Enhanced Pharmacology Data of Next-generation IMA203CD8 TCR-T Monotherapy Targeting PRAME

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Declaration of Interests

Martin Wermke

Financial Interests

Amgen, Invited Speaker, Personal
AstraZeneca, Advisory Board, Personal
Bayer, Advisory Board, Personal
Boehringer Ingelheim, Advisory Board, Personal
Boehringer-Ingelheim, Invited Speaker, Personal
Bristol Myers Squibb, Advisory Board, Personal
Daiichi Sankyo, Advisory Board, Personal
EMD Merck Serono, Invited Speaker, Personal
GWT TUD GmbH, Invited Speaker, Personal
ImCheck Therapeutics, Advisory Board, Personal
Immatics, Advisory Board, Personal
ISA Therapeutics, Other, Personal, Member of DSMC
Janssen, Invited Speaker, Personal
Novartis, Invited Speaker, Personal
Novartis, Advisory Board, Personal
Pfizer, Advisory Board, Personal
Regeneron, Advisory Board, Personal
Synlab GmbH, Invited Speaker, Personal
Tacalyx GmbH, Advisory Board, Personal
Zymeworks, Advisory Board, Personal
Roche, Funding, Institutional, Financial interest

Non-Financial Interests

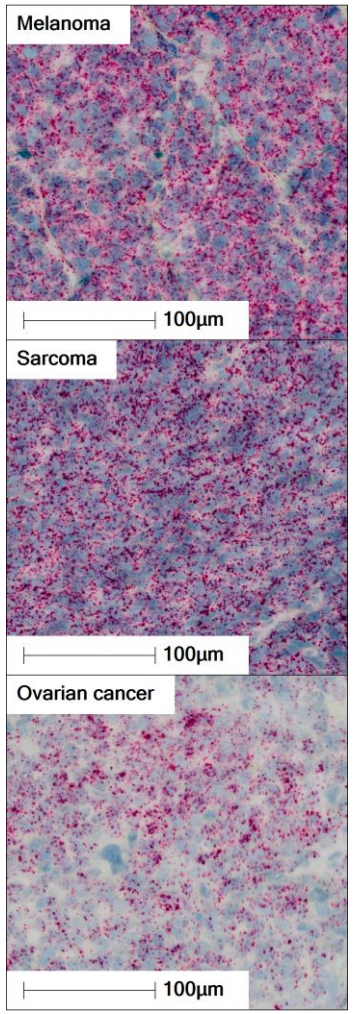
AstraZeneca, Other, Congress Travel Cost Support
Boehringer Ingelheim, Other, Congress Travel Cost Support
Daiichi Sankyo, Other, Congress Travel Cost Support
EMD Merck Serono, Other, Congress Travel Cost Support
Immatics, Other, Congress Travel Cost Support
Iovance, Other, Congress Travel Cost Support
Janssen, Other, Congress Travel Cost Support

The Multi-Cancer Opportunity of PRAME

PRAME Prevalences

Indication	% PRAME positive patients
Uterine Carcinosarcoma	100%
Sarcoma Subtypes	up to 100%
Uterine Carcinoma	95%
Cut. Melanoma	95%
Uveal Melanoma[2]	90%
Ovarian Carcinoma	85%
Squamous NSCLC	70%
TNBC	65%
Small Cell Lung Cancer	45%
Kidney Carcinoma Subtypes	up to 40%
Cholangiocarcinoma	35%
Adeno NSCLC	25%
Breast Carcinoma	25%
HNSCC	25%
Esophageal Carcinoma	25%
HCC	20%
Bladder Carcinoma	20%

PRAME RNA detection (ISH)

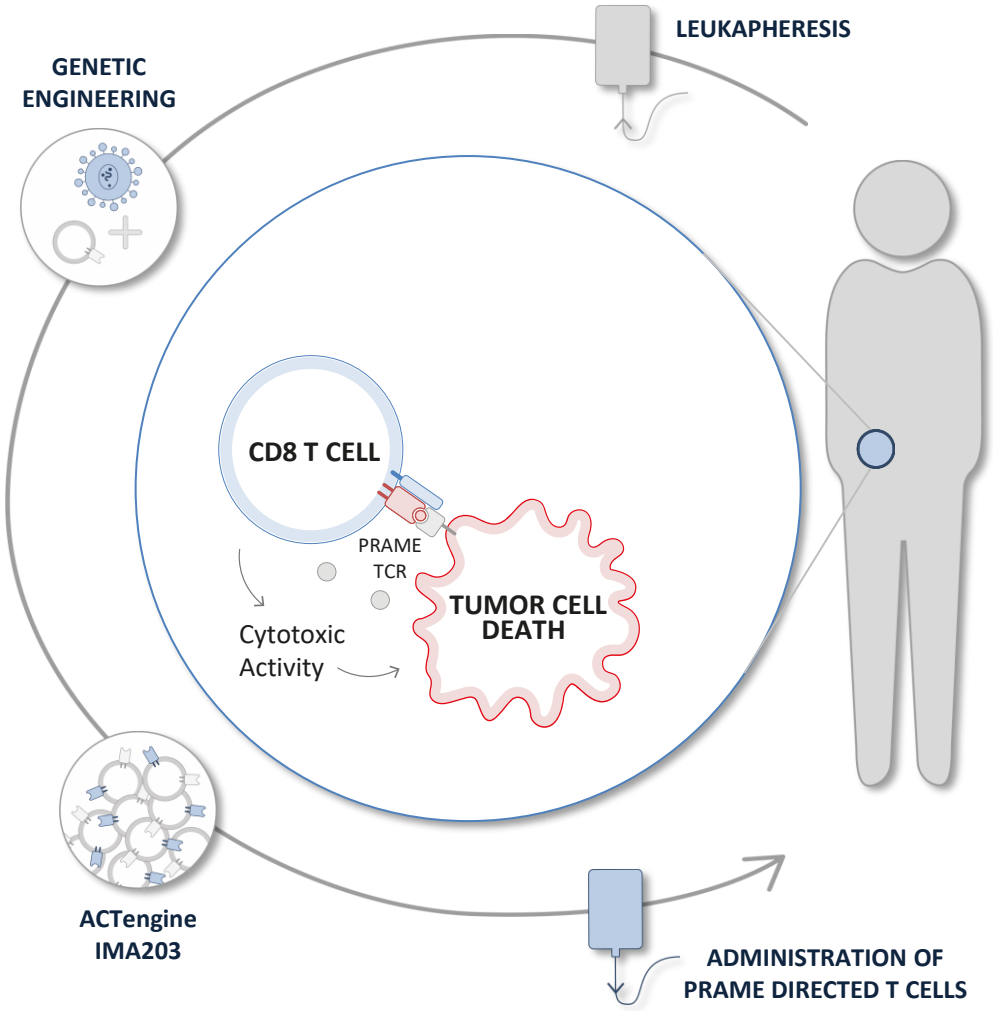


PRAME fulfills all properties of an ideal target for TCR-based therapies

- High prevalence[1]
- High target density
- Homogeneous expression
- “Clean” expression profile[3]

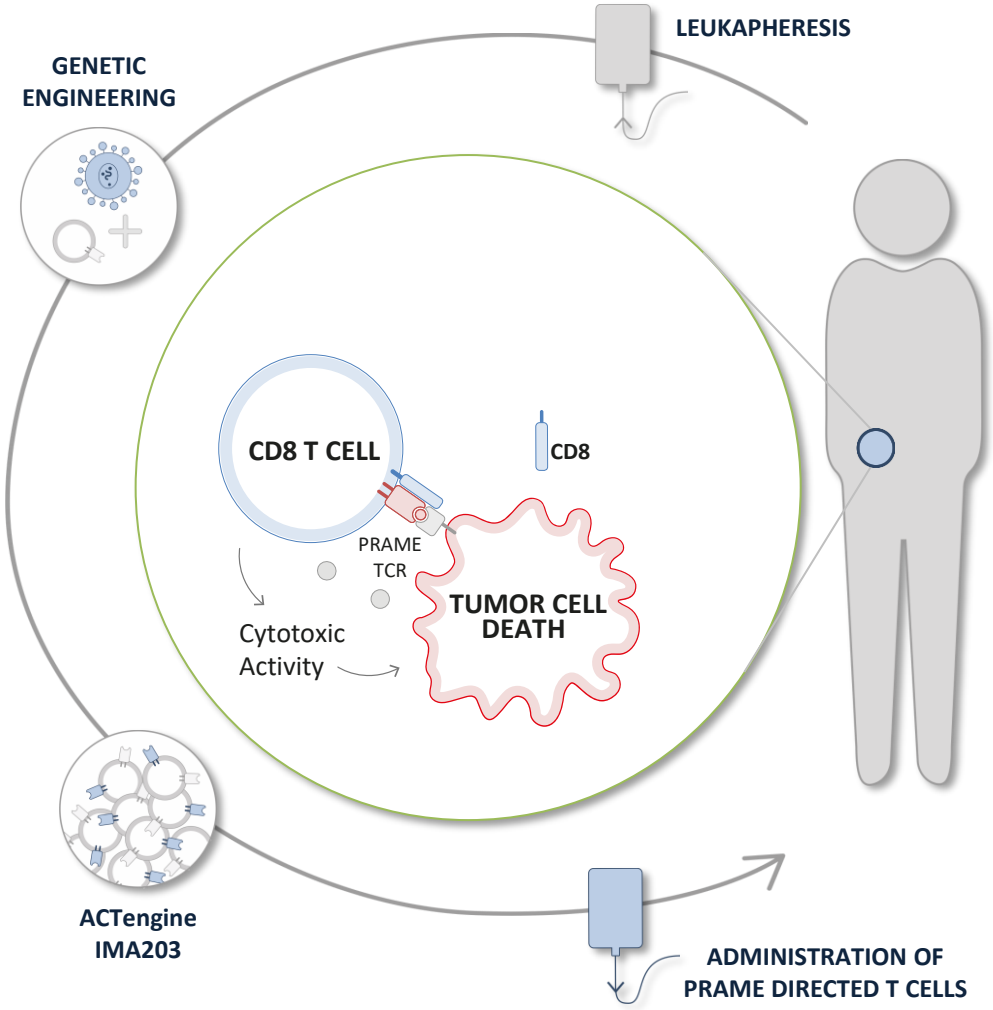
[1]Target prevalence based on TCGA (SCLC: in-house) RNAseq data combined with proprietary mass spec-guided RNA expression threshold; [2]Uveal melanoma target prevalence based on IMADetect qPCR testing of screening biopsies from 61 trial patients; [3]presented at SITC 2022

IMA203 – Mechanism of Action



- Autologous T cells transduced with PRAME specific TCR
- Targets HLA-A*02:01-presented PRAME peptides
- Engineered $CD8^+$ T cells designed to specifically recognize and destroy PRAME-positive tumor cells

IMA203CD8 (GEN2) – IMA203 TCR-T Monotherapy Leveraging CD8 and CD4 cells



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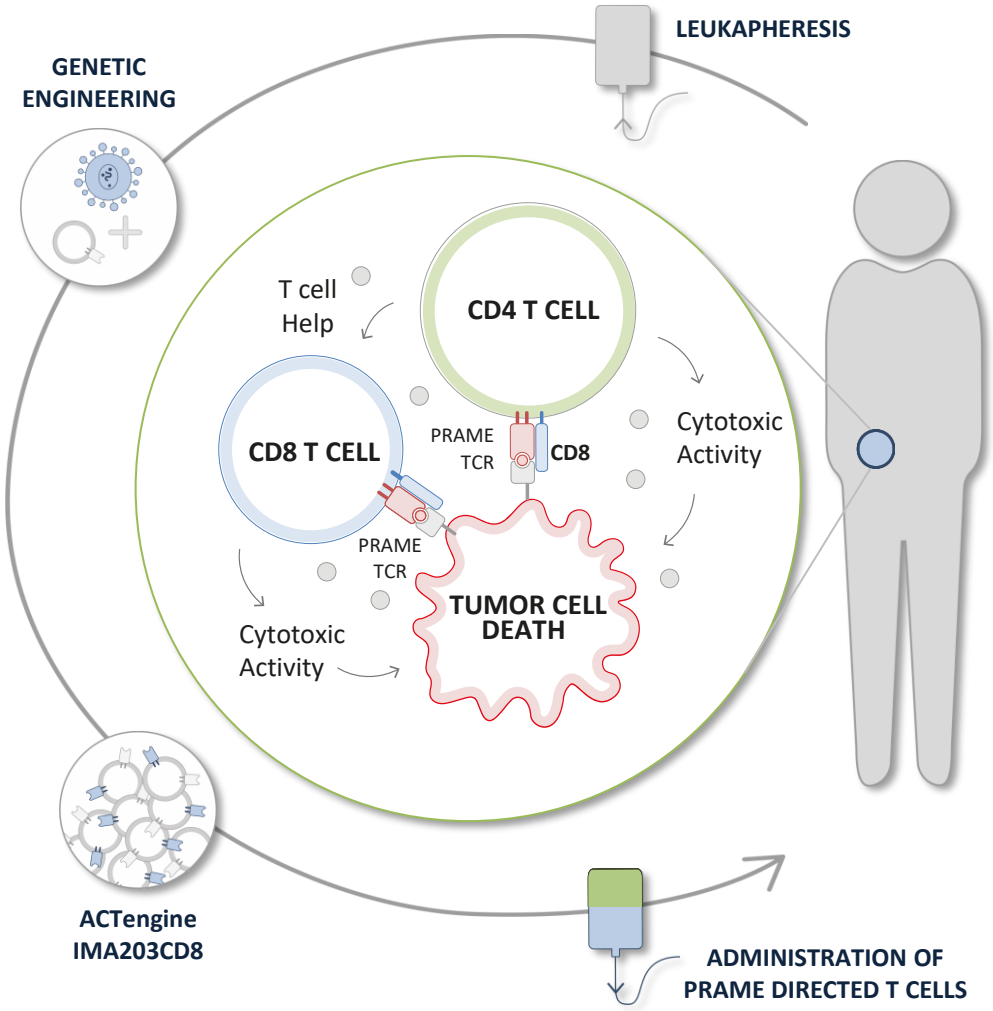


- Autologous T cells transduced with PRAME specific TCR
- Targets HLA-A*02:01-presented PRAME peptides
- Engineered CD8⁺ T cells designed to specifically recognize and destroy PRAME-positive tumor cells
- Co-transduction of CD8αβ alongside PRAME TCR
- Adds functional CD4⁺ T cells designed to boost activity/cytotoxicity
- Proof of concept from preclinical experiments[1] and CD19 CAR T cell studies in leukemia[2]

[1] Data not shown here, published in Bajwa *et al.* 2021 Journal for Immunotherapy of Cancer; [2] Melenhorst *et al.* 2022 Nature, Bai *et al.* 2022 Science Advances

Phase 1 Trial Design in Advanced Solid Tumors

IMA203

Concurrent Session 106c: Oral Abstract Session

Friday, Nov. 8, 2024

1:45–3:20 p.m.

Grand Ballroom A

Total Safety Population (N=70)

Phase 1a Dose Escalation: Dose Level 1-4 (N=[illegible])

Phase 1b Dose Expansion: Dose Level 4/5(N=42[2])

Efficacy Population (N=41[3])

IMA203CD8

Phase 1a Dose Escalation

DL3 (N=5)

DL4a[1] (N=33)
Cleared for safety, defined as provisional MTD

DL4b (N=4)

DL4c[2] Without IL-2 (N=2)

DL4c[2] With IL-2 (planned)

Dose Escalation with and without IL-2 ongoing

Data cut-off Sep 30, 2024; [1] DL4a cleared in Dec 2023; [2] DLTs at DL4b triggered modifications of the eligibility criteria, adapted patient population is treated with DL4c.

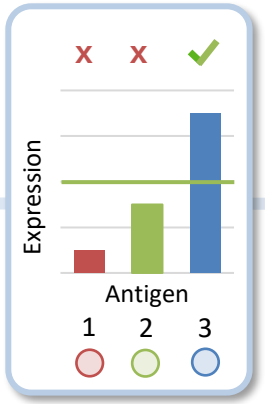
Patient Flow

SCREENING/MANUFACTURING | TREATMENT / OBSERVATION | LTFU

HLA-A*02 Testing

Leukapheresis

Lymphodepletion
Fludarabine 30mg/m^2 and Cyclophosphamide 500mg/m^2 for 4 days



Target Profiling
IMADetect mRNA assay using Immatics' MS-guided threshold; Biopsy or archived tissue

ACTengine Manufacturing
by Immatics

IMA203CD8

Process time of 14 days
7-day manufacturing process applying CD8/CD4 T cell selection
7-day QC release testing

Low Dose IL-2
1m IU, daily d1-5 and twice daily d6-10

Escalation cohorts with and without IL-2 starting from cohort DL4c

ACTengine IMA203CD8 Infusion

Key Objectives and Eligibility Criteria

Key Objectives

Primary: Tolerability

- Investigation of Adverse Events
- Determination of a RP2D

Secondary: Biological and Clinical Activity

- IMA203CD8 T cell engraftment, persistence
- Objective responses (RECIST1.1) & Duration of Response

Exploratory

- IMA203CD8 tumor infiltration

Key Eligibility Criteria

- Patients ≥ 18 years of age with ECOG 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
- No serious autoimmune disorder
- No immunosuppressive medication

Patient Characteristics

	Total Safety Population	Efficacy Population
Number of patients	N=44[1]	N=41[2]
Prior lines of systemic treatment (median, min, max)	3 (0, 8)	3 (0, 8)
LDH at baseline >1 x ULN [% of patients]	47.7	43.9
Baseline tumor burden Median target lesion sum of diameter [mm] (min, max)	84.5 (12.4, 434.4)	83.0 (12.4, 434.4)
With liver/brain lesions at baseline [% of patients]	45.5	43.9
Infused dose levels TCR-T cells/m^2 BSA [$x10^9$]	DL3: 0.2-0.48 DL4a: 0.481-0.8 DL4b: 0.801-1.2 DL4c: 0.801-1.2	DL3: 0.2-0.48 DL4a: 0.481-0.8 DL4b: 0.801-1.2 DL4c: 0.801-1.2
Total infused dose TCR-T cells [$x10^9$] (median, min, max)	1.48 (0.44, 2.05)	1.47 (0.44, 2.05)

Data cut-off Sep 30, 2024; [1] All patients who started lymphodepletion. [2] All infused patients with at least one tumor assessment postbaseline.

Tolerability Profile Across Dose Levels

TEAEs by maximum severity for all patients (N=44)

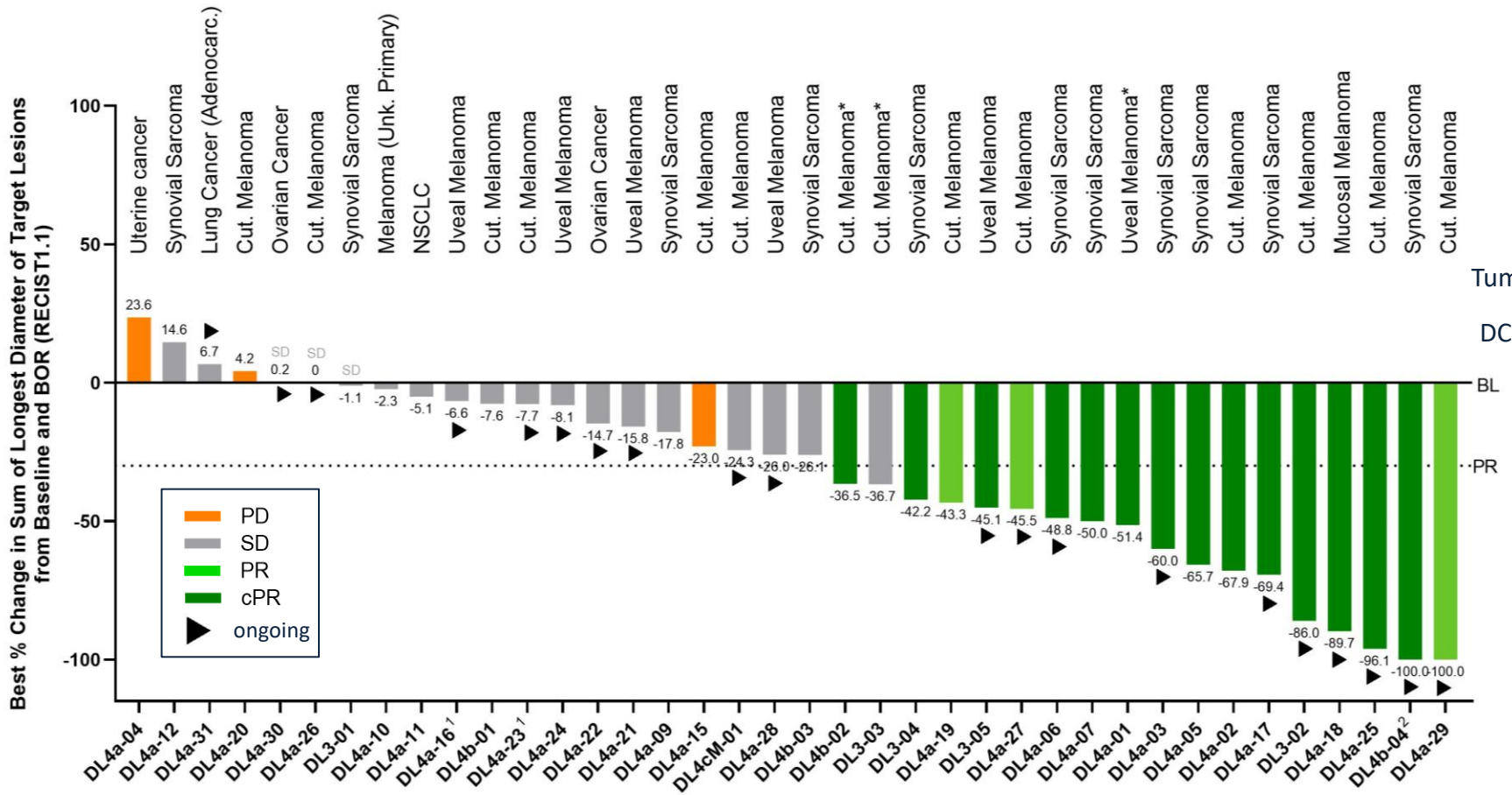
Adverse event (System organ class, preferred term)	≥ Grade 3 No.	≥ Grade 3 %
Patients with any adverse event	**44**	**100.0**
Adverse events of special interest	**7**	**15.9**
Cytokine release syndrome[1]	6	13.6
Immune effector cell-associated neurotoxicity syndrome	1	2.3
Blood and lymphatic system disorders	**44**	**100.0**
Neutropenia	40	90.9
Anaemia	25	56.8
Lymphopenia	25	56.8
Thrombocytopenia	15	34.1
Leukopenia	11	25.0
Febrile neutropenia	2	4.5
Investigations	**9**	**20.5**
Alanine aminotransferase increased	5	11.4
Aspartate aminotransferase increased	5	11.4
Blood creatinine increased	2	4.5
Blood alkaline phosphatase increased	1	2.3
Blood bilirubin increased	1	2.3
Gamma-glutamyltransferase increased	1	2.3
Metabolism and nutrition disorders	**6**	**13.6**
Hypophosphataemia	2	4.5
Acidosis	1	2.3
Decreased appetite	1	2.3
Hyperglycaemia	1	2.3
Hypermagnesaemia	1	2.3
Hypoalbuminaemia	1	2.3
General disorders and administration site conditions	**5**	**11.4**
Fatigue	5	11.4
Oedema peripheral	1	2.3
Musculoskeletal and connective tissue disorders	**5**	**11.4**
Bone pain	3	6.8
Myalgia	2	4.5
Back pain	2	4.5
Arthralgia	1	2.3

Adverse event (System organ class, preferred term)	≥ Grade 3 No.	≥ Grade 3 %
… table continued		
Immune system disorders	**4**	**9.1**
Haemophagocytic lymphohistiocytosis[2]	4	9.1
Infections and infestations	**4**	**9.1**
Pneumonia	2	4.5
Infection	1	2.3
Sepsis[3]	1	2.3
Systemic candida	1	2.3
Gastrointestinal disorders	**3**	**6.8**
Diarrhoea	2	4.5
Abdominal pain	1	2.3
Skin and subcutaneous tissue disorders	**3**	**6.8**
Rash	2	4.5
Alopecia	1	2.3
Rash maculo-papular	1	2.3
Vascular disorders	**3**	**6.8**
Hypertension	3	6.8
Nervous system disorders	**2**	**4.5**
Neurotoxicity[2]	1	2.3
Syncope	1	2.3
Renal and urinary disorders	**2**	**4.5**
Acute kidney injury	1	2.3
Urinary tract obstruction	1	2.3
Hepatobiliary disorders	**1**	**2.3**
Hepatic function abnormal	1	2.3
Reproductive system and breast disorders	**1**	**2.3**
Pelvic pain	1	2.3

Data cut-off Sep 30, 2024; All treatment-emergent adverse events (TEAEs) with ≥ Grade 3 regardless of relatedness to study treatment that occurred in at least 1 patient are presented; [1] DLT: Dose limiting toxicity in patient DL4b-04. [2] DLTs in patient DL4b-01; [3] The patient's immediate cause of death was considered to be fatal sepsis, aggravated by the immunosuppression, a high-grade Immune Effector Cell-Associated Hemophagocytic Lymphohistiocytosis-Like Syndrome (IEC-HS), and the fast-progressing disease. Event was reported in Annual Report 2023.

- **Overall manageable tolerability profile**
- Expected cytopenia
- Mostly mild to moderate CRS:
  - 36% (16/44) Grade 1
  - 48% (21/44) Grade 2
  - 11% (5/44) Grade 3
  - 2% (1/44) Grade 4
- DLTs in 2 patients at DL4b as previously reported by the Company:
  - Patient DL4b-01: high *in vivo* T cell expansion, Grade 4 neurotoxicity, Grade 4 CRS, Grade 3 HLH
  - Patient DL4b-04: Grade 3 CRS defined by Grade 3 ALT resolved to Grade 2 within 10 days; no need for vasopressors or ventilation
- One possibly-related Grade 5 adverse event as previously reported by the Company:
  - Cause of death: fatal sepsis - aggravated by immunosuppression, IEC-HS, fast-progressing disease
- Consecutive modification I/E criteria + IL2 scheme
- **Dose escalation ongoing** based upon manageable tolerability in patients at DL4a

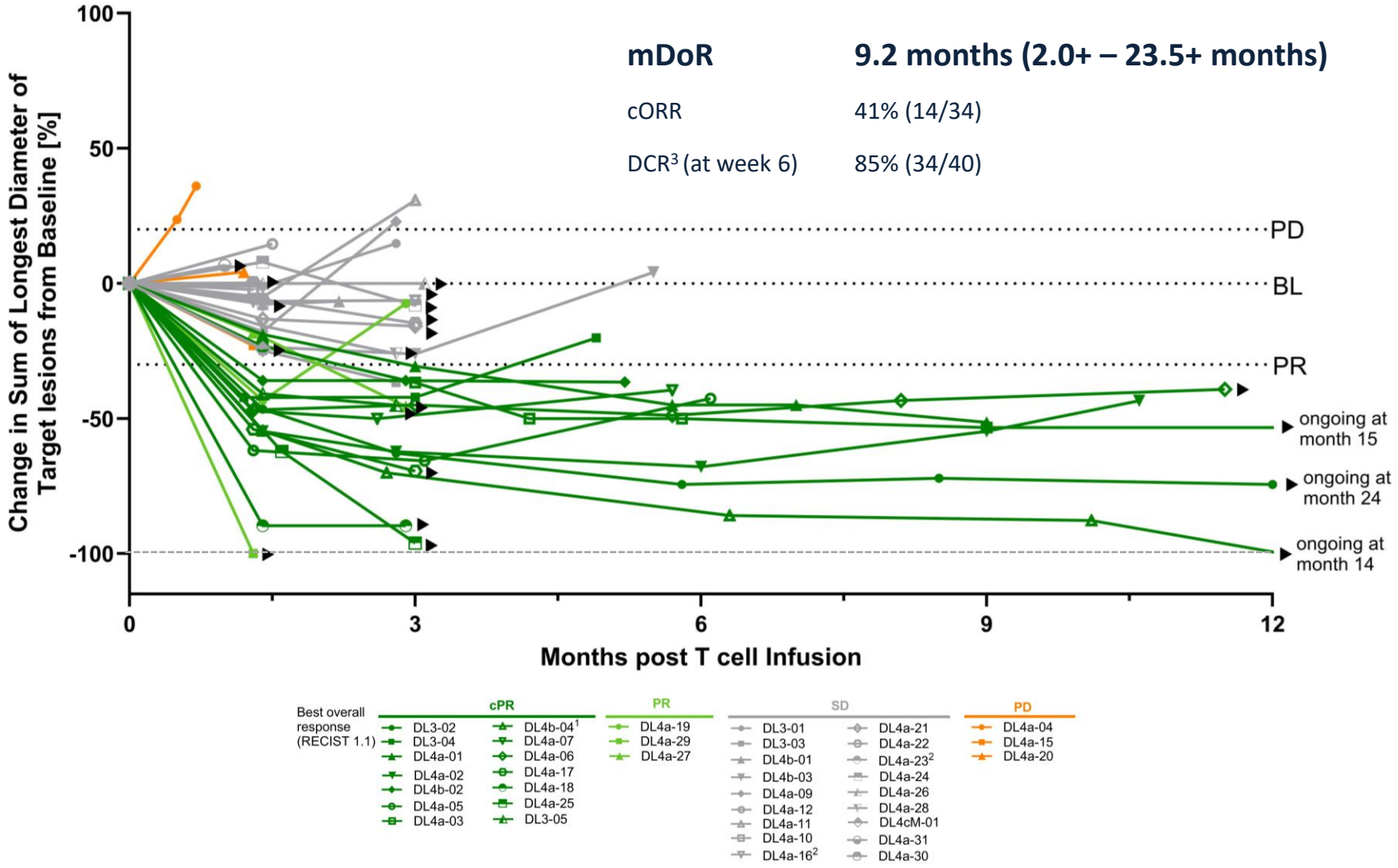
Best Overall Response for IMA203CD8 in Dose Escalation



cORR	**41% (14/34)**
ORR	41% (17/41)
Tumor shrinkage[3]	84% (32/38)
DCR[4] (at week 6)	85% (34/40)

Data cut-off Sep 30, 2024; *Maximum change of target lesions and RECIST1.1 response at different timepoints; [1]Patients off study at data-cut; [2]Metabolic CR according to PET-CT; [3] three patients excluded from tumor shrinkage analysis and figures due to lack of post-treatment assessment; [4] One patient had an early tumor assessment, outside the first assessment visit window and is not included in DCR calculation.

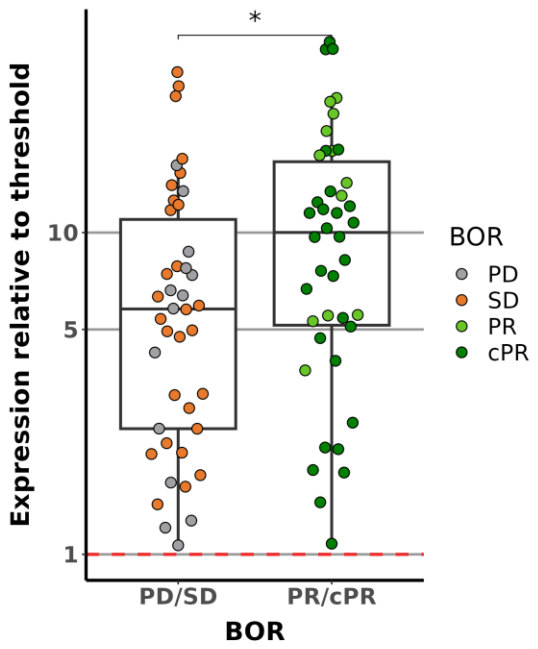
Response over Time of IMA203CD8 in Dose Escalation



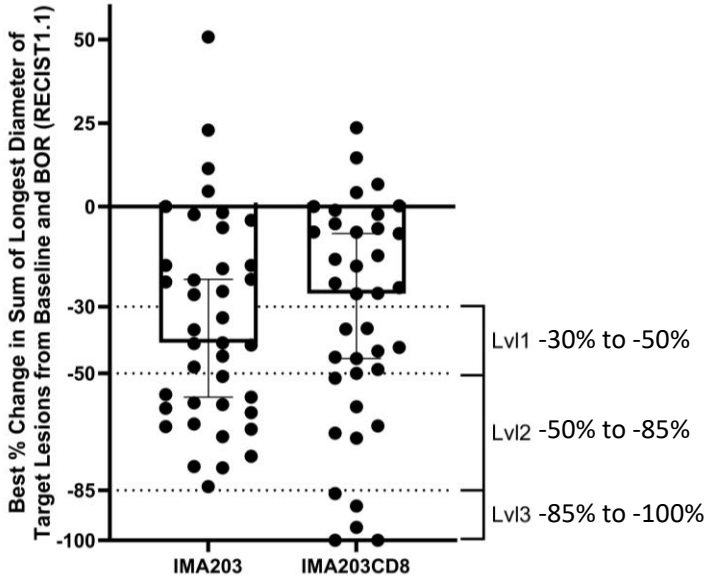
Data cut-off Sep 30, 2024; [1] Metabolic CR according to PET-CT [2] Patients off study at data-cut; [3] One patient had an early tumor assessment, outside the first assessment visit window and is not included in DCR calculation.

Opportunity of IMA203CD8 in Medium-level PRAME-Expressing Indications

PRAME expression associates with IMA203 and IMA203CD8 activity

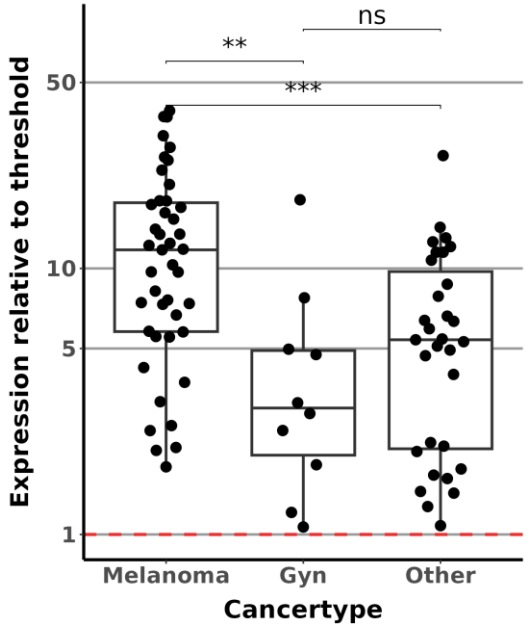


Deep responses with IMA203CD8 at low doses



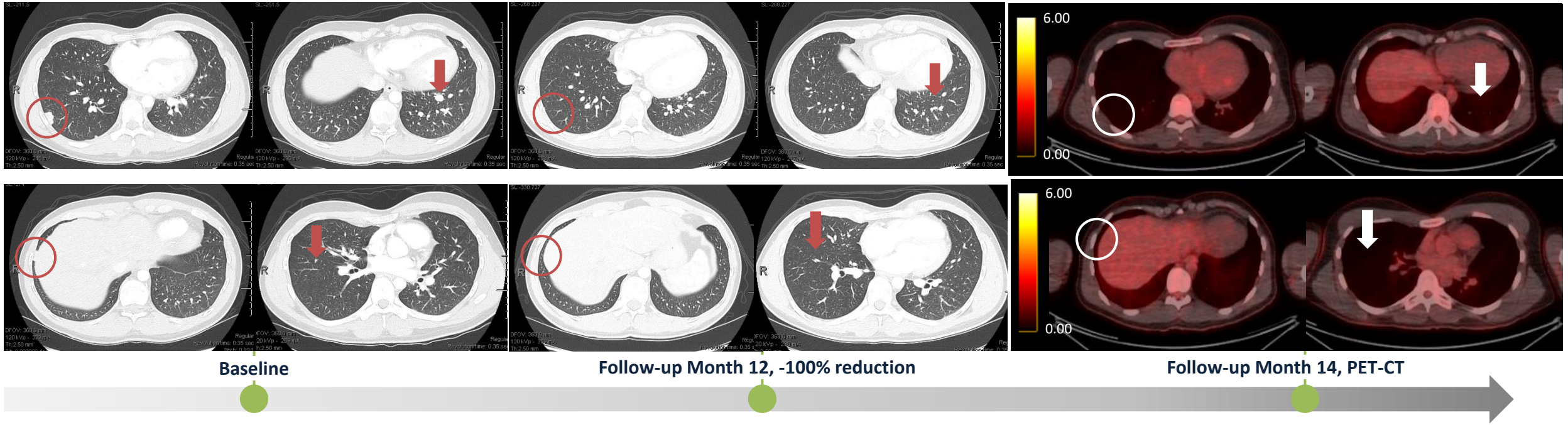
Number of patients	N=39*	N=38
Total infused dose TCR-T cells [x10^9]	**5.09** (1.0, 10.2)	**1.48** (0.443, 2.05)

Potential for targeting medium-level PRAME expressing tumors with IMA203CD8



Data cut-off IMA203CD8: Sep 30, 2024; *Patients treated at RP2D during Ph1b with evaluable post baseline assessments at data cut-off IMA203: Aug 23, 2024

Patient Case DL4b-04: Synovial Sarcoma



24-year-old male patient with complete remission according to PET imaging after 14 months post infusion

- 1 prior systemic treatment line: Doxorubicin + Ifosfamide + Mesna
- 3 years of cancer history
- At BL: 33.4 mm TL sum in lung, NTL in lymph nodes and lung
- Received ~$2.05x10^9$ IMA203CD8 TCR-T cells
- Metabolic CR on investigator-initiated PET month 14 post infusion
- Ongoing PR at 14+ months post infusion with -100% reduction according to RECIST 1.1

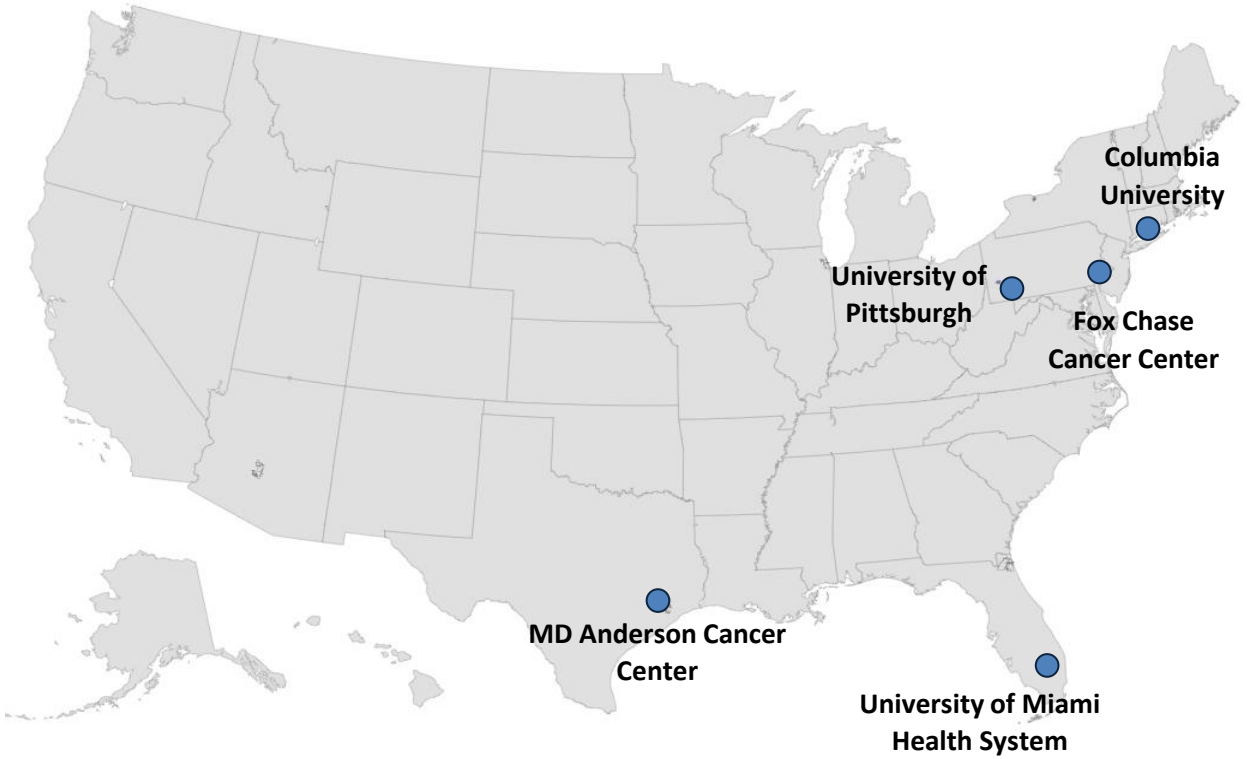
Data cut-off Sep 30, 2024; Images courtesy of treating physician (Dr. Dejka Araujo, University of Texas, MD Anderson Cancer Center)

IMA203CD8 (GEN2) - Summary

- Manageable tolerability with most frequent ≥Grade 3 AEs being expected cytopenia
  - DLTs in 2 patients at DL4b triggered dosing adjustment to DL4a
  - Manageable tolerability in patients at DL4a combined with modifications of the eligibility criteria and IL-2 scheme allows further exploration of higher doses
- Deep and durable objective responses already observed at low doses (median: 1.48 x10^9 T cells)
  - 41% (14/34) cORR and tumor shrinkage in 84% (32/38) of patients including two patients with complete response of target lesions
  - 9.2 months median DOR with 3 confirmed responses ongoing at 1+ year
- Opportunity of IMA203CD8 in medium-level PRAME expressing indications
  - Association of PRAME expression with clinical activity in IMA203 and IMA203CD8 treated patients
  - Deep responses with IMA203CD8, even though applied dose still lower than IMA203
- **Dose escalation with and without post-infusion low-dose IL-2 is ongoing** to investigate the full clinical potential of IMA203CD8 in hard-to-treat solid tumors

Thank you Patients, Families, participating IMA203 Clinical Trial Sites

United States



Germany

Sponsor: Immatics