

ACTengine IMA203 TCR-T targeting PRAME in PD1 refractory metastatic melanoma

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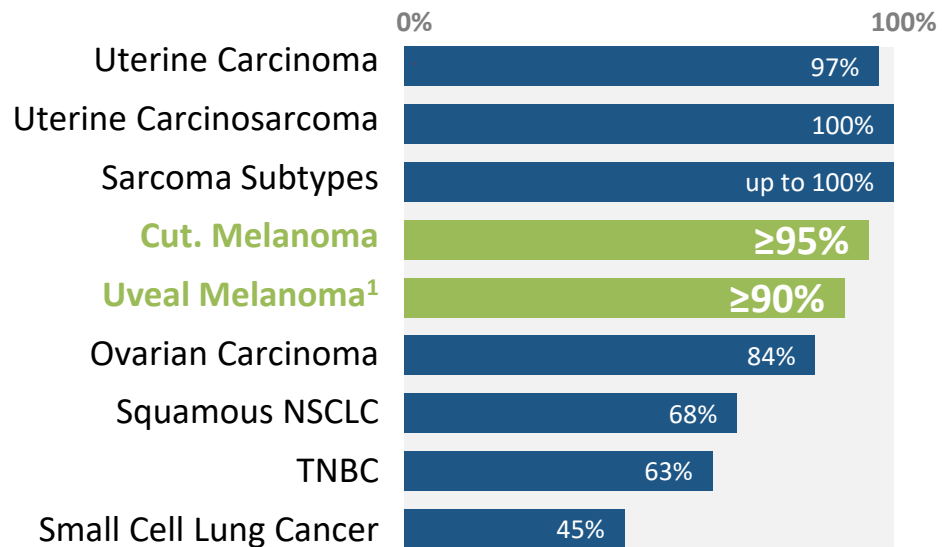
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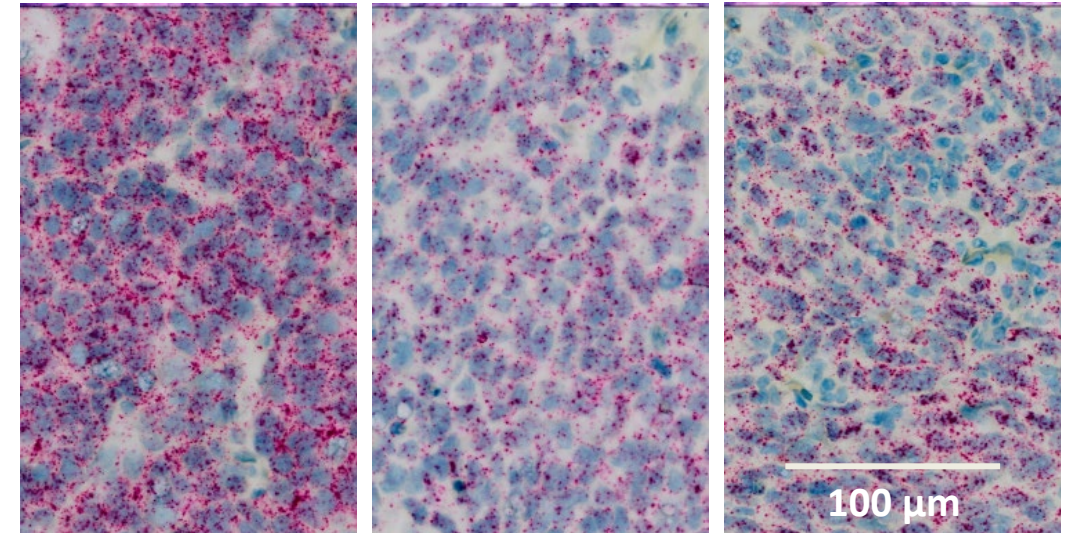
PRAME – a Widely Expressed Cancer Testis Antigen

% PRAME Positive Patients in Selected Indications



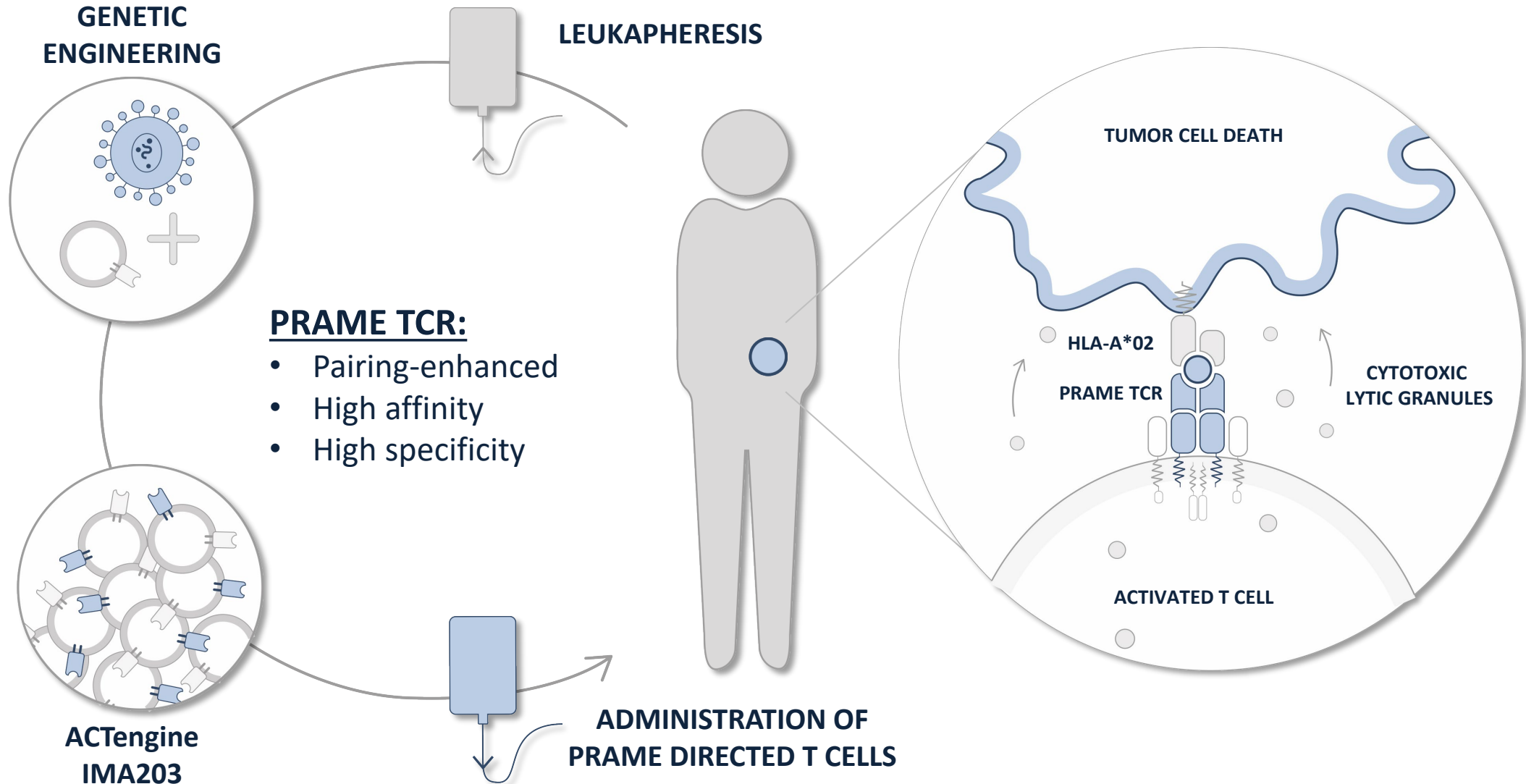
Target prevalence based on TCGA (SCLC: in-house) RNAseq data combined with proprietary mass spec-guided RNA expression threshold;
¹ Uveal melanoma target prevalence based on IMADetect qPCR testing of screening biopsies from 33 trial patients.

PRAME RNA Detection in Melanoma Samples (ISH)



% PRAME+ cells

ACTengine IMA203 TCR-T – Mechanism of Action

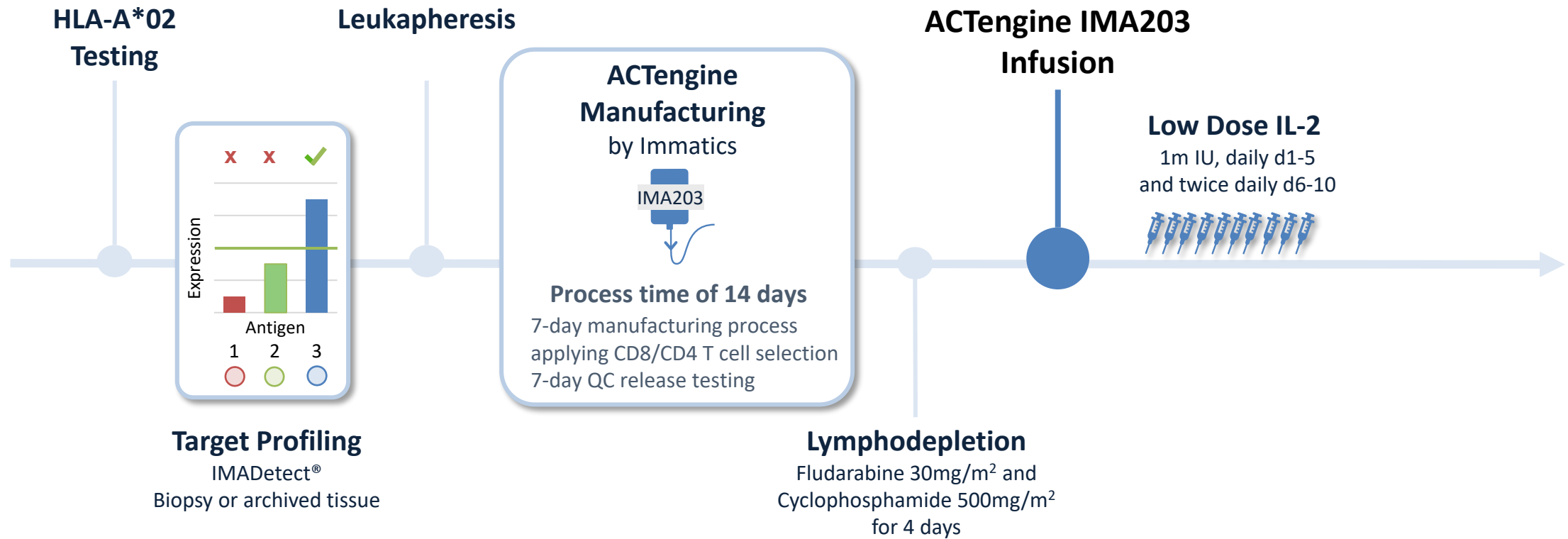


Patient Flow

SCREENING/MANUFACTURING

TREATMENT / OBSERVATION

LTFU



Key Objectives and Eligibility Criteria

Key Objectives

Primary: Safety

- Investigation of Adverse Events
- Determination of a RP2D

Secondary: Biological and Clinical Activity

- IMA203 T cell engraftment, persistence
- Objective responses (RECIST1.1) & Duration of Response

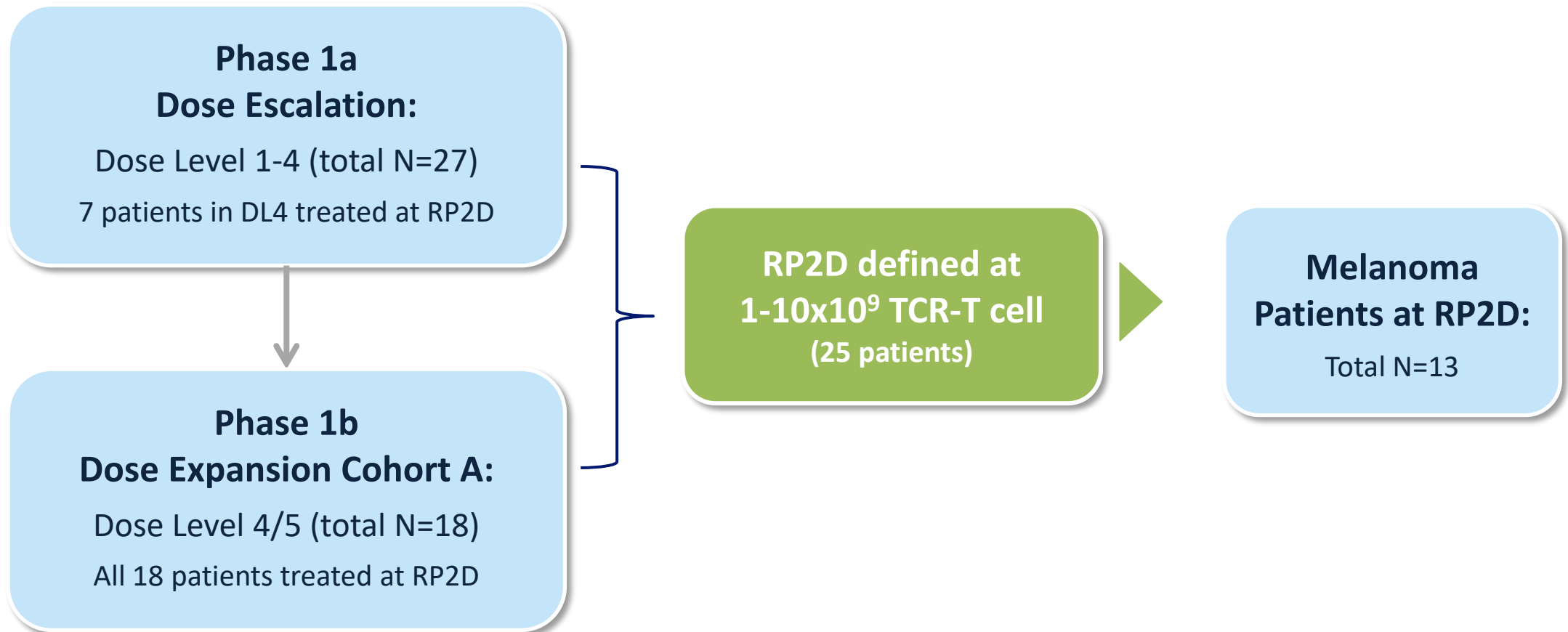
Exploratory

- IMA203 tumor infiltration

Key Eligibility Criteria

- Patients \geq 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

Phase 1 Trial Design in Advanced Solid Tumors



All Patients: Patient Characteristics

Characteristic	Phase 1a Dose Escalation	Phase 1b Cohort A	Melanoma Subgroup at RP2D
Safety population	28 [#]	21 [*]	16 [*]
Efficacy population	27	18	13
Melanoma	11	8	13
Ovarian cancer	1	4	
Synovial sarcoma	6	3	
Others	9	3	
Age	55.0	52.5	51
Median (min, max)	(18, 72)	(31, 79)	(24, 79)
Prior lines of treatment	4.0	3.0	4.0
Median (min, max)	(1,8)	(0, 10)	(0, 7)
LDH at baseline	66.7	50.0	53.8
>1 x ULN [% of patients]			
Baseline tumor burden	133.0	58.9	52.0
Target lesion sum of diameter [mm]			
Median (min, max)	(29.0, 219.7)	(21.0, 207.3)	(21.0, 178.7)
Dose Level	DL1-4	DL4/5 (RP2D)	DL4/5 (RP2D)
Total infused dose	0.41	4.33	1.73
Median transduced viable CD8 T cells infused [x10 ⁹] (min, max)	(0.08, 2.09)	(1.30, 9.36)	(1.07, 5.12)

Detailed Patient Characteristics

Melanoma Subgroup at RP2D	N=13
Melanoma subtype, n (%)	
Cutaneous	8 (61.5)
Uveal	4 (30.8)
Unk. Primary	1 (7.7)
Prior therapies for <u>cut. melanoma patients</u>	N=8
Prior lines of treatment, median (min, max)	5.5 (3, 7)
BRAF inhibitor pretreated, n (%)	5 (62.5)
Anti-CTLA-4, n (%)	7 (87.5)
Anti-PD-1 + anti-CTLA-4 combination, n (%)	7 (87.5)
Median lines of CPI (min, max)	3.0 (1, 4)
Retreated with CPI, n (%)	7 (87.5)

[#]One patient died from sepsis of unknown origin and did not receive IMA203 TCR-T cells; ^{*}Three cutaneous melanoma patients treated with IMA203, and pending post infusion scan included in safety population, but not efficacy population; Data cut-off Sep 30, 2023

All Patients: Tolerability Profile

TEAEs by maximum severity for all patients in Phase 1a dose escalation and Cohort A dose expansion (N=49)¹

Adverse event (System organ class, Preferred term)	≥ Grade 3		Adverse event (System organ class, Preferred term)	≥ Grade 3	
	No.	%		No.	%
Patients with any adverse event	49	100.0	table continued...		
Adverse Events of Special Interest	2	4.1	General disorders and administration site conditions	4	8.2
Cytokine release syndrome	2	4.1	Condition aggravated ²	1	2.0
ICANS	0	0.0	Fatigue	1	2.0
Blood and lymphatic system disorders	48	98.0	Pyrexia	1	2.0
Neutropenia	36	73.5	Swelling face	1	2.0
Lymphopenia	27	55.1	Metabolism and nutrition disorders	4	8.2
Leukopenia	26	53.1	Hypokalaemia	3	6.1
Anaemia	24	49.0	Failure to thrive	1	2.0
Thrombocytopenia	17	34.7	Hypophosphataemia	1	2.0
Cytopenia	1	2.0	Gastrointestinal disorders	2	4.1
Leukocytosis	1	2.0	Abdominal pain	1	2.0
Lymphocytosis	1	2.0	Diarrhoea	1	2.0
Investigations	9	18.4	Vomiting	1	2.0
Neutrophil count decreased	4	8.2	Injury, poisoning and procedural complications	2	4.1
Alanine aminotransferase increased	2	4.1	Humerus fracture	1	2.0
Aspartate aminotransferase increased	2	4.1	Infusion related reaction	1	2.0
White blood cell count decreased	2	4.1	Renal and urinary disorders	2	4.1
Blood alkaline phosphatase increased	1	2.0	Acute kidney injury	1	2.0
Blood creatinine increased	1	2.0	Proteinuria	1	2.0
Blood fibrinogen decreased	1	2.0	Skin and subcutaneous tissue disorders	2	4.1
Infections and infestations	7	14.3	Rash maculo-papular	2	4.1
Appendicitis	1	2.0	Cardiac disorders	1	2.0
COVID-19	1	2.0	Atrial fibrillation ¹	1	2.0
Enterococcal infection	1	2.0	Endocrine disorders	1	2.0
Infection	1	2.0	Inappropriate antidiuretic hormone secretion	1	2.0
Orchitis	1	2.0	Eye disorders	1	2.0
Sepsis ^{2,3}	1	2.0	Ulcerative keratitis	1	2.0
Septic shock ²	1	2.0	Hepatobiliary disorders	1	2.0
Urinary tract infection	1	2.0	Cholangitis	1	2.0
Respiratory, thoracic and mediastinal disorders	6	12.2	Immune system disorders	1	2.0
Hypoxia	3	6.1	Contrast media allergy	1	2.0
Bronchial obstruction	1	2.0	Musculoskeletal and connective tissue disorders	1	2.0
Laryngeal inflammation	1	2.0	Muscle spasms	1	2.0
Pleural effusion	1	2.0	Nervous system disorders	1	2.0
Respiratory failure	1	2.0	Headache	1	2.0
Vascular disorders	6	12.2	Reproductive system and breast disorders	1	2.0
Hypertension	4	8.2	Vaginal haemorrhage	1	2.0
Hypotension	2	4.1			

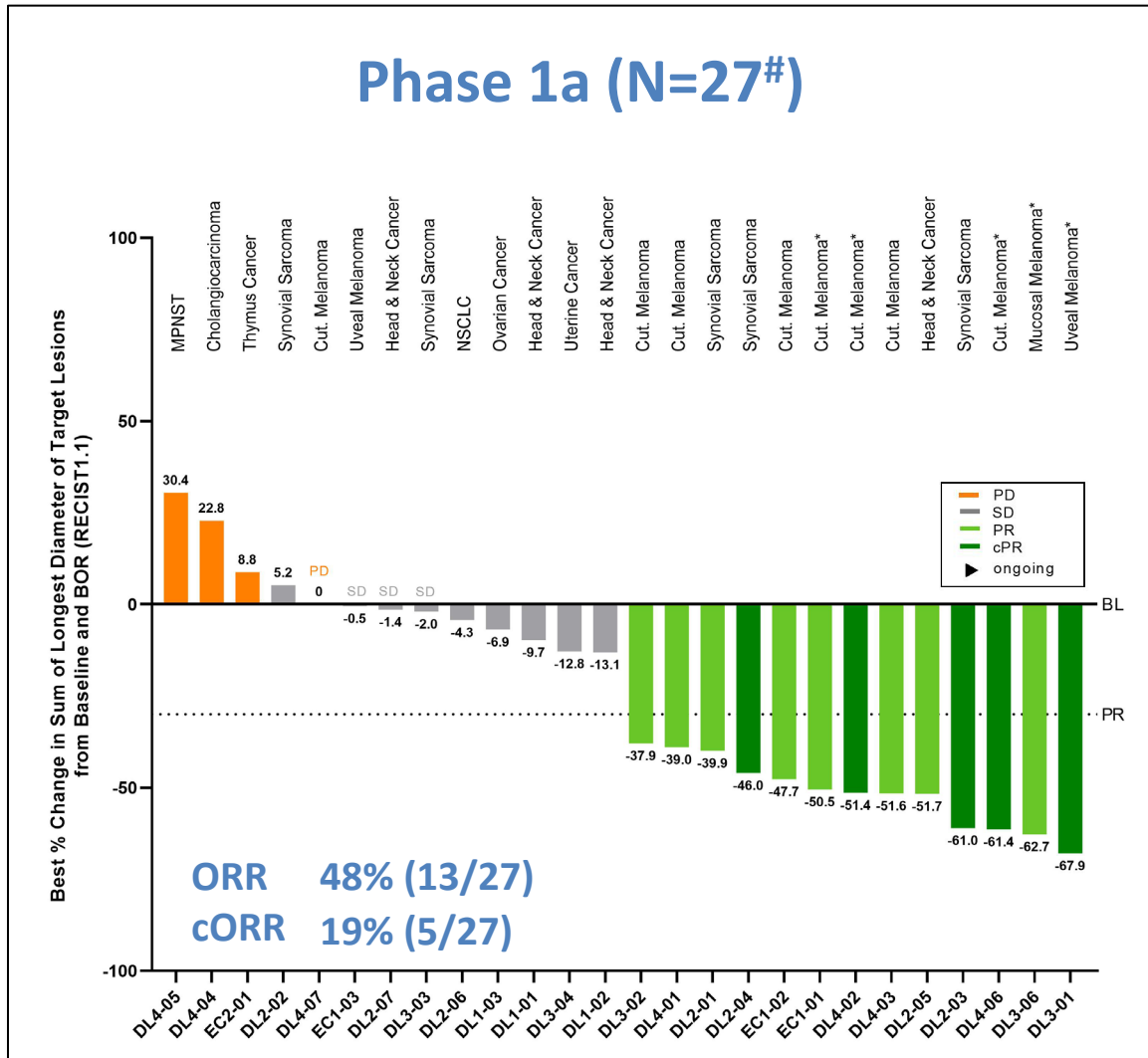
- Well tolerated at doses as high as ~10x10⁹ TCR-T cells
- Expected cytopenia (Grade 1-4) associated with lymphodepletion in all infused patients
- No AE ≥Grade 3 was observed with a frequency ≥10% when excluding expected cytopenias associated with lymphodepletion
- One DLT in Phase 1a at DL2
- No IMA203-related Grade 5 Adverse Events

All ≥Grade 3 TEAEs regardless of relatedness to study treatment, experienced by at least 1 patient (except for ICANS with only Grade 1-2; listed for completeness due to being an adverse event of special interest). Patients are counted only once per adverse event and severity classification (CTCAE v5.0 or CARTOX criteria for CRS/ICANS, Neelapu et al., 2018). Two patients with disease progression after first IMA203 infusion received exploratory second IMA203 infusion and 9 ≥Grade 3 TEAEs included in the table occurred only after second infusion. ¹ DLT: Dose limiting toxicity in phase 1a at DL2 reported on March 17, 2021; ² Fatal adverse events were not considered related to any study drug; ³ Patient died from sepsis of unknown origin and did not receive IMA203 TCR-T cells.

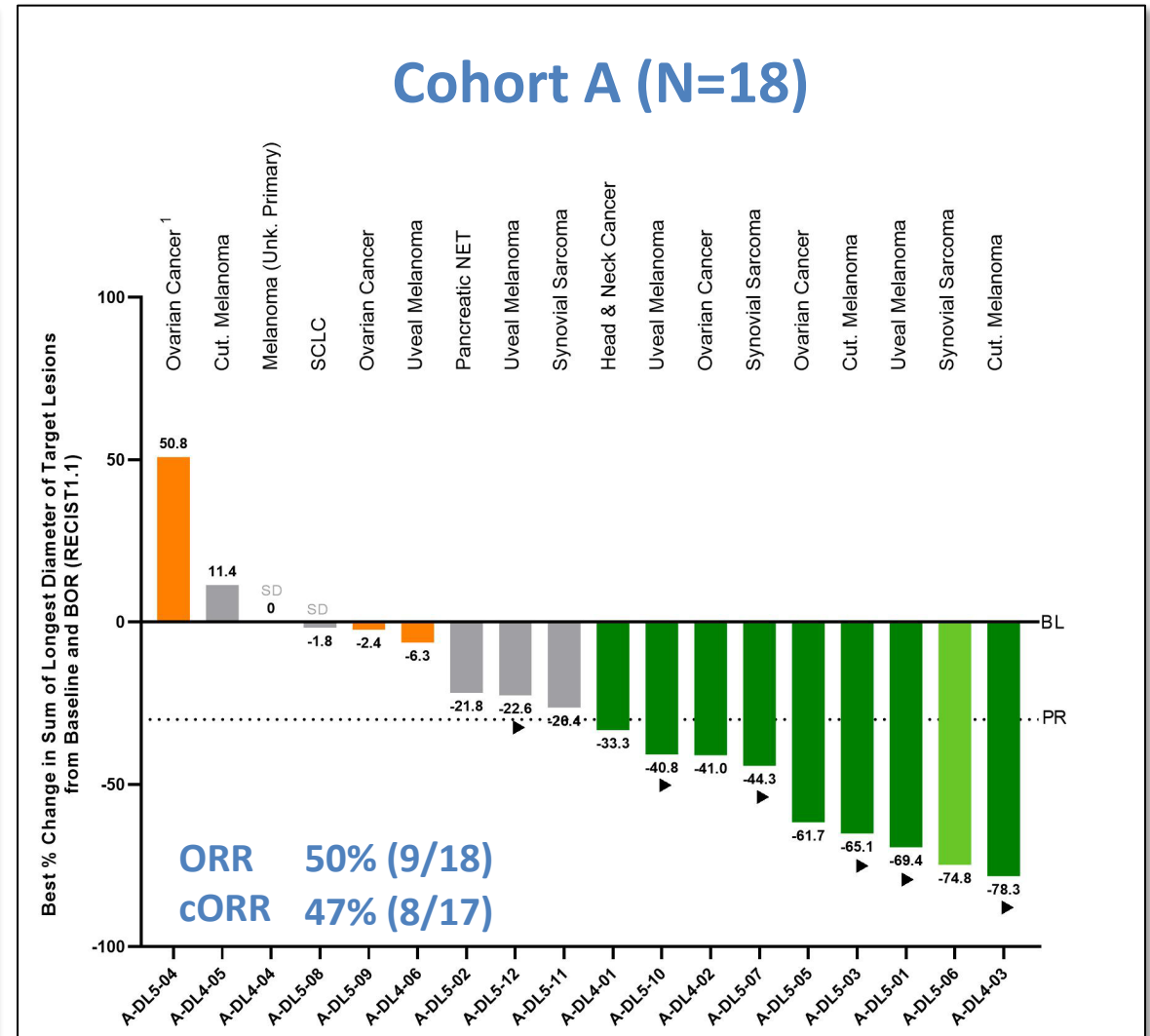
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All Patients: Best Overall Response

Phase 1a (N=27#)

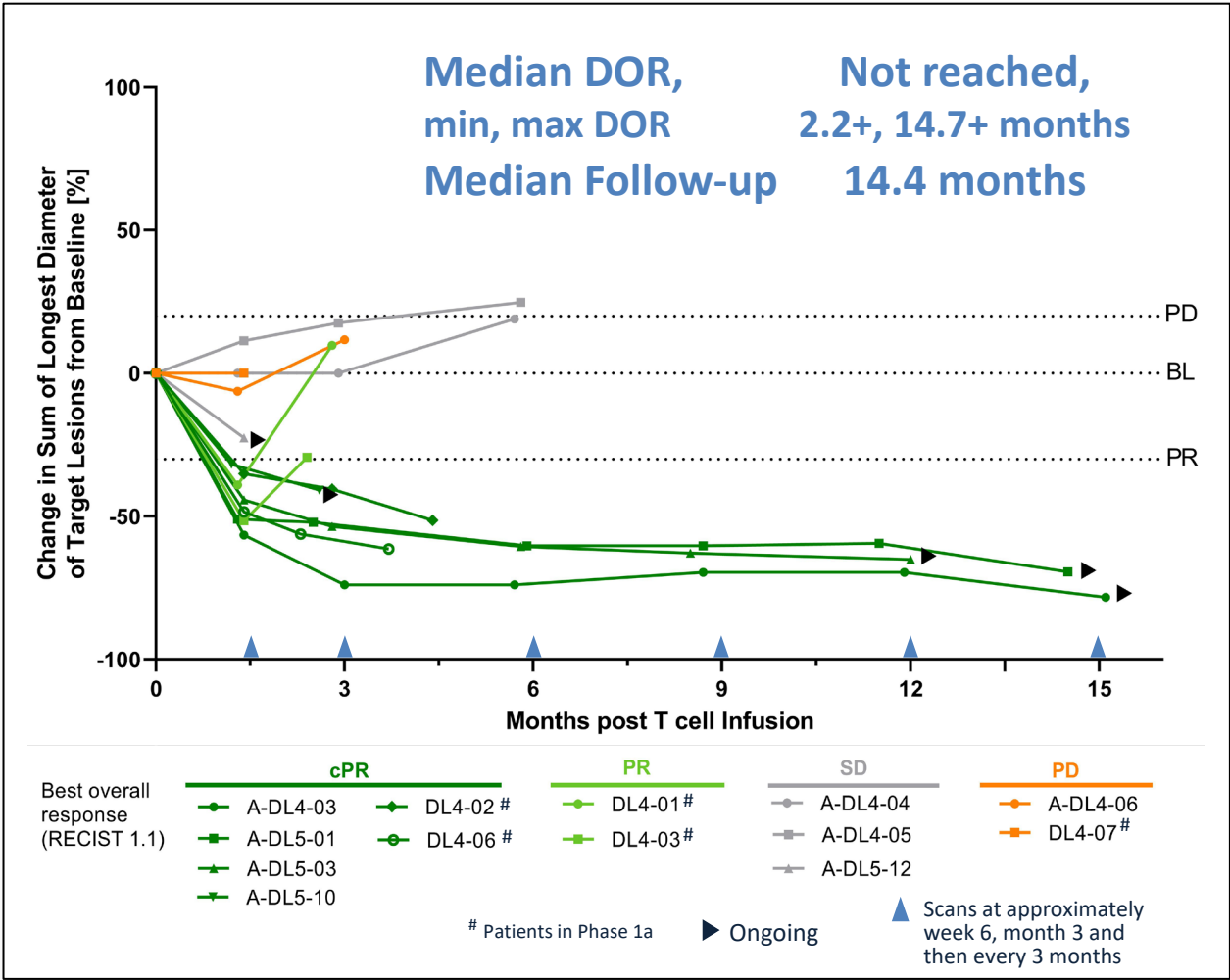
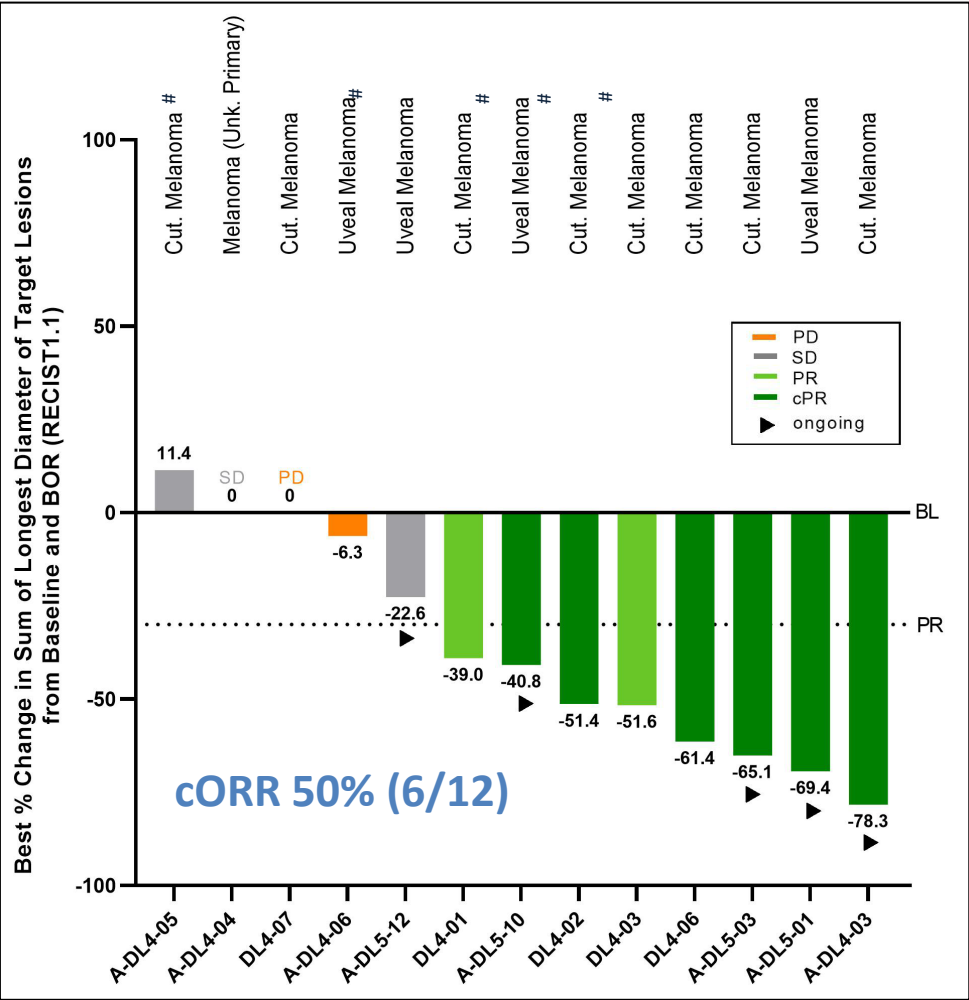


Cohort A (N=18)

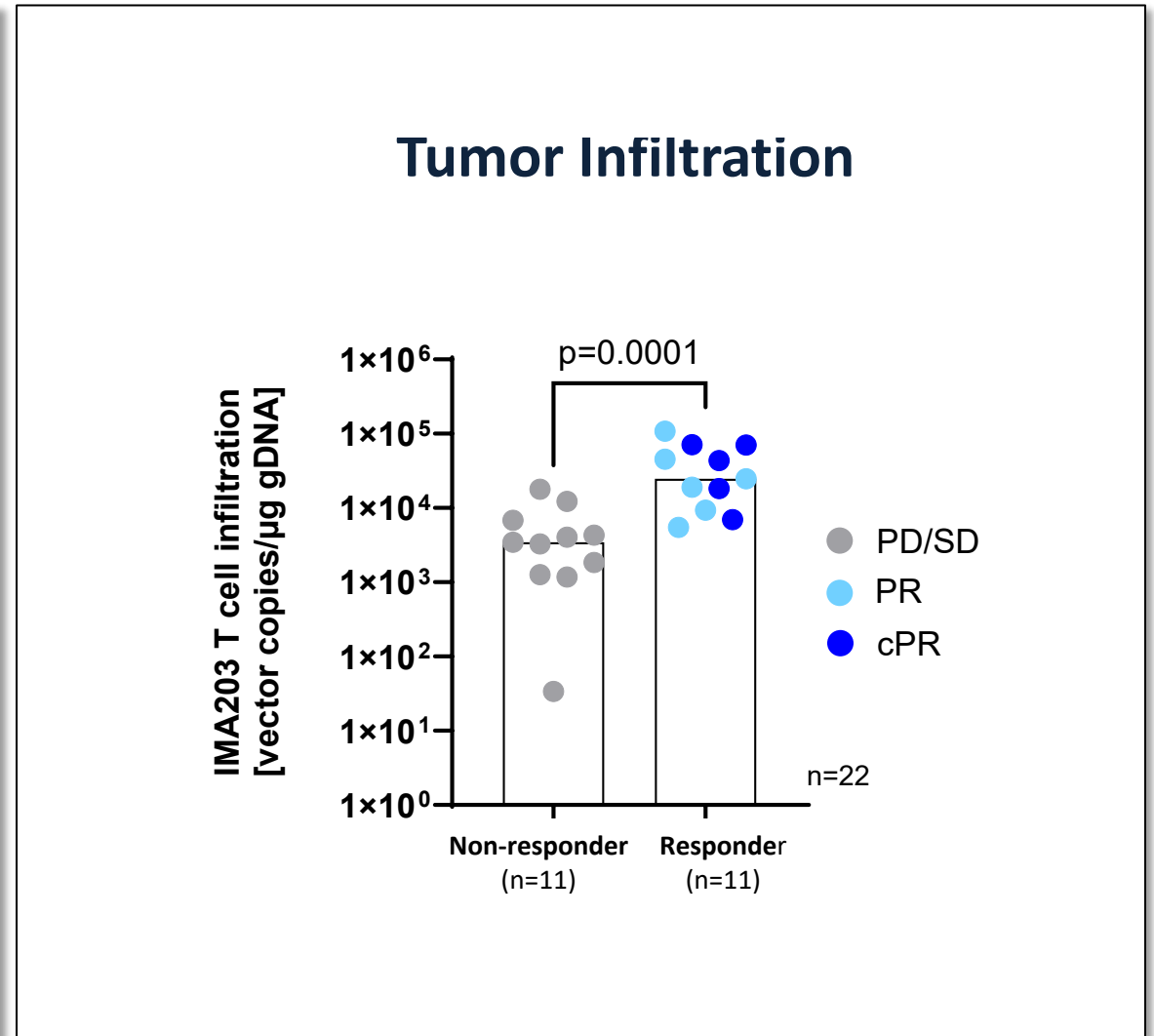
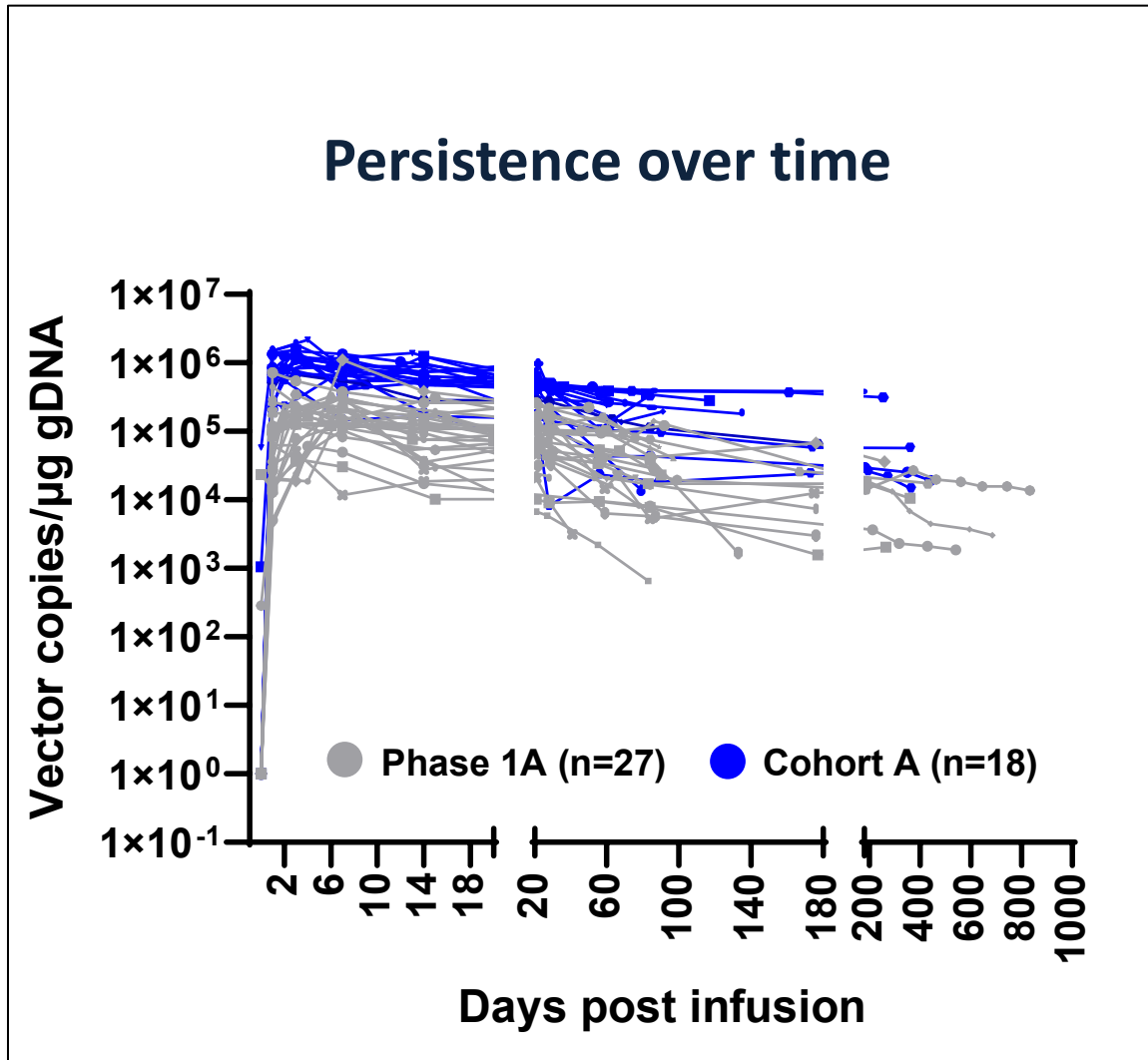


* Maximum change of target lesions and RECIST 1.1 BOR at different timepoints; # Synovial sarcoma patient (DL3) PD at week 6 not shown as target lesions were not evaluable; ¹ Patient received one dose nivolumab erroneously; Data cut-off Sep 30, 2023

Melanoma Subgroup at RP2D: BOR and Durability of Response



All Patients: Biological Data Consistent with Clinical Data

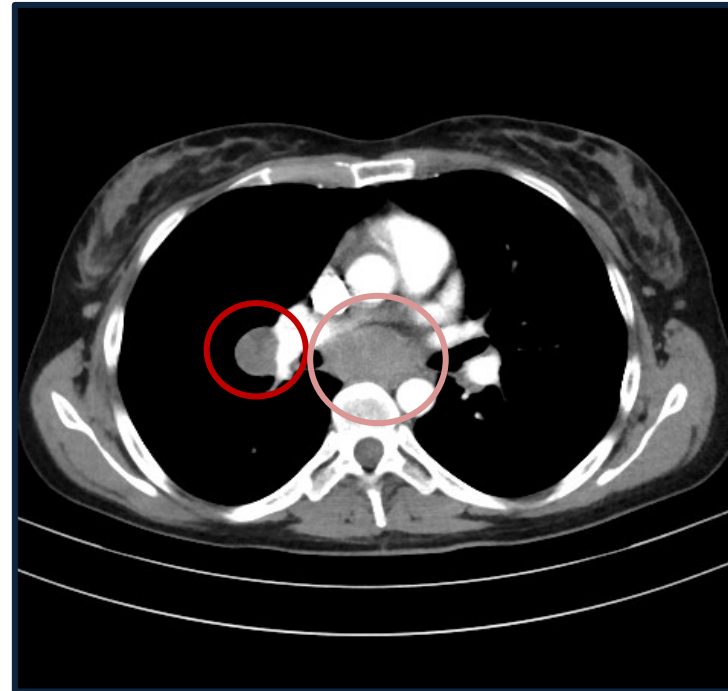


Patient Case A-DL5-03: Metastatic Cutaneous Melanoma

Patient characteristics:

- 31-year-old female patient with stage 4 metastatic cutaneous melanoma
- Treated with IMA203 after failing 3 prior lines of therapy incl. 2 lines of checkpoint inhibitors
- Dose: 5.12×10^9 TCR-T cells

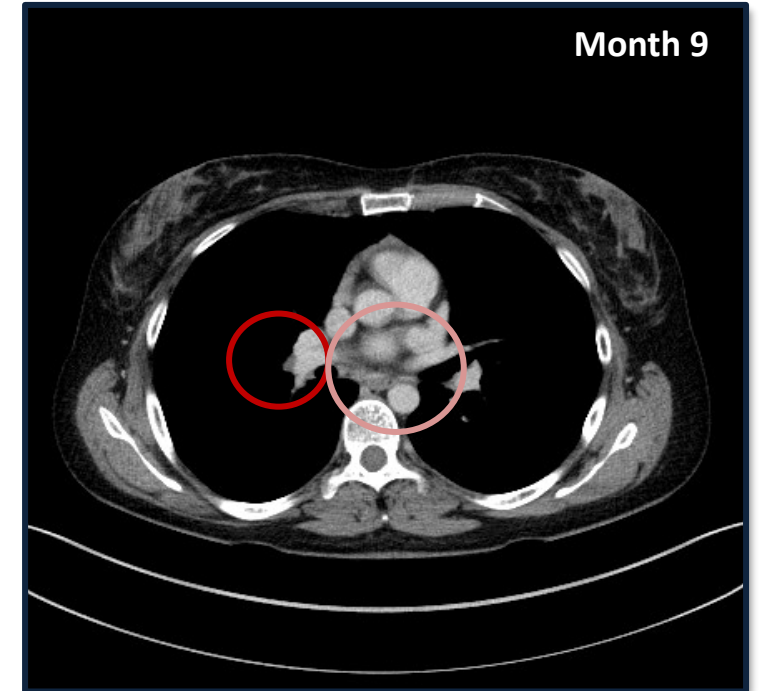
Baseline



target lesion (right hilar lymph node)

non-target lesion

Post-Treatment



Tumor Response

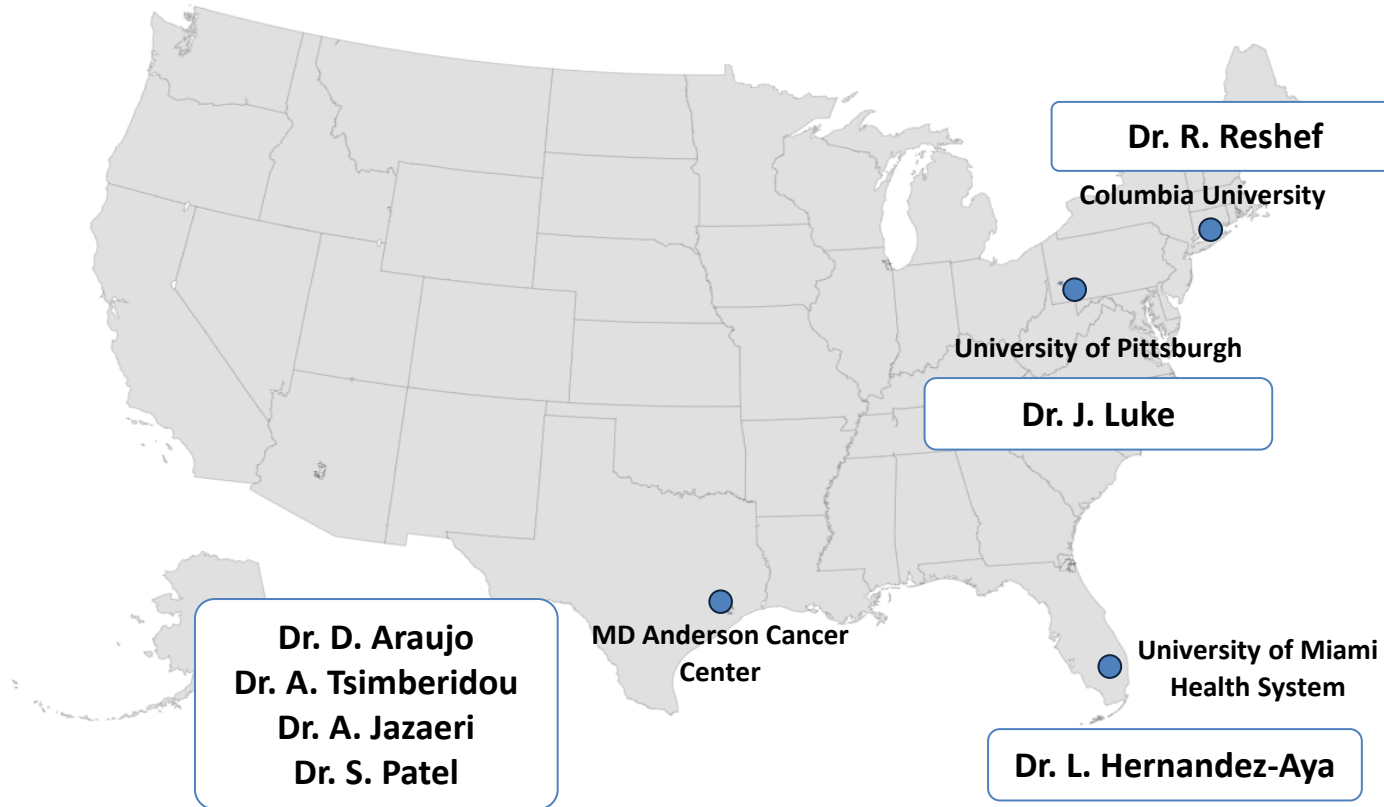
- Best overall response: Confirmed PR (RECIST 1.1)
- Ongoing partial response >12 months post treatment

Conclusions

- IMA203 is well tolerated
- Objective Responses (RECIST1.1) in CPI-refractory and BRAF inhibitor-refractory cutaneous melanoma, platinum-resistant ovarian cancer, uveal melanoma, head and neck cancer, synovial sarcoma
- Anti-tumor activity in melanoma patients at RP2D: 50% (6/12) cORR, mDOR not reached at mFU of 14.4 months
- Durability in some patients with three ongoing responses beyond 12 months
- Biological data consistent with clinical outcomes
- FDA RMAT designation for multiple PRAME+ cancers including cutaneous & uveal melanoma received
- Targeted registration-enabling Phase 2 trial in melanoma to start in 2024

Participating IMA203 Clinical Trial Sites

United States



Germany

