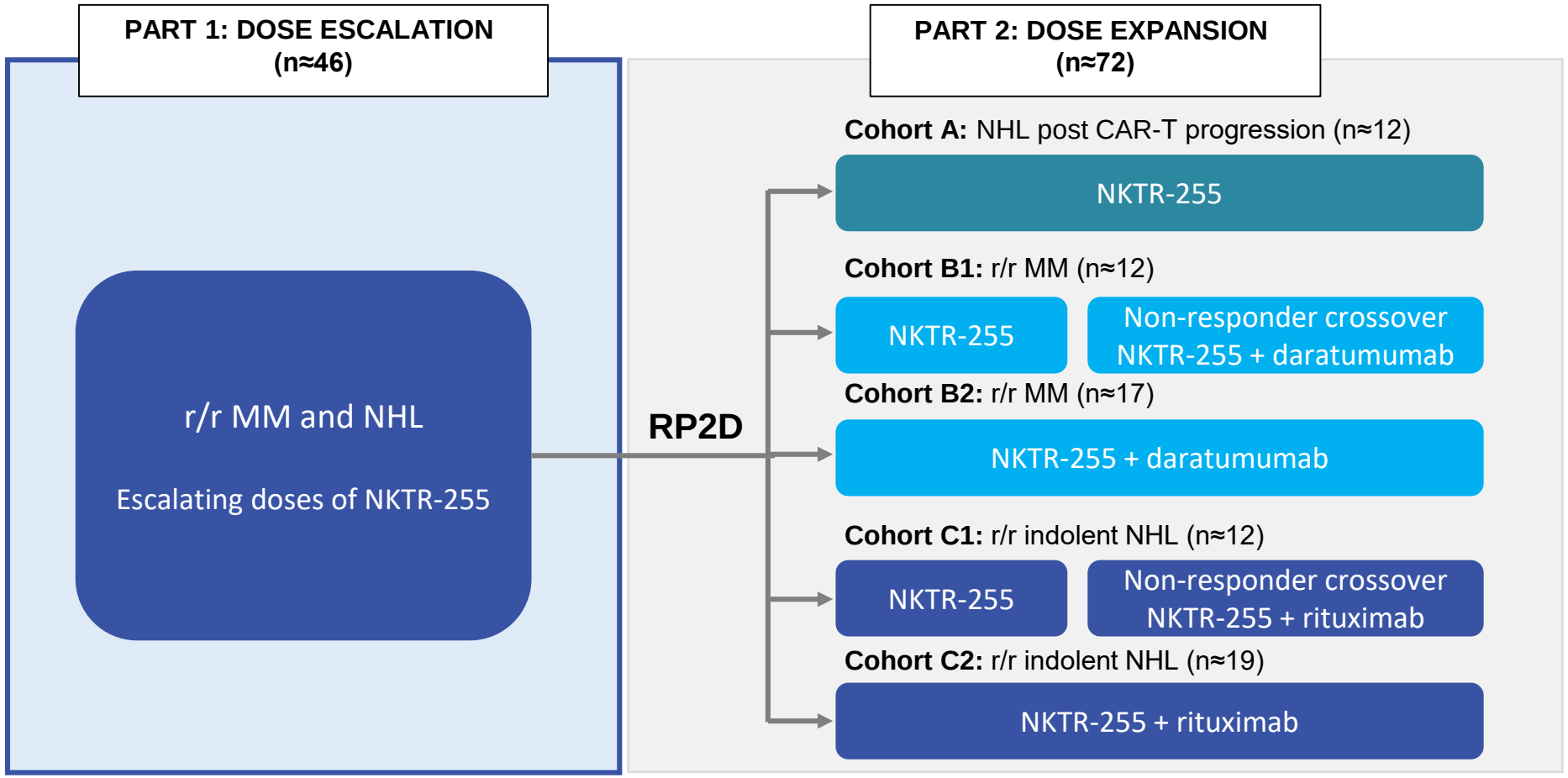
[1]University of California San Francisco, San Francisco, CA, USA; [2]Rush University Medical Center, Chicago, IL, USA; [3]City of Hope Comprehensive Cancer Center, Duarte, CA, USA; [4]Winship Cancer Institute of Emory University, Atlanta, GA, USA; [5]Division of Medical Oncology, University of Washington, Seattle, WA, USA; [6]H. Lee Moffitt Cancer Center and Research Institute, Tampa, FL, USA; [7]Rogel Cancer Center, University of Michigan, Ann Arbor, MI, USA; [8]New York Medical College, Valhalla, NY, USA; [9]Duke University School of Medicine, Durham, NC, USA; [10]Virginia Cancer Specialists; Fairfax, VA, USA; [11]Nektar Therapeutics, San Francisco, CA, USA; [12]The University of Texas MD Anderson Cancer Center, Houston, TX, USA

NKTR-255 Engages With IL-15Rα/IL-2Rβγ Receptor Complex to Boost NK Cell Number and CD8+ T-cell Expansion, Proliferation, Activation, Function and Survival



ADCC, antibody-dependent cellular cytotoxicity; CAR-T, chimeric antigen receptor T-cell; IL-15R, interleukin-15 receptor; NK, natural killer.

Phase 1, Open-Label, Multicenter Dose-Escalation and Dose-Expansion Study in Patients With R/R MM or NHL



PRIMARY ENDPOINT

- Safety and tolerability

SECONDARY AND EXPLORATORY ENDPOINTS

- Pharmacodynamic effects
- Pharmacokinetics
- Efficacy

CAR-T, chimeric antigen receptor T-cell therapy; MM, multiple myeloma; NHL, non-Hodgkin lymphoma; r/r, relapsed/refractory.

NKTR-255 was Well Tolerated With No DLTs or Serious AEs (Safety Data During the DLT Period Only)

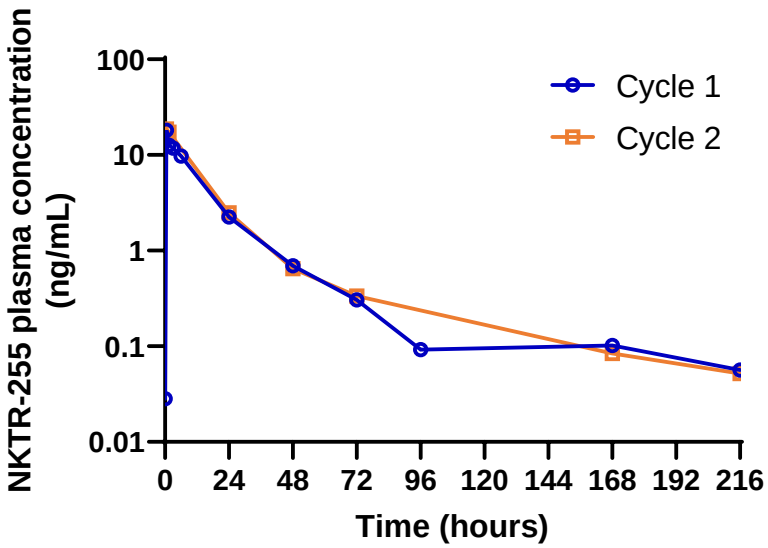
Number of AEs, n (%)[a]	NKTR-255 1.5 µg/kg (n=3)	NKTR-255 3.0 µg/kg (n=1)
Patients reporting ≥1 TRAE	3 (100.0)	1 (100.0)
Grade 1/2 TRAE		
Flu-like symptoms[b]	1 (33.3)	1 (100.0)
Headache	0	1 (100.0)
Hypercalcemia	0	1 (100.0)
Hypotension	0	1 (100.0)
Liver function test	0	1 (100.0)
Muscle tightness	1 (33.3)	0
Myalgia	1 (33.3)	0
Platelet count decreased	0	1 (100.0)
Grade 3 TRAE		
Flu-like symptoms[c]	1 (33.3)	0
Lymphocyte count decreased	0	1 (100.0)
White blood cell count decreased	0	1 (100.0)
Patients with AEs leading to discontinuation	0	0

- As of July 6, 2020, 4 patients aged 59–66 years were enrolled:
  - NKTR-255 1.5 µg/kg
    - Male MM patient (n=1)
    - Female NHL patient (n=1)
    - Male NHL patient (n=1)
  - NKTR-255 3.0 µg/kg
    - Male MM patient (n=1)
- NKTR-255 was well tolerated
- No serious TRAE, no delayed DLT, and no dose modifications during the DLT period

Data cutoff: July 6, 2020. [a]Worst toxicity grades are summarized. [b]Grade 1/2 flu-like symptoms comprise influenza-like illness (1 patient: worst Grade 1 [n=1]), pyrexia (2 patients: worst Grade 1 [n=2]), and chills (2 patients: worst Grade 1 [n=1], Grade 2 [n=1]). [c]Grade 3 flu-like symptoms comprise Grade 3 pyrexia (n=1), which resolved <24 hours with over-the-counter medications.
AE, adverse event; DLT, dose-limiting toxicity; TRAE, treatment-related adverse event.

NKTR-255 1.5 µg/kg Exhibited a Long Half-life With No Accumulation After Every 21-day Dosing

Concentration–time profiles



Preliminary PK analyses

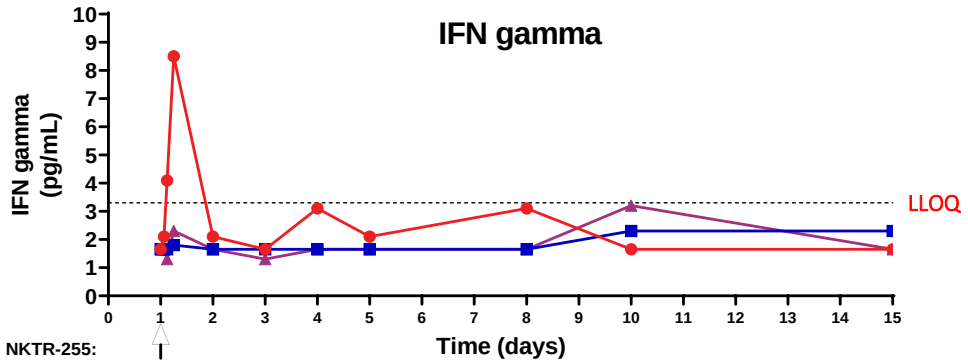
Cycle	N	C_{max} (ng/mL)	$AUC_{0\text{-last}}$ (ng•hr/mL)	$T_{1/2}$ (hr)
1	3	18.1 (46)	212 (69)	27 (10)
2	2	19.8 (26)	250 (39)	27 (67)

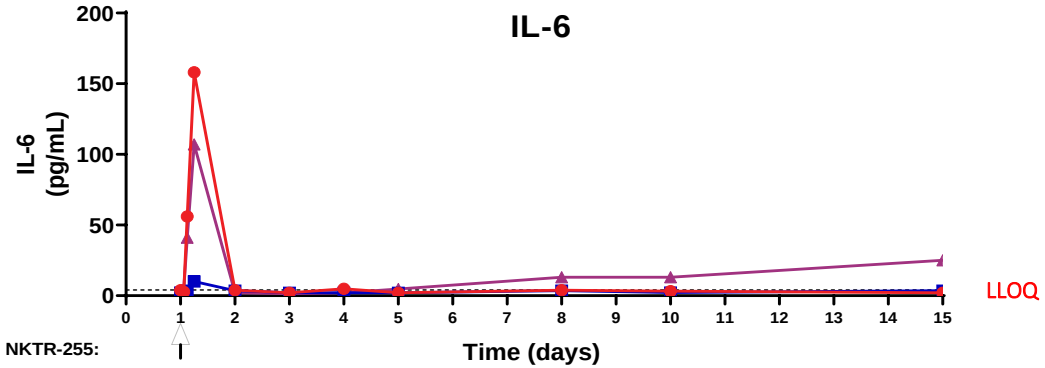
PK parameters: Mean (coefficient of variance %).
All pre-dose NKTR-255 concentrations at Cycle 2+ were below the lower limit of quantification of 0.05 ng/mL.

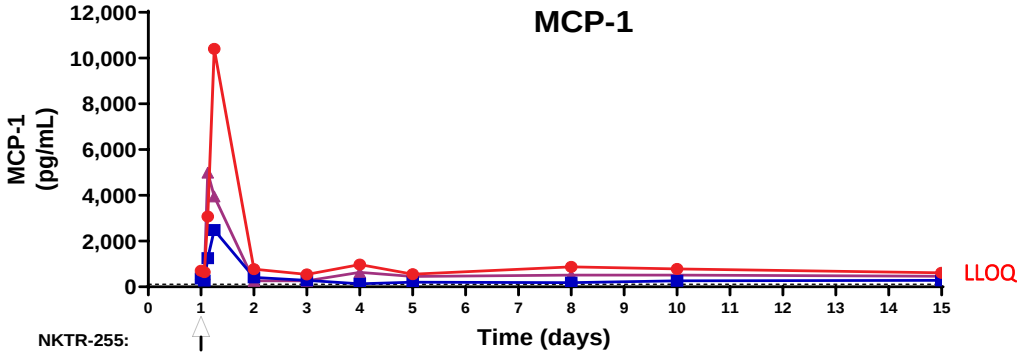
- Mean plasma NKTR-255 1.5 µg/kg concentration–time profiles were superimposable for cycles 1 and 2
- Mean half-life of NKTR-255 was 27 hours, which is over 10-fold longer than that reported for rhIL-15 IV dose,[3] with no accumulation following repeat dosing

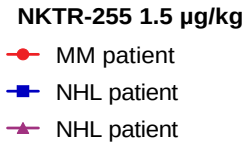
Data cutoff: July 6, 2020.
Validated bioassay method was used to measure plasma concentration of NKTR-255, which was expressed in IL-15 content.
AUC, area under the curve; C_{max}, peak concentration; PK, pharmacokinetic; $T_{1/2}$; half life.

Transient Upregulation and Rapid Decline of Cytokines to Baseline Levels by Day 2 With No Further Increases







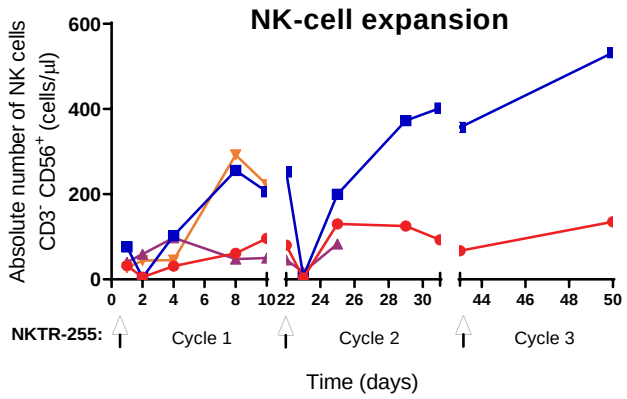


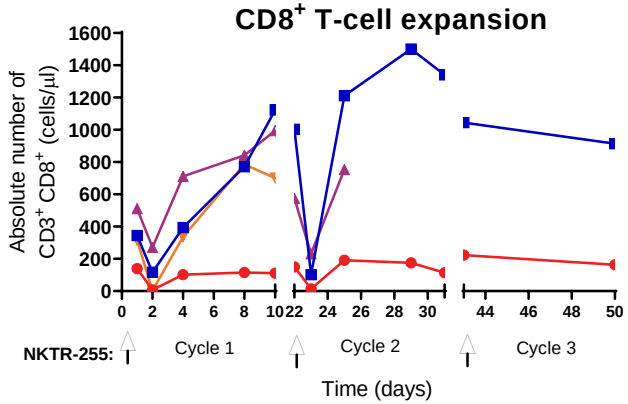
- NKTR-255-dependent changes in inflammatory cytokines were transient, supporting the safety of NKTR-255
- No further changes observed after Day 15

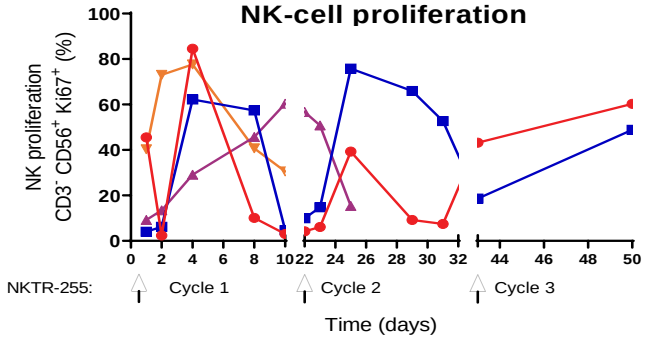
*Values below LLOQ are approximate but calculated based on standard control curve.

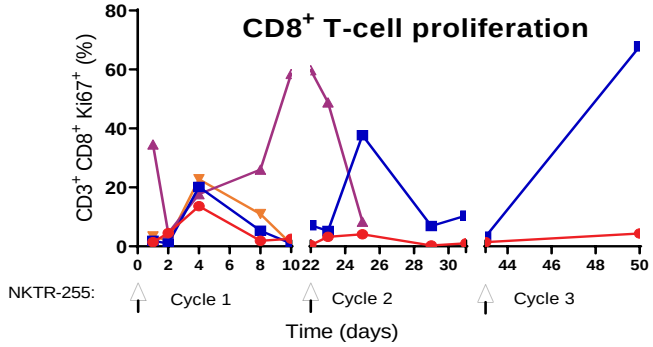
IFN, interferon; IL, interleukin; MCP, monocyte chemoattractant protein; MM, multiple myeloma; NHL, non-Hodgkin lymphoma.

NKTR-255 Increased Total Expansion and Proliferative Capacity (Ki67+) of NK and CD8+ T Cells in Blood, Peaking Around Days 8–10 Per Cycle









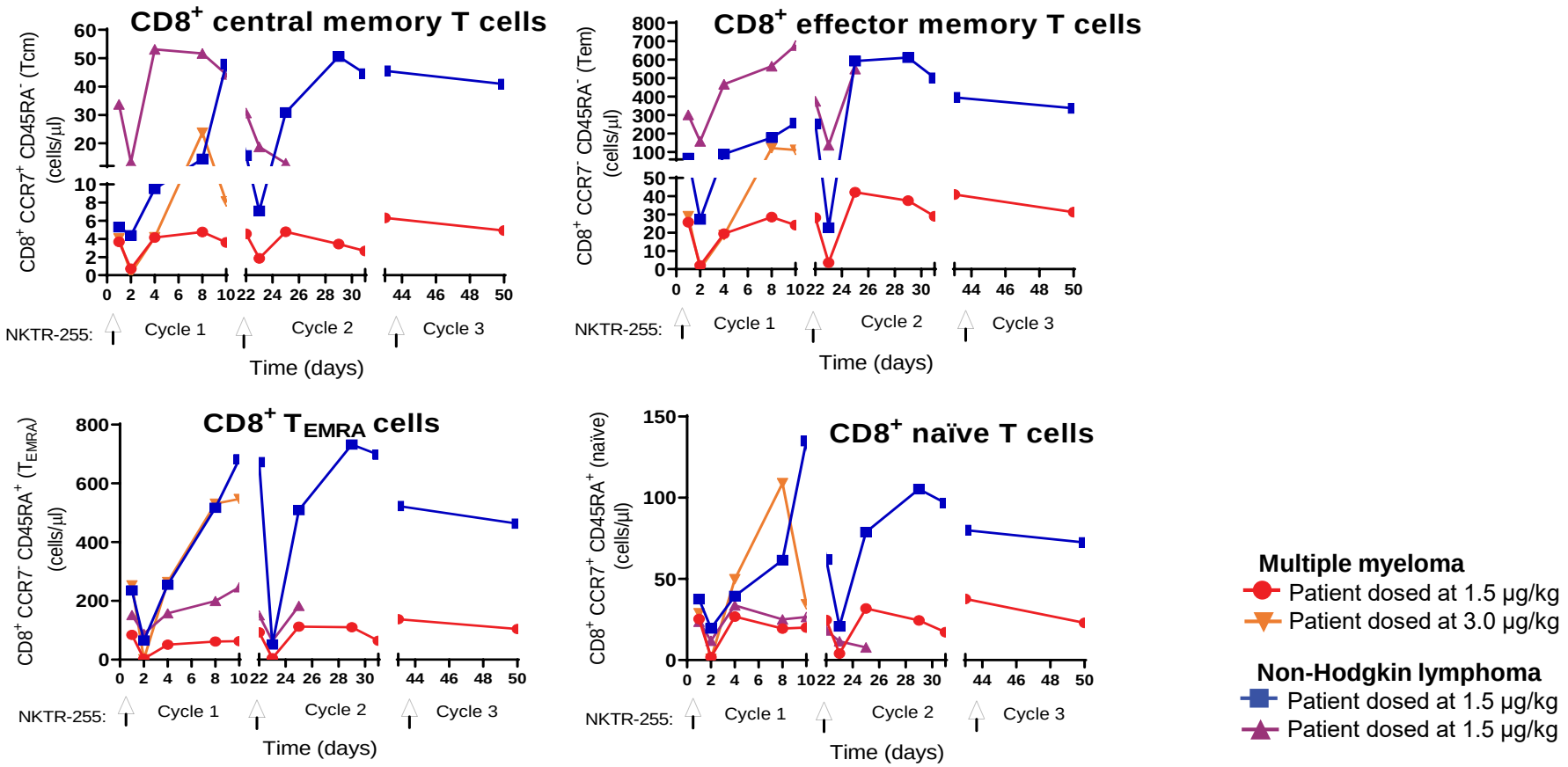
Multiple myeloma
- Patient dosed at 1.5 µg/kg
- Patient dosed at 3.0 µg/kg

Non-Hodgkin lymphoma
- Patient dosed at 1.5 µg/kg
- Patient dosed at 1.5 µg/kg

NK, natural killer.

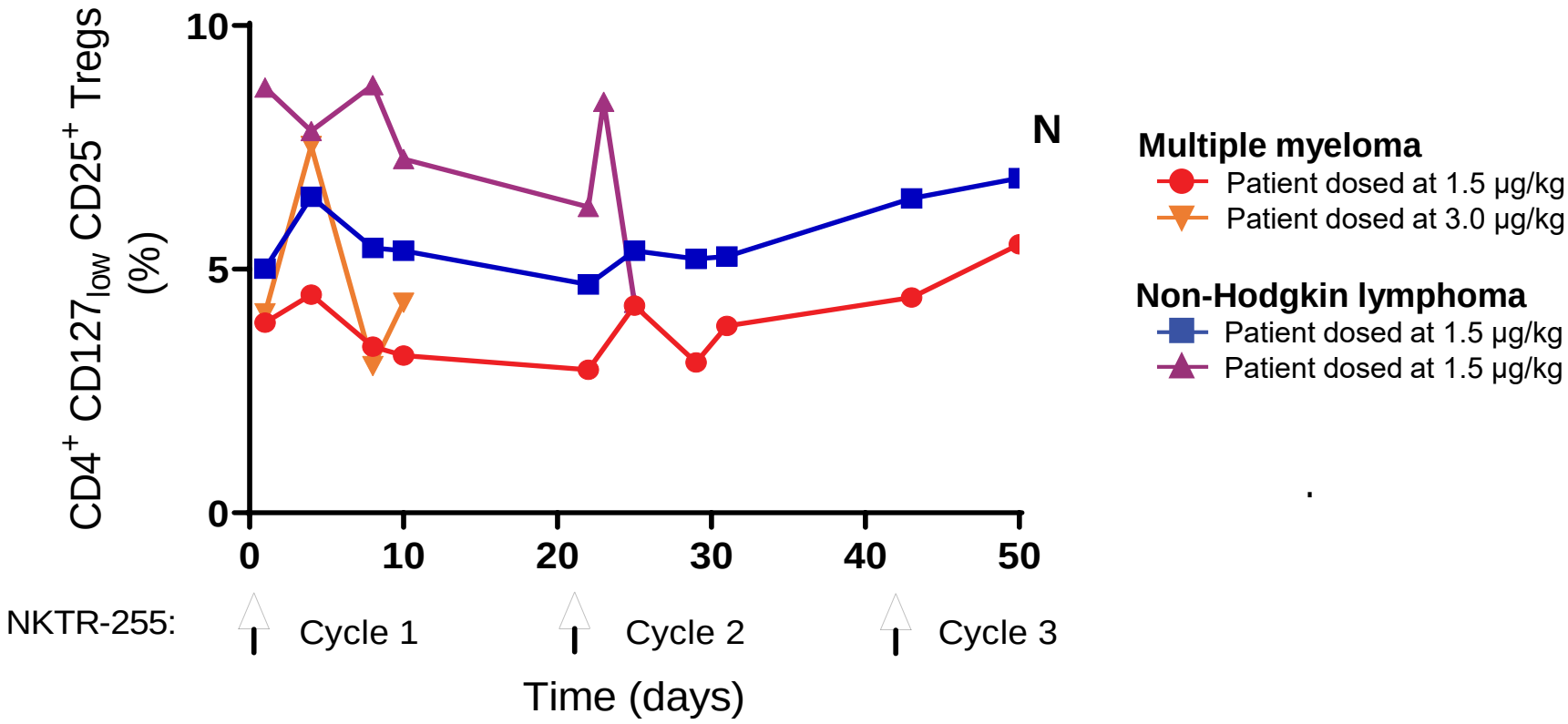
- NKTR-255 1.5 µg/kg expanded NK cells by ~5-fold and CD8+ T cells by ~3-fold
- Proliferative capacity (Ki67+) was maintained across multiple cycles of NKTR-255 1.5 µg/kg
- NKTR-255 3 µg/kg increased NK cell numbers in cycle 1 by ~10-fold in the heavily pretreated patient with MM
- Differences in baseline levels and fold increases of NK and CD8+ cells may be due to different disease types (MM vs NHL), disease severity and bone marrow capacity

NKTR-255 Increased Memory and Naïve CD8+ T-cell Subpopulations



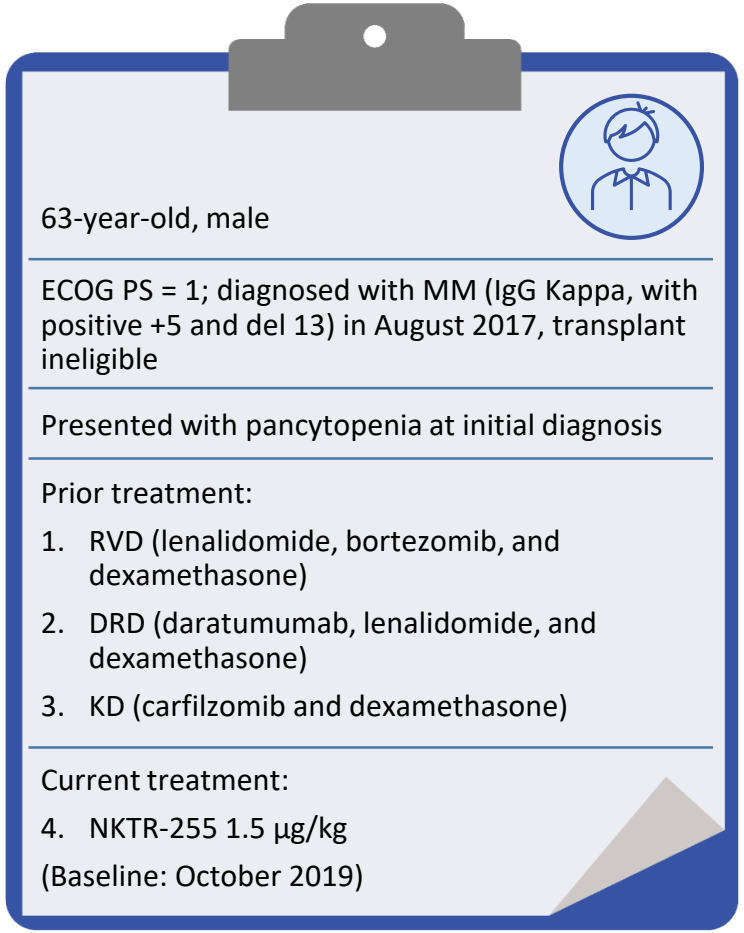
- NKTR-255 induced CD8+ memory T-cell expansion in all patients, including a >9-fold increase in one patient receiving NKTR-255 1.5 µg/kg

No Meaningful Changes Were Observed in CD4+ Tregs With NKTR-255 Treatment*



*Day 2 timepoint data for cycle 1 and 2 are artifacts of gating and so were removed from the plot.

Clinical Vignette: First Patient Enrolled in the NKTR-255 1.5 µg/kg Cohort (Stable Disease per IMWG)



- Patient received NKTR-255 as monotherapy at 1.5 µg/kg IV for 9 cycles

	Baseline (Oct 2019)	Cycle 3 (Dec 2019)	Cycle 7 (Feb 2020)	Cycle 9 (Apr 2020)
K/L chain ratio	638	632	128	554
Lambda/L	2.08	<2.0	5.44	6.0
Kappa K	1328	1265	693	2223
M Protein	1.9	1.9	2.1	2.0
IgG	1340	1757	1928	2004
Bone marrow	44% $CD138^+$ core	NA	30% $CD138^+$ core	40% $CD138^+$ core
Bone marrow FACS	NA	NA	13–17%	6%

ECOG PS, Eastern Cooperative Oncology Group Performance Status; IMWG, International Myeloma Working Group; MM, multiple myeloma; NA, not available.

Clinical Vignette: First Patient Enrolled in the NKTR-255 1.5 µg/kg Cohort (Stable Disease per IMWG)

63-year-old, male

ECOG PS = 1; diagnosed with MM (IgG Kappa, with positive +5 and del 13) in August 2017, transplant ineligible

Presented with pancytopenia at initial diagnosis

Prior treatment:

1. RVD (lenalidomide, bortezomib, and dexamethasone)
2. DRD (daratumumab, lenalidomide, and dexamethasone)
3. KD (carfilzomib and dexamethasone)

Current treatment:

4. NKTR-255 1.5 µg/kg

(Baseline: October 2019)

- Patient received NKTR-255 as monotherapy at 1.5 µg/kg IV for 9 cycles

BM FACS	Baseline (09/20)	Cycle 5 (01/20)	Cycle 9 (April 9)
+CD4%	2.1%	2.3%	3.9%
+CD8%	**2.5%**	**4.7%**	**4.4%**
+CD56% *	**0.4%**	**2.7%**	**5.3%**

13 fold

*indirect gating strategy for CD56+

NK cells can form long term memory pool and can migrate to niche tissue like BM and liver

The increase in BM may suggest that NKTR-255 the expanded NK cells may be converting to memory like NK cells and migrating to NK memory niche like BM

NEKTAR

ECOG PS, Eastern Cooperative Oncology Group Performance Status; IMWG, International Myeloma Working Group; MM, multiple myeloma; NA, not available.

Clinical Vignette: First Patient Enrolled in the NKTR-255 1.5 µg/kg Cohort (Stable Disease per IMWG)

Infusion (Baseline: October 2019)

4–5 hours post-infusion

- Mild rigors (Grade 1) and flu-like symptoms (Grade 1), which were treated with acetaminophen and resolved by Day 2
  - Reproducible pattern was observed in Cycle 2, 3 and 4
- Neutropenia (Grade 3) and low platelet counts (Grade 3) related to study drug – required stimulating factors and platelet transfusion in order to schedule bone marrow biopsy

Treatment-related AEs during the DLT period (November 2019)

	NKTR-255 (1.5 µg/kg) MM patient
Grade 1 flu-like symptoms (fever and rigors)	Resolved
Grade 1 muscle aches	Resolved

AEs, adverse events; DLT, dose-limiting toxicity; MM, multiple myeloma.

Clinical Vignette: Second Patient Enrolled NKTR-255 Metabolic Response in Splenic Target Lesion on Cycle 5

66-year-old, female

ECOG PS = 0; diagnosed with NHL (DLBCL (splenic biopsy(+)), BM Bx clear; Target lesions: spleen SUV+, LVEF: 60-65%) in August 2017, transplant ineligible

Prior treatment:

1. RCHOP (rituximab, cyclophosphamide, doxorubicin, vincristine and prednisone) + enzastaurin maintenance
2. RICE (rituximab, ifosfamide, carboplatin, etoposide)
3. BEAM conditioning (BCNU, etoposide, Ara-C, and melphalan) + ASCT

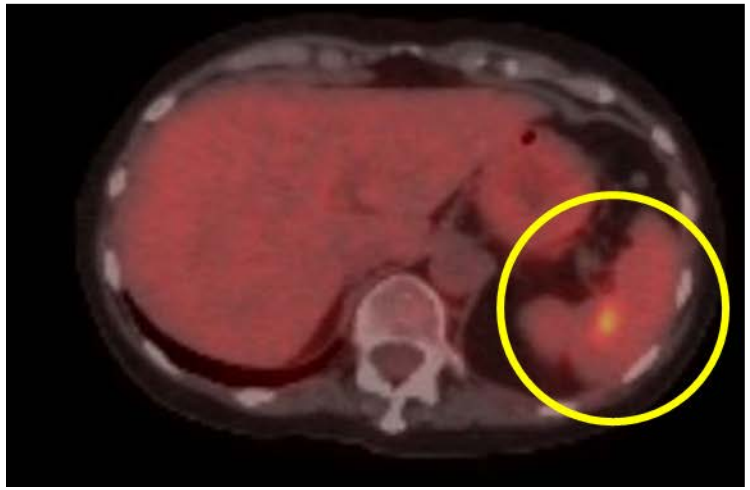
Disease progressed March 2020 with splenic lesion

Current treatment:

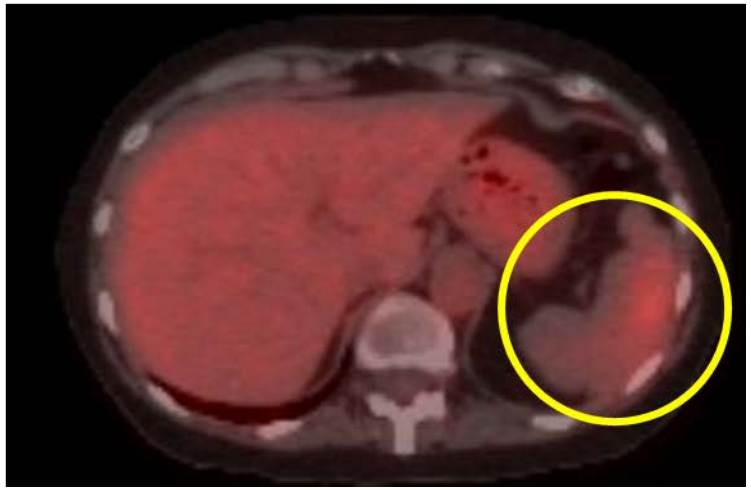
4. NKTR-255 1.5 µg/kg for 7 cycles
   (Baseline: March 2020)
   Last Cycle: C7D1 – 13-Jul-2020

- Patient received 7 cycles of NKTR-255 as monotherapy at 1.5 µg/kg IV

Baseline Scan



Cycle 5 Scan



NEKTAR

ECOG PS, Eastern Cooperative Oncology Group Performance Status; DLBCL, diffuse large B-cell lymphoma; BM Bx, bone marrow biopsy; LVEF, left ventricular ejection fraction; NHL, non-hodgkin lymphoma; NA, not available.

Clinical Vignette: Second Patient Enrolled NKTR-255 Metabolic Response in Splenic Target Lesion on Cycle 5

Infusion (Baseline: March 2019)

24 hours post-infusion

- Muscle tension (Grade 1), which resolved same day
  - Reproducible pattern was observed in Cycle 2, 3, 4 and etc. were treated with acetaminophen

Treatment-related AEs during the DLT period (Late March 2020)

	NKTR-255 (1.5 µg/kg) NHL patient
Grade 1 muscle tension	Resolved

AEs, adverse events; DLT, dose-limiting toxicity; NHL, non-hodgkin lymphoma

- SAEs: None
- AEs Grade ≥2: None
- Other Related AEs Ongoing: None
- Other Non-related AEs: None

Clinical Vignette: Third Patient Enrolled NKTR-255 Pharmacodynamic Analysis of CD19 CAR-T

66-year-old, male

ECOG PS = 2; diagnosed with NHL (DLBCL, BM Bx clear; Target lesions: para-spinal and abdominal lymphs SUV+, LVEF: 63%)

Prior treatment:

1. RCHOP (rituximab, cyclophosphamide, doxorubicin, vincristine and prednisone)
2. RICE (rituximab, ifosfamide, carboplatin, etoposide)
3. R-Gem-Ox
4. polatuzumab vedotin + bendamustine
5. **Yescarta (axicabtagene ciloleucel)**

Complete Response January 2020

Disease progressed March 2020 (PET CT increased pelvic nodules and lymph nodes)

Current treatment:

4. NKTR-255 1.5 µg/kg for 2 cycles
   (Baseline: May 2020)
   Last Cycle: C2D1 – 01-Jun-2020

- Patient received 2 cycles of NKTR-255 as monotherapy at 1.5 µg/kg IV

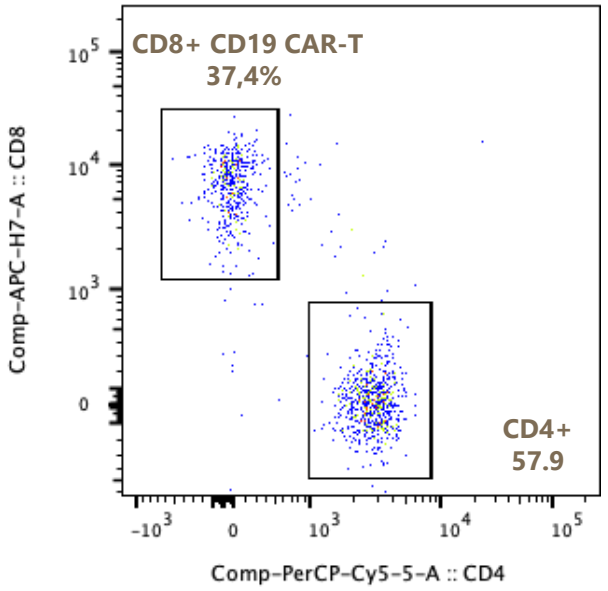
Baseline **Cycle 2**

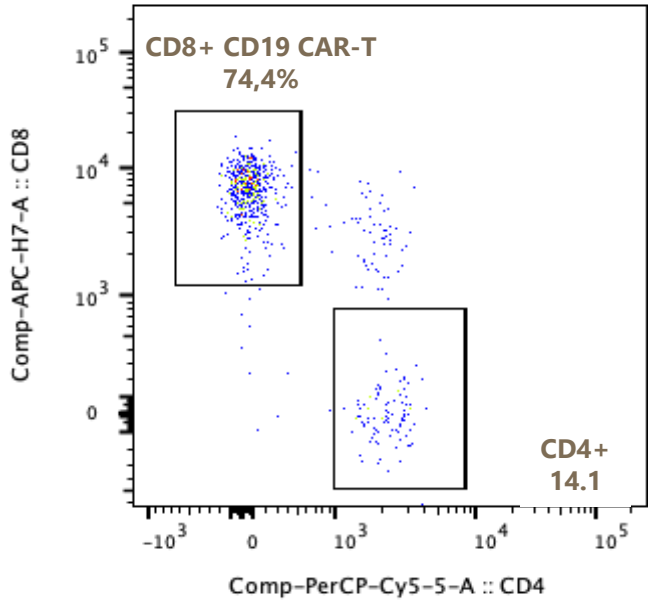
Total CD19 CAR-T in Peripheral Blood

2.05% or 16.0 CAR-T cells/µl*

3.34% or 23.1 CAR-T cells/µl*

CD4/CD8 Phenotype Analysis





ECOG PS, Eastern Cooperative Oncology Group Performance Status; DLBCL, diffuse large B-cell lymphoma; BM Bx, bone marrow biopsy; LVEF, left ventricular ejection fraction; NHL, non-hodgkin lymphoma; NA, not available; FACS: fluorescence-activated cell sorting; Scan Source: Dr. Cameron Turtle - Fred Hutchinson Cancer Center; *Out of the total CD+3 T-cell population

Clinical Vignette: Third Patient Enrolled NKTR-255 PD Analysis of CD19 CAR-T

Infusion (Baseline: March 2019)

24 hours post-infusion

- Muscle tension (Grade 1), which resolved same day
  - Reproducible pattern was observed in Cycle 2, 3, 4 and etc. were treated with acetaminophen

Treatment-related AEs during the DLT period (May 2020)

	NKTR-255 (1.5 µg/kg) NHL patient
Grade 3 fever	Resolved
Grade 2 chills	Resolved

AEs, adverse events; DLT, dose-limiting toxicity; MM, multiple myeloma.

- SAEs: None
- Other Related AEs Ongoing: None
- Other Non-related AEs:
  - Grade 1 fever – Resolved
  - Grade 1 intermittent fatigue – Ongoing

FACS: fluorescence-activated cell sorting

NKTR-255: Conclusions

- Patients with relapsed or refractory (r/r) MM or NHL, who had exhausted all available therapeutic options, were eligible for the dose-escalation portion of this study
- For dose-escalation, successive cohorts of three patients each received escalating doses of NKTR-255 monotherapy to determine the maximum tolerated dose (MTD)*
- NKTR-255 was well tolerated with low-grade, cytokine-related AEs that were transient and easily managed
  - No DLTs were observed
  - No drug-related AEs led to treatment discontinuation, dose delay or dose modification
- NKTR-255 exhibited a long half-life with no evidence of accumulation
- NKTR-255 was biologically active and demonstrated consistent expansion of lymphocytes, with durable and sustained increases in NK and $CD8^+$ T cells in this highly refractory population of patients with MM and NHL
- These data support continued dose escalation of NKTR-255, and subsequent evaluation in combination with other anticancer agents

Interim cutoff July 6, 2020 presented; *Following the first dose, patients were observed for a 3-week dose-limiting toxicity (DLT) window; 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 six patients have been evaluated at a dose and the posterior probability of targeted toxicity is at least 50% for that dose

Q&A Session

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Dr. Brendan D. Curti

Director of the Melanoma Program, Cytokine and Adoptive Immunotherapy and Genitourinary Oncology Research at Providence Cancer Institute

Dr. Nina Shah

Associate Professor, Department of Medicine at University of California San Francisco

Dr. Alan Tan

Assistant Professor Department of Internal Medicine, Division of Hematology, Oncology and Cell Therapy at Rush Medical College

Dr. Jonathan Zalevsky

Chief Research & Development Officer at Nektar Therapeutics

Dr. Wei Lin

Senior Vice President and Head of Development at Nektar Therapeutics