Phase 1 Clinical Update of IMA203, an Autologous TCR T Targeting PRAME in Patients with PD1 Refractory Metastatic Melanoma

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Background and Key Takeaways

- Frequent recurrence and limited long-term survival with unresectable or metastatic melanoma highlight the critical need for new treatments that deliver deeper, more durable responses[1-3]
- IMA203 is a PRAME-directed TCR T-cell therapy engineered to recognize an intracellular PRAME-derived peptide presented by HLA-A*02:01 on the cell surface and initiate a potent and specific anti-tumor response[4]

- IMA203 exhibited favorable tolerability, with anticipated lymphodepletion-associated cytopenias, mostly mild-to-moderate CRS, infrequent ICANS, and no IMA203-related grade 5 events
- One-time infusion of IMA203 has promising clinical activity in heavily pretreated patients with metastatic melanoma (n=33):
  - cORR: 56% (18/32)
  - mDOR: 12.1 mo (range: 1.8+, 32.6+) at mFU of 13.4 mo
  - mPFS: 6.1 mo (range: 1.4, 34.0+) at mFU of 14.4 mo
  - mOS: 15.9 mo (range: 2.4, 34.2+) at mFU of 14.4 mo
- Encouraging activity was seen in both cutaneous melanoma (cORR 50%) and uveal melanoma (cORR 67%)

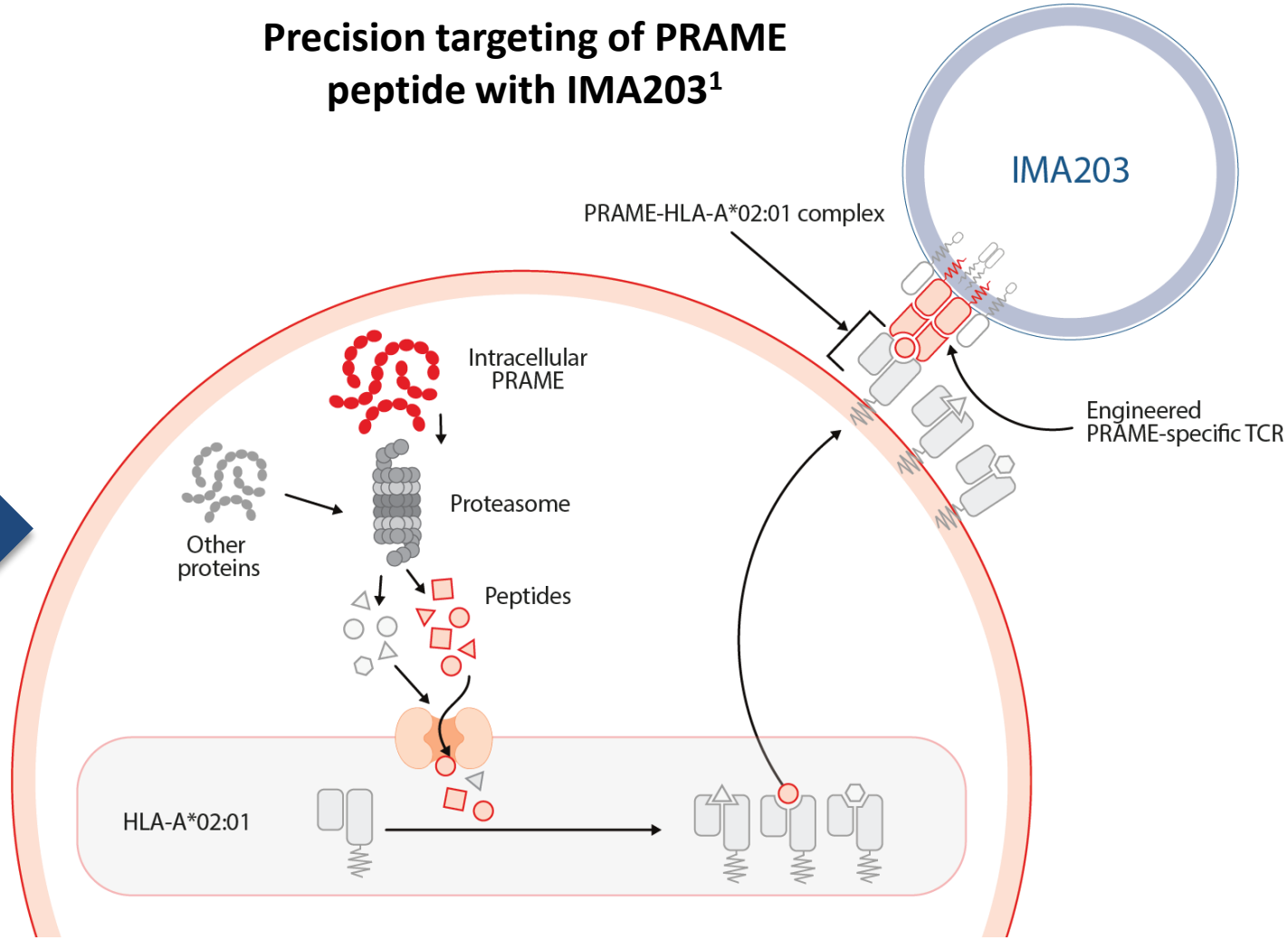
Data cutoff: April 7, 2025.
HLA, human leukocyte antigen; PRAME, preferentially expressed antigen in melanoma; TCR, T-cell receptor.
1. Mooradian MJ, et al. Oncology (Williston Park). 2019;33:141-148. 2. Hamid O, et al. Ann Oncol. 2019;30:582-588. 3. Goldinger SM, et al. Eur J Cancer. 2022;162:22-33. 4. Wermke M, et al. Na*t Med.* 2025; doi: 10.1038/s41591-025-03650-6 [online ahead of print].

IMA203 TCR T-cell Therapy is Designed to Target PRAME

PRAME is expressed in more than 50 cancers

PRAME prevalence in selected indications	
Indication	**% PRAME positive tumors[a]**
Cutaneous Melanoma	**95%**
Uterine Carcinoma	95%
Uterine Carcinosarcoma	95%
Synovial Sarcoma	95%
Uveal Melanoma	**90%**
Mucosal melanoma	90%
Ovarian Carcinoma	85%
Squamous Cell NSCLC	70%
TNBC	65%

Precision targeting of PRAME peptide with IMA203[1]



[a] Data on file: PRAME target prevalence is based on a proprietary mass spec-guided expression threshold applied to RNAseq data (approximate values; values between 95-100% shown as 95%).
HLA, human leukocyte antigen; NSCLC, non-small cell lung cancer; PRAME, preferentially expressed antigen in melanoma; TCR, T-cell receptor; TNBC, triple-negative breast cancer.

[1] Wermke M, et al. Nat *Med.* 2025; doi: 10.1038/s41591-025-03650-6 [online ahead of print].

Phase 1 Study Design: IMA203 in Advanced Solid Tumors Expressing PRAME

Key Objectives

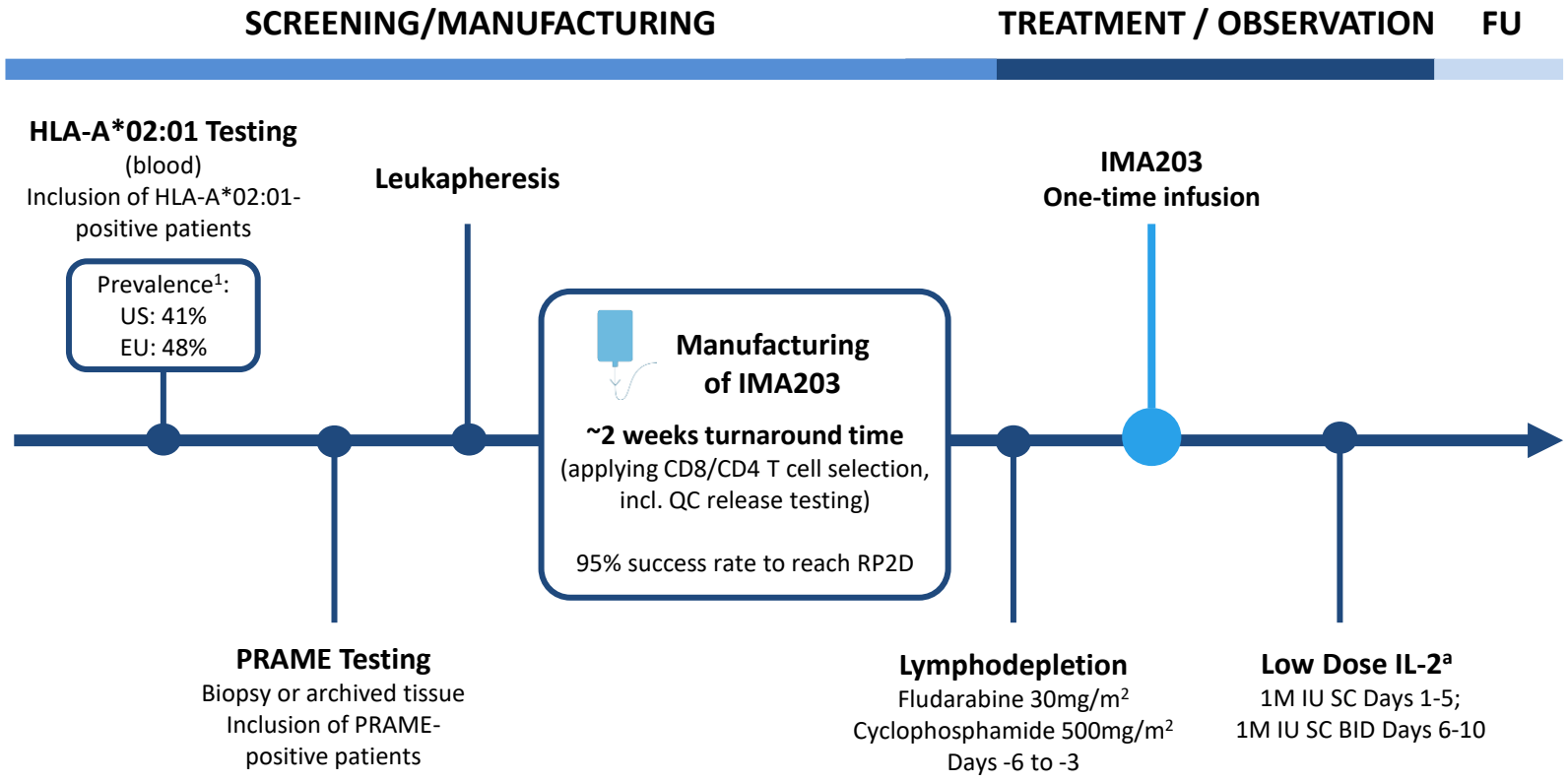
Primary:
- Tolerability
- Determination of RP2D (Phase 1a)

Secondary:
- IMA203 T cell engraftment, persistence
- Efficacy

Key Eligibility Criteria

- Confirmed advanced and/or metastatic solid tumor
- Patients ≥ 18 years of age
- ECOG performance status 0-1
- HLA-A*02:01 and PRAME positive
- Patients having received, or not been eligible for all available indicated SOC treatment
- Adequate organ function
- No active brain metastasis

Patient Journey



Data cutoff: April 7, 2025.

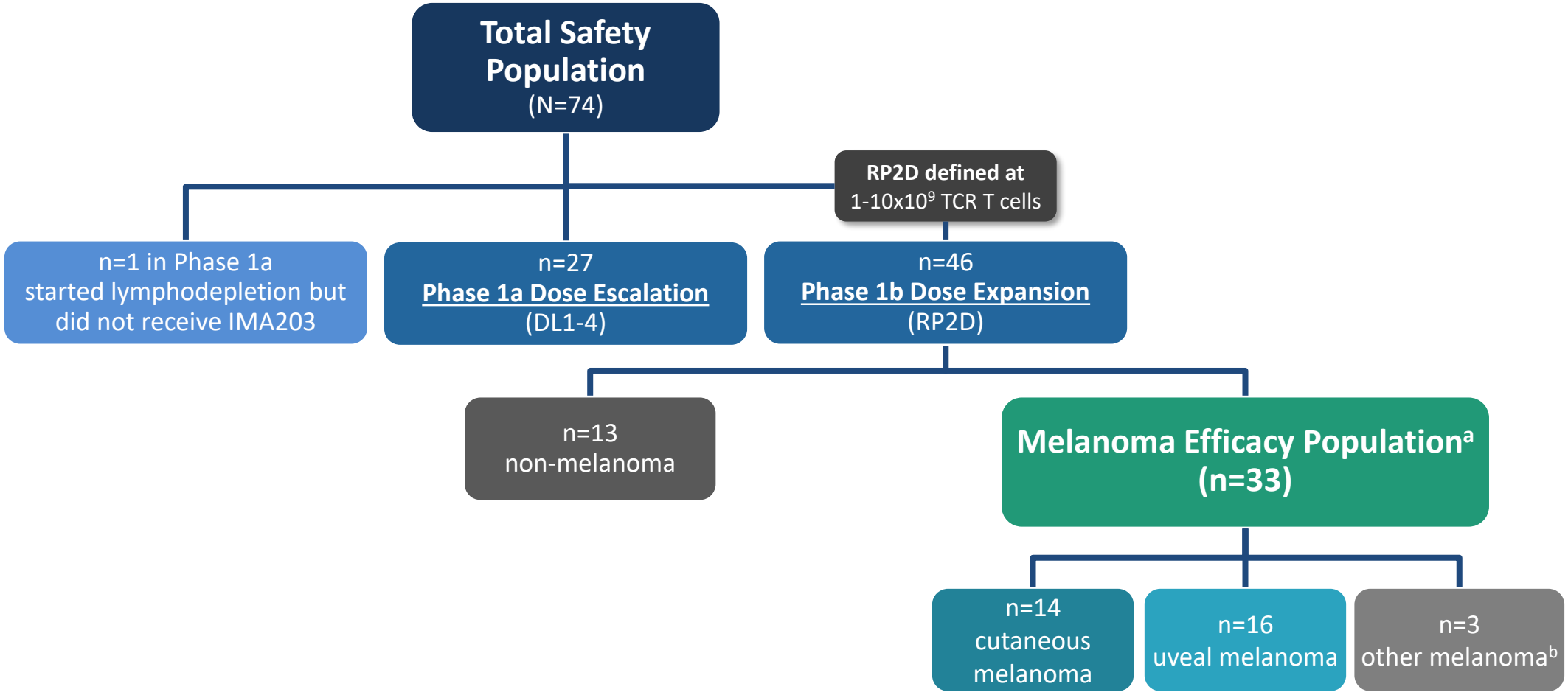
[a] Outpatient administration at investigator's discretion.

BID, twice daily; ECOG, Eastern Cooperative Oncology Group; FU, follow-up; IL, interleukin; IU, international unit; QC, quality control; RP2D, recommended phase 2 dose at 1-10x10^9 TCR T cells; SC, subcutaneous; SOC, standard of care.

1. Gragert et al. 2013 and census numbers.

Manufacturing success rate as of Apr 7, 2025

IMA203 Phase 1 Study: Patient Disposition



Data cutoff: April 7, 2025.

[a] Melanoma efficacy population excludes 1 patient with uveal melanoma with ongoing unconfirmed PR from cORR; [b] Mucosal melanoma n=2, melanoma of unknown primary n=1; RP2D: 1-10x10^9 TCR T cells; DL4: 0.2-1.2x10^9 TCR T cells/m^2 BSA.

BSA, body surface area; cORR, confirmed overall response rate; DL, dose level; PR, partial response; RP2D, recommended phase 2 dose; TCR, T-cell receptor.

IMA203 Phase 1 Study: Baseline Characteristics & Treatment Experience

Baseline Characteristics	Total Safety Population N=74	Cutaneous Melanoma n=14	Uveal Melanoma n=16	All Melanoma n=33
Age, median (range)	54 (18, 79)	54.5 (31, 79)	62 (32, 74)	57 (31, 79)
Female, %	52.7	21.4	62.5	48.5
Baseline ECOG status 1, %	51.4	35.7	43.8	39.4
Prior lines of systemic treatment, median (range)	**3** (0, 10)	**2.5** (1, 5)	**2** (0, 6)	**2** (0, 6)
Prior ICI treatment, median (range)	---	2 (1, 3)	1 (0, 4)	1 (0, 4)
≥1 line of ICI treatment, % (n/N)	---	100 (14/14)	62.5 (10/16)	81.8 (27/33)
Prior tebentafusp, % (n/N)	---	---	62.5 (10/16)	---
Elevated LDH at baseline, %	63.5	64.3	56.3	57.6
Median target lesion sum of diameter, mm (range)	116.1 (15.0, 309.8)	120.5 (15.0, 309.8)	101.6 (30.8, 210.0)	104.0 (15.0, 309.8)
Patients with **liver metastasis,** %	62.2	64.3	93.8	78.8
Patients with **brain metastasis,** %	12.2	0.0	0.0	3.0
Metastatic staging, % (CM, MM, UkM only)				
IIIb/IIIc/IVM1a	---	0.0	---	0.0
IVM1b/c/d	---	100.0	---	100.0
Metastatic staging, % (UM only)				
IVM1a	---	---	18.8	---
IVM1b/c/d	---	---	81.3	---
Treatment Experience	**Total Safety Population**	**Cutaneous Melanoma**	**Uveal Melanoma**	**All Melanoma**
Infused TCR T cell dose ($x10^9$), median (range)	2.34 (0.078, 10.20)	4.58 (1.30, 10.20)	3.94 (1.62, 8.43)	4.04 (1.30, 10.20)

Data cutoff: April 7, 2025.

CM, cutaneous melanoma; ECOG, Eastern Cooperative Oncology Group; ICI, immune checkpoint inhibitor; LDH, lactate dehydrogenase; MM, mucosal melanoma; TCR, T-cell receptor; UkM, melanoma of unknown primary; UM, uveal melanoma.

IMA203 Safety: Adverse Events Occurring in ≥20% of Patients
(Total Safety Population)

TEAEs in ≥20% of patients

Preferred terms, n (%)	N=74	
	Any grade	Grade ≥3
Blood and lymphatic system disorders	73 (98.6)	73 (98.6)
Neutropenia[a]	68 (91.9)	67 (90.5)
Anaemia	57 (77.0)	38 (51.4)
Thrombocytopenia[a]	50 (67.6)	27 (36.5)
Leukopenia	39 (52.7)	38 (51.4)
Lymphopenia	39 (52.7)	39 (52.7)
Gastrointestinal disorders	65 (87.8)	2 (2.7)
Nausea	45 (60.8)	0 (0.0)
Diarrhoea[a]	28 (37.8)	1 (1.4)
Vomiting	25 (33.8)	1 (1.4)
Constipation	23 (31.1)	0 (0.0)
General disorders and administration site conditions	49 (66.2)	2 (2.7)
Fatigue	29 (39.2)	1 (1.4)
Pyrexia	22 (29.7)	1 (1.4)
Edema peripheral	17 (23.0)	0 (0.0)
Investigations	35 (47.3)	10 (13.5)
Aspartate aminotransferase increased	29 (39.2)	5 (6.8)
Alanine aminotransferase increased	28 (37.8)	7 (9.5)
Blood creatinine increased	15 (20.3)	2 (2.7)
Skin and subcutaneous tissue disorders	35 (47.3)	6 (8.1)
Rash	18 (24.3)	0 (0.0)
Rash maculo-popular	18 (24.3)	6 (8.1)
Metabolism and nutrition disorders	33 (44.6)	6 (8.1)
Hyponatraemia	22 (29.7)	3 (4.1)
Hypokalaemia	21 (28.4)	3 (4.1)

Adverse events of special interest

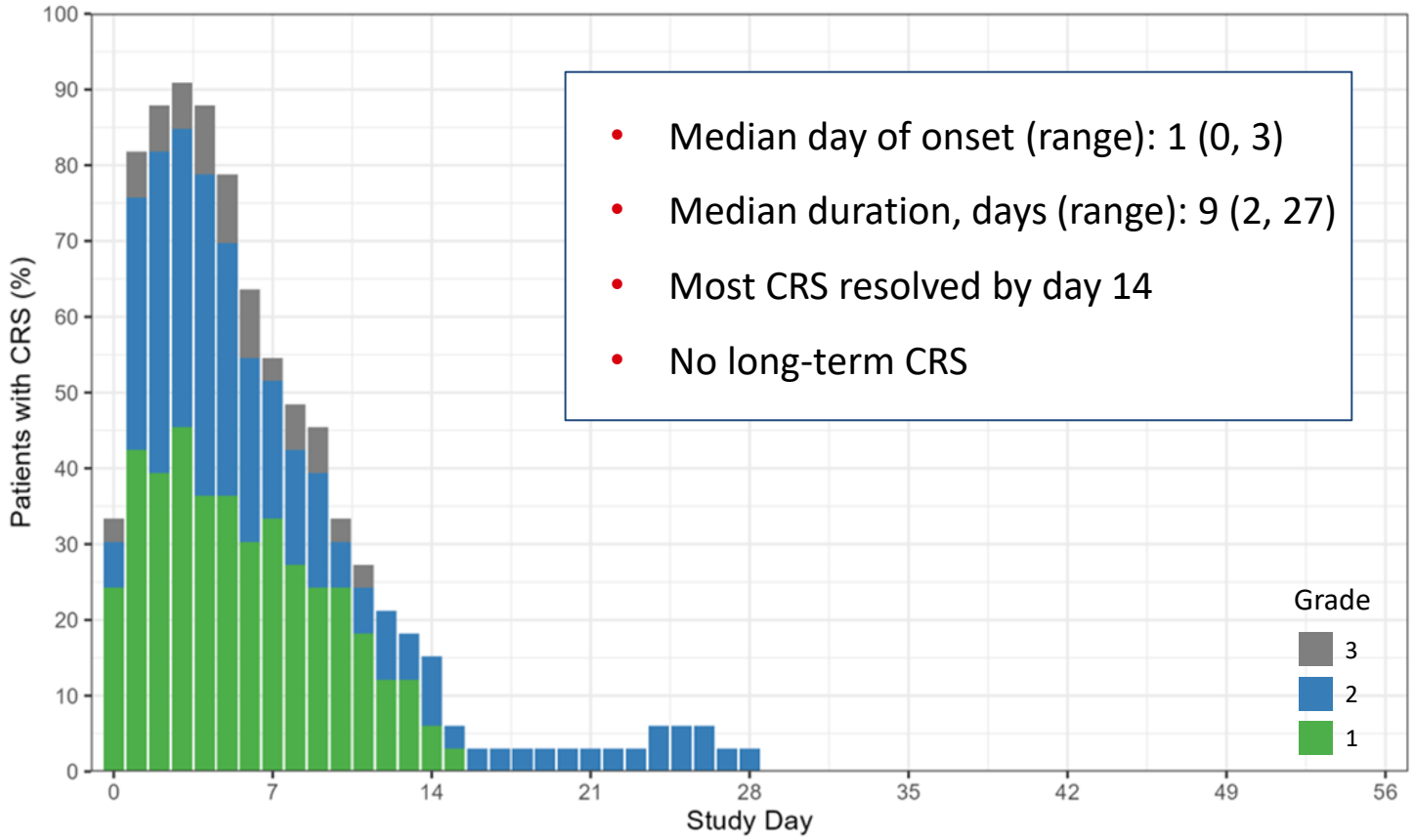
	N=74
CRS, any grade, n (%)	**70 (94.6)**
Grade 1	27 (36.5)
Grade 2	35 (47.3)
Grade 3[a]	8 (10.8)
Grade 4	0 (0.0)
Grade 5	0 (0.0)
ICANS, any grade, n (%)	**10 (13.5)**
Grade 1	4 (5.4)
Grade 2	3 (4.1)
Grade 3	3 (4.1)
Grade 4	0 (0.0)
Grade 5	0 (0.0)
HLH, any grade, n (%)	**2 (2.7)**
Grade 1	0 (0.0)
Grade 2	1 (1.4)
Grade 3	1 (1.4)
Grade 4	0 (0.0)
Grade 5	0 (0.0)

- Tolerability consistent with previous report
- Most frequent TEAEs were anticipated cytopenias associated with lymphodepletion
- Expected and manageable CRS, mostly Grade 1/2, consistent with mechanism of action
- Infrequent, manageable, and mostly mild ICANS
- No IMA203-related Grade 5 events
- Tolerability in the melanoma subset generally consistent with the full IMA203 tolerability profile

Data cutoff: April 7, 2025.
Patients are counted only once per adverse event and severity classification.
[a] Two patients with disease progression after first IMA203 infusion received exploratory second IMA203 infusion. They had these ≥ Grade 3 TEAEs only after second infusion, which are included in the table: First patient: CRS, diarrhea; Second patient: neutropenia, thrombocytopenia.
CRS, cytokine release syndrome; ICANS, immune effector cell-associated neurotoxicity syndrome; HLH, hemophagocytic lymphohistiocytosis; TEAE, treatment-emergent adverse event.

CRS Events and Interventions After IMA203 Infusion in Melanoma Efficacy Population

CRS Dynamics



- Median day of onset (range): 1 (0, 3)
- Median duration, days (range): 9 (2, 27)
- Most CRS resolved by day 14
- No long-term CRS

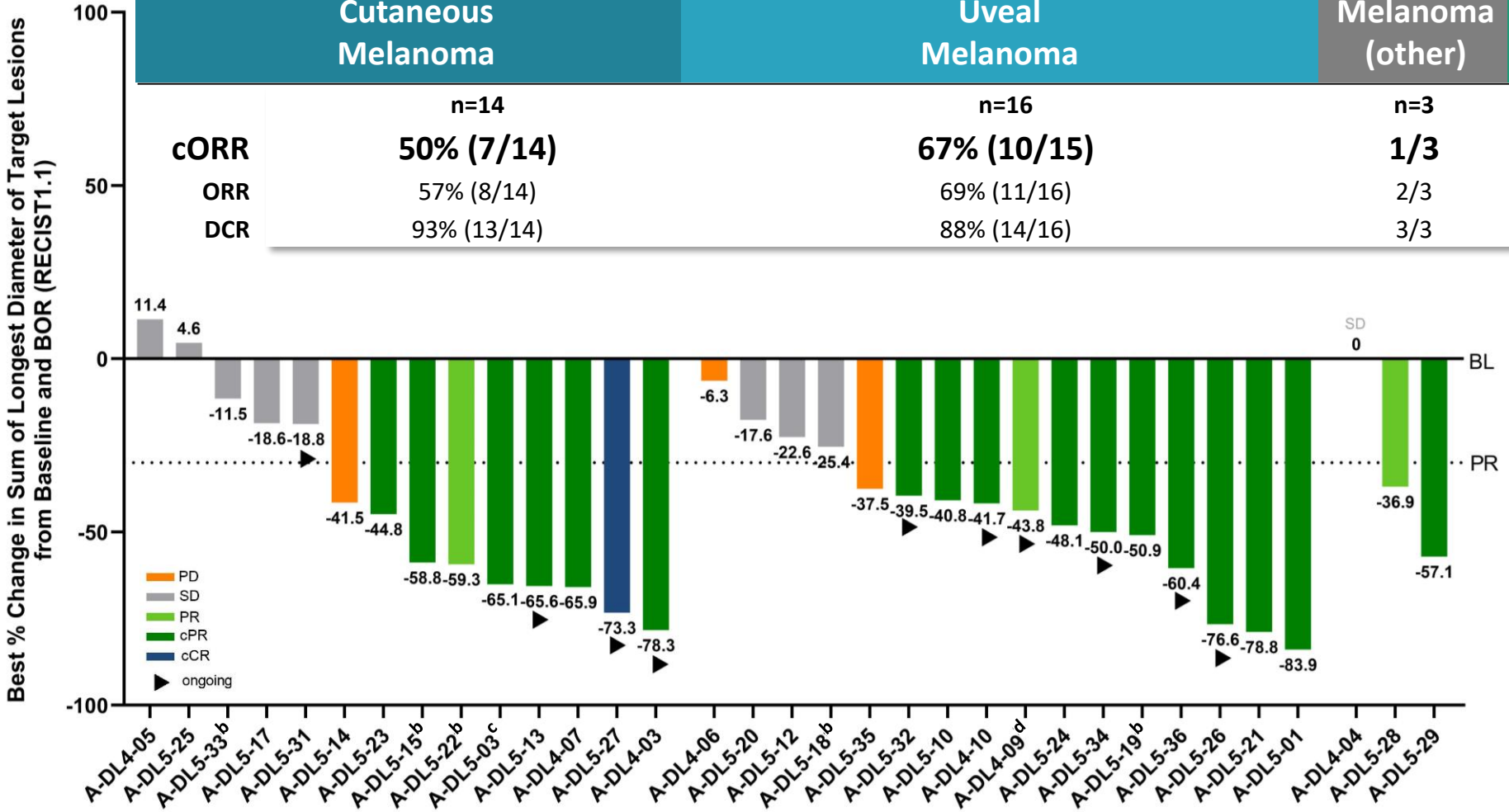
CRS Interventions

	n=33
Interventions, n (%)	24 (72.7)
Tocilizumab	23 (69.7)
Steroids	11 (33.3)

Data cutoff: April 7, 2025.
CRS, cytokine release syndrome.

IMA203: Best Overall Response in Melanoma Efficacy Population

	Cutaneous Melanoma	Uveal Melanoma	Melanoma (other)	All Melanoma[a]
	n=14	n=16	n=3	n=33
cORR	**50% (7/14)**	**67% (10/15)**	**1/3**	**56% (18/32)**
ORR	57% (8/14)	69% (11/16)	2/3	64 % (21/33)
DCR	93% (13/14)	88% (14/16)	3/3	91% (30/33)



Data cutoff: April 7, 2025.

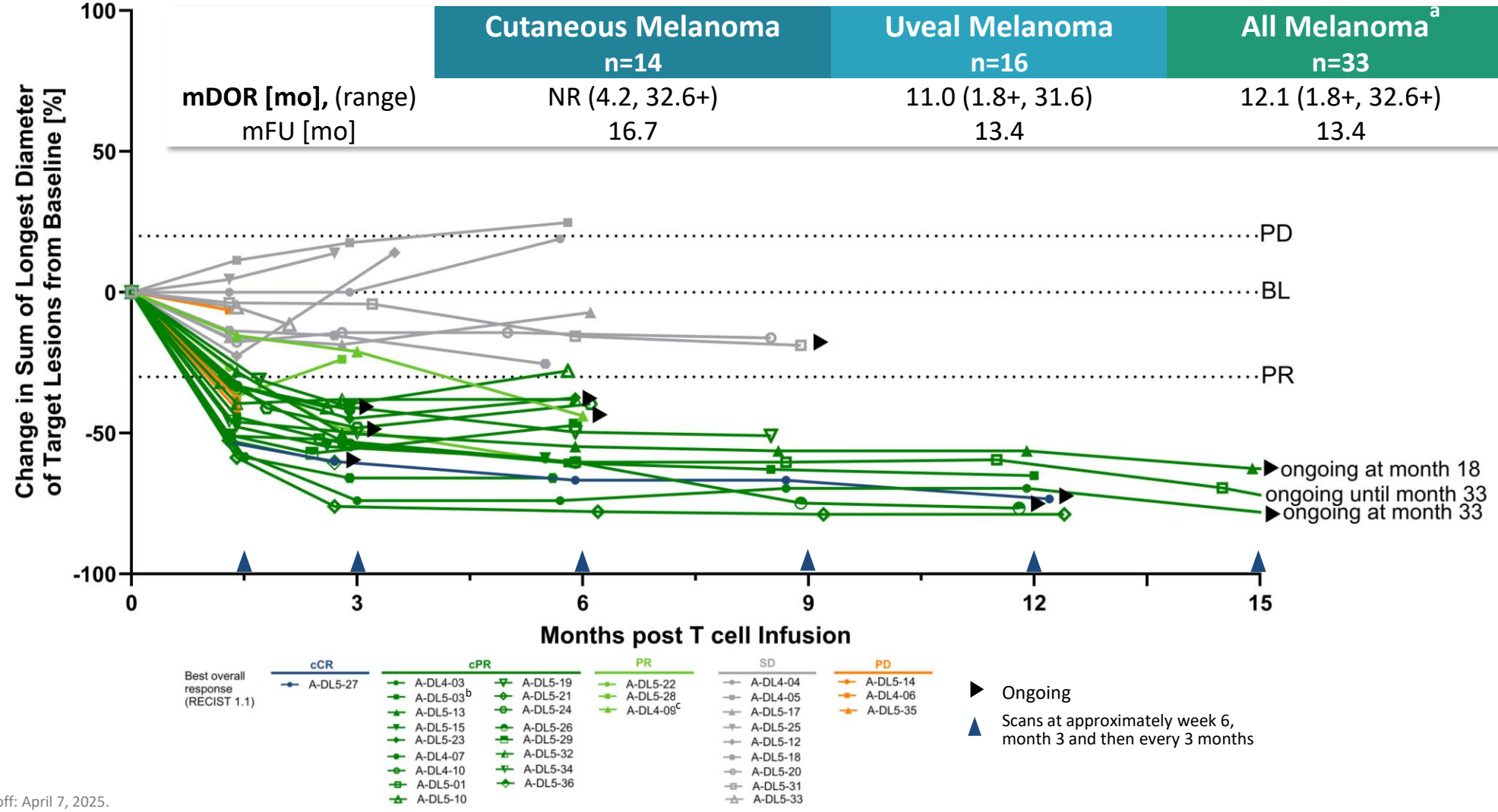
[a] Includes melanoma (other) n=3: mucosal melanoma n=2, melanoma of unknown primary n=1; Melanoma efficacy population excludes 1 uveal melanoma patient with ongoing unconfirmed PR from cORR

[b] Maximum change of target lesions and RECIST1.1 response at different timepoints. [c] Patient out of study due to PD (external assessment); [d] Patient out of study at data-cut (withdrew consent)

BL, baseline; BOR, best overall response; (c)CR, (confirmed) complete response; (c)ORR, (confirmed) objective response rate; (c)PR, (confirmed) partial response; DCR, disease control rate at week 6; PD, progressive disease; RECIST, Response Evaluation Criteria in Solid Tumors; SD, stable disease.

IMA203: Duration of Response in Melanoma Efficacy Population

	Cutaneous Melanoma n=14	Uveal Melanoma n=16	All Melanoma[a] n=33
mDOR [mo], (range)	NR (4.2, 32.6+)	11.0 (1.8+, 31.6)	12.1 (1.8+, 32.6+)
mFU [mo]	16.7	13.4	13.4



Data cutoff: April 7, 2025.

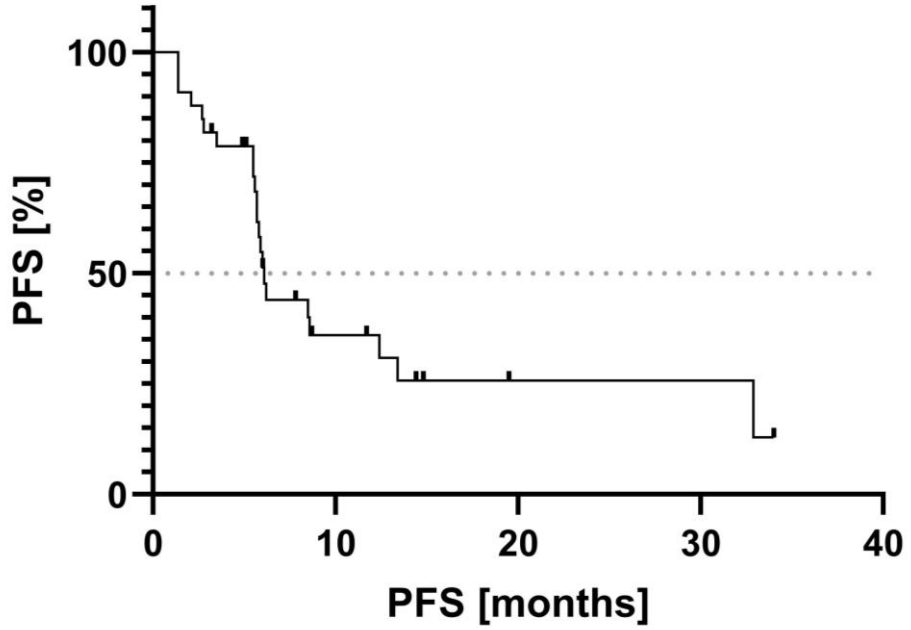
[a] Includes melanoma (other) n=3: mucosal melanoma n=2, melanoma of unknown origin n=1; [b] Patient out of study due to PD (external assessment); [c] Patient out of study at data-cut (withdrew consent)

BL, baseline; (c)CR, (confirmed) complete response; (c)PR, (confirmed) partial response; mDOR, median duration of response; mFU, median follow-up; PD, progressive disease; RECIST, Response Evaluation Criteria in Solid Tumors; SD, stable disease.

IMA203: Survival Outcomes in Melanoma Efficacy Population

Median Progression Free Survival

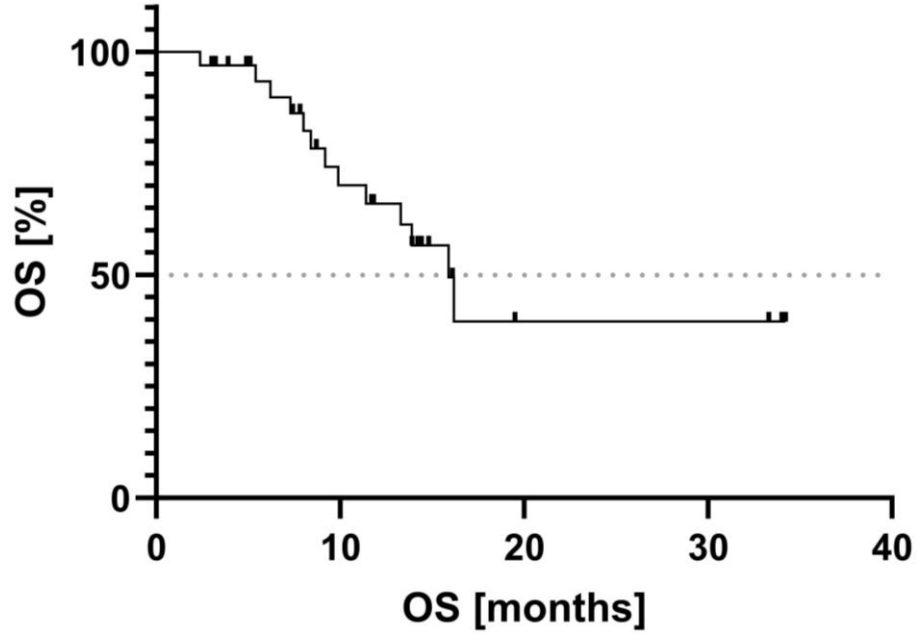
	Cutaneous Melanoma n=14	Uveal Melanoma n=16	All Melanoma[a] n=33
mPFS [mo] (range)	6.0 (1.4 , 34.0+)	8.5 (1.4, 32.9)	**6.1** (1.4, 34.0+)
mFU [mo]	14.4	8.7	14.4



6-month PFS rate: 53%
12-month PFS rate: 27%

Median Overall Survival

	Cutaneous Melanoma n=14	Uveal Melanoma n=16	All Melanoma[a] n=33
mOS [mo] (range)	13.9 (2.4, 34.0+)	16.2 (3.2+, 34.2+)	**15.9** (2.4, 34.2+)
mFU [mo]	14.4	14.5	14.4



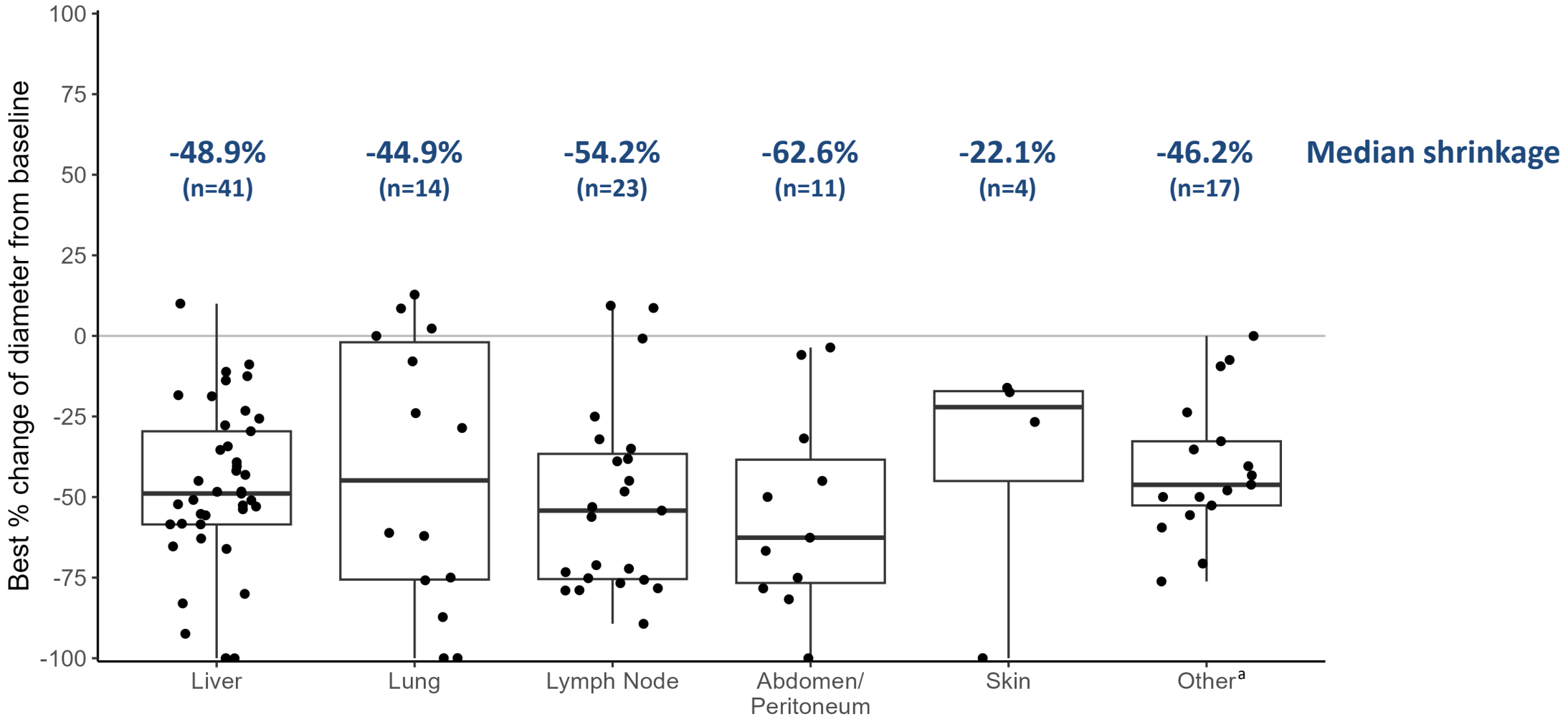
12-month OS rate: 61%

Data cutoff: April 7, 2025.

[a] Includes melanoma (other) n=3: mucosal melanoma n=2, melanoma of unknown origin n=1; PFS and OS censored at data-cut; PFS and OS rate shown as % of evaluable patients at indicated timepoint.

mFU, median follow-up; mOS, median overall survival; mPFS, median progression-free survival.

IMA203: Responses of Metastases Throughout the Body in Melanoma Efficacy Population



Data cutoff: April 7, 2025.

[a] Other: brain, kidney, pelvis, pericardium, pleura, bone, adrenal, retroperitoneum, rectum, soft tissue, gluteal, dorsal.

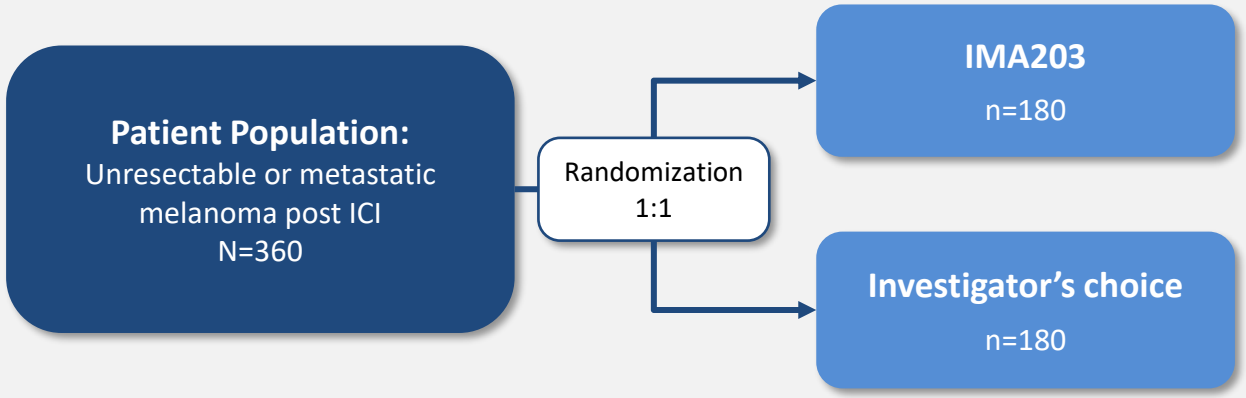
Conclusions

- IMA203 PRAME-directed TCR T-cell therapy exhibited favorable tolerability, with anticipated lymphodepletion-associated cytopenias, mostly mild-to-moderate CRS, infrequent ICANS, and no IMA203-related grade 5 events
- One-time infusion of IMA203 has promising clinical activity in heavily pretreated patients with metastatic melanoma (n=33):
  - cORR: 56% (18/32)
  - mDOR: 12.1 mo (range: 1.8+, 32.6+) at mFU of 13.4 mo
  - mPFS: 6.1 mo (range: 1.4, 34.0+) at mFU of 14.4 mo
  - mOS: 15.9 mo (range: 2.4, 34.2+) at mFU of 14.4 mo
- Encouraging activity was observed in both cutaneous melanoma (cORR 50%) and uveal melanoma (cORR 67%)
- Given its promising Phase 1 profile with high PRAME prevalence in melanoma, a registration-directed Phase 3 trial (SUPRAME; NCT06743126) is underway in previously treated advanced or metastatic cutaneous melanoma

Data cutoff: April 7, 2025.
cORR, confirmed objective response rate; CRS, cytokine release syndrome; ICANS, Immune effector cell-associated neurotoxicity syndrome; mDOR, median duration of response; mFU, median follow-up; mPFS, median progression-free survival; mOS, median overall survival.

SUPRAME: A Randomized Phase 3 Trial of IMA203 PRAME-directed TCR T-cell Therapy vs Investigator's Choice in Unresectable or Metastatic Melanoma post ICI

Actively Enrolling, >50 Sites Planned across North America and Europe



Primary Endpoint
- PFS

Key Secondary Endpoint
- Overall survival

Secondary Endpoints
- **Efficacy:** ORR
- **Safety:** TESAEs, AEs of special interest
- **Quality of life:** EORTC QLQ-C30 and EQ-5D-5L

Trial-in-progress Poster

Abstract #: TPS2673

Title: "SUPRAME: A phase 3 trial comparing IMA203, an engineered T-cell receptor expressing T-cell therapy (TCR T) vs investigator's choice in patients with previously treated advanced cutaneous melanoma"

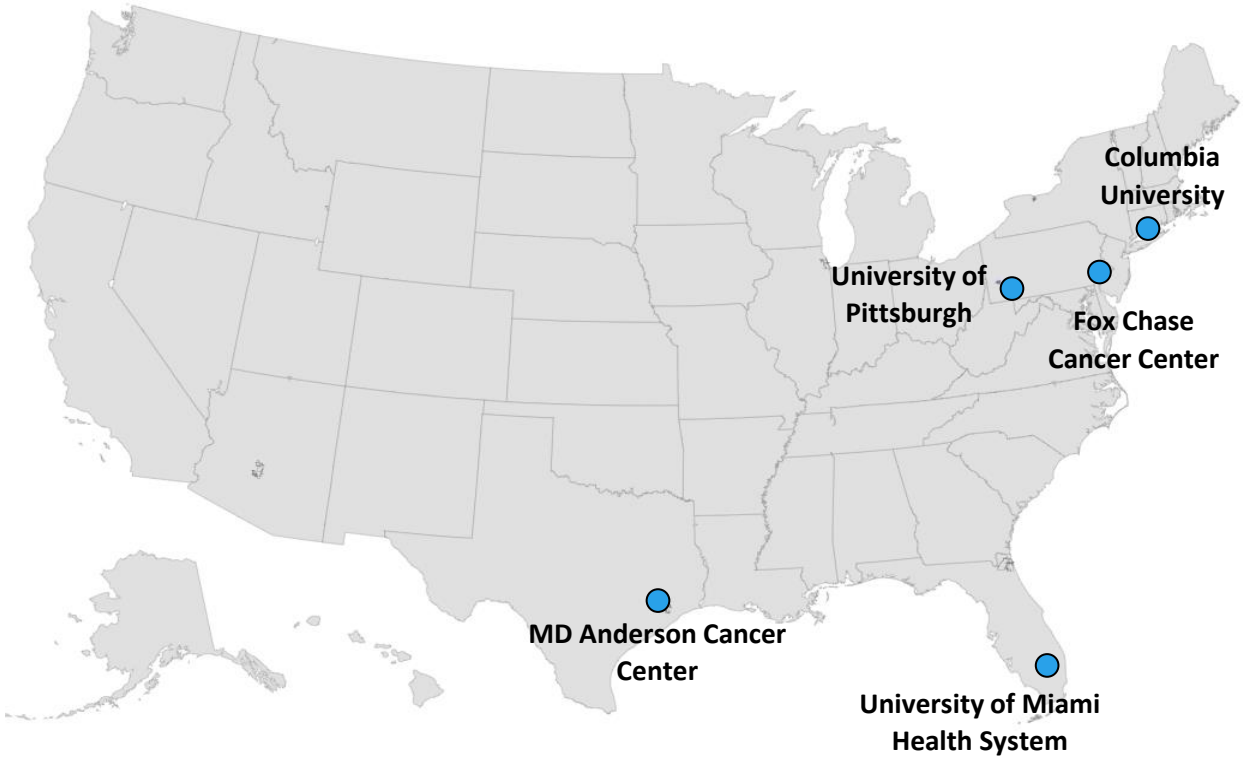
Date & Time: Monday, June 2, 1:30 PM – 4:30 PM CDT

Presenter: Jason J. Luke, MD, FACP, FASCO

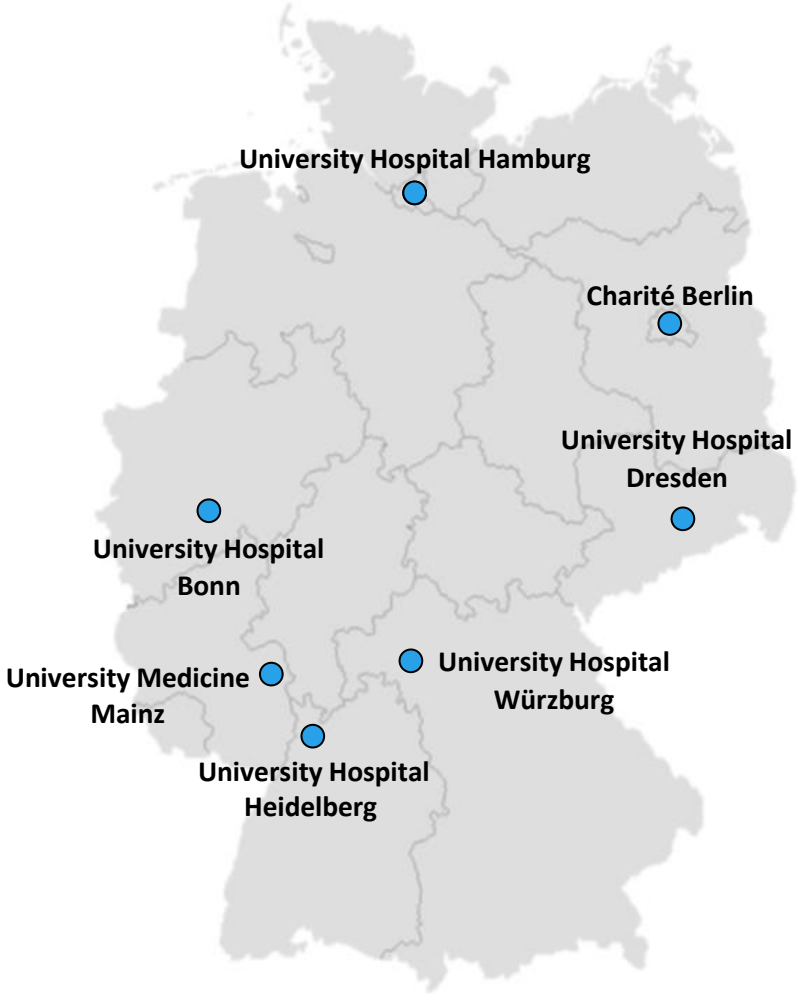
AE, adverse event; EORTC, European Organization for Research and Treatment of Cancer; EQ-5D-5L, European Quality of Life 5 Dimensions 5 Level; ICI, immune checkpoint inhibitor; ORR, objective response rate; PFS, progression-free survival; QLQ-C30, Core Quality of Life questionnaire; TESAE, treatment-emergent serious adverse event.

Thank You to the Patients, their Families and the Participating Clinical Trial Sites

United States



Germany



IMA203 Phase 1 Study
Sponsor: Immatics