



NEKTAR
NEW PATHWAYS TO
SMARTER MEDICINE™

ASCO 2017
Nektar Therapeutics
Investor Meeting

Saturday, June 3, 2017

Today's Speakers and Panelists



Dr. Adi Diab

Assistant
Professor of
Melanoma
Medical
Oncology
MD Anderson



Dr. Michael Hurwitz

Assistant Professor
of Medicine,
Medical Oncology
Yale Cancer Center



Dr. Nizar M. Tannir

Professor of
Genitourinary
Medical Oncology &
Deputy Department
Chair of the
Department of
Genitourinary
Medical Oncology
MD Anderson



Dr. Mary Tagliaferri

Senior Vice
President,
Clinical
Development
Nektar
Therapeutics



Dr. Jonathan Zalevsky

Senior Vice
President,
Biology & Preclinical
Development
Nektar
Therapeutics

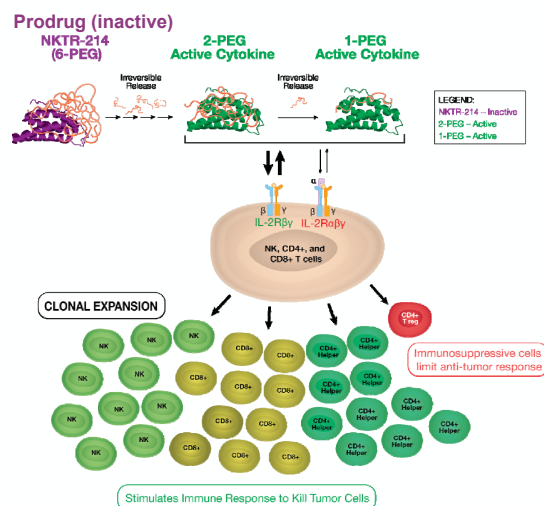


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Phase 1 EXCEL Monotherapy Clinical Trial of NKTR-214

Dr. Adi Diab, Assistant Professor of Melanoma Medical Oncology
MD Anderson Cancer Center
Co-Chair Scientific Advisory Board for PIVOT Program

Harnessing the IL-2 Pathway the Right Way to Increase TILs



- Prodrug design to enable safe, outpatient dosing Q2W or Q3W
- Active cytokine species bias signaling through the heterodimeric IL-2 receptor pathway (IL-2Rβγ)
- Biased and sustained signaling to preferentially activate and expand effector CD8+ T and NK cells over Tregs in the tumor microenvironment

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EXCEL Phase 1 Dose Escalation, Stage IV Patients (N=28)

Phase 1

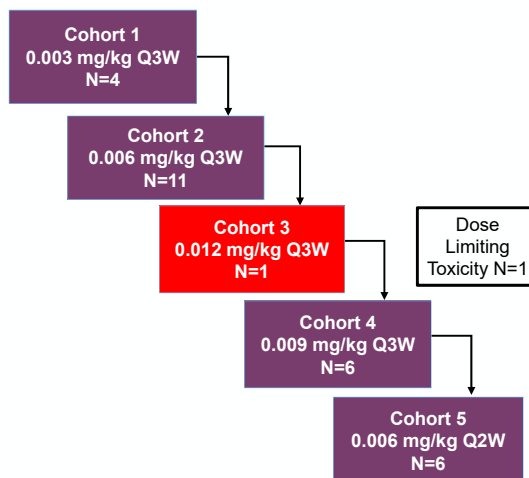
- Monotherapy Dose Escalation

Primary Objectives

- Define the MTD
- ORR

Eligibility

- Confirmed locally advanced or metastatic solid tumors
- Measurable disease
- ECOG 0 or 1



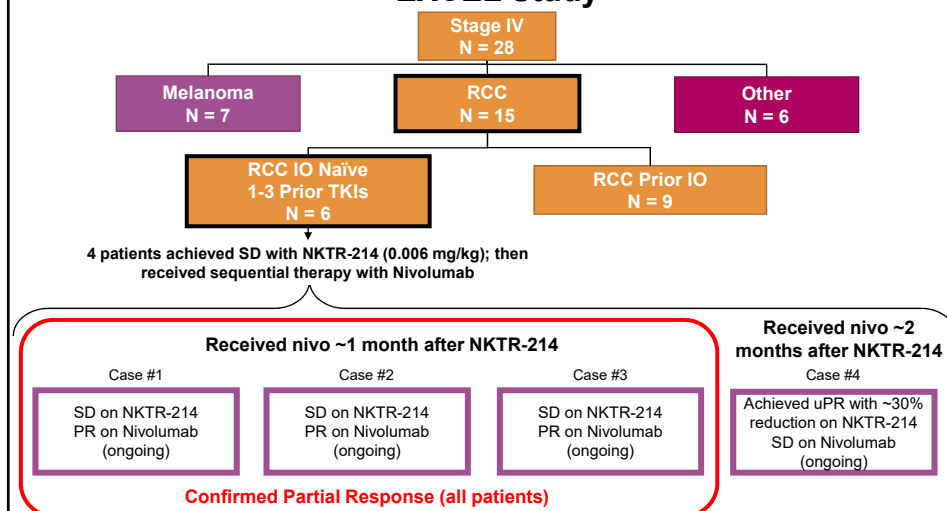
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Serial collection of blood samples and tumor biopsies for biomarker analysis

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NKTR-214 Monotherapy Followed by Dosing With Nivolumab in RCC IO Naïve Patients

EXCEL Study



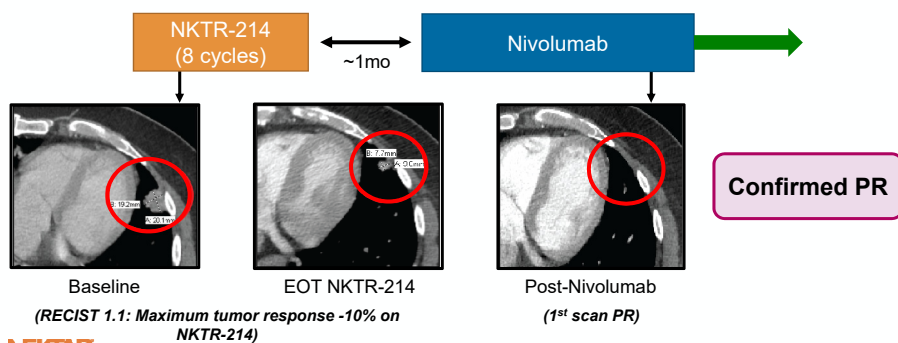
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RCC, renal cell carcinoma; IO, immuno-oncology; TKI, tyrosine-kinase inhibitor; PR, confirmed partial response; uPR, unconfirmed partial response; SD, stable disease.

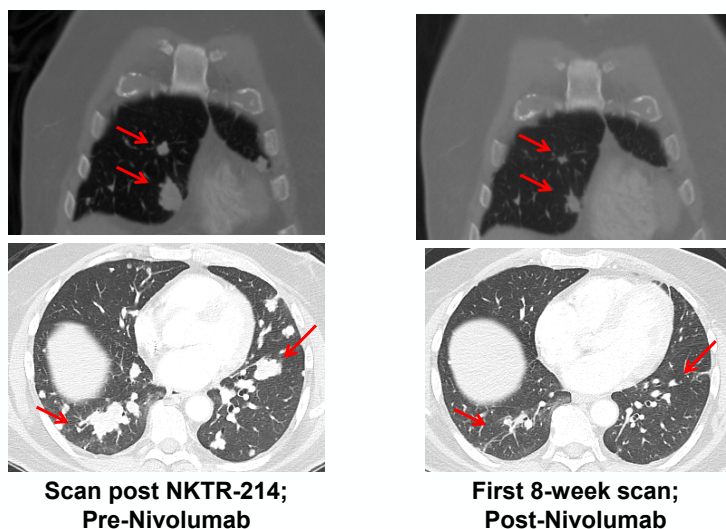
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Case #1: Patient with RCC Stage IV, Age 59, Male, Progressed on Prior TKI

	Treatment	Duration of Treatment	Time Interval to Next Treatment
Prior Therapies	Sunitinib	~67 mos (PD)	~2 mos
Therapies Administered	NKTR-214	~5 mos (SD)	~1 mo
	Nivolumab	>9 mos	Ongoing

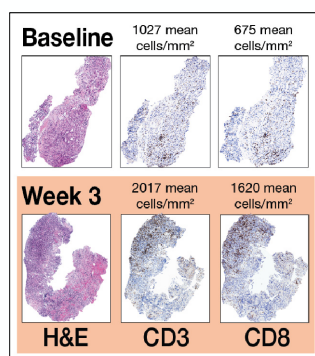


Case #1: Patient with RCC Stage IV, Age 59, Male, Progressed on Prior TKI



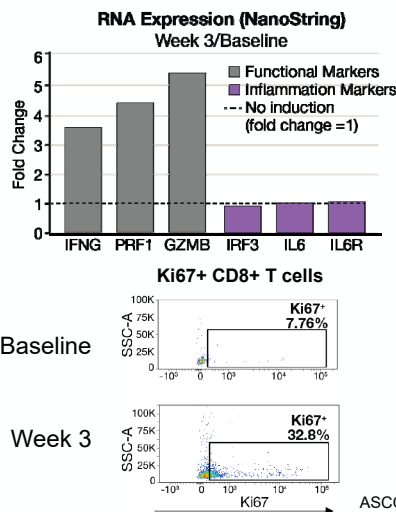
Case #1: Patient with RCC Stage IV, Age 59, Male, Progressed on Prior TKI

Tumor Biopsy: Observed Immunological Changes on NKTR-214
(IHC, Gene Expression, Flow Cytometry)



IHC, Immunohistochemistry; IFNG, interferon gamma; PRF1, perforin; GZMB, granzymeB; IRF3, interferon response factor 3.

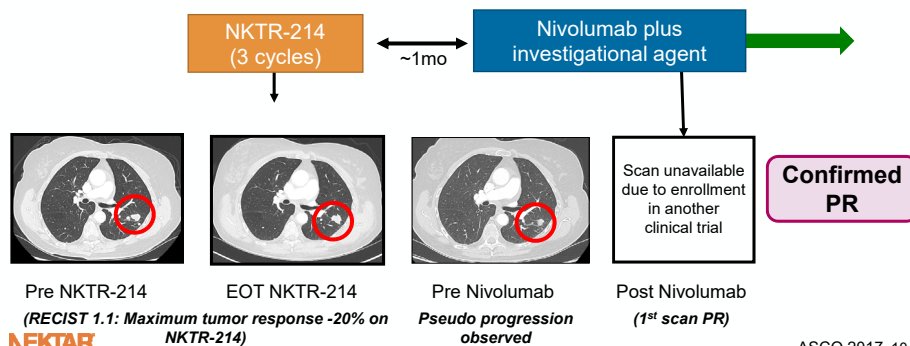
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Case #2: Patient with RCC Stage IV, Age 66, Female, Prior TKI

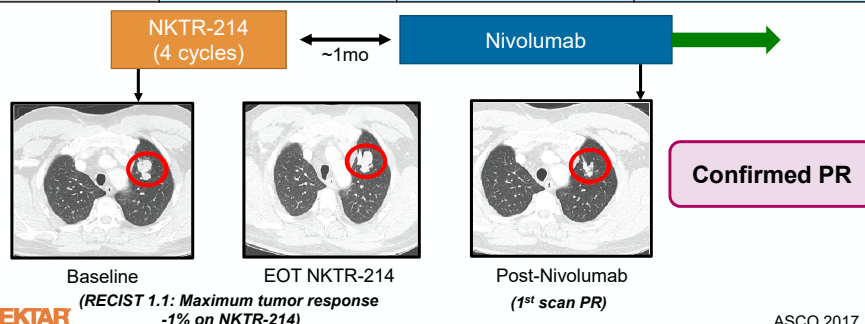
	Treatment	Duration of Treatment	Time Interval to Next Treatment
Prior Therapies	Sunitinib	~8 mos (AE disc.)	~1.5 mos
Therapies Administered	NKTR-214	~1.5 mos (SD)	~1 mo
	Nivolumab	>9 mos	Ongoing



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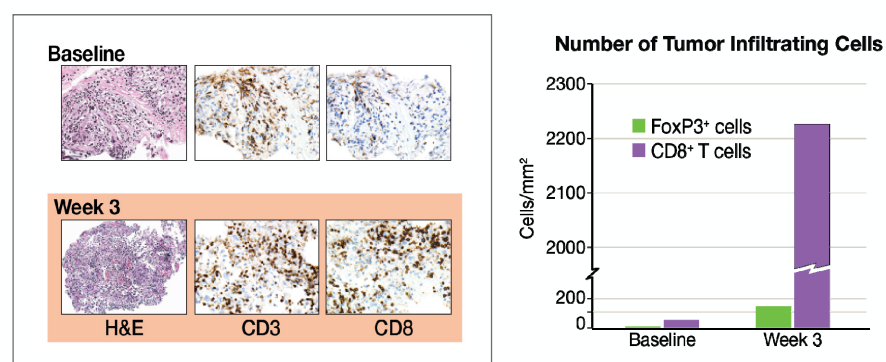
Case #3: Patient with RCC Stage IV, Age 61, Male, Progressed on Prior TKI

	Treatment	Duration of Treatment	Time Interval to Next Treatment
Prior Therapies	Sunitinib	~2.5 mos (PD)	0
	Axitinib	~1.5 mos (PD)	~2 mos
	Bevacizumab + CRLX101	~3.5 mos (unknown)	~4.5 mos
Therapies Administered	NKTR-214	~1.5 mos (SD)	~1 mo
	Nivolumab	>7 mos	Ongoing



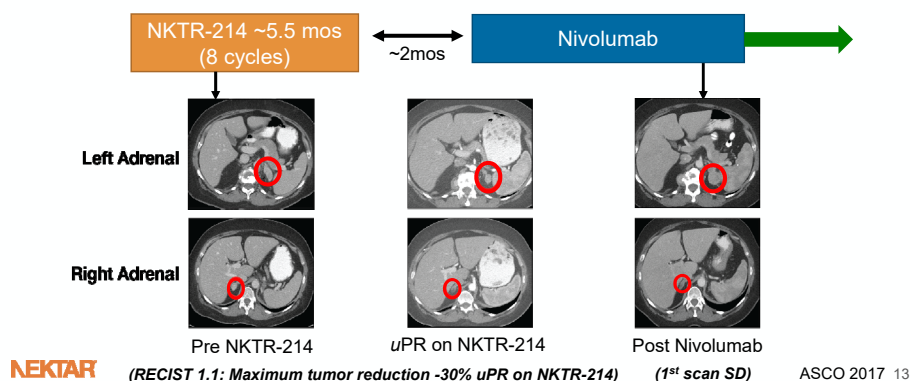
Case #3: Patient with RCC Stage IV, Age 61, Male, Progressed on Prior TKI

Tumor Biopsy: Observed Immunological Changes on NKTR-214 (IHC)



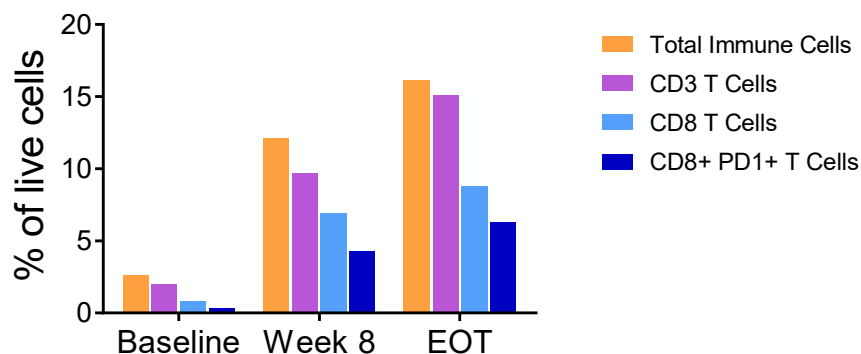
Case #4: Patient with RCC Stage IV, 60 Year Old Female, Progressed on Prior TKI

	Treatment	Duration of Treatment	Time Interval to Next Treatment
Prior Therapies	Pazopanib	~10.5 mos	~1 mo
	Axitinib	~5 mos (PD)	~2.5 mos
Therapies Administered	NKTR-214	~5.5 mos (SD)	~2 mos
	Nivolumab	>4 mos	Ongoing



Case #4: Patient with RCC Stage IV, Age 60, Female, Progressed on Prior TKI

Tumor Biopsy: Observed Immunological Changes on NKTR-214 (Flow Cytometry)

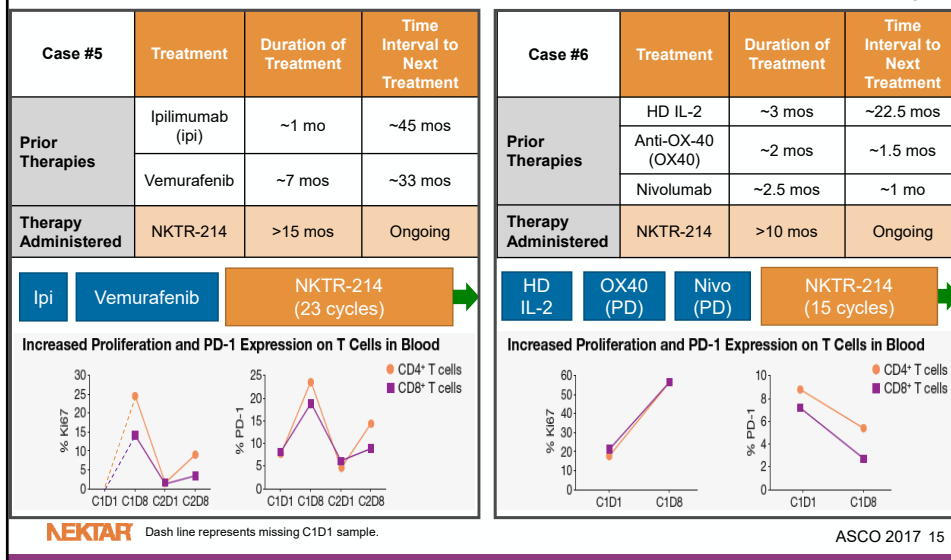


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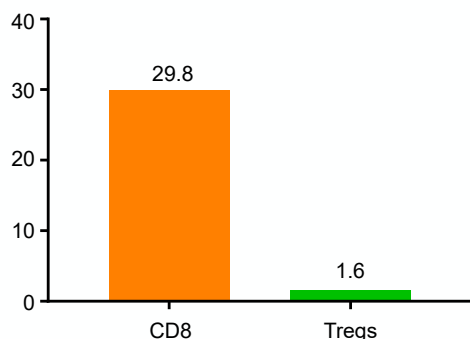
Two Patients in EXCEL with Durable Disease Control on NKTR-214 (Ongoing)

Robust Immune Activation in Patients Who Have Failed Prior Immunotherapy



NKTR-214 Selectively Grows T Cells, NK Cells in Tumor Microenvironment in Cancer Patients

Analysis of T cell Populations in Tumor



Fold change expressed as Week 3 / pre-dose
Shown are results from N=10 patients
Q3W dose schedules

NKTR-214 drives immune activation in the tumor

- Increase in total T cells, NK and CD8 T cells
- No increase in Tregs
- Increase in PD-1 positive CD8 T cells
- Increase in newly proliferating CD8 T cells
- Activation and expression of anti-tumor genes
- Change in T cell clonality in the tumor

Combination of increased TILs and increased expression of PD-1 provides strong mechanistic rationale with anti-PD-1

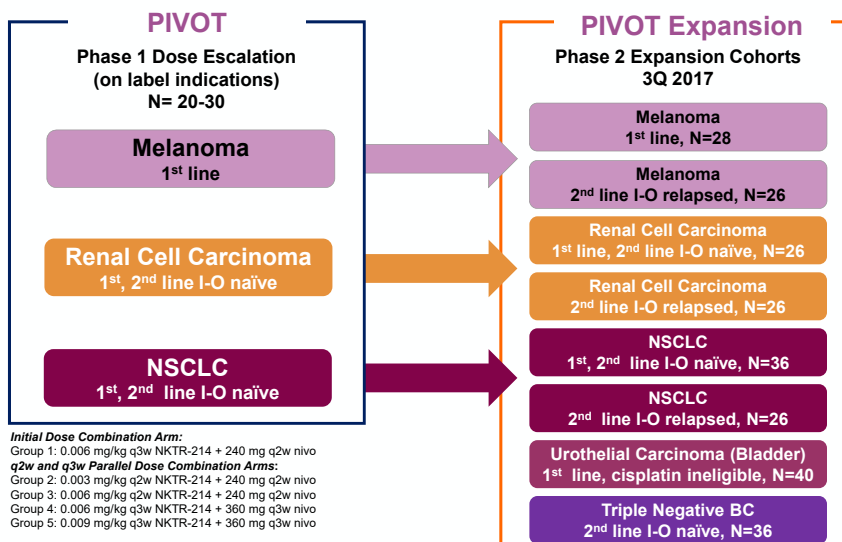
NEKTAR Source: SITC Nov, 2016; JPM Jan, 2017

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Phase 1 PIVOT Combination Clinical Trial of NKTR-214 + Nivolumab

Dr. Adi Diab, Assistant Professor of Melanoma Medical Oncology
MD Anderson Cancer Center
Co-Chair Scientific Advisory Board for PIVOT Program

PIVOT Program: NKTR-214 plus Opdivo® with Eight Expansion Cohorts Planned



PIVOT Dose Escalation Patient Demographics (as of June 1, 2017)

Patient Characteristics Safety Population: Dose Escalation	N=20	
Sex		
Male	15	
Female	5	
Age (years)		
Median		58
Range		22-70
Tumor Type		
Melanoma (0-1 prior therapies)	8	
Renal Cell Carcinoma (0-1 prior therapies)	9	
Non-Small Cell Lung Cancer (0-1 prior therapies)	3	
Stage		
Unresectable Stage III	1	
IV	19	
ECOG Performance Status (0-1)	20	
Prior Therapies		
Chemotherapy	2	
Cancer Vaccine	2	
Targeted Therapy (TKI or anti-VEGF)	3	

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PIVOT Dose Escalation: Treatment-Related Adverse Events

- No DLTs or grade 3/4 treatment-related adverse events (TRAEs)
- No grade 3 or above immune-related AEs observed to date
- No patients discontinued treatment due to AE and no deaths

AE, N (%)	Total (N=20)	NKTR-214 0.006 mg/kg q3w + Nivo 240 mg q2w (N=4)	NKTR-214 0.006 mg/kg q3w + Nivo 360 mg q3w (N=10)	NKTR-214 0.006 mg/kg q2w + Nivo 240 mg q2w (N=3)	NKTR-214 0.003 mg/kg q2w + Nivo 240mg q2w (N=3)
≥ G3 AE Reported	0	0	0	0	0
Grade 1&2 (>25%)					
Fatigue	15 (75)	4 (100)	6 (60)	2 (67)	3 (100)
Flu-Like Symptoms*	15 (75)	3 (75)	7 (70)	3 (100)	2 (67)
Rash**	12 (60)	4 (100)	5 (50)	1 (33)	2 (67)
Pruritus	11 (55)	2 (50)	5 (50)	2 (67)	2 (67)
Headache	9 (45)	3 (75)	4 (40)	1 (33)	1 (33)
Flushing	8 (40)	3 (75)	2 (20)	2 (67)	1 (33)
Decreased Appetite	6 (30)	3 (75)	1 (10)	2 (67)	0

* Flu-like symptoms includes the following MedDRA preferred terms: influenza-like illness, pyrexia, and chills.

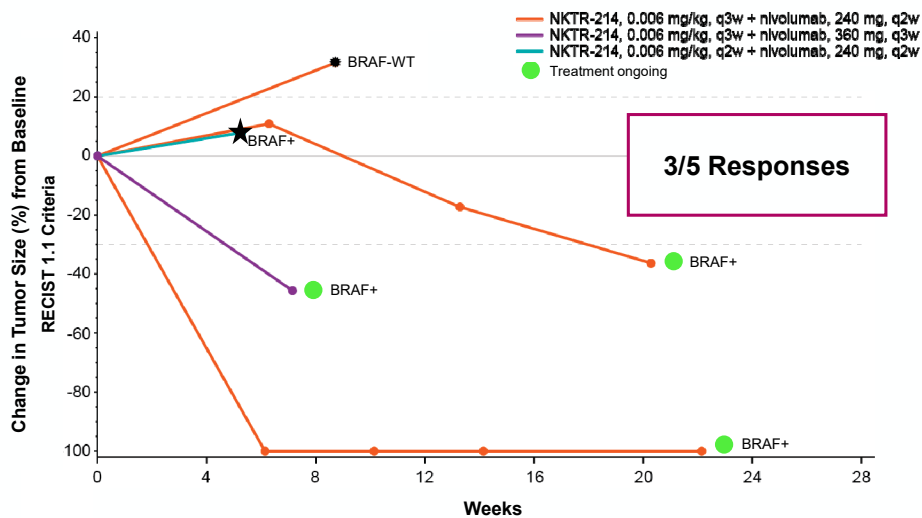
**Rash includes the following MedDRA preferred terms: Rash, rash erythematous, rash macular and rash maculo-popular.

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Melanoma Patients in PIVOT Dose Escalation Study

Melanoma Stage IV Patients 1st Line



● Discontinued due to PD

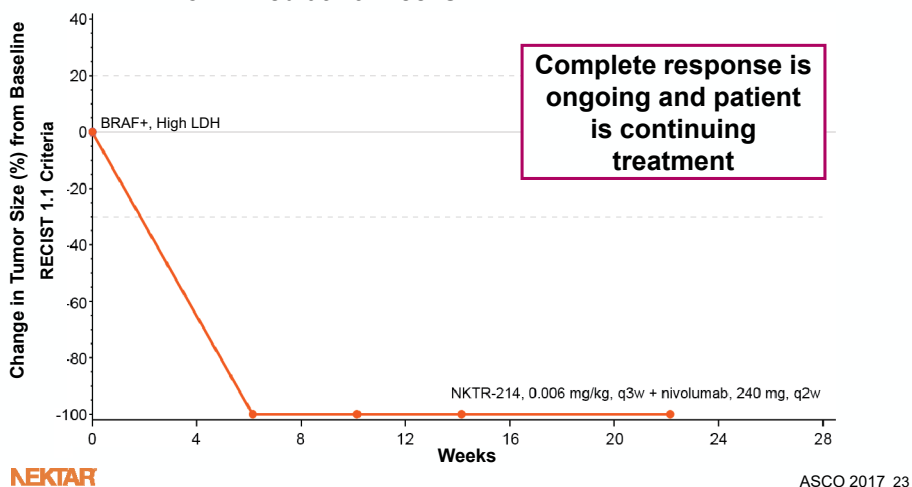
★ Discontinued with stable disease because of travel constraints to treatment center.

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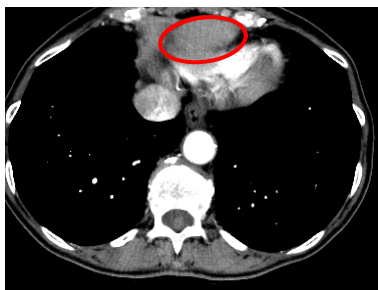
Patient with Stage IV Melanoma, Age 69, BRAF+, Prior Adjuvant Interferon

- Complete Response After 6 Weeks of Treatment
- Confirmed at 10 Weeks



Patient with Stage IV Melanoma, Age 69, BRAF+, Prior Adjuvant Interferon

Pericardial Lesion, 45 mm



Baseline

Pericardial Lesion, Undetectable



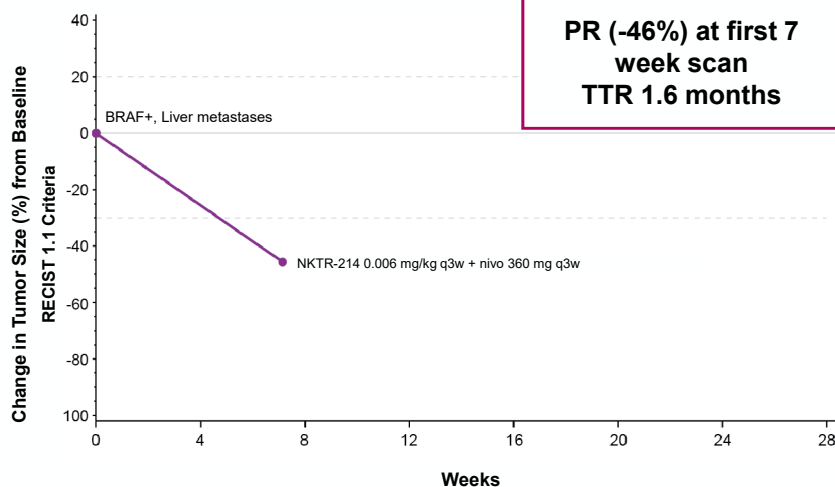
6 Weeks

Lesion	Baseline Scan (mm)	1 st Scan on Treatment (mm) 6-weeks
Pericardial	45	0
Peritoneal	21	0
Peritoneal	20	0
Peritoneal	17	0
Peritoneal	16	0
Peritoneal	10	0

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Patient with Stage IV Melanoma, Age 54, BRAF+, No Prior Therapy

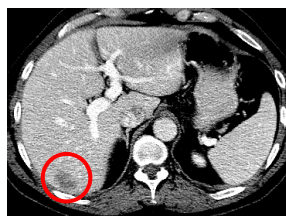


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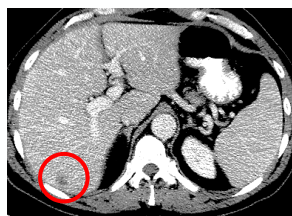
Patient with Stage IV Melanoma, Age 54, BRAF+, No Prior Therapy

Liver Lesion, 30 mm



Baseline

Liver Lesion, 14 mm



7 Weeks

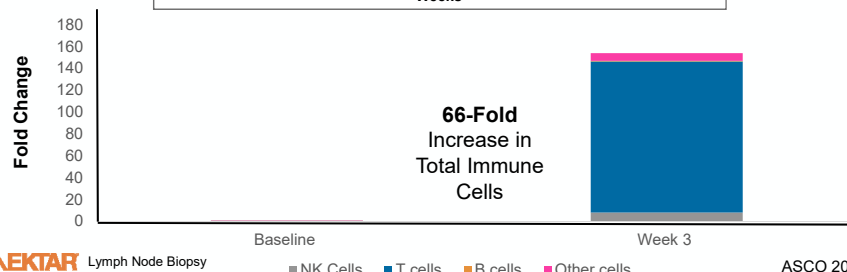
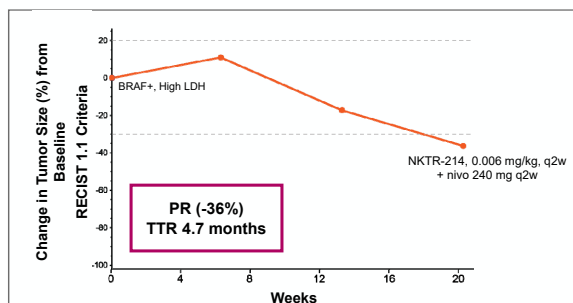
Lesion	Baseline Scan (mm)	1 st Scan on Treatment (mm) 7 Weeks
Liver	30	14
Skin (trunk)	16	11
Sum/% Change	46	25 (-46%)

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Correlation of Response with Tumor Infiltrating Immune Cells

Patient with Stage IV Melanoma, Age 43, No Prior Therapies



NEKTAR Lymph Node Biopsy

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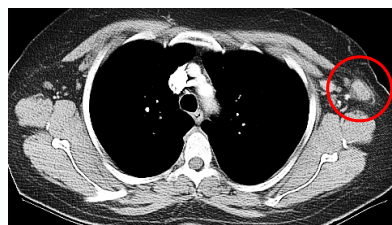
Patient with Stage IV Melanoma, Age 43, No Prior Therapies

Lymph Node, 30 mm



Baseline

Lymph Node, 11 mm



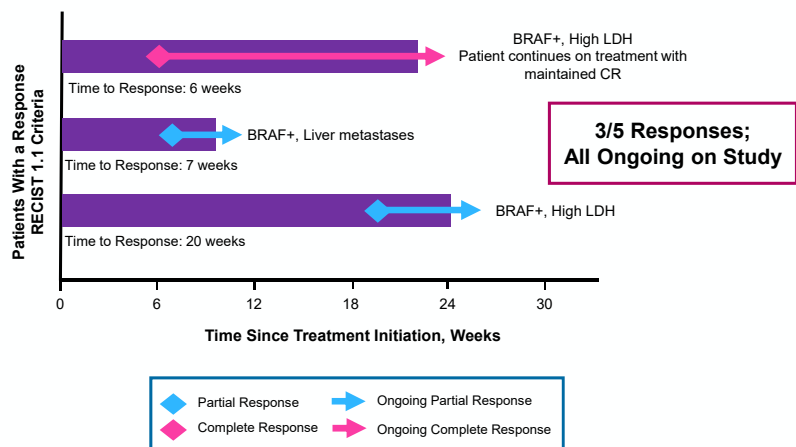
21 Weeks

Lesion	Baseline Scan (mm)	3 rd Scan on Treatment 21 Weeks
Lymph Node	30	11
Chest Wall	30	31
Kidney	11	9
Lymph Node	25	11
Spleen	14	8
Sum/% Change	110	70 (-36%)

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NKTR-214 and Nivolumab Responses in BRAF+ Melanoma



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RCC Patients in PIVOT Dose Escalation Study

RCC Stage IV Patients, 0-1 Prior Therapies (Ongoing)

Patient	Prior Therapy	Dose	Ongoing Response
#1	Pazopanib (PD)	NKTR-214 0.006 mg/kg Q3W + Nivolumab 240 mg Q2W	PR (-39%), Week 15
#2	Bevacizumab (PD)	NKTR-214 0.006 mg/kg Q2W + Nivolumab 240 mg Q2W (first scan only)	SD (-9%), Week 8
#3	None	NKTR-214 0.006 mg/kg Q2W + Nivolumab 240 mg Q2W	SD (0%), Week 7
#4	Sunitinib (PD)	NKTR-214 0.003 mg/kg Q2W + Nivolumab 240 mg Q2W	SD (-4%), Week 7
#5	Adjuvant oncopophage vaccine (relapsed)	NKTR-214 0.003 mg/kg Q2W + Nivolumab 240 mg Q2W	SD (-9%), Week 7
#6	None	NKTR-214 0.006 mg/kg Q3W + Nivolumab 360 mg Q3W	SD of target lesions, PD of non-target lesion, Week 7

Only First Scan Available

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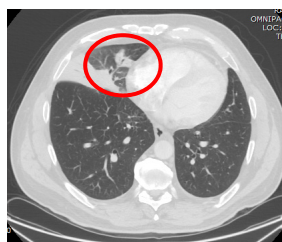
Patient with Stage IV RCC, Age 56, Progressed on a TKI

Pulmonary Lesion, 61 mm



Baseline

Pulmonary Lesion, 29 mm



Week 15

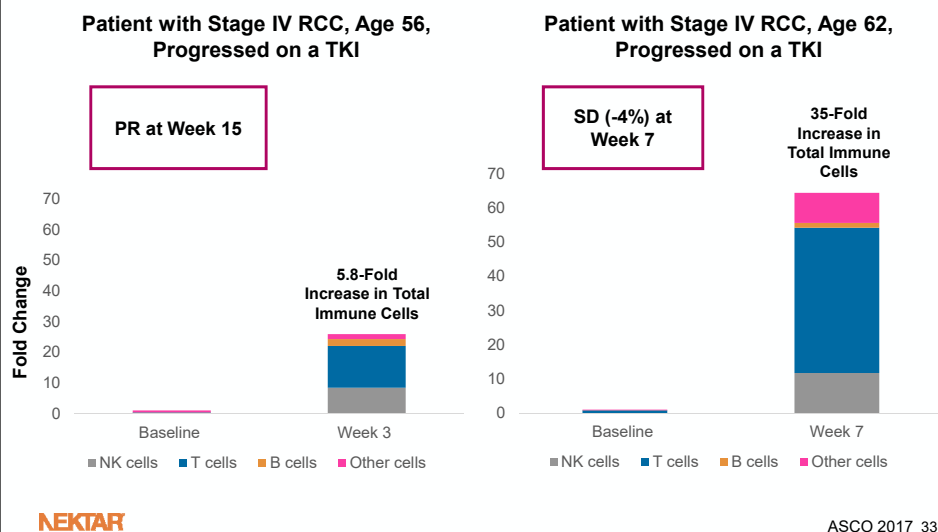
Lesion	Baseline Scan (mm)	2 nd Scan on Treatment (mm) Week 15
Bronchopulmonary lymph Node	28	20
Lymph nodes: subcarinal	37	27
Lung: left upper pulmonary	61	29
Lung: left basal pulmonary nodule	13	9
Liver: hepatic dome	27	16
Sum/% Change	166	101 (-39%)

Confirmed
PR

NEKTAR Complete resolution of hemoptysis with the decrease in pulmonary lesions

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Robust Increase in Tumor Infiltrating Immune Cells in RCC Patients

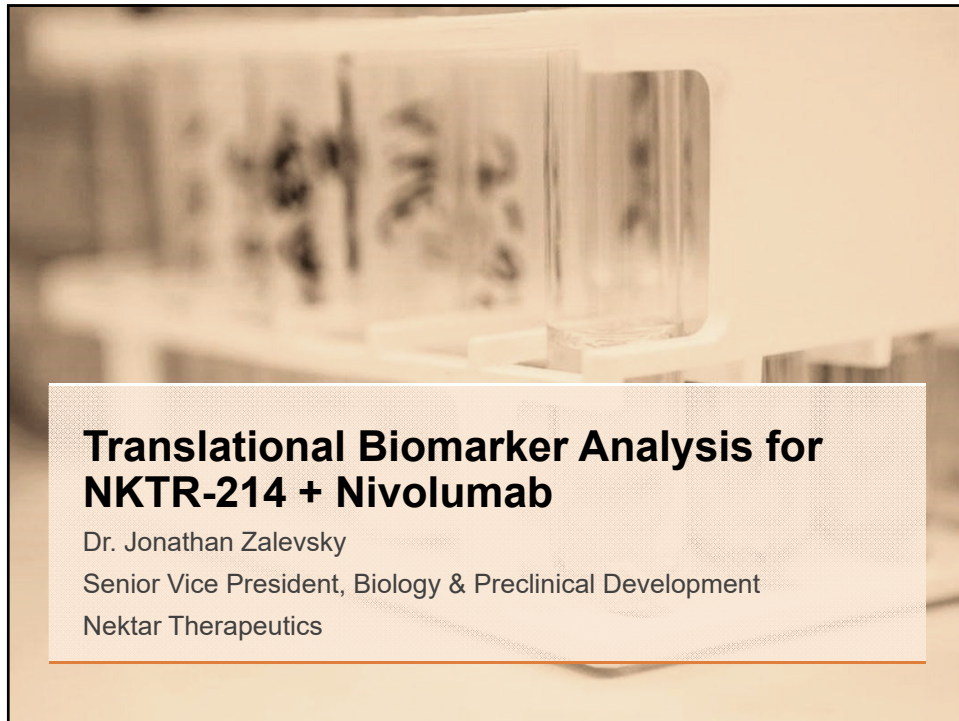


NKTR-214 + Nivolumab Combination: Conclusions to Date

- Enrolling patients to dose escalation of PIVOT 02 to identify the RP2D
 - Last dosing cohort NKTR-214 0.009 mg/kg q3w + nivo 360 mg q3w
- Favorable safety profile and well tolerated combination
 - Low-grade AEs are predictable, manageable and of short duration
 - No DLTs and grade 3 or above TRAEs
 - No immune-related AEs were observed to date (e.g. colitis, dermatitis, hepatitis, pneumonitis, adrenal insufficiency)
- Clinical benefit observed early with NKTR-214 and Nivolumab
 - Responses in 3/5 patients with Stage IV Melanoma (1 CR, 2 PR)
 - Time to responses: 6 weeks, 7 weeks, 20 weeks
 - PR in RCC patient who progressed on prior TKI (PD-L1 negative)
 - Responses in 3/4 RCC IO naïve patients with SD on NKTR-214 who received sequential therapy with Nivolumab
 - Total time on treatment to reach response is much shorter with concurrent dosing
- On treatment biopsies show robust elevation in immune cell frequency and activation
- Anticipate enrollment to expansion cohorts in 3Q 2017

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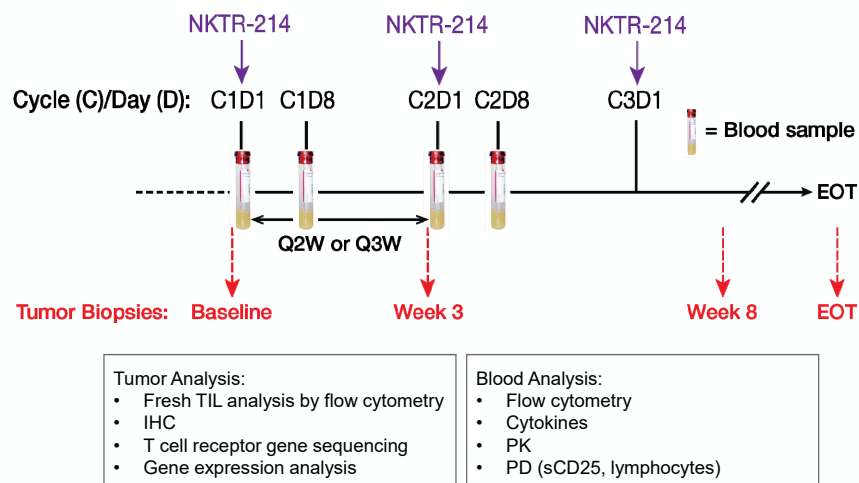
Translational Biomarker Analysis for NKTR-214 + Nivolumab

Dr. Jonathan Zalevsky
Senior Vice President, Biology & Preclinical Development
Nektar Therapeutics

Biomarker Program Overview

- Understanding the human immunology obtained from NKTR-214 monotherapy and NKTR-214 + Nivolumab studies
 - Does Nivolumab impact the primary PK/PD relationship of NKTR-214?
 - Is there a measurable immunological difference between NKTR-214 and NKTR-214 + Nivolumab?
 - Which biomarkers are specific to NKTR-214 or NKTR-214 + Nivolumab?
- Early evaluation (03Jun2017) includes assessment of:
 - Primary PK/PD
 - Flow cytometry analysis of peripheral blood cells
 - Flow cytometry of serial tumor biopsy samples

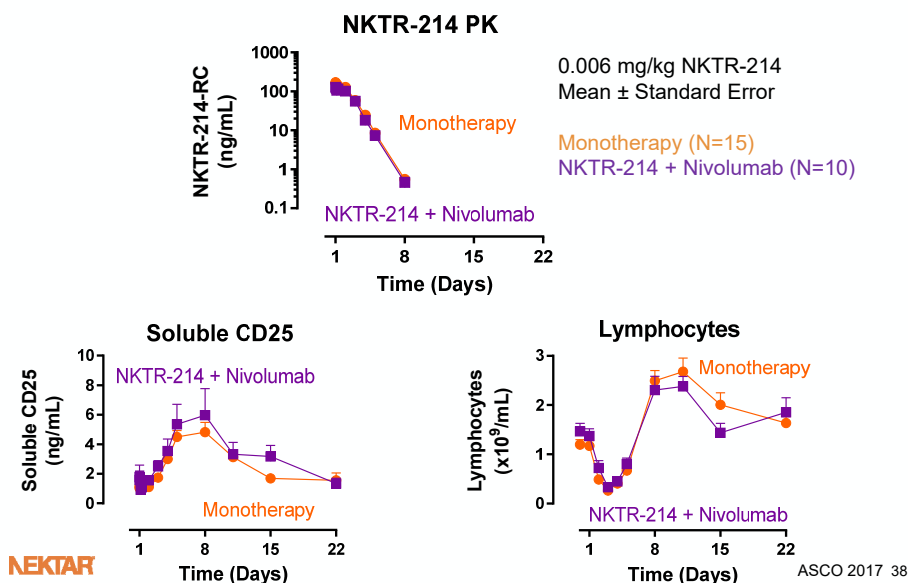
Blood and Tumor Biopsy Analysis



NEKTAR EOT, end of treatment.

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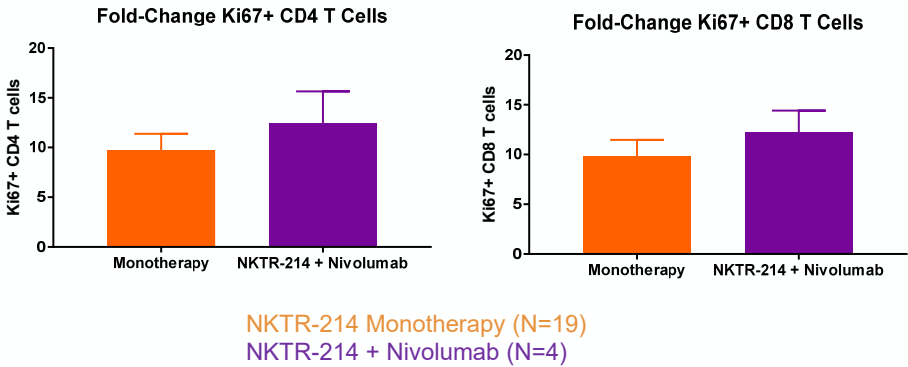
Nivolumab Does Not Change the PK/PD Relationship for NKTR-214



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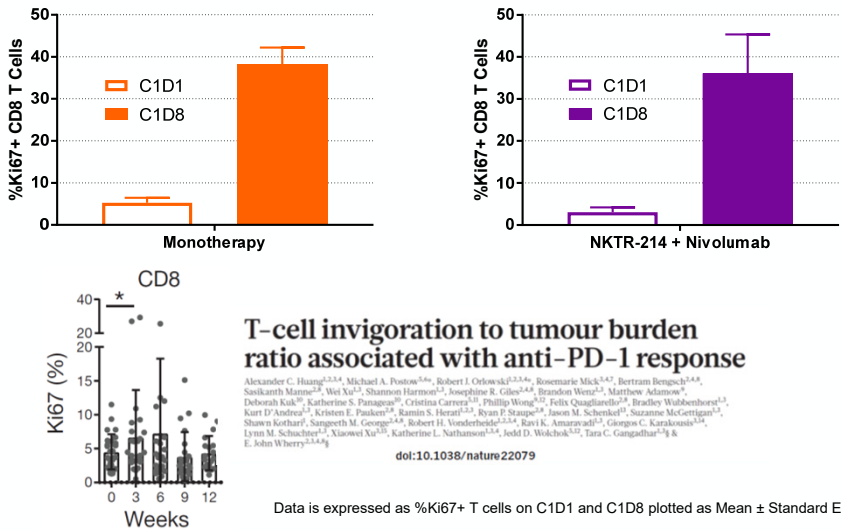
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T Cell Proliferation is Primarily Driven by NKTR-214 in Blood



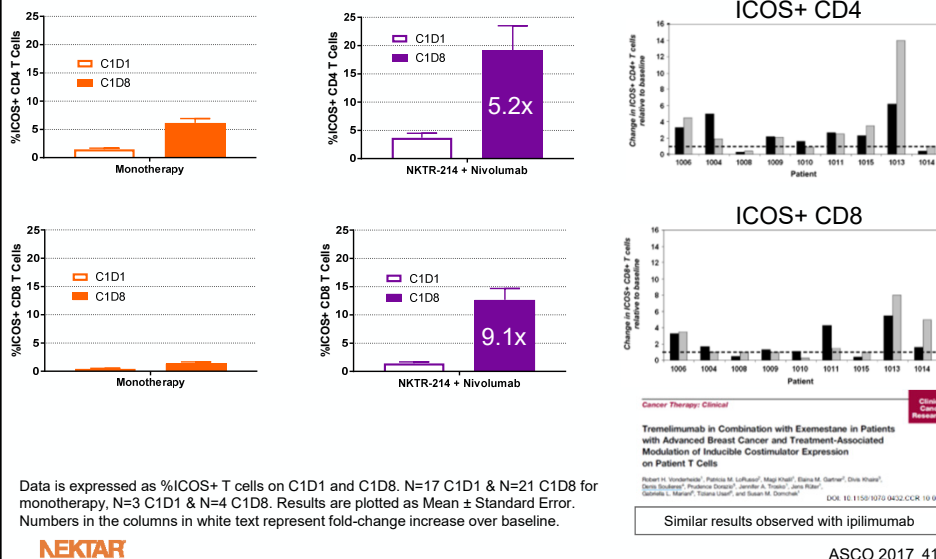
Data is expressed as fold-change %Ki67+ T cells on C1D8 + %Ki67+ T cells on C1D1. In some cases where a C1D1 specimen was not available (N=3 in monotherapy and N=1 in NKTR-214 + Nivolumab), average baseline values were calculated and used for C1D1 values. Data is plotted as Mean ± Standard Error.

NKTR-214 Promotes T Cell Invigoration in Blood

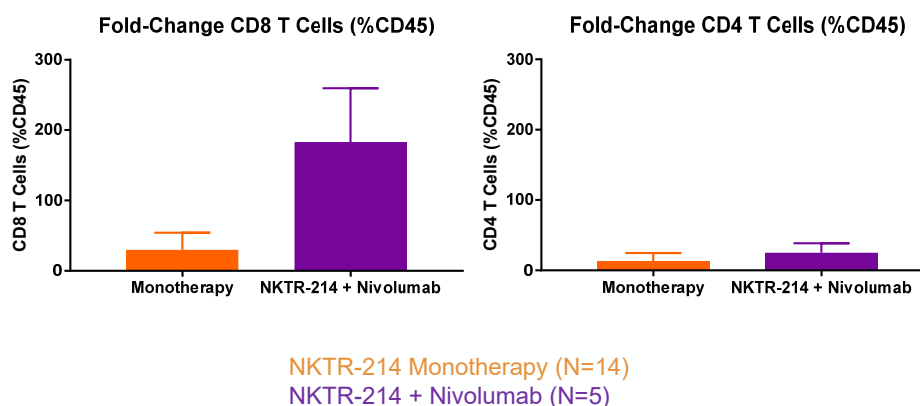


Data is expressed as %Ki67+ T cells on C1D1 and C1D8 plotted as Mean ± Standard Error.

NKTR-214 + Nivolumab Promotes Expansion of ICOS+ T Cells in Blood



NKTR-214 + Nivolumab Drives Large Increase in Tumor Infiltrating Immune Cells

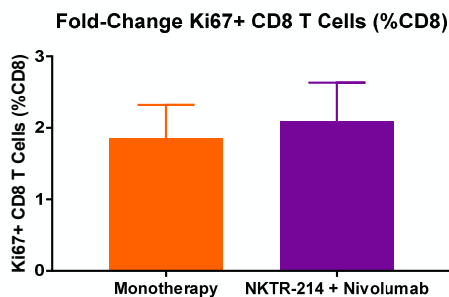


Data is expressed as fold-change CD45+ cells, or CD4 T cells (of CD45), or CD8 T cells (of CD45) treatment + baseline. Data is plotted as Mean ± Standard Error. For monotherapy, CD8 T Cells shown for monotherapy are for the q3w dose cohorts (n=10) and the CD4 T Cells shown for monotherapy includes q3w and q2w dose cohorts.

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NKTR-214 Promotes CD8 T Cell Proliferation in Tumor



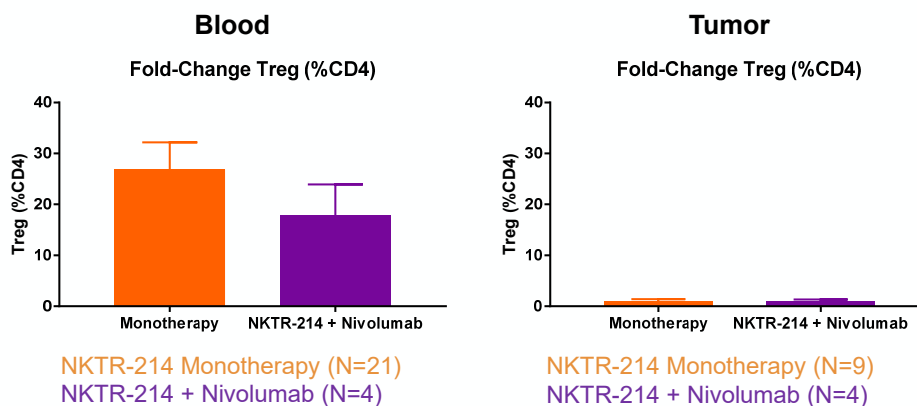
NKTR-214 Monotherapy (N=11)
NKTR-214 + Nivolumab (N=4)

Data is expressed as fold-change Ki67+ CD8 T cells treatment + baseline. Data is plotted as Mean \pm Standard Error.

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Monotherapy v. Combination: Comparison of CD4 Tregs in Blood and Tumor



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Data is expressed as fold-change Tregs (CD3+CD4+CD25+FoxP3+) treatment + baseline. Data is plotted as Mean \pm Standard Error. For monotherapy the data includes both q3w and q2w regimens.

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Biomarker Conclusions

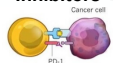
- Does Nivolumab impact the primary PK/PD relationship of NKTR-214?
 - No
 - No effect on PK, sCD25, or lymphocyte levels
- Is there a measurable immunological difference between NKTR-214 and NKTR-214 + Nivolumab?
 - Yes
 - ICOS+ cells in blood and massive immune cell infiltrates, especially CD8 T cells in tumors
- Which biomarkers are specific to NKTR-214 or NKTR-214 + Nivolumab?
 - Proliferation (Ki67) appears to be driven by NKTR-214 in blood and tumor
 - ICOS+ CD4 and CD8 T cells are greatly expended by NKTR-214 + Nivolumab
 - Treg levels, elevation in blood and no change in tumor, appear to be driven by NKTR-214



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NKTR-214: Additional Clinical Development Programs in 2H 2017/1H 2018

Checkpoint Inhibitors



Start triplet combination of NKTR-214 with anti-PD-1 and anti-CTLA-4 agents

Start Phase 1 trial of NKTR-214 and TECENTRIQ

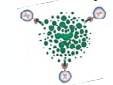
Start IST in Sarcoma with NKTR-214 and Opdivo® at Memorial Sloan Kettering and MD Anderson

TLR Agonist



Start Phase 1 trial of NKTR-214 and NKTR-262 (TLR Agonist 7/8)

Cell Therapies



Start Phase 1/2 trial of NKTR-214 in combination with Endogenous T Cell regimen in NSCLC patients (with MDA)

Vaccines



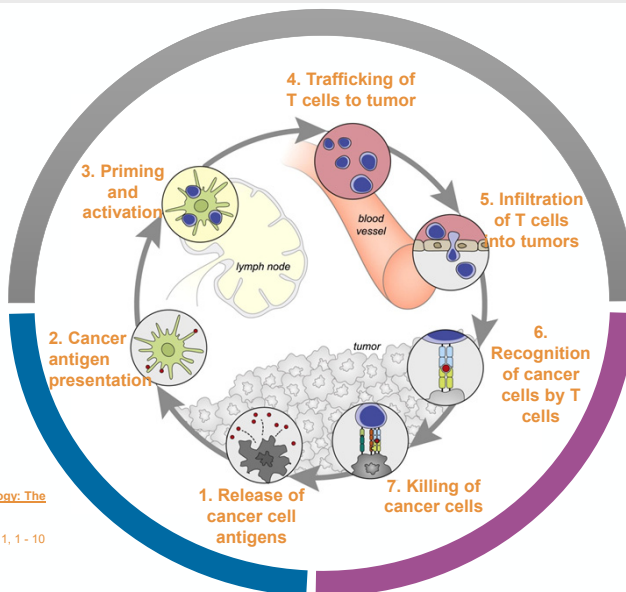
Preclinical studies underway with NKTR-214 and vaccines with potential for clinical advancement in 2018



Opdivo is a registered trademark of Bristol-Myers Squibb

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The Immunity Cycle and Multiple Points of Intervention for I-O Therapies

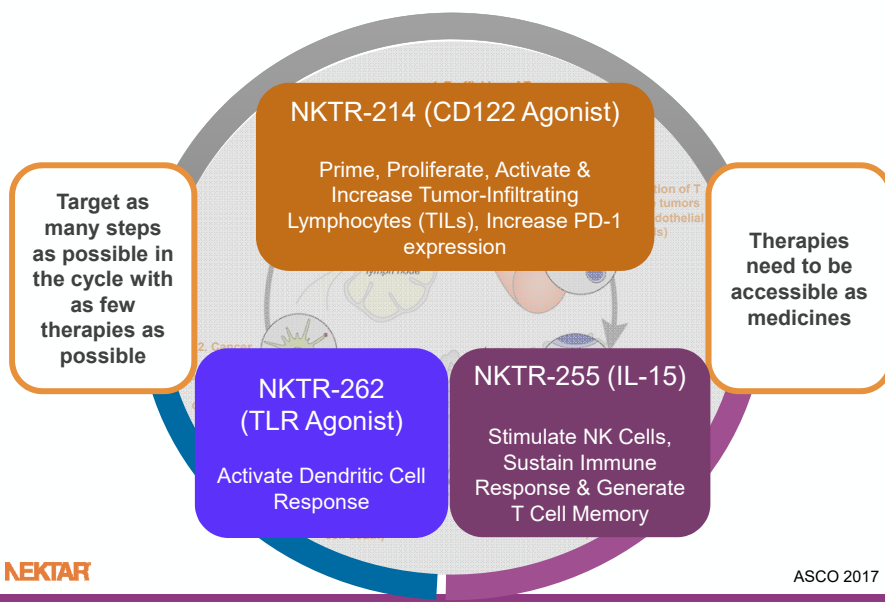


Source:
Oncology Meets Immunology: The
Cancer-Immunity Cycle
Chen and Mellman
Immunity, Volume 39, Issue 1, 1 - 10

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Nektar's Immuno-Oncology Strategy to Create Therapies that Cover the Immunity Cycle

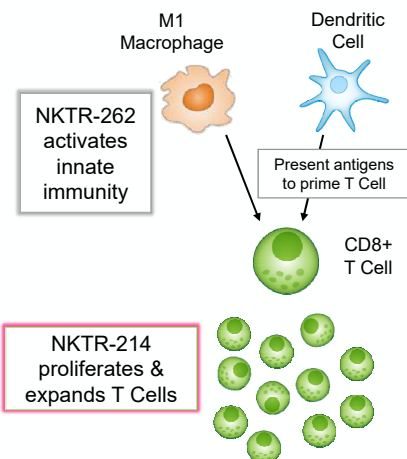


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NKTR-262: Adding a Unique Intratumoral TLR Agonist to Nektar's Immuno-Oncology Portfolio

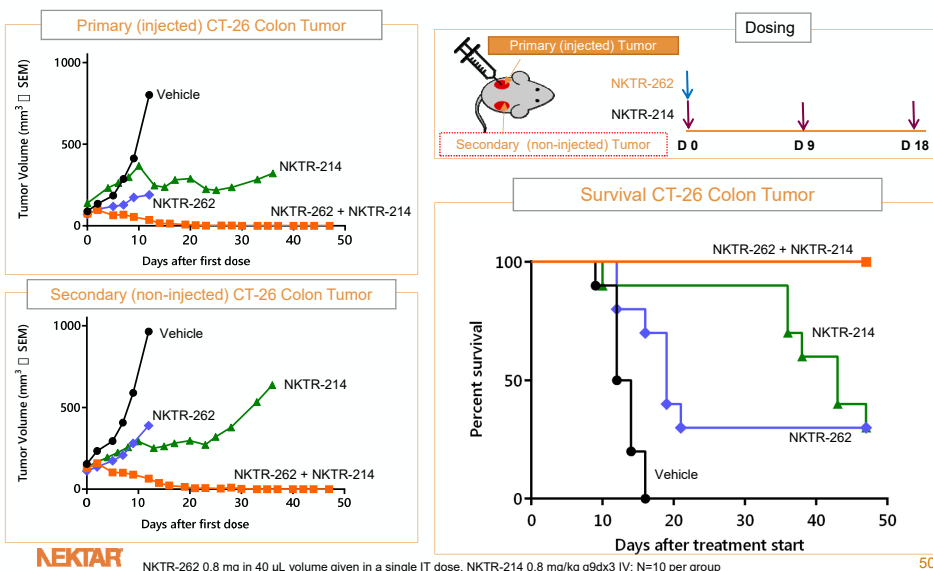
- TLR agonists activate innate immunity, myeloid cell response and increase tumor antigen presentation
 - Creates tumor-suppressing micro-environment by mimicking local infection
- Nektar technology optimizes specific abscopal effect in tumors without systemic exposure of TLR agonist
- NKTR-262 designed to be highly synergistic with NKTR-214
- NKTR-262 with NKTR-214 represent a novel, wholly-owned combination regimen in immuno-oncology

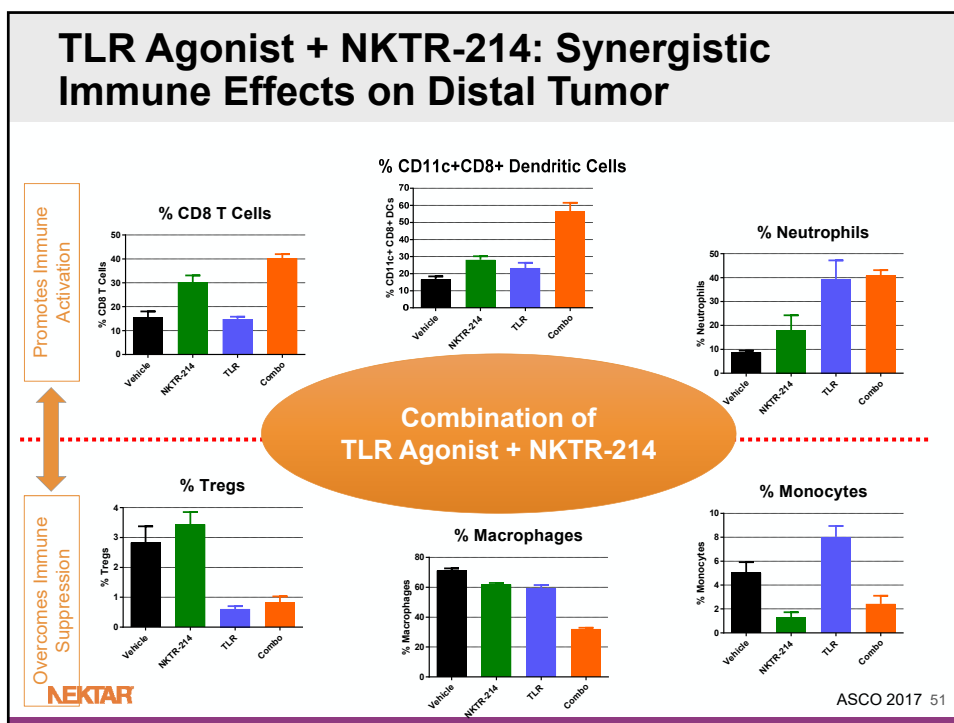


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Complete Regression and Abscopal Effect with Combination of NKTR-262 and NKTR-214

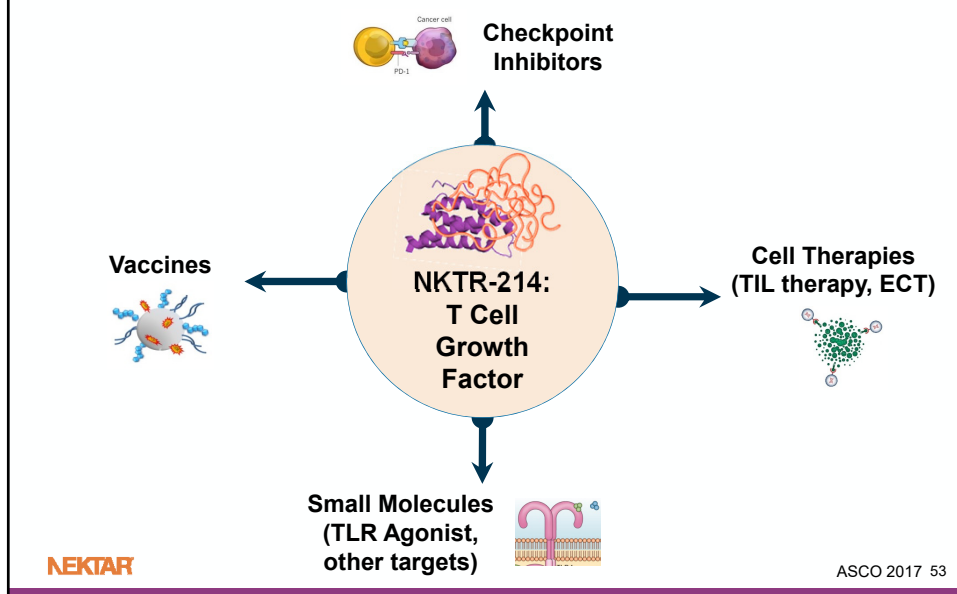




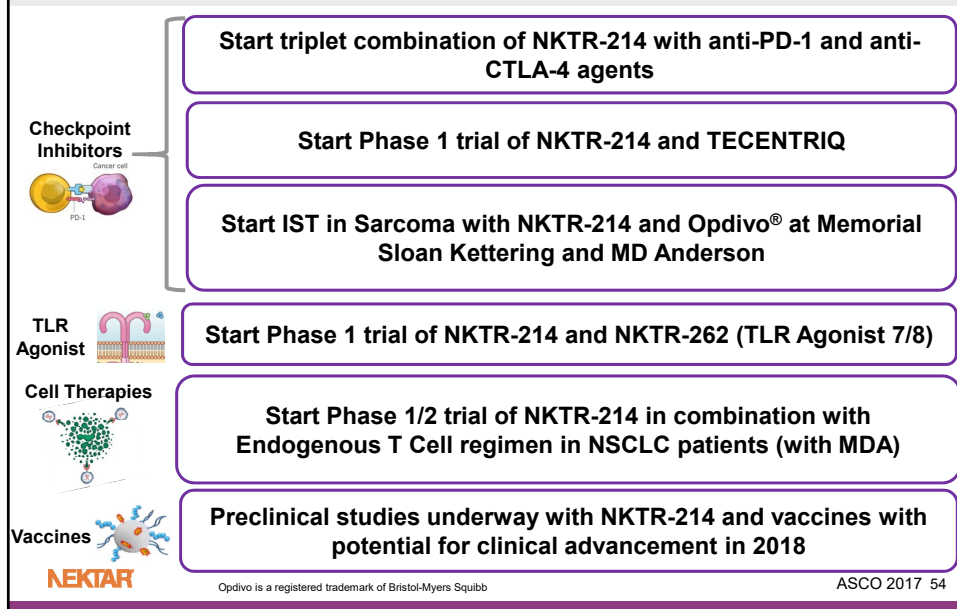
NKTR-214 Development Program

Dr. Mary Tagliaferri
Senior Vice President, Clinical Development
Nektar Therapeutics

NKTR-214 Provides A Central Mechanism to Combine with Multiple Modalities in Immuno-Oncology



NKTR-214: Additional Clinical Development Programs in 2H 2017/1H 2018



PROPEL Program: NKTR-214 plus TECENTRIQ® (atezolizumab)

PROPEL

Phase 1 Dose Escalation
(on label indications)
N= 20-30

NSCLC

2nd line – metastatic disease
with progression following
platinum regimen or
targeted therapy

Urothelial Carcinoma

2nd line locally advanced or
metastatic disease with
progression following
platinum regimen

- NKTR-214 in combination with Roche's anti-PD-L1 agent, atezolizumab
- Nektar sponsored program supporting checkpoint inhibitor combination strategy
- Study is expected to initiate mid-2017

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Investigator Initiated Study: Sarcoma

Phase 2 Study Proposed by Dr. Sandra D'Angelo (MSKCC) and Tony Conley (MD Anderson)

- Both investigators with proven track record of high enrollment to IO studies in sarcoma
- Initiate study with RP2D of NKTR-214 plus Opdivo
- Can amend proposal to evaluate triplet regimen

Eligibility:

At least one
prior line of
systemic
therapy

Basket Study:

2 Bone
Sarcomas and
4 Soft Tissue
Sarcomas

Endpoints

- Safety and tolerability
- PFS at 24 weeks, median PFS, OS at 12 months and median OS
- RECIST 1.1
- Radiographic scans every 8 weeks
- Measure biomarkers in blood and tumor

Osteosarcoma
N=10

Chondrosarcoma
N=10

Undifferentiated pleomorphic
sarcoma/malignant fibrous
histiosarcoma
N=10

Angiosarcoma
N=10

Dedifferentiated/
pleomorphic liposarcoma
N=10

Leiomyosarcoma
N=10

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Takeda and Nektar Research Collaboration

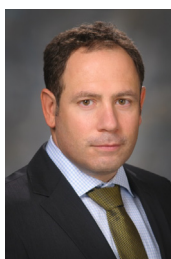
- Takeda and Nektar collaborating on combining NKTR-214 with five Takeda oncology compounds
- Collaboration will explore five targeted mechanisms in Takeda's oncology portfolio including:
 - SYK-inhibitor
 - Proteasome inhibitor
- Combinations will be tested in preclinical models of lymphoma, melanoma and colorectal cancer
- Takeda and Nektar will share costs and each will maintain global commercial rights to respective drugs/candidates



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Q&A Panel



Dr. Adi Diab

Assistant Professor of Melanoma Medical Oncology
MD Anderson



Dr. Michael Hurwitz

Assistant Professor of Medicine, Medical Oncology
Yale Cancer Center



Dr. Nizar M. Tannir

Professor of Genitourinary Medical Oncology & Deputy Department Chair of the Department of Genitourinary Medical Oncology
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Dr. Mary Tagliaferri

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- Michael Wong, MD

Yale University

- Michael Hurwitz, MD
- Harriet Kluger, MD
- Mario Sznol, MD

Providence Cancer Center

- Brendan Curti, MD

New York University

- Daniel Cho, MD

Roswell Park Cancer Institute

- Igor Puzanov, MD

Seattle Cancer Center

- Scott Tycodi, MD



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