TCR Bispecific Molecule TCER® IMA402 Targeting PRAME

- Phase 1 Dose Escalation Clinical Data Update

November 18, 2024

Data cut-off Nov 6, 2024

Delivering the Power of T cells to Cancer Patients

IMA402 Phase 1 Dose Escalation Study

Summary as of Nov 6, 2024

- **Study design and patient population**
  - BLRM-model based dose escalation with currently 33 patients treated with IMA402 at a dose range from 0.02 mg to 4 mg

  → *preclinical in-vivo data suggested relevant anti tumor efficacy starting at ~3 mg human equivalent dose (DL7)*
  - Advanced metastatic solid cancer patients with no available treatment option, PRAME expression tested retrospectively
  - Efficacy-evaluable population: N=21 patients (per protocol and excluding PRAME-negative patients)
  - Relevant patient population: N=9 patients received ≥3 mg (DL7) via initial or escalated dose (N=8 DL7, N=1 DL8)
- **Favorable tolerability profile with CRS and transient lymphopenia being most common AE, dose escalation ongoing**
- **Early PK data indicates median half-life of ~7 days, potentially enabling bi-weekly dosing**
- **Initial signs of clinical activity, associated with PRAME expression and IMA402 dose**
  - No relevant tumor shrinkage in PRAME-*negative* patients
  - Dose-dependent clinical activity in PRAME-*positive/NT* patients with DCR of 52% across all doses
  - Tumor shrinkage in 25% of patients at low doses (DL1-6) including one unconfirmed partial response
  - **Tumor shrinkage in 78% (7/9) of patients at relevant doses (DL7+, ≥3 mg) including**
    - **1 cPR in cutaneous melanoma (-40.2% and ongoing at 3 months)**
    - **2 SD with significant tumor shrinkage in cutaneous/uveal melanoma (-27.5%/-25% and ongoing at 6+ weeks/8+ months)**
    - **1 SD in ovarian cancer (-13% and ongoing at 3 months)**

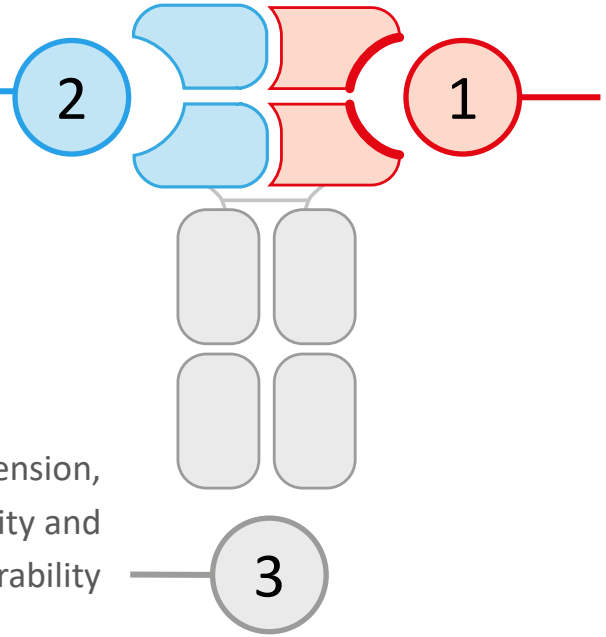
For comprehensive patient flow chart, see appendix

NT: not tested or not evaluable for PRAME expression; CRS: Cytokine release syndrome; DCR: Disease control rate

TCER® – Immatics' Next-generation, Half-Life Extended Bispecifics

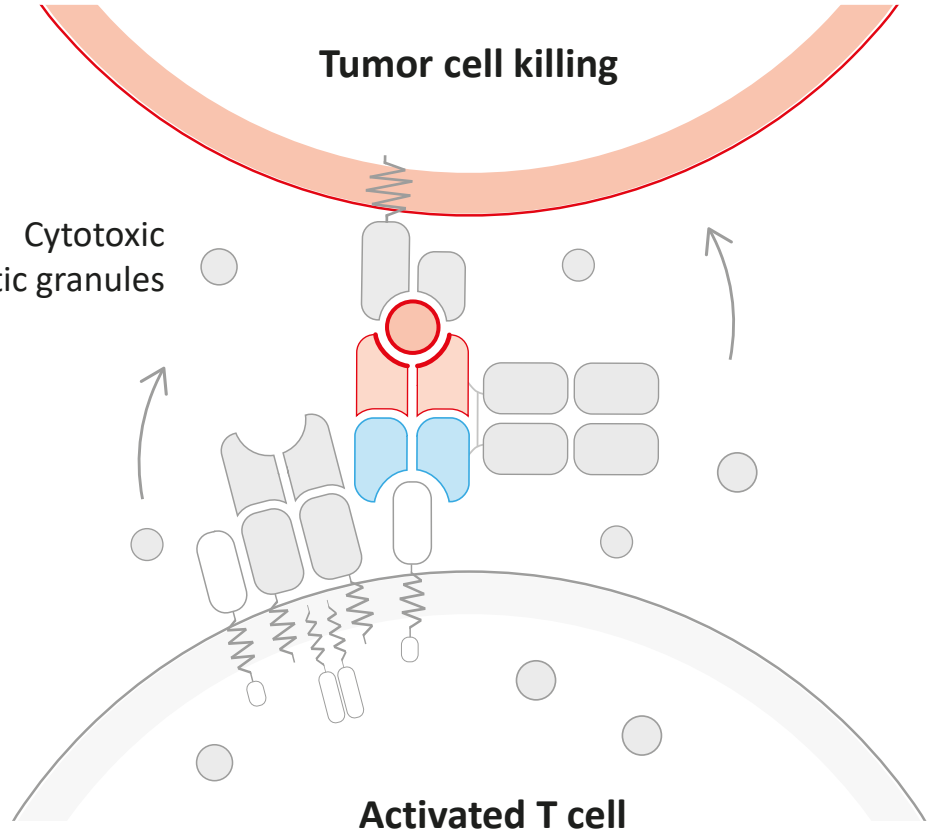
Proprietary TCER® Format Consisting of Three Distinct Elements

Low-affinity
T cell recruiter
against CD3/TCR



High-affinity TCR domains targeting **XPRESIDENT®-selected** tumor-specific peptide-HLA molecules

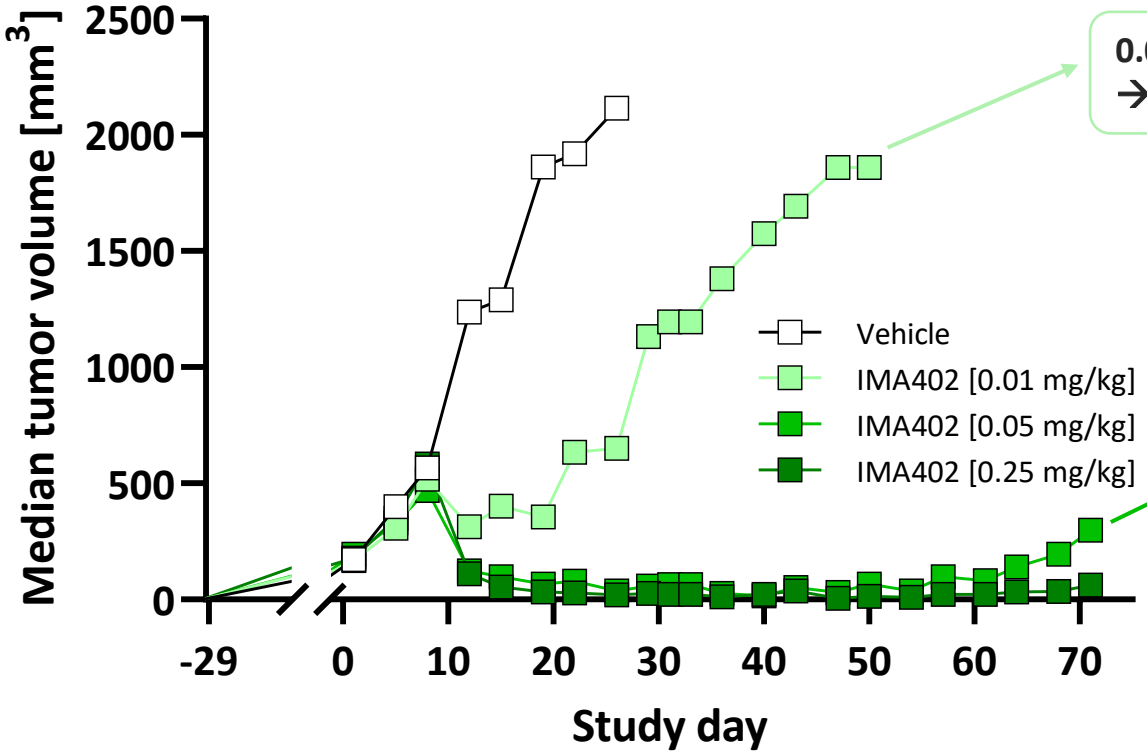
Fc part for half-life extension, favorable stability and manufacturability



Next-gen, half-life extended TCER® format designed to
→ safely apply high drug doses for activity in a broad range of tumors
→ achieve optimized scheduling

TCER® IMA402 Achieves Dose-Dependent Durable Tumor Control *in vivo*

Dose-response Relationship in Mouse Xenograft Model



0.01 mg/kg mouse dose
→ equivalent to approximately 0.6 mg human dose (~DL5)

0.05 mg/kg mouse dose
→ equivalent to approximately 3 mg human dose (DL7)

Preclinical data suggest that a dose of ≥3mg of IMA402 (DL7 in Phase 1 trial) is expected to start showing relevant efficacy in humans

Phase 1/2 Clinical Trial to Evaluate TCER® IMA402 Targeting PRAME

Trial Overview

Phase 1/2 clinical trial to evaluate safety, tolerability and anti-tumor activity of IMA402

- HLA-A*02:01-positive patients with recurrent and/or refractory solid tumors with high PRAME prevalence
- Initially weekly i.v. infusions
- Potential for early adjustment of treatment interval based on PK data of half-life extended TCER® format

Phase 1: Dose Escalation

Adaptive design aimed at accelerating dose escalation

MTD/ RP2D

- Basket trial in focus indications to accelerate signal finding
- Melanoma, ovarian cancer, lung cancer, uterine cancer and others

Phase 2a: Dose Expansion

Expansion cohort

Expansion cohort

Expansion cohort

- Specific indications plus ongoing basket
- Combination therapies
- Optional dose/application optimization

MTD: maximum tolerated dose, RP2D: recommended phase 2 dose

Baseline Characteristics
Heavily Pre-treated Patients

Characteristic	Safety population (N=33)	Efficacy-evaluable population[1] (N=21 excl. PRAME neg.)		
	All patients dosed DL1-DL8	PRAME-negative patients across DLs N=7	PRAME-positive/NT patients DL1-DL6 N=12	**DL7+ N=9**
Age Median (min, max)	61 (28, 82)	62 (56, 75)	62 (28, 82)	**61 (40, 74)**
ECOG performance status				
0 - n [%]	18 [54.5]	4 [57.1]	5 [41.7]	**7 [77.8]**
1 - n [%]	15 [45.5]	3 [42.9]	7 [58.3]	**2 [22.2]**
2 - n [%]	0 [0.0]	0 [0]	0 [0]	**0 [0.0]**
Prior lines of systemic treatment Median (min, max)	3 (1, 5)	3 (1, 4)	3.5 (2, 5)	**3 (1, 5)**
LDH at baseline				
≤ 1xULN [%]	15 [45.5]	4 [57.1]	4 [33.3]	**5 [55.6]**
1-2xULN [%]	15 [45.5]	2 [28.6]	7 [58.3]	**4 [44.4]**
> 2xULN [%]	3 [9.1]	1 [14.3]	1 [8.3]	**0 [0.0]**
Baseline tumor burden Median target lesion sum of diameter [mm] (min, max)	76.5 (24.5, 398)	80.0 (30.1, 180)	76.4 (46, 398)	**61.4 (24.5, 258)**
Number of organs with metastases Median (min, max)	3 (1, 8)	2 (1, 5)	3 (2, 7)	**3 (1, 6)**
Liver and/or Brain Lesions [% of patients]	54.5	71.4	41.7	**55.6**

[1]Efficacy Analysis Set prospectively defined in the study protocol: patients who received at least four IMA402 infusions and had at least one post-baseline efficacy assessment or clinical progression.
LDH: Lactate dehydrogenase; ULN: Upper limit of normal; NT: not tested or not evaluable for PRAME expression

IMA402 Demonstrates Favorable Tolerability in N=33 Patients

Most Frequent Related AEs were Lymphopenia and CRS

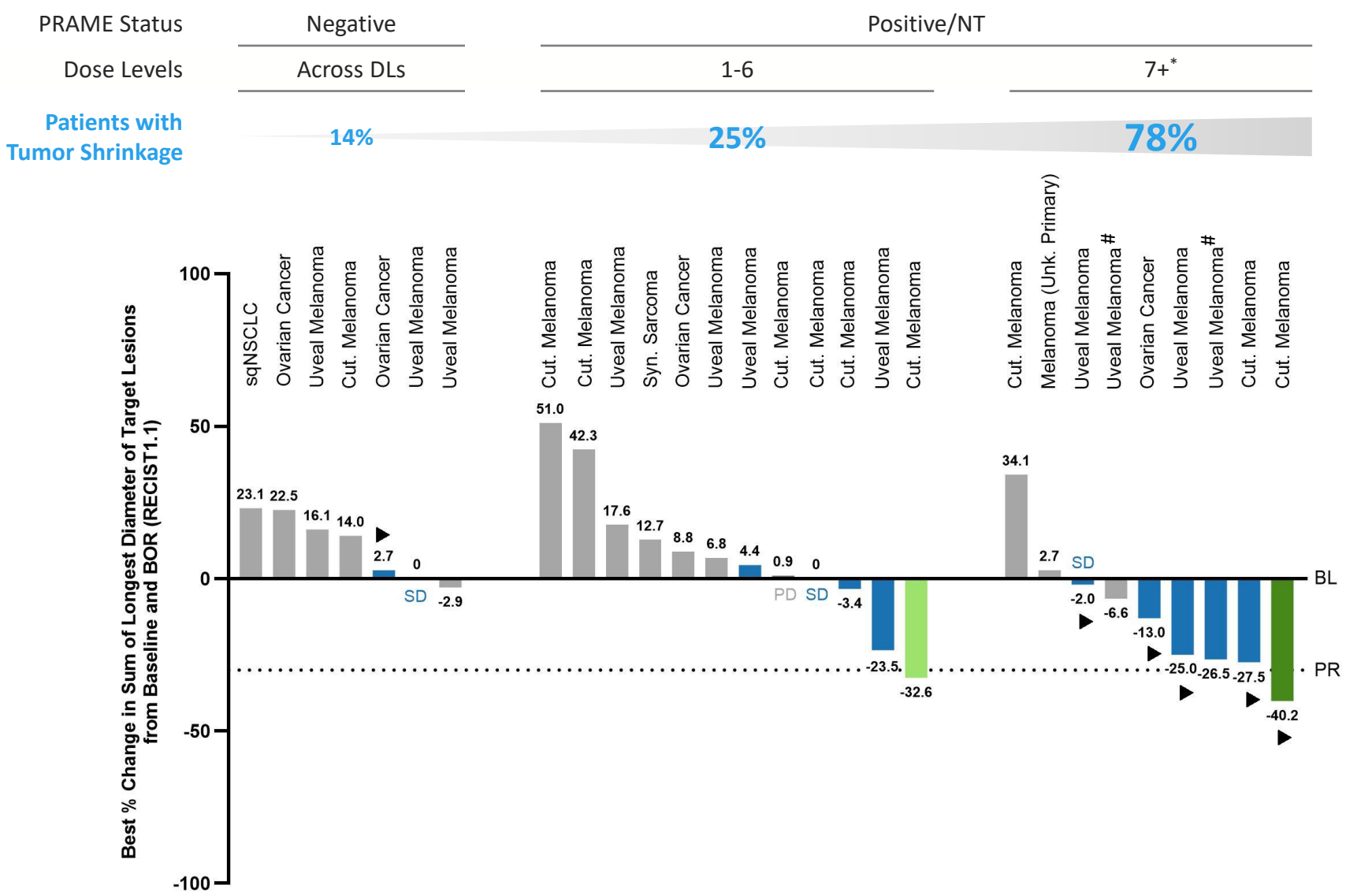
Treatment-related AEs[1], n [%]	All Grades	≥ Grade 3
Lymphopenia	17 [52]	10 [30]
Cytokine release syndrome	16 [48]	1 [3]
Arthralgia	9 [27]	0
Fatigue	9 [27]	0
Pruritus	7 [21]	0
Rash	7 [21]	0
Aspartate aminotransferase increased	6 [18]	2 [6]
Alanine aminotransferase increased	5 [15]	1 [3]
Pyrexia	5 [15]	0
Anaemia	4 [12]	2 [6]
Vomiting	4 [12]	0
C-reactive protein increased	3 [9]	0
Headache	3 [9]	0
Rash maculo-papular	3 [9]	0
Neutropenia	2 [6]	2 [6]
Stomatitis	2 [6]	1 [3]
Blood creatinine increased	1 [3]	1 [3]
Electrocardiogram abnormal	1 [3]	1 [3]
Gamma-glutamyltransferase increased	1 [3]	1 [3]
Hypertension	1 [3]	1 [3]
Immune-mediated arthritis	1 [3]	1 [3]
Tumor lysis syndrome	1 [3]	1 [3]
Tumor pain	1 [3]	1 [3]

TEAEs, n [%]	All Grades	≥ Grade 3
Any	33 [100]	17 [52]
Treatment-related	32 [97]	15 [45]

- **Favorable tolerability** profile
- **Most frequent/relevant related AEs** were
  - transient lymphopenia,
  - mostly mild to moderate CRS (42% Grade 1, 3% Grade 2, 0% Grade 3, 3% Grade 4), majority at first dose
  - One DLT: Grade 4 CRS (fully resolved)
- No IMA402-related Grade 5 events
- **MTD not reached**

[1]All treatment-emergent adverse events (TEAEs) at least possibly related to IMA402 infusion with grade 1-2 occurring in at least 9% of patients and all events with grade 3-5;
CRS: Cytokine release syndrome; MTD: Maximum tolerated dose.; One AE "Rash, Intermittent" was not coded at data cut-off, but added to the preferred term "Rash"

Early Signs of Clinical Activity Associated with PRAME Expression and IMA402 Dose



BOR (RECIST 1.1)

- PD
- SD
- PR
- cPR
- ▶ Ongoing response / SD (RECIST1.1/ iRECIST)

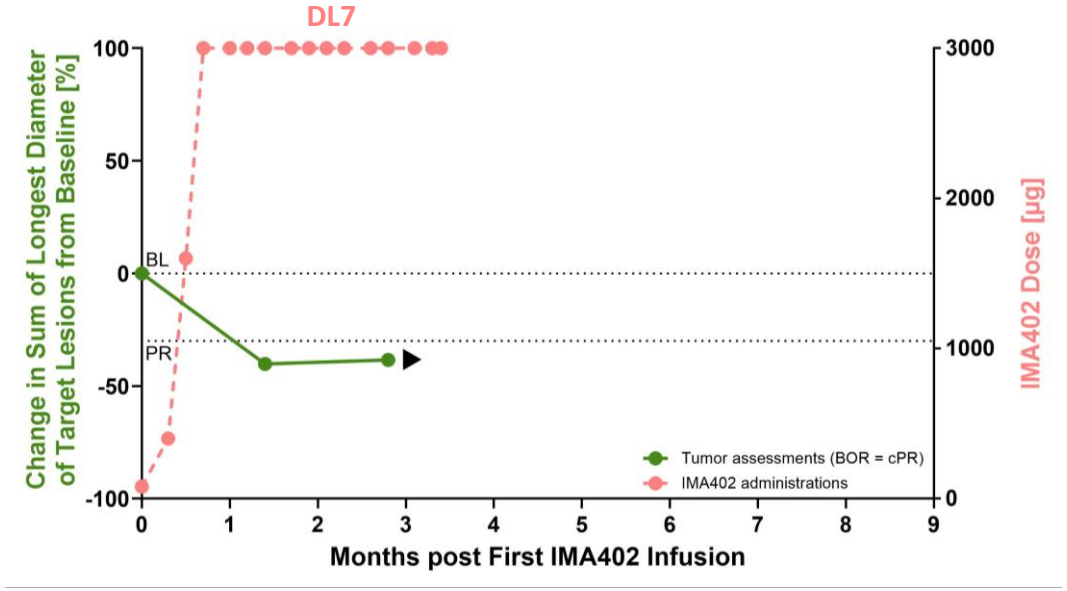
- Melanoma patient with confirmed partial response ongoing at 3 months (DL7, see next slide)
- Melanoma patient with -27.5% tumor shrinkage ongoing at first scan (DL8)
- Uveal melanoma patient with -25.0% tumor shrinkage deepening over time and ongoing (started at DL4 and currently at DL7, see next slide)
- Ovarian cancer patient with -13% tumor shrinkage ongoing at 3 months (started at DL6 and currently at DL7)

* Patients who received DL7 or higher, either from start or as part of intra-patient dose-escalation; #continuing treatment; PD: Progressive Disease; SD: Stable Disease; PR: Partial Response; cPR: Confirmed Partial Response; BOR: Best Overall Response; BL: Baseline; NT: not tested or not evaluable for PRAME expression

Exemplary Patient Cases Suggesting Dose-Dependent Tumor Response

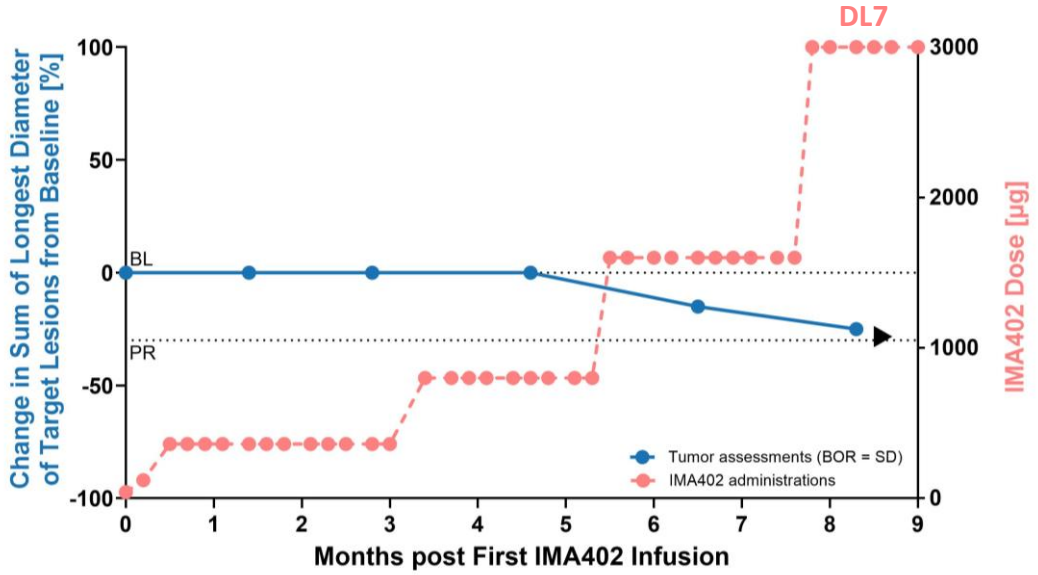
Patients with Disease Control (RECIST1.1) at Relevant Doses (DL7+)

Case 1



Patient Characteristics & Outcomes
52-year-old female with cutaneous melanoma
Lesions in lung, lymph nodes, gall bladder, fat tissue, pancreas
1 prior line of therapy and maintenance with anti-PD-1
Patient received DL7 from start (after step-up dosing)
Ongoing cPR at 3 months post treatment start with -40.2% reduction of target lesion size

Case 2

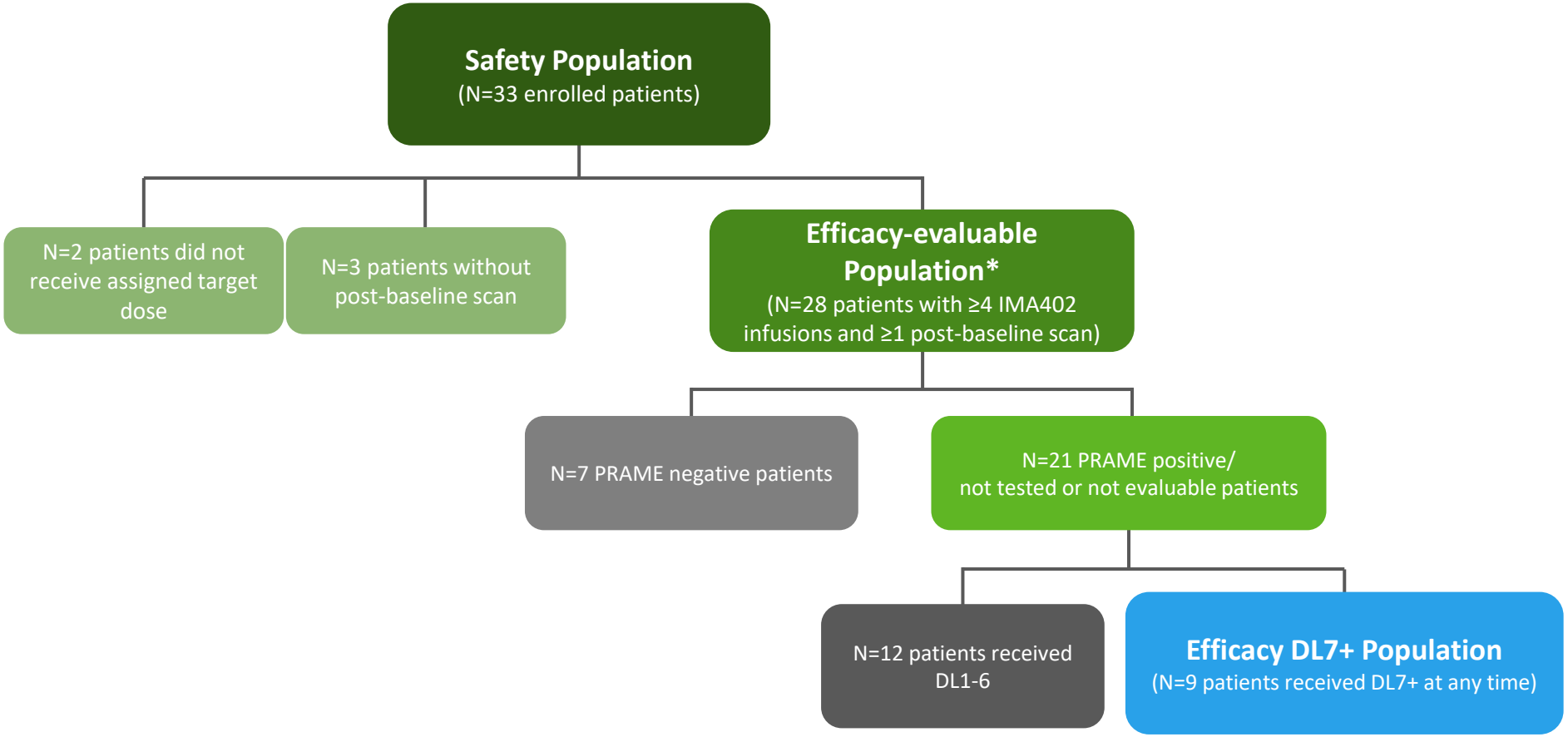


Patient Characteristics & Outcomes
46-year-old female with uveal melanoma
Lesions in liver
3 prior lines of therapy with anti-PD1 and tebentatafusp
Patient received DL4 and went up to DL7 through intra-patient dose escalation
Ongoing SD at 8+ months post-treatment start with -25% reduction of target lesion size

BOR: Best Overall Response; SD: Stable Disease; cPR: Confirmed Partial Response; arrow: Ongoing response / stable disease (RECIST 1.1/ iRECIST)

Appendix

IMA402 Phase 1a Patient Population Flow Chart



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Delivering

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