2025 ESMO IMMUNO-ONCOLOGY
Annual Congress

SCOPE, a phase 2 trial with off-the-shelf DNA vaccine in first line advanced melanoma in combination with check point inhibition

Data Update: Safety and Efficacy

Dr Heather Shaw
Department of Medical Oncology, Mount Vernon Cancer Centre and University College London Hospital

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Declaration of Interests

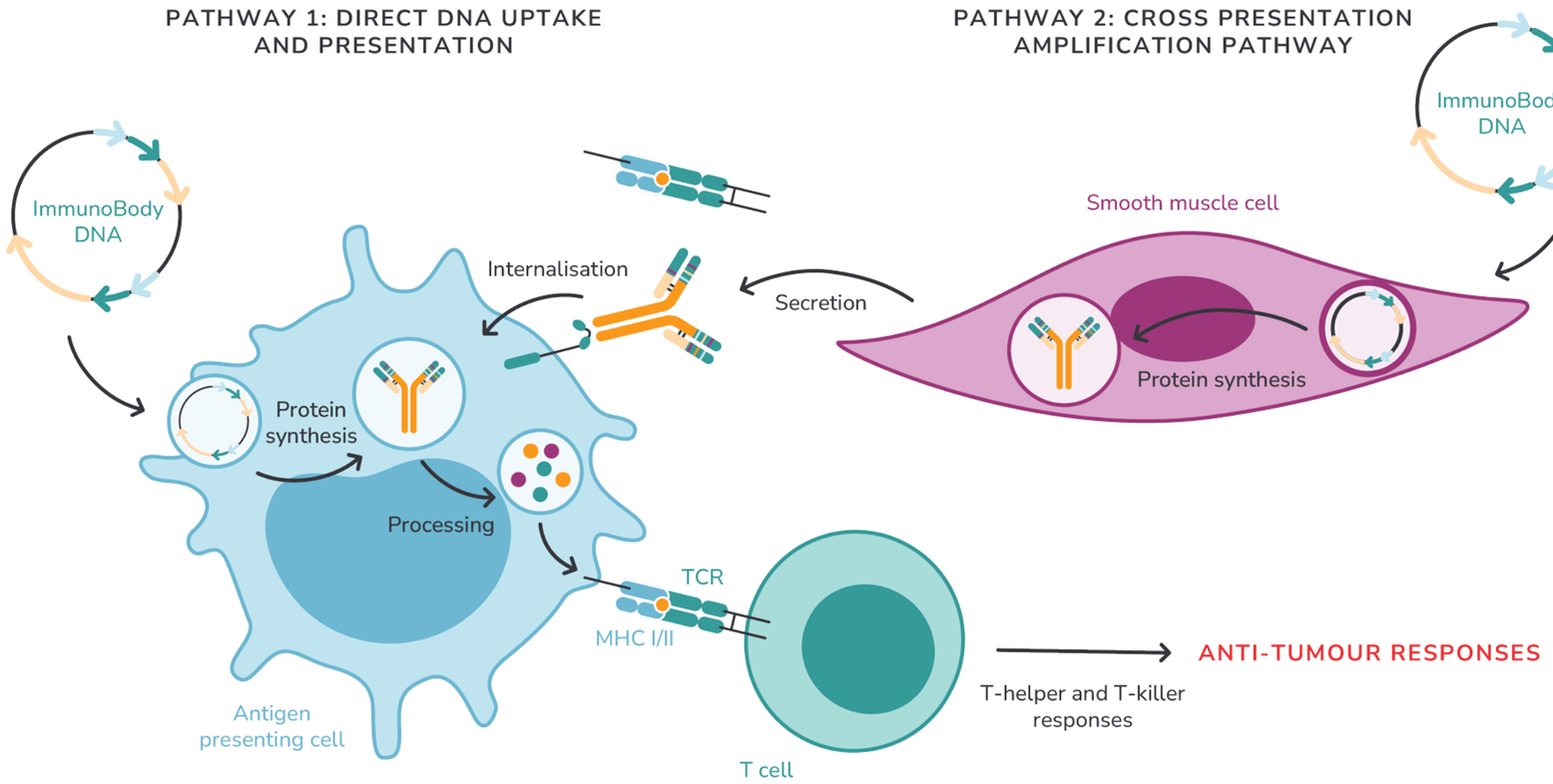
Consulting

- Novartis, BMS, MSD, Immunocore, Idera, Iovance, Genmab, Sanofi Genzyme, Regeneron, Macrogenics, Roche, Agenus, Ideaya, iOnctura, CDR-Life, NovalGen, Therakos/Mallinkrodt Pharmaceuticals, Scancell Ltd

Speakers bureau

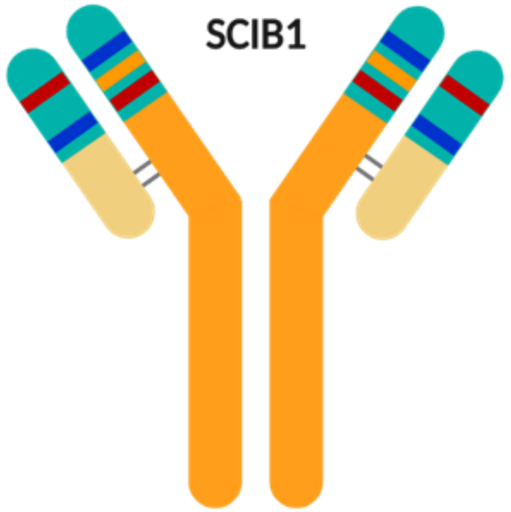
- Novartis, BMS, MSD, Sanofi Genzyme, Regeneron, AstraZeneca, Eisai, Pierre-Fabre

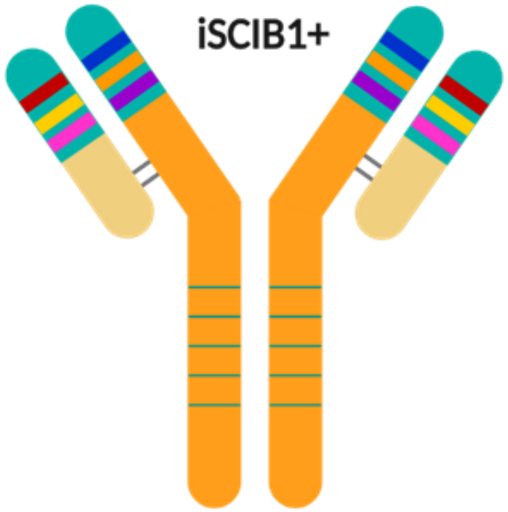
Immunobody dual mode of action to maximise anti-tumour immune response following needle free injection



- By **Direct Presentation** ImmunoBody targets antigen presenting cells (APCs) via CD64 resulting in engineered antibodies
- By **Cross Presentation** secretion of engineered antibodies that via Fc domain target APCs
- Mediated by MHC class1, melanoma specific epitopes bind specific HLA restricted T-cell receptors to effect targeted CD-8 and CD-4 anti-tumour response

SCIB1 & iSCIB1+ are off-the-shelf DNA plasmid cancer vaccines with CD8 & CD4 epitopes from TRP-2 and gp100 .





SCIB1		Amino acids
✓		H1: gp100 173-190
✓		H2: TRP2 180-188
		H3: gp100 471-492
✓		L1: gp100 44-59
		L2: TRP2 177-205
		L3: TRP2 60-91

Amino acids	iSCIB1+
A2/DR7/DR53/DQ6	✓
A2	✓
DP4/A1/B35	✓
DR4	✓
A2/DP4/A31/A33/A3	✓
DR3/B35/B44	✓

- SCIB1 and iSCIB1 + incorporate CD8 and CD4 epitopes from TRP-2 and gp100 into an antibody framework to allow direct and Fc targeting of activated dendritic cells
- TRP-2 and gp 100 epitopes have a key role in melanin production and were isolated from T-cells of patients who achieved spontaneous complete response from melanoma
- Next generation iSCIB1 + has additional epitopes applicable to more HLA MHC – class 1 haplotypes, **A2, A3, A31, Bw4, B35 & B44** that represent 80% of the population
- iSCIB1+ is modified for additional avidity

SCOPE Program - advanced melanoma with checkpoint inhibitors

Phase 2 open label multi cohort translational study enrolling over 140 patients at 16 clinical trial sites in the UK initiated in 2022.

STUDY POPULATION

Advanced melanoma in combination with standard of care checkpoint inhibition (CPI)

Inclusion Criteria (Summary)

- Histologically confirmed, unresectable Stage III or Stage IV Melanoma
- Not received prior systemic treatment for advanced disease.

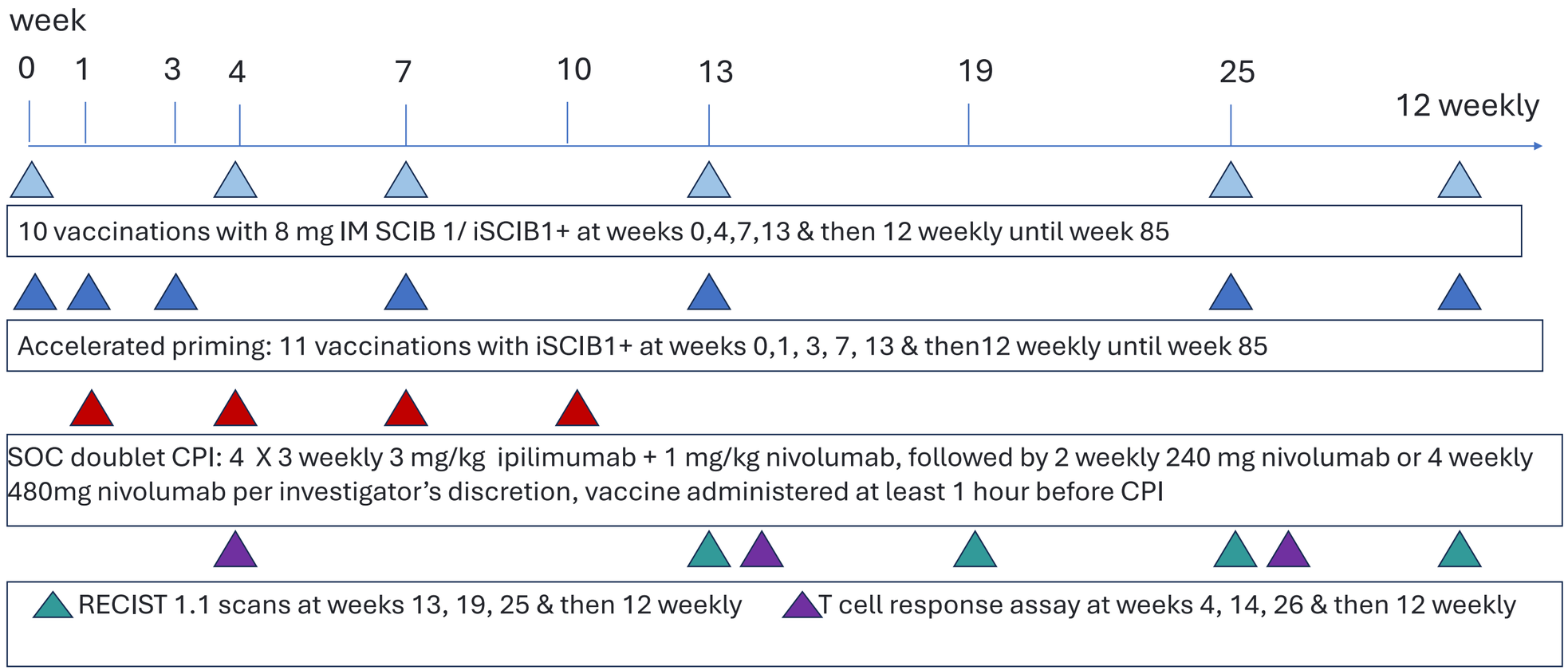
ECOG Performance Status 0 or 1.

- At least one measurable RECIST 1.1 lesion
- HLA status known

Exclusion Criteria (Summary)

- Acral, Ocular & Mucosal Melanoma
- CNS Metastases
- Exposure to CPI as adjuvant treatment in previous 6 months
- LDH >2 X ULN

STUDY SCHEDULE



EOT Visit – 4 weeks after last vaccination, Final Follow-up Visit at week 97 (22 months)

Patient Characteristics of Combined SCIB1 & iSCIB1+ HLA eligible population

Characteristic	SCOPE HLA eligible
Number of patients	80
Age in years	
Mean	58
Range	25 - 81
Sex: female %	46.3
ECOG Performance Status in %	
0-1	98.8
not reported	1.25
Stage at treatment start in %	
M0	2.5
M1a, M1b	61.2
M1c	36.3
Baseline LDH (ULN = 250 U/L)	
<ULN	88.7
>ULN	7.5
Missing	3.8
Brain Mets %	0
BRAF status %	
Mutated	48.1
Wild Type	51.9
Previous treatment with adjuvant CPI %	22.5

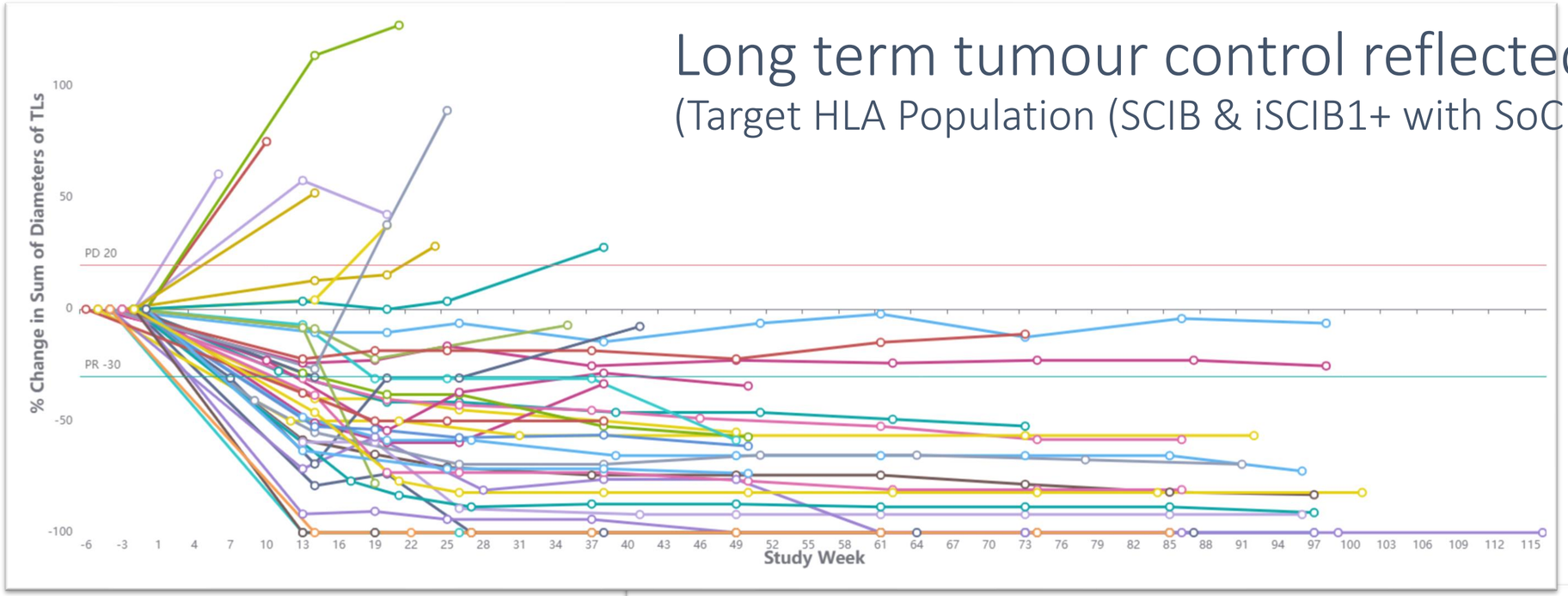
SCOPE: Data Update 27.10.25 data cut

Cohort	No of patients	Mean follow-up	PFS	DCR	ORR
SCIB1 HLA Restricted	41	13 mths	55% @ 26 mths	83% (34/41)	63% (26/41)
iSCIB1+ Broad HLA	39	8 mths	74% @16 mths	79% (31/39)	56% (22/39)
Combined	80	10.5 mths	60% @ 26 mths	81% (65/80)	60% (48/80)
HLA Ineligible	13	NA	20% @ 14 mths	30% (4/13)	15% (2/13)
Comparator	PFS with Ipi/Nivo at 24 months = 48% (Checkmate 067) ORR 58% on confirmation & 50% unconfirmed (Checkmate 067)				

- **Vaccine induced T-cell responses peak at week 25 hence largest impact on PFS, strongly correlated with DCR.**
- **T-cell memory response drives durability with continued PFS benefit, emphasizing the need for booster immunizations until week 85.**

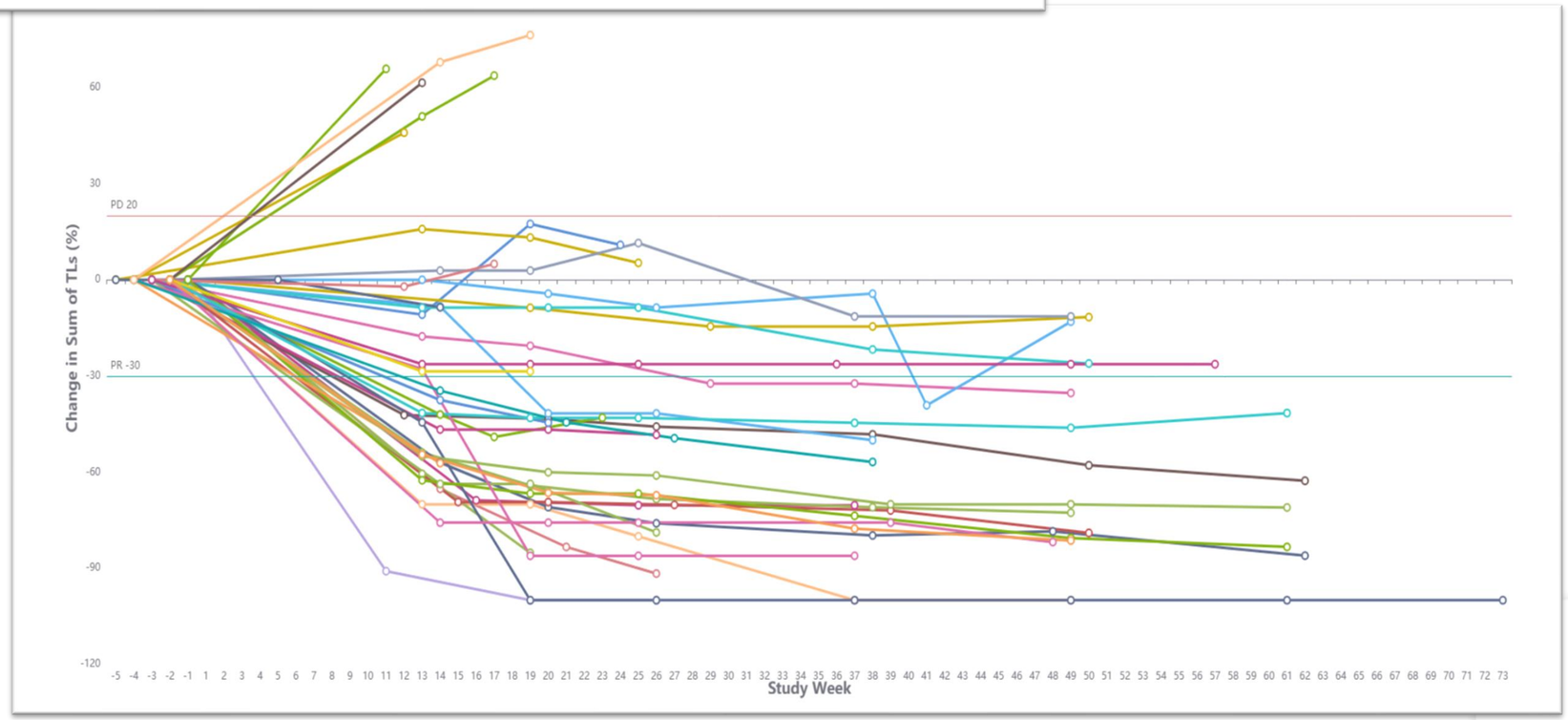
Long term tumour control reflected in durability

(Target HLA Population (SCIB & iSCIB1+ with SoC ipilimumab/nivolumab (n= 80))

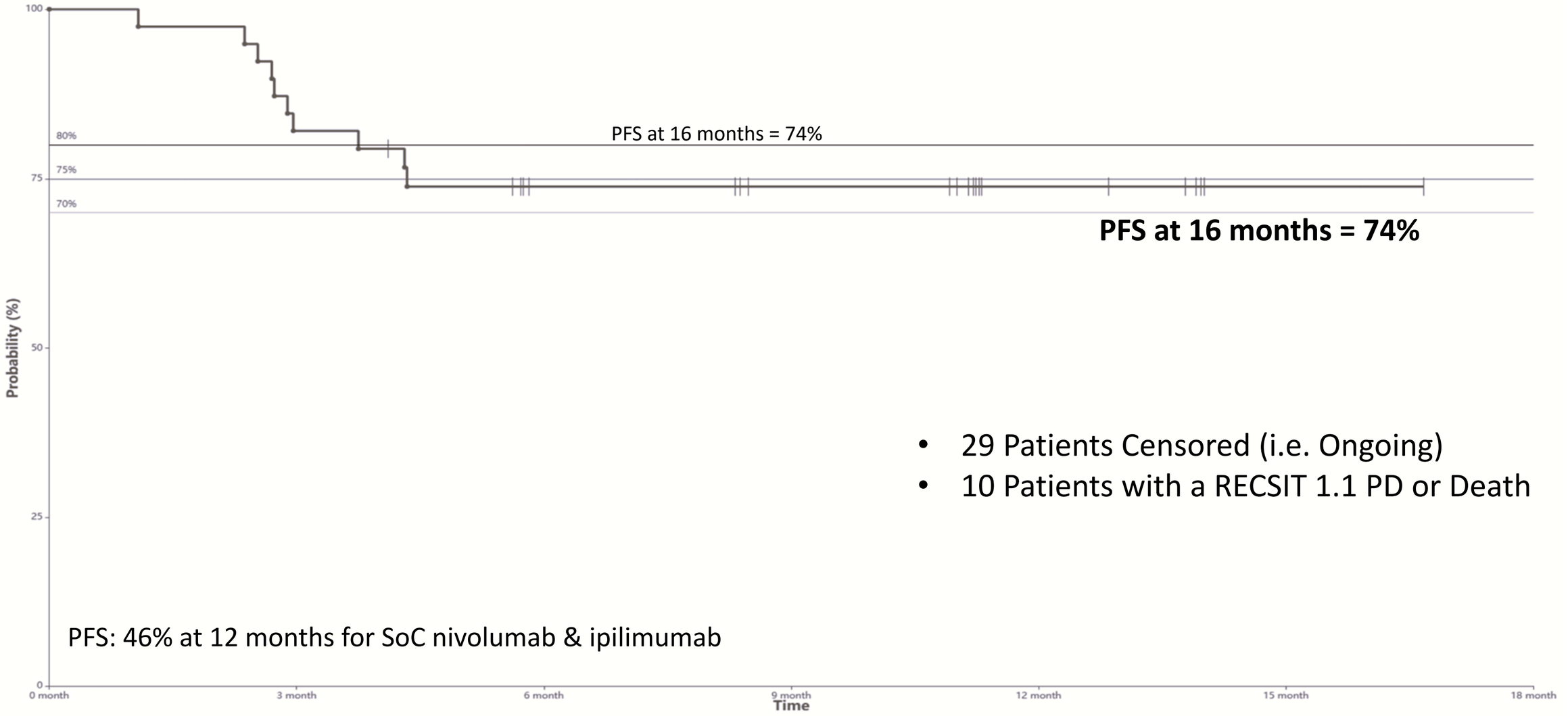


SCIB1: Target Population (HLA-A2) (n=41)

iSCIB1+: Target Population (HLA-A2, A3, A31, B35,Bw4, A33, B44 (n=39)



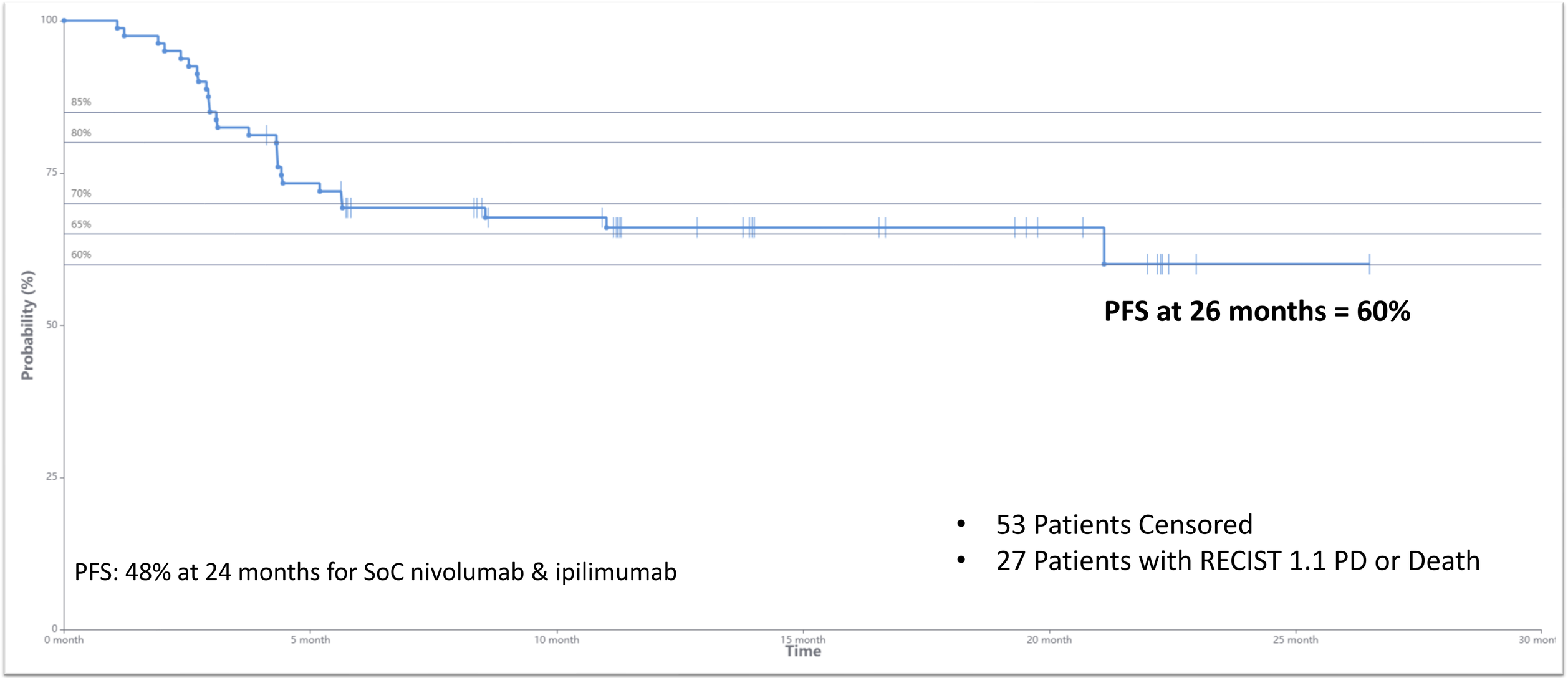
PFS: Target HLA Population **iSCIB1+** (n=39).



- 29 Patients Censored (i.e. Ongoing)
- 10 Patients with a RECSIT 1.1 PD or Death

PFS: 46% at 12 months for SoC nivolumab & ipilimumab

PFS Combined SCIB1 & iSCIB1+ in HLA eligible patients (n=80)

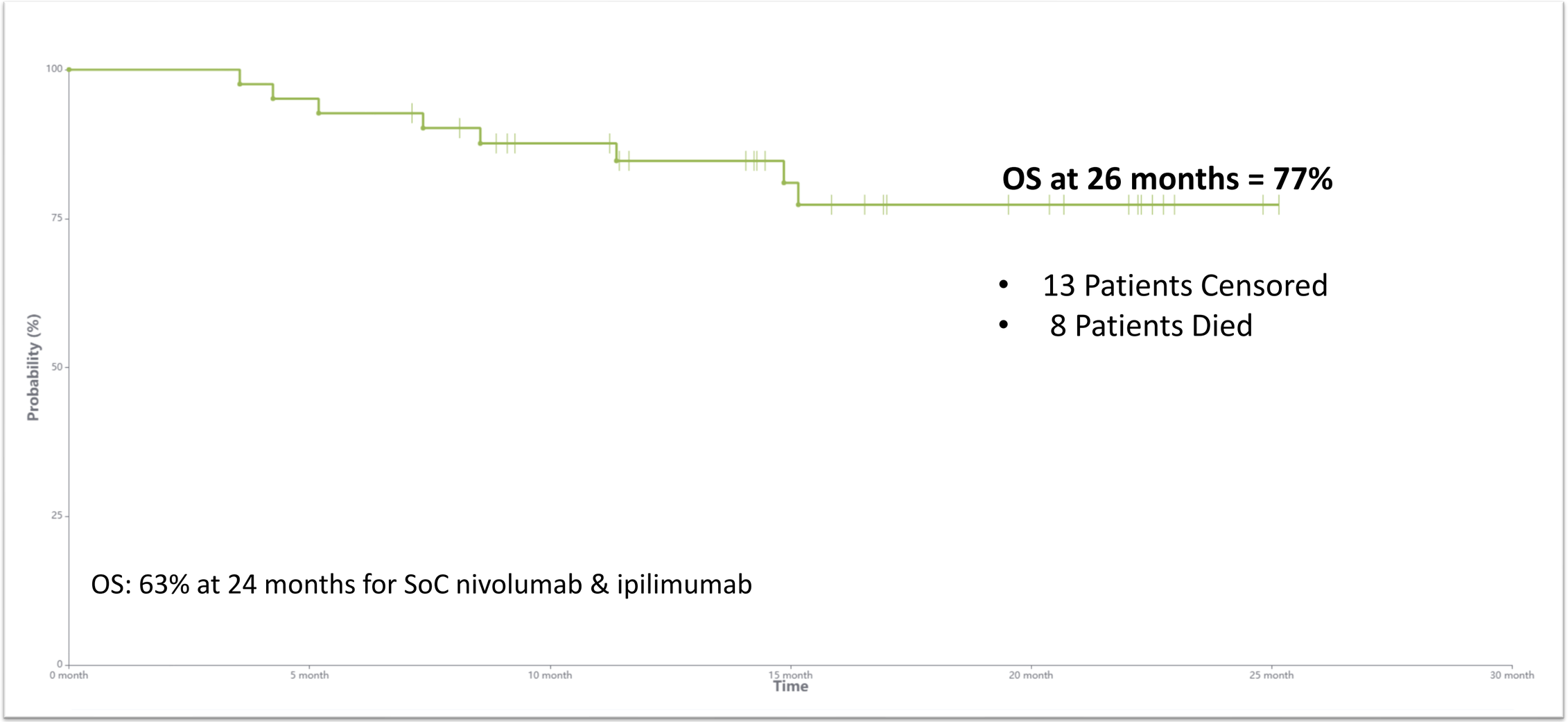


PFS at 26 months = 60%

PFS: 48% at 24 months for SoC nivolumab & ipilimumab

- 53 Patients Censored
- 27 Patients with RECIST 1.1 PD or Death

Overall Survival SCIB1 in HLA – A2 (n=41) with 26 months follow up



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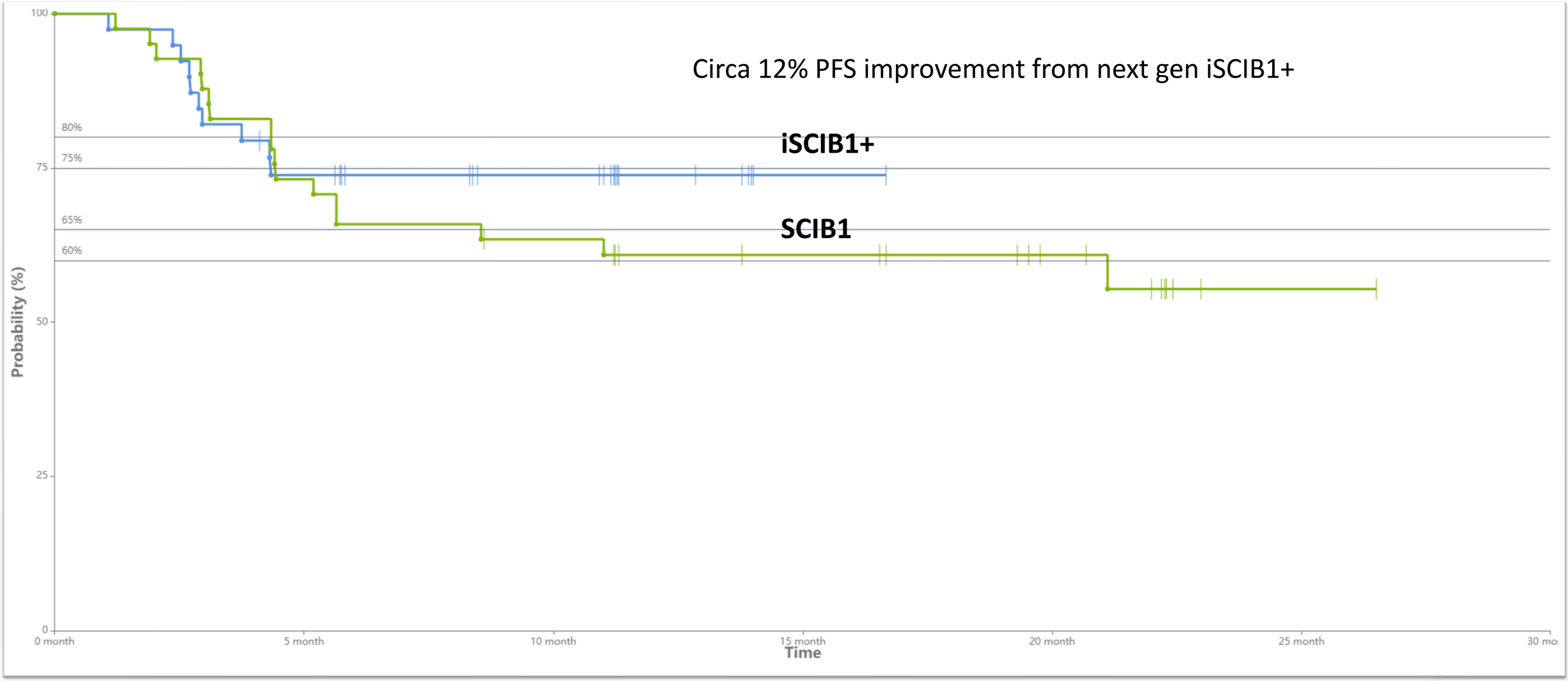
PFS: SCIB1 (41) vs iSCIB1+ (39)



SCANCELL

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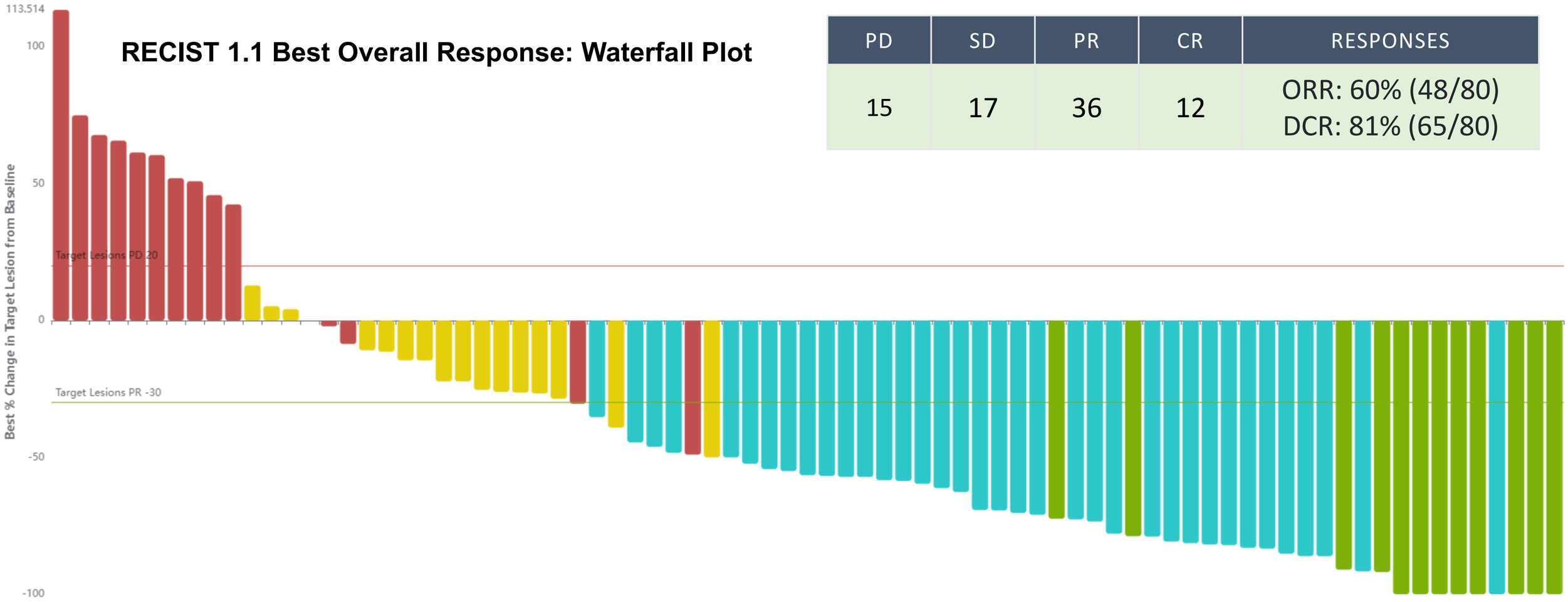
Combined SCIB1 & iSCIB1+ in HLA eligible patients (n=80)



PD	SD	PR	CR	RESPONSES
15	17	36	12	ORR: 60% (48/80) DCR: 81% (65/80)

SCIB1 and iSCIB1+ tolerability

The administration of SCIB1 and iSCIB1^{+} in combination with ipilimumab and nivolumab was generally **safe and well tolerated** in a dose range from **0.4 - 8mg**.

Overall incidence and profile of AEs consistent with those reported for ipilimumab and nivolumab combination therapy, indicating that **neither SCIB1 or iSCIB1^{+} potentiate or alter the known CPI toxicity spectrum**.

The exception: Immune-mediated or melanocyte-related **ocular inflammatory events, classified as eye disorders**

- Ocular inflammatory events are observed at a higher frequency than typical of CPI alone (21% of patients; 30 events; 28 events <G3; 2 events at G3, 1 of which was dose limiting), all of which were transient
- These events reflect inflammation of the uveal tract possibly caused by T-cell cross-reactivity against gp100 and TRP-2–expressing uveal melanocytes
- Precautionary fundoscopy and ophthalmic examinations would be scheduled during the first 25 weeks of vaccine administration

Interim Safety Summary – SCIB1 and iSCIB1+ (n = 133)

	Related to SCIB1 or iSCIB1+	Related to checkpoint inhibitors
TEAE (Total 2156 in 130 (98%) patients)	305 in 75 (55%) patients Majority comprised of elevated ALT/AST, injection site bruising, fatigue, gastrointestinal & skin disorders	940 in 120 (90%) patients Majority comprised of elevated ALT/AST, gastrointestinal and skin disorders
TEAE ≥ G3 (Total 200 in 90 (68%) patients)	32 in 19 (14%) patients SCIB1 = 14 & iSCIB1+ = 18 Most common: elevated ALT/AST and hypophysitis.	137 in 76 (57%) patients Most commonly colitis, diarrhea, hepatitis, increased transaminases
	One DLT of Posterior Uveitis was reported as related to iSCIB1+ and Ipilimumab with Nivolumab (combination phase)	
SAEs (Total 154 in 83 (60%) patients)	11 in 10 (7%) patients All SUSARs are dually related to CPI therapy; No SUSARs are reported as only related to SCIB1 or iSCIB1+.	109 in 65 (49%) patients Most commonly colitis, diarrhea, hepatitis, increased transaminases

Conclusions

- Efficacy benefit, durability & tolerability of iSCIB1+ confirmed with Progression Free Survival improvement is a critically important signal
- HLA matched population with MHC – class 1 A2, A3, A31, Bw4, B44, B35 comprising 80% of the patient population identified
- Stable (at -20C) off-the-shelf product delivered IM by needle free injection with an accelerated priming dosing schedule
- Further data awaited with ongoing maturity & follow-on phase 3 registration RCT planned along with evaluation in the neoadjuvant setting
- Potential to achieve meaningful clinical benefit in malignant melanoma

Poster Presentation: T-cell response data with clinical correlation

A DNA plasmid melanoma cancer vaccine, SCIB1 and iSCIB1+ combined with nivolumab and ipilimumab in advanced unresectable melanoma induces potent clinically meaningful CD8 T cell responses in 80% of the patient population.

Kate Young, et al.

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Scancell Team

Nermeen Varawalla
Joe Thornton
Georgia Goodhew
Olivia Howard
Robert Miller
Samantha Paston
Lindy Durrant

Partners

Cancer Vaccine Launch Pad
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Pharmajet
Rivia

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European Society for Medical Oncology (ESMO)
Via Ginevra 4, CH-6900 Lugano
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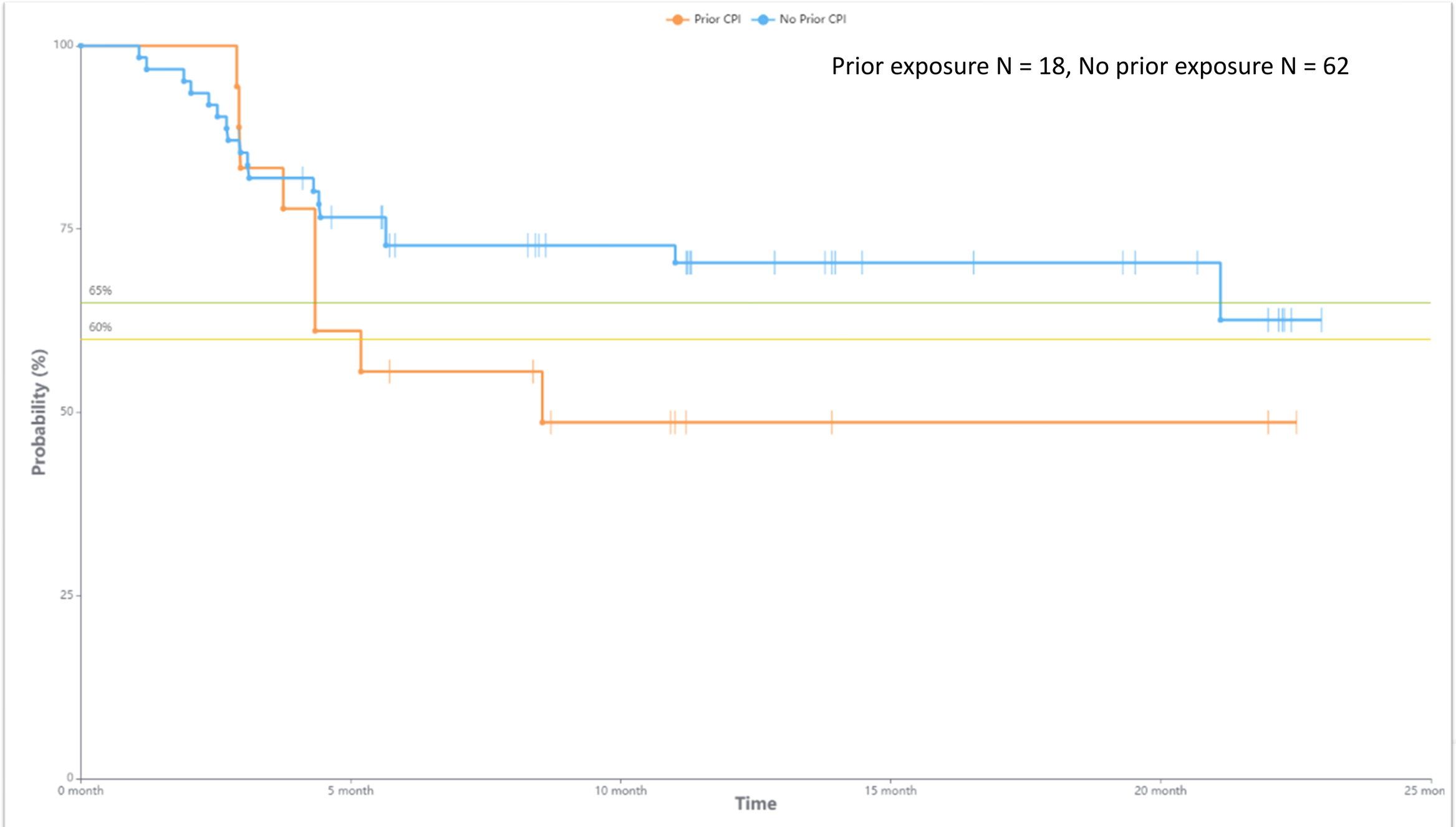
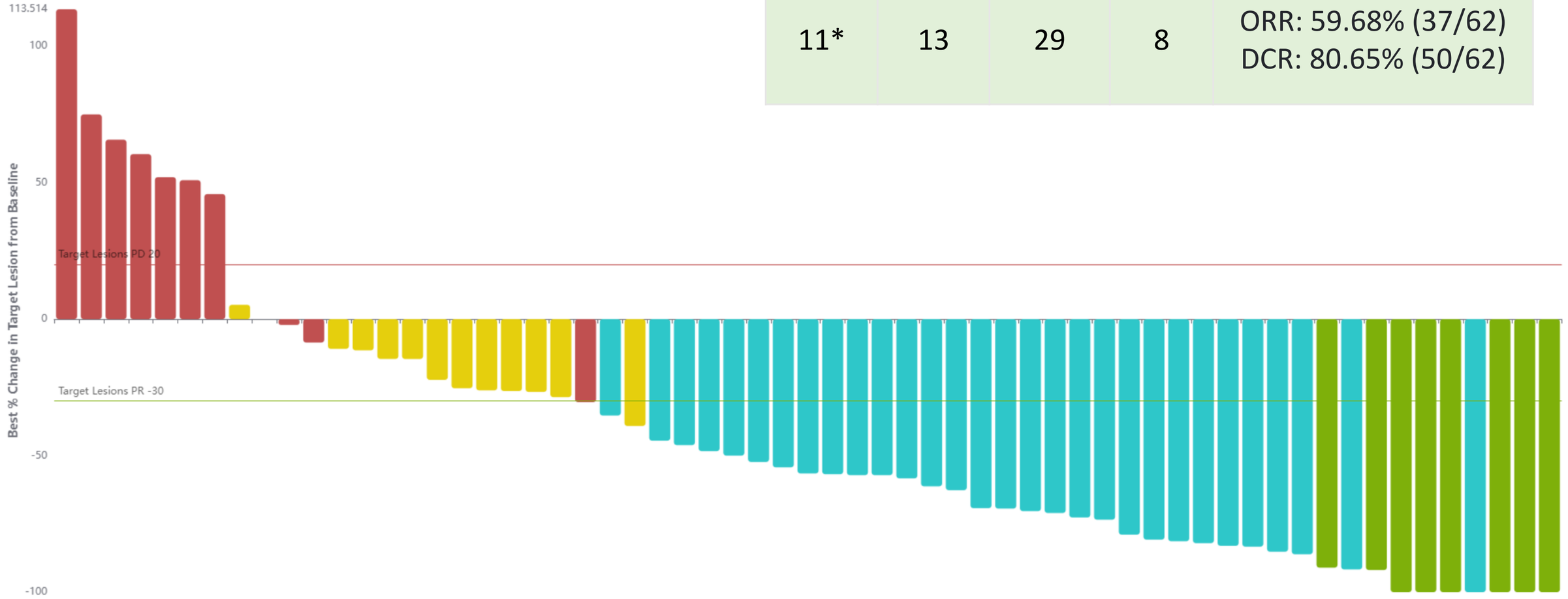
Patients with no previous CPI exposure fare better



Combined SCIB1 & iSCIB1+ in HLA eligible patients with no prior CPI exposure (n=62)

PD	SD	PR	CR	RESPONSES
11*	13	29	8	ORR: 59.68% (37/62) DCR: 80.65% (50/62)

RECIST 1.1 Best Overall Response: Waterfall Plot



Overview of Categories of TEAEs (N=123)

	No. of patients (%)	No of Events (n)				
		Total	Related to IMP / vaccine	Related to Nivo	Related to Ipi/Nivo	Related to needle free procedure
All AEs	129 (97)	2148	305	167	750	154
SAEs	80 (60.2)	152	12	13	97	0
AEs ≥ Grade 3	90 (67.7)	197	32	12	125	3
AEs leading to treatment discontinuation	16 (12)	56	4	0	29	0
AEs resulting in death	3 (2.2)	4	0	0	2	0

Summary of Most Frequently Reported TEAEs Considered Related to iSCIB1+ or SCIB1 (in >5% participants Treated with Either IMP)

Preferred Term	**iSCIB1+, n (%) patients [events]N=80**		**SCIB1, n (%) patients [events]** N=53	
	All	**Grade ≥3**	**All**	**Grade ≥3**
Injection site bruising	9 (11.3) [16]	0	6 (11.3) [11]	0
ALT increased	6 (7.5) [12]	3 (3.8) [3]	5 (9.4) [6]	1 (1.9) [1]
Fatigue	8 (10.0) [9]	0	9 (18.9) [10]	0
Rash	7 (8.8) [9]	1 (1.3) [1]	7 (17.0) [9]	1 (1.9) [1]
AST increased	3 (3.8) [8]	2 (2.5) [2]	3 (5.7) [4]	1 (1.9) [1]
Nausea	1 (1.3) [1]	0	3 (5.7) [8]	0
Eye Disorders	5 (0.7) [3]	0	5 (3.7) [5]	0

SCIB1-002: Serious Adverse Events in >1 Participant Overall, by SOC and PT (n =133)

Primary System Organ Class	Preferred Term	n (%) patients [events]
Endocrine disorders	Hypophysitis	5 (3.8) [5]
Gastrointestinal disorders	Colitis	12 (9.0) [13]
	Diarrhea	12 (9.0) [17]
	Enterocolitis	2 (1.5) [2]
	Immune-mediated enterocolitis	4 (3.0) [4]
	Mesenteric panniculitis	2 (1.5) [2]
	Vomiting	2 (1.5) [2]
General disorders & administration site conditions	Pyrexia	4 (3.0) [4]
Hepatobiliary disorders	Hepatitis	4 (3.0) [4]
	Immune-mediated hepatitis	6 (4.5) [8]
Infections and infestations	Pneumonia	4 (3.0) [4]
	Sepsis	2 (1.5) [2]
Investigations	ALT increased	2 (1.5) [2]
	Transaminases increased	6 (4.5) [6]
Metabolism and nutrition disorders	Hyperglycemia	4 (3.0) [4]
	Hypoglycemia	2 (1.5) [3]
	Hyponatremia	4 (3.0) [4]
Psychiatric disorders	Delirium	2 (1.5) [2]
Renal and urinary disorders	Acute kidney injury	2 (1.5) [2]
Respiratory, thoracic and mediastinal disorders	Cough	2 (1.5) [2]