NEKTAR®

NEW PATHWAYS TO SMARTER MEDICINE™

SITC 2018

Nektar Therapeutics Investor & Analyst Call with Melanoma Specialists

November 10, 2018

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Today’s Speakers

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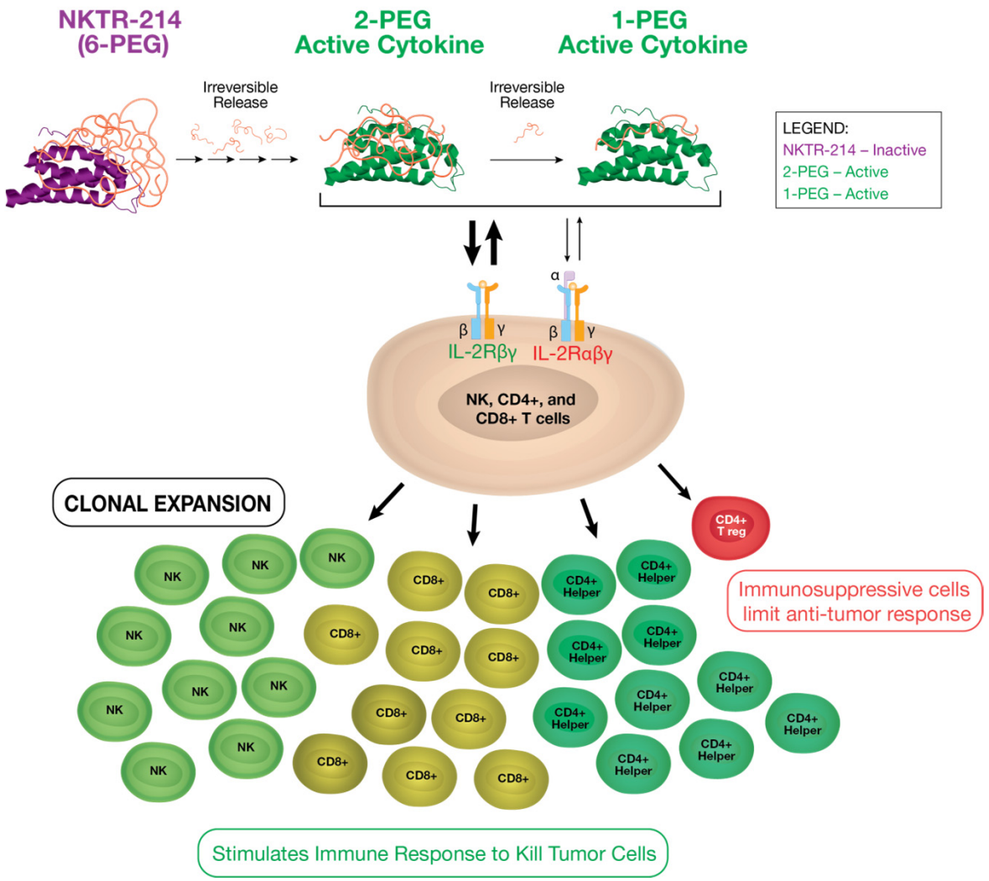
Today's Agenda

- PIVOT-02: Immune Monitoring After NKTR-214 Plus Nivolumab in Previously Untreated Patients with Metastatic Stage IV Melanoma
  - First 8 Registrational Trials for NKTR-214 with Opdivo
- Introduction to NKTR-262: A Unique TLR 7/8 Agonist
- REVEAL Study: Doublet of NKTR-262 with NKTR-214
  - Preliminary Biomarker Data
  - Case Studies: Melanoma Patients R/R to Prior CPIs
- Investigator Panel Discussion

NKTR-214 Background: Harnessing the IL-2 Pathway to Increase TILs



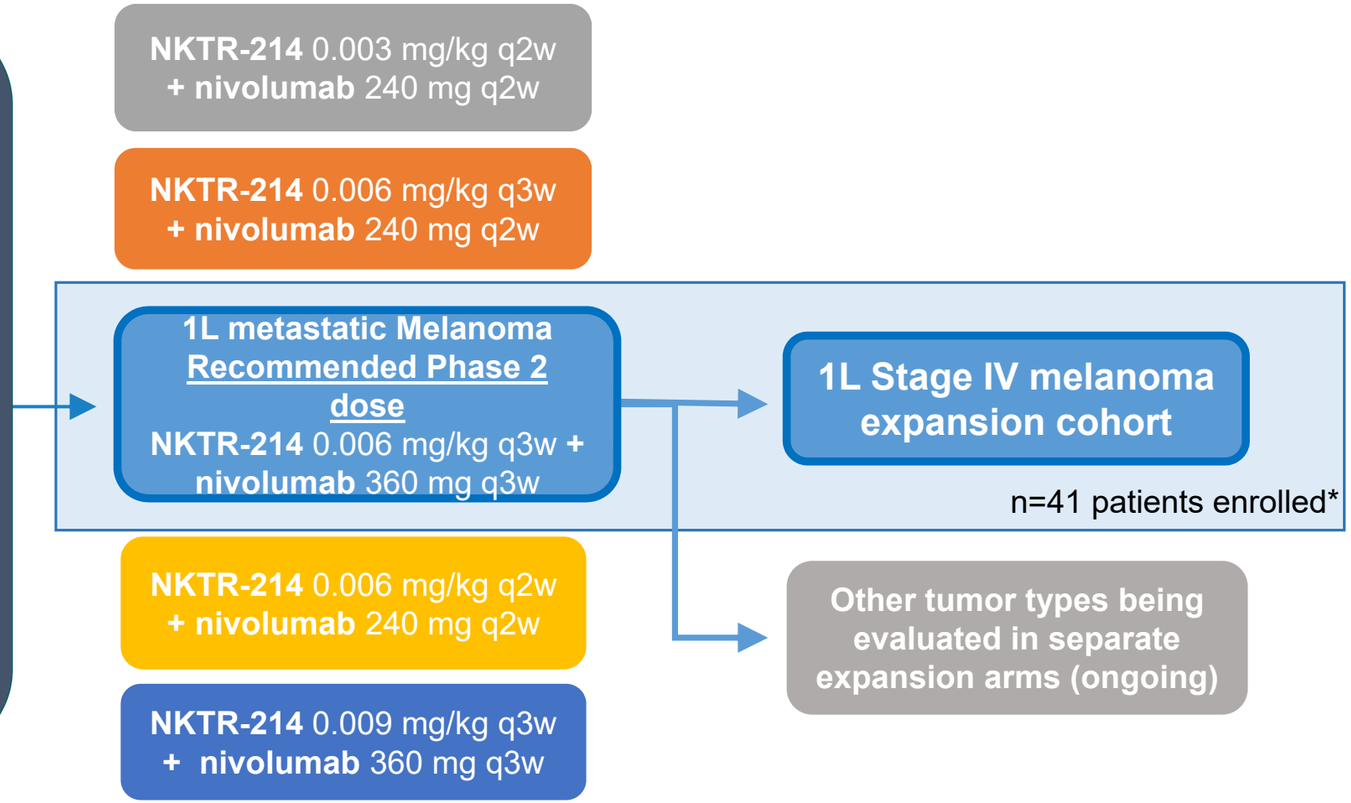
- NKTR-214 prodrug design results in potent immune activation with every 3 week dosing
- Biased signaling through IL-2bg receptor preferentially activates and expands effector T cells and NK cells over Tregs in the tumor microenvironment
- NKTR-214 creates a favorable tumor microenvironment for combination with checkpoint inhibitors including increased TILs, CD8+ PD1 expression and T cell clonality
- NKTR-214 has been shown to convert baseline PD-L1(-) tumors to PD-L1(+)*
- NKTR-214 is a systemic therapy with broad mechanistic applicability across multiple tumors

NEKTAR *Diab, A., et al., ASCO 2018; Bentebibel, S. et al., SITC 2017; Diab, A., SITC 2016

PIVOT-02: Dose-Escalation and Recommended Phase 2 Dose Expansion Trial of NKTR-214 + Nivolumab

Key inclusion criteria

- Locally advanced or metastatic solid tumour
  - 1L Melanoma (with known BRAF status)
  - 1L–2L RCC
  - 1L–2L NSCLC (EGFR and ALK WT)
- Measurable disease per RECIST v1.1
- ECOG PS 0–1
- Adequate organ function
- Fresh biopsy and archival tissue



RP2D: recommended Phase 2 dose.
*41 1L melanoma patients enrolled across 12 clinical sites; includes 7 patients from dose escalation cohort

Primary endpoints:

- Safety and tolerability per CTCAEv4.03
- ORR per RECIST v1.1 assessed every 8 (±1) weeks
- Per protocol, efficacy evaluable is defined as patients with ≥ 1 post baseline scan

Secondary and exploratory endpoints:

- Duration of response, OS, PFS, clinical benefit rate, PK

Biomarker endpoints (subset of patients in each cohort):

- Absolute Lymphocyte Count, Blood immuno-phenotyping
- Baseline and on-treatment biopsies (3 weeks) were collected in patients, when clinically feasible.

Patient Demographics and Disease Characteristics at Study Entry: 1st-Line Stage IV Melanoma

	Total (n=41)
Sex	
Female	17 (41.5%)
Male	24 (58.5%)
Age (years)	
Median (Range)	63 (22-80)
ECOG Performance Status	
0	32 (78.0%)
1	9 (22.0%)

	Total (n=38)
PD-L1 status* (Efficacy Evaluable)	
Positive ≥1%	19 (50.0%)
Negative <1%	14 (36.8%)
Unknown	5 (13.2%)

	Total (n=41)
BRAF status	
Mutant (V600E, V600K)	13 (32%)
Wild-Type or non-V600 mutation	27 (66%)
Unknown	1 (2%)
LDH‡	
Normal	29 (70.7%)
Elevated >ULN#	12 (29.3%)
Stage (7th edition AJCC)	
M0	0 (0%)
M1a	5 (12%)
M1b	16 (39%)
M1c	20 (49%)
Liver metastases	
Yes**	11 (26.8%)
No	30 (73.2%)

Demographics of biomarker subgroup are representative of overall population
*PD-L1 status determined by 28-8 diagnostic on fresh or archival tumor, or investigator reported
‡Based on maximum value prior to dosing
#8 patients with ≥ 2X ULN; 1 patient with elevated LDH not evaluable for efficacy
**1 patient with liver metastases not evaluable for efficacy

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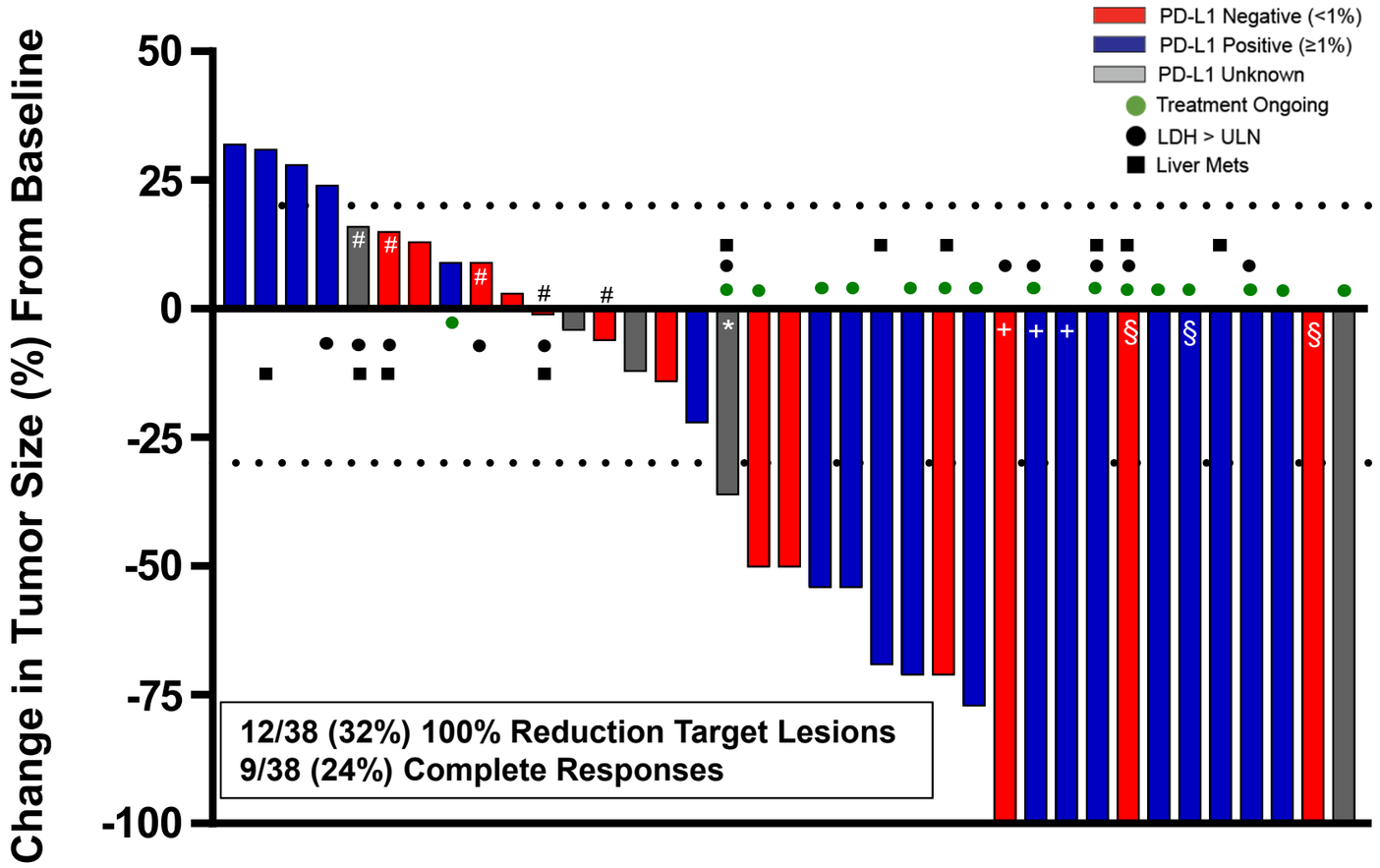
Stage IV IO-Naïve 1L Melanoma Cohort at RP2D Best Overall Response by Independent Radiology

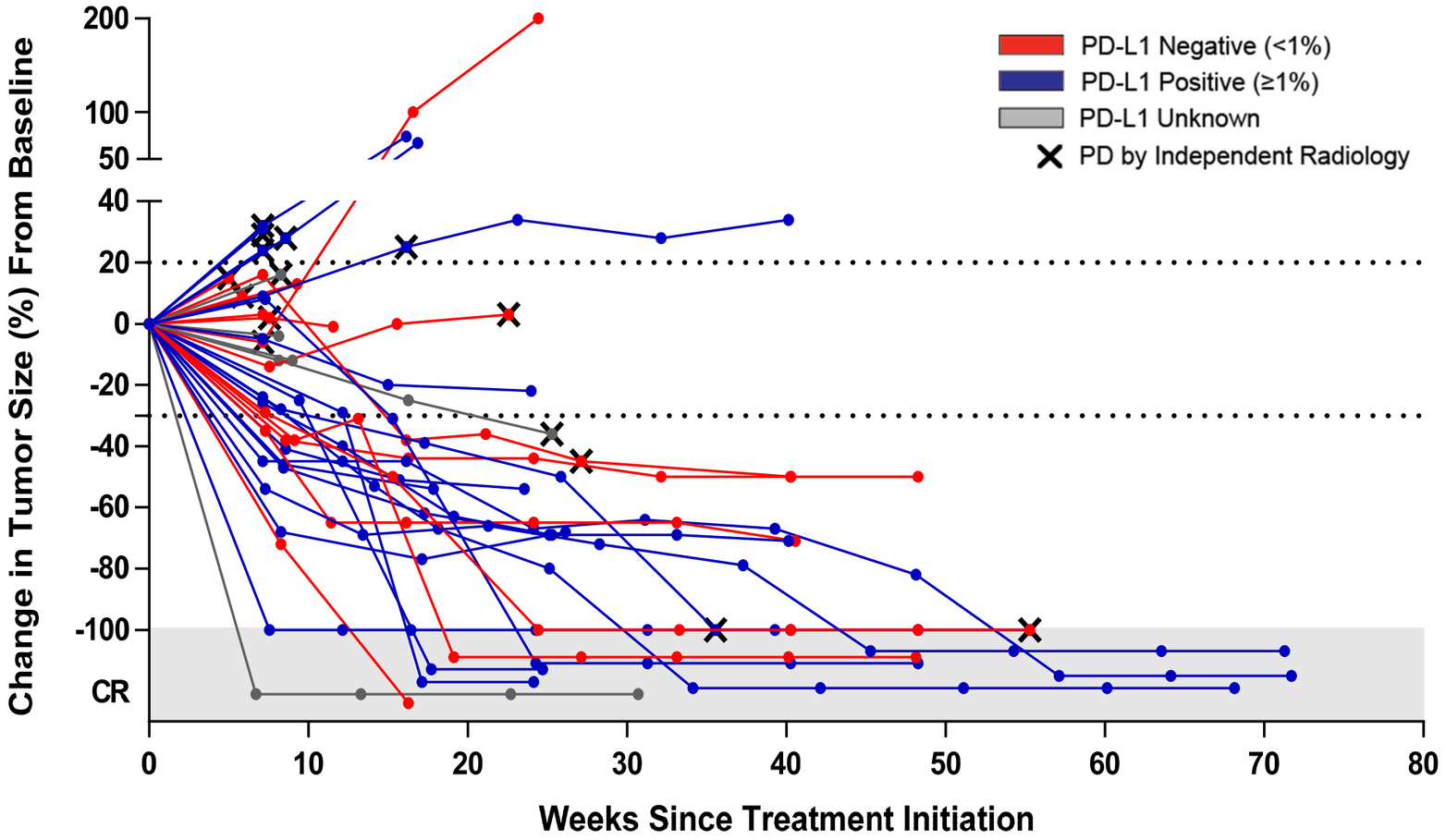


1L Melanoma (n=38 Efficacy Evaluable)	Overall Response Rate
Confirmed ORR (CR+PR)	20 (53%)
CR	9 (24%)
DCR (CR+PR+SD)	29 (76%)
PD-L1 negative (n=14)	6 (43%)
PD-L1 positive (n=19)	13 (68%)
PD-L1 unknown (n=5)	1 (20%)
LDH > ULN (n=11)	5 (45%)
Liver metastases (n=10)	5 (50%)

High level of concordance in ORR between independent central radiology (53%) and investigator-assessed 19/38 (50%).

Per protocol, efficacy evaluable is defined as patients with ≥ 1 post baseline scan. 3 patients discontinued prior to 1st scan due to an unrelated TEAE [n=1] and Patients Decision [n=2].
One patient not represented in plot had target lesions per protocol by investigator assessment but did not have target lesions at baseline by independent central radiology; patient achieved SD based on non-target lesions during the study.
#: Best overall response is PD. *: Best overall response is SD. + Best overall response is PR with -100% reduction of target lesions. §: Best overall response of CR is unconfirmed; PR confirmed.

Stage IV IO-Naïve 1L Melanoma Cohort at RP2D
Target Lesion Change Over Time Per Independent Radiology



1L Melanoma (n=38)	
Median Time of Follow-Up (months)	7.2
Patients with Ongoing Responses	17/20 (85%)
Median Duration of Response (months)	NR (2.6, NR)
Median Time to Response (months)	2.0
Median % Reduction from Baseline as of 1Oct2018 (ongoing)	-50%

Per protocol, efficacy evaluable is defined as patients with ≥ 1 post baseline scan. 3 patients discontinued prior to 1st scan due to TEAE [n=1] and Patients Decision [n=2].
Three responders progressed after 6 months of treatment. All three patients sustained tumor control of target lesions (-100%, -100%, -50%) with 2 patients having non-target, new subcutaneous lesions and one patient with new mediastinal lymph node deemed as progression by independent radiology. One patient not represented in plot had target lesions per protocol by Investigator assessment but did not have target lesion at baseline by BICR. Patient achieved non-target SD based on non-target lesion during the study.

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Stage IV IO-Naïve 1L Melanoma Treatment-Related Adverse Events (AEs) at RP2D

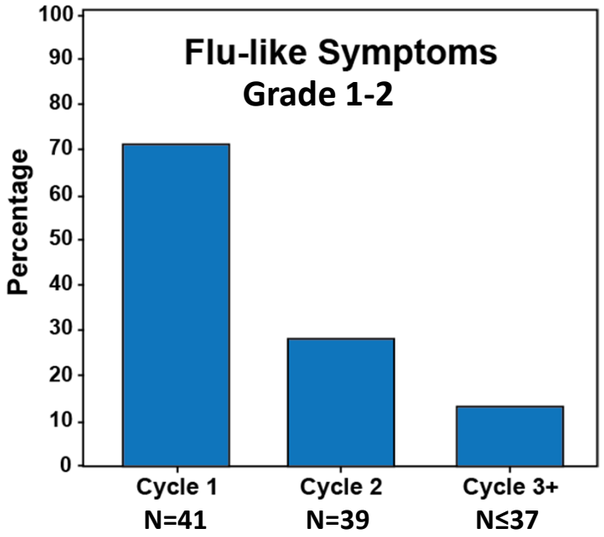
Preferred Term[1]	Total (N=41)
Grade 3-4 Treatment-Related AEs	8 (19.5%)
Lipase increased	3 (7.3%)
Atrial fibrillation*	2 (4.9%)
Acute kidney, injury, Blood creatinine increased, Cellulitis, Dyspnea, Hyperglycemia, Hypoxia	1 each (2.4%)
Grade 1-2 Treatment-Related AEs (>30% listed below)	
Flu like symptoms**	32 (78.0%)
Rash***	29 (70.7%)
Fatigue	26 (63.4%)
Pruritus	19 (46.3%)
Nausea	18 (43.9%)
Arthralgia	15 (36.6%)
Myalgia	13 (31.7%)
Any imAE (Grade ≥3) (blood creatinine increased, lipase increased)	2 (4.9%)
Patients requiring dose reductions of NKTR-214 (serum amylase increase, fatigue, pharyngitis)	3 (7.3%)
Patients who discontinued due to a TRAE (blood creatinine increased, stroke)	2 (4.9%)

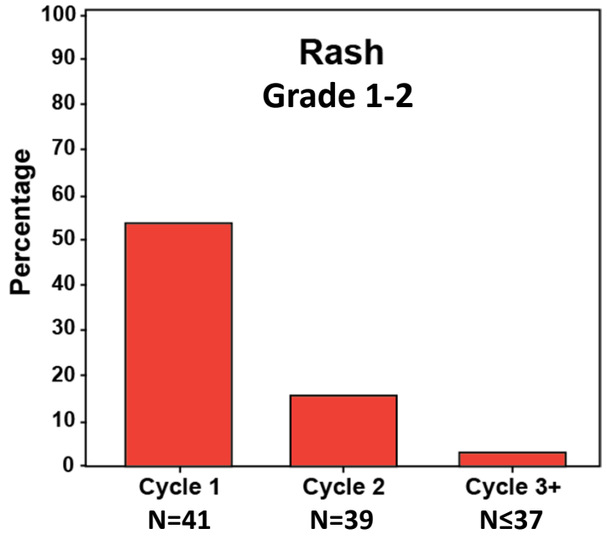
Median number of cycles = 9. Median duration of exposure = 5.8 months. Per protocol, safety evaluable is defined as patients with ≥ 1 dose of study treatment. (1) Patients are only counted once under each preferred term using highest grade.

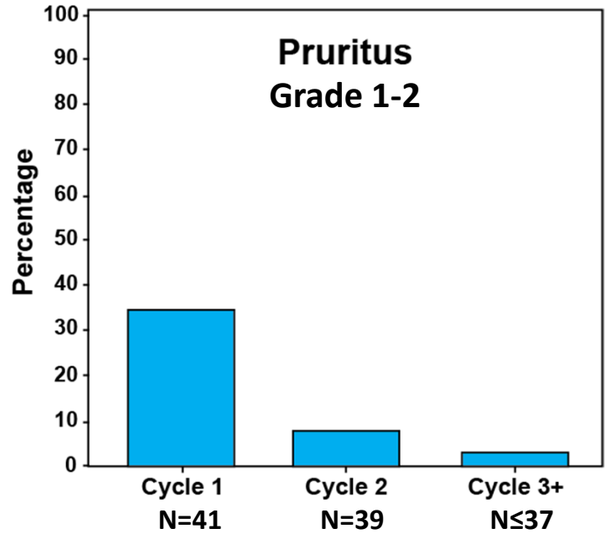
*1 patient with previous history of atrial fibrillation since 2015; 1 patient experienced atrial fibrillation 1 month after last dose of study drug. ** Flu-like symptoms included the following MedDRA PTs: Chills, Influenza, Influenza-like Illness, Pyrexia.

***Rash included the following MedDRA PTs: Erythema, Rash, Rash erythematous, Rash generalised, Rash macular, Rash maculo-papular, Rash maculovesicular, Rash papular, Rash pruritic, Rash pustular, Rash vesicular, Exfoliative rash

Cytokine Related AEs: Decreased Frequency with Continuous Dosing



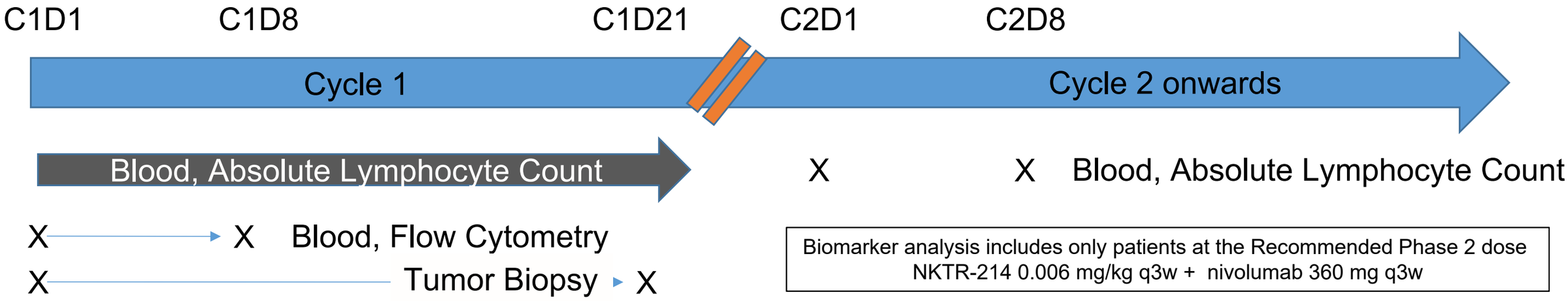




- Cytokine related AEs decreased with subsequent cycles of treatment.
  - All were low grade (no Grade ≥3 or higher).
  - Easily managed with NSAIDs/OTCs.
  - No dose delays, dose reductions or study discontinuations due to cytokine related AE's.
- Hydration guidelines effective: no Grade ≥3 cases of hypotension.
- Prodrug design of NKTR-214 accounts for lower frequency of cytokine-related AE's compared to high dose IL-2.

NEKTAR Cycle 3+ symptoms equals average of % per cycle for cycles 3-25.

Biomarker Sampling and Methodology for Stage IV Melanoma Cohort

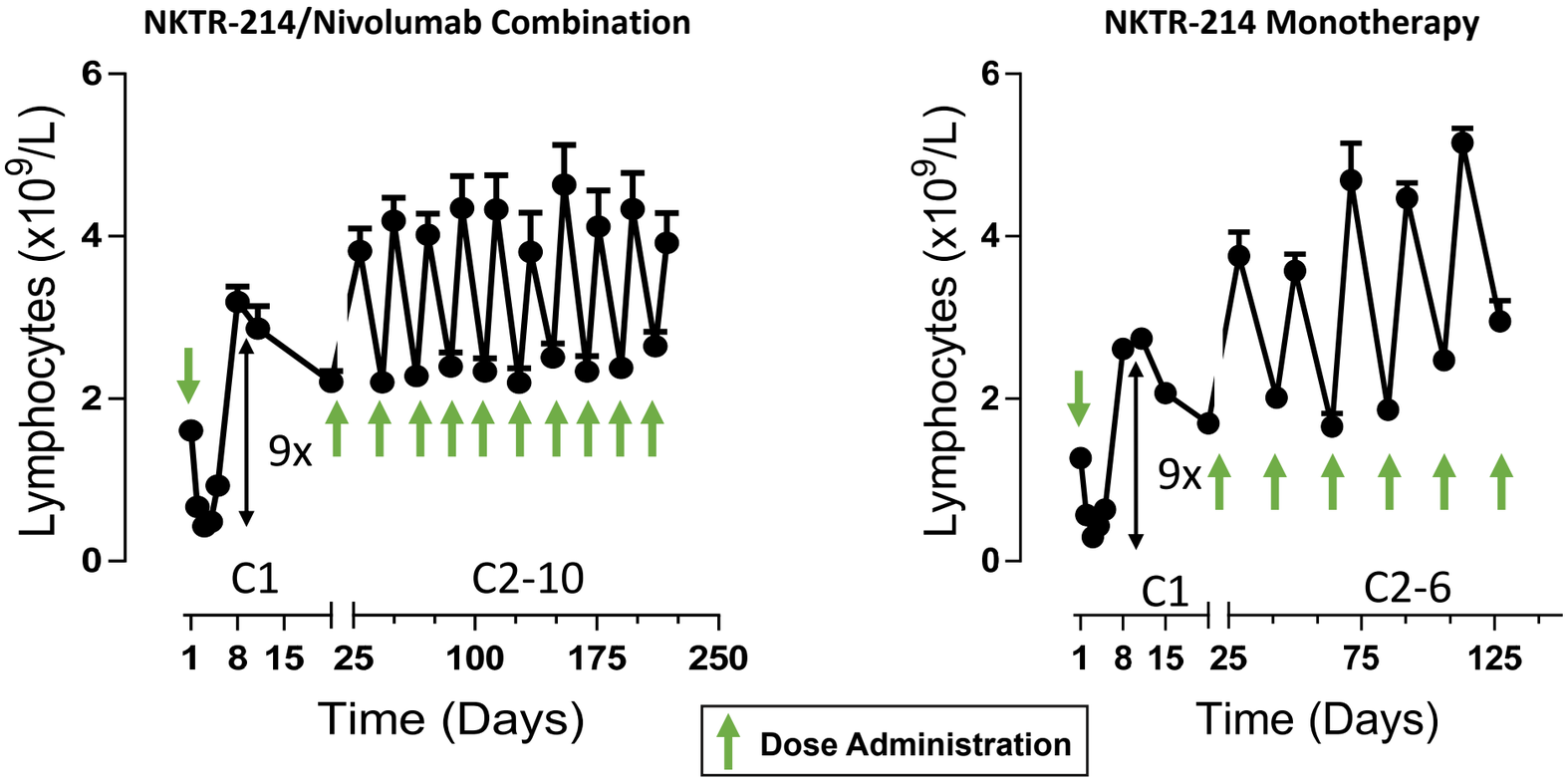


Biomarker analysis includes only patients at the Recommended Phase 2 dose
NKTR-214 0.006 mg/kg q3w + nivolumab 360 mg q3w

Multiple methods included in the biomarker plan to demonstrate activation of the IL-2 receptor pathway:

- Lymphocyte analysis in blood for all patients over duration of treatment (n=41)
- Baseline tumor biopsies evaluated for PD-L1, CD8 T cells (n=26)
- Baseline tumor biopsies evaluated for gene expression using EdgeSeq (n=11)
- Immunophenotype analysis for matched Day 1 and Day 8 samples (n=9)
- Cellular analysis of tumor biopsy using immunofluorescence (n=4) and IHC (n=8) with matched Day 1 and Day 21 samples
- TCR repertoire analysis using immunoSEQ (n=7)

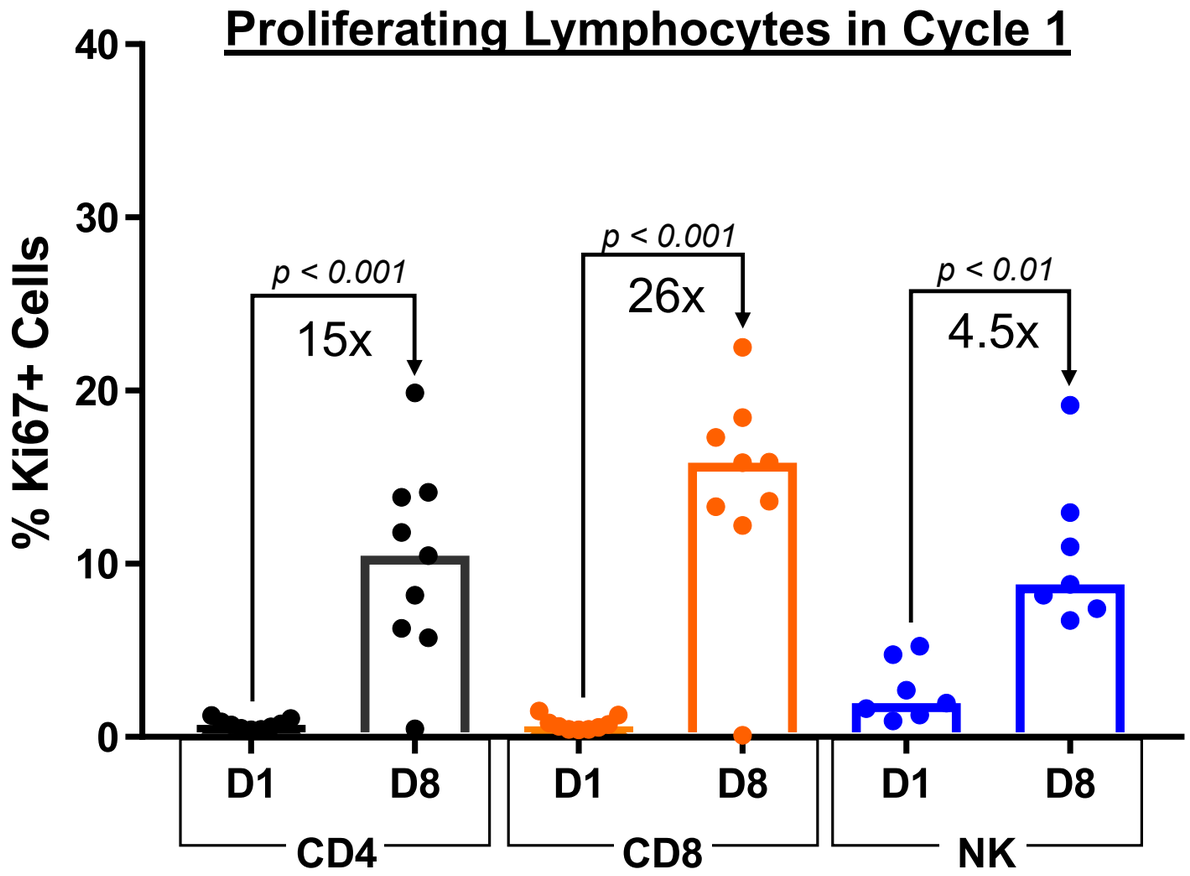
NKTR-214 Drives Continuous Mobilization of Lymphocytes After Every Cycle



- NKTR-214 provides rapid activation of the immune system.
- Effect of lymphocyte mobilization is consistent and maintained with successive treatment cycles.
- Lymphocyte effects of the NKTR-214/nivolumab combination are driven by NKTR-214, as a similar pattern is observed with monotherapy

Lymphocyte levels were obtained from standard hematology analysis. All patients with data from the monotherapy trial EXCEL (N=17) and all 1L Melanoma patients in the NKTR-214/nivolumab combination enrolled in PIVOT-02 (N=41, Mean±SE) were included in the analyses.

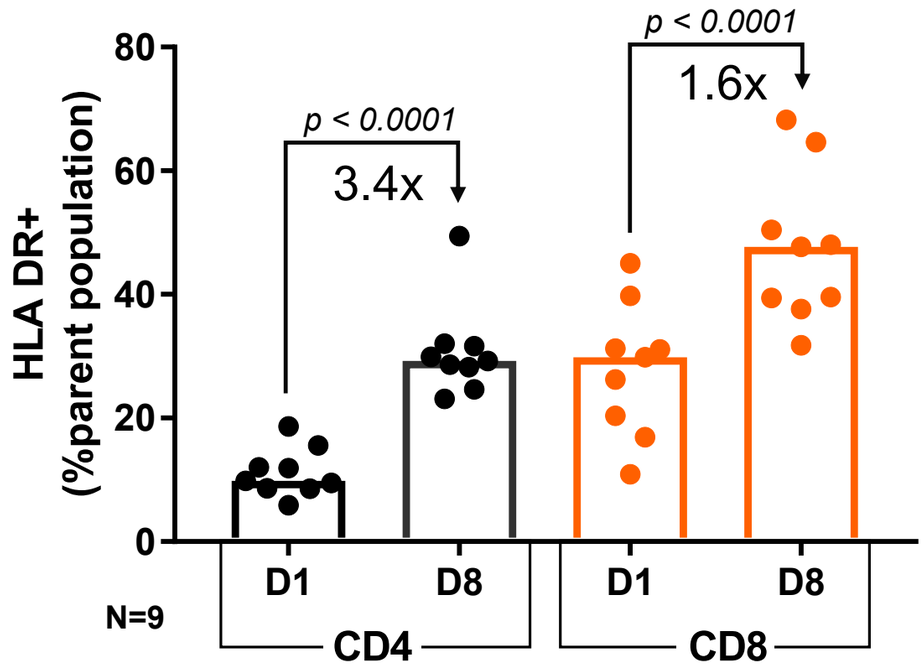
Peripheral Blood Demonstrates Proliferation of CD4, CD8 and NK Cells 1L IO-Naïve Melanoma



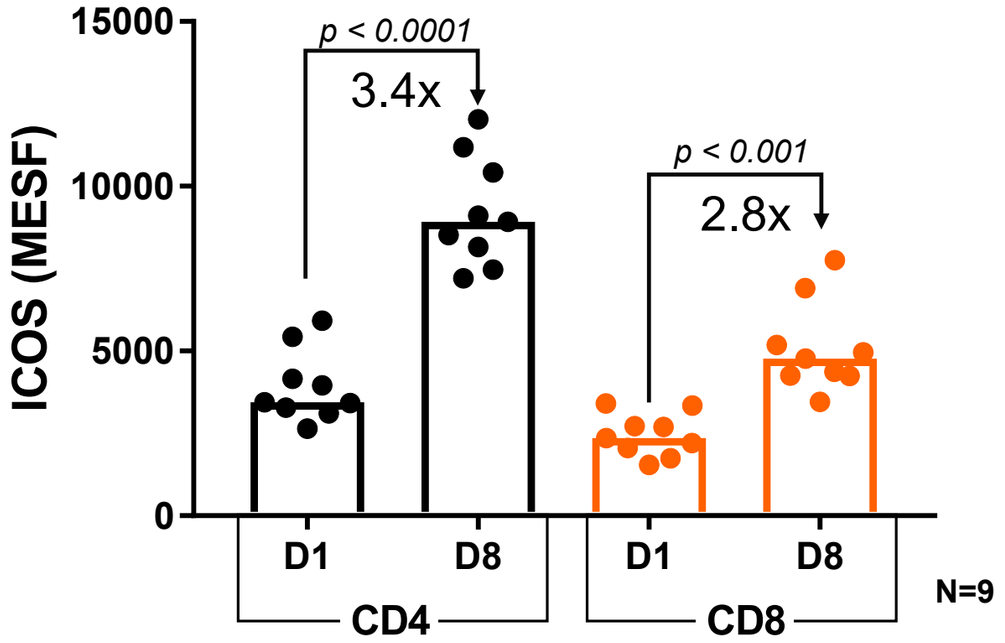
Ki67 positive lymphocytes were enumerated using flow cytometry and presented as proportion (%) of each cell population. All patients at RP2D with matched D1 and D8 samples were included in the analysis (CD4: N=9, CD8: N=9, NK: N=7). Median is shown, fold change and paired T-test was used for statistical significance.

Peripheral Lymphocytes Mobilized by NKTR-214 + Nivolumab Exhibit an Activated Phenotype

Antigen-Experienced T Cells in Cycle 1



Increased Cell Surface Expression of ICOS on T Cells in Cycle 1



- ICOS increase also observed with NKTR-214 monotherapy

HLA-DR positive T cells were enumerated using flow cytometry and presented as proportion (%) of each parent cell population. All patients at RP2D with matched D1 and D8 Cycle 1 samples were included in the analysis. (N=9; bars show median for each population). Median fold change and statistical analysis is paired T-test between D8 and D1.

ICOS positive T cells were enumerated using flow cytometry and cell surface expression of ICOS was calculated from a reference curve of Molecules of Equivalent Staining Fluorochrome (MESF). All patients at the RP2D with matched D1 and D8 Cycle 1 samples were included in the analysis (N=9, bars show median for each population). Median fold change and statistical analysis is paired T-test between D8 and D1.

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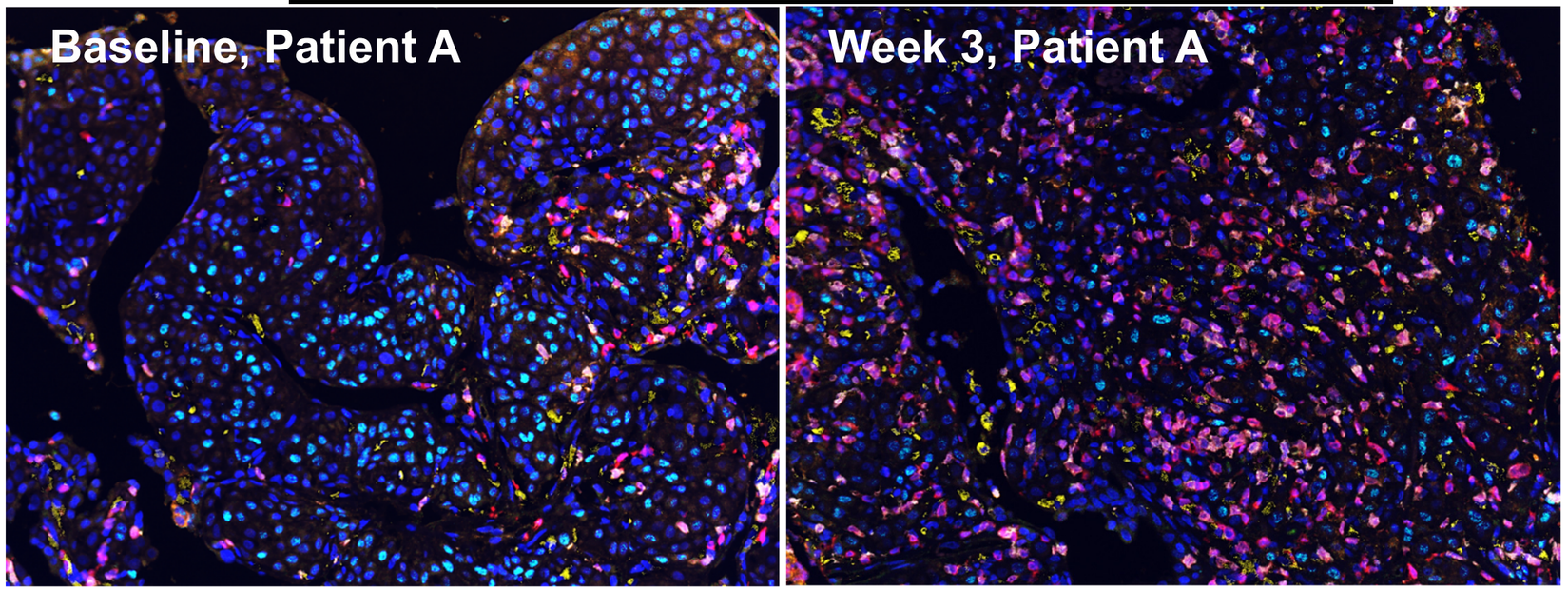
NKTR-214 + Nivolumab Promotes Increase of T cells

Immunofluorescence Microscopy of Tumor Biopsy

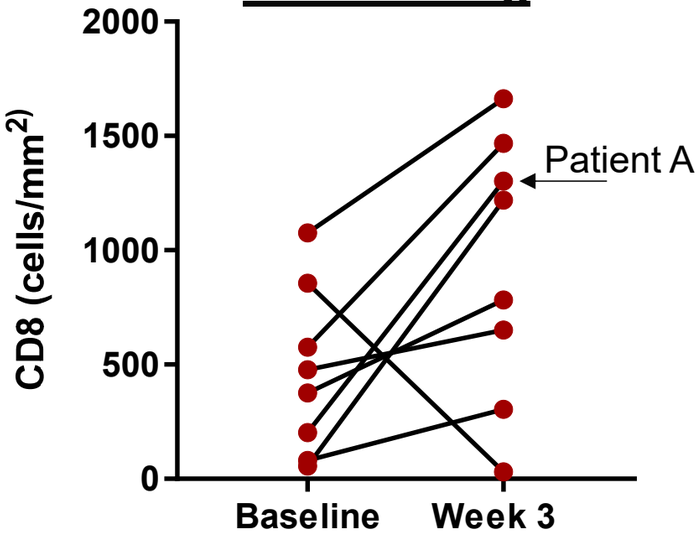


CD8 T cells: Baseline – 108 cells/mm2

CD8 T cells: Week 3 – 712 cells/mm2

DAPI SOX-10 CD3 CD8 PD-L1 PD-1 CD68

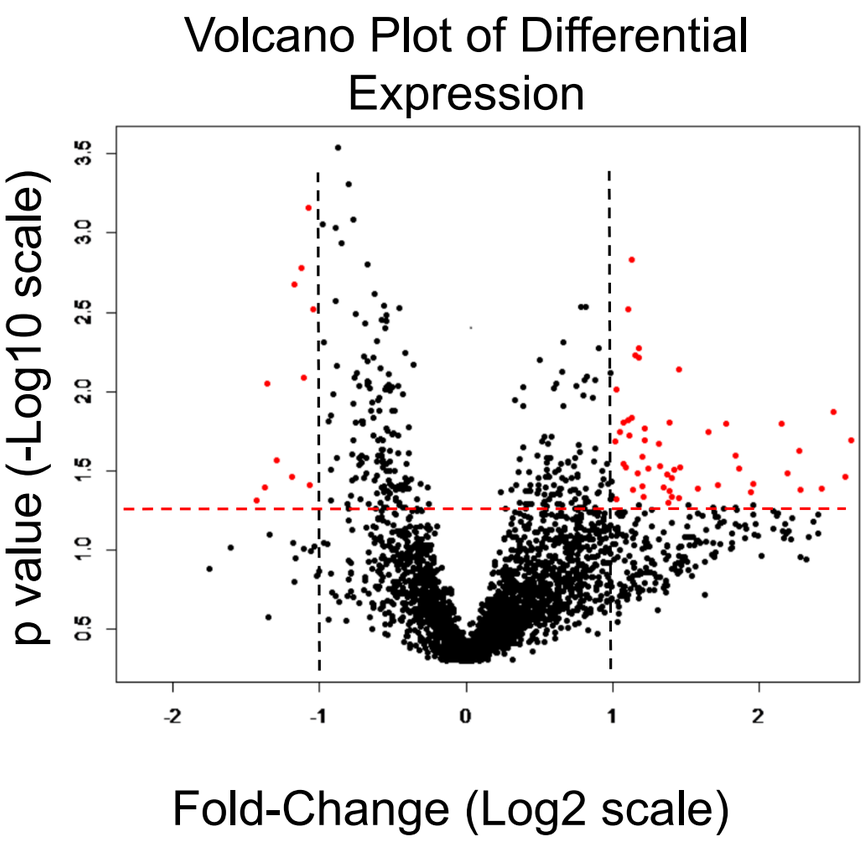
Change in CD8 Infiltrate IHC Staining

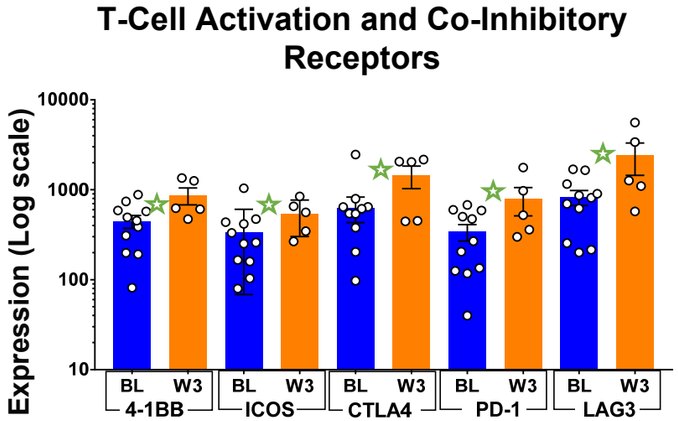


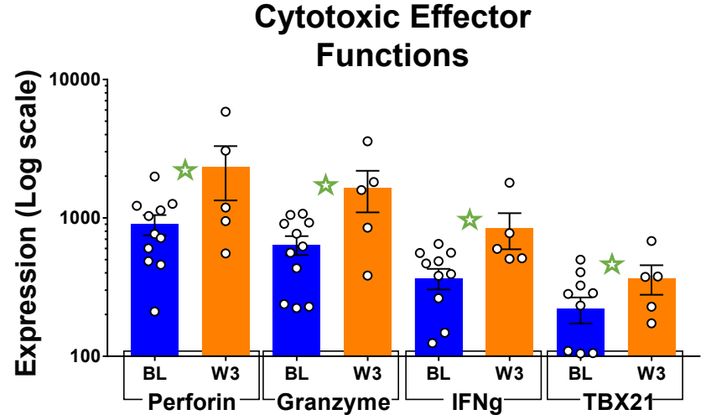
Good concordance between immunofluorescence and IHC methods

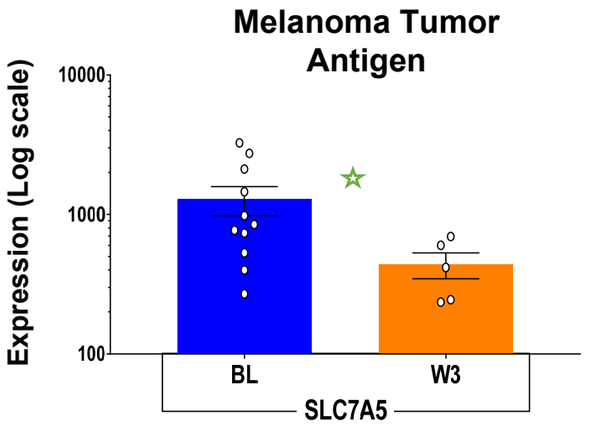
Immunofluorescence staining was performed using Vectra with the indicated staining reagents. Images shown obtained at 20X magnification. DAPI stains DNA, SOX-10 is a melanoma tumor antigen, CD3/CD8 stain T cells, CD68 stains macrophage. IHC for CD8 was obtained by standard methods. All 1L Melanoma patients with matched Baseline and Week 3 biopsy (N=8) were included in the analysis.

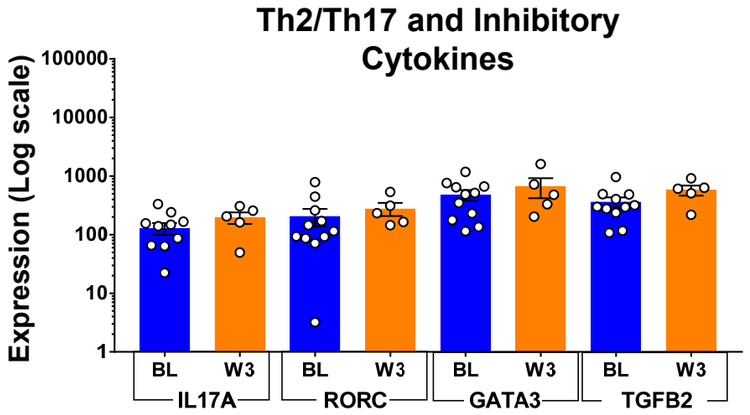
NKTR-214 + Nivolumab Promotes Favorable Anti-Tumor Gene Expression Changes and Antigen Reduction in the Tumor





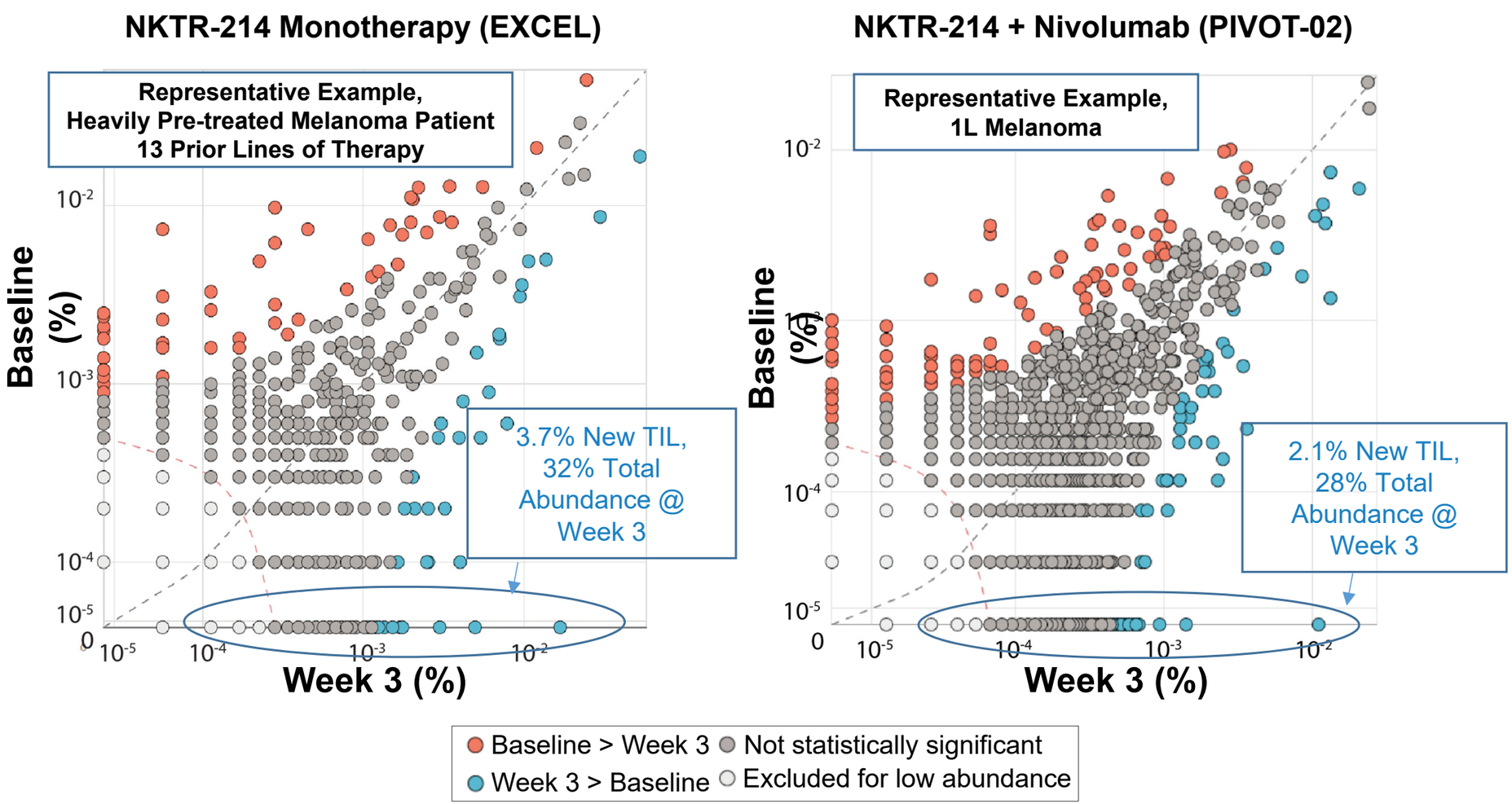






EdgeSeq was performed on all available samples, Baseline (BL) N=11 and Week 3 (W3) N=5. Only 2 patients had matched BL and W3 samples. Volcano Plot N=2: red points are both statistically significant (p-value<=0.05) and are over 2 fold higher (in linear space). Black dashed lines show 2-fold increase/decrease, red dashed line shows threshold for statistical significance. Bar Charts / Scatter Plots: Green stars indicate statistically significant genes (p-value<=0.05).

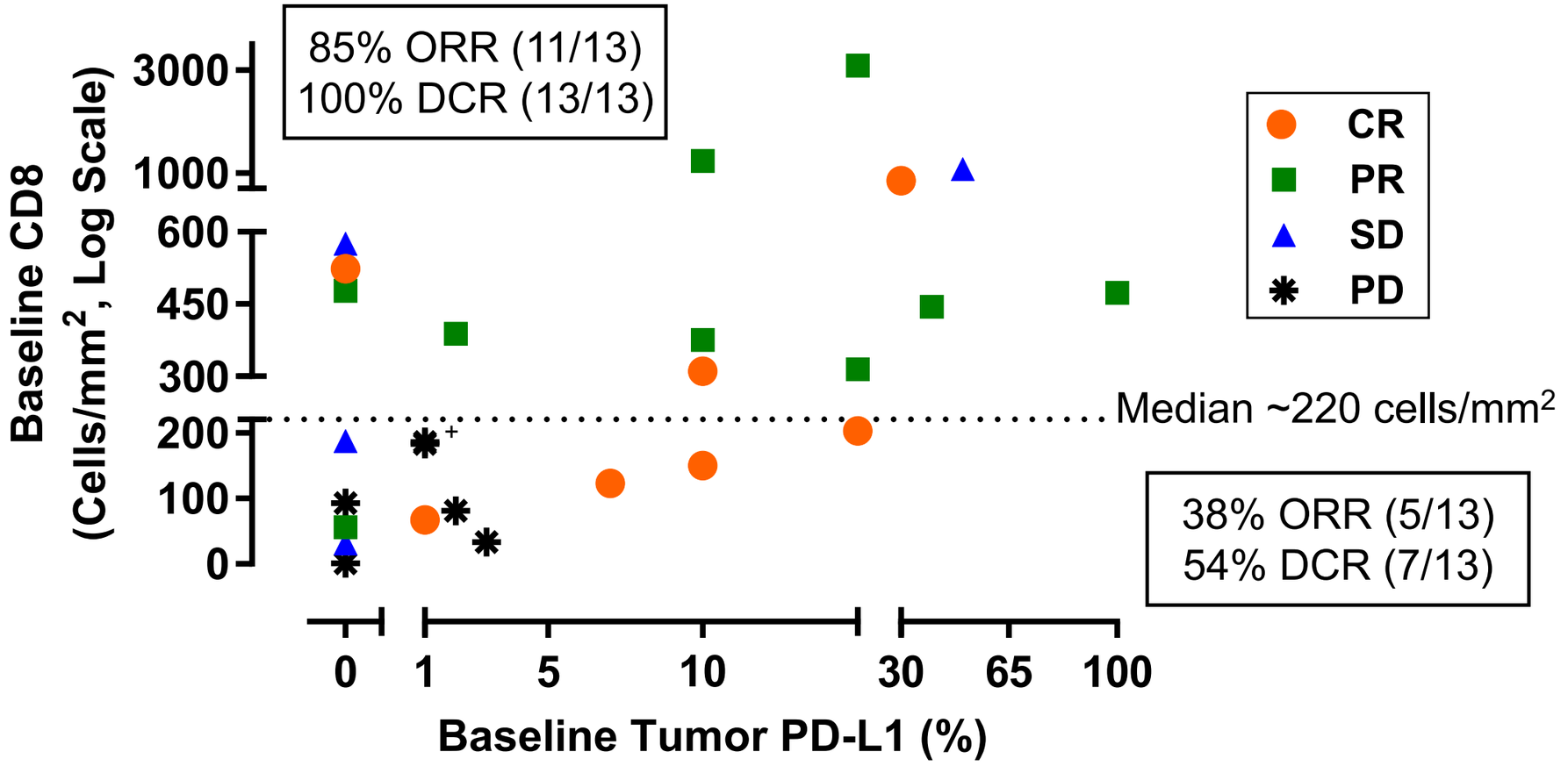
NKTR-214 Drives New T Cell Clones into the Tumor Microenvironment



- All patients evaluated demonstrated new clones at Week 3 that were not present at Baseline
- New TIL fraction and proportional abundance driven by NKTR-214 since effects are similar in monotherapy and combination
- Results indicate that therapy promotes new priming and T cell trafficking into the tumor

Tumor biopsy was processed to nucleic acid and used for TCR repertoire analysis using immunoSEQ. All 1L Melanoma patients (N=7) with matched Baseline and Week 3 samples are reported as % productive frequency. TCR Clones more abundant at Baseline are shown in red and clones more abundant at Week 3 are shown in blue. Dark grey dots are not significant between timepoints and light gray dots are excluded for low abundance. The gray dashed line lists frequency equality and the red dashed line identifies the population used for statistical comparison. New T Cell infiltrates are shown in the oval and summarized for N=7 in the box above. EXCEL: NKTR-214 Monotherapy clinical trial.

NKTR-214 + Nivolumab Provides Efficacy Regardless of Baseline CD8 Tumor Infiltrating Lymphocytes and PD-L1 Expression



+: 2 patients with PD

Baseline tumor biopsies were evaluated by immunohistochemistry for CD8 cell counts (N=26), and PD-L1 expression (N=26) using the 28-8 method, or tumor mutation burden (TMB, N=12) using the Foundation TMB method. Each patient with matched baseline CD8 and %PD-L1 were plotted as x/y coordinates and correlated with BOR. Each symbol represents an individual patient (CR: N=7, PR: N=9, SD: N=4, and PD: N=6).

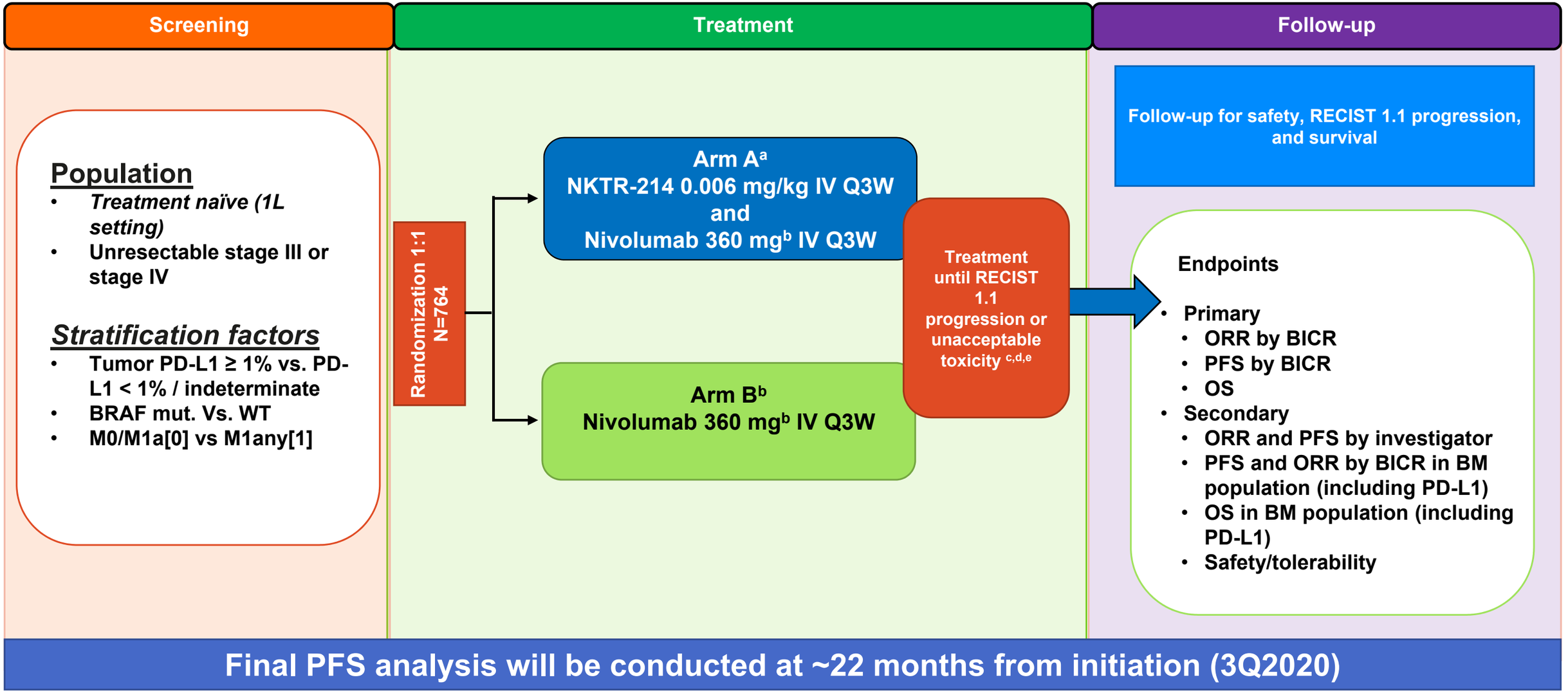
Conclusions

- NKTR-214 plus nivolumab is well tolerated with deep and durable responses in 1L Stage IV melanoma patients, including a high rate of complete responses
- Clear activation of the IL-2 pathway demonstrated by increase in absolute lymphocyte count with activated and proliferating CD4, CD8 and NK cells in blood
- Combination demonstrated T cell infiltration and activation in the tumor microenvironment
- TCR repertoire analysis demonstrates the presence of newly trafficked clonal infiltrates after treatment with NKTR-214 plus nivolumab
- These findings support further evaluation of NKTR-214 plus nivolumab in randomized clinical trials, including the recently initiated 1L melanoma phase 3 trial (CA045-001/NCT03635983)

First Set of Registrational Trials Initiated or Being Initiated

		Patient Population	Study Design	Number Patients
Melanoma	1	1L metastatic melanoma	Phase 3 study of NKTR+Nivo vs. Nivo	764
RCC	2	1L metastatic RCC (intermediate/poor risk)	Phase 3 study of NKTR+Nivo vs. Physicians Choice TKI	600
	3	1L metastatic RCC (intermediate/poor risk)	Phase 3 study of NKTR+Nivo+Ipi vs. Nivo+Ipi	820
	4	1L metastatic RCC	Phase 2/3 study of NKTR/Nivo/TKI vs. Nivo+TKI	~400
Bladder	5	1L metastatic cis-ineligible urothelial cancer (PD-L1 negative baseline patients)	NKTR-214 + nivo with gem/carbo reference arm	165
	6	Muscle-invasive bladder cancer	NKTR-214 + nivo vs nivo	540
	7	1L metastatic urothelial cancer (all comers, cis-eligible and cis-ineligible)	Chemo inclusive and chemo sparing arms with NKTR-214 + nivo	TBD
NSCLC	8	2L metastatic NSCLC (post CPI/chemo combo in 1L)	New cohort of NKTR-214 + nivo in PIVOT-02	100

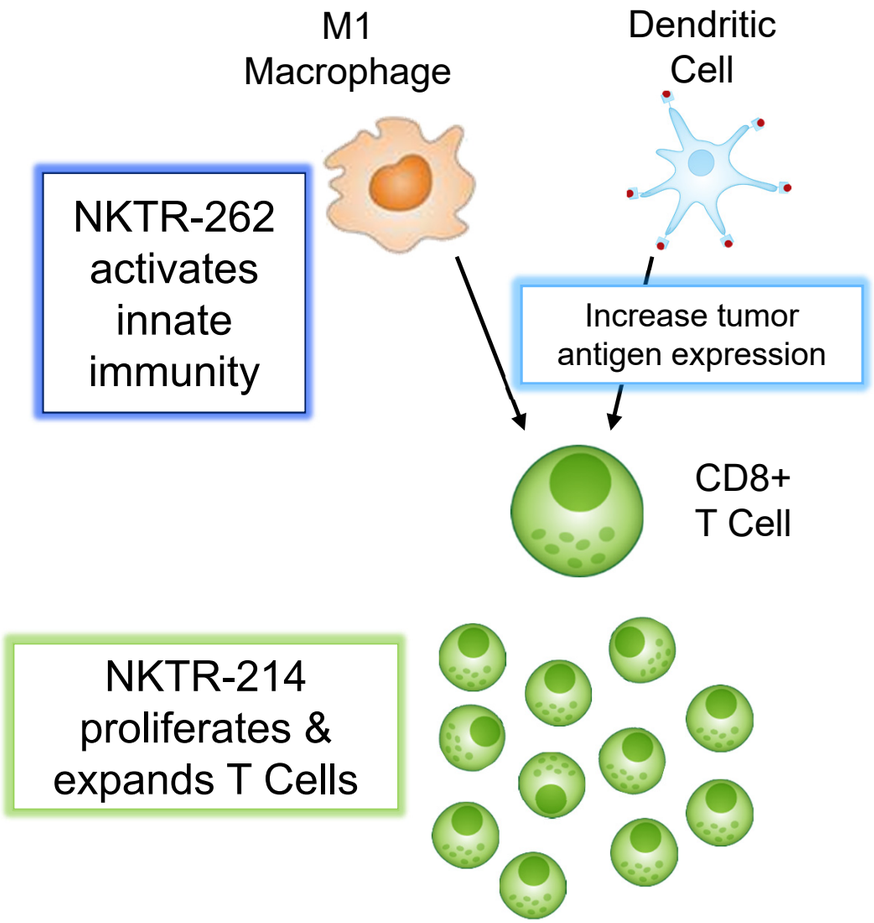
Phase 3 1L Melanoma Trial Design



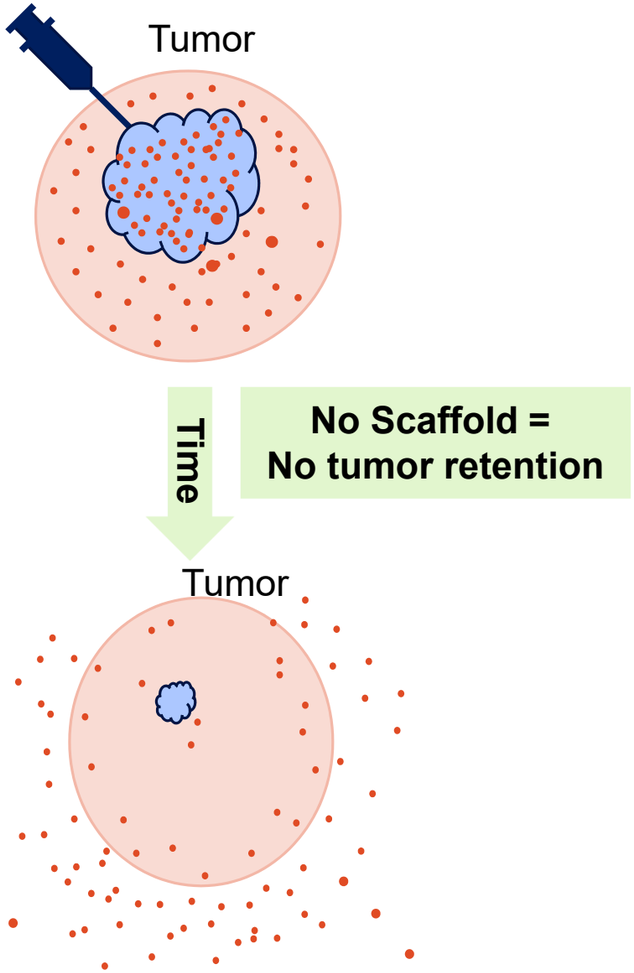
NKTR-262: A Unique TLR 7/8 Agonist

NKTR-262: A Unique Intratumoral TLR Agonist to Target the Innate Immune Response

- Activates myeloid cell response and increases tumor antigen presentation
  - Overcomes tumor-suppressing micro-environment by mimicking local infection
- NKTR-262 designed to be synergistic with NKTR-214 and is a novel, wholly-owned I-O combination for Nektar
- Nektar technology optimizes abscopal anti-tumor effects with minimal systemic exposure
- Phase 1 Study Open for Recruitment in March 2018



Our Strategy: PEGylation Will Keep Scaffold in Tumor And Reduces Systemic Exposure



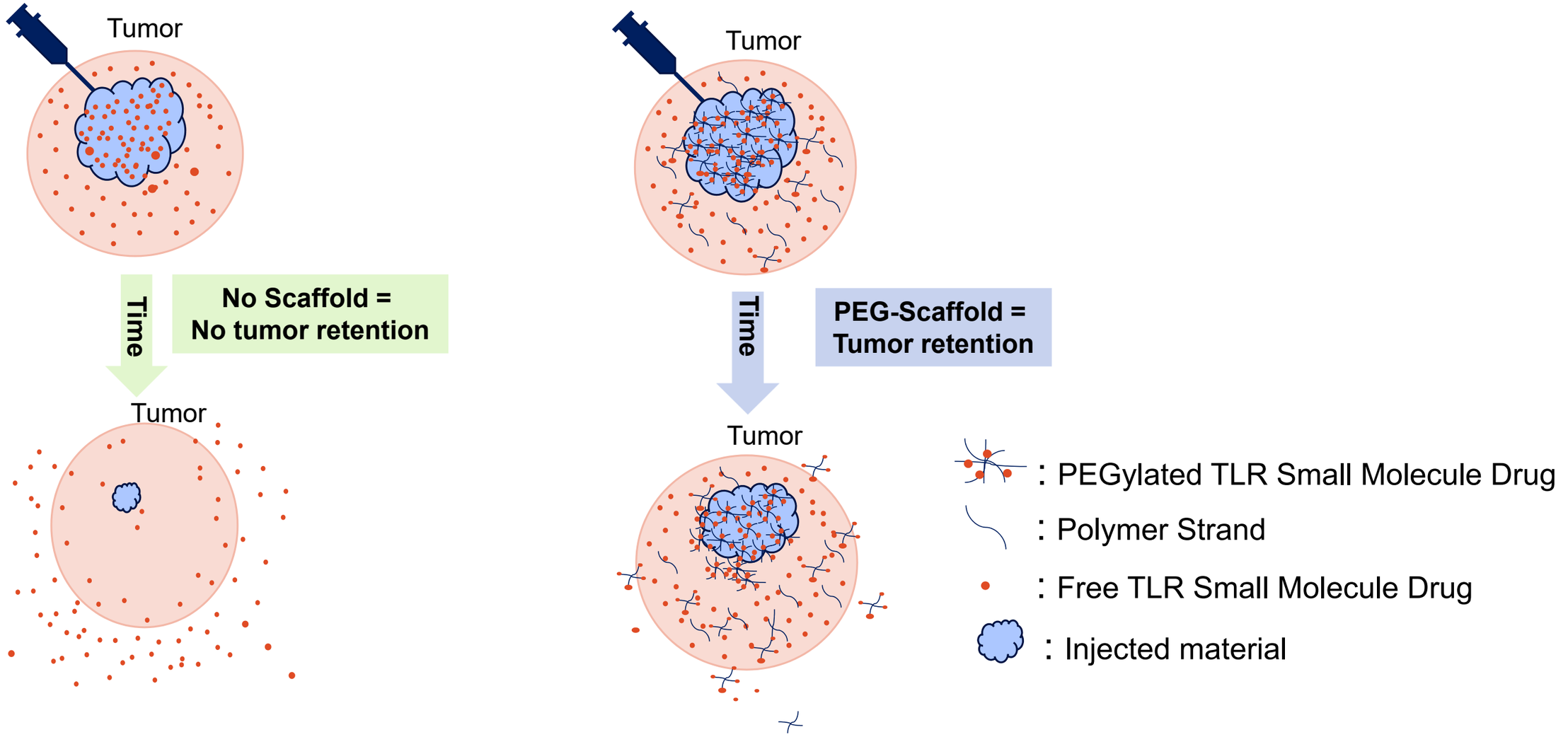
：PEGylated TLR Small Molecule Drug

：Polymer Strand

：Free TLR Small Molecule Drug

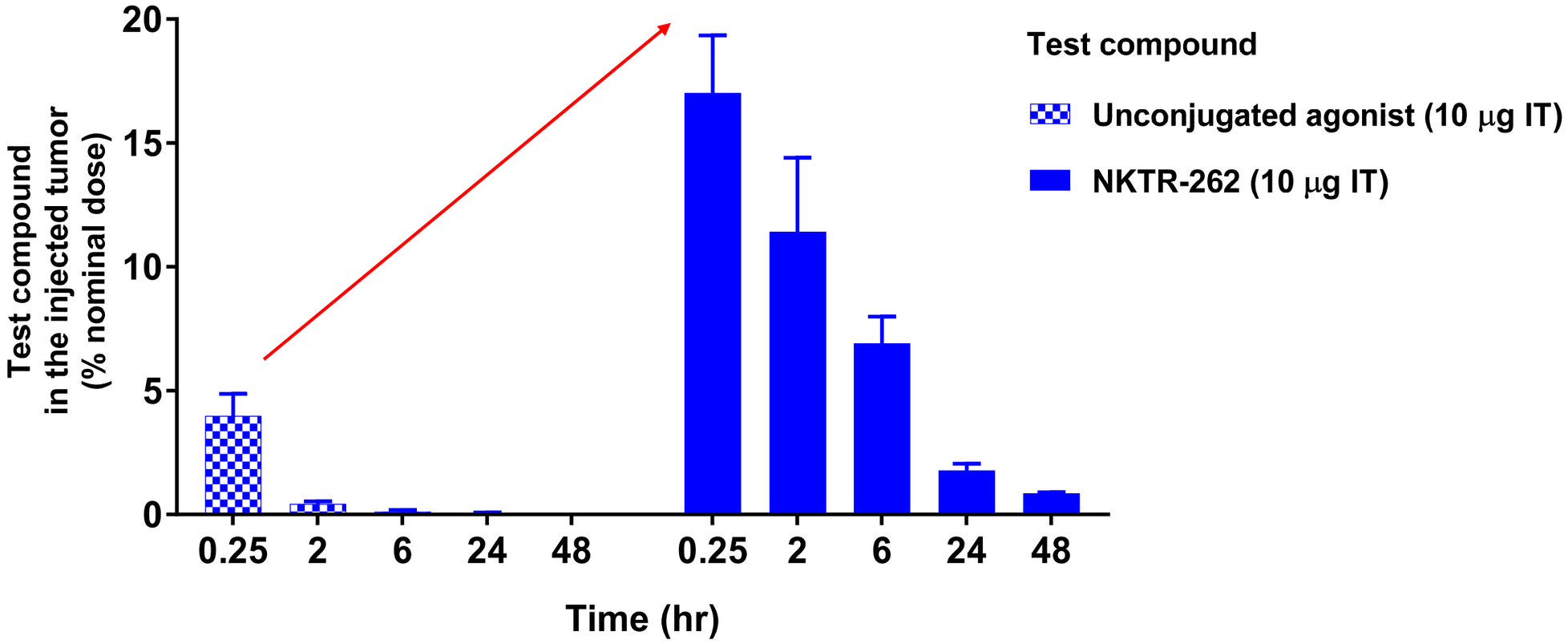
：Injected material

Our Strategy: PEGylation Will Keep Scaffold in Tumor And Reduces Systemic Exposure

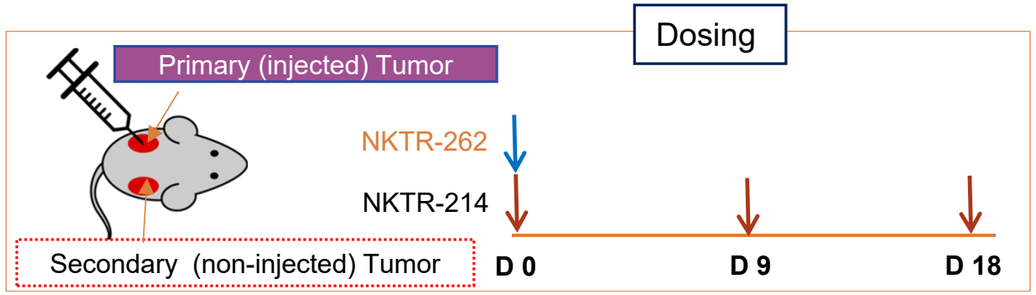


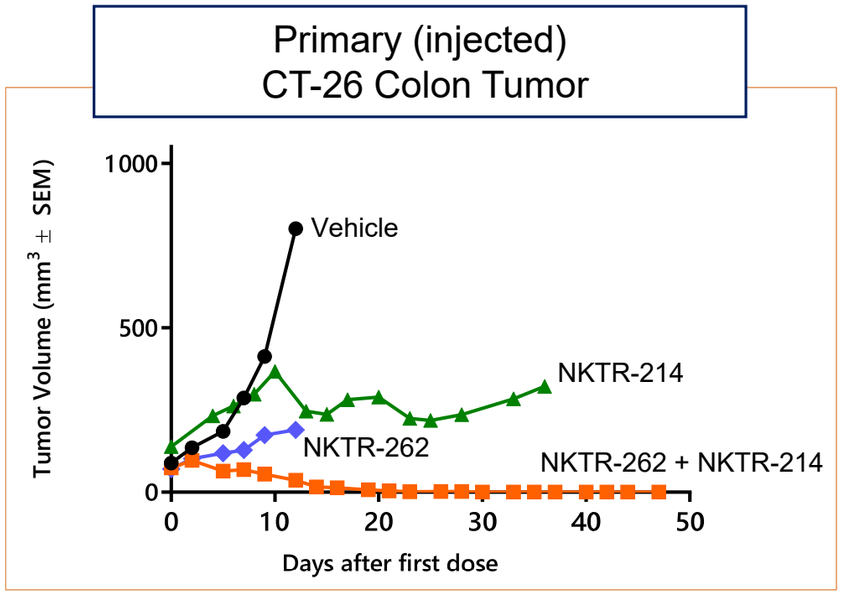
NKTR-262 is Retained More Effectively in Injected Tumors Compared to Unconjugated TLR7/8 Agonist

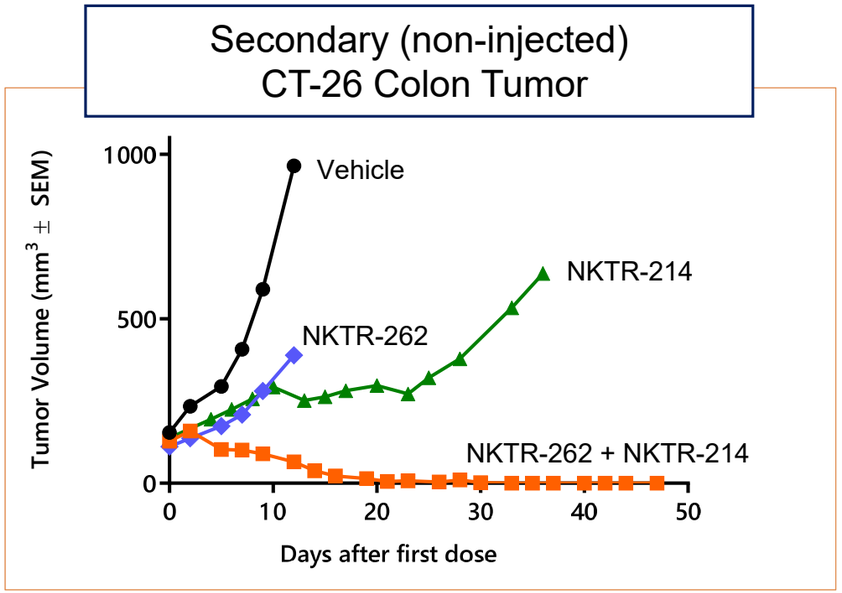
Intratumoral retention of unconjugated TLR7/8 agonist vs NKTR-262 in the injected tumor



Complete Regression and Abscopal Effect with Combination of NKTR-262 and NKTR-214







NKTR-262 0.8 mg in 40 µL volume given in a single IT dose, NKTR-214 0.8 mg/kg q9dx3 IV; N=10 per group

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The REVEAL Study: Doublet of NKTR-262 with NKTR-214

REVEAL Phase 1b/2 Study Objectives

Primary Objectives:

- **Phase 1b:** Evaluate safety and determine recommended phase 2 dose (RP2D) of doublet therapy of NKTR-262+NKTR-214
- **Phase 1b/2:** Assess objective response rate (ORR) by RECIST 1.1

Secondary Objectives:

- **Phase 1b/2:** Evaluate the proportion of patients with an abscopal response by RECIST 1.1
- **Phase 1b/2:** Evaluate immune activity in the blood and tumor including cellular analysis of tumor biopsy, gene expression analysis and TCR repertoire analysis
- **Phase 2:** Once RP2D is established in Phase 1b, NKTR-262 and NKTR-214 will be administered as doublet therapy in expansion cohorts in specific solid tumor types

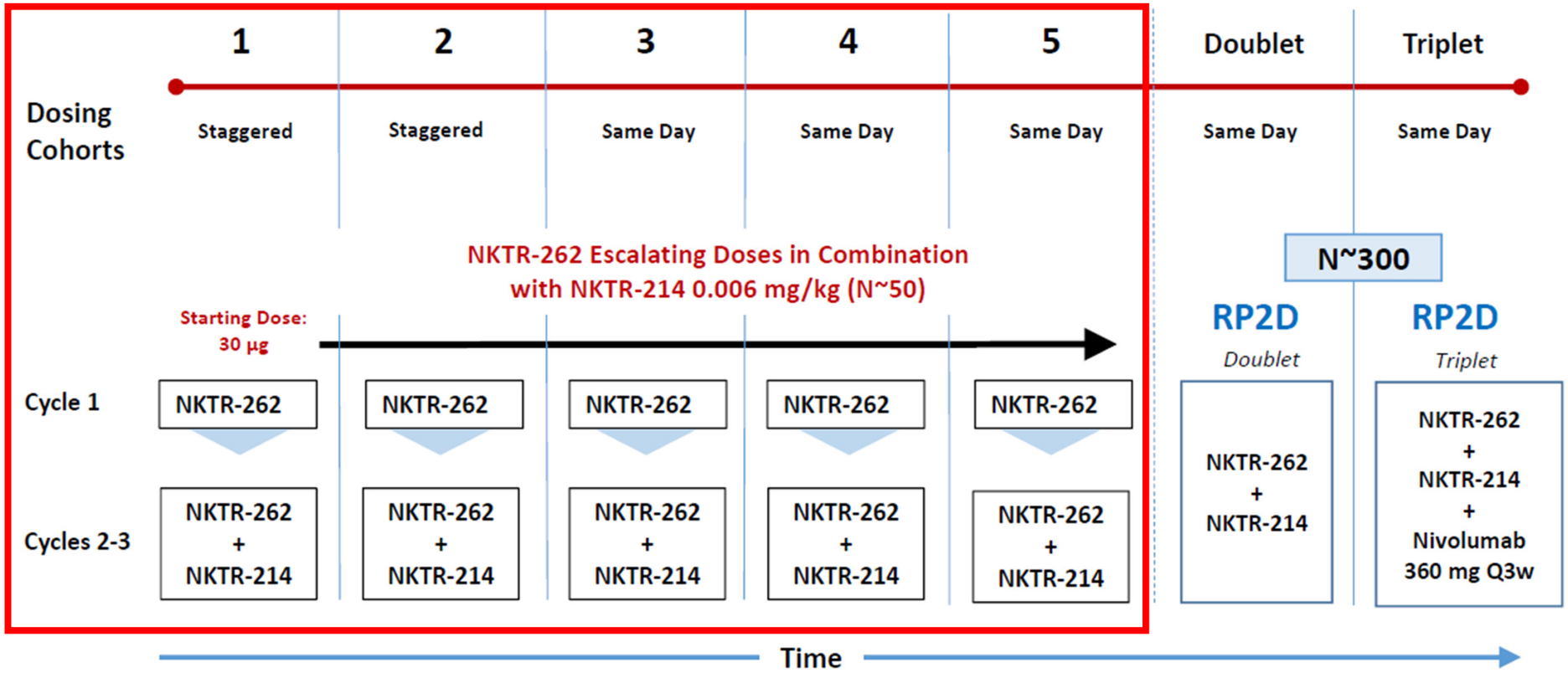
Eligibility Criteria for Doublet Phase 1b:

- Patients with metastatic R/R MEL, RCC, TNBC, SARC, UC, CRC, MERKEL CELL or OVARIAN
- Patients must be refractory to all therapies known to confer clinical benefit to their disease

REVEAL: Phase 1/2 of NKTR-262 and NKTR-214 in Locally Advanced or Metastatic Solid Tumors

REVEAL Cohorts:

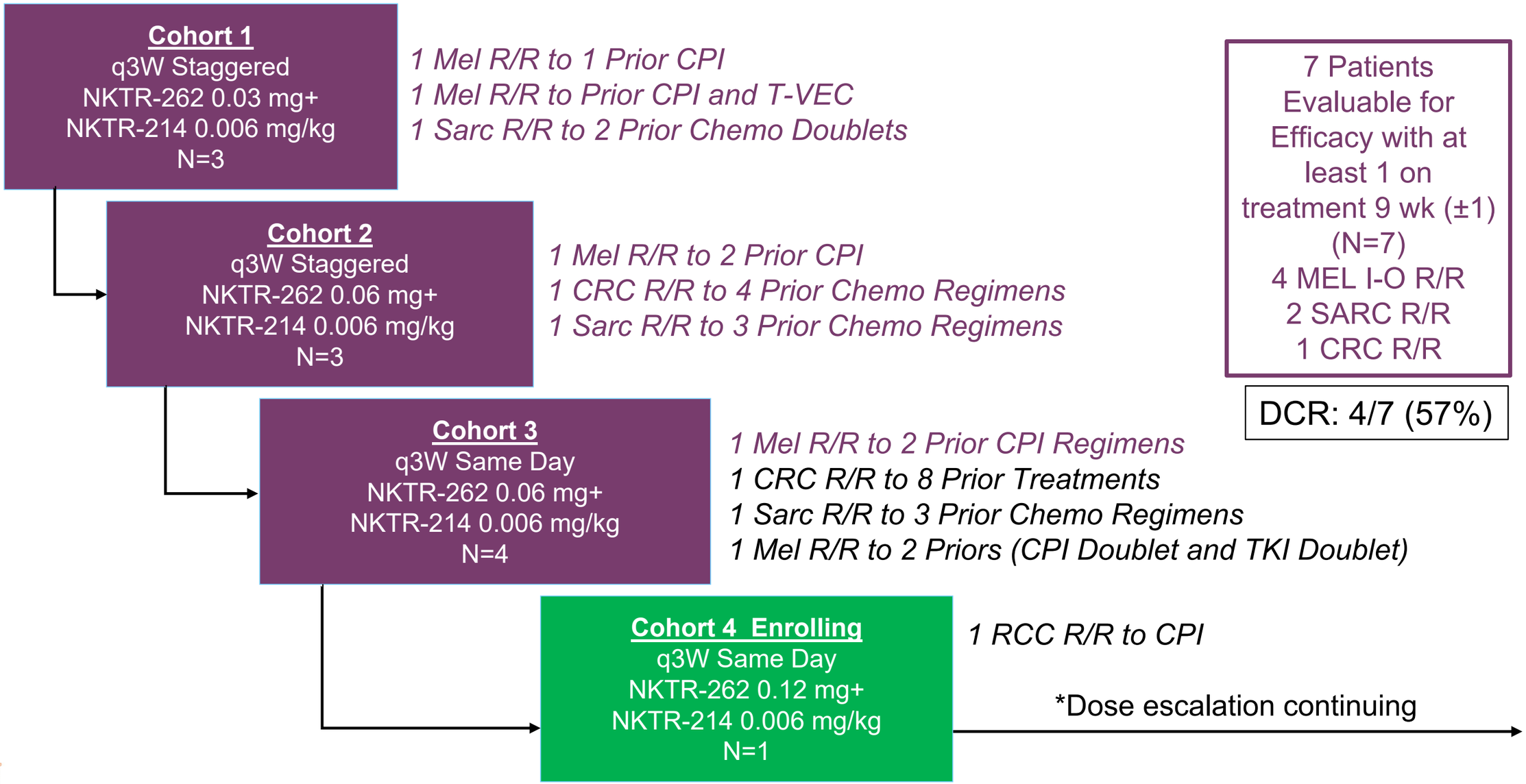
Enrolling Cancer Patients with Melanoma, Merkel Cell, Renal, Urothelial, Triple Negative Breast Cancer, Ovarian, Colorectal, Sarcoma (1L & 2L, I-O Naïve & Refractory)



REVEAL: NKTR-262 + NKTR-214 Doublet Administration in Ongoing Dose-Escalation Phase 1b

- Intratumoral (IT) NKTR-262 Q3W; starting dose 0.03 mg
- During dose escalation phase
  - **Cycle 1:** NKTR-262 IT is administered in Cycle 1 to assess single agent safety
  - **Cycle 2 and beyond:** NKTR-214 fixed dose of 0.006 mg/kg IV is combined with NKTR-262 IT starting in Cycle 2
- NKTR-262 injected lesions (up to two) must be between 20 mm and 90 mm in diameter for IT injection
- Target lesions chosen for RECIST response assessment **must be** lesions that have not been injected with NKTR-262
- Evaluation of nivolumab with RP2D of NKTR-262 and NKTR-214 permitted per protocol

REVEAL Phase 1b Dose Escalation: Starting Dose Cohorts and Characteristics of Relapsed/Refractory Patients (N=11)



Safety for Starting Dose Cohorts of Doublet Administration (N=11)

- No DLTs observed in starting dose cohorts
- No Grade ≥ 3 TRAEs observed to-date
- Most common treatment-related AEs are flu-like symptoms easily managed with NSAIDs/OTCs
- No dose delays, no dose reductions and no discontinuations due to TRAEs
- Dose-escalation ongoing; MTD not reached

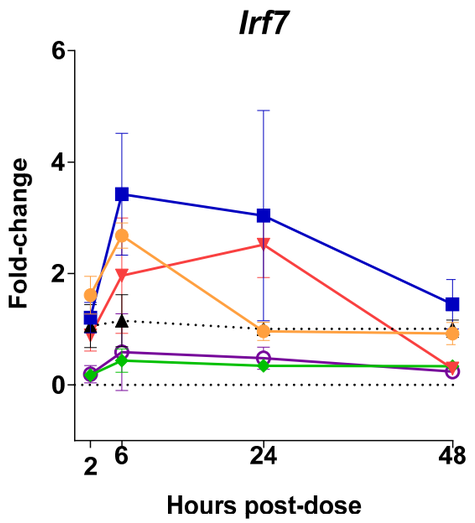
Preliminary Biomarker Data

NKTR-262 Target Engagement in Tumor: Gene Expression in Mouse Models

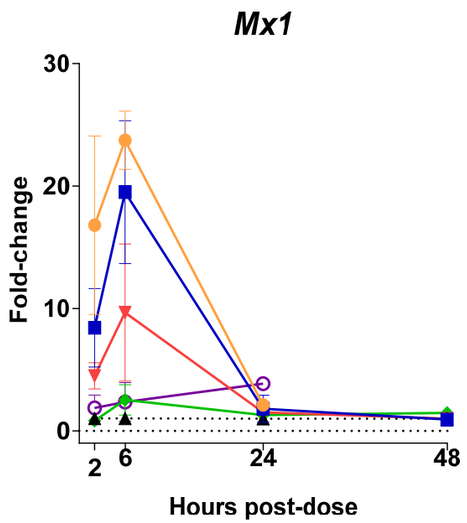
Rapid and transient activation of TLR7 pathway and type I interferon response genes in NKTR-262 treated tumors

Examples from Interferon Inducible Gene Family

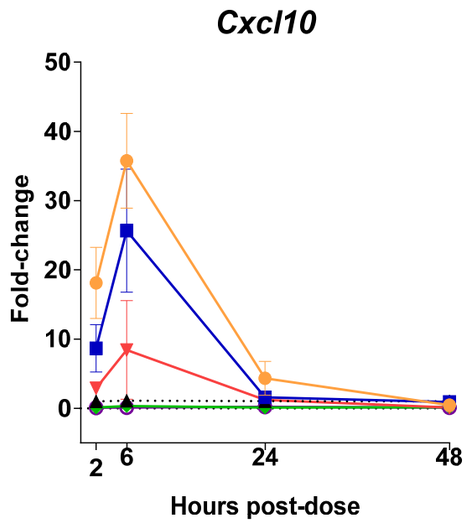
Interferon regulatory factor 7

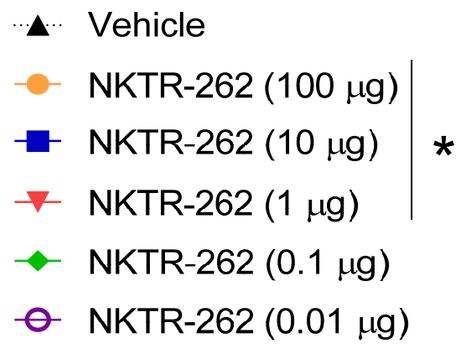


Mx Dynamin Like GTPase 1



C-X-C Motif Chemokine Ligand 10

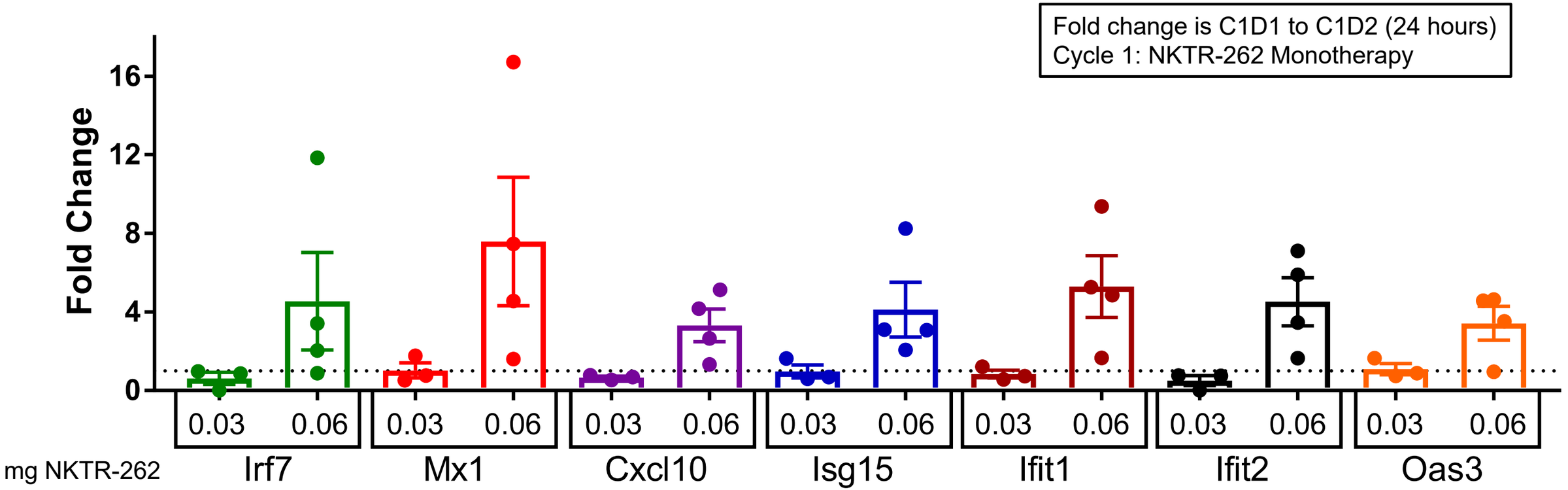




TLR7 and type I interferon pathway gene expression induction after NKTR-262 dose response measured by qRT-PCR relative to vehicle in CT26 subcutaneous tumors. (*, $p<0.05$ relative to vehicle at T_{max})

REVEAL: NKTR-262 Target Engagement Validation in Patients at Lowest Starting Doses

Induction of type I IFN response genes in NKTR-262 injected tumor lesions



NKTR-262 was injected intratumorally at 0.03mg dose in Cohort 1 and at 0.06mg dose in Cohorts 2 and 3. Gene expression changes were compared between pre-dose and 24 hrs post-dose tumors biopsies in Cycle 1 (NKTR-262 single agent) from the injected lesions utilizing nCounter platform from Nanostring Technologies.

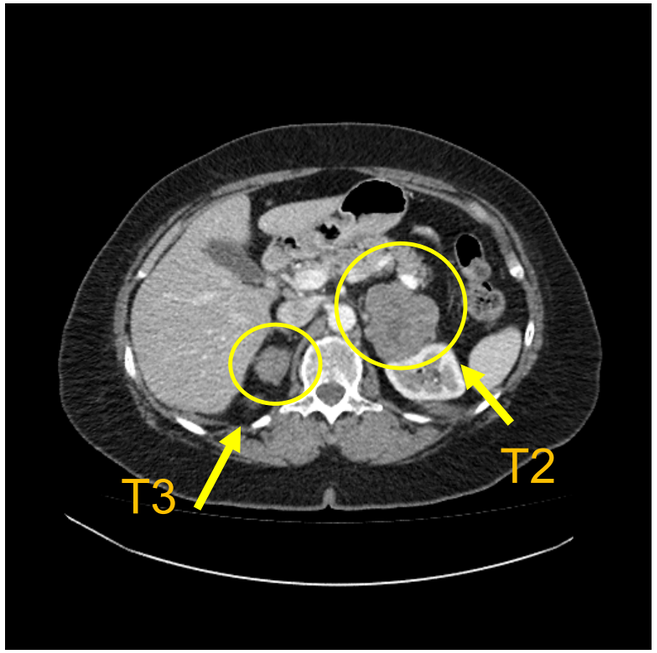
Case Studies
Melanoma Patients R/R to Prior CPIs

Case 1: Stage IV Melanoma IO Refractory

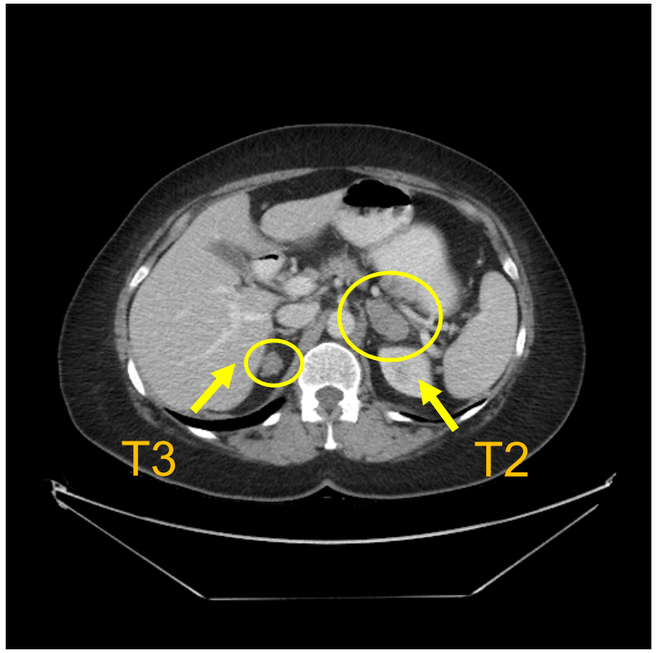
- Treatment Center: Providence Cancer Center in Portland Oregon
- 71 year old female diagnosed with metastatic melanoma 2/15/18
- Metastatic disease to the lung, adrenal glands, bone, lymph nodes and soft tissue
- ECOG 0 with LDH > ULN
- Prior CPI Treatment Regimens:
  - March 2018 - May 2018: Treated with Nivolumab with Best Overall Response of PD
  - May 2018 - July 2018: Treated with Ipilimumab + Nivolumab with Best Overall Response of PD
- NKTR-262 Intratumoral Injection Site: Left Inguinal Lymph Node
- Treatment Ongoing in Dose Cohort 3 (q3W IT NKTR-262 0.06 mg with IV NKTR-214 0.006 mg/kg)

Case 1: Stage IV Melanoma CPI-Refractory Patient Unconfirmed Partial Response (-38%) with Treatment Ongoing

Baseline



Scan 1



	Lesion Description	Baseline	Scan 1
Target Lesions (Non Injected Lesions)	Exam/Scan Date	2018-08-29	2018-11-05
	Target Lesion 1 (T1): Right Anterior Lung	11	4
	Target Lesion 2 (T2): Left Adrenal Gland	55	35
	Target Lesion 3 (T3): Right Adrenal Gland	25	18
	Target Lesion 4 (T4): Right Lateral Intra-Abdominal	21	12
	Sum of the Diameters (% Change from Baseline)	112	69 (-38.3%)
Overall Response	RECIST 1.1		Partial Response

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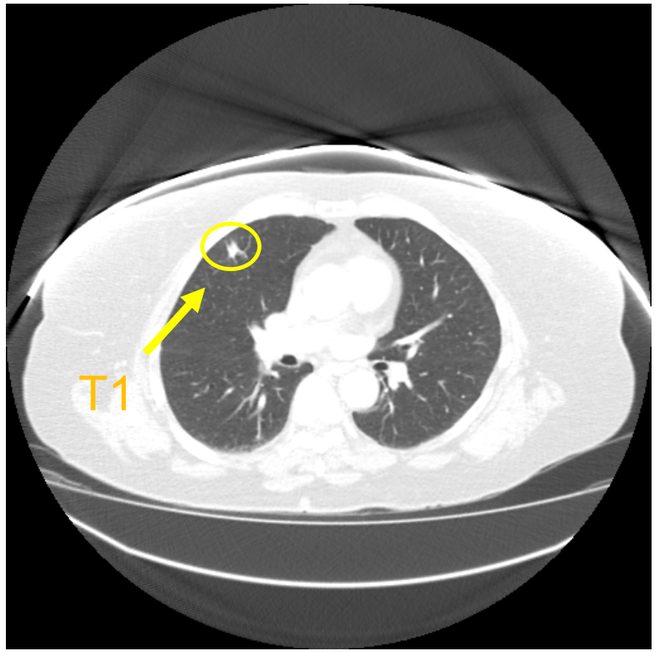
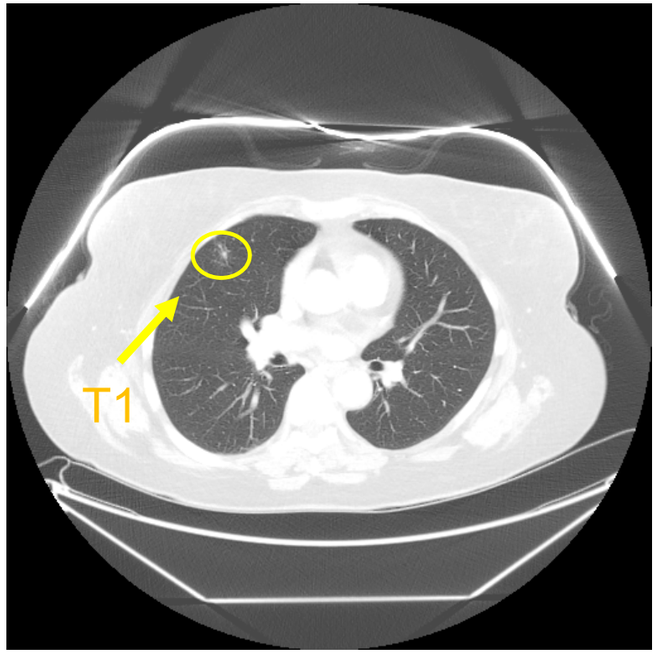
Case 1: Stage IV Melanoma CPI-Refractory Patient Unconfirmed Partial Response (-38%) with Treatment Ongoing

Baseline



Scan 1



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NEKTAR

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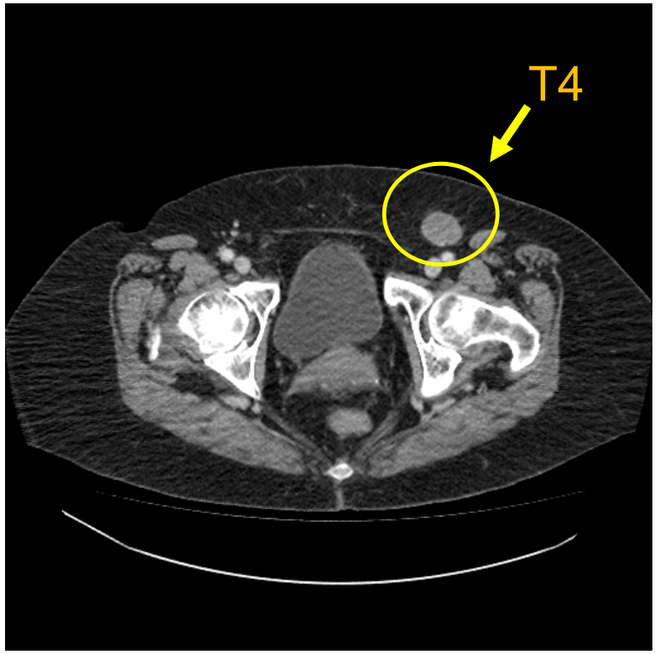
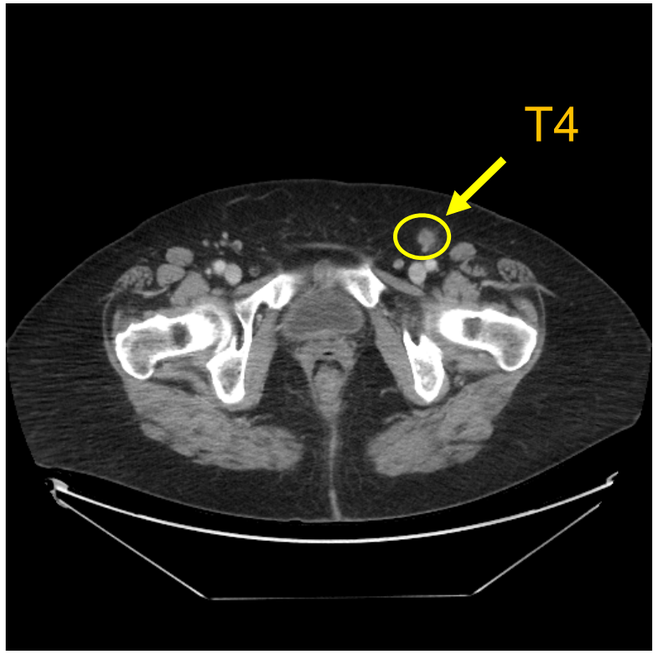
Baseline



Scan 1



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	Target Lesion 3 (T3): Right Adrenal Gland	25	18
	Target Lesion 4 (T4): Right Lateral Intra-Abdominal	21	12
	Sum of the Diameters (% Change from Baseline)	112	69 (-38.3%)
Overall Response	RECIST 1.1		Partial Response

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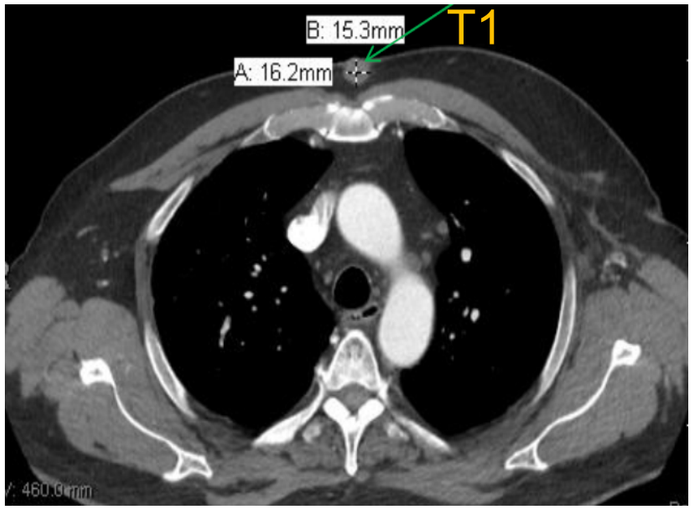
Case 2: Stage IV Melanoma IO Refractory
Confirmed Partial Response (-100%) – Treatment Ongoing

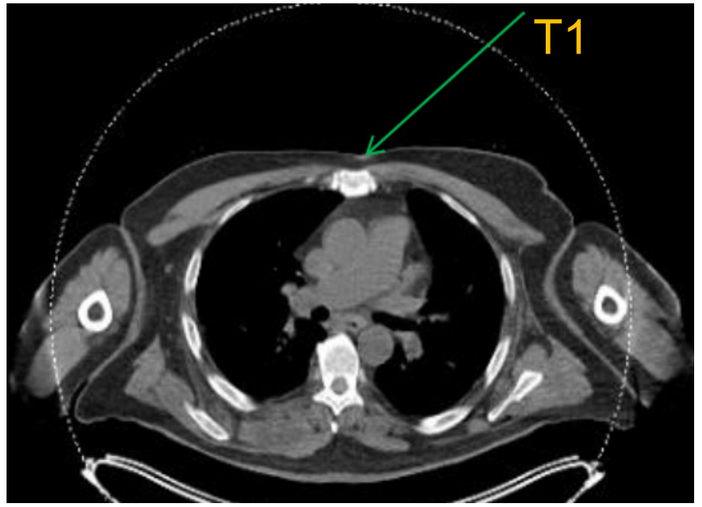
- Treatment Center: MD Anderson Cancer Center
- 63 year old male diagnosed with metastatic melanoma 2/25/17
- Metastatic disease to chest wall (multiple lesions), brain
- ECOG 0
- Prior Cancer Treatment
  - May 2017 - July 2017: Treated with Pembrolizumab (AE disc.) with Best Overall Response of PD
  - January 2018 – March 2018; Treated with IMLYGIC™(T-VEC) with Radiation; Best Overall Response of PD
- NKTR-262 Intratumoral Injection Site: Right posterior chest wall
- Partial Response at Scan 2 and confirmed at scan 3
- Treatment Ongoing in Dose Cohort 1 (q3W IT NKTR-262 0.03 mg with IV NKTR-214 0.006 mg/kg)

Case 2: Stage IV Melanoma IO Refractory
Confirmed Partial Response (-100%) – Treatment Ongoing

Baseline

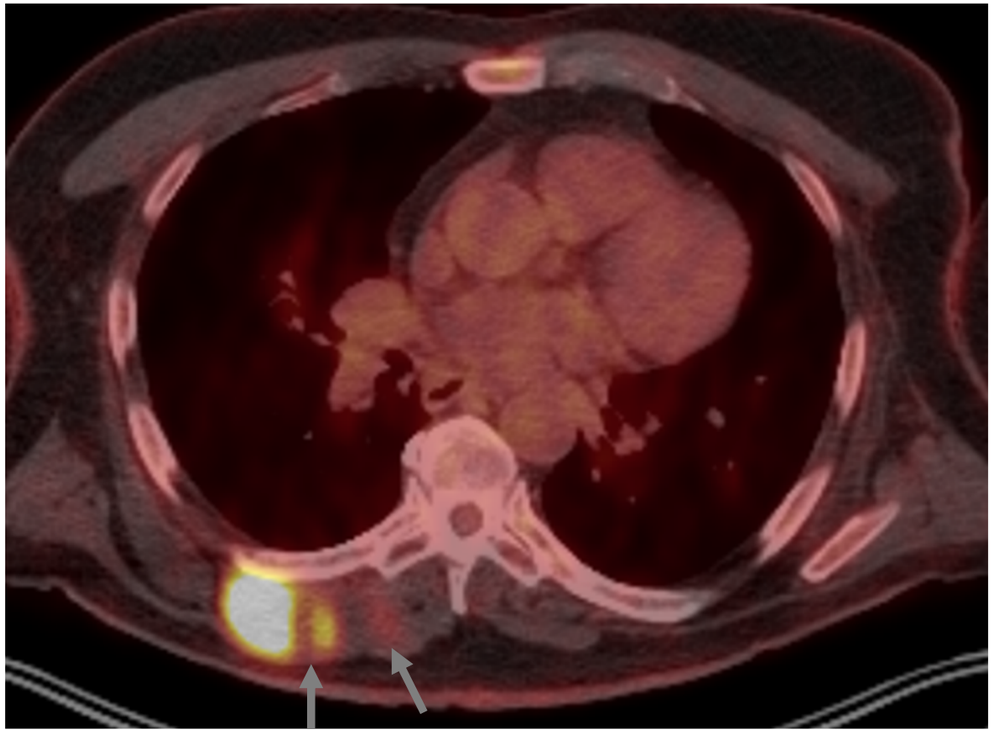


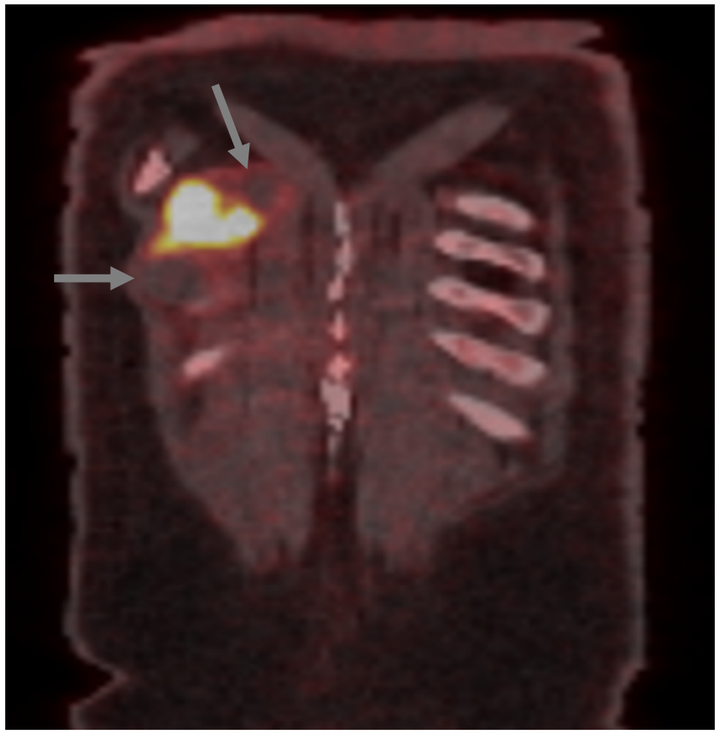
Scan 3



	Lesion Description	Baseline	Scan 1	Scan 2	Scan 3
Target Lesions	Exam/Scan Date	2018-04-13	2018-07-02	2018-09-12	2018-10-11
	Target Lesion 1 (T1): Anterior Chest Wall	16	18	11	0
	Sum of the Diameters (% Change from Baseline)	16	18 (+12.5%)	11 (-31.3%)	0 (-100%)
Overall Response	RECIST 1.1 from Site		Stable Disease	Stable Disease	Partial Response

Case 2: Stage IV Melanoma IO Refractory
Confirmed Partial Response (-100%) – Treatment Ongoing





Only remaining lesions on PET scan showed multiple areas of fibrosis, necrosis and melanophages upon pathology analysis (October 18, 2018)

Key Takeaways from Ongoing Dose Escalation of REVEAL Study

Preliminary Safety and Tolerability

- MTD not reached and dose escalation continues
- No observed DLTs in starting dose cohorts of escalating NKTR-262 with fixed-dose NKTR-214
- No grade 3 or higher TRAEs observed to-date with no treatment study discontinuations or treatment delays from TRAEs
- Most common side effects were flu like symptoms that were predictable, short lived and easily managed

Preliminary Efficacy and Biomarker Data

- Early evidence of clinical activity in Phase 1 dose escalation
- 2 out of 4 evaluable patients with R/R metastatic melanoma experienced responses and continue on treatment; DCR rate of 4/7 (57%)
  - Both melanoma responders were refractory to 2 prior IO regimens
- Induction of interferon genes observed with NKTR-262 only with dose-dependent increase in first two dose cohorts

Q&A Session