DGHO DEUTSCHE GESELLSCHAFT FÜR HÄMATOLOGIE UND ONKOLOGIE

JAHRESTAGUNG 2024 BASEL 11.–14. Oktober

CHARITÉ UNIVERSITÄTSMEDIZIN BERLIN

14. Oktober 2024

Multiples Myelom - Zugang zu neuen Arzneimitteln: Theorie und Praxis

CAR-T-Zellen

Jan Krönke

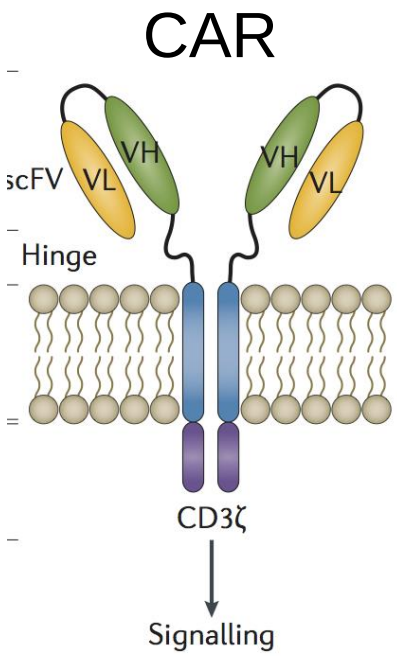
Medizinische Klinik m.S.
Hämatologie, Onkologie
und Tumorimmunologie

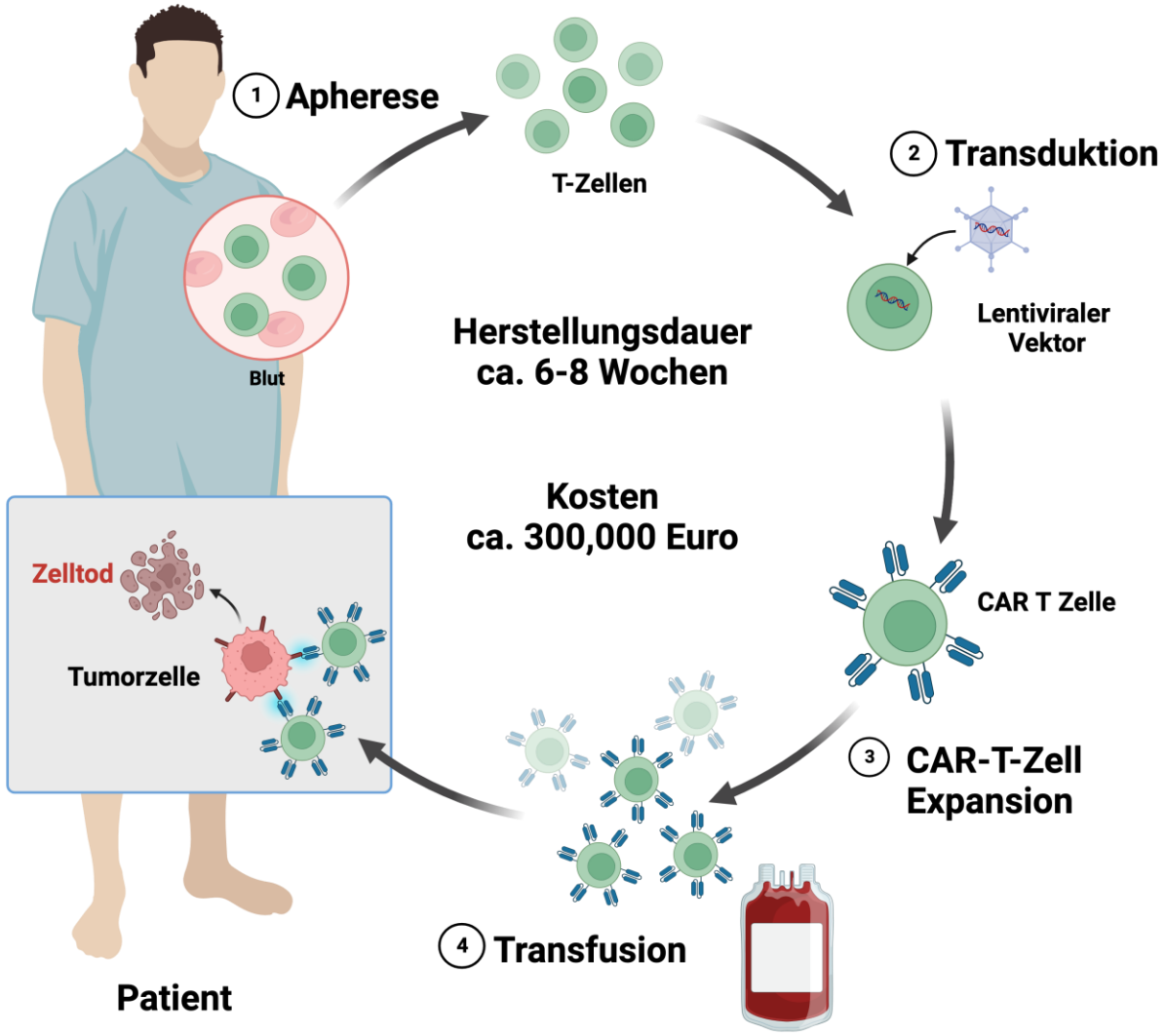
Conflict of Interests

Advisory Board/ Speaker/ Honoraria/ Travel support

BMS, Janssen, Abbvie, Sanofi , Pfizer, Jazz

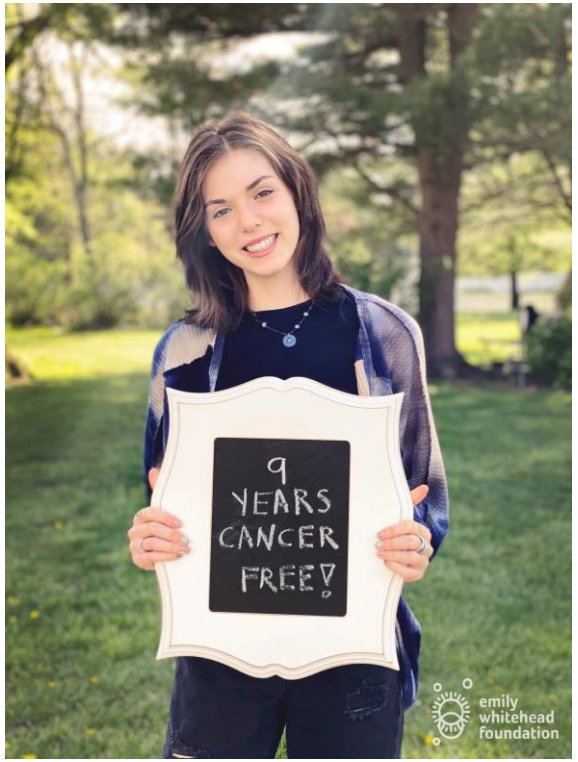
Chimeric Antigen Receptor (CAR)-T-Zellen





CAR-T-Zellen: Therapie mit kurativem Potential

2012
EMILY WITHEHEAD

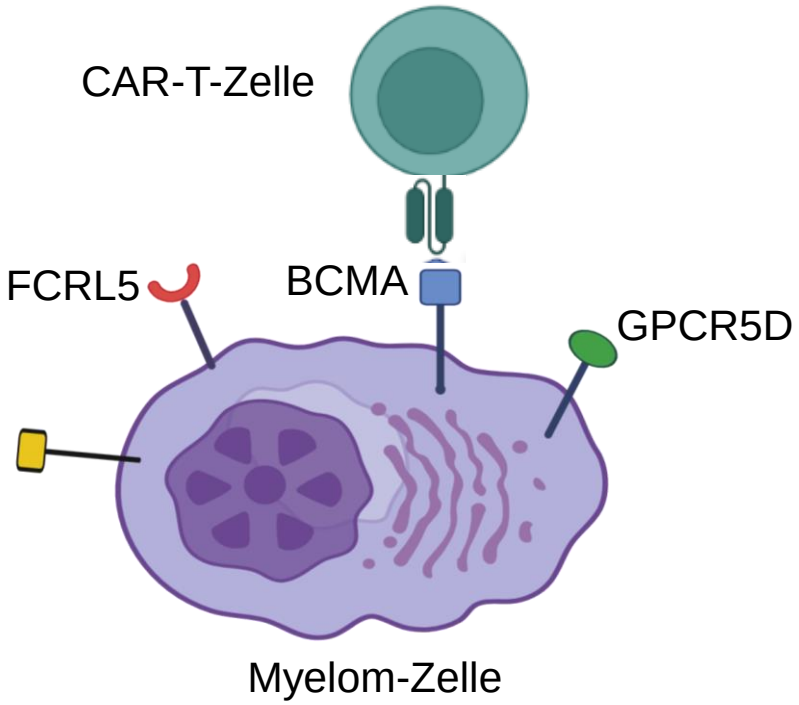


2021

CAR-T-Zellen 2024
→B-ALL
→B-Zell Lymphome
→Multiples Myelom

Studien
→T-Zell-Lymphome/T-ALL
→ AML
→Solide Tumore
→Autoimmunerkrankungen

CAR-T Zelltherapie beim Multiplen Myelom



Zielantigen	CAR	Verfügbarkeit	Line
BCMA	Ide-Cel (Abecma)	2022	3+
BCMA	Cilta-Cel (Carvykti)	2023	2+

Weitere Targets: GPCR5D, SLAMF, FCRL5, ROR2, CD138

Dual-targeting CAR-T

Allo CAR-T

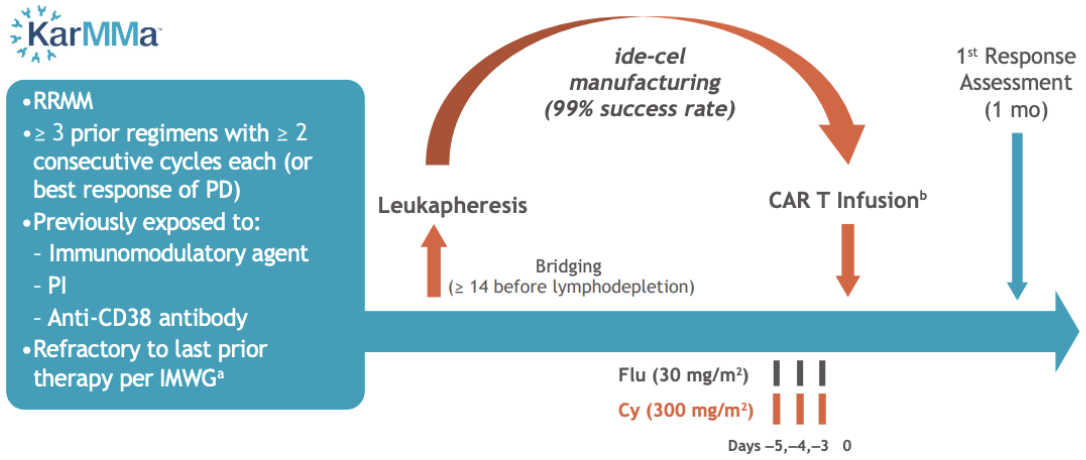
} Studien

BCMA CAR-T-Zellen, Phase 1-Studien

Idecabtagen Vicleucel (Ide-Cel, Abecma)

Table 1. Baseline Characteristics of the Patients Who Received Idecabtagene Vicleucel (Ide-cel).*

Characteristic	Ide-cel Target Dose of CAR+ T Cells			Total (N=128)
	150×10^6 (N=4)	300×10^6 (N=70)	450×10^6 (N=54)	
Median age (range) — yr	54 (49–69)	61 (33–76)	62 (43–78)	61 (33–78)
Male sex — no. (%)	4 (100)	38 (54)	34 (63)	76 (59)
Median time from initial diagnosis to screening (range) — yr	10 (6–12)	7 (2–18)	6 (1–17)	6 (1–18)
Extramedullary disease — no. (%)†	0	34 (49)	16 (30)	50 (39)
High tumor burden — no. (%)‡	3 (75)	34 (49)	28 (52)	65 (51)
Median no. of previous antimyeloma regimens (range) — no. (%)	9 (4–12)	6 (3–16)	5 (3–13)	6 (3–16)
>1 Previous antimyeloma regimen per year — no. (%)	2 (50)	36 (51)	22 (41)	60 (47)
Previous autologous HSCT — no. (%)	4 (100)	67 (96)	49 (91)	120 (94)
>1 transplantation	3 (75)	23 (33)	18 (33)	44 (34)
Refractory status — no. (%)††				
Immunomodulatory agent	4 (100)	70 (100)	52 (96)	126 (98)
Proteasome inhibitor	4 (100)	63 (90)	49 (91)	116 (91)
Anti-CD38 monoclonal antibody	4 (100)	66 (94)	50 (93)	120 (94)
Daratumumab	3 (75)	61 (87)	45 (83)	109 (85)
Double-refractory disease‡‡	4 (100)	63 (90)	47 (87)	114 (89)
Triple-refractory disease§§	4 (100)	60 (86)	44 (81)	108 (84)
Penta-refractory disease¶¶	1 (25)	24 (34)	8 (15)	33 (26)



Endpoints

- **Primary**: ORR
- **Secondary**: CRR (key secondary), safety, DOR, PFS, OS, PK, MRD,[c] QOL, HEOR

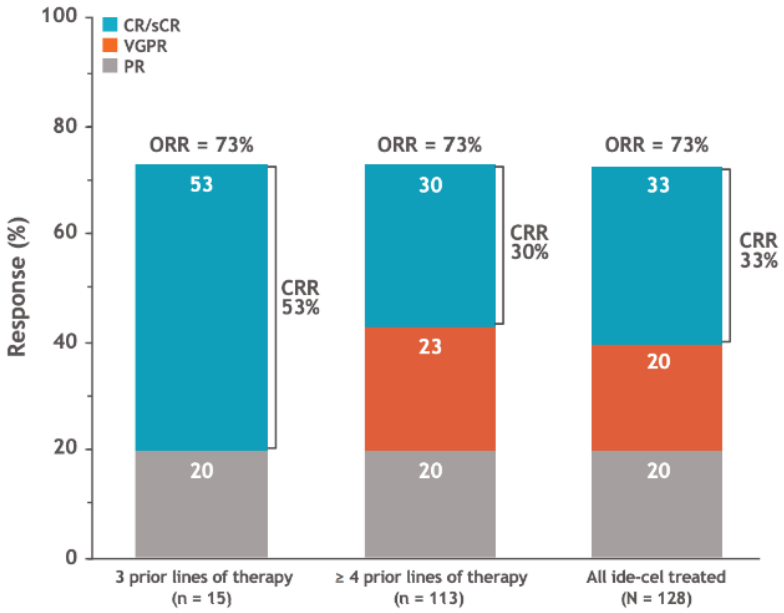
- Dosiseskalation 150, 300, 400 x10^6 CAR-T-Zellen
- 128 der 140 (91%) Patienten erhielten CAR-T-Zellen

Munshi et al. NEJM 2021

BCMA CAR-T-Zellen, Phase 1 Studien

Ide-Cel (Abecma)
KarMMa-1

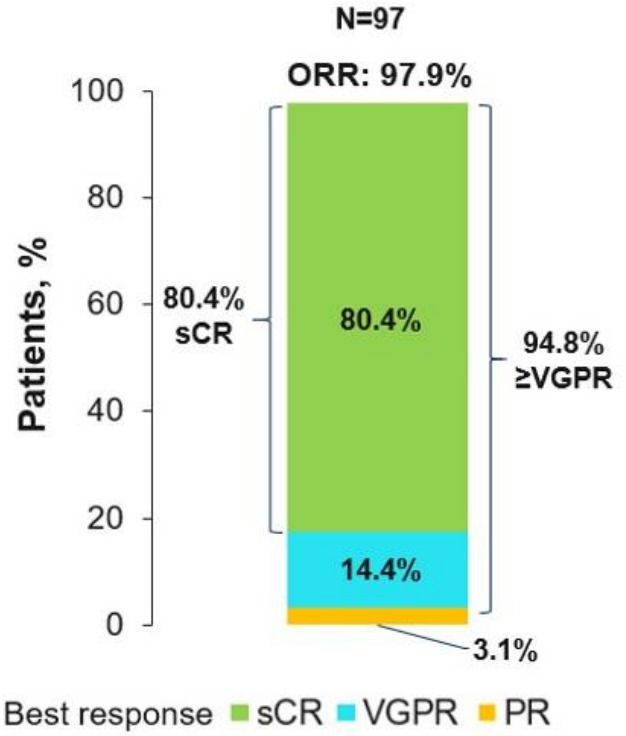
>3 Vortherapien



Munshi et al. NEJM 2021
Lin et al. Nat Med 2023

Cilta-Cel (Carvykti)
Cartitude-1

>3 Vortherapien

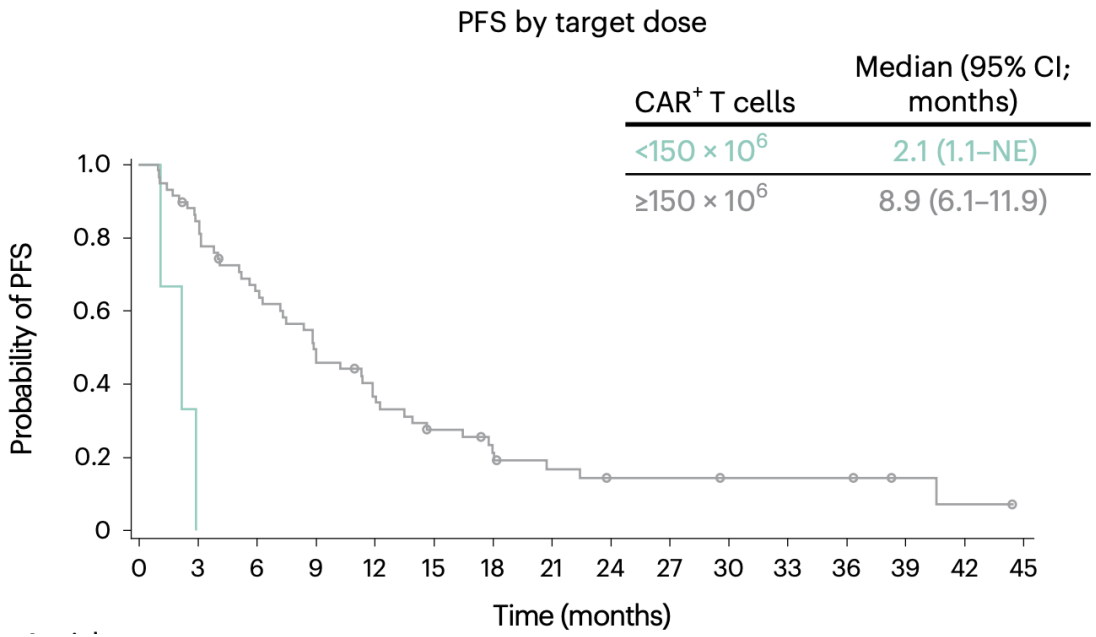


Berdeja et al. Lancet 2021
Martin et al. JCO 2022

BCMA CAR-T-Zellen, Phase 1 Studien

Ide-Cel (Abecma)
KarMMa-1

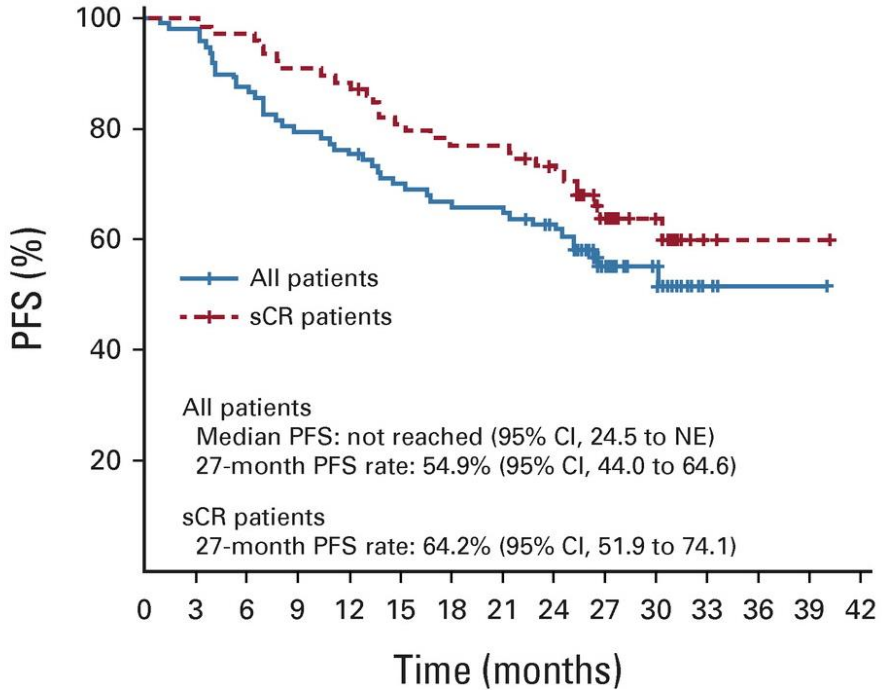
>3 Vortherapien



Munshi et al. NEJM 2021
Lin et al. Nat Med 2023

Cilta-Cel (Carvykti)
Cartitude-1

>3 Vortherapien

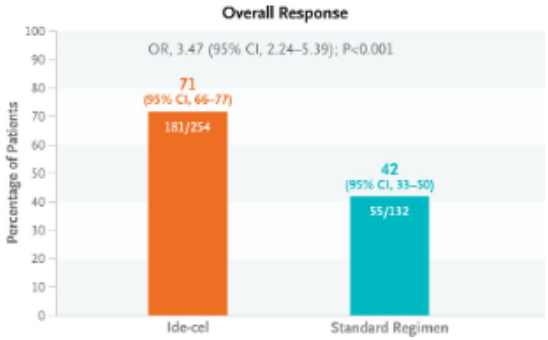


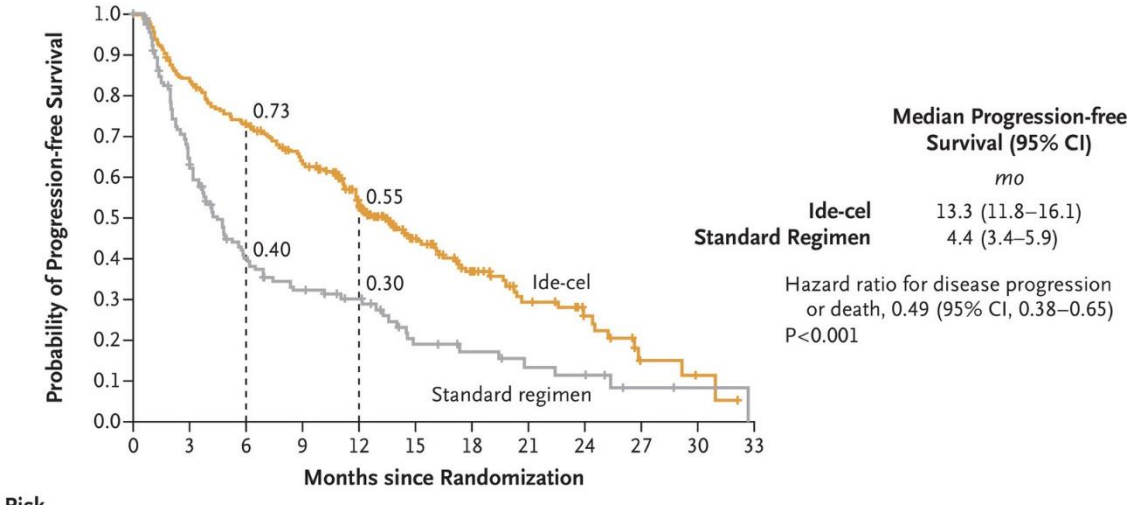
Berdeja et al. Lancet 2021
Martin et al. JCO 2022

BCMA CAR-T, Phase 3 Studien

Ide-Cel (Abecma) KarMMa-3

2-4 Vortherapien, Ide-Cel vs SOC

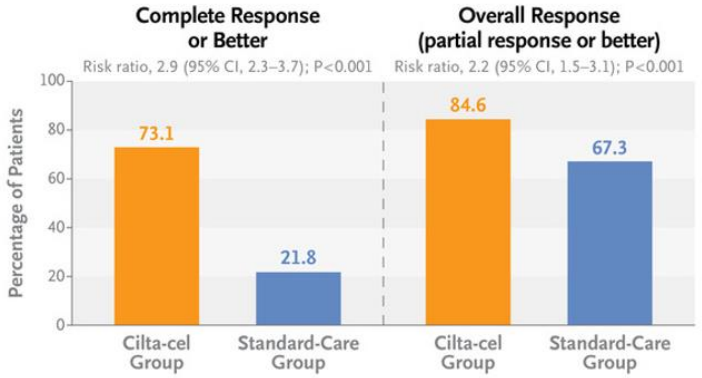


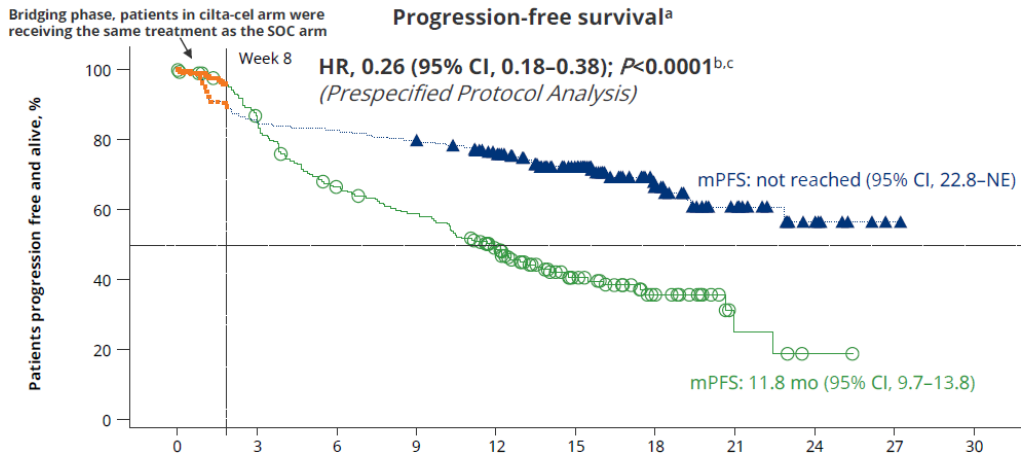


Rodriguez-Otero et al. NEJM 2023

Cilta-Cel (Carvykti) Cartitude-4

1-3 Vortherapien, Cilta-Cel vs PVd oder DPd

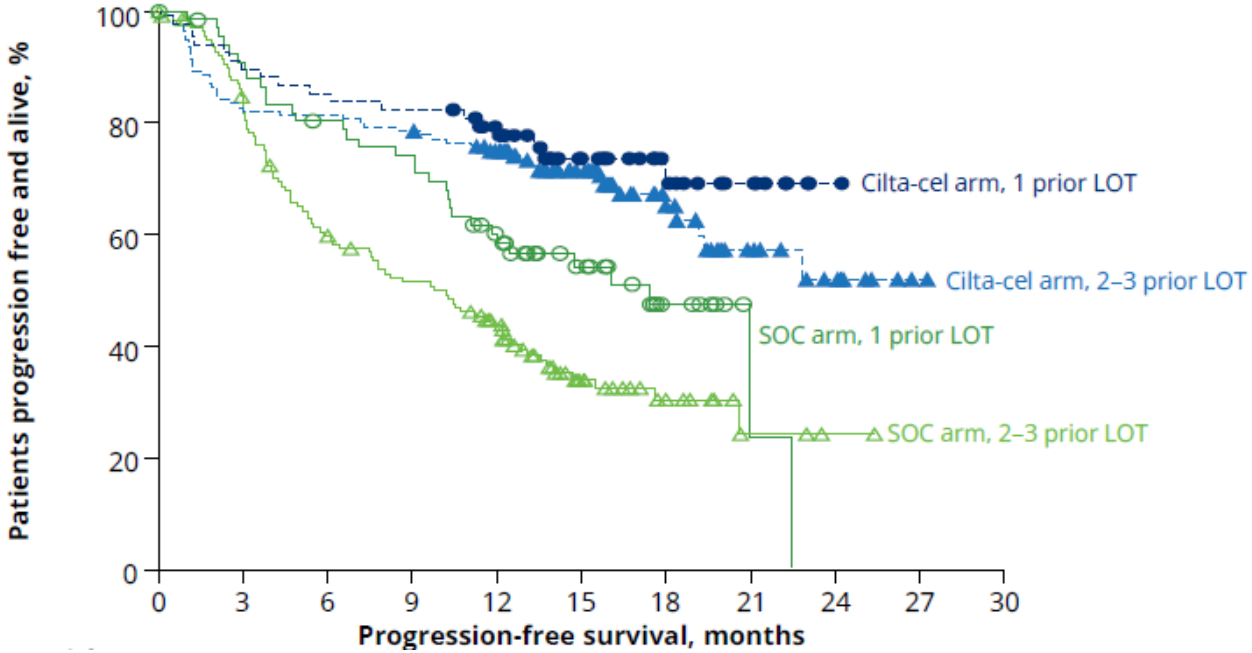




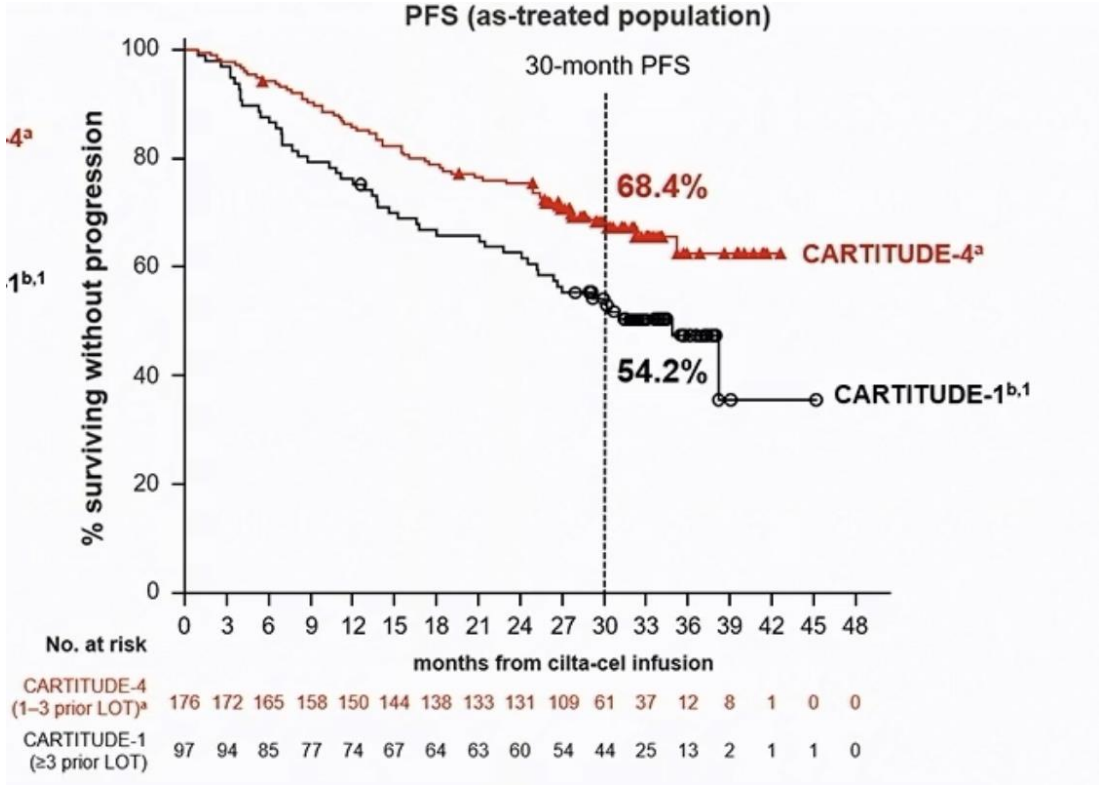
San-Miguel et al. NEJM2023, Einsele et al. EHA 2023

Einfluss der Therapielinie auf die Effektivität

Cilta-Cel, Cartitude-4



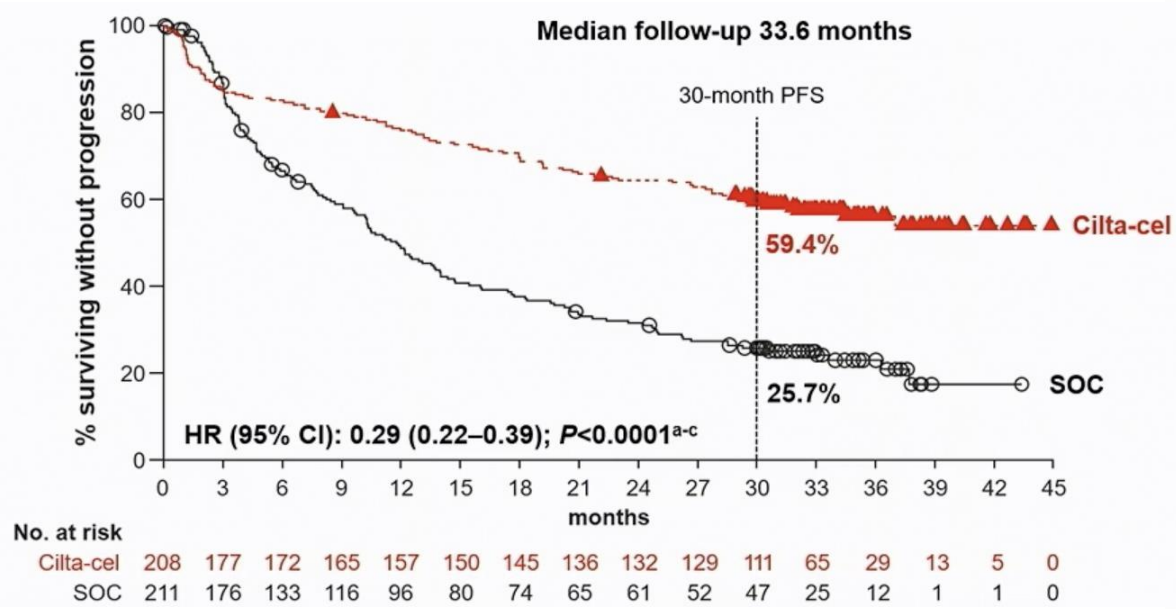
Einsele et al. EHA 2023



Mateos et al. IMS 2024 Abstr. OA-065

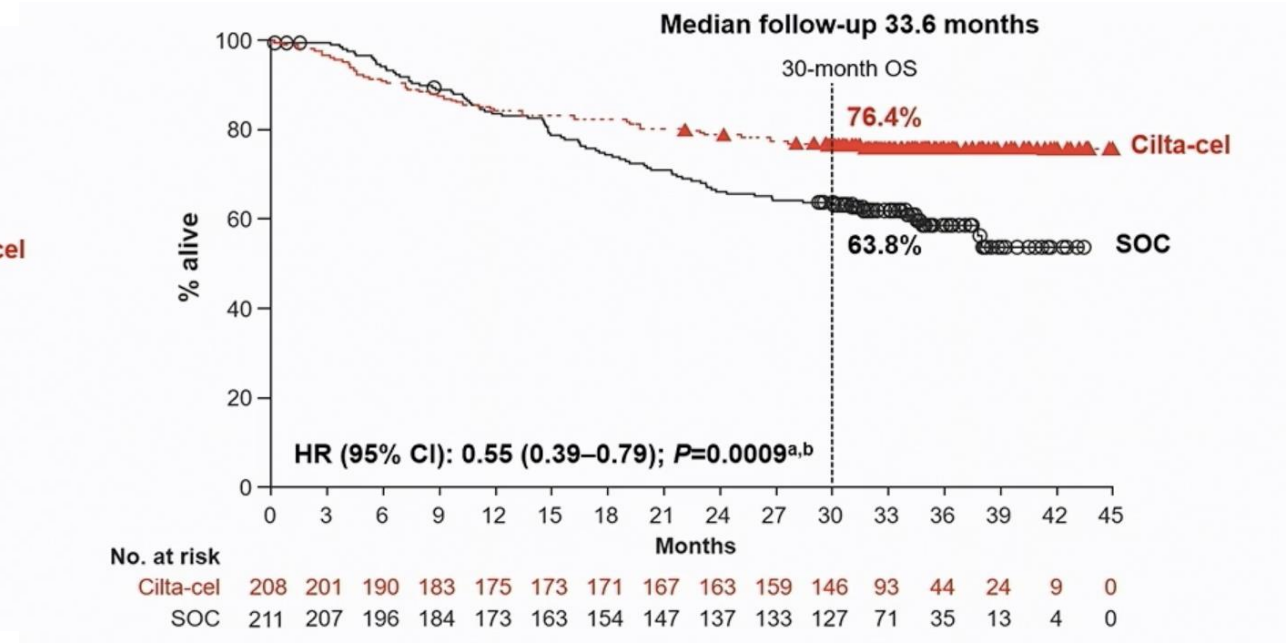
CARTITUDE-4: Update

Progression Free Survival



Mateos et al. IMS 2024 Abstr. OA-065

Overall Survival

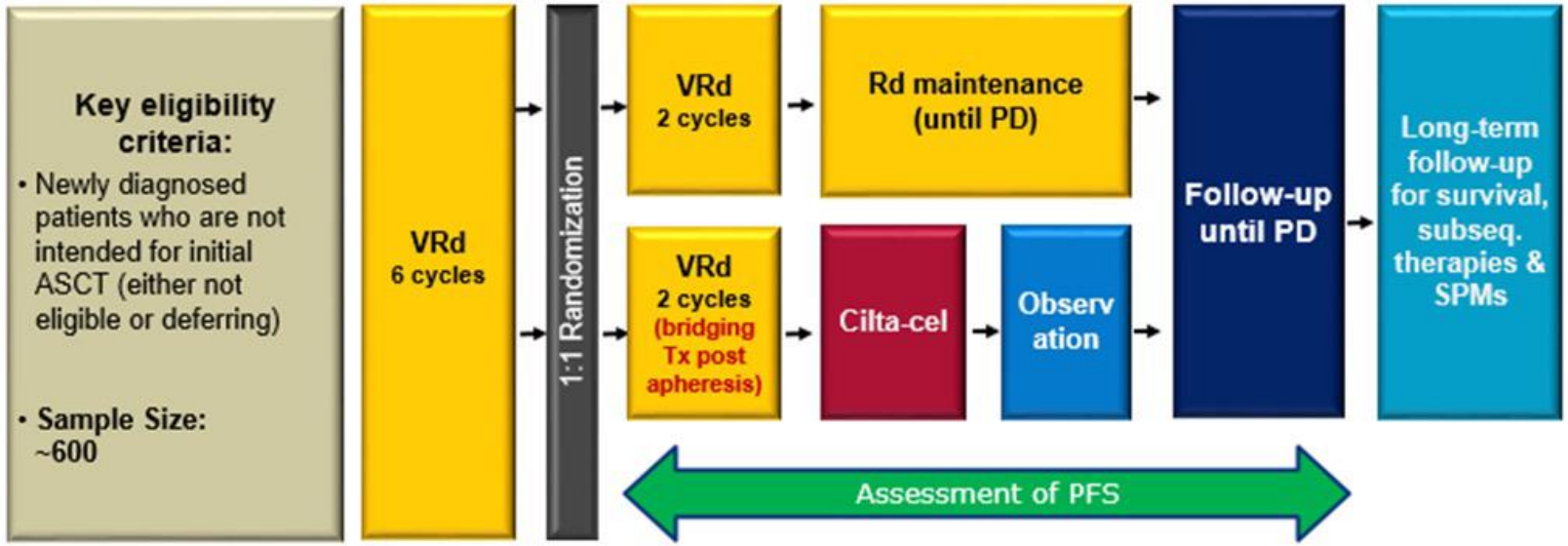


→ Kein Cross-over
→ Cilta-Cel nicht verfügbar als SOC

CAR-T in der Erstlinie

Transplant-ineligibel

CARTITUDE-5



Transplant-eligibel

KarMMA-9: Ide-Cel nach Hochdosistherapie

CARTITUDE-6: Cilta-Cel vs Hochdosistherapie

} Lenalidomid-Erhaltung nach CAR-T

BCMA CAR-T-Zellen beim Multiplen Myelom

BCMA CAR-T Zellen sind die effektivste Monotherapie beim Multiplen Myelom

Ansprechen, PFS, OS, QoL sind dem Standard-of-Care überlegen

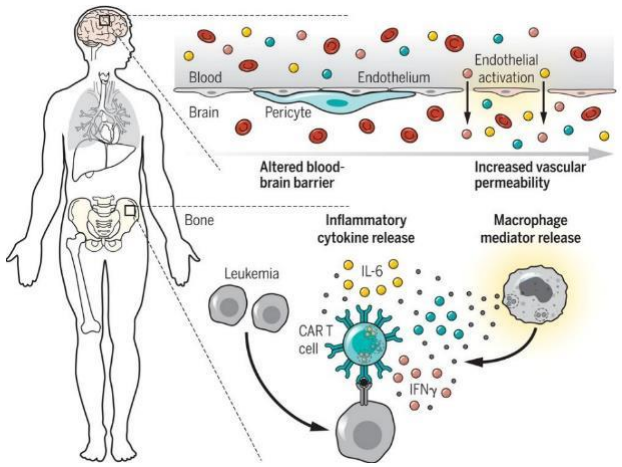
EMA-Zulassung 04/2024

Cilta-Cel (Carvykti): ab der 2. Therapielinie, PI Vorbehandlung, Lenalidomid-refraktär

Ide-Cel (Abecma): ab der 3. Therapielinie, IMID, PI und Anti-CD38 Vorbehandlung

→ CAR-T für alle Patienten mit rezidiviertem Multiplen Myelom

Nebenwirkungen von T-Zelltherapien



June et al., Science 2018

	Ide-Cel KarMMa-1	Cilta-Cel Cartitude-1	Teclistamab Majestec-1	Elranatamab MagnetisMM-3	Talquetamab MonumenTAL-1
CRS	84%	95%	72%	56%	77%
CRS °3+	6%	4%	0,6%	0%	3%
CRS onset, d	1 (1-12)	7(1-12)	2 (1-6)	NR	2 (1-6)
ICANS	18%	17%	3%	3%	3%
ICANS °3+	4%	2%	0%	0%	0%
Infections °3+	22%	20%	55%	40%	15%
Infections °5	2%	NR	12%	6.5%	2%

Cytokine Release Syndrom (CRS)

→ Tocilizumab, Dexamethason

Immune effector cell–associated neurotoxicity (ICANS)

→ Dexamethason

Munshi et al. NEJM 2021, Berdeja et al. Lancet 2021, Rajeski et al., Blood 2022, Verdun et al. NEJM 2024; Lesokhin et al., Nat. Med. 2023

Hämatotoxizität nach CAR-T

Cilta-Cel

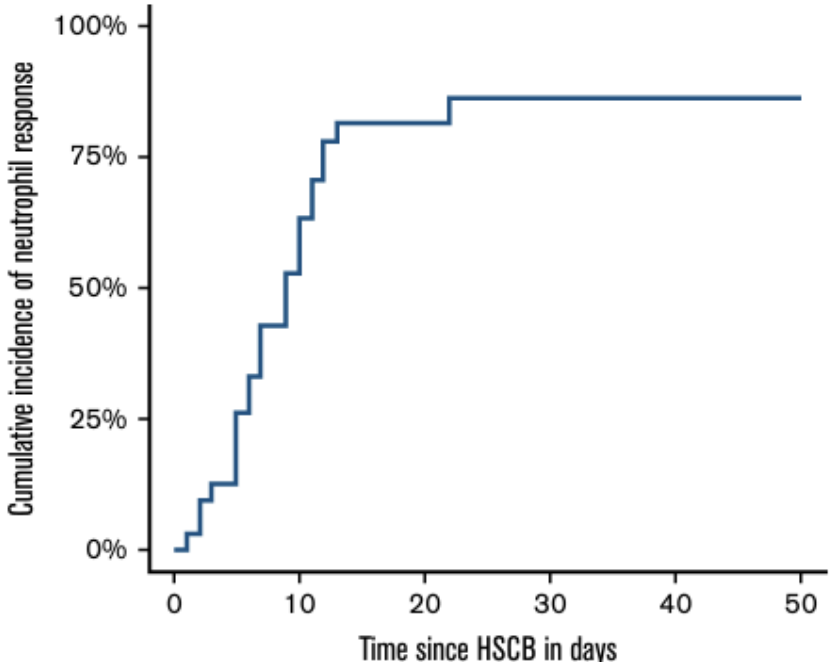
	Any grade	Grade 3–4
Any adverse event	97 (100%)	91 (94%)
Haematological*	97 (100%)	96 (99%)
Neutropenia	93 (96%)	92 (95%)
Anaemia	79 (81%)	66 (68%)
Thrombocytopenia	77 (79%)	58 (60%)
Leukopenia	60 (62%)	59 (61%)
Lymphopenia	51 (53%)	48 (50%)

Ide-Cel

Event	Ide-cel (N=250)		
	Any Grade	Grade 3 or 4	Grade 5
Any adverse event — no. (%)*	248 (99)	233 (93)	36 (14)†
Hematologic event	224 (90)	218 (87)	0
Neutropenia	195 (78)	189 (76)	0
Anemia	165 (66)	127 (51)	0
Thrombocytopenia	136 (54)	106 (42)	0
Lymphopenia	73 (29)	70 (28)	0
Leukopenia	72 (29)	71 (28)	0

Berdeja et al. Lancet 2021
Rodriguez-Otero et al. NEJM 2023

Autologe Stammzellen Boost



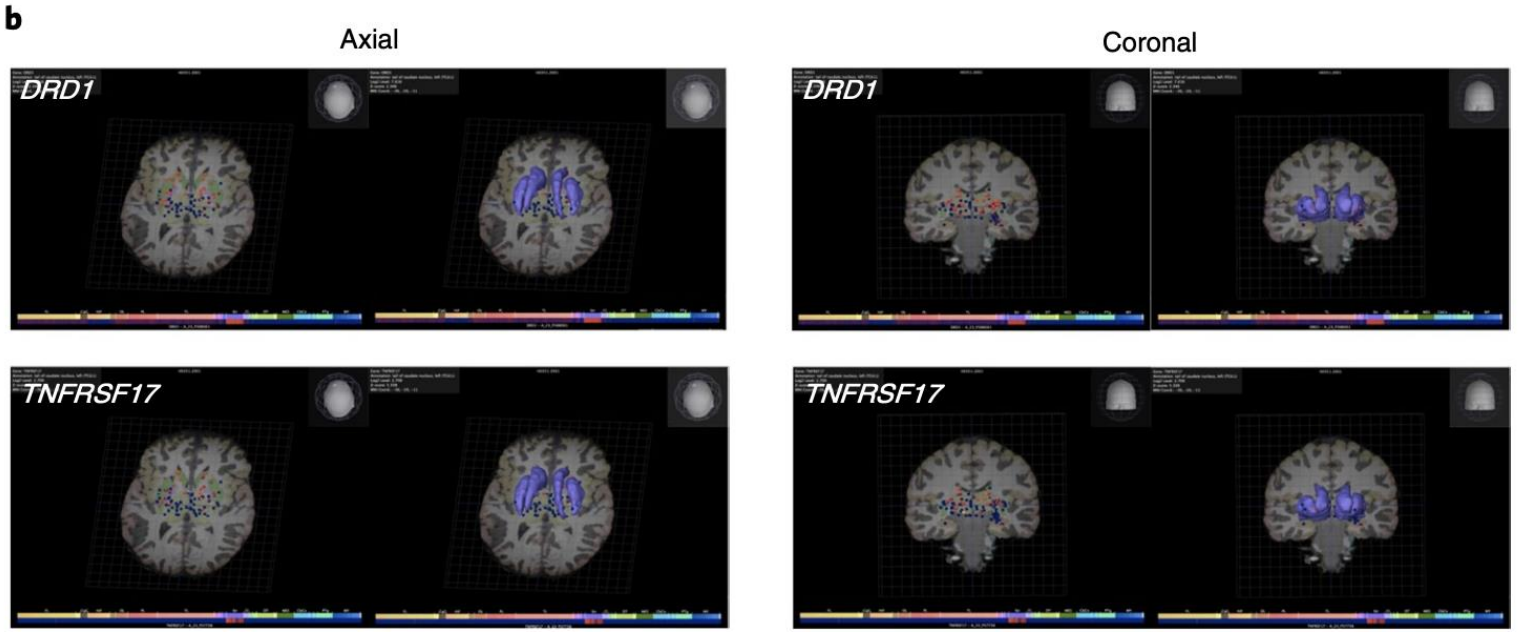
Gagelmann et al. Blood Adv 2023

Parkinson nach BCMA CAR-T-Zelltherapien

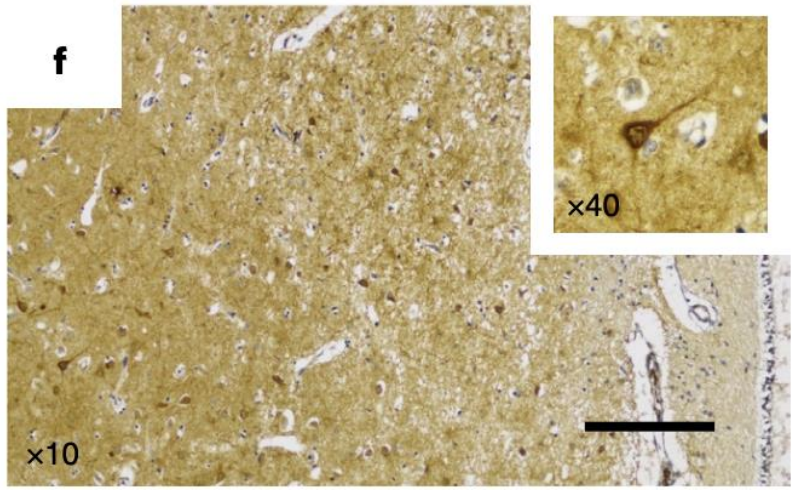
Parkinson Symptome: Tremor, Bewegungsstörung, Bradykinesie, Mikrographie, Gedächtnisstörung

1-3 Monate nach BCMA-CAR-T-Zelltherapie

Expression von BCMA in neuronalen Zellen des Nucleus Caudatus



BCMA=TNFRSF17



→ Suppression der CAR-T-Zellen: Dexamethason, Cyclophopshamid

Van Oekelen et al., Nat Med 2021

Sekundäre Neoplasien nach CAR-T-Zellen

CARTITUDE-4

SPM	Cilta-cel (n=208)	SOC (n=208)
SPMs, n (%)	**27 (13.0)**	**24 (11.5)**
Hematologic[a]	7 (3.4)	1 (0.5)
MDS, n	4	0
Progressed to AML, n	2	–
AML, n	1	0
Peripheral T-cell lymphoma, n	2	0
EBV-associated lymphoma, n	0	1
Cutaneous/non-invasive[a]	15 (7.2)	15 (7.2)
Non-cutaneous/invasive[a]	6 (2.9)	8 (3.8)

Mateos et al. IMS 2024 Abstr. OA-065

→ CAR-T-NHL: unter 1%

nature medicine

Brief Communication https://doi.org/10.1038/s41591-024-02826-w

T cell lymphoma and secondary primary malignancy risk after commercial CAR T cell therapy

Received: 19 December 2023

Accepted: 22 January 2024

Guido Ghilardi[1,2,3], Joseph A. Fraietta[2,4], James N. Gerson[1,3], Vivianna M. Van Deerlin[5,6], Jennifer J. D. Morrissette[5,6], Gabriel C. Caponetti[5], Luca Paruzzo[1,2,3], Jaryse C. Harris[5], Elise A. Chong[1,2,3],

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE | BRIEF REPORT

Aggressive Lymphoma after CD19 CAR T-Cell Therapy

Authors: Guido Kobbe, M.D., Monika Brüggemann, M.D., Ben-Niklas Baermann, M.D., Laura Wiegand, I

ORIGINAL ARTICLE | BRIEF REPORT

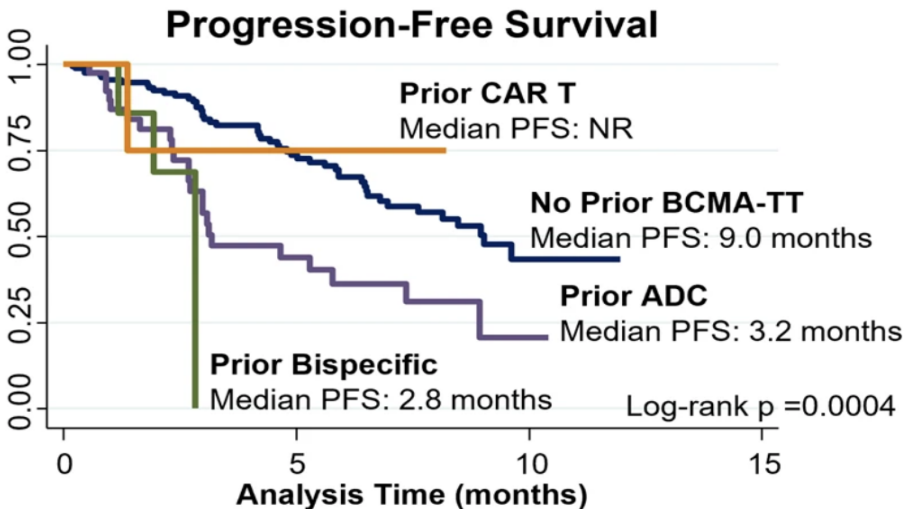
Indolent CD4+ CAR T-Cell Lymphoma after Cilta-cel CAR T-Cell Therapy

Authors: Metin Ozdemirli, M.D., Ph.D., Thomas M. Loughney, M.D., Emre Deniz, Ph.D., Joeffrey J. Chahine, Ph.D., Maher

„CAR auf BiTE ist nicht gescheit“

CAR-T after Bispecific

Ide-Cel

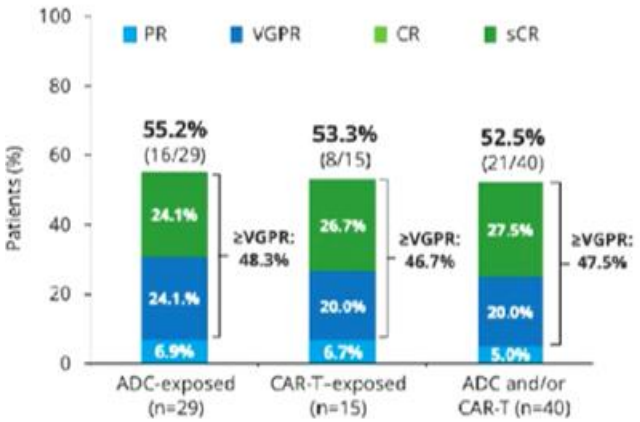


Ferreri et al BCJ 2023

„BiTE auf CAR ist doch klar“

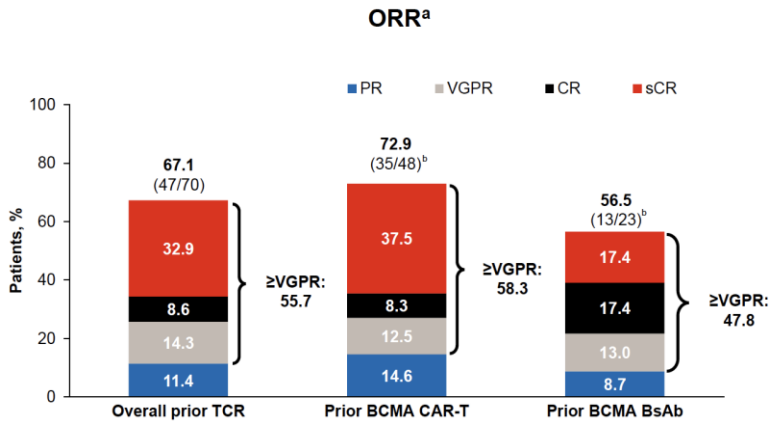
Bispecific after CAR-T

Teclistamab



Touzeau et al EHA 2022

Talquetamab



Jakubowiak et a.l ASH 2023

Talquetamab als Bridging Therapie

Teclistamab → Progress → T-Zell-Apherese → CAR-T 👎

Talquetamab → Response → T-Zell-Apherese → Talquetamab→ CAR-T 👍

BCMA CAR-T Verfügbarkeit

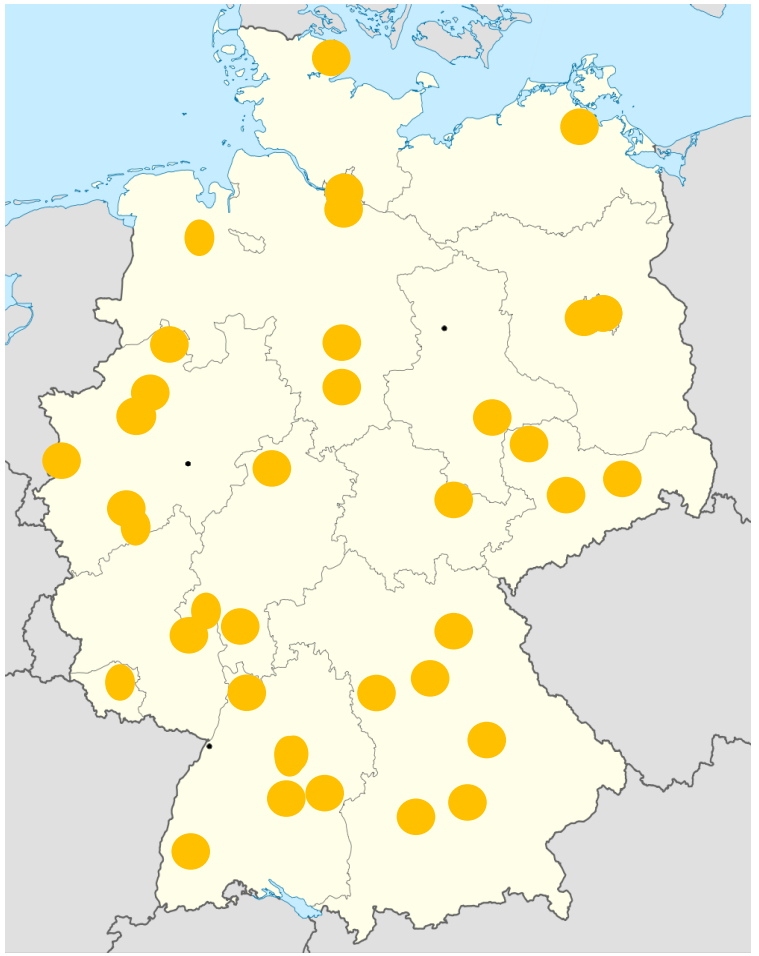
Nur an zertifizierten CAR-T-Zentren möglich!

Ide-Cel (Abecma) 40 Zentren

Cilta-Cel (Carvykti) 23 Zentren

Ide-Cel: Verfügbarkeit ab Dezember 2024 unklar

Cilta-Cel: aktuell eingeschränkte Verfügbarkeit



DAG HSZT

www.dag-hszt.de/CAR-T.html

BCMA CAR-T Stationäre Therapie?

AT THE FOREFRONT UChicagoMedicine Comprehensive Cancer Center

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Outpatient CAR T-cell Therapy

CAR T-cell Therapy

- How CAR T-cell Therapy Works
- Frequently Asked Questions
- Outpatient CAR T-cell Therapy
- Meet Our Team
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PRESSEMITTEILUNGEN | 21.07.2021 | MEDIZIN, FORSCHUNG

KREBSIMMUNTHERAPIE

Erste ambulante CAR-T-Zell-Therapie

Eine neue Studie an der Medizinischen Klinik III zeigt neue Wege auf

www.lmu-klinikum.de

CAR-T beim Myelom – Hohe Therapie-Kosten

CAR-T	
Ide-Cel (Abecma)	240,000 Euro einmalig
Cilta-Cel (Carvykti)	~280,000 Euro einmalig
Bispezifische	
Teclistamab	240,000 Euro/ Jahr
Elranatamab	280,000 Euro/ Jahr
Alternativen	
Dara/ Carf/ Dex	280,000 Euro/ Jahr
Isa/ Carf/ Dex	220,000 Euro/ Jahr
Dara/ Pom/ Dex	240,000 Euro/ Jahr
Isa/ Pom/ Dex	180,000 Euro/ Jahr

freeimages.com

https://www.g-ba.de/

CAR-T beim Myelom – Organisatorische Herausforderungen

- Termin zur Beratung und Aufklärung am CAR-T-Zentrum
- Planung der Apherese 1 bis 2 Wochen, Cilta-Cel aktuell ca. 4 bis 8 Wochen
- Herstellung 6 bis 10 Wochen

- Bridging-Therapie notwendig?
- Bridging-Therapie vor/ nach Apherese?
- Welche Bridging Therapie?
- Qualität der T-Zellen beeinflusst durch Vortherapie aber auch Krankheitsaktivität

→ Patienten frühzeitig am CAR-T-Zentrum vorstellen!!!

Vielen Dank für Ihre Aufmerksamkeit!