BERLIN 2025 ESMO congress

Efficacy and Safety of Anzutresgene Autoleucel (IMA203), a PRAME-directed T-cell Receptor T-cell Therapy, in Patients with Previously Treated Advanced or Metastatic Uveal Melanoma from a Phase 1 Trial

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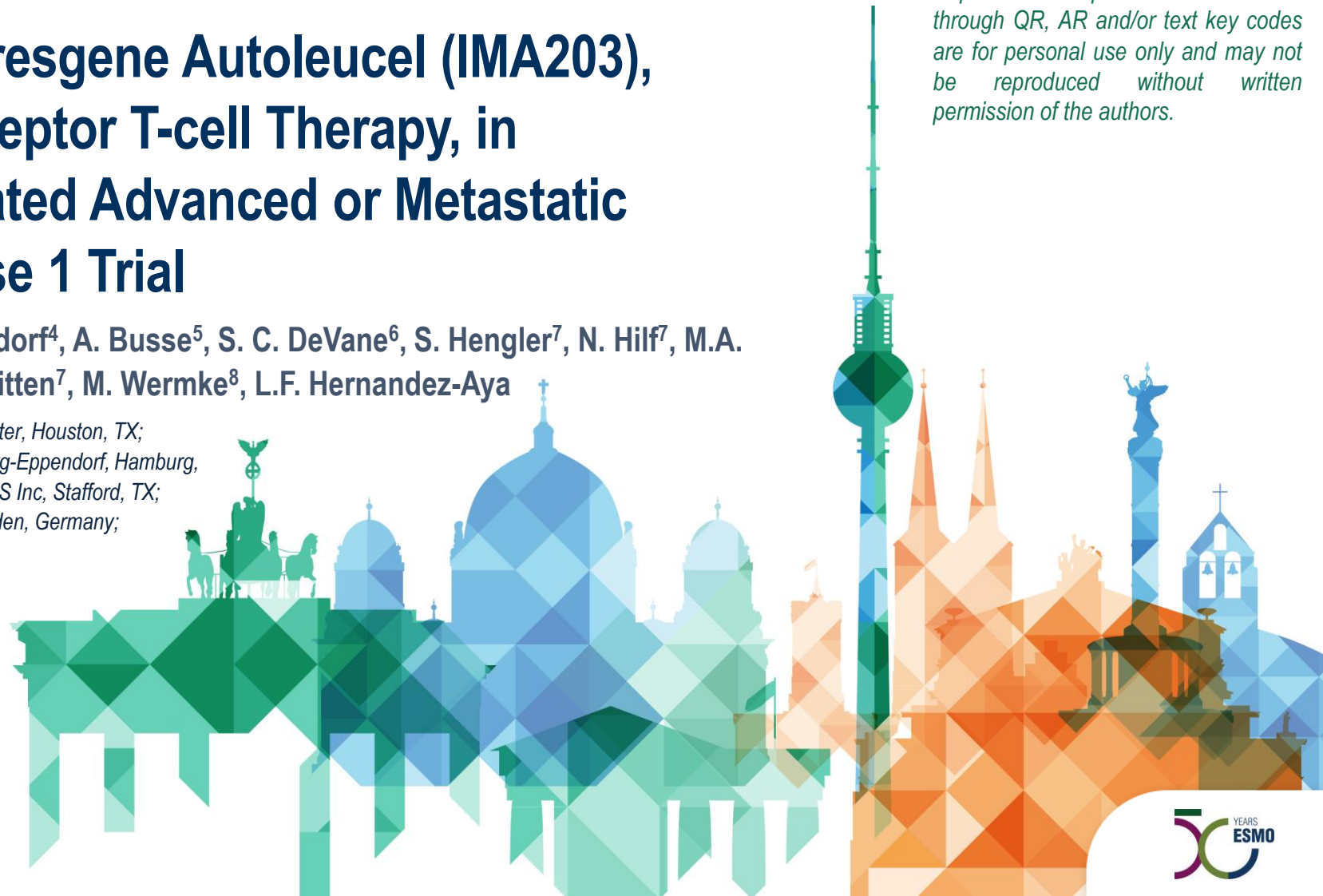

Sapna Patel, MD

Presidential Symposium III
Proffered Paper #1600O
20 October 2025

50 YEARS ESMO

DECLARATION OF INTERESTS

Institutional clinical trial support: Linnaeus, Replimune

Advisory board, steering committee, data safety monitoring board, consulting: Bristol-Myers Squibb, Daiichi Sankyo, Fortvita, Ideaya, Immatics, IO Biotech, MSD, Natera, Novartis, Obsidian, Pfizer, Replimune, Scancell, TriSalus Life Sciences, T3 Pharmaceuticals, Sun Pharmaceuticals, Veda Trials

Commercial Medical Education providers: Clinical Education Alliance, Clinical Care Options, MJH Life Sciences, Melanoma Research Foundation, Vindico Medical

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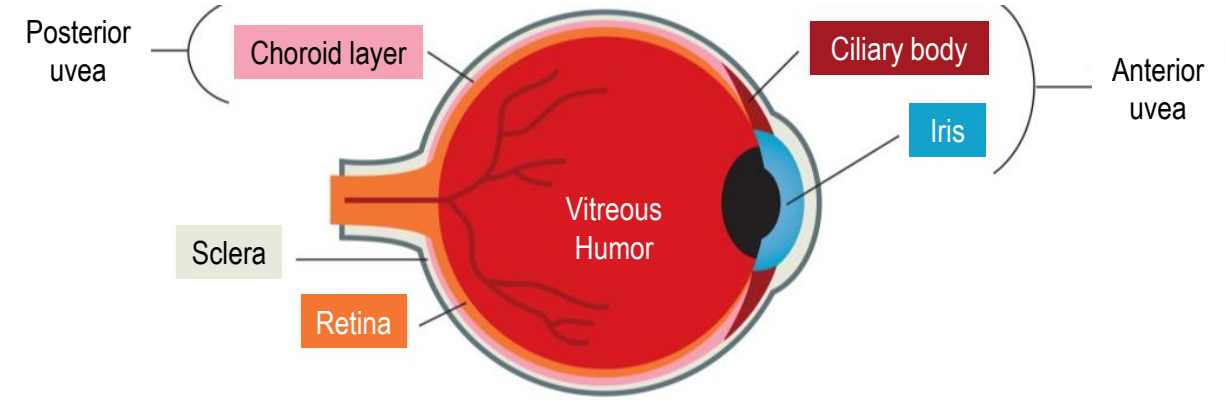
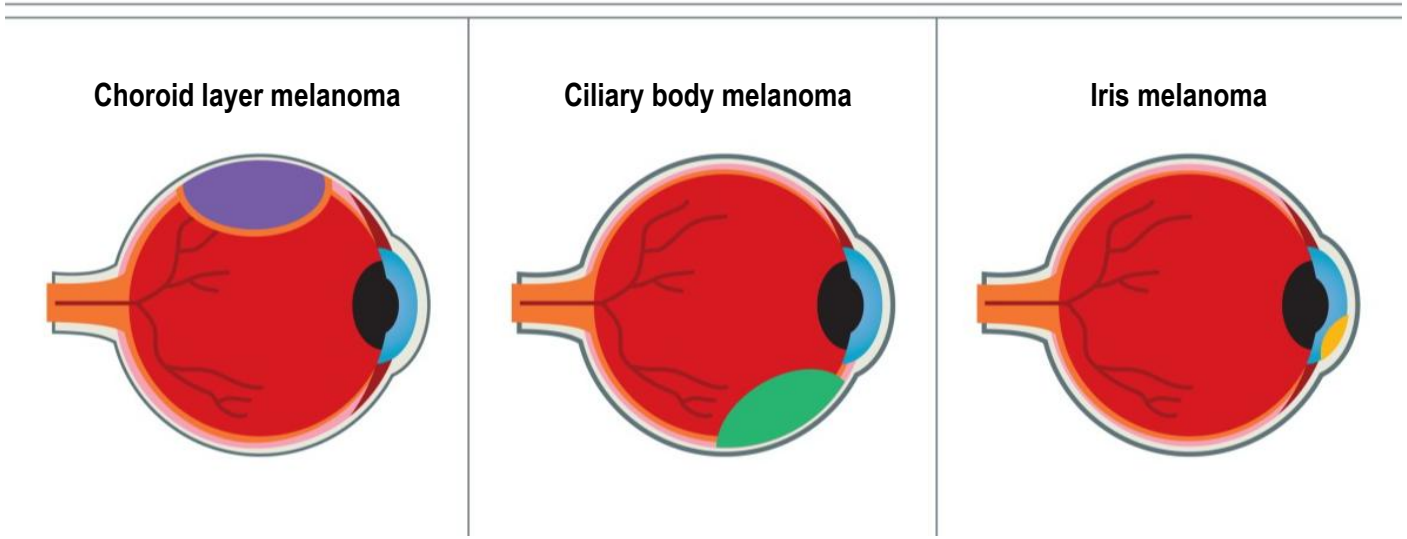
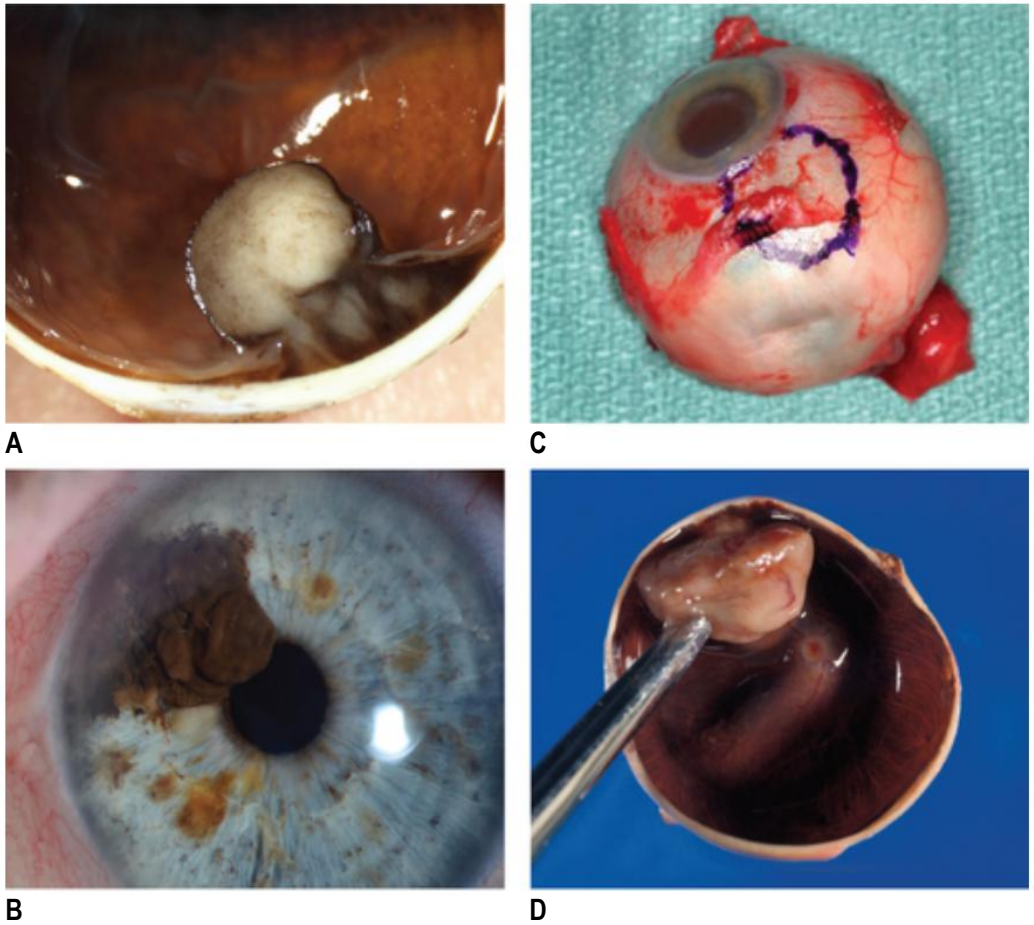
In a cold tumour, does targeting a highly expressed antigen with TCR T-cell therapy lead to clinical benefit?

Uveal Melanoma: The Disease

- Most common tumor of the adult eye
- Worldwide incidence of 0.6-0.7 per 100,000
- Hepatic failure most common cause of death



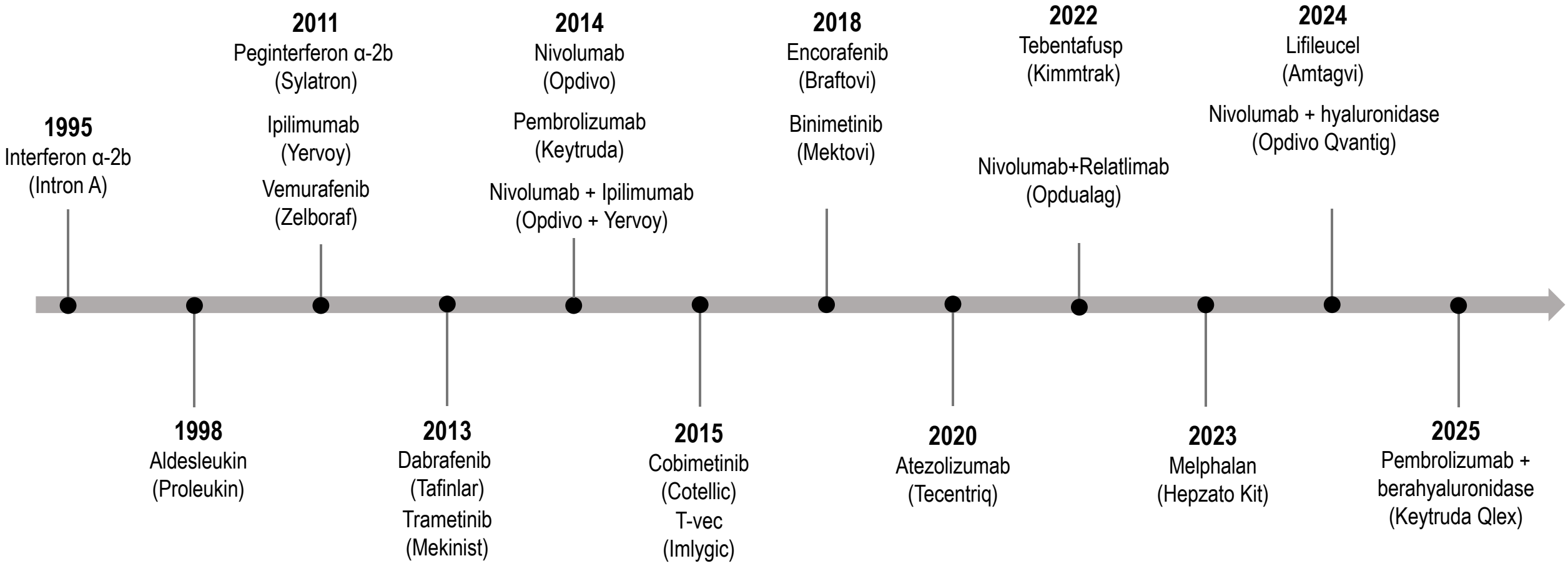




Chattopadhyay C,… Patel SP. *Cancer*. 2016. Reproduced with corresponding author permission.

Uveal Melanoma: The Dilemma

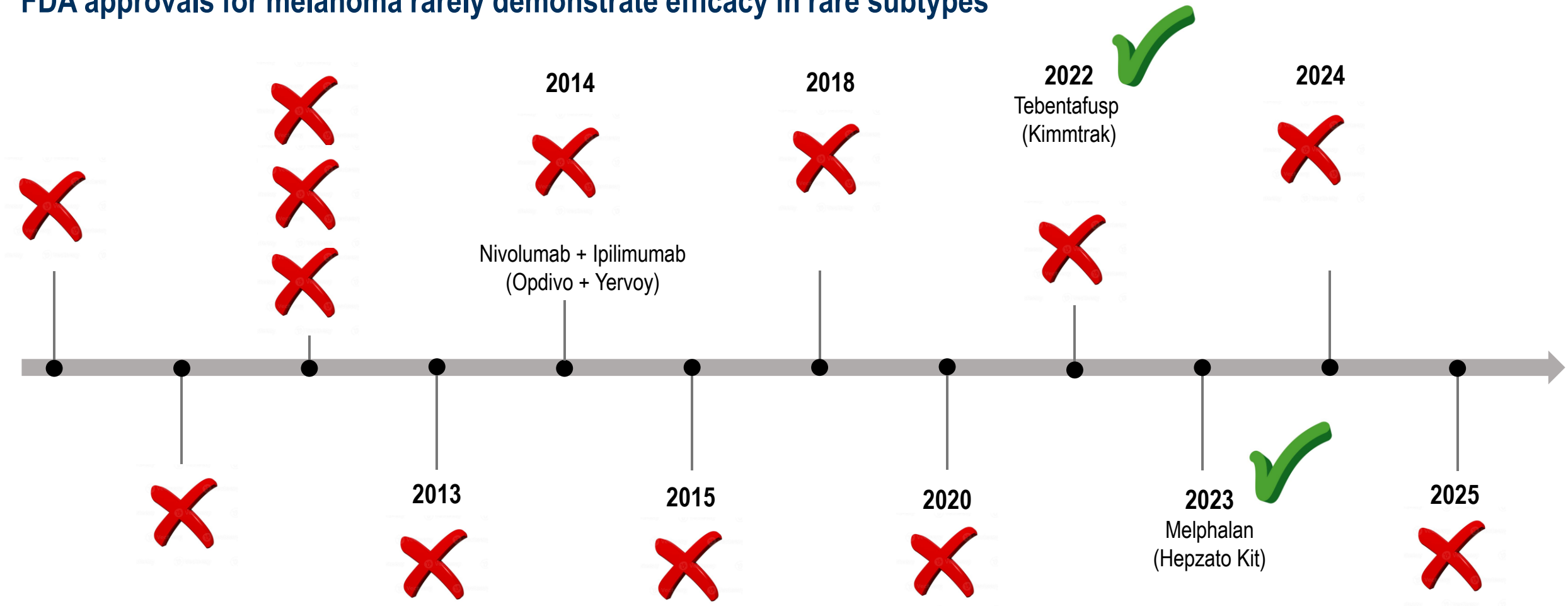
FDA approvals for melanoma rarely demonstrate efficacy in rare subtypes



Adapted from Citeline Disease Analysis (updated Oct 2024) for most approvals; FDA announcements for Kimmtrak (2022) and Amtagvi (2024).

Uveal Melanoma: The Dilemma

FDA approvals for melanoma rarely demonstrate efficacy in rare subtypes



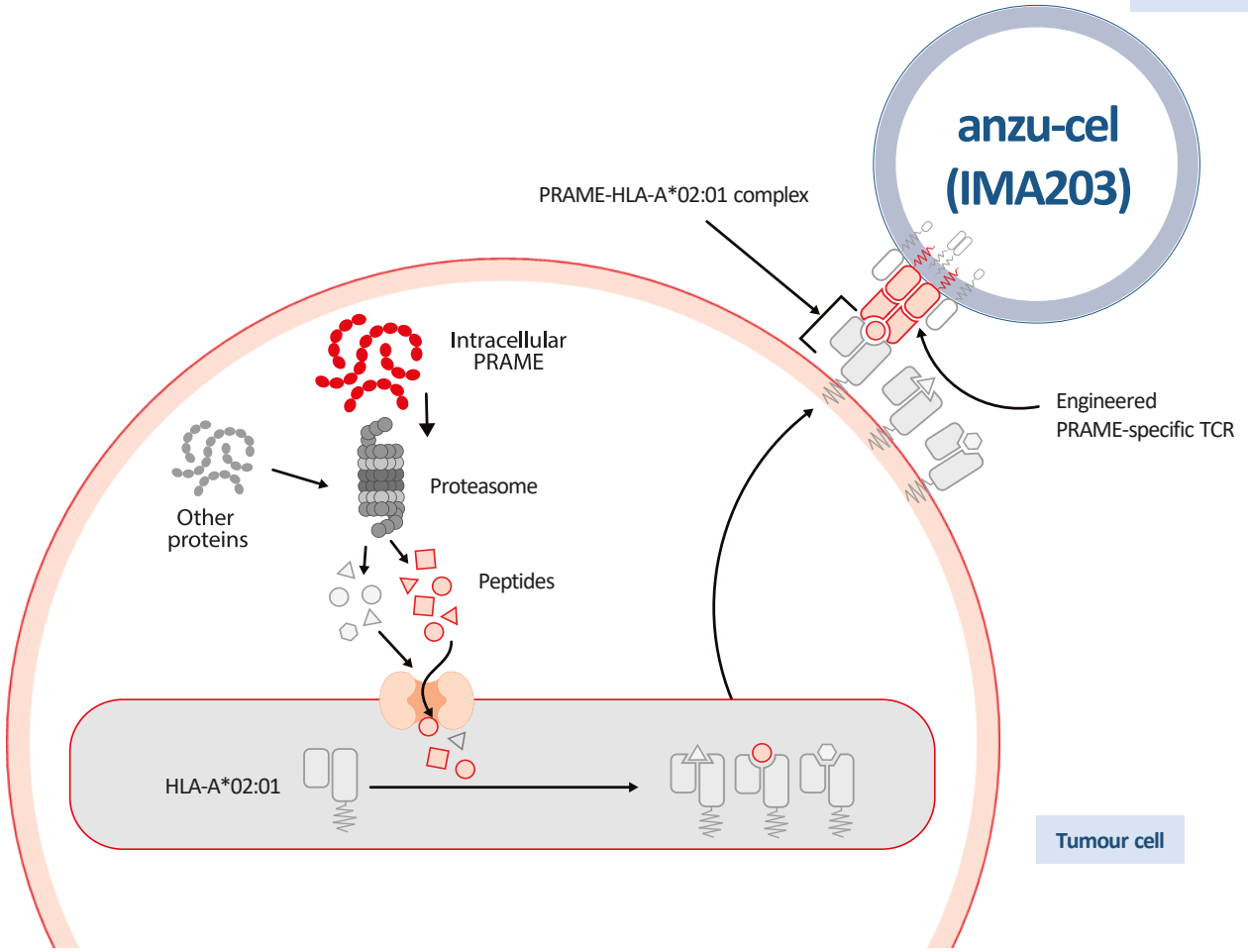
Adapted from Citeline Disease Analysis (updated Oct 2024) for most approvals; FDA announcements for Kimmtrak (2022) and Amtagvi (2024).

Anzu-cel (IMA203): TCR-based Therapy Targeting PRAME

PRAME is expressed in more than 50 cancers

Indication	% PRAME+ Patients[1]
Cutaneous melanoma	95%
Uterine carcinoma	95%
Uterine carcinosarcoma	95%
Synovial sarcoma	95%
Uveal melanoma[2]	**90%**
Mucosal melanoma	90%
Ovarian carcinoma (clear cell, endometroid)	85%
Squamous cell NSCLC	70%
Triple-negative breast carcinoma	65%
Small cell lung cancer	45%
Esophageal small cell carcinoma	45%
Renal papillary cell carcinoma	40%
Cholangiocarcinoma	35%
HER2-enriched breast carcinoma	30%
Adenocarcinoma NSCLC	25%
Head & neck squamous cell carcinoma	25%
Hepatocellular carcinoma	20%
Bladder carcinoma	20%

Mechanism of action of anzu-cel



Anzutresgene autoleucel (anzu-cel, formerly IMA203), [1]Data on file: PRAME target prevalence is based on a proprietary mass spec-guided expression threshold applied to RNAseq and/or IHC data (approximate values; values between 95-100% shown as 95%); [2]PRAME target prevalence in uveal melanoma based on IMADetect® qPCR testing of screening biopsies from 61 clinical trial patients demonstrates substantial higher prevalence of ~90% compared to prevalence based on TCGA data of 50%, TCGA: early & late-stage primary tumor samples, Immatics clinical trials: primarily late-stage/metastatic tumor samples; HER2, Human epidermal growth factor receptor 2; HLA, human leukocyte antigen; NSCLC, non-small cell lung cancer; PRAME, preferentially expressed antigen in melanoma; TCR, t-cell receptor.

Phase 1 Study Design: Anzu-cel in Advanced Solid Tumours Expressing PRAME

Key Objectives

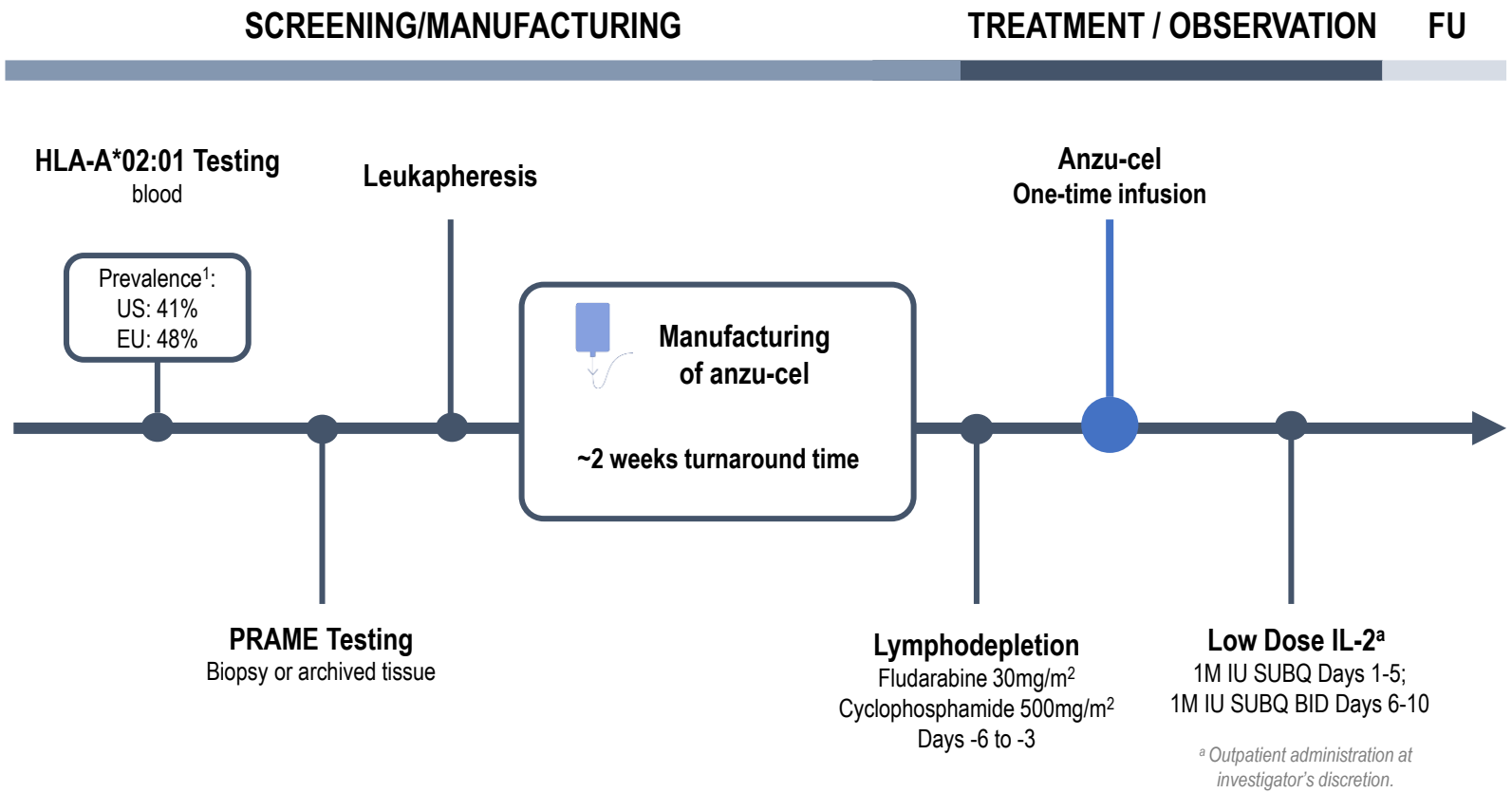
Primary:
- Tolerability
- Determination of RP2D

Secondary:
- Anzu-cel T-cell engraftment, persistence
- Efficacy

Key Eligibility Criteria

- Advanced and/or metastatic solid tumor
- Age ≥ 18 years
- ECOG PS 0-1
- HLA-A*02:01 positive (blood)
- PRAME positive (mRNA)
- No active brain metastasis

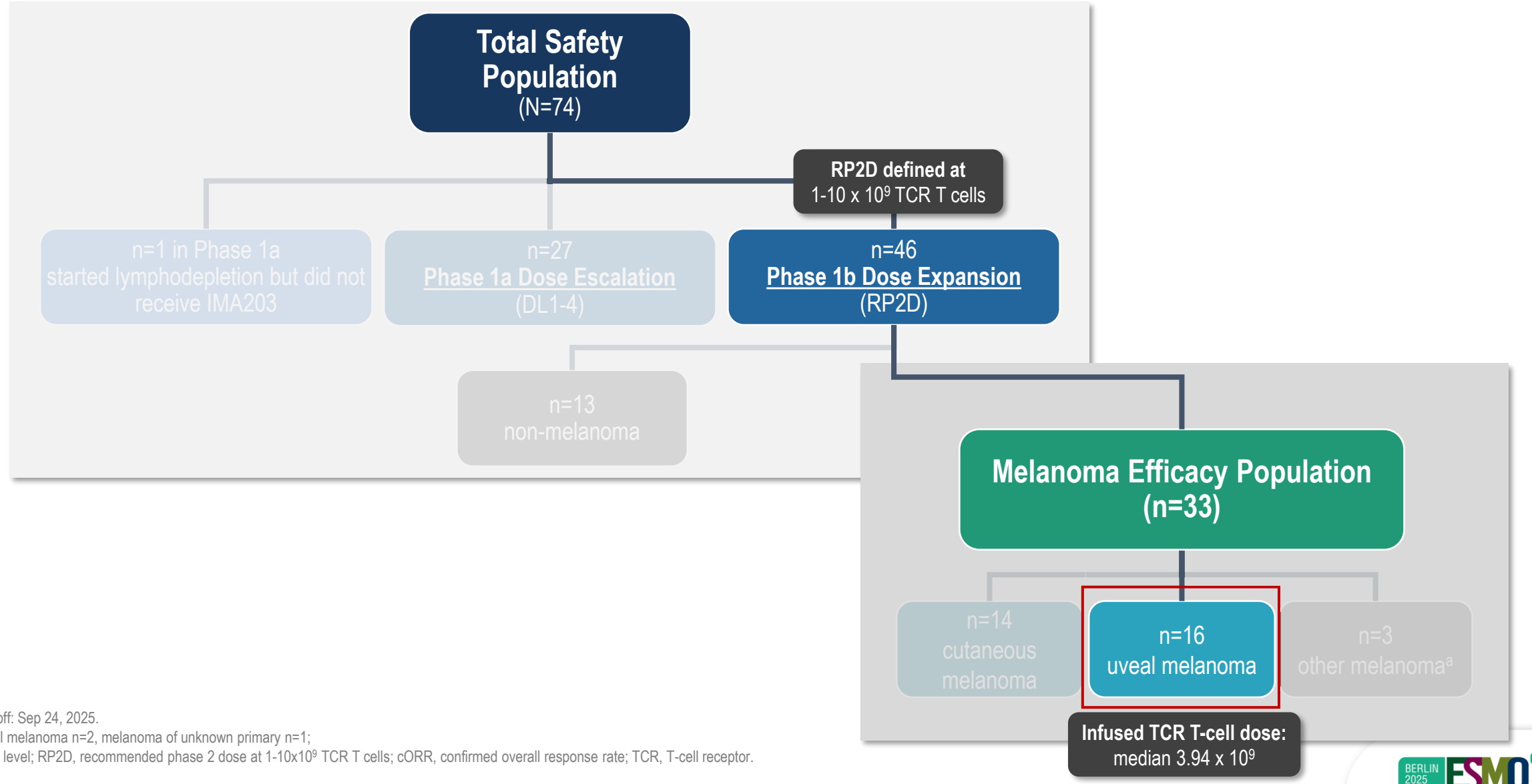
Patient Journey



BID, twice daily; ECOG PS, Eastern Cooperative Oncology Group performance status; FU, follow-up; HLA, human leukocyte antigen; IL, interleukin; IU, international unit; mRNA, messenger ribounucleic acid; QC, quality control; RP2D, recommended phase 2 dose at 1-10x10^9 TCR T cells; SUBQ, subcutaneous.

1. Gragert L et al. Hum Immunol, 2013;74:1313-1320 and census numbers

Anzu-cel Phase 1 Study: Patient Disposition



Data cutoff: Sep 24, 2025.

[a] Mucosal melanoma n=2, melanoma of unknown primary n=1;

DL, dose level; RP2D, recommended phase 2 dose at 1-10x10^9 TCR T cells; cORR, confirmed overall response rate; TCR, T-cell receptor.

Demographics: Uveal Melanoma

Baseline Characteristic	N=16
Age, median (range)	62 (32, 74)
Female, n (%)	10 (63)
Baseline ECOG status 1, n (%)	7 (44)
LDH ≥ ULN, n (%)	9 (56)
AJCC stage*, IV M1a/b/c, %	19 / 75 / 6
Median target lesion SPD, cm (range)	10 (3, 21)
Liver and extrahepatic metastasis, n (%)	**13 (81)**
Liver metastasis only, n (%)	2 (13)
Extrahepatic metastasis only, n (%)	1 (6)

Prior therapy	N=16
Systemic therapies, median (range)	**2 (0, 6)**
Tebentafusp, n (%)	10 (63)
Brenetafusp, n (%)	1 (6)
Liver-directed therapies, n (%)	**16 (100)**
Melphalan hepatic delivery system, n (%)	2 (13)

*AJCC Uveal Melanoma 8th ed.
M1a = largest tumor up to 3 cm
M1b = 3.1-8 cm
M1c = >8 cm

Data cutoff: Sep 24, 2025.
ECOG, Eastern Cooperative Oncology Group; LDH, lactate dehydrogenase; ULN, upper limit of normal.

Anzu-cel: Safety in Uveal Melanoma

TEAEs in ≥25% of patients, n (%)	n=16 Any Grade	n=16 Grade 3/4
Blood and lymphatic system disorders	**15 (94)**	**15 (94)**
Neutropenia	15 (94)	15 (94)
Anemia	12 (75)	8 (50)
Thrombocytopenia	9 (56)	6 (38)
Leukopenia	6 (38)	6 (38)
Lymphopenia	4 (25)	4 (25)
Gastrointestinal disorders	**15 (94)**	**0 (0)**
Nausea	13 (81)	0 (0)
Constipation	4 (25)	0 (0)
Diarrhea	4 (25)	0 (0)
Vomiting	4 (25)	0 (0)
General disorders/administration. site conditions	**10 (63)**	**0 (0)**
Fatigue	8 (50)	0 (0)
Pyrexia	5 (31)	0 (0)
Chills	4 (25)	0 (0)
Investigations	**9 (56)**	**2 (13)**
ALT/AST increased	8 (50)	2 (13)
Blood creatinine increased	5 (31)	0 (0)
C-reactive protein increased	4 (25)	0 (0)
Metabolism and nutrition disorders	**7 (44)**	**2 (13)**
Hyponatremia	5 (31)	2 (13)
Hypokalemia	4 (25)	0 (0)
Skin and subcutaneous tissue disorders	**7 (44)**	**2 (13)**
Rash/rash maculo-popular	7 (44)	2 (13)
Nervous system disorders	**6 (38)**	**0 (0)**
Headache	6 (38)	0 (0)

Adverse Events of Special Interest, n (%)	n=16 Any Grade
CRS, any grade	**16 (100)**
Grade 1	6 (38)
Grade 2	7 (44)
Grade 3	3 (19)
ICANS, any grade	**2 (13)**
Grade 1	0
Grade 2	0
Grade 3	2 (13)
HLH[1], any grade	**1 (6)**
Grade 1	0
Grade 2	1 (6)
Grade 3	0

No Grade 4 or 5 AESIs were observed

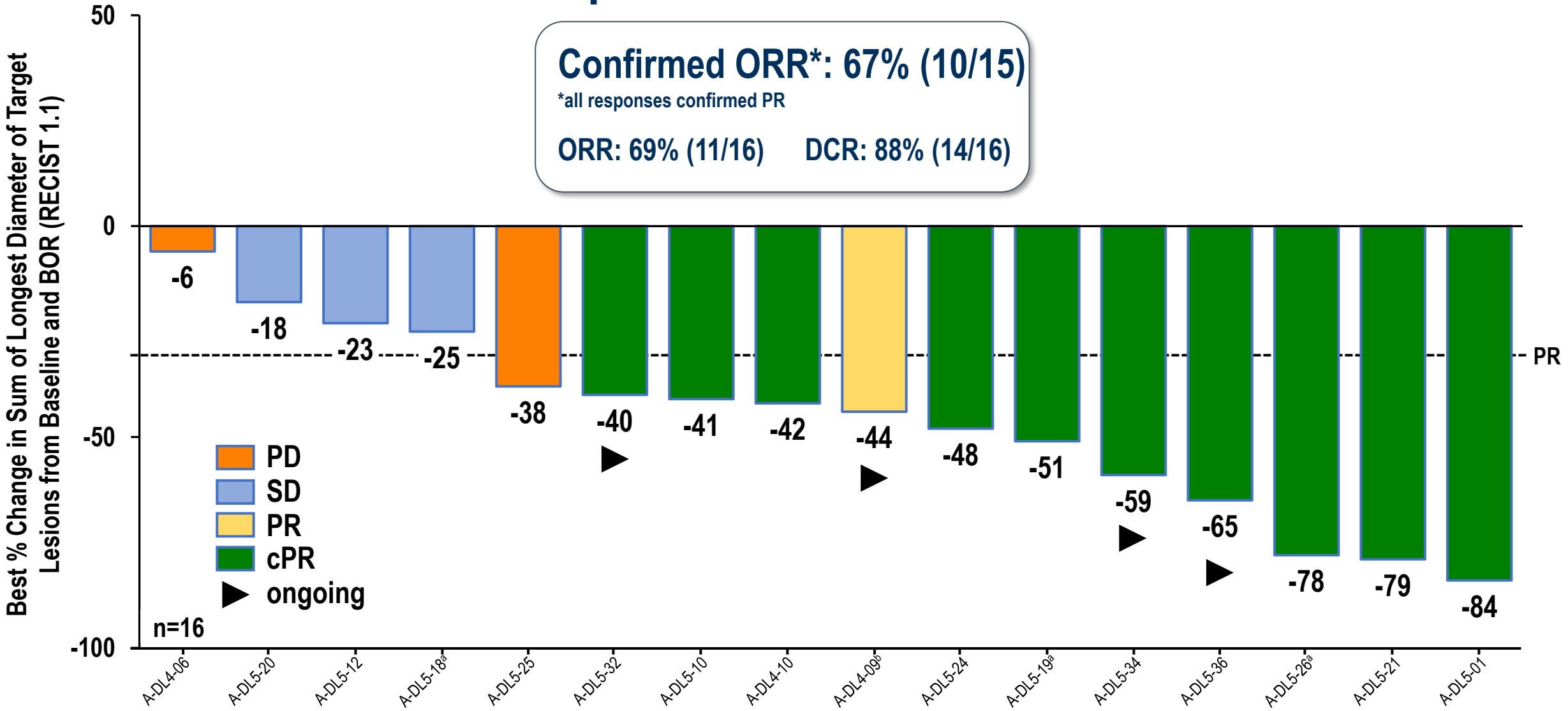
- Most frequent TEAEs were anticipated cytopenias associated with lymphodepletion
- Expected and manageable CRS, mostly Grade 1-2, consistent with mechanism of action
  - Median day of onset (range): 1 (0, 3)
  - Median duration, days (range): 9 (2, 28)
  - Most CRS resolved by day 14
  - No long-term CRS
- No anzu-cel-related Grade 5 events

Tolerability in uveal melanoma is generally consistent with full anzu-cel tolerability profile

Data cutoff: Sep 24, 2025. Patients are counted only once per adverse event and severity classification.

[1] HLH was reported as HLH-like syndrome; AESI, adverse event of special interest; ALT, alanine aminotransferase; AST, aspartate aminotransferase; CRS, cytokine release syndrome; HLH, hemophagocytic lymphohistiocytosis; ICANS, immune effector cell-associated neurotoxicity syndrome; TEAE, treatment-emergent adverse event.

Anzu-cel: Best Overall Response in Uveal Melanoma



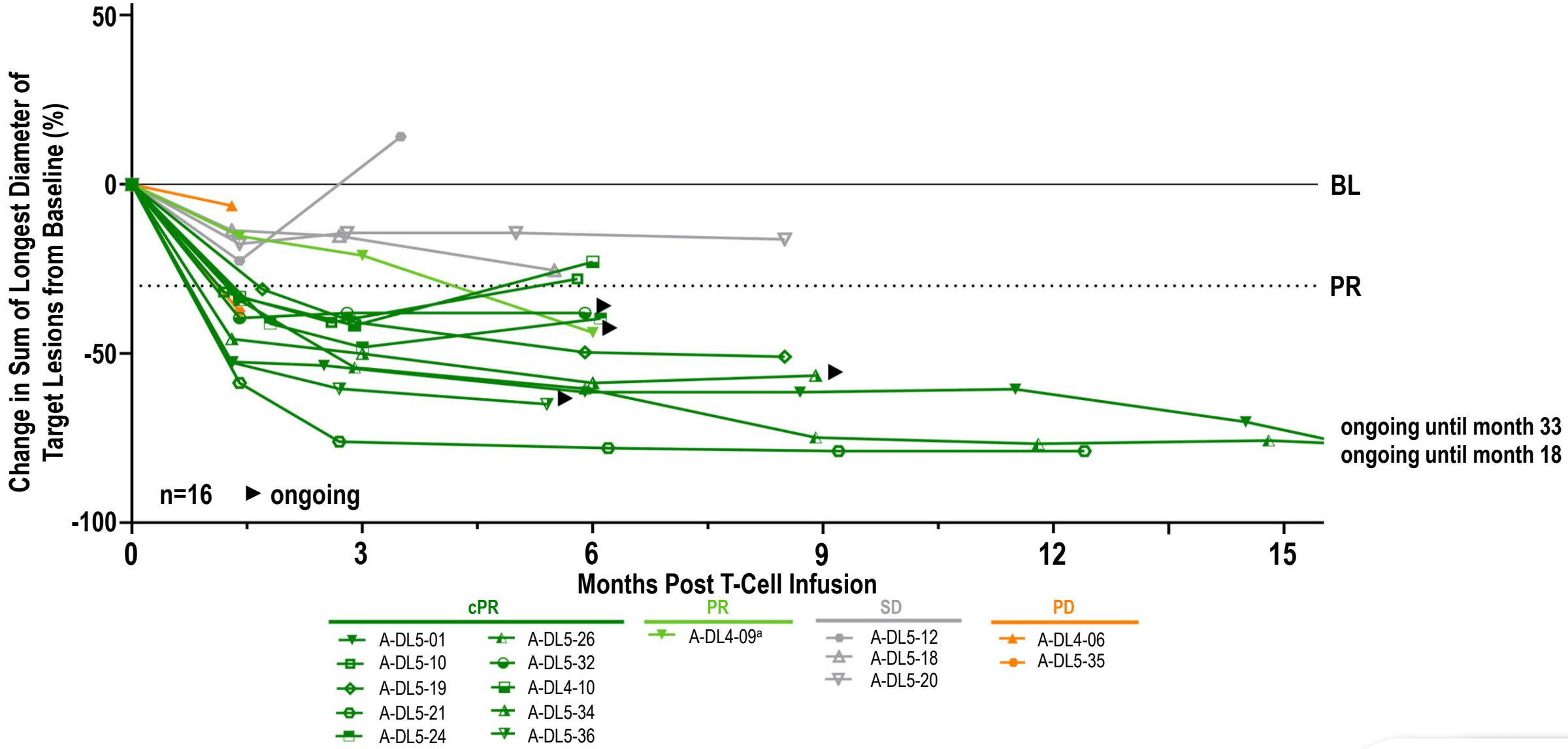
Data cutoff: Sep 24, 2025.

Uveal melanoma population excludes 1 patient with ongoing unconfirmed PR from cORR; [a]Maximum change of target lesions and RECIST1.1 response at different timepoints. [b]Patient off study at data cutoff date (withdrew consent).

14/16 patients had liver target lesions with median best change of longest diameter of liver target lesions (range) of -49.6% (-100, 10).

cPR, (confirmed) partial response; RECIST, Response Evaluation Criteria in Solid Tumors; SD, stable disease; PD, progressive disease; ORR, objective response rate; DCR, disease control rate at week 6.

Anzu-cel: Duration of Response in Uveal Melanoma



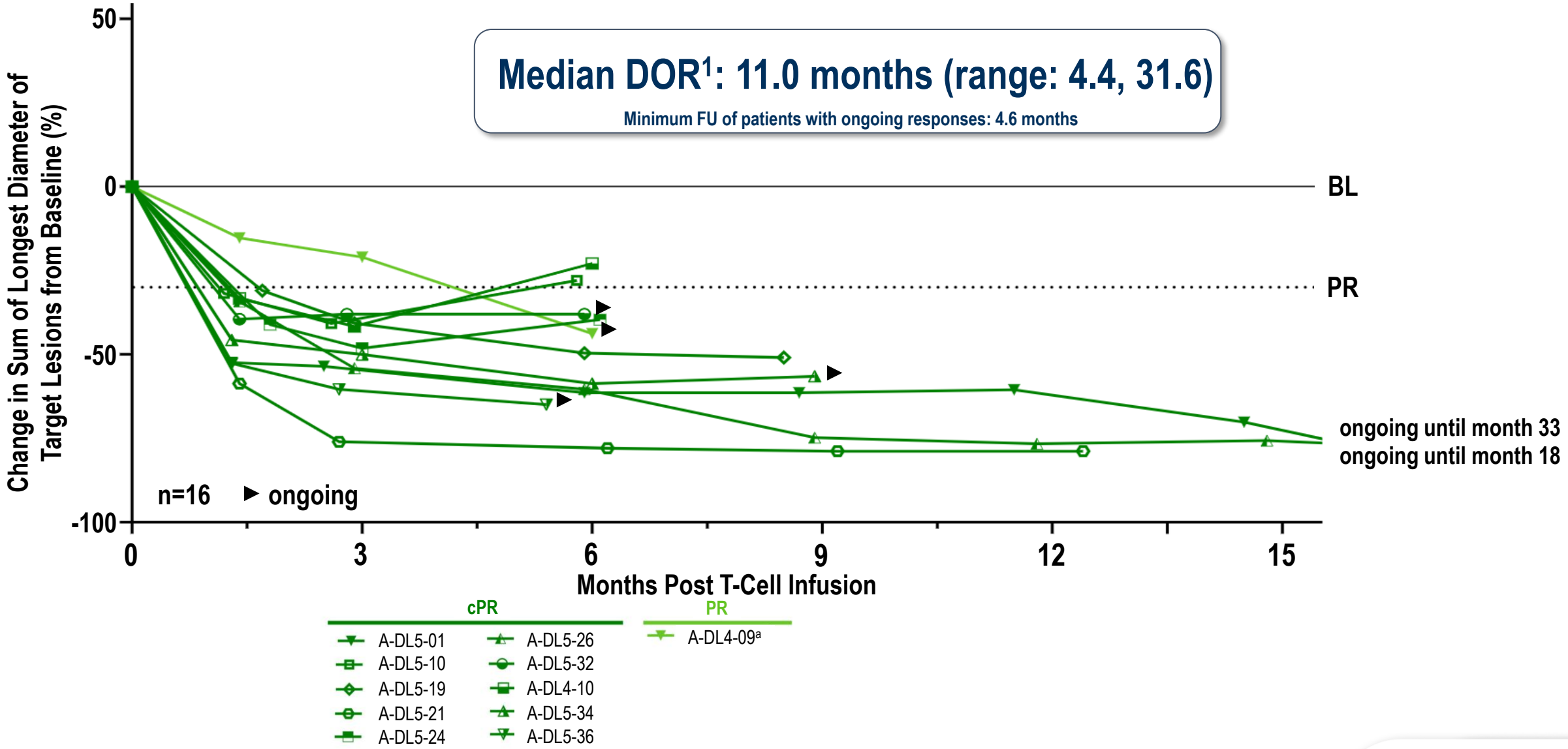
Data cutoff: Sep 24, 2025.

[a]Patient out of study at data cutoff (withdrew consent); BL, baseline; (c)PR, (confirmed) partial response; DOR, duration of response; PD, progressive disease; SD, stable disease.

Anzu-cel: Duration of Response in Uveal Melanoma

Median DOR[1]: 11.0 months (range: 4.4, 31.6)

Minimum FU of patients with ongoing responses: 4.6 months



Data cutoff: Sep 24, 2025. [1] DOR: time from the first documented evidence of a partial response (PR) until disease progression or death

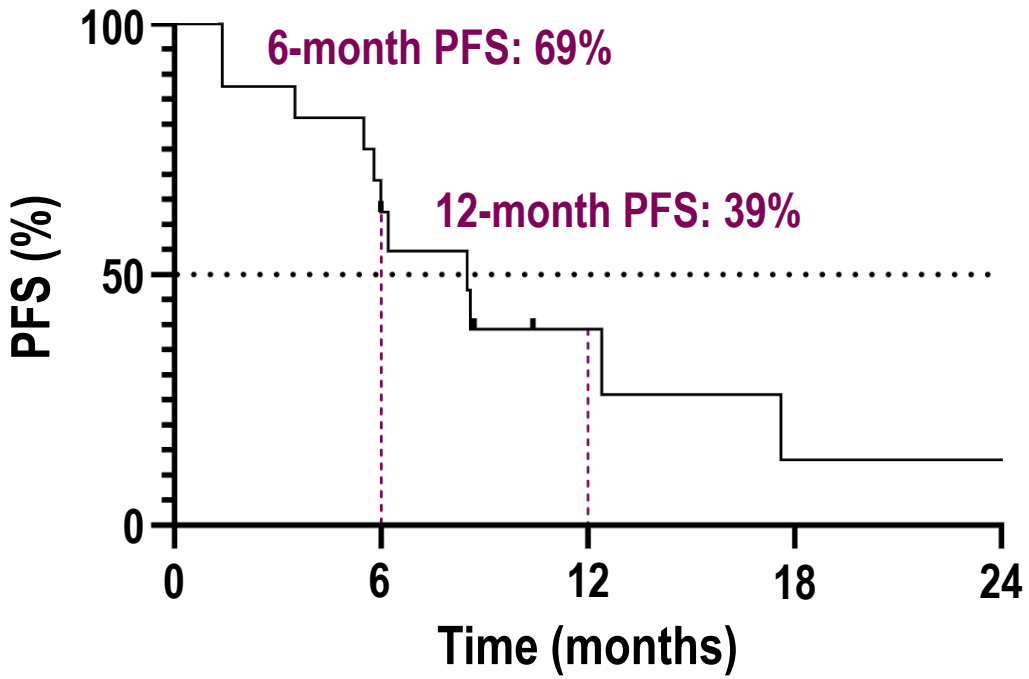
[a]Patient out of study at data cutoff (withdrew consent); BL, baseline; (c)PR, (confirmed) partial response; DOR, duration of response; PD, progressive disease; SD, stable disease.

Anzu-cel: Survival Outcomes in Uveal Melanoma

Progression-Free Survival

(median follow-up: 10.4 months)

Median PFS: 8.5 months (range: 1.4, 32.9)

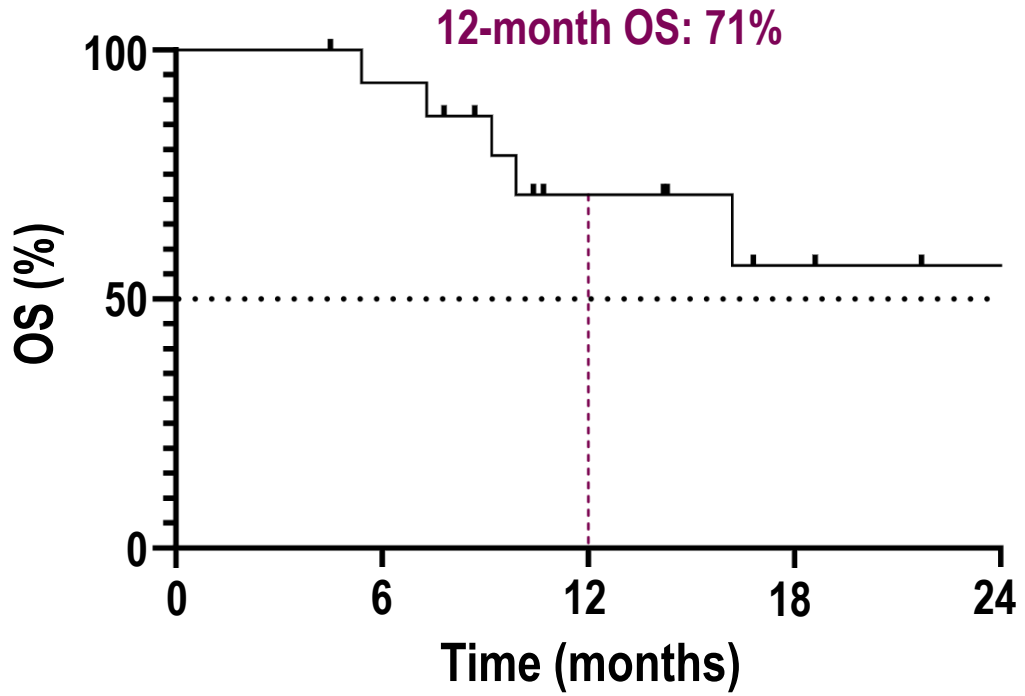


Patients at risk	16	10	3	1	1
Events	0	6	9	9	9

Overall Survival

(median follow-up: 14.3 months)

Median OS: not reached (range: 4.3+, 34.2+)



Patients at risk	16	14	7	3	1
Events	0	1	4	5	5

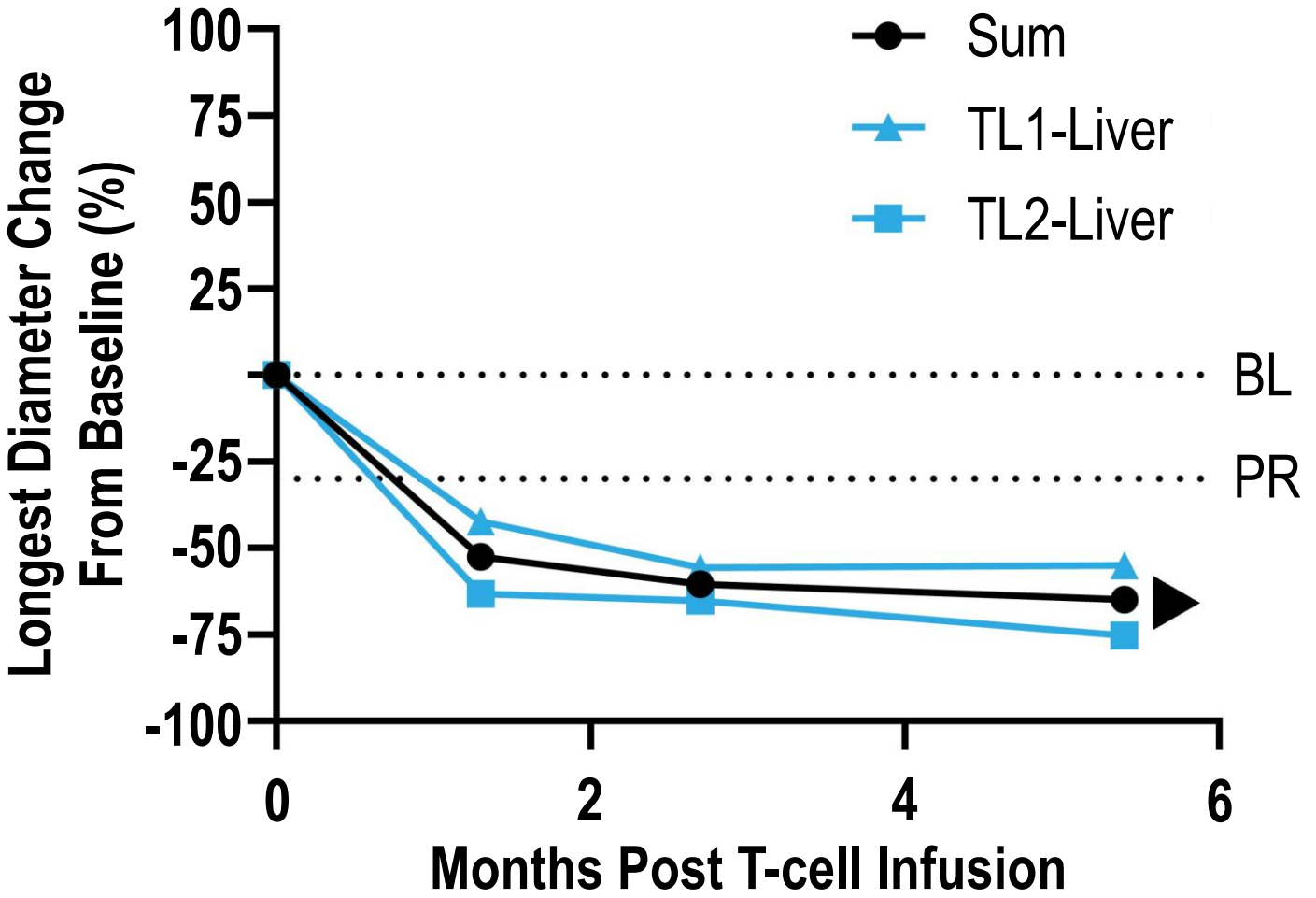
Data cutoff: Sep 24, 2025.

PFS and OS censored at data cutoff; OS, overall survival; PFS, progression-free survival.

Patient Case: Response After Prior PRAME-directed Treatment

A-DL5-36

- 44 years of age (female)
- Prior lines of treatment = 1
  - PRAME-directed treatment
  - Time on treatment: Oct 2023-Dec 2024
  - BOR: SD/No Response
  - Anzu-cel infusion: Jan 2025
- Tumor burden
  - Hepatic-only disease
  - Two target lesions
- T-cell dose
  - 7.93×10^9 infused TCR T cells
- Best overall response
  - cPR, -65%
  - Ongoing at 8.7 months



Data cutoff: Sep 24, 2025.

CT scans courtesy of treating physician (Diwakar Davar, University of Pittsburgh); BOR, best overall response; cPR: confirmed partial response; PRAME, preferentially expressed antigen in melanoma; SOD: sum of diameter; TL: target lesion

Conclusions

- **Anzu-cel tolerability profile:**
  - Most frequent TEAEs: anticipated cytopaenias
  - CRS was mostly grade 1-2
- **One-time infusion of anzu-cel in this cohort shows high response rates to immunotherapy for patients with metastatic uveal melanoma:**
  - 67% cORR and 11.0 months mDOR
  - mPFS: 8.5 months (mFU: 10.4 months) and mOS not reached (mFU: 14.3 months)
- **Antitumor activity of anzu-cel was observed in patients with prior TCR-based or PRAME-targeted therapies**

Data cutoff: Sep 24, 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.

In a cold tumour, targeting a highly expressed antigen (PRAME) with TCR-specific T cells results in clinical activity.

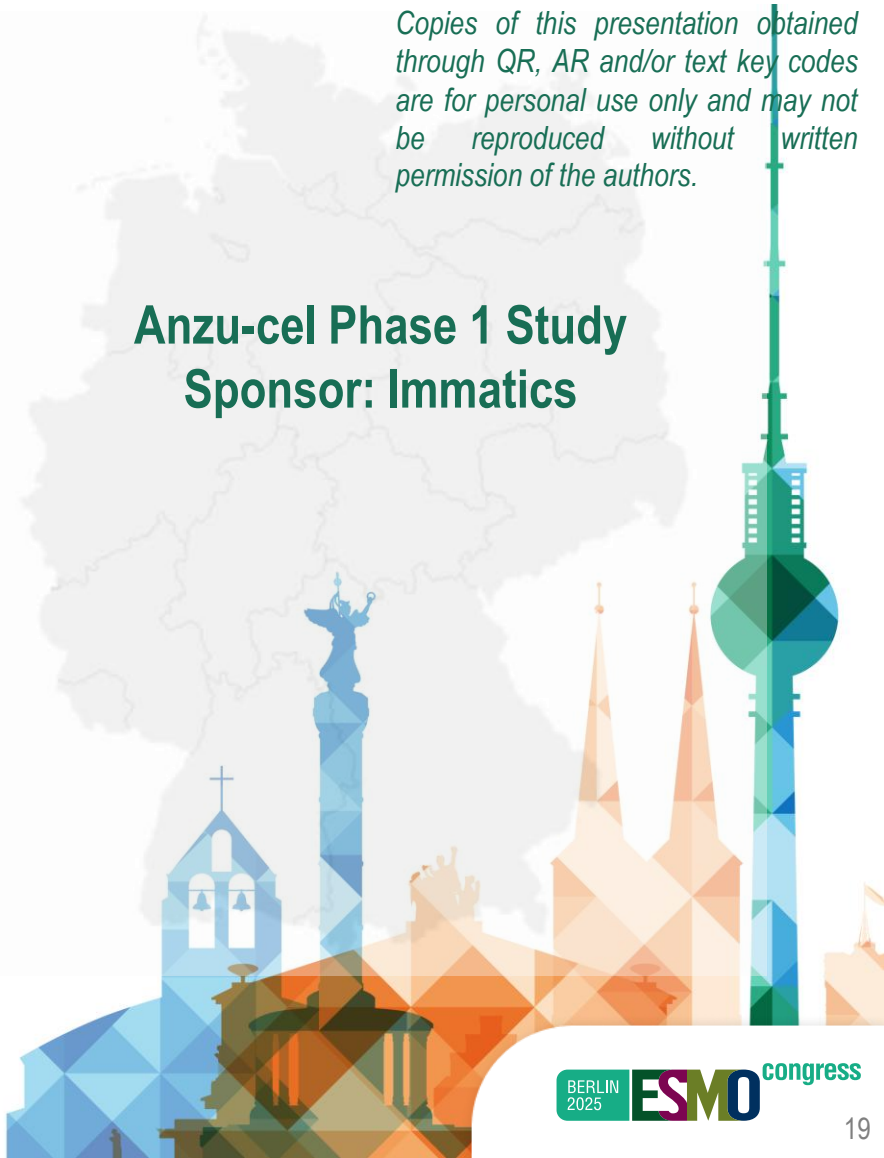
These results are being verified in a Phase 2 extension cohort.

Thank You – Study Participants & Caregivers

Clinical Trial Sites

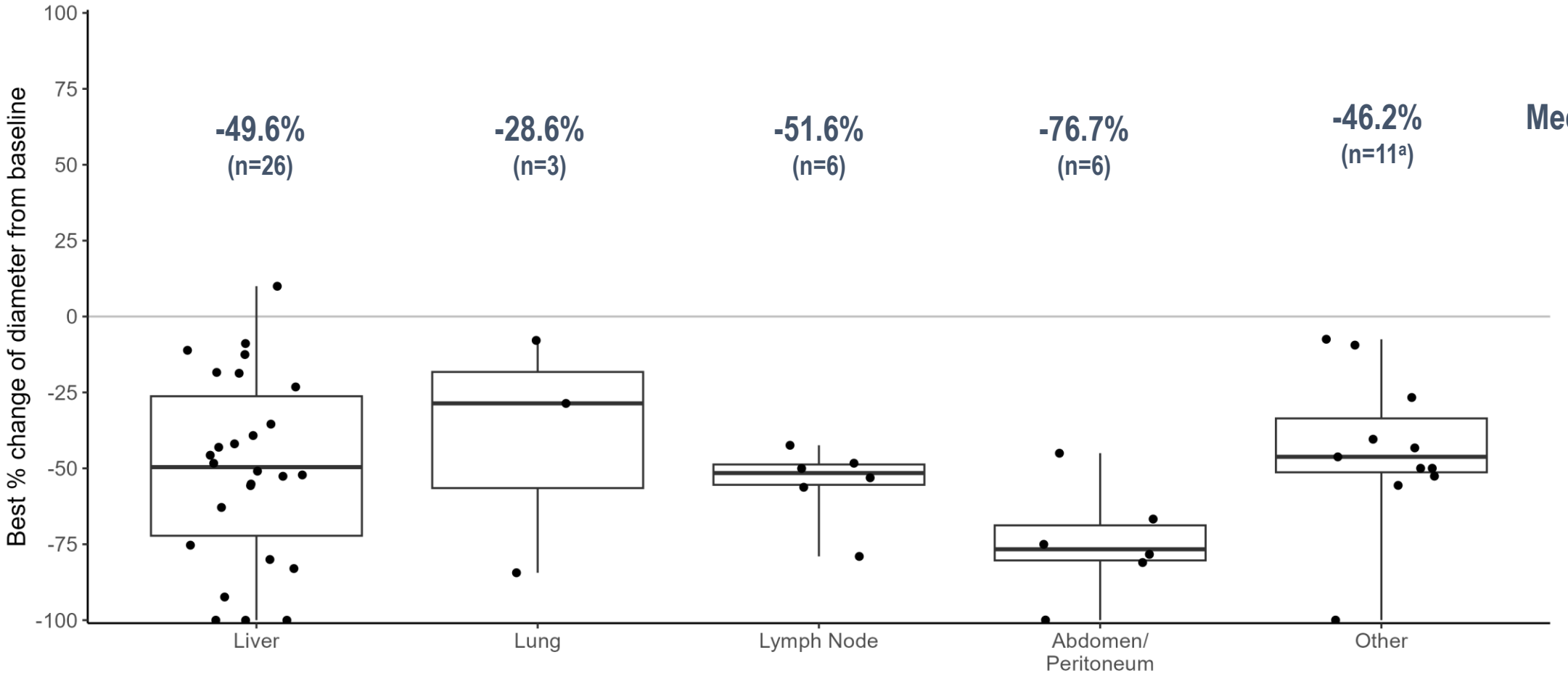
Sapna Patel	University of Colorado Cancer Center Aurora, CO, USA (current) University of Texas MD Anderson Cancer Center Houston, TX, USA (during study conduct)
Apostolia Tsimberidou	University of Texas MD Anderson Cancer Center Houston, TX, USA
Jason Luke	Strand Therapeutics (current) University of Pittsburgh Medical Center Pittsburgh, PA, USA (during study conduct)
Winfried Alsdorf	University Medical Center Hamburg – Eppendorf Hamburg, Germany
Antonia Busse	Charite University Medicine Berlin, Germany
Martin Wermke	University Hospital Dresden Dresden, Germany
Leo Hernandez-Aya	University of Miami, Miller School of Medicine Miami, FL, USA

Anzu-cel Phase 1 Study
Sponsor: Immatics



Supplemental Data

Anzu-cel in UM: Responses of Metastatic Lesions



[a] Other: kidney, pelvis, pericardium, pleura, retroperitoneum, skin, soft tissue, gluteal, dorsal.
Each data point represents shrinkage of a target lesion, respectively.

Data cut-off Sep 24, 2025

Patients with Uveal Melanoma Treated with Anzu-cel in Phase 1b Dose Expansion (n=16)

Patient ID	Indication	No of prior treatment lines	Prior treatments	Prior local liver-directed treatments	Total infused dose TCR-T cells[1] [x10^9]	BOR	BOR (Max % change of target lesions)	Comment	Reason for Progression
A-DL5-34	Uveal Melanoma	1	Tebentafusp		3.68	cPR	-58.7	Ongoing response at 10.4 months PFS	
A-DL5-36	Uveal Melanoma	1	Brenetafusp	*Liver ablation*	7.93	cPR	-64.9	Ongoing response at 8.7 months PFS	
A-DL5-32	Uveal Melanoma	6	Ipilimumab + Nivolumab Tebentafusp Melphalan Ipilimumab + Nivolumab DYP-688 Ipilimumab + Nivolumab	*1.Local radiopharmaceutical therapy with Y-90* *2.Melaphlan*	3.18	cPR	-39.5	Patient discontinued tumor assessments; censored at last assessment with ongoing response and 6 months PFS	
A-DL4-09	Uveal Melanoma	3	Ipilimumab + Nivolumab Darovasertib Tebentafusp	*Embolization of right hepatic artery*	1.62	PR	-43.8	Patient withdrew consent with unconfirmed PR, last evaluable scan prior to termination at 6.0 months PFS	
A-DL5-01	Uveal Melanoma	1	ARRY614 + Nivolumab		4.16	cPR	-84.2	Response until 32.9 months PFS	New lesions
A-DL5-26	Uveal Melanoma	2	Melphalan Tebentafusp	*Melphalan*	8.14	cPR	-78.4	Response until 17.6 months PFS	New lesion
A-DL5-21	Uveal Melanoma	2	Valproic acid + Sunitinib Tebentafusp		7.19	cPR	-78.8	Response until 12.4 months PFS	Non-target lesion progression
A-DL5-20	Uveal Melanoma	5	Ipilimumab + Pembrolizumab Tebentafusp Ipilimumab + Nivolumab IDE196 + Binimetinib FHD-286		8.43	SD	-17.6	Stable disease until 8.6 months PFS	Non-target lesion progression

[1] Transduced viable CD8 T cells;
BOR: Best overall response; DL: Dose level; PD: Progressive Disease; SD: Stable Disease; PR: Partial Response; cPR: Confirmed Partial Response; PFS: Progression-free survival (censored at data-cut)

Data cut-off Sep 24, 2025

Patients with Uveal Melanoma Treated with Anzu-cel in Phase 1b Dose Expansion (n=16)

Patient ID	Indication	No of prior treatment lines	Prior treatments	Prior liver-directed treatments	Total infused dose TCR-T cells[1] [x10^9]	BOR	BOR (Max % change of target lesions)	Comment	Reason for Progression
A-DL5-19	Uveal Melanoma	6	Pembrolizumab Clinical trial intrahepatic PV10 Ipilimumab + Nivolumab Clinical trial Anti-CTLA-4 NF AB + XRT Clinical trial foghorn FHD-286 Pembrolizumab	*Clinical trial intrahepatic PV10*	5.42	cPR	-50.9	Response until 8.5 months PFS	Non-target lesion progression
A-DL5-24	Uveal Melanoma	3	NOX66-005 Idronoxil with radiotherapy IDE196 + Crizotinib LVGN3616 + LVGN6051 + LVGN7409 + Bevacizumab + Cyclophosphamide		2.89	cPR	-48.1	Response until 6.2 months PFS	Non-target lesion progression and new lesions
A-DL4-10	Uveal Melanoma	1	Tebentafusp		1.62	cPR	-41.7	Response until 6.0 months PFS	Target lesion progression and new lesion
A-DL5-10	Uveal Melanoma	1	SEAGEN CD40 Agonist + Pembrolizumab		2.68	cPR	-40.8	Response until 5.8 months PFS	Target lesion progression
A-DL5-18	Uveal Melanoma	2	Tebentafusp Ipilimumab + Nivolumab		5.71	SD	-25.4	Disease stabilization until 5.5 months PFS	New lesion
A-DL5-12	Uveal Melanoma	3	Tyrosinase peptides Nivolumab + Ipilimumab Tebentafusp		4.50	SD	-22.6	Disease stabilization until 3.5 months PFS	Target and non-target lesion progression, new lesions
A-DL5-35	Uveal Melanoma	2	Tebentafusp Ipilimumab + Nivolumab		3.71	PD	-37.5	Progressive disease at 1.4 months PFS	Non-target lesion progression
A-DL4-06	Uveal Melanoma	0	NA		2.56	PD	-6.3	Progressive disease at 1.4 months PFS	New lesion

Data cut-off Sep 24, 2025

[1] Transduced viable CD8 T cells;
BOR: Best overall response; DL: Dose level; PD: Progressive Disease; SD: Stable Disease; PR: Partial Response; cPR: Confirmed Partial Response; PFS: Progression-free survival (censored at data-cut)