Immunorad

September 2025 Data on Phase 1 Trial

Safety and preliminary efficacy of NBTXR3/SBRT in combination with Immune Checkpoint Inhibitors in anti-PD-1 resistant patients with melanoma treated in the phase I trial Study 1100

Cohort 3 – Melanoma Subgroup Analysis

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Study 1100 – Expansion Cohort 3 – Melanoma Extract

Study objective: RP2D and safety

HNSCC- Cohort 1	HNSCC- Cohort 2	Lung/ Liver/ Soft tissue Mets- Cohort 3
Inoperable LRR or R/M HNSCC Tumor to be injected is in HN region, lungs, or liver or soft tissue **Resistant** to prior anti-PD-1/ anti-PD-L1	The same as Cohort 1 except: **Naïve** to prior anti-PD-1/ anti-PD-L1	Primary tumor must be originating from any solid tumor that is: **Resistant** to a prior anti-PD-1/ anti-PD-L1 Tumor to be injected is in lung, liver, or soft tissue

Melanoma Extraction

Study Treatments

Day 1: One- time pre-med steroid then NBTXR3 IT injection (% of baseline)

Day 7-16: Begin tumor-site specific RT (35-45Gy in 3-5 fractions)

Day after RT: Begin or Resume PD-1 (pembrolizumab or nivolumab)

Objectives and Endpoints

Primary: Recommended Phase 2 Dose

Secondary: ORR, Safety and Feasibility, and Body-Kinetics

Exploratory: Survival Outcomes, Duration of Responsibility, and Biomarkers of Response

Treating Melanoma Patients After Multiple Lines of Treatment[1]

Study 1100 third cohort results: Focus on melanoma

- Resistance to immune checkpoint inhibitor in melanoma is common and remains a clinical challenge
- Primary and secondary resistance to anti-PD-1 therapy occurs in ~50% and ~25% of melanoma patients
- In this resistant patient population and with no standard approach, response rate is generally low (e.g. 20% ORR and 50% DCR respectively[2])

"This patients represent one of the more difficult clinical challenges […] as many have exhausted standard therapies"

Colette Shen, MD, PhD, Assistant Professor of Radiation Oncology, University of North Carolina Lineberger Comprehensive Cancer Center

1 Lim SY, et al. The molecular and functional landscape of resistance to immune checkpoint blockade in melanoma. Nat Commun. 2023 Mar 18;14(1):1516. doi: 10.1038/s41467-023-36979-y. PMID: 36934113; PMCID: PMC10024679. 2 Ascierto, et al. (2017). Initial efficacy of anti-lymphocyte activation gene-3 (anti–LAG-3; BMS-986016) in combination with nivolumab (nivo) in pts with melanoma (MEL) previously treated with anti–PD-1/PD-L1 therapy.. Journal of Clinical Oncology. 35. 9520-9520. 10.1200/JCO.2017.35.15_suppl.9520.

Baseline Characteristics of Melanoma Patients

Melanoma primary cancer diagnosis		N = 21
Median age, years (Min-Max)		63 (29 - 90)
Gender, n (%)	Male	14 (66.7)
ECOG, n (%)	0 -1	20 (95.2)
Lactate dehydrogenase level, n (%)	Unknown	2
	Above normal range	4 (21.1)
	Within normal range	15 (78.9)
Median number of lesions (Min-Max)		3 (1 - 22)
Clinical stage group at study entry, n (%)	III	10 (47.6)
	IV	11 (52.4)

Safety

Radiation, PD1, Injection, NBTXR3

All TEAEs	Patients (%) (N = 21)		
	Grade 1-2	Grade 3+	All grades
Overall	16 (76.2)	2 (9.5)	17 (81.0)
Patient incidence over 5%			
Fatigue	8 (38.1)	0	8 (38.1)
Diarrhoea	5 (23.8)	0	5 (23.8)
Nausea	4 (19.0)	0	4 (19.0)
Lymphocyte count decreased	3 (14.3)	0	3 (14.3)
C-reactive protein increased	2 (9.5)	0	2 (9.5)
Hypotension	1 (4.8)	1 (4.8)	2 (9.5)
Pyrexia	2 (9.5)	0	2 (9.5)

All TEAEs related to NBTXR3 and/or Injection	Patients (%) (N = 21)		
	Grade 1-2	Grade 3+	All grades
Overall	5 (23.8)	1 (4.8)	5 (23.8)
All events			5 (23.8)
Hypotension	1 (4.8)	1 (4.8)	2 (9.5)
Erythema	1 (4.8)	0	1 (4.8)
Hiccups	1 (4.8)	0	1 (4.8)
Hyperhidrosis	1 (4.8)	0	1 (4.8)
Injection site pain	1 (4.8)	0	1 (4.8)
Nausea	1 (4.8)	0	1 (4.8)
Pleuritic pain	0	1 (4.8)	1 (4.8)
Tachycardia	1 (4.8)	0	1 (4.8)

No Grade 4-5, No SAEs

Patients Failed Multiple Treatment Lines Prior Entering The Study

Melanoma patients, N=19

Melanoma Patient	Anti-PD-1	Anti CTLA4	Anti-LAG3	TLR9 agonist	TIL	BRAFi	MEKi	RANKLi	ATRi	TVEC	CT?	Prior RT
1	PD											
2	PD									PD		
3	PD	PD				PD	PD					
4	PD											
5	PD	PD	PD							PD		
6	PD	PD								PD		
7	PD		PD									
8	PD		PD									
9	PD											
10	PD	PD										
11	PD							PD		PD		
12	PD	PD										
13	PD	PD	PD								PD	
14	PD	PD	PD			PD	PD					PD
15	PD	PD	PD		PD							
16	PD	PD	PD						PD			
17	PD	PD										
18	PD											
19	PD	PD		PD								

Patients Resistant to Anti-PD1 and Multiple Line of Treatments

Melanoma primary cancer diagnosis		N = 21
Prior immunotherapies, n (%)	Anti-PD-1	21 (100)
	Anti-CTLA4	11 (52.4)
	Anti-LAG3	7 (33.3)
	TVEC	5 (23.8)
	Other	2 (9.5)
Prior BRAF/MEK therapy, n (%)		2 (9.5)
Prio other systemic treatment, n (%)		3 (14.3)
Prior RT, n (%)		5 (23.8)

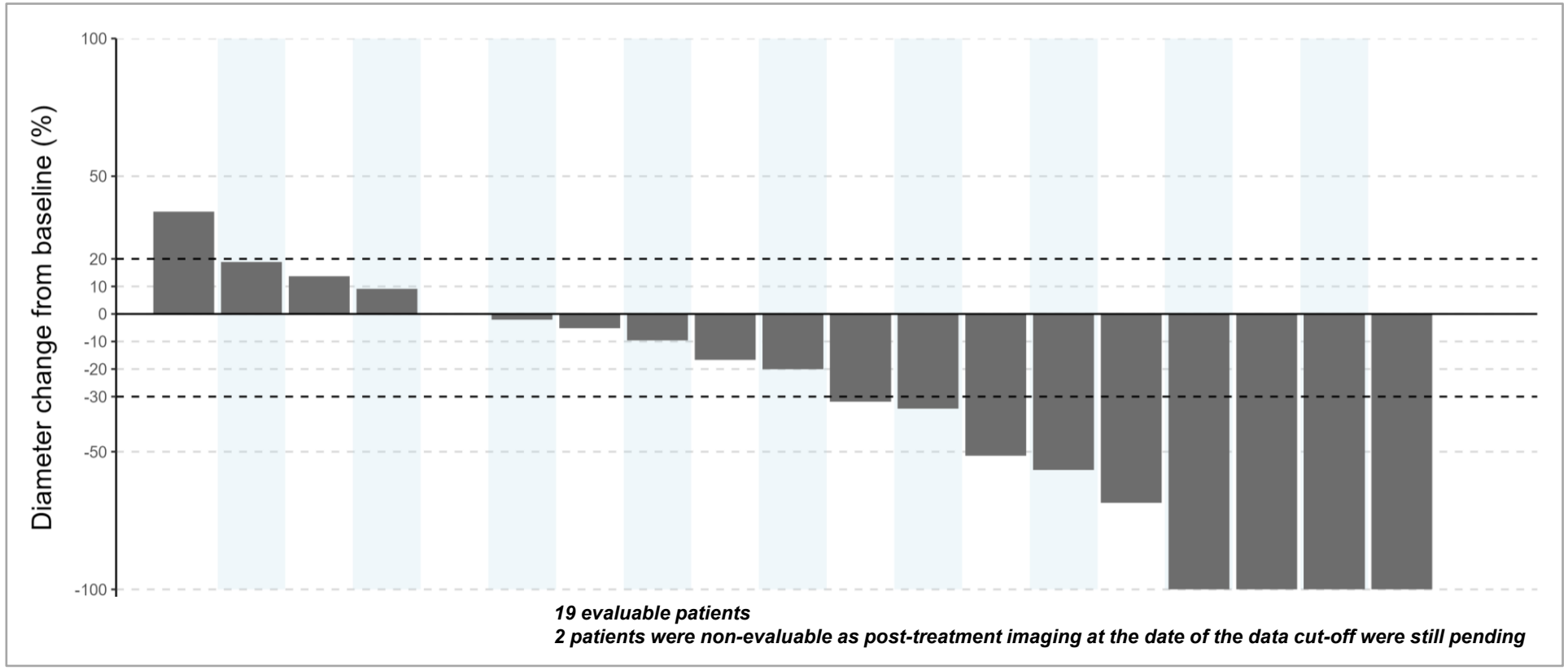
Multi-resistance patient population

SITC definition of primary resistance: Occurs when a patient receives adequate exposure to a PD-1 or PD-L1 inhibitor (usually ≥ 6 weeks or 2–3 doses), yet fails to achieve any objective clinical benefit (i.e., no partial response [PR] or better) and disease progression is confirmed on follow-up imaging .

Cut-Off: 21 Aug 2025

Best Sum of Target Lesion Diameter Change from Baseline

1100 study, primary melanoma evaluable subjects



Efficacy (RECIST 1.1): 47.4% of ORR

Evaluable for Efficacy	Primary melanoma N=19*			
	Overall response by number of lesions at baseline			Injected response
	1-4 (N = 14)	5+ (N = 5)	All (N = 19)	All (N = 19)
CR	4 (28.6)	0	4 (21.1)	5 (26.3)
PR	4 (28.6)	1 (20.0)	5 (26.3)	5 (26.3)
SD	3 (21.4)	3 (60.0)	6 (31.6)	9 (47.4)
PD	3 (21.4)	1 (20.0)	4 (21.1)	0
ORR (= CR + PR)	8 (57.1)	1 (20.0)	9 (47.4)	10 (52.6)
95% CI	[28.9 - 82.3]	[0.5 - 71.6]	[24.4 - 71.1]	[28.9 - 75.6]
DCR (= SD + CR + PR)	11 (78.6)	4 (80.0)	15 (78.9)	19 (100)
95% CI	[49.2 - 95.3]	[28.4 - 99.5]	[54.4 - 93.9]	[82.4 - 100]

ORR is 47.4%
DCR is 78.9%

*2 patients were non-evaluable as post-treatment imaging at the date of the data cut-off were still pending
1 patient received additional SBRT on target lesions without JNJ-1900.This patient didn't show response at the date of the cutoff.

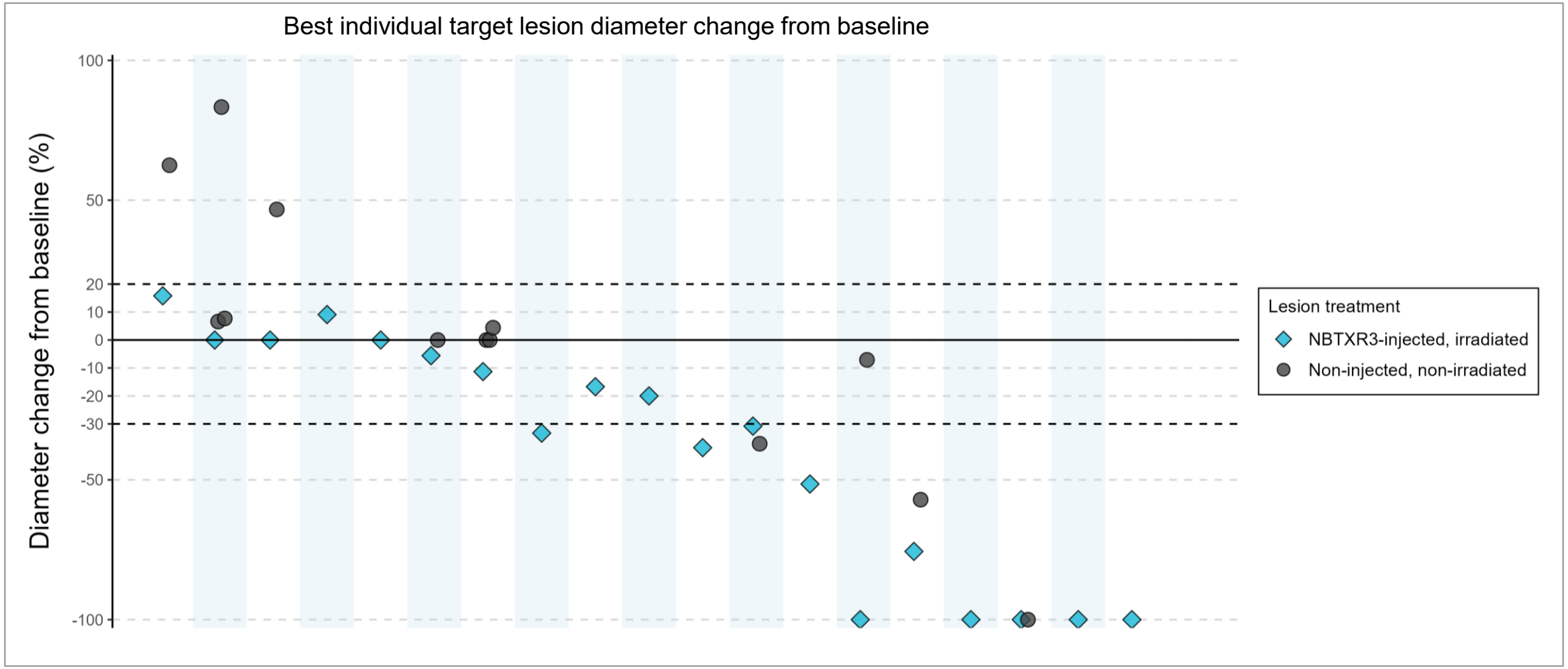
Treatment Outcome After Each Prior Treatment, and After NBTXR3/RT

Melanoma patients, N=19

Melanoma Patient	Anti-PD-1	Anti CTLA4	Anti-LAG3	TLR9 agonist	TIL	BRAFi	MEKi	RANKLi	ATRi	TVEC	CT?	Prior RT	OR (RECIST 1.1) NBTXR3/RT
1	PD												SD
2	PD									PD			CR
3	PD	PD				PD	PD						PD
4	PD												CR
5	PD	PD	PD							PD			PR
6	PD	PD								PD			CR
7	PD		PD										PD
8	PD		PD										PR
9	PD												PR
10	PD	PD											CR
11	PD							PD		PD			PR
12	PD	PD											SD
13	PD	PD	PD								PD		PD
14	PD	PD	PD			PD	PD					PD	SD
15	PD	PD	PD		PD								PD
16	PD	PD	PD						PD				SD
17	PD	PD											SD
18	PD												SD
19	PD	PD		PD									PR

Local Response Linked to Systemic Activity

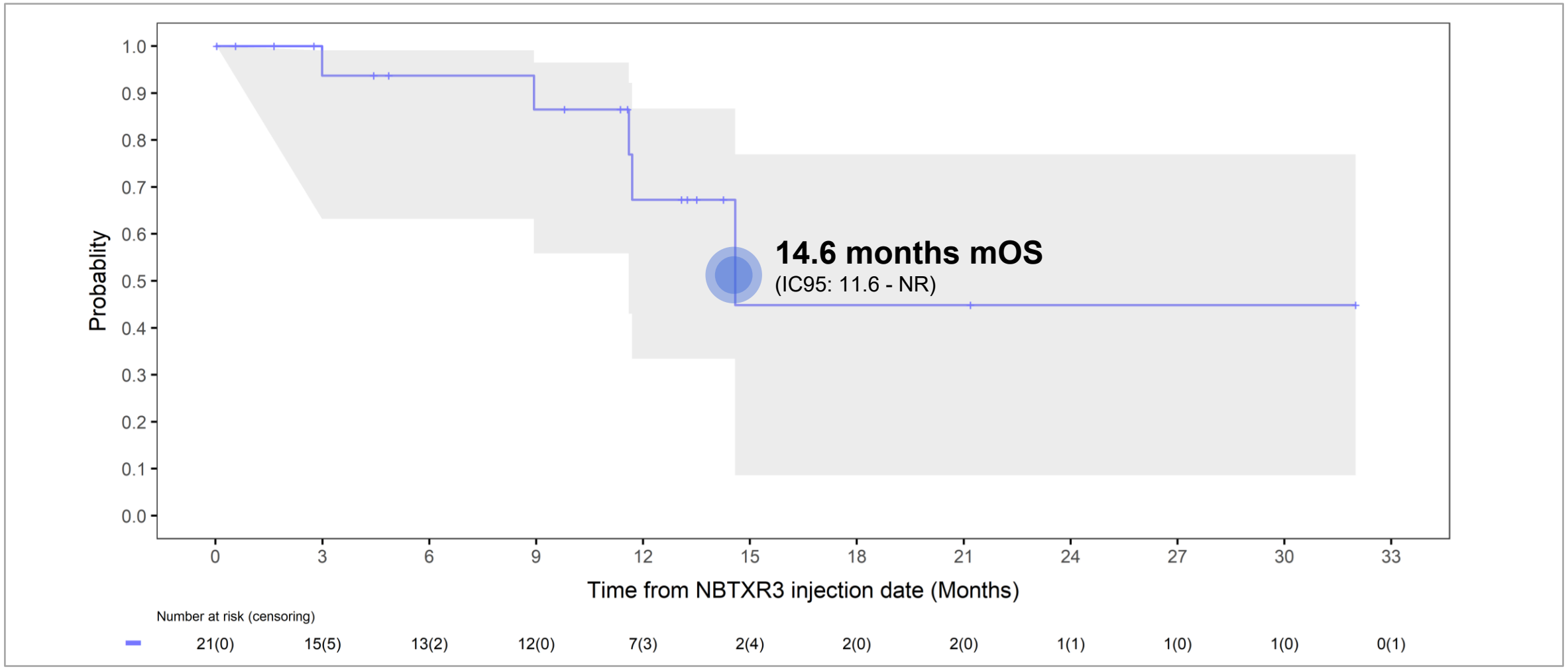
1100 study, primary melanoma NBTXR3-injected evaluable subjects



19 evaluable patients. 2 patients were non-evaluable as post-treatment imaging at the date of the data cut-off were still pending

Early signs of efficacy: 14.6 months Median Overall Survival

1100 study, all treated melanoma subjects – Early data, OS under maturation



Patient Case: Melanoma Patient, 81 yo, Refractory to ICI (Part 2)

Dose level 33% GTV – Still in study

Patient Case : RECIST Best Overall Response SD – Response Ongoing For 19 Months, Patient Still On Study

<u>Prior to study entry</u>, patient progressed on multiple lines of treatment:

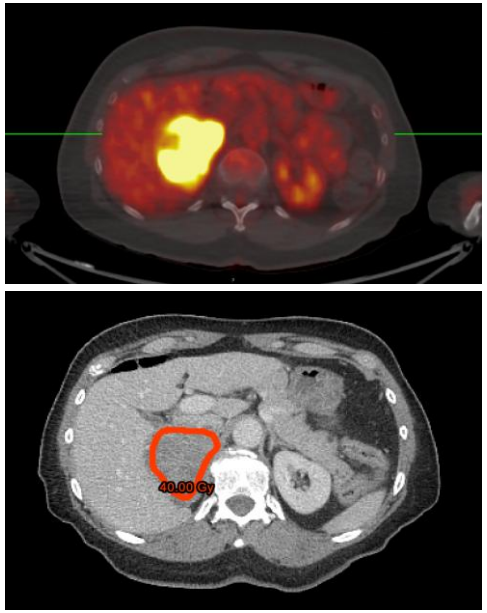
Pembrolizumab monotherapy,

Ipilumimab monotherapy,

RT (pelvis/R adrenal 40 Gy/10fx in 2020)

LXH254 trial (BRAF and CRAF inhibitor), relatlimab/nivolumab

NRAS-mutant cutaneous melanoma



FDG PET/CT for Local Response

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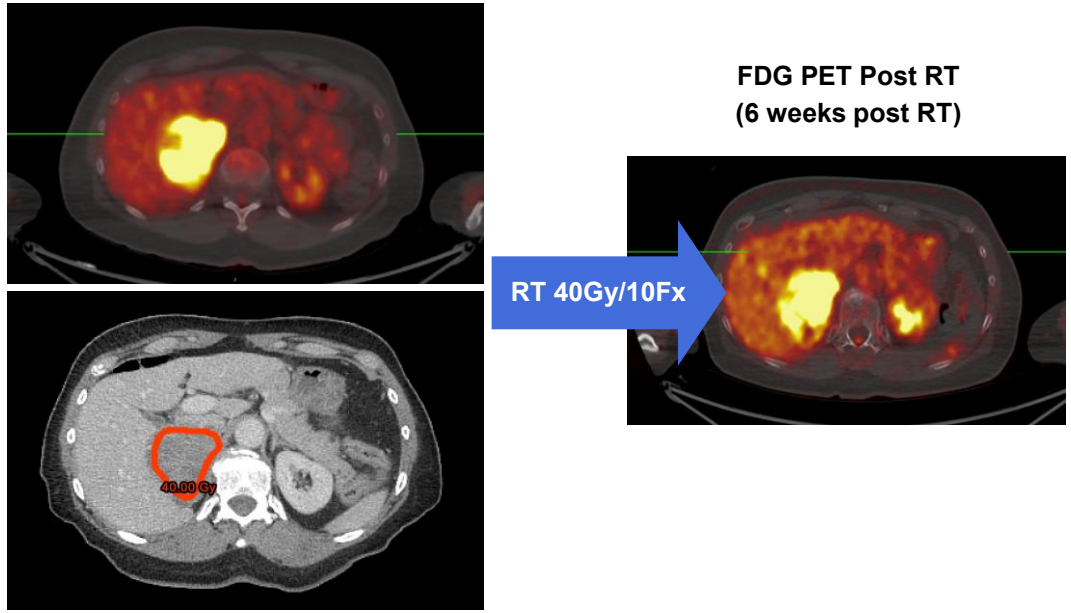

FDG PET Post RT
(6 weeks post RT)

FDG PET/CT for Local Response

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Dose level 33% GTV – Still in study

Patient Case : RECIST Best Overall Response SD – Response Ongoing For 19 Months, Patient Still On Study

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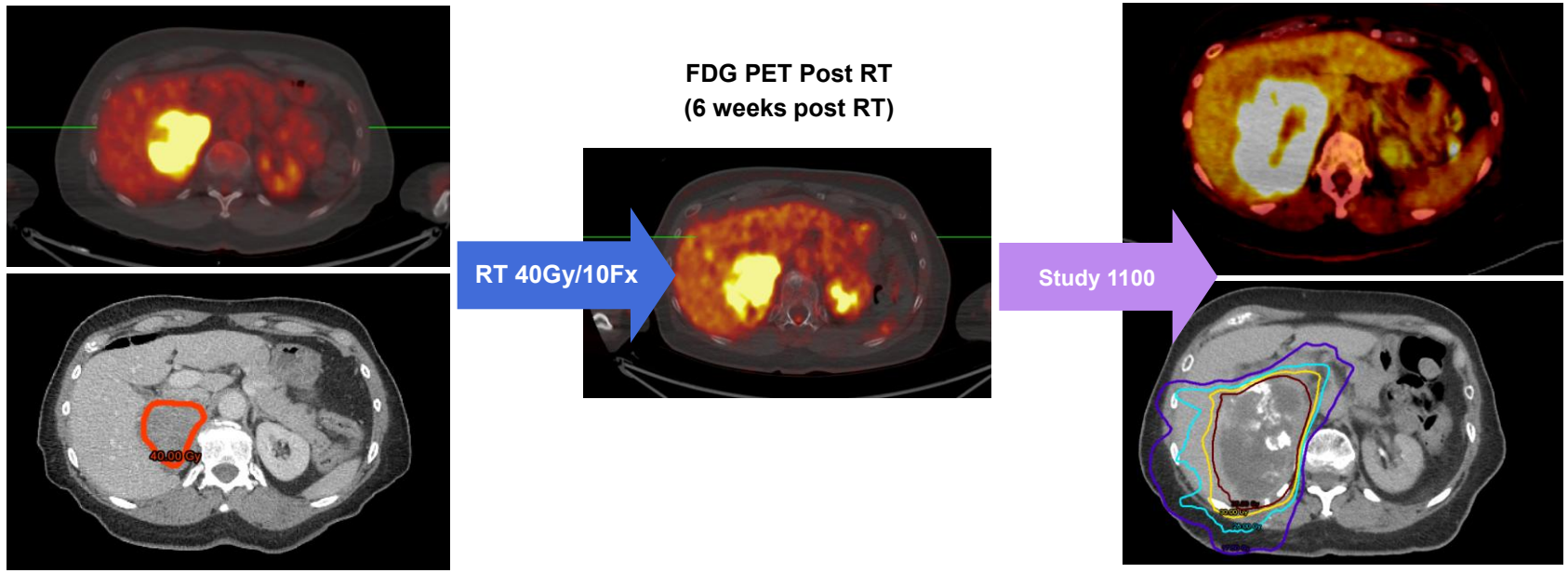
Post-NBTXR3+ re-irradiation to right adrenal (35 Gy/5Fx)

NRAS-mutant cutaneous melanoma



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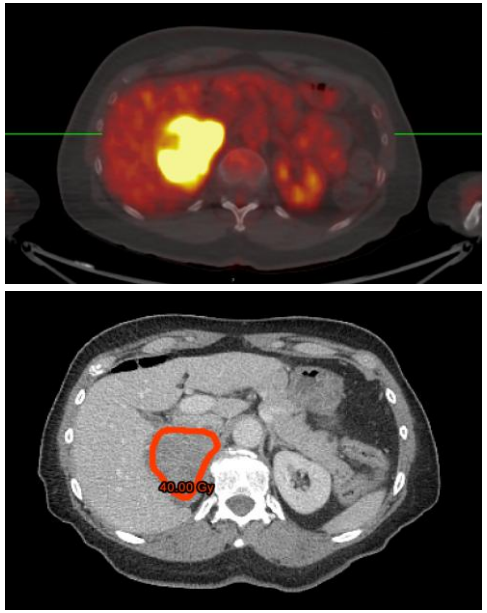
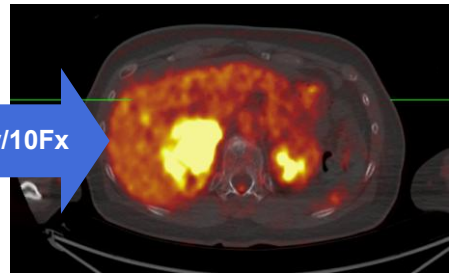


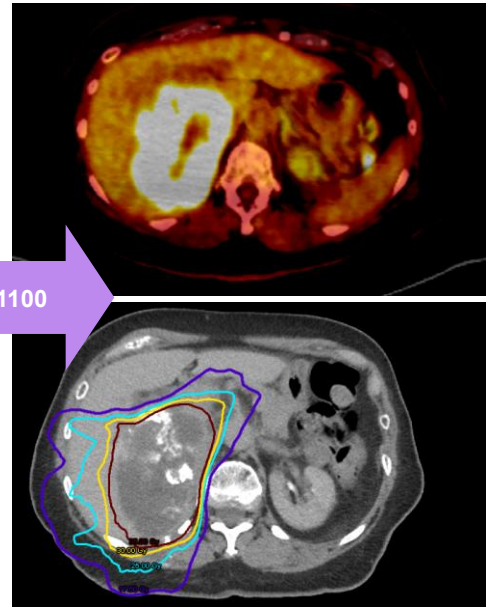
RT 40Gy/10Fx

FDG PET Post RT
(6 weeks post RT)



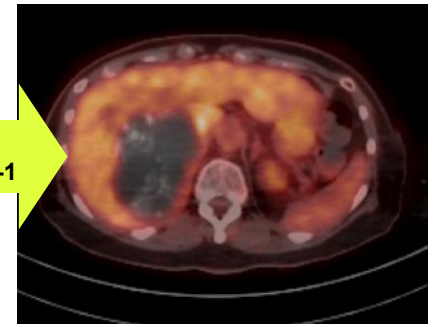
Study 1100

Pre-NBTXR3/RT



NBTXR3+SBRT
35Gy/5F +anti-PD-1

FDG PET Post NBTXR3/RT
(4 weeks post RT and start of anti-PD-1)



FDG PET/CT for Local Response

Stable Disease BOR per RECIST, however PET scan suggests Complete Metabolic Response

Conclusion for NBTXR3 in Metastatic Melanoma

NBTXR3 could represent a new option in this patient population

- **NBTXR3 injection** in a single melanoma lesion at the RP2D dose (33% of the GTV) was **feasible and well tolerated**
- NBTXR3/RT was also **well tolerated in** combination **with anti-PD-1**
- **Promising local and systemic control** observed with:
  - **47.4% ORR as per RECIST 1.1** in evaluable patients
  - **100% DCR in injected lesions, and 78.9% overall**
- Early analysis of OS shows a **Median OS of 14.6 months** in the all treated population

With promising preliminary efficacy results, this data warrants further evaluation of NBTXR3/RT in combination with ICI in a randomized trial