Safety and anti-tumor activity of TCR-engineered autologous, PRAME-directed T cells across multiple advanced solid cancers at low doses – clinical update on the ACTengine® IMA203 trial

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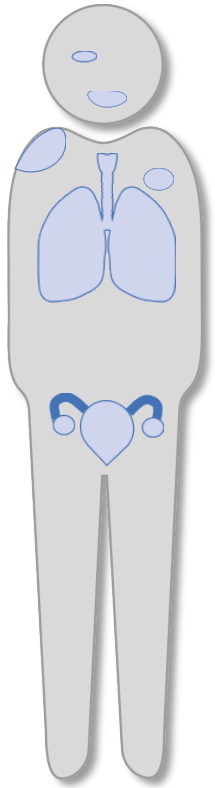
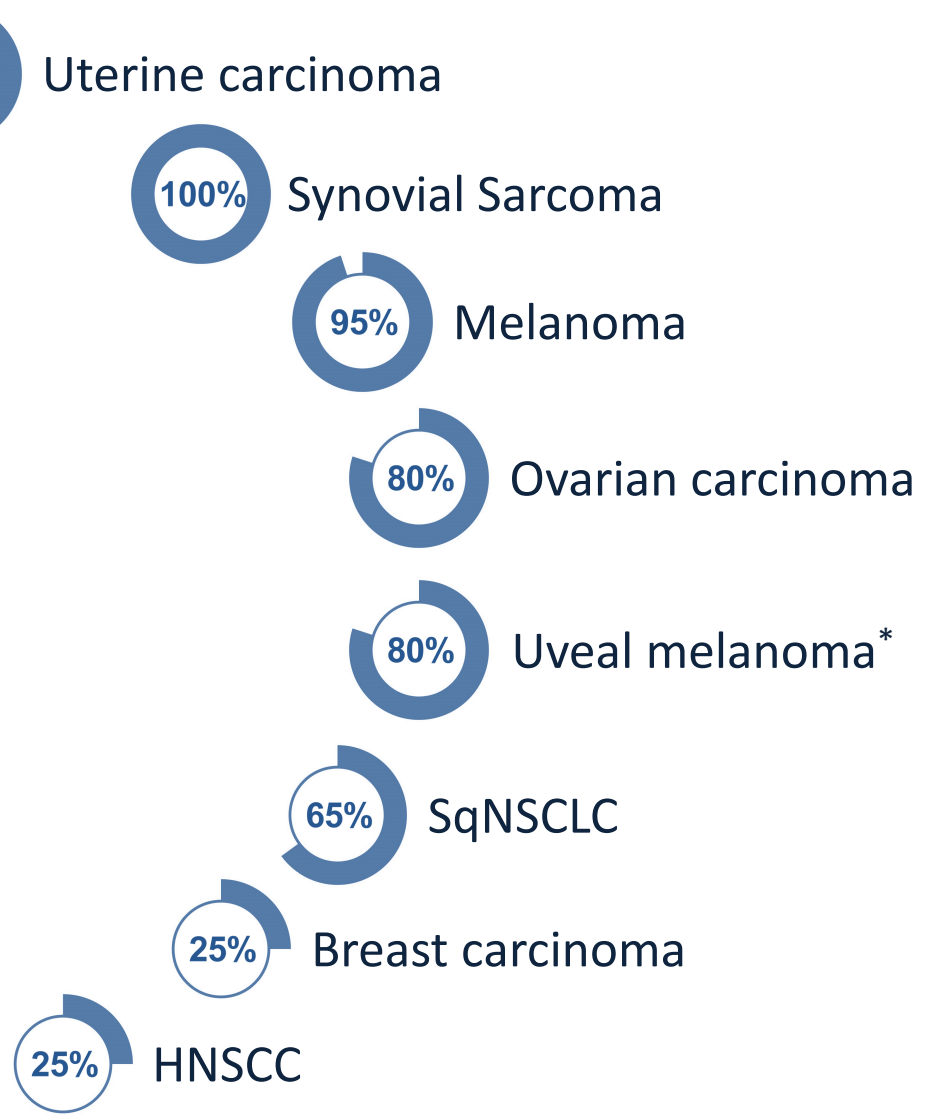
Peptide Target Derived From PRAME

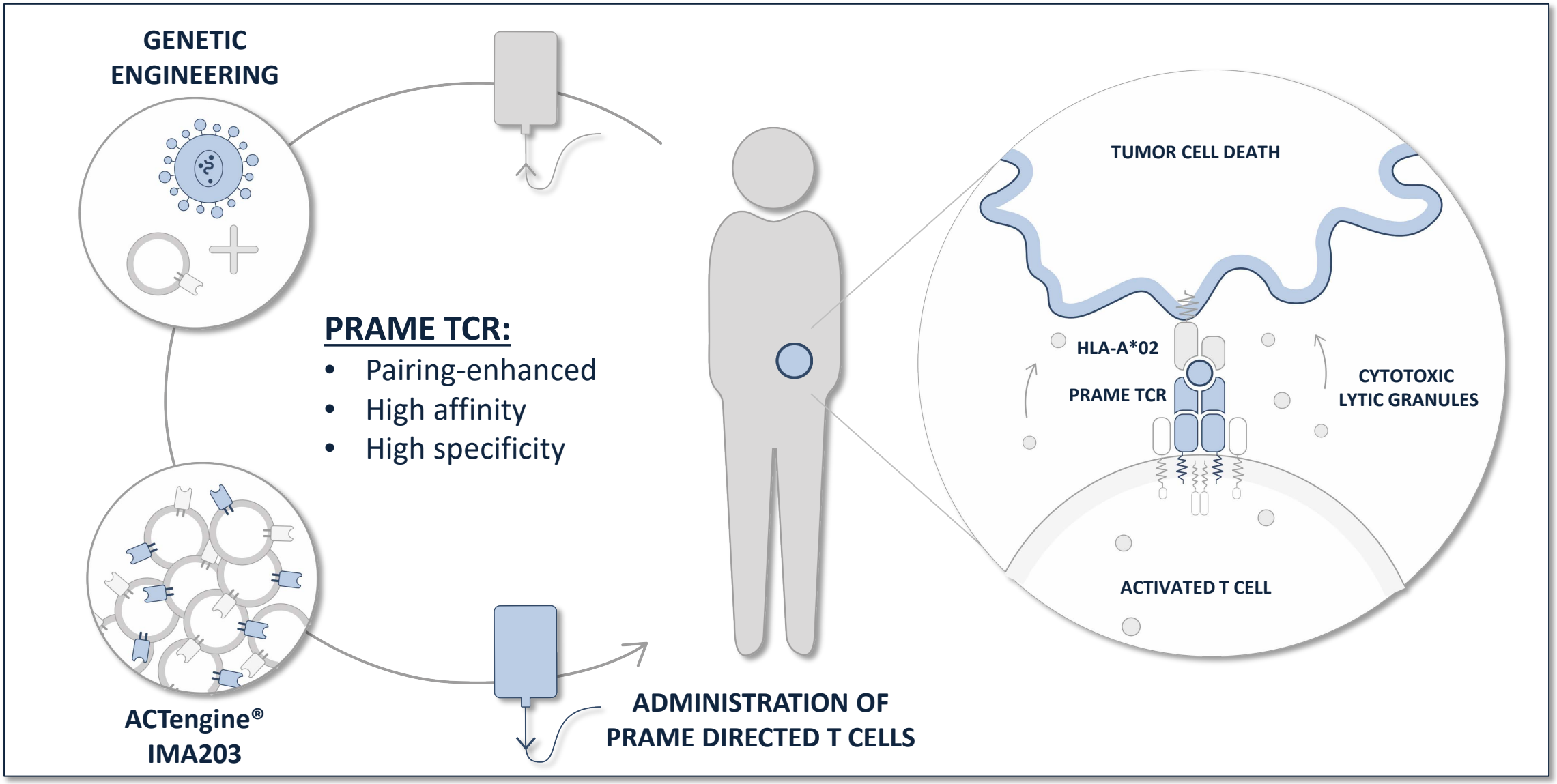
- Cancer testis antigen
- Homogenously expressed
- Expressed at high target density (100-1000 copies/cell)





Target prevalence based on mRNA expression (TCGA and Immatics inhouse experiments), * Based on metastatic uveal melanoma patients screened in IMA203 study (N=12)

Mechanism of Action



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 standard-of-care treatment
- Adequate organ function
- No active brain metastasis
- No serious autoimmune disorder
- No immunosuppressive medication

Key Objectives

Primary: Safety

- Investigation of Adverse Events
- Determination of a recommended Phase 2 dose

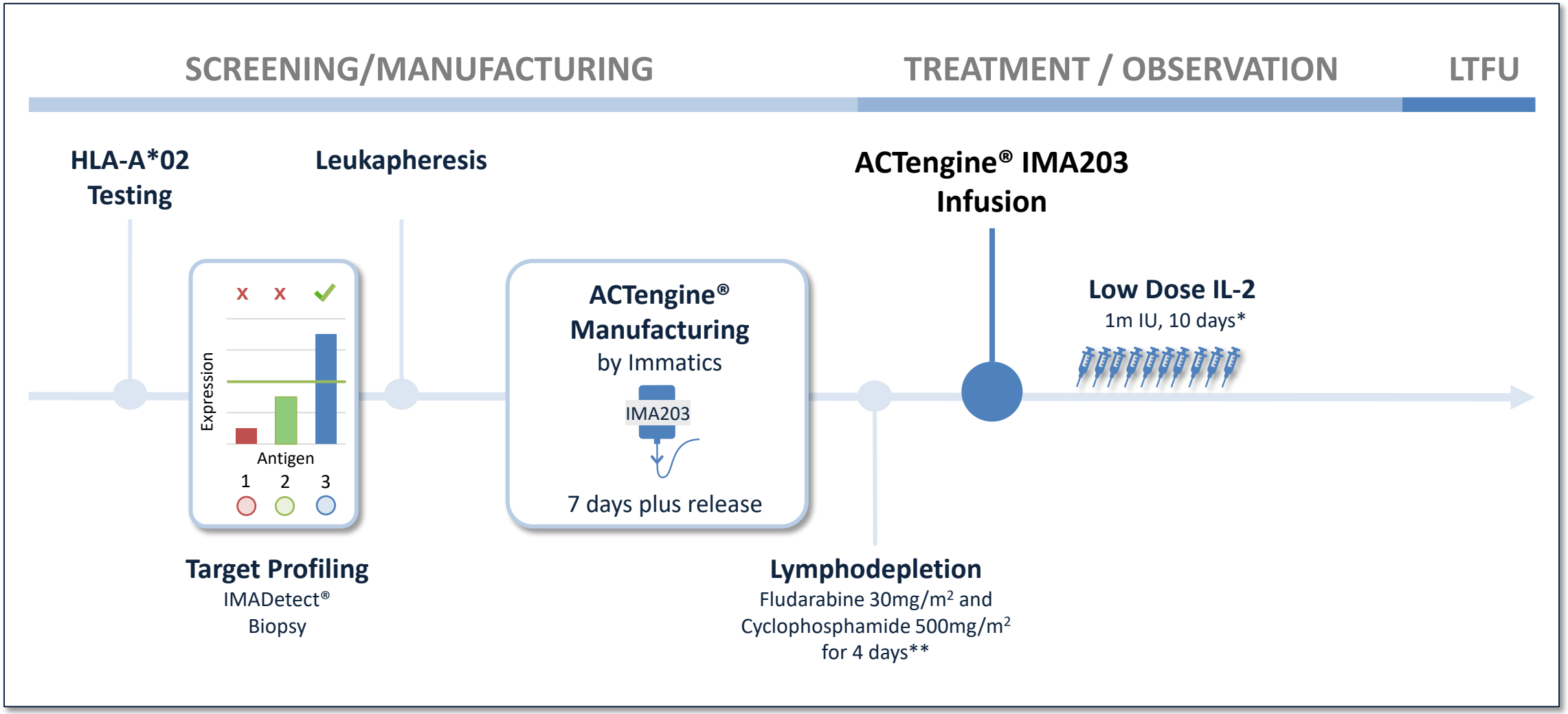
Secondary: Biological and Clinical Activity

- T cell engraftment, persistence
- Objective responses as per RECIST1.1 & duration of response

Exploratory:

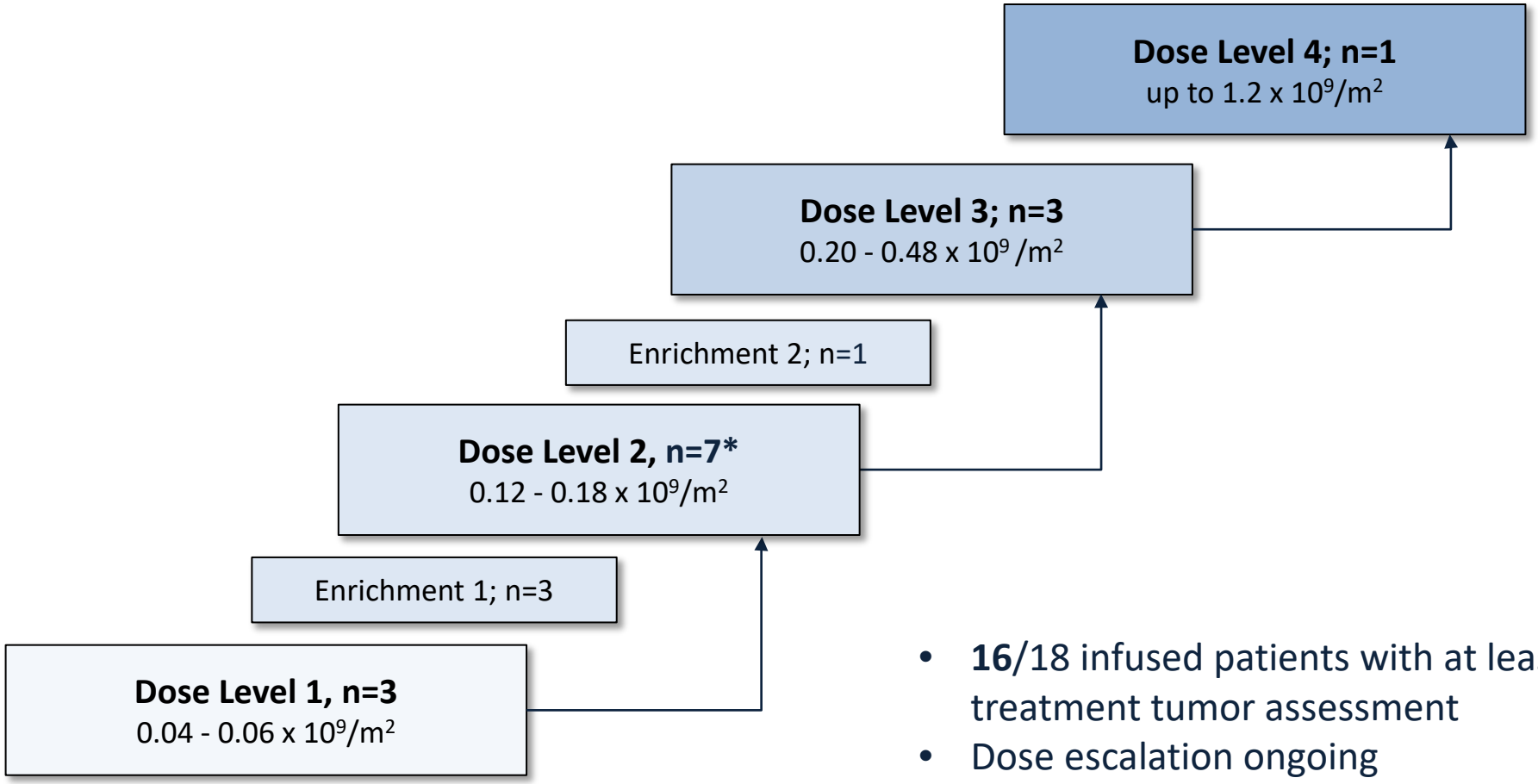
- Tumor Infiltration

Patient Flow



* IL-2 dose reduction (BID to QD and 14 to 10 days) starting on dose level 3, daily for day 1-5, twice daily for day 6-10, ** Fludarabine dose reduction (40mg/m² to 30mg/m²) starting on dose level 3

Trial Design & Recruitment Status



- **16**/18 infused patients with at least one post treatment tumor assessment
- Dose escalation ongoing

Standard 3+3 dose escalation design with 2 optional enrichment cohorts, dose shown as transduced viable CD8+ T cells per m^2 total body surface area;
* One patient infused at the same dose level as part of the enrichment cohort; Data cut-off – 05-Oct-2021

Patient Characteristics

Patient Characteristics (Patients with at least one post infusion tumor assessment, **N=16**)*	**Median (range)**
Age [years]	53 (18 - 65)
Number of prior lines of systemic therapies	4 (2 - 8)
Years from diagnosis	4 (1 - 25)
Disease Entity	**N**
Synovial Sarcoma	5
Head & Neck Cancer	3
Cutaneous Malignant Melanoma	3
Uveal Melanoma	2
Other (NSCLC, Ovarian & SCC)	3

* 2 patients infused but pending first tumor assessment

Data cut-off – 05-Oct-2021

Safety Profile

TEAEs by maximum severity (N=19)[1]

Adverse event	All grades No.	All grades %	≥ Grade 3 No.	≥ Grade 3 %
Patients with any adverse event	19	100.0	19	100.0
Adverse Events of Special interest				
Cytokine release syndrome	17	89.5	0	0.0
ICANS[2]	4	21.1	0	0.0
Blood and lymphatic system disorders				
Neutropenia*	16	84.2	15	78.9
Anaemia	16	84.2	9	47.4
Thrombocytopenia	15	78.9	7	36.8
Lymphopenia*	14	73.7	14	73.7
Leukopenia*	12	63.2	11	57.9
Cytopenia	1	5.3	1	5.3
Infections and infestations				
Enterococcal infection	1	5.3	1	5.3
COVID-19	1	5.3	1	5.3
Appendicitis	1	5.3	1	5.3
Sepsis[3]	1	5.3	1	5.3
Respiratory, thoracic and mediastinal disorders				
Hypoxia	2	10.5	1	5.3
Pleural effusion	2	10.5	1	5.3
Bronchial obstruction	1	5.3	1	5.3
Metabolism and nutrition disorders				
Hyponatraemia	7	36.8	1	5.3
Hypokalaemia	5	26.3	1	5.3
Decreased appetite	3	15.8	0	0.0

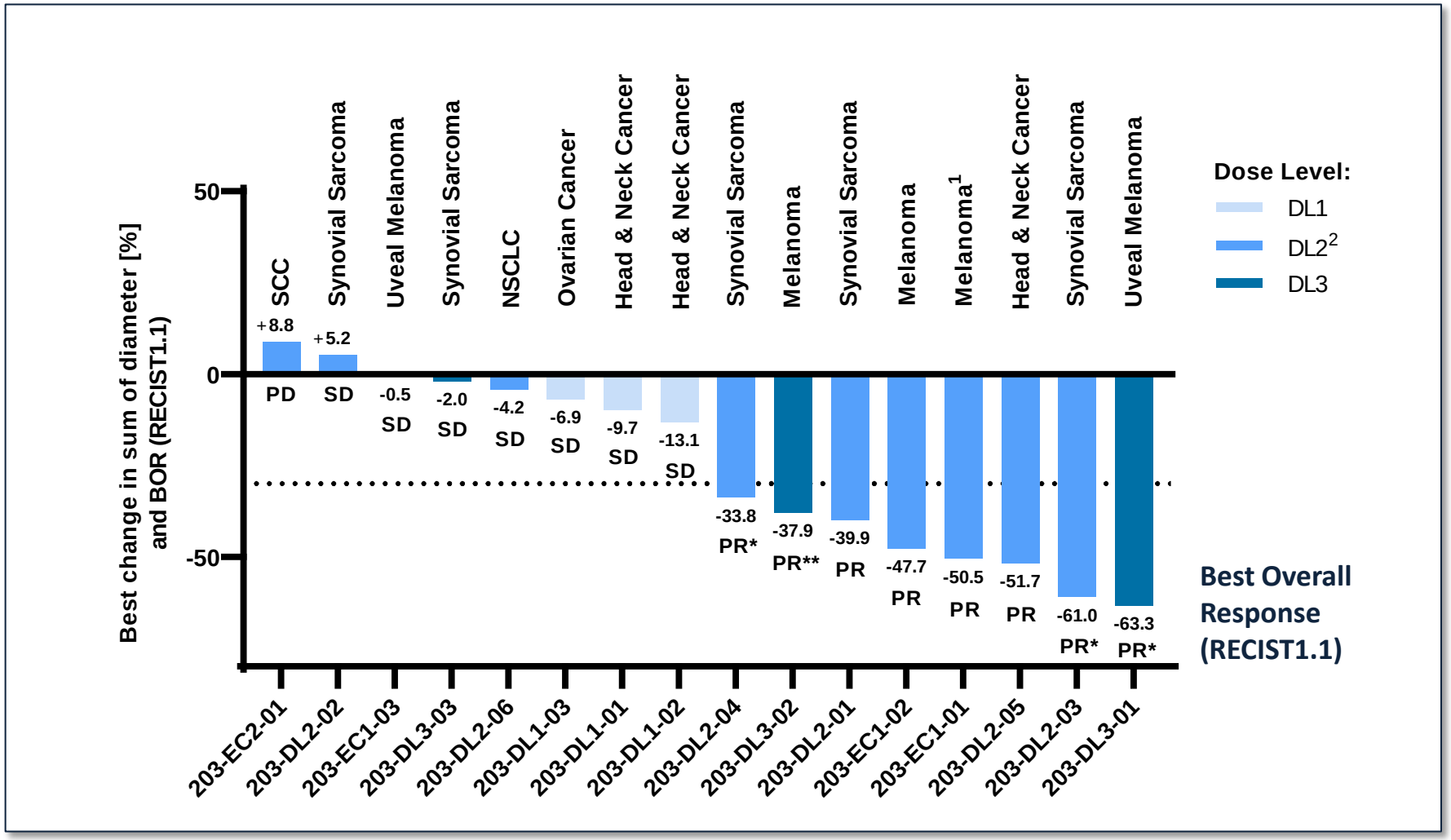
Adverse event	All grades No.	All grades %	≥ Grade 3 No.	≥ Grade 3 %
table continued…				
Cardiac or vascular disorders				
Hypertension	3	15.8	2	10.5
Atrial fibrillation	2	10.5	1[4]	5.3
General disorders and administration site conditions				
Fatigue	7	36.8	1	5.3
Pyrexia	5	26.3	0	0.0
Oedema peripheral	3	15.8	0	0.0
Gastrointestinal disorders				
Nausea	12	63.2	0	0.0
Vomiting	7	36.8	0	0.0
Diarrhoea	7	36.8	0	0.0
Constipation	6	31.6	0	0.0
Investigations				
Aspartate aminotransferase increased	5	26.3	0	0.0
Alanine aminotransferase increased	4	21.1	0	0.0
Blood creatinine increased	4	21.1	0	0.0
Other				
Rash	5	26.3	0	0.0
Myalgia	4	21.1	0	0.0
Arthralgia	3	15.8	0	0.0
Alopecia	3	15.8	0	0.0
Rash maculo-papular	2	10.5	1	5.3
Orchitis	1	5.3	1	5.3
Contrast media allergy	1	5.3	1	5.3

DLT:
Transient, Grade 3 atrial fibrillation. Resolved within 48h. DLT triggered expansion of DL2

[1]All treatment-emergent adverse events (TEAEs) with grade 1-2 occurring in at least 3 patients (incidence ≥15.8%) and additionally all events with grade 3-5 regardless of relatedness to study treatment are presented. Data source: clinical database. Adverse events were coded using the Medical Dictionary for Regulatory Activities. Grades were determined according to National Cancer Institute Common Terminology Criteria of Adverse Events (CTCAE), version 5.0. Grades for Cytokine release syndrome and ICANS were determined according to CARTOX criteria (Neelapu et al, 2018). Patients are counted only once per adverse event and severity classification.; [2]ICANS: Immune effector cell-associated neurotoxicity syndrome; [3]Patient died from sepsis of unknown origin and did not receive IMA203 T cells; [4]DLT: Dose limiting toxicity; *100% of patients experienced transient cytopenias ≥ Grade 3 (CTCAE v5.0)

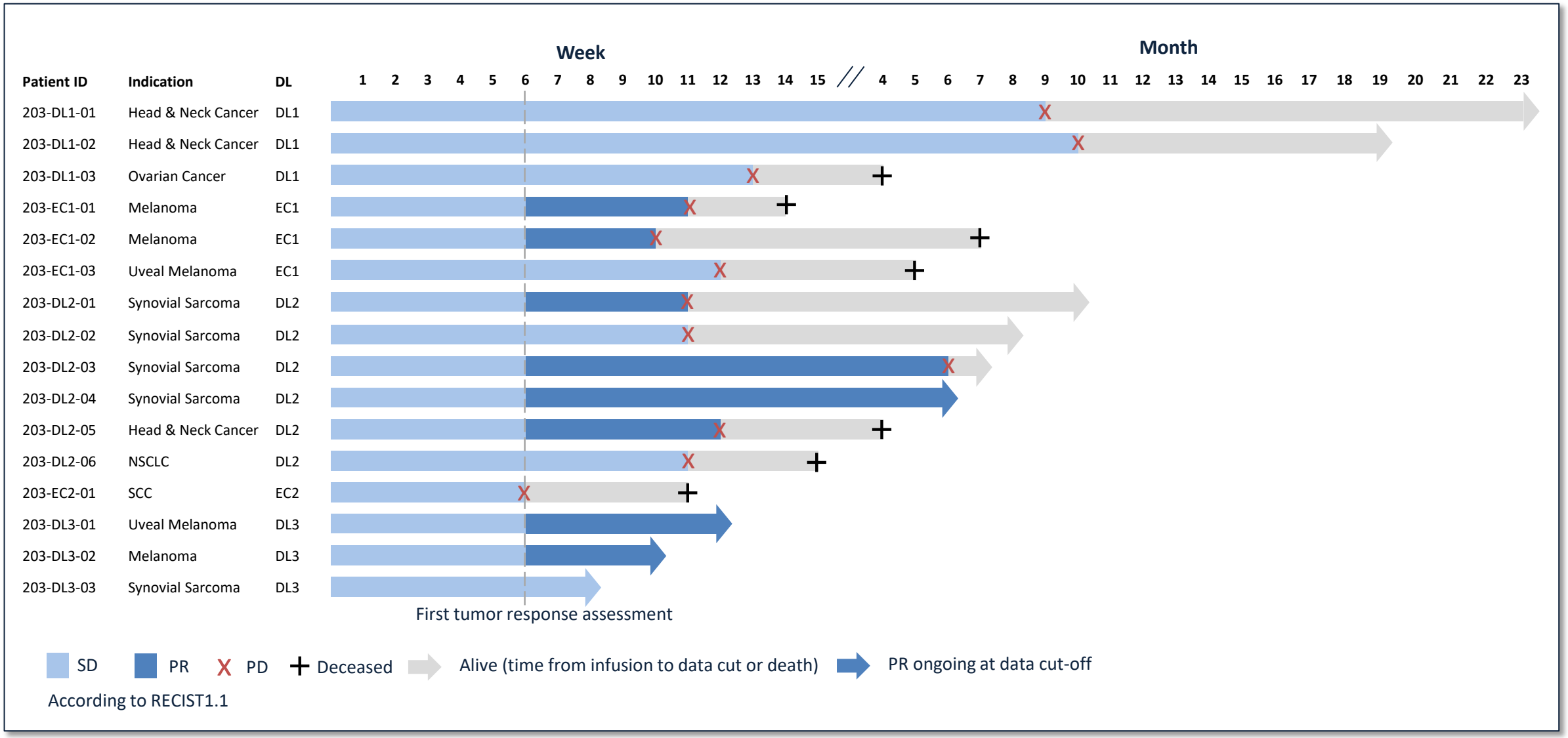
Data cut-off – 05-Oct-2021

Tumor Response



[1] RECIST1.1 response at the timepoint of maximum change of target lesions (week 12): PD due to leptomeningeal disease; [2] Patients dosed with DL2, EC1 and EC2;
*Confirmed responses; ** Confirmation pending as of data cut-off; Data cut-off – 05-Oct-2021

Patient Response over Time



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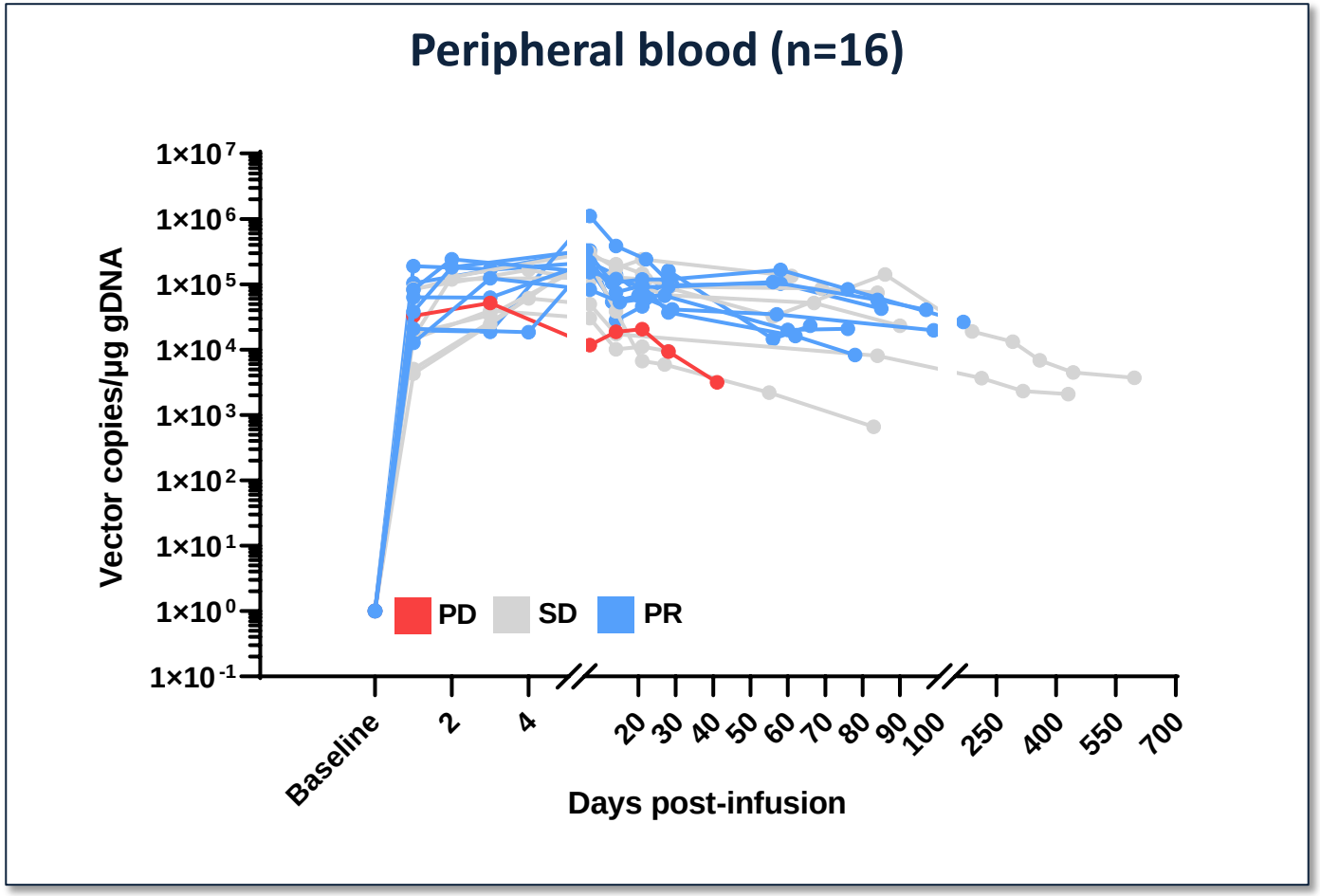
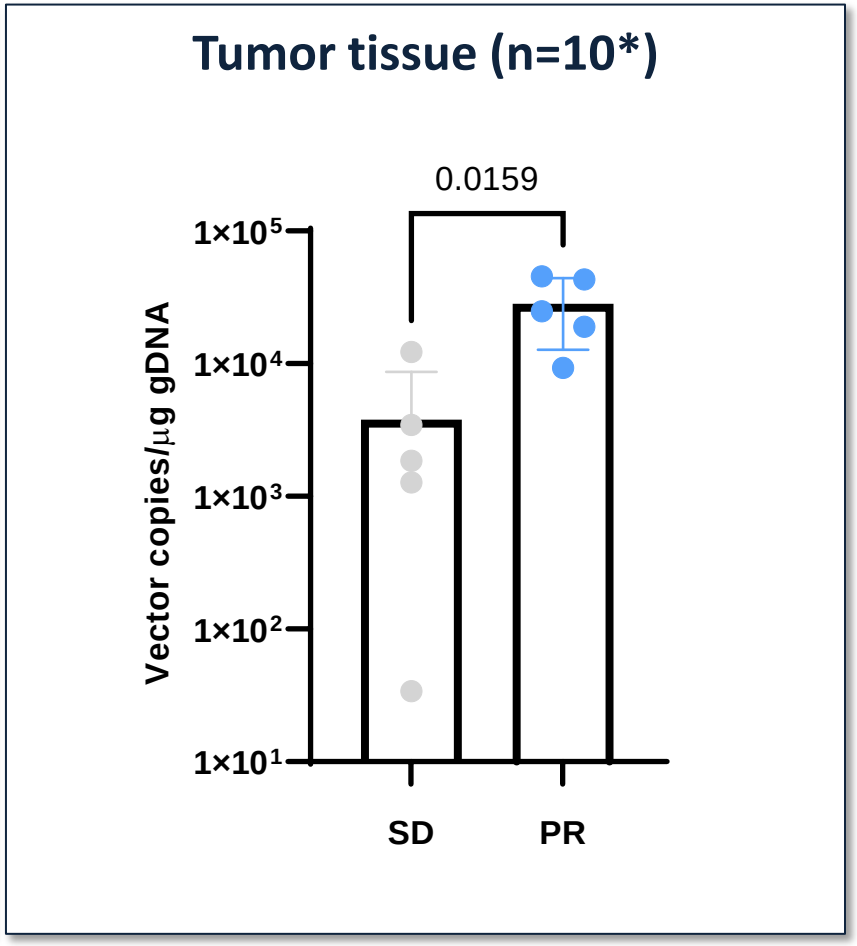
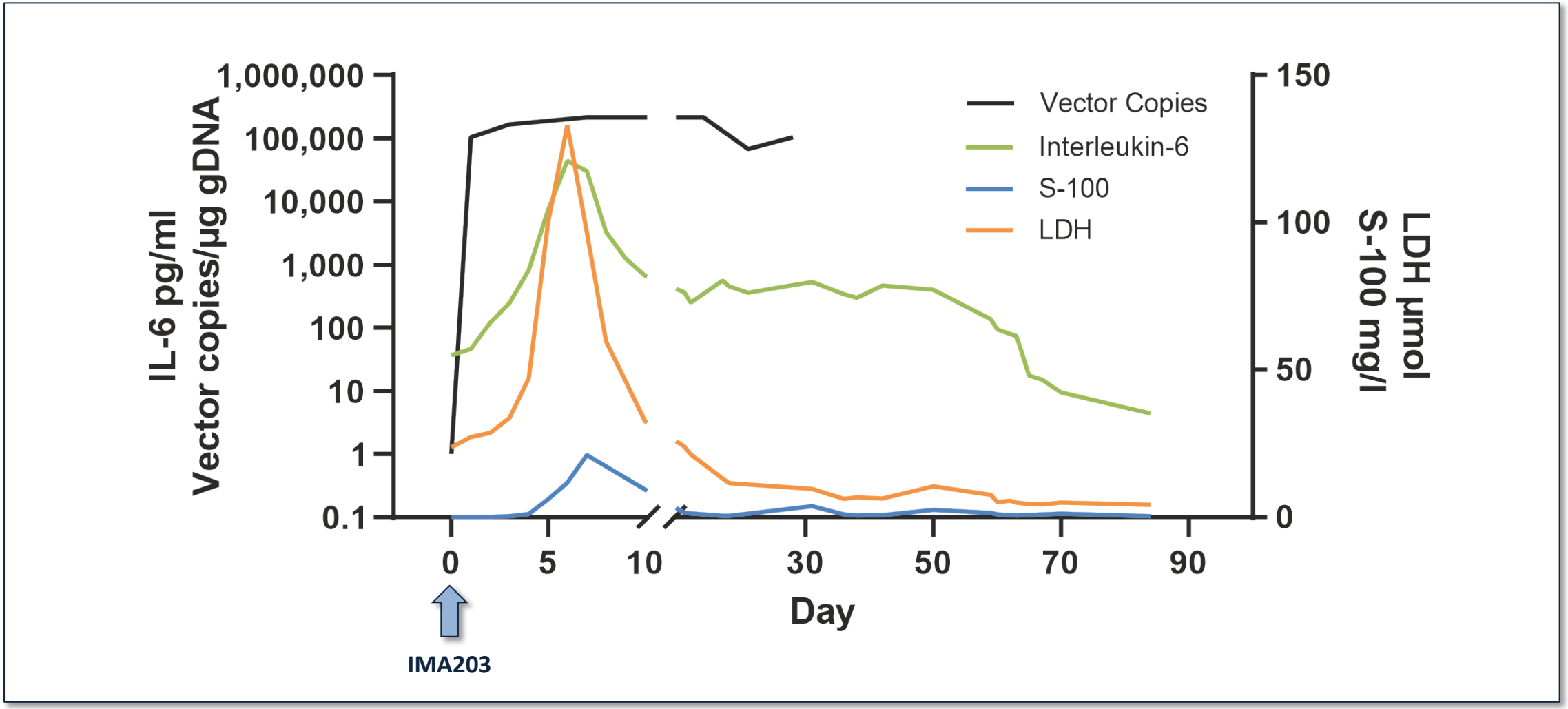
T cell Detection in Blood and Tumor





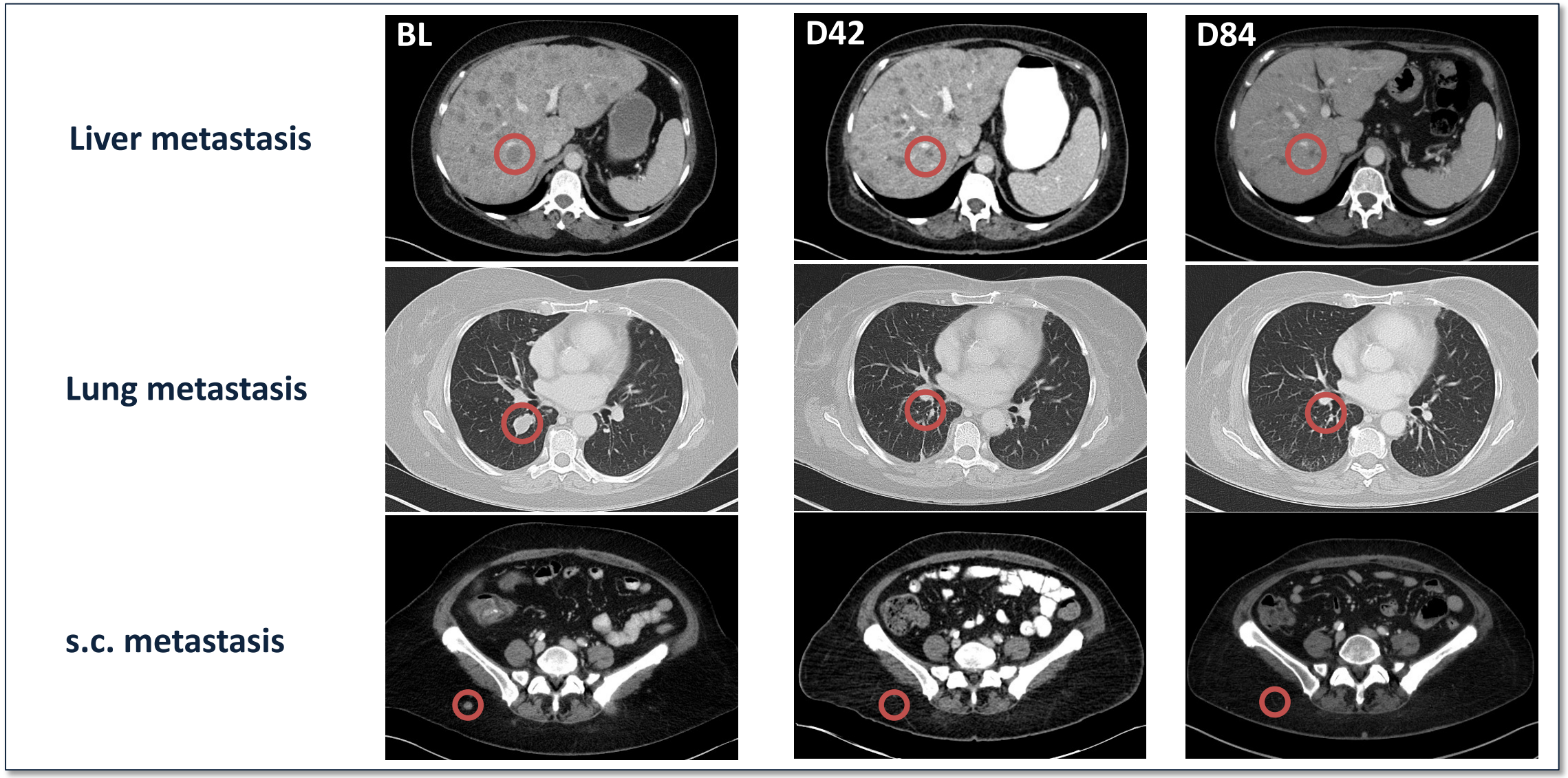
*Post-teatment ACTengine® IMA203 infiltration in 10/12 patients with available biopsy, for 2/12 patients, infiltration was not evaluable due to insufficient tumor size or tumor content in the biopsy; Biopsy not available for 4/16 patients, Data cut-off – 05-Oct-2021

Case Study: Biomarkers in Patient 203-DL3-01



All laboratory analyses done locally at site; vector copies numbers assessed by PCR at Immatics

Case Study: Response in Patient 203-DL3-01

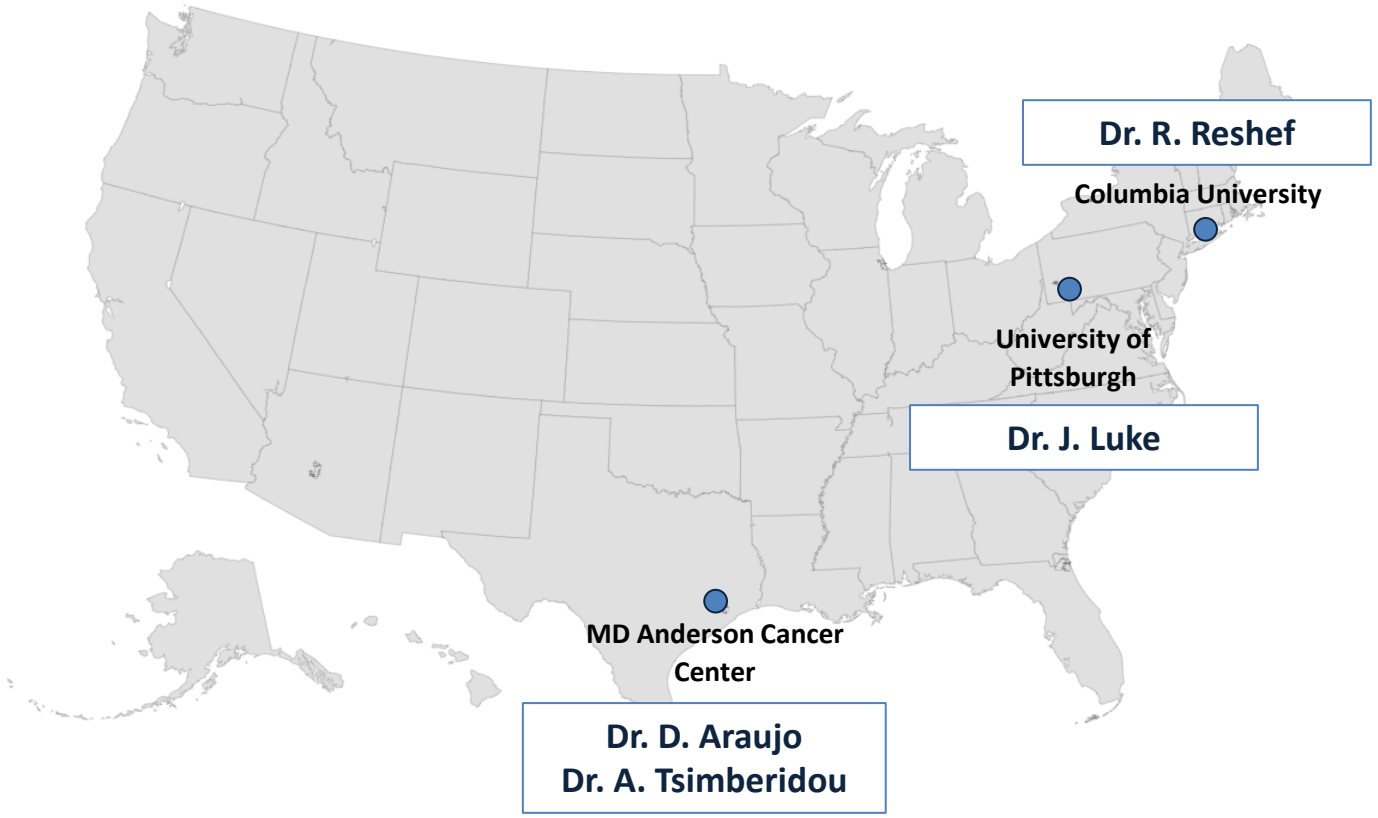


Conclusions

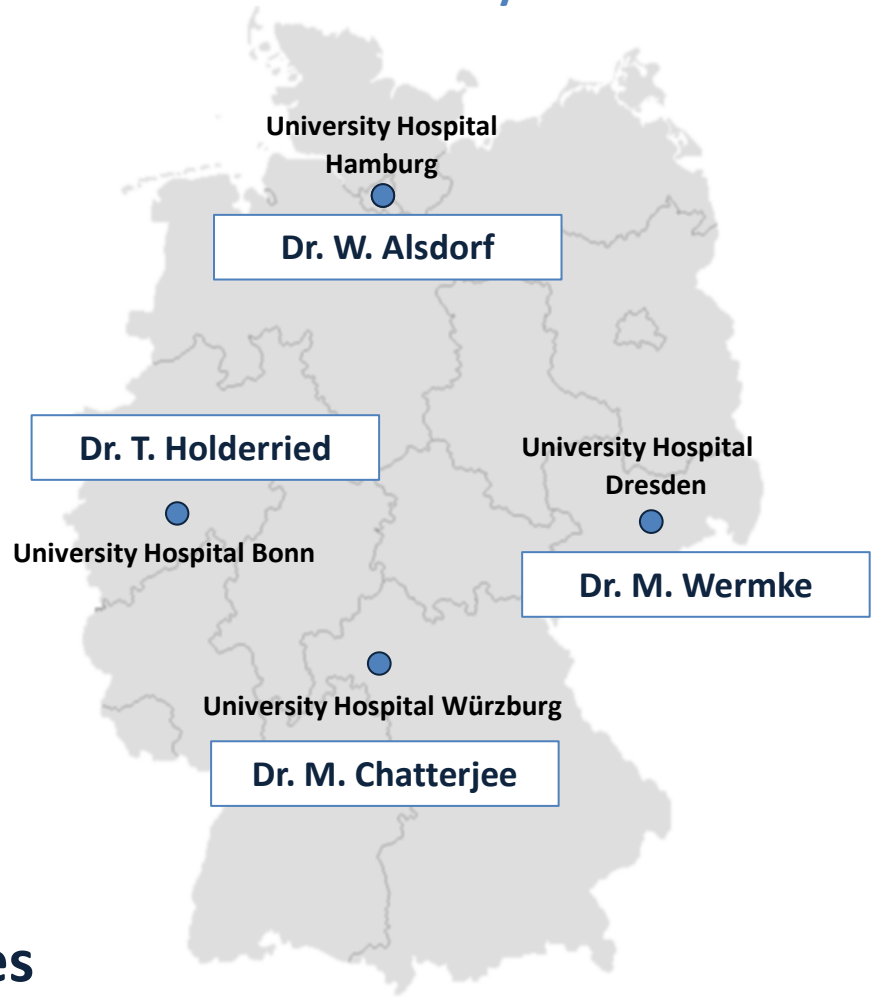
- Transient and manageable treatment-emergent adverse events as expected for cell therapies without signs of autoreactivity
- High T cell engraftment, persistence and infiltration into tumor tissue
- Objective Responses (RECIST1.1) in 8/16 patients across multiple solid cancers – all responses occurring above dose level 1

Special Thanks to the Patients, their Families

United States



Germany



… and IMA203 Investigators at the Clinical Sites