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NATIONALES CENTRUM
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DRESDEN

Technische
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Dresden

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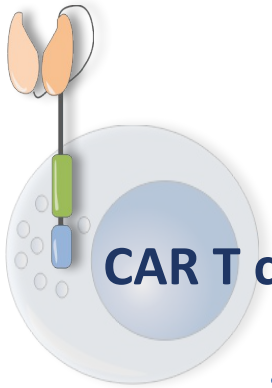
Carl Gustav Carus
DIE DRESDNER.

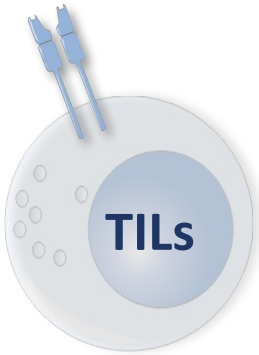
TCRs/ TILs in solid tumors – „state of the art“

Katrin Wetzko

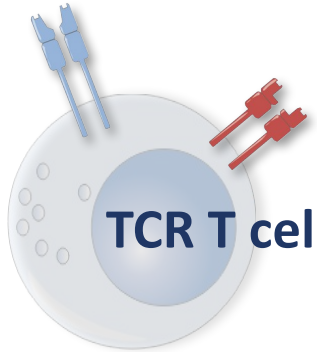
Side-by-side comparison



CAR T cells



TILs



TCR T cells

DIFFICULT FOR SOLID TUMORS

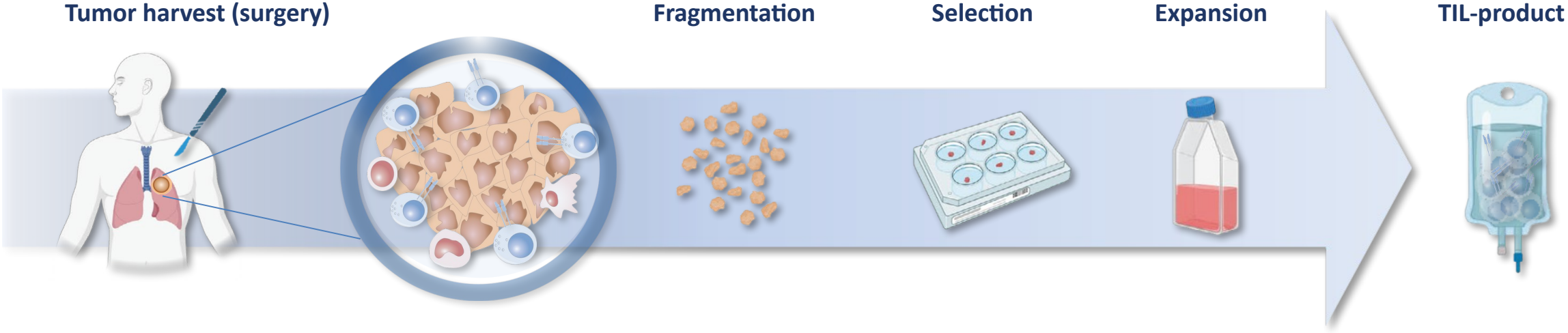
	CAR T cells	TILs	TCR T cells
Source:	Blood	Tumor tissue	Blood
Engineering:	Yes (CAR added)	No (natural)	Yes (TCR added)
Target recognition:	Synthetic CAR	Natural TCR	Engineered TCR
MHC dependence:	No	Yes	Yes
Targets:	Surface proteins only	Broad (incl. private neoantigens)	Intracellular + surface (via MHC)

"Give T-cells a new artificial receptor."

"Use what the body already found in the tumor."

"Upgrade T cells with a better natural receptor."

How TIL therapy works? - preparing



PRO

+ naturally „pre-selected“ t-cells
multiple target antigens/neoantigens

Cons

- surgical removement
- expansion can be diffcult

pionieerd for treating solid cancers by
Dr. Steven Rosenberg in 1986

Modified according to Veatch 2021 10.1038/s41591-021-01445-z

The first FDA-approved cellular therapeutic for a solid tumor

https://www.fda.gov/drugs/resources-information-approved-drugs/fda-grants-accelerated-approval-lifileucel...

An official website of the United States government Here's how you know

U.S. FOOD & DRUG ADMINISTRATION

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FDA grants accelerated approval to lifileucel for unresectable or metastatic melanoma

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Resources for Information | Approved Drugs

Oncology (Cancer) /

On February 16, 2024, the Food and Drug Administration granted accelerated approval to lifileucel (Amtagvi, Iovance Biotherapeutics, Inc.), a tumor-derived autologous T cell immunotherapy, for adult patients with unresectable or metastatic melanoma previously treated with a PD-1 blocking antibody, and if BRAF V600 positive, a BRAF inhibitor with or without a MEK inhibitor.

Content current as of: 02/16/2024

Regulated

Approval based on C-144-01 Study

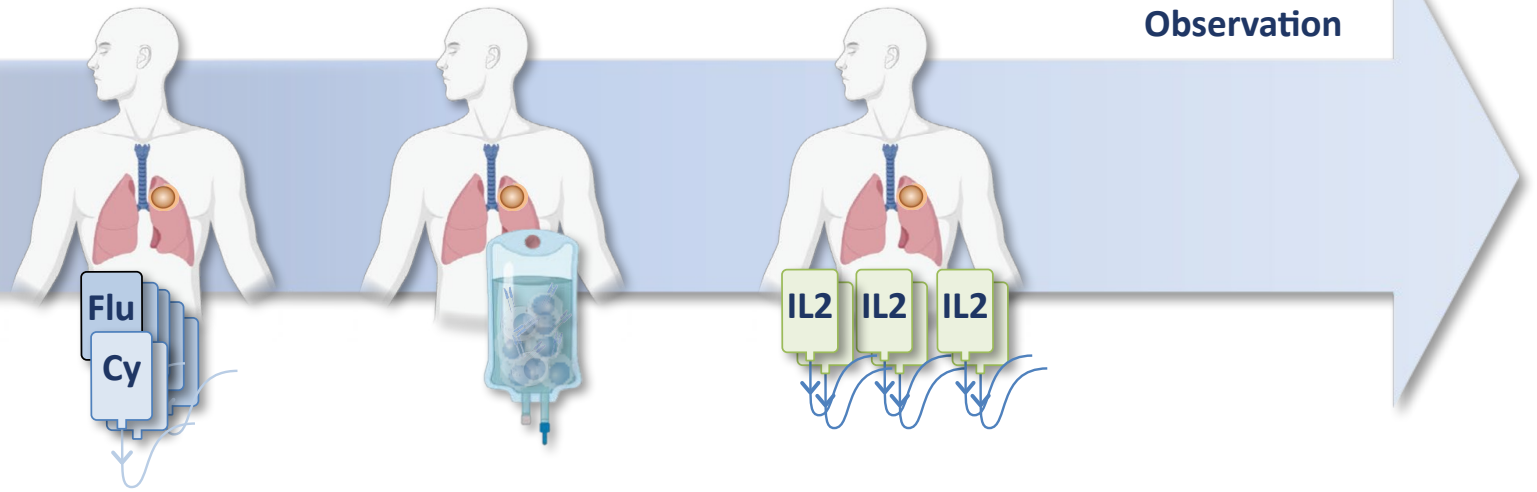
Update: 5-Year Analysis of C-144-01 Study published in June 2025

https://www.fda.gov/drugs/resources-information-approved-drugs/fda-grants-accelerated-approval-lifileucel-unresectable-or-metastatic-melanoma

How TIL therapy works? – IOVANCE C144-01

Melanoma
- After CPI/TKI failure
- Median 3 prior lines
- 100% prior PD-1/PD-L1
- 84% prior CTLA4

n = 153 received lifileucel



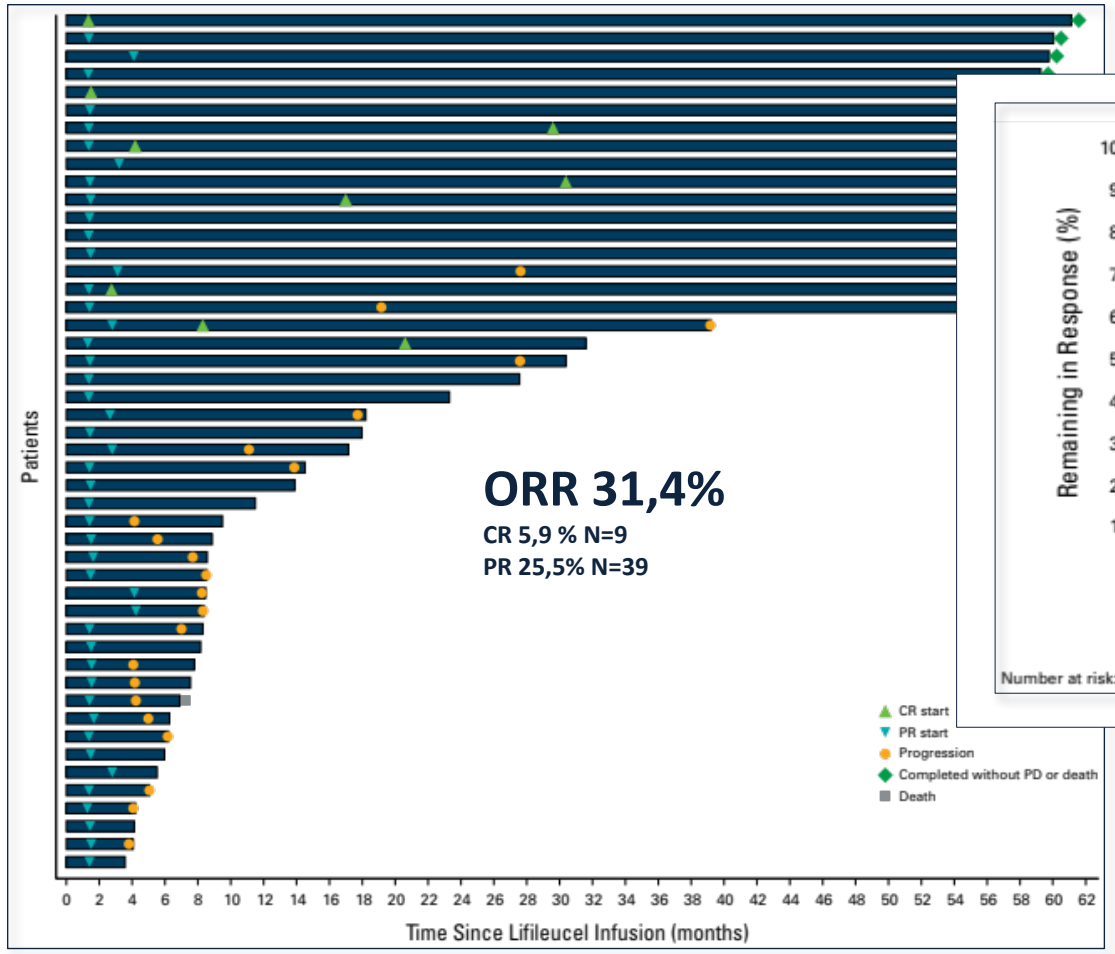
Flu 2x 60mg/kg
Cy 5x 25mg/m^2

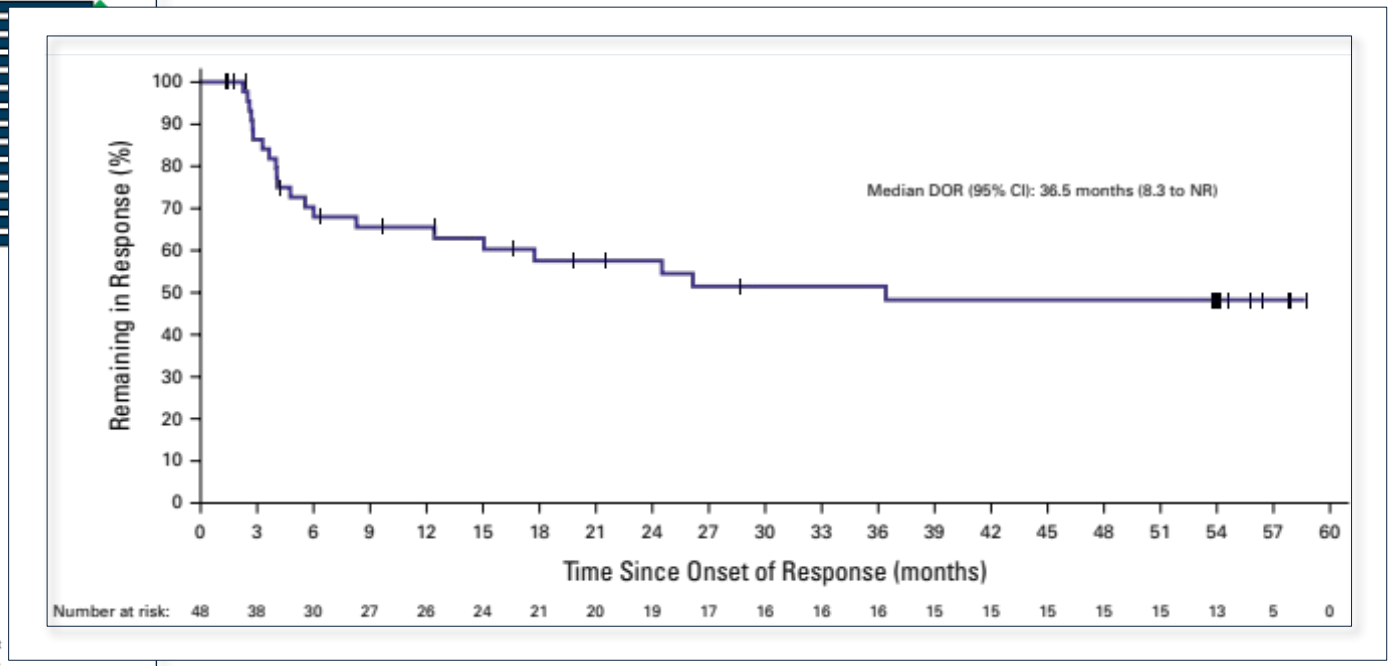
Lifileucel (1-150x 10^9)

IL2 6x 0.6x10^6 IU/kg

Modified according to Veatch 2021 10.1038/s41591-021-01445-z, Flu- Fludarabin, Cy –Cyclophosphamid, IL2 – Interleukin 2

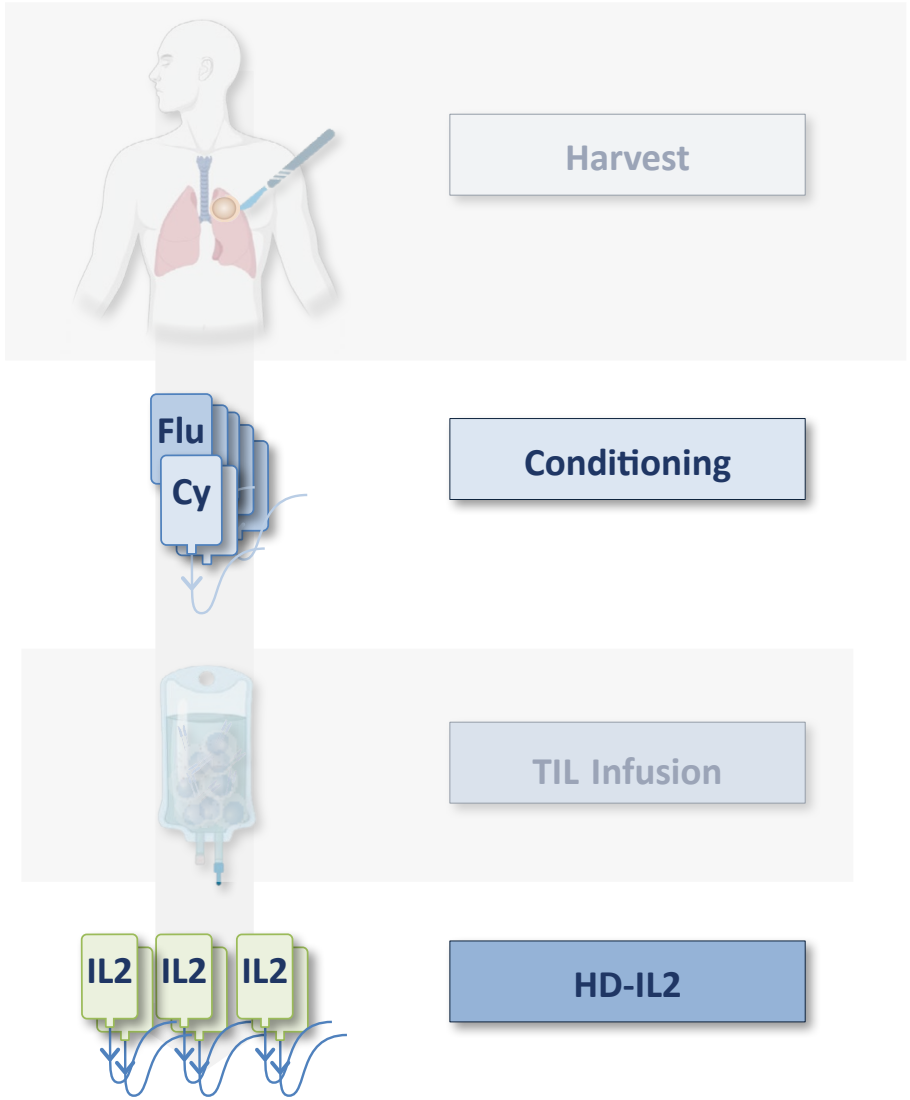
TIL in melanoma: Iovance C144-01; 5-year data



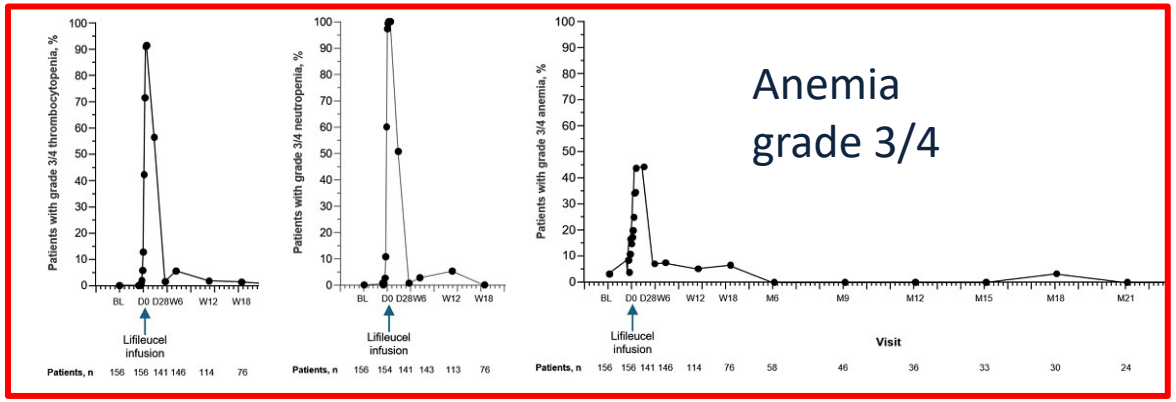


Medina et al 2025, https://doi.org/10.1200/JCO-25-00765

Tumor- infiltrating Lymphocytes - Safety



	Any Grade	Grade 3/4
Surgical AE	32%	3%

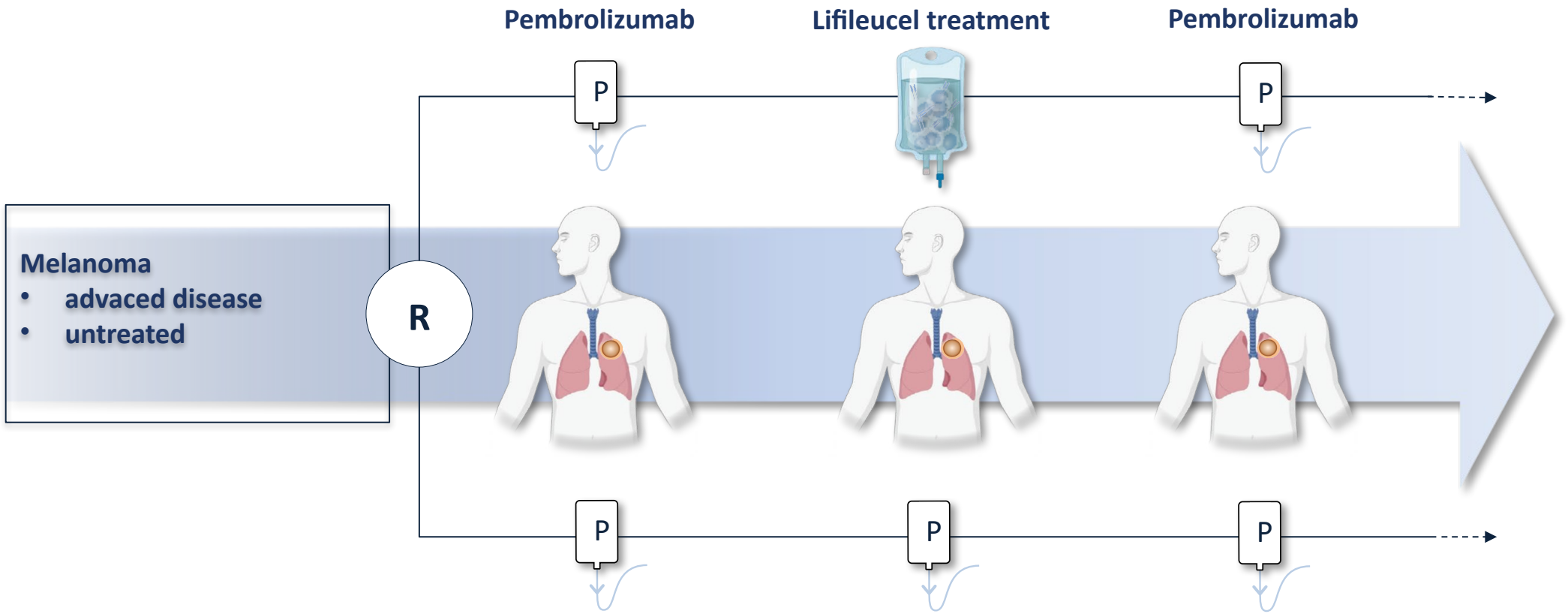


IRR/anaphylaxis	5%	1%

Modified according to Veatch 2021 10.1038/s41591-021-01445-z, Chesney 2022 doi: 10. 1136/jitc-2022-005755, Medina et al 2025, https://doi.org/10.1200/JCO-25-00765

TILVANCE - Phase 3 Trial

Recruiting



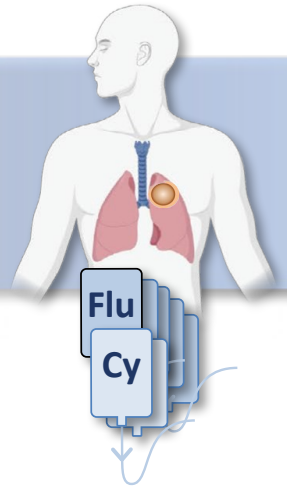
Modified according to Veatch 2021 10.1038/s41591-021-01445-z, Flu- Fludarabin, Cy –Cyclophosphamid, IL2 – Interleukin 2, P –Pembrolizumab, doi.org/10.1158/1538-7445.AM2024-CT286

Is Lifileucel also working in lung cancer?

Recruiting

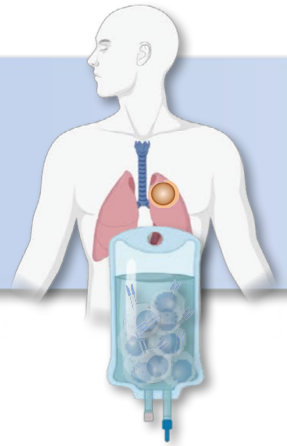
NSCLC
- **Phase 2 study**
- **Stage IV disease**
- **100% prior PD-1/PD-L1**
- **2nd line treatment**

Conditioning Chemotherapy



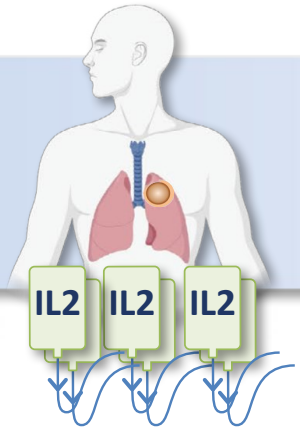
Flu 2x 60mg/kg
Cy 5x 25mg/m^2

TIL infusion



Lifileucel (1-53x 10^9)

High dose IL2 infusion



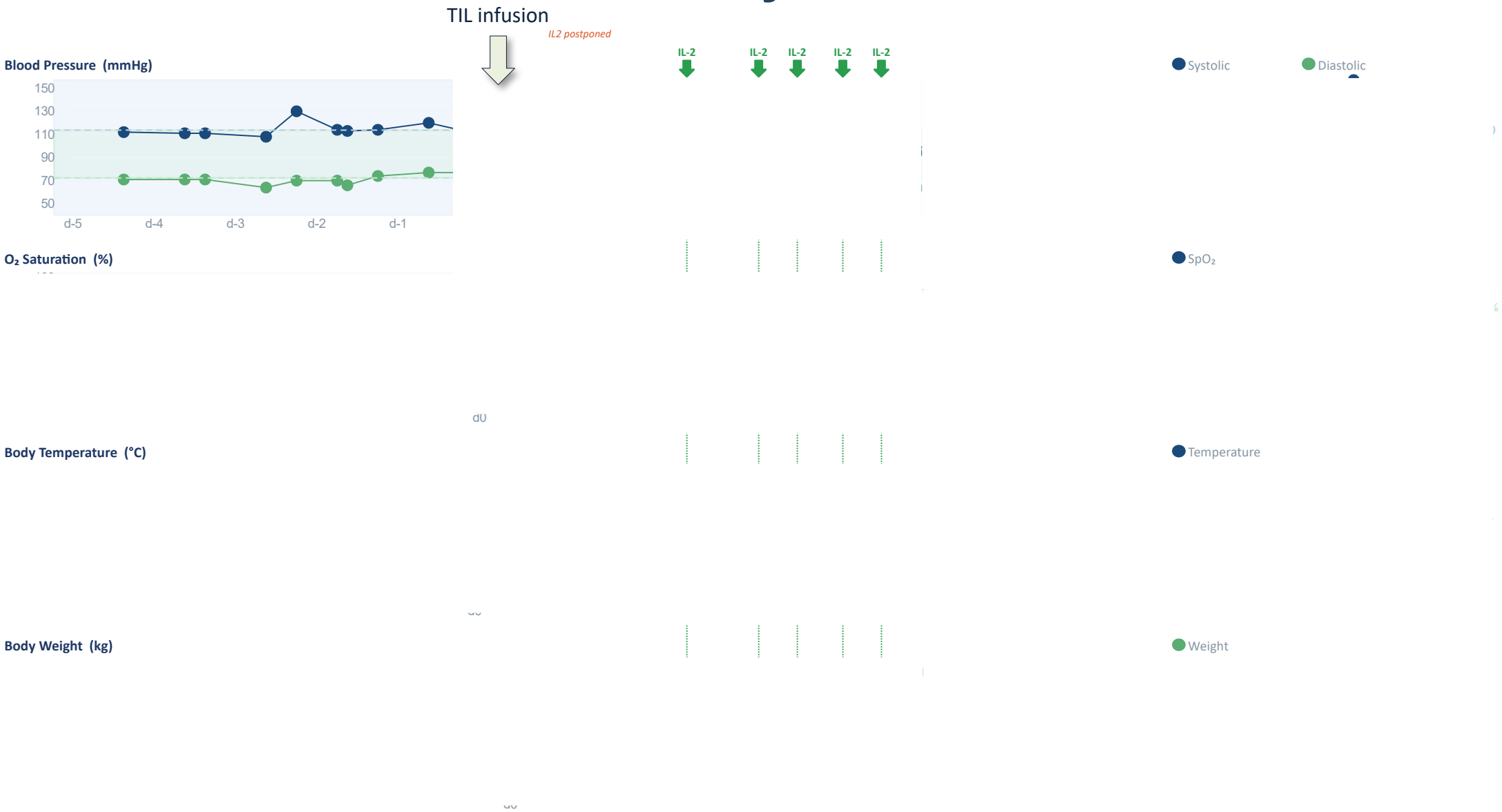
IL2 6x 0.6x10^6 IU/kg

ORR?

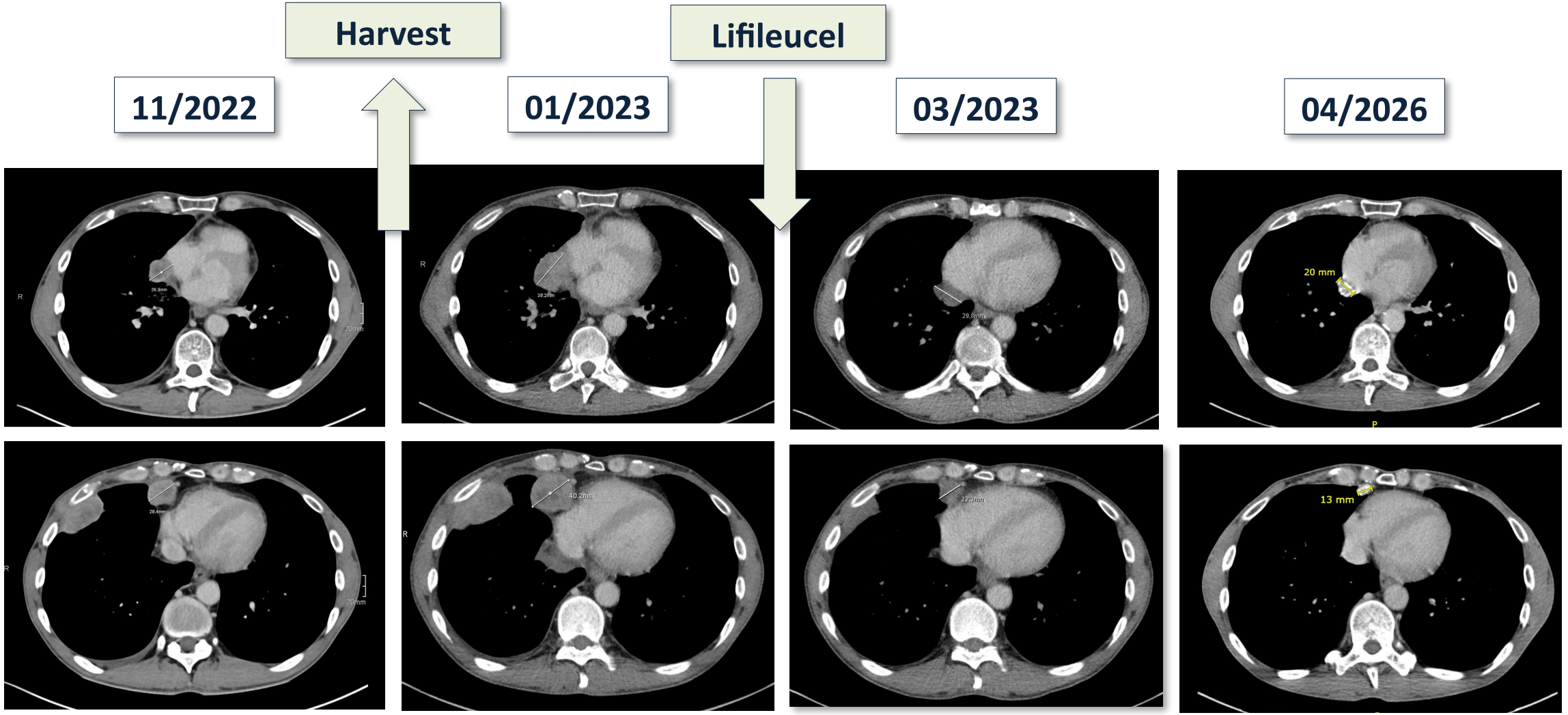
Schoenfeld 2024 doi: 10.1158/2159-8290.CD-23-1334, 2020-003629-45 (EudraCT Number)

Clinical course - Male, 39y, SMARCA4-deficient NSCLC

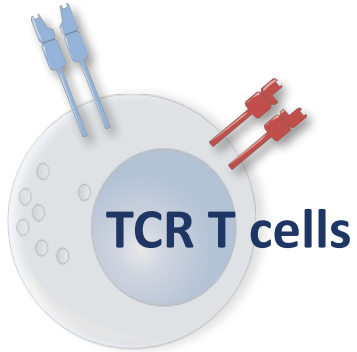
Clinical course - Male, 39y, SMARCA4-deficient NSCLC



Response - Male,39 y, SMARCA4-deficient NSCLC



Side-by-side comparison



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Target recognition:	Synthetic CAR	Natural TCR	Engineered TCR
MHC dependence:	No	Yes	Yes
Targets:	Surface proteins only	Broad (incl. private neoantigens)	Intracellular + surface (via MHC)

TCR therapy - IMA203-101 Phase-I-trial (IMA203)

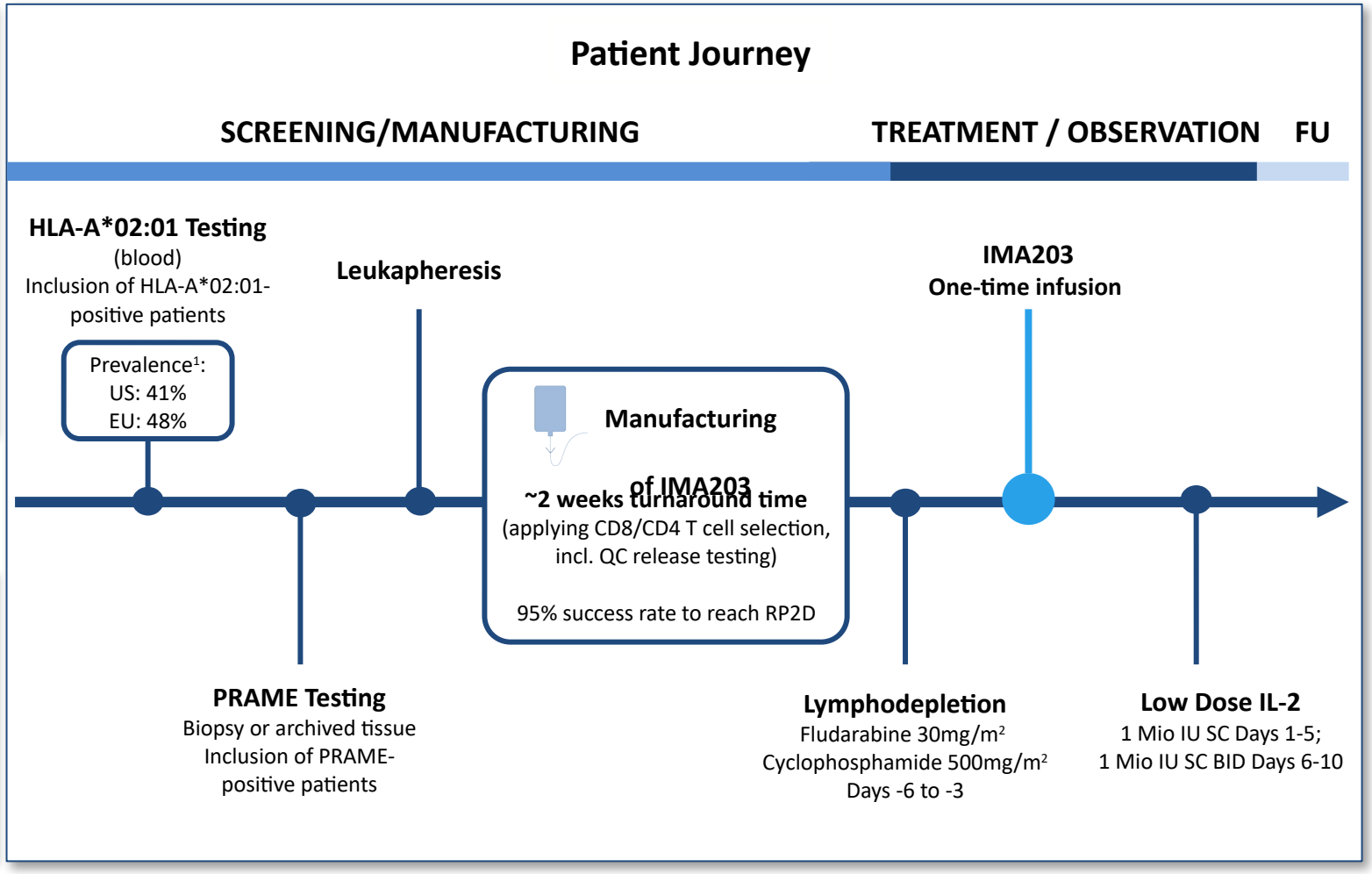
Key Eligibility Criteria

- Confirmed **advanced and/or metastatic solid tumor**
- Patients having received, or not been eligible for all available indicated SOC treatment
- Adequate organ function
- No active brain metastasis

Key Objectives

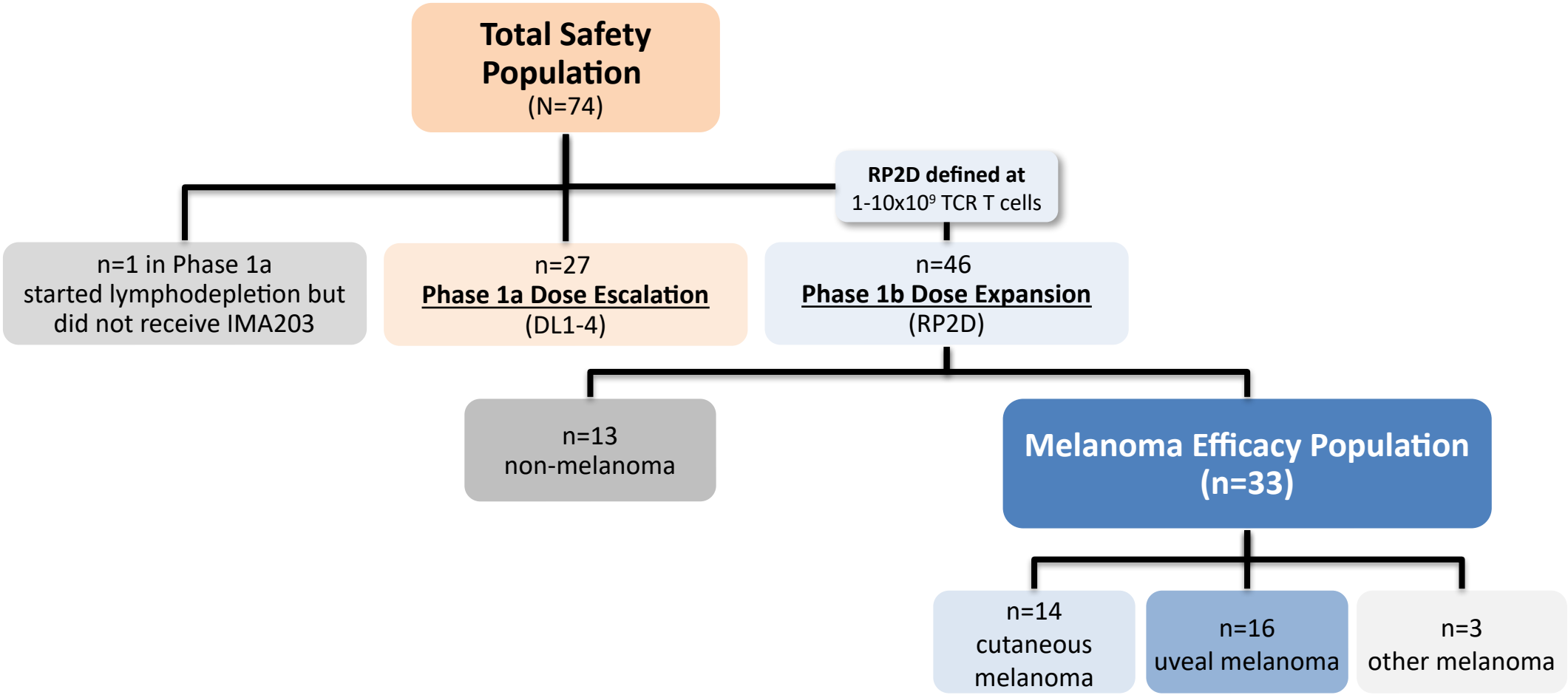
Primary:
- Tolerability
- Determination of RP2D (Phase 1a)

Secondary:
- IMA203 T cell engraftment, persistence
- Efficacy



Wermke 2025 doi: 10.1038/s41591-025-03650-6 / ASCO 2025 doi: 10.1200/JCO.2025.43.16_suppl.2508

IMA203-101 Patient disposition



Wermke 2025 doi: 10.1038/s41591-025-03650-6 / ASCO 2025 doi: 10.1200/JCO.2025.43.16_suppl.2508

Anzu-cel (IMA203) safety profile

TEAEs in ≥20% of patients

Preferred terms, n (%)	Any grade	Grade ≥3
Blood and lymphatic system disorders	73 (98.6)	73 (98.6)
Neutropenia[a]	68 (91.9)	67 (90.5)
Anaemia	57 (77.0)	38 (51.4)
Thrombocytopenia[a]	50 (67.6)	27 (36.5)
Leukopenia	39 (52.7)	38 (51.4)
Lymphopenia	39 (52.7)	39 (52.7)
Gastrointestinal disorders	65 (87.8)	2 (2.7)
Nausea	45 (60.8)	0 (0.0)
Diarrhoea[a]	28 (37.8)	1 (1.4)
Vomiting	25 (33.8)	1 (1.4)
Constipation	23 (31.1)	0 (0.0)
General disorders and administration site conditions	49 (66.2)	2 (2.7)
Fatigue	29 (39.2)	1 (1.4)
Pyrexia	22 (29.7)	1 (1.4)
Edema peripheral	17 (23.0)	0 (0.0)
Investigations	35 (47.3)	10 (13.5)
Aspartate aminotransferase increased	29 (39.2)	5 (6.8)
Alanine aminotransferase increased	28 (37.8)	7 (9.5)
Blood creatinine increased	15 (20.3)	2 (2.7)
Skin and subcutaneous tissue disorders	35 (47.3)	6 (8.1)
Rash	18 (24.3)	0 (0.0)
Rash maculo-popular	18 (24.3)	6 (8.1)
Metabolism and nutrition disorders	33 (44.6)	6 (8.1)
Hyponatraemia	22 (29.7)	3 (4.1)
Hypokalaemia	21 (28.4)	3 (4.1)

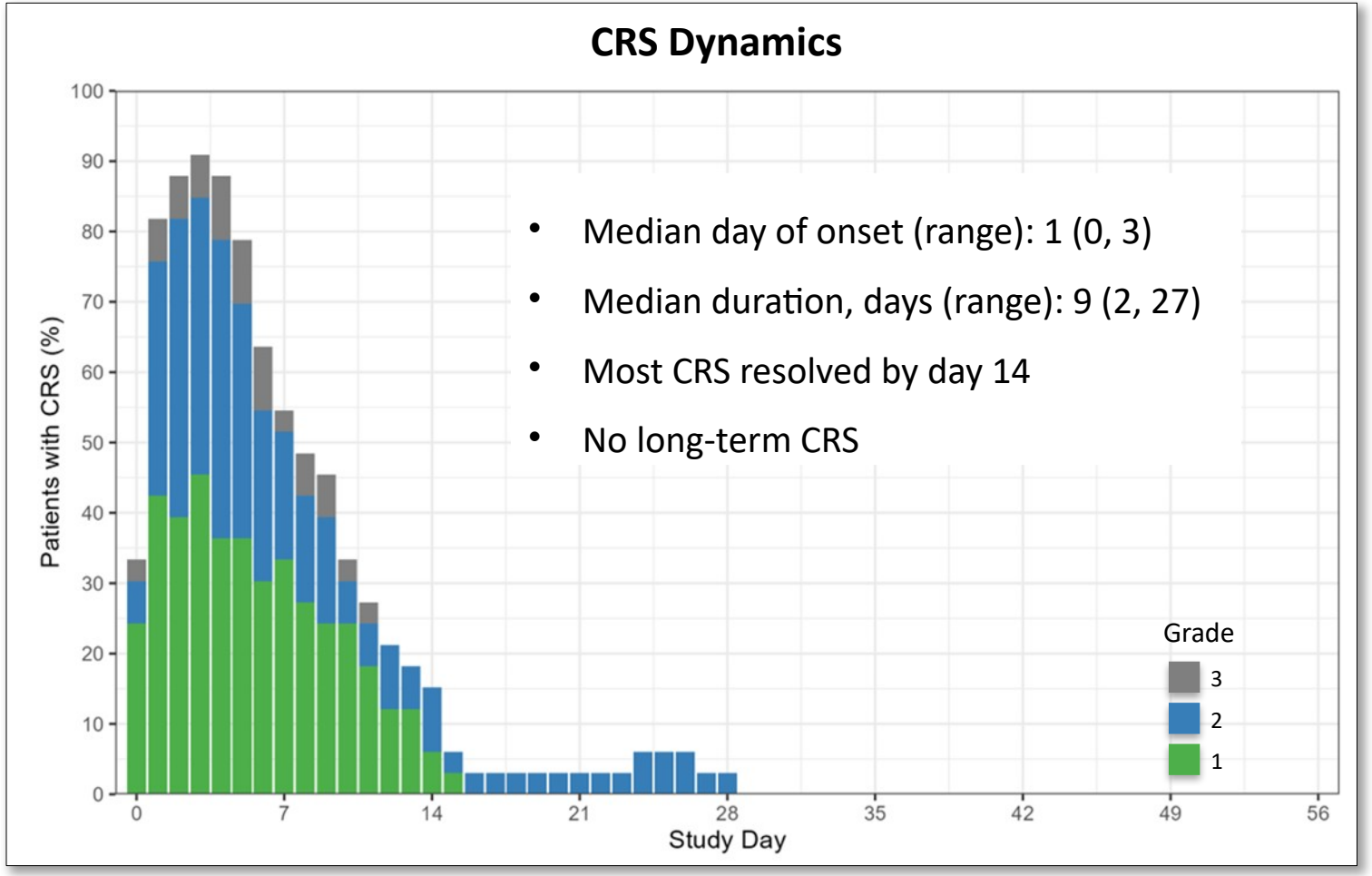
Adverse events of special interest

	N=74
CRS, any grade, n (%)	**70 (94.6)**
Grade 1	27 (36.5)
Grade 2	35 (47.3)
Grade 3[a]	8 (10.8)
Grade 4	0 (0.0)
Grade 5	0 (0.0)
ICANS, any grade, n (%)	**10 (13.5)**
Grade 1	4 (5.4)
Grade 2	3 (4.1)
Grade 3	3 (4.1)
Grade 4	0 (0.0)
Grade 5	0 (0.0)
HLH, any grade, n (%)	**2 (2.7)**
Grade 1	0 (0.0)
Grade 2	1 (1.4)
Grade 3	1 (1.4)
Grade 4	0 (0.0)
Grade 5	0 (0.0)

- Anticipated LD-chemo side effects
- CRS mostly grade 1/2
- Infrequent ICANS
- No Anzu-Cel related deaths

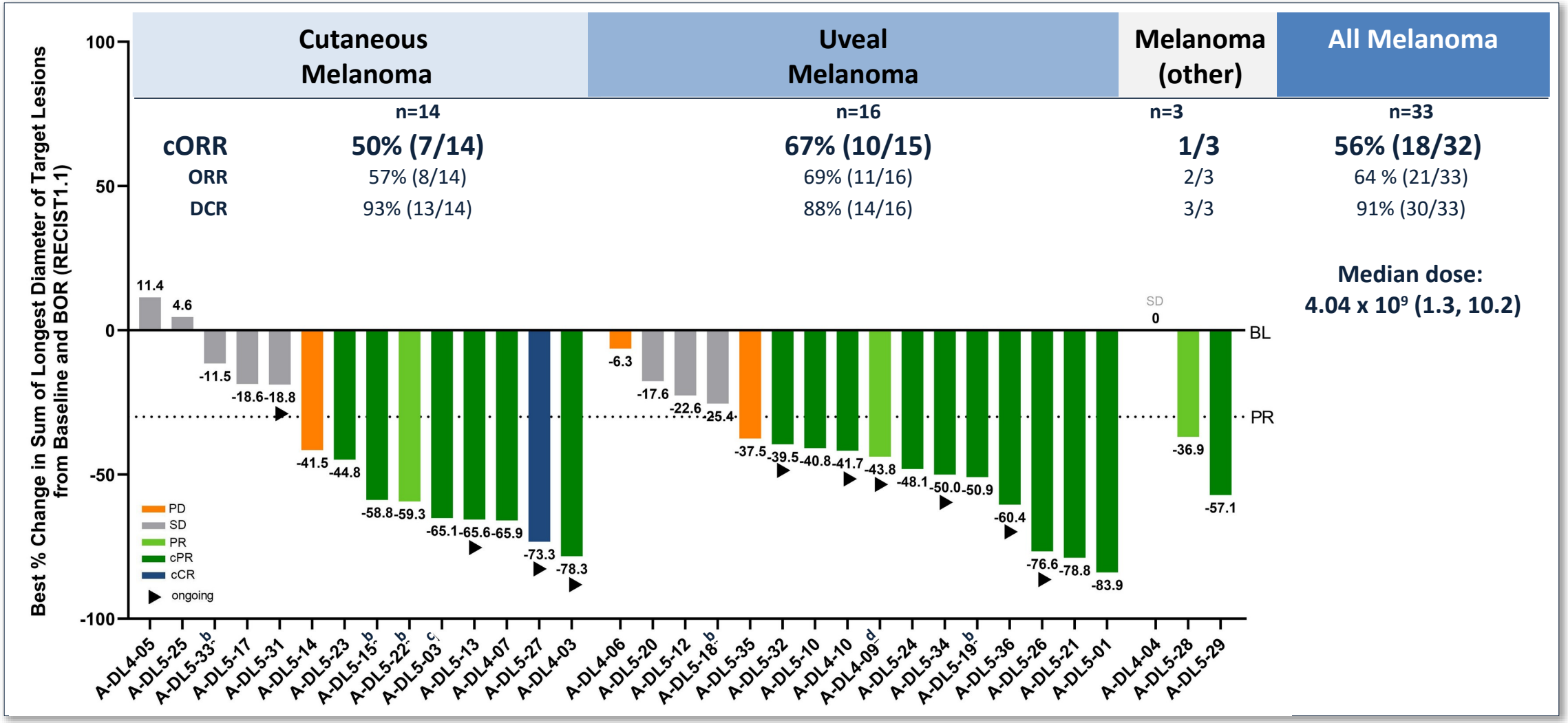
Wermke 2025 doi: 10.1038/s41591-025-03650-6 / ASCO 2025 doi: 10.1200/JCO.2025.43.16_suppl.2508

CRS severity and kinetics in melanoma efficacy population



Wermke 2025 doi: 10.1038/s41591-025-03650-6 / ASCO 2025 doi: 10.1200/JCO.2025.43.16_suppl.2508

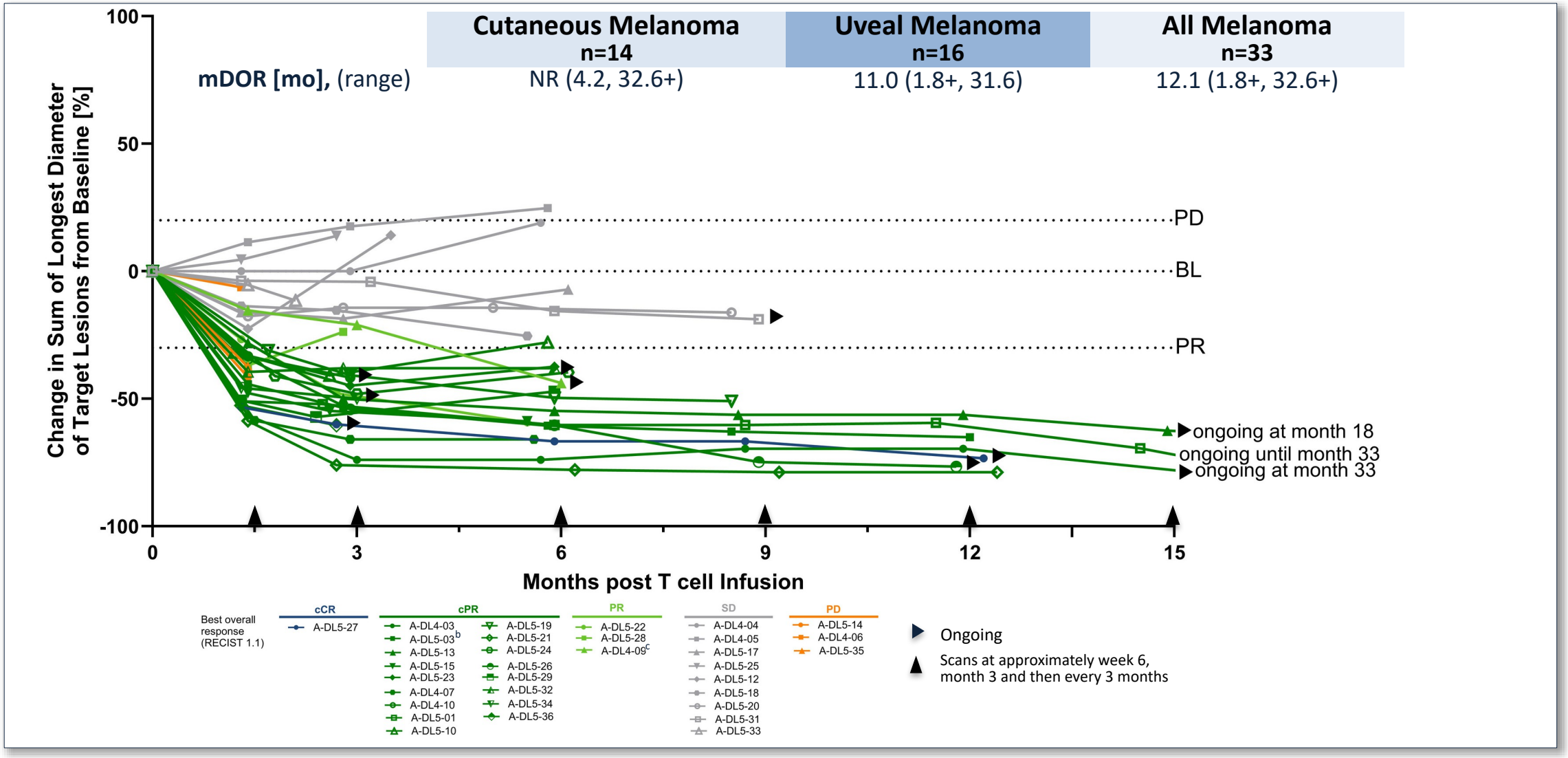
Best overall response in the melanoma efficacy population



Wermke 2025 doi: 10.1038/s41591-025-03650-6 / ASCO 2025 doi: 10.1200/JCO.2025.43.16_suppl.2508

Durability of reponses in the melanoma efficacy population

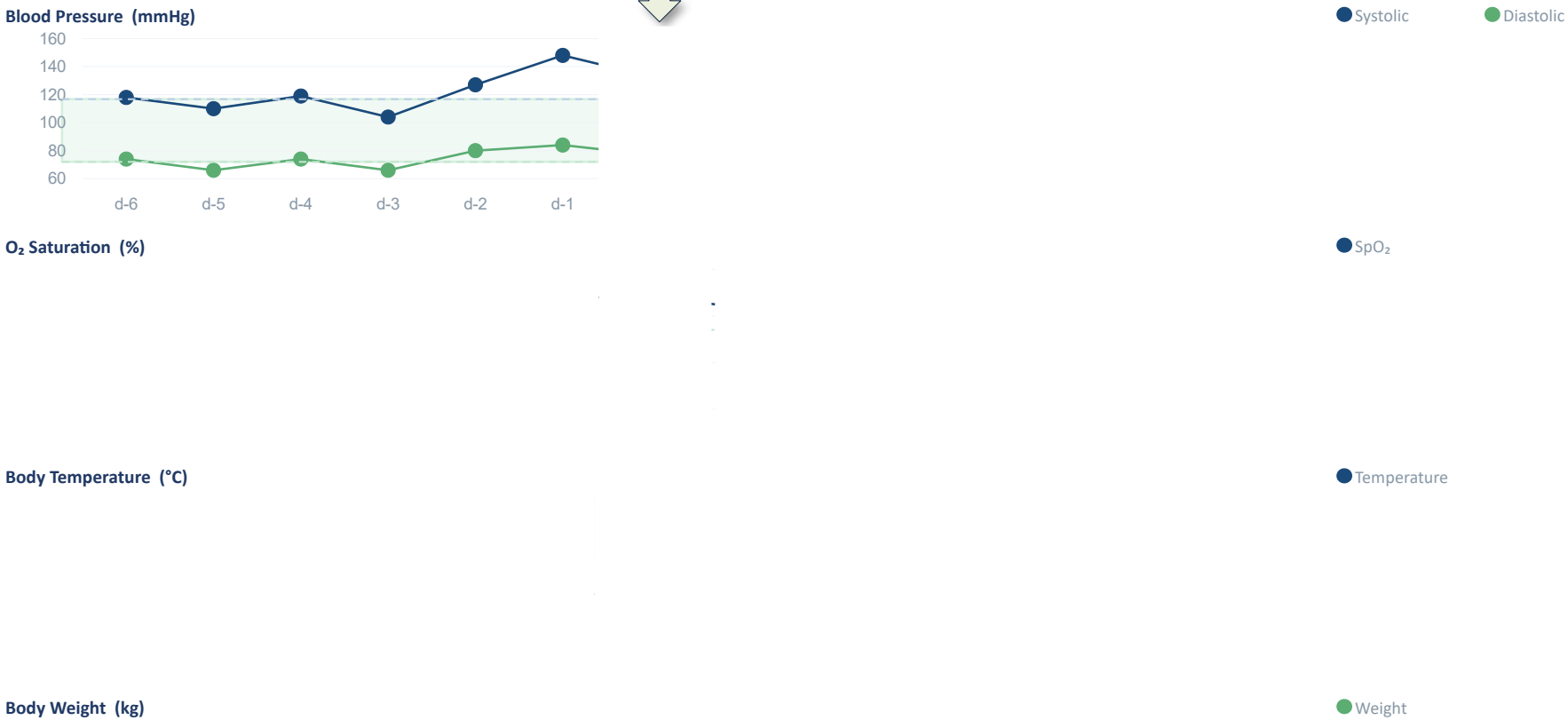
	Cutaneous Melanoma n=14	Uveal Melanoma n=16	All Melanoma n=33
mDOR [mo], (range)	NR (4.2, 32.6+)	11.0 (1.8+, 31.6)	12.1 (1.8+, 32.6+)



Wermke 2025 doi: 10.1038/s41591-025-03650-6 / ASCO 2025 doi: 10.1200/JCO.2025.43.16_suppl.2508

Clinical course - Male, 66 y, synovial sarcoma

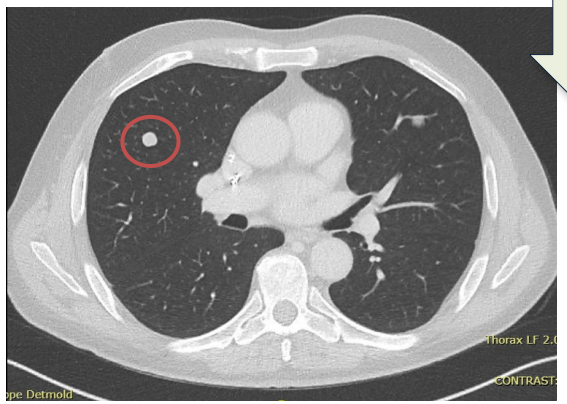
TCR infusion



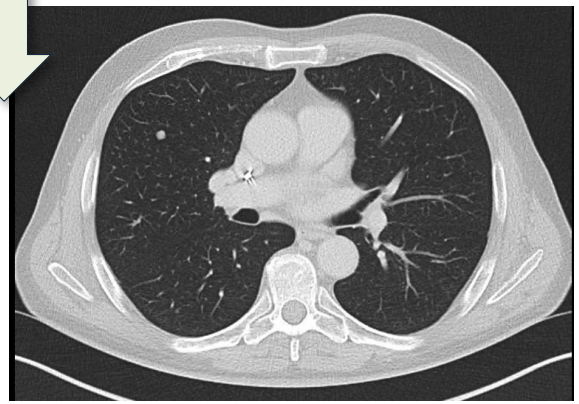
Response - Male, 66 y, synovial sarcoma

TCR T

04/2023



06/2023



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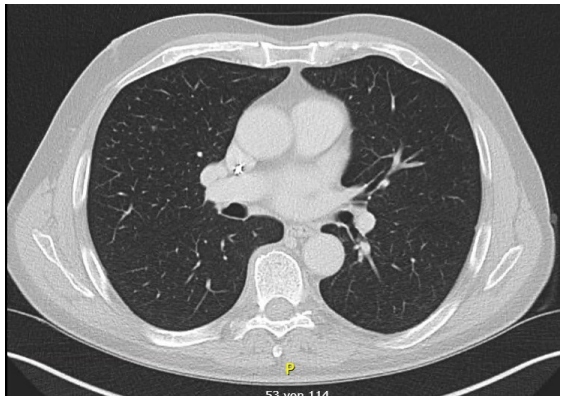
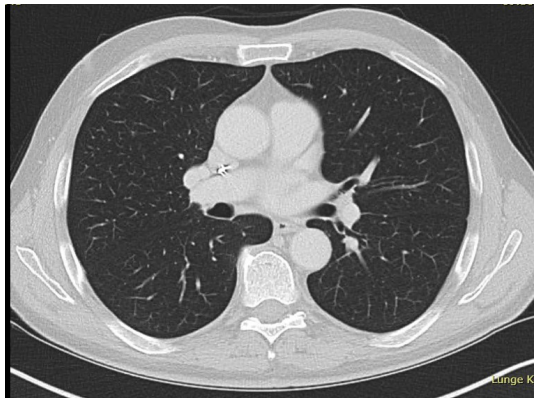
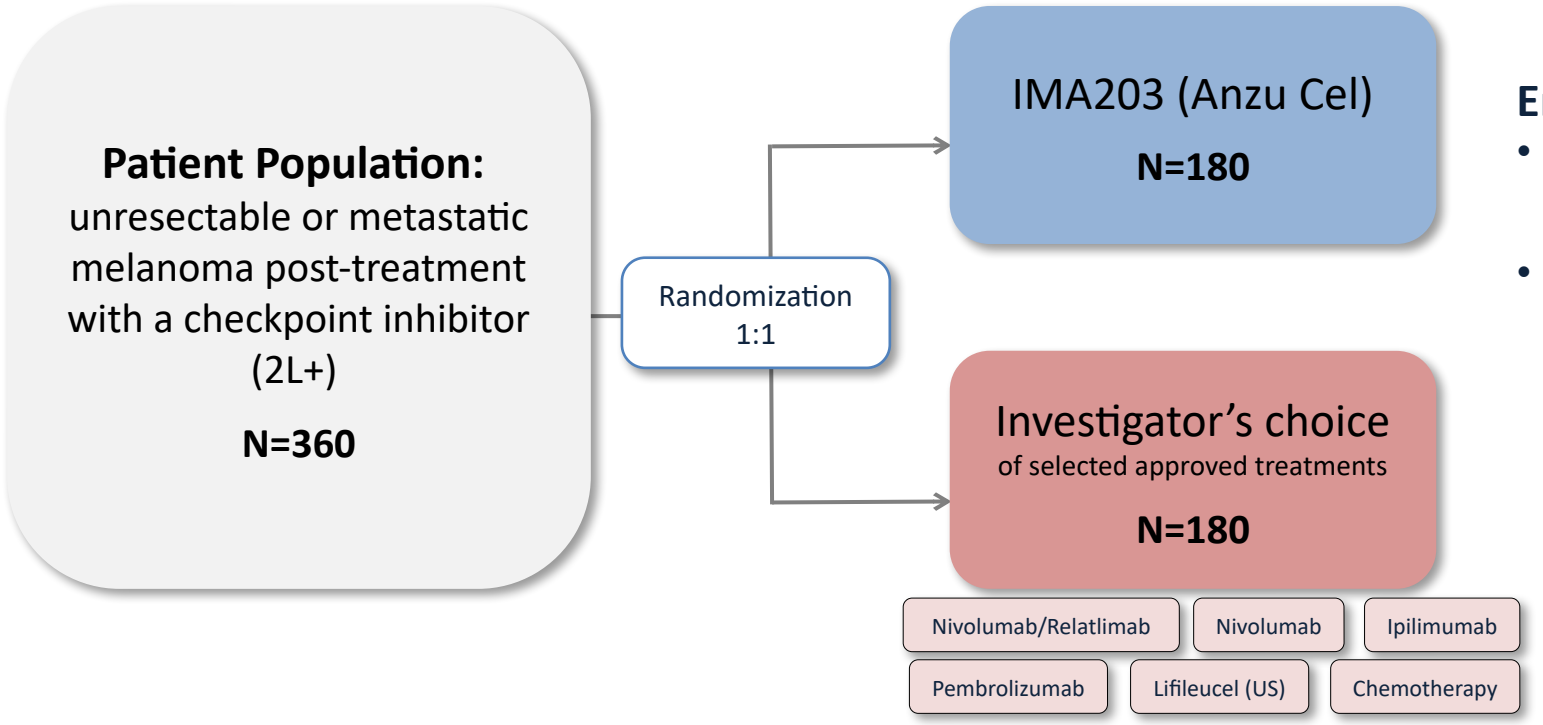


02/2026



SUPRAME: Registration-enabling Randomized Phase 3 Tri

Recruiting

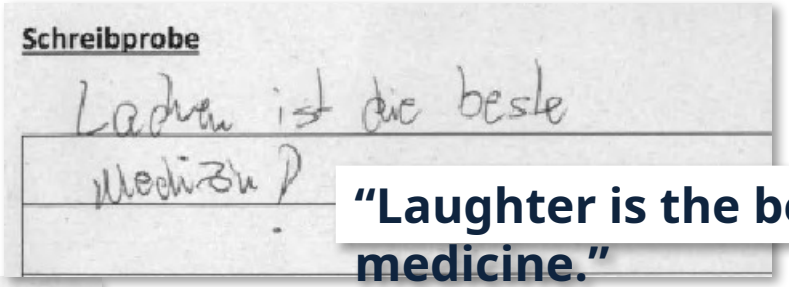


Endpoints

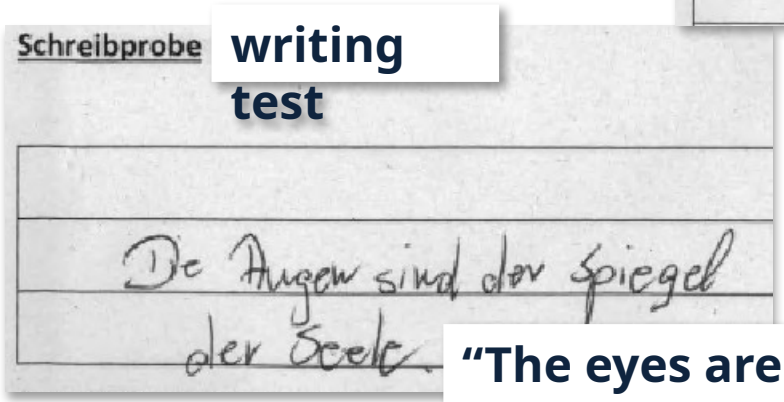
- **Primary Endpoint**
  - **PFS**
- **Secondary Endpoints**
  - Safety
  - ORR + DOR
  - No OS detriment
  - Patient-reported outcomes (EORTC QLQ-C30, EQ-5D-5L)

NCT06743126

Best of writing tests

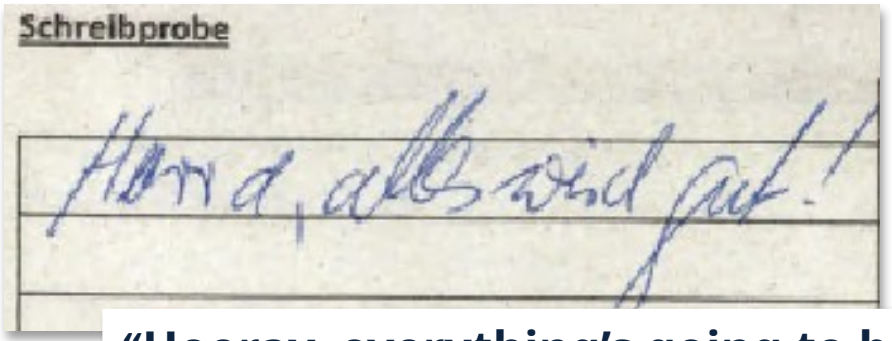


“Laughter is the best medicine.”



writing test

“The eyes are the windows to the soul.”



“Hooray, everything’s going to be alright!”

“My greatest happiness in life, is my wife Gabi.”

Thank you for your attention!

TCR-T trials in Dresden:

IMA203-101 (Endomet.-Ca. 2nd+ line)

SUPRAME (kut. Melanom 2nd+ line)

VIDAR (Pankreas G12V 1st line)

TIL trials in Dresden:

IOV-LUN202 (NSCLC 2nd line)

TILVANCE (Melanom 1st line)

Martin.wermke@ukdd.de

NCT/UCC ECTU-Studienregister:

Universitätsklinikum Carl Gustav Carus DIE DRESDNER.

Technische Universität Dresden

NCT NATIONALES CENTRUM FÜR TUMORERKRANKUNGEN DRESDEN