Lymphoma · Leukemia & Myeloma Congress
Celebrating 25 Years of Excellence

Evolving Strategies for CAR T Cell Therapy in Relapsed/Refractory Multiple Myeloma

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Supported by an educational grant from Johnson & Johnson.

Disclosures

- **Adam D. Cohen, MD:** Consulting/Advisory Boards—BMS, Janssen, Genentech/Roche, GlaxoSmithKline, ArcelIx, Ichnos, Abbvie, Pfizer, iTeos, AstraZeneca, Legend, Sanofi, Moderna, Regeneron, Prothena, Kite, Caribou; research support—Novartis, GlaxoSmithKline, Genentech, Janssen; intellectual property licensed by institution to—Novartis
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Learning Objectives

- Evaluate the clinical and individual factors influencing access to and treatment planning for BCMA-directed CAR T-cell therapy in R/R MM
- Assess the latest clinical trial and emerging data that inform patient selection, therapeutic bridging strategies, and sequencing of BCMA-directed CAR T-cell therapies in R/R MM
- Describe evolving best practices for the care of patients undergoing CAR T-cell therapy, emphasizing interdisciplinary care coordination, shared decision-making, and the early identification and mitigation of treatment-related AEs

R/R = relapsed/refractory; MM = multiple myeloma; AE = adverse event.

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CAR T Cell Therapies for R/R MM: A Focus on Evolving Indications and Emerging Therapeutics

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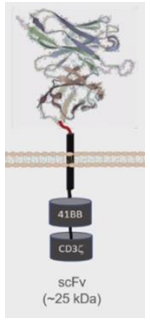
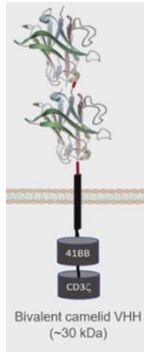
Outline

- FDA-approved CAR T cell therapies for multiple myeloma
  - Safety/efficacy data and indications
  - Evolving considerations for patient selection and therapeutic sequencing
- Emerging CAR T cell therapies for MM
- CAR T cell therapy-associated adverse events
  - Common adverse events
  - Anticipating and mitigating risk

FDA = US Food and Drug Administraion; MM = multiple myeloma.

FDA-Approved BCMA CAR T Cell Products

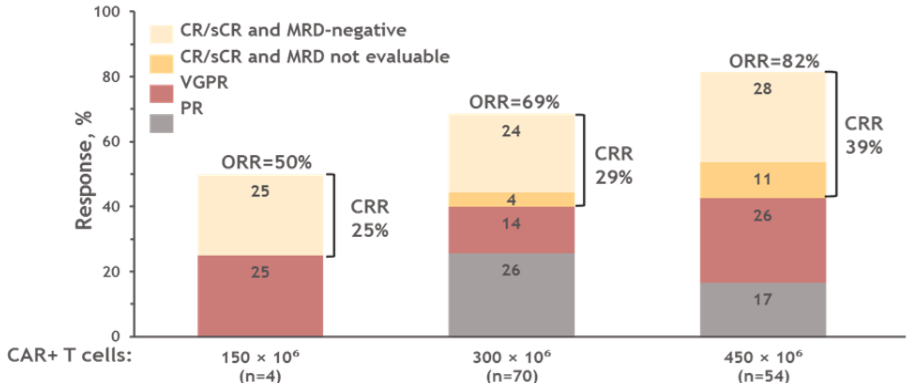
	Ide-cel	Cilta-cel
		
• Initial approvals - ≥4 prior lines, including PI, IMID, and anti-CD38 mAb	**Mar. 2021** **FDA Approves First Cell-Based Gene Therapy for Adult Patients with Multiple Myeloma**	**Feb. 2022** **FDA approves ciltacabtagene autoleucel for relapsed or refractory multiple myeloma**
• Updated labels:	• April 2024 - ≥2 prior lines, including PI, IMID, and anti-CD38 mAb	• April 2024 - ≥1 prior line, including PI, IMID, and refractory to lenalidomide

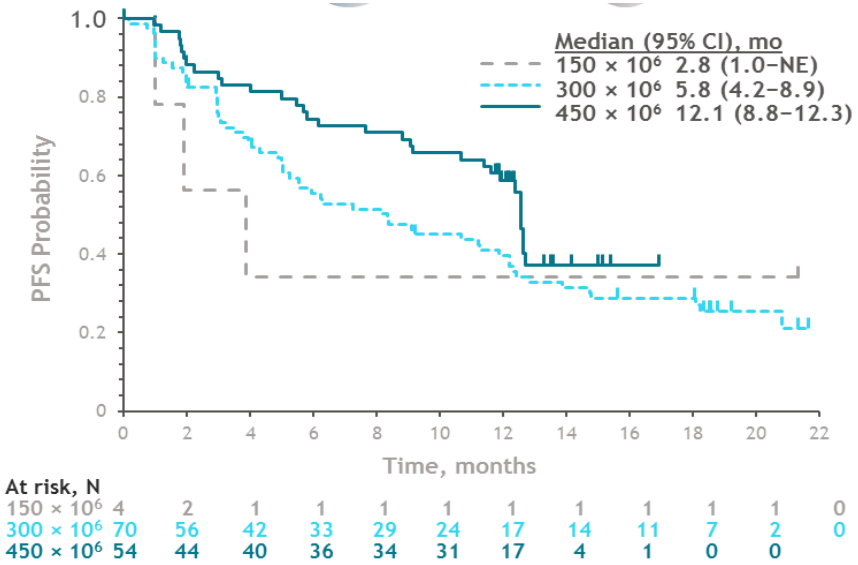
PI = protease inhibitor; IMiD = immunomodulatory drug; mAb = monoclonal antibody.

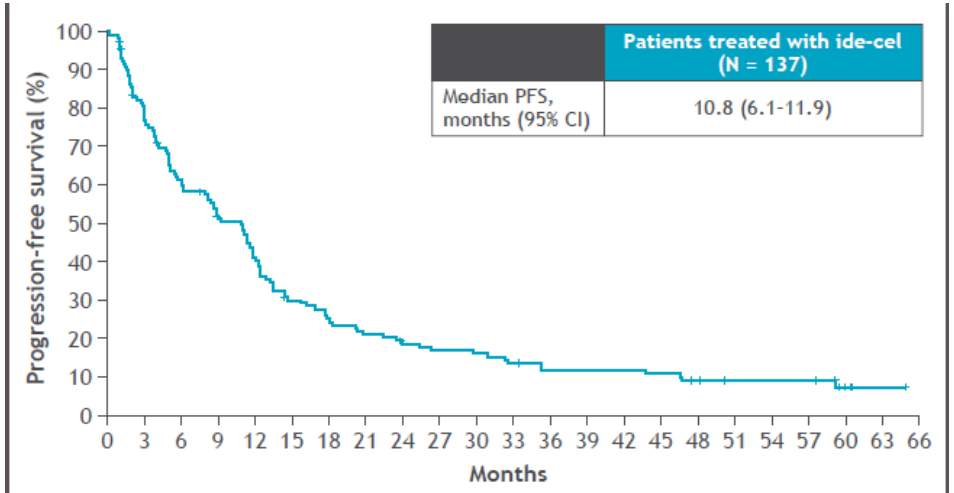
US Food and Drug Administration [www.fda.gov]. Last updated March 27, 2021. https://www.fda.gov/news-events/press-announcements/fda-approves-first-cell-based-gene-therapy-adult-patients-multiple-myeloma. US Food and Drug Administration [www.fda.gov]. Last updated March 7, 2022. https://www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-ciltacabtagene-autoleucel-relapsed-or-refractory-multiple-myeloma. Bishop MR, et al. *Blood*. 2024;144(Suppl 1):4825.

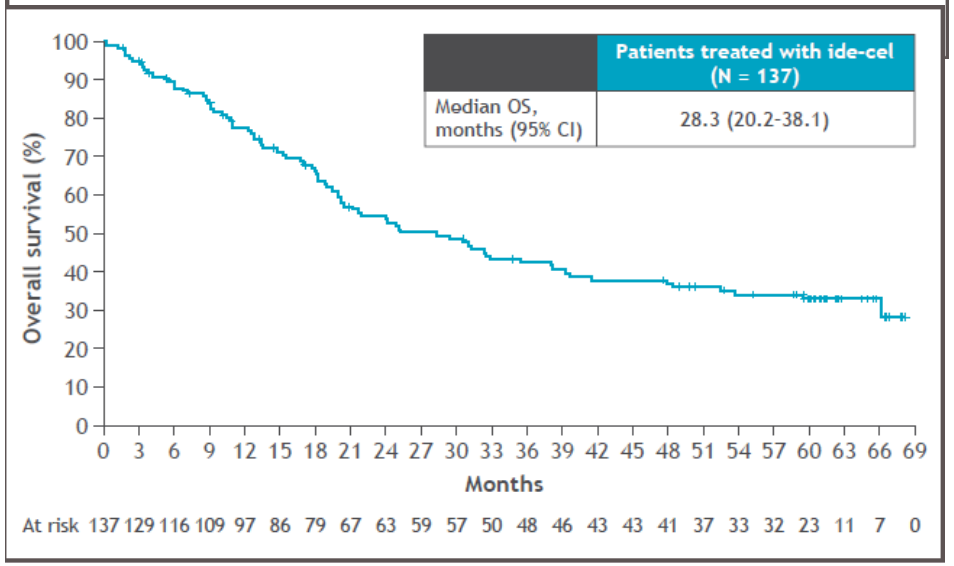
Ide-Cel: Long-Term Follow-Up of KarMMa Study

Median 6 prior lines, 84% triple-refractory







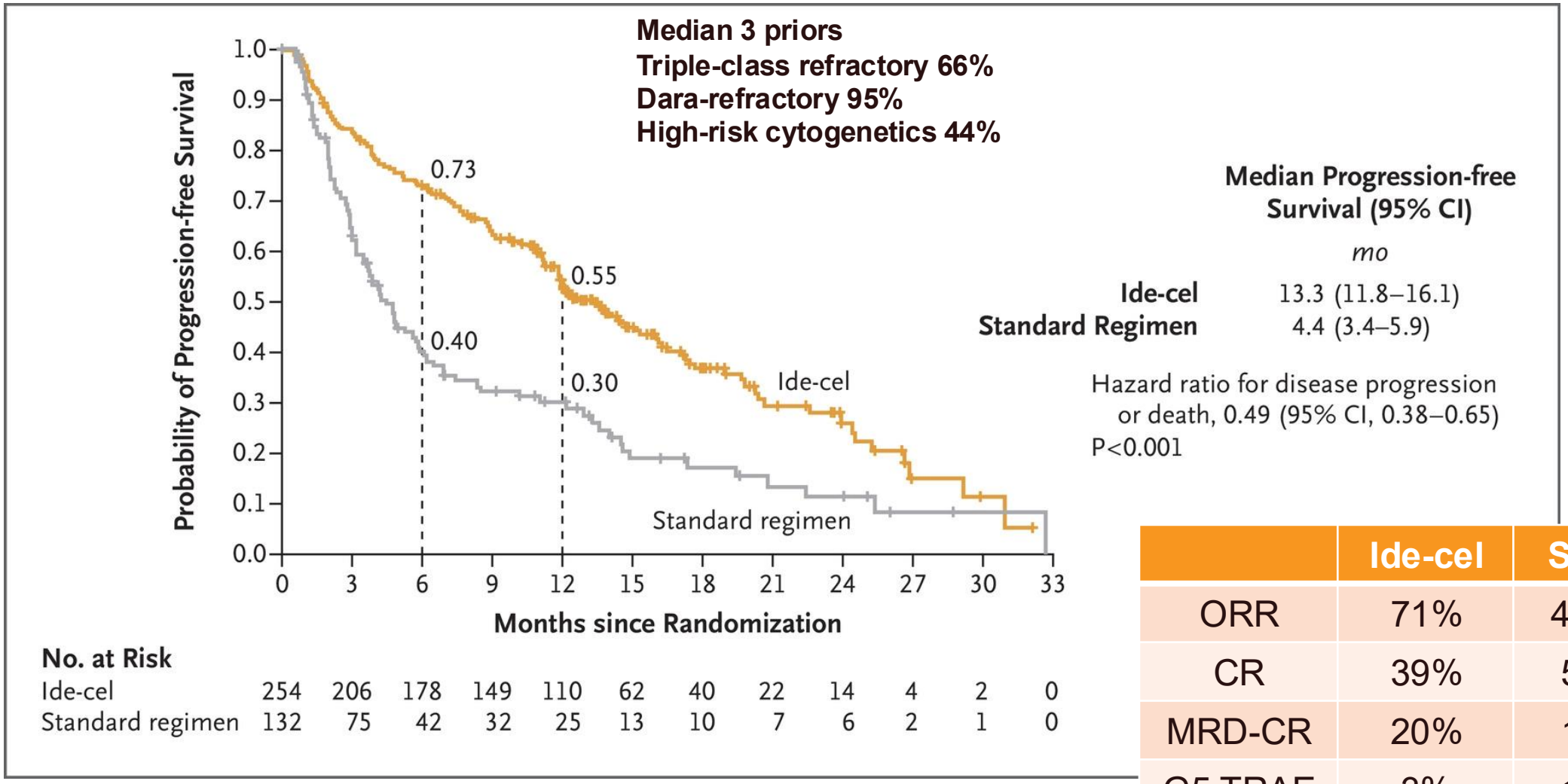


Med f/up = 63.6 mos.

CR = complete response; sCR = stringent complete response; MRD = minimal/measurable residual disease; VGPR = very good partial response; PR = partial response; ORR = objective response rate; CRR = complete response rate; PFS = progression-free survival; OS = overall survival; f/up = follow-up.

Munshi NC, et al. *N Engl J Med*. 2021;384(8):705-716. Anderson L, et al. Presented at: 21st International Myeloma Society (IMS) Annual Meeting; 2024.

KarMMa-3: Ide-cel vs SOC in MM Pts with 2-4 Prior Therapies



	Ide-cel	SOC
ORR	71%	42%
CR	39%	5%
MRD-CR	20%	1%
G5 TRAE	3%	1%

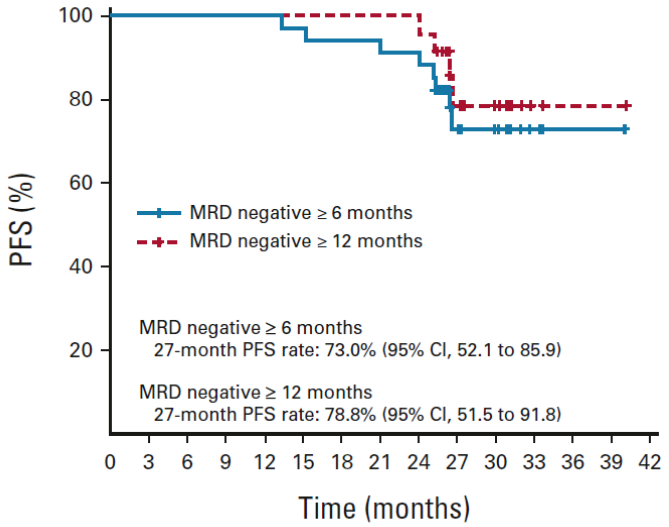
SOC = standard of care; TRAE = treatment-related adverse event.

Rodriguez-Otero P, et al. *N Engl J Med*. 2023;388(11):1002-1014.

Cilta-cel: Long-Term Follow-Up of CARTITUDE-1 Study

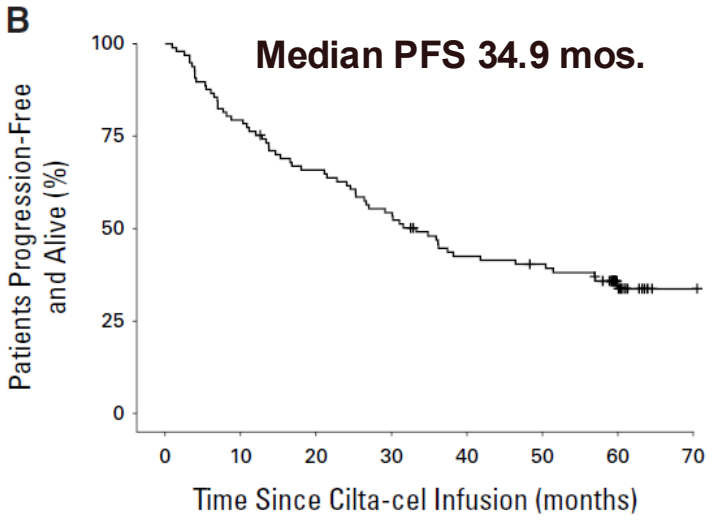
Median 6 prior lines, 88% triple-refractory

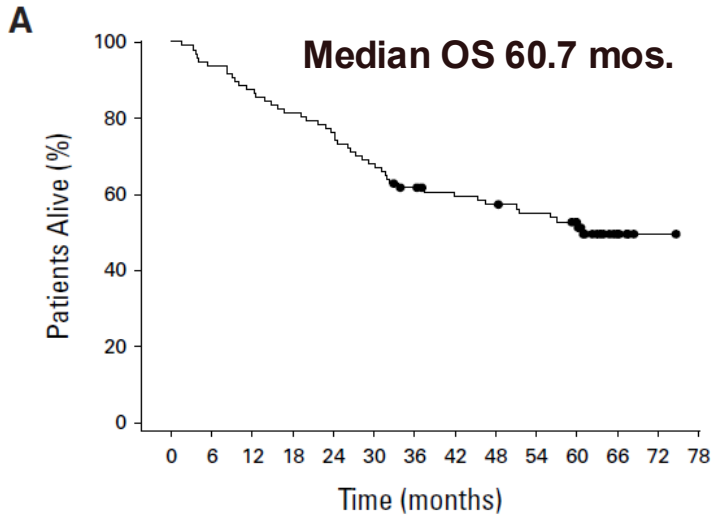
- ORR = 98%
  - CR/sCR = 83%
  - MRD-neg = 92%
    - (n=61 evaluable at 10^{-5})

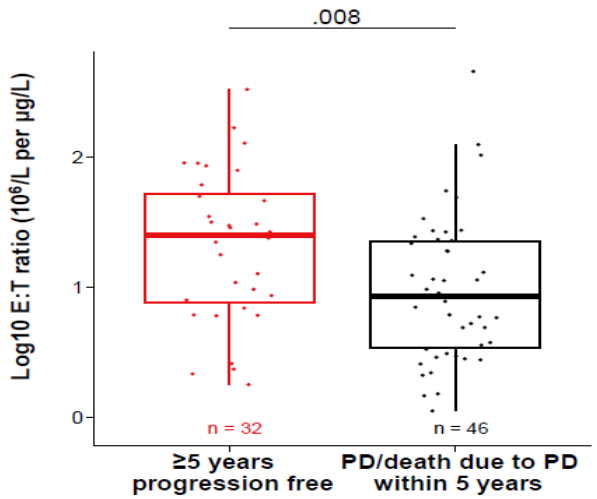


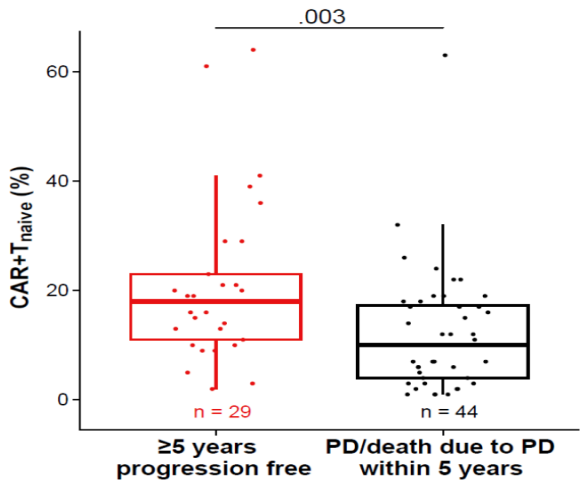
No. at risk:

MRD negative ≥ 6 months	34	34	34	34	34	33	32	32	31	13	10	3	1	1	0
MRD negative ≥ 12 months	24	24	24	24	24	24	24	24	24	11	8	2	1	1	0





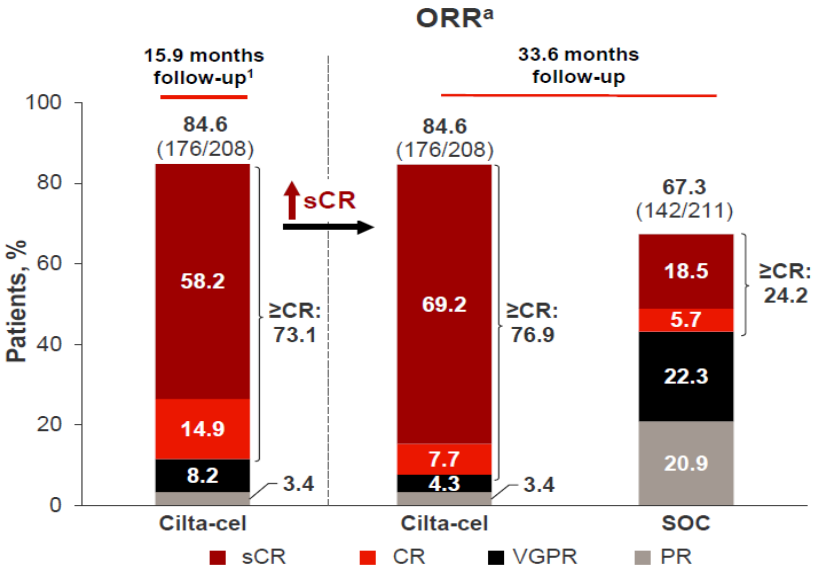


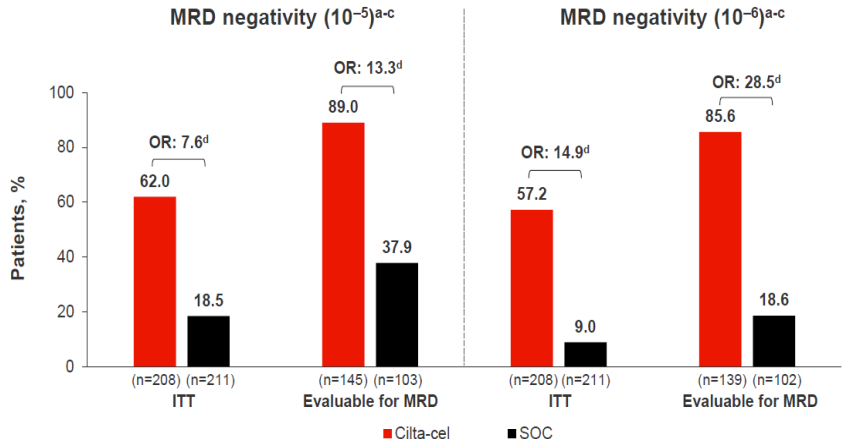


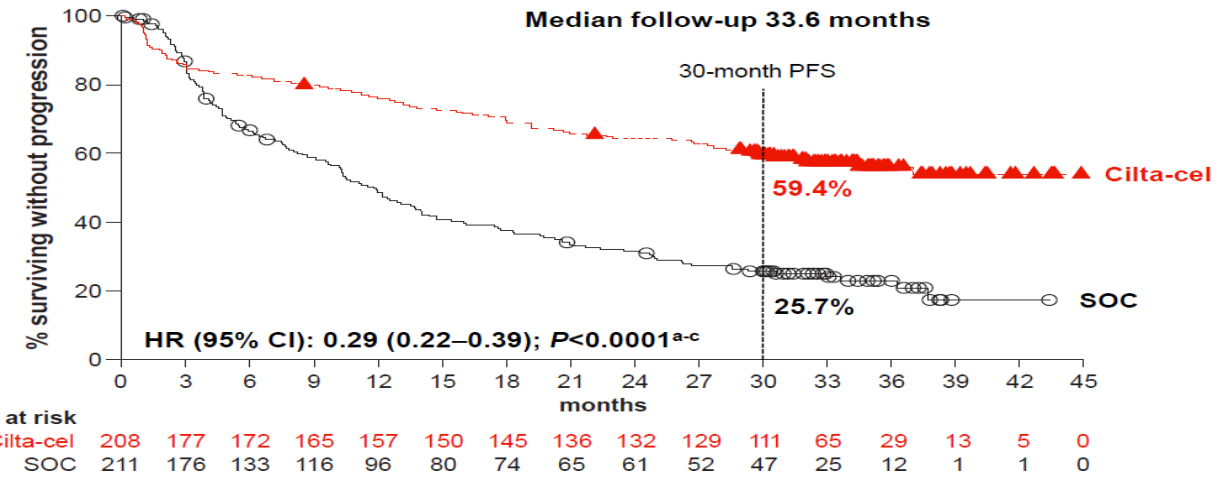
PD = progressive disease; E:T = effector-to-target.

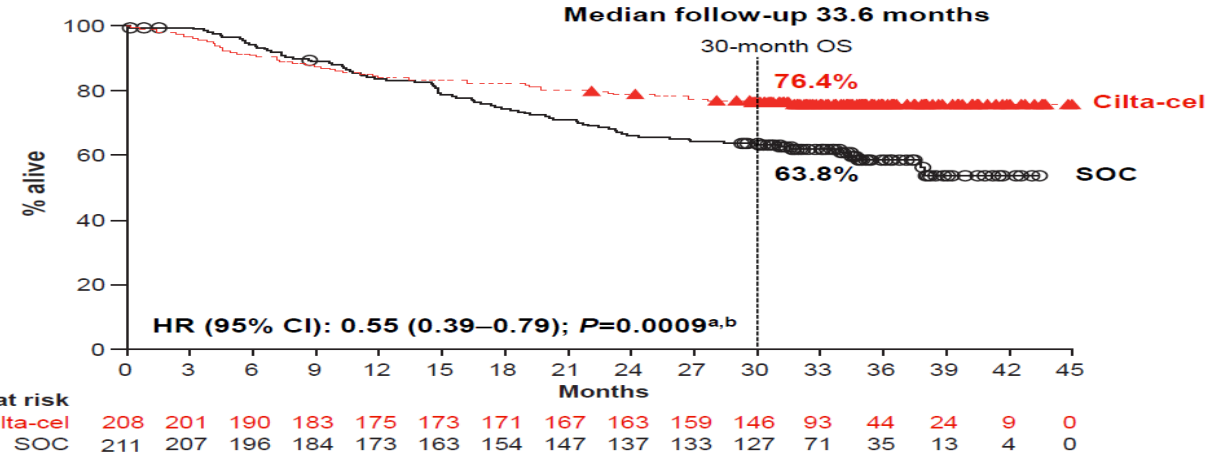
Martin T, et al. *J Clin Oncol*. 2023;41(6):1265-1274.
Jagannath S, et al. *J Clin Oncol*. 2025;43(25):2766-2771.

CARTITUDE-4: Cilta-Cel vs DPd or VPd in 1-3 Prior Lines









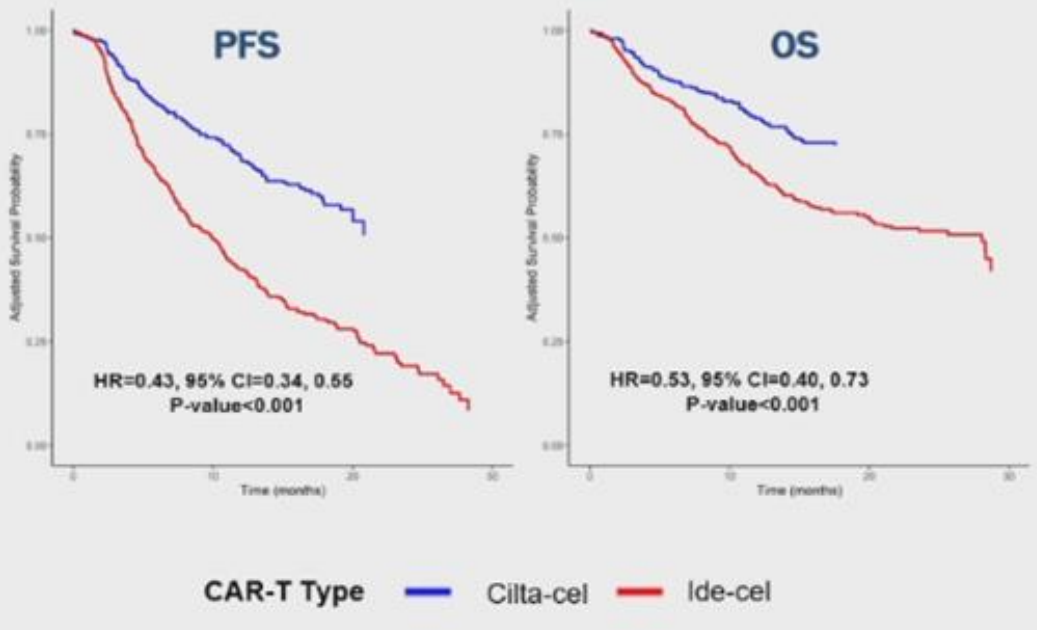
DPd = daratumumab, pomalidomide, dexamethasone; VPd = bortezomib, pomalidomide, dexamethasone; ITT = intent-to-treat.

Mateos MV, et al. Presented at: 21st IMS Annual Meeting; 2024.

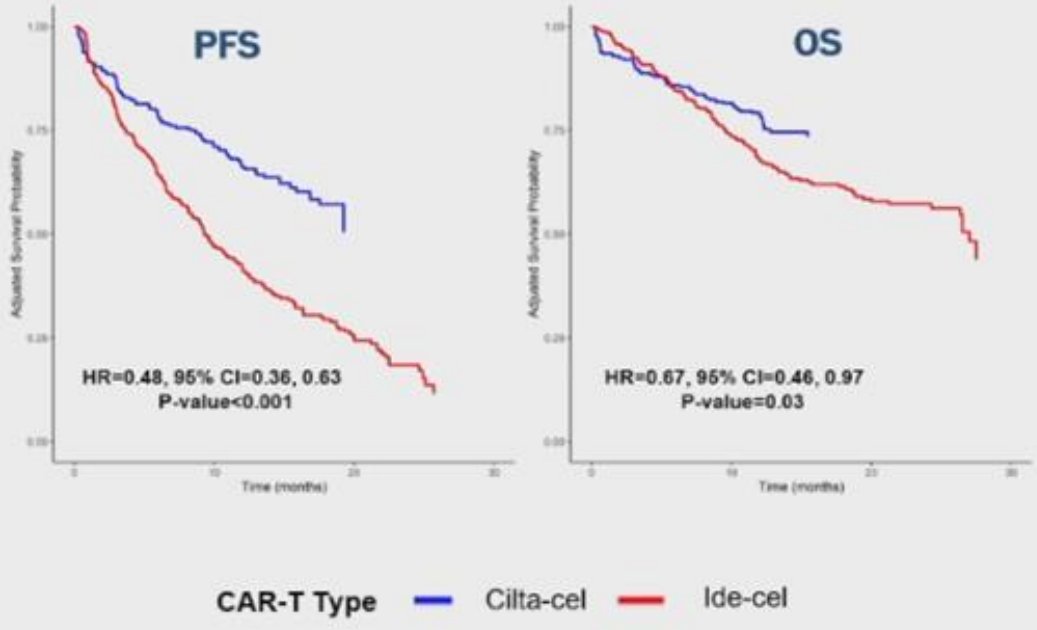
Ide-Cel vs Cilta-Cel Real-World Analysis

PFS and OS by Therapy Type

Intention to Treat Cohort (ITT) n=641



Infused Cohort n=586



Hansen DK, et al. Presented at: 66th American Society of Hematology (ASH) Annual Meeting & Exposition; 2024.

Ide-Cel vs Cilta-Cel Real-World Analysis

Safety and Response

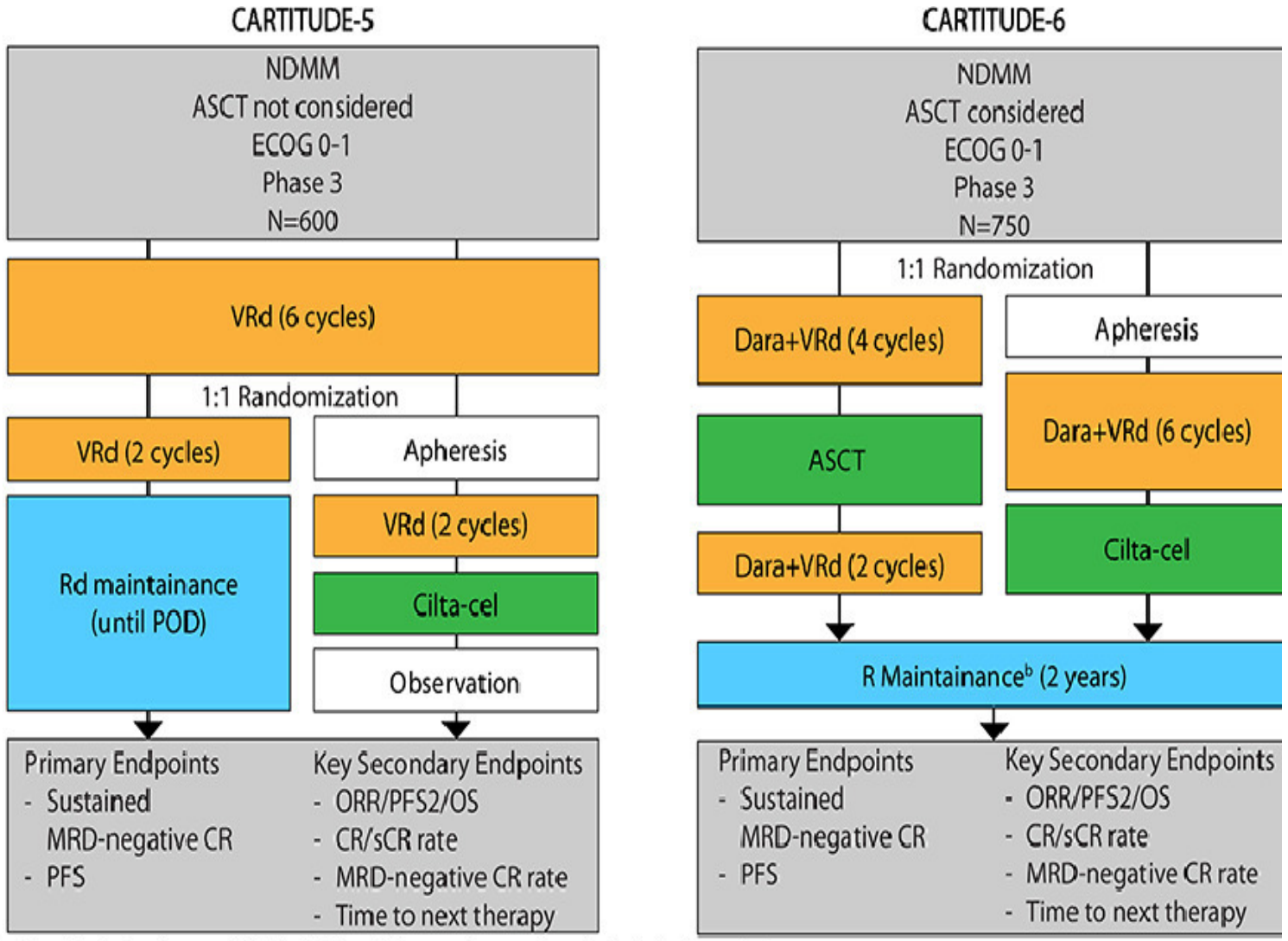
	Ide-cel		Cilta-cel		
Outcomes	n (%)	OR (95% CI)	n (%)	OR (95% CI)	P
Safety					
Any CRS	294 (84)	1.00 (Referent)	176 (75)	0.69 (0.45, 1.08)	0.10
Severe CRS (≥ Grade 3)	6 (2)	1.00 (Referent)	12 (5)	6.80 (2.28, 20.33)	<0.001
Any ICANS	72 (22)	1.00 (Referent)	30 (14)	0.82 (0.49, 1.37)	0.4
Severe ICANS (≥ Grade 3)	14 (4)	1.00 (Referent)	8 (4)	1.54 (0.53, 4.48)	0.4
Delayed neurotoxicity	2 (0.6)	1.00 (Referent)	24 (10)	20.07 (4.46, 90.20)	<0.001
Infections	122 (35)	1.00 (Referent)	112 (47)	2.03 (1.41, 2.92)	<0.001
Second Malignancies (SPM)	18 (5)	1.00 (Referent)	20 (9)	1.77 (0.89, 3.56)	0.11
SPM: MDS, AML, lymphoma	6 (2)	1.00 (Referent)	4 (2)	0.94 (0.26, 3.47)	>0.9
Severe cytopenia, day 30	199 (58)	1.00 (Referent)	111 (50)	0.97 (0.68, 1.39)	0.9
Severe cytopenia, day 90	92 (31)	1.00 (Referent)	41 (25)	0.92 (0.61, 1.38)	0.7
Response					
Best ORR (≥ PR)	275 (79)	1.00 (Referent)	205 (89)	1.60 (0.90, 2.83)	0.11
Best CR or better	165 (47)	1.00 (Referent)	161 (70)	2.42 (1.63, 3.60)	<0.001

Models were fitted using IPTW weights

CRS = cytokine release syndrome; ICANS = immune effector cell-associated neurotoxicity syndrome; SPM = second primary malignancy; MDS = myelodysplastic syndrome; AML = acute myeloid leukemia; IPTW = inverse probability of treatment weighting.

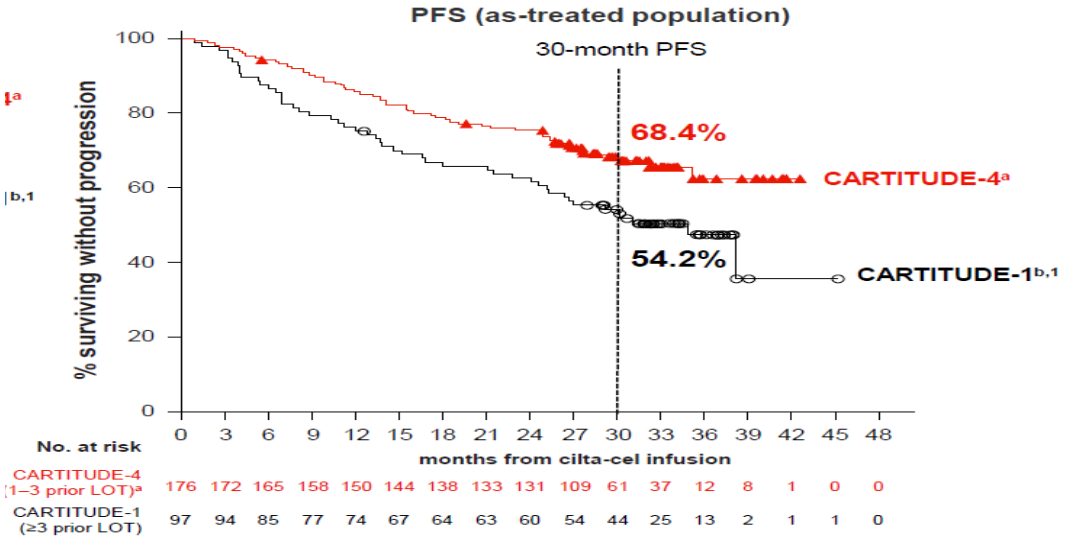
Hansen DK, et al. Presented at: 66th ASH Annual Meeting & Exposition; 2024.

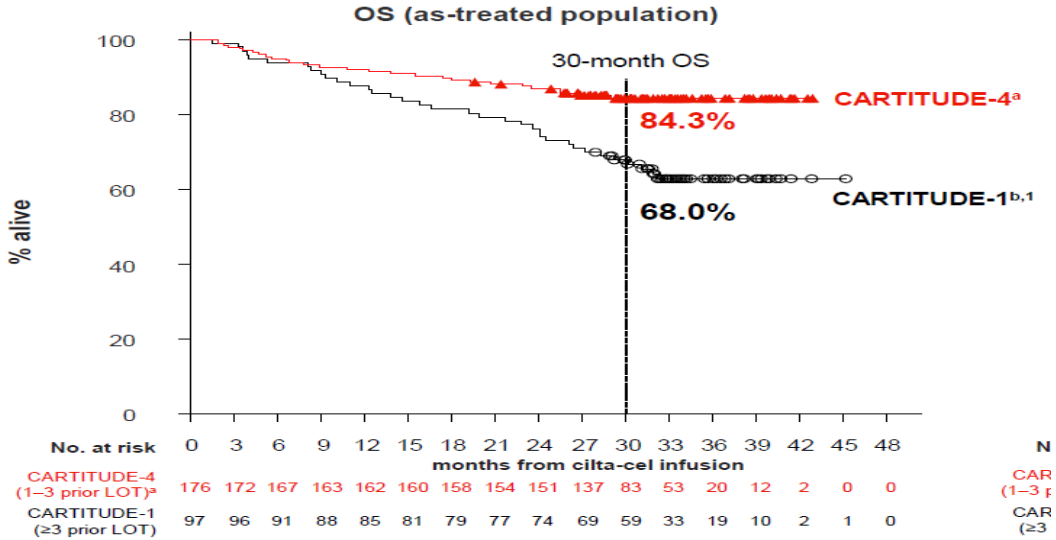
CAR T as Consolidation of Induction Therapy

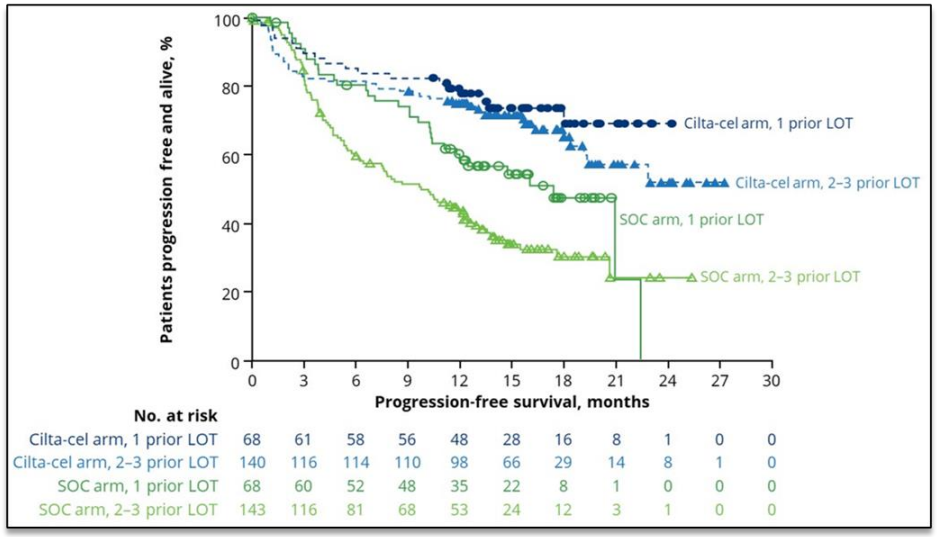


From Jurgens E, Usmani SZ. *Clin Lymphoma Myeloma Leuk*. 2024 ;24(5):277-284.

When to Use CAR T Cells for RRMM: Lessons from Cilta-Cel Studies





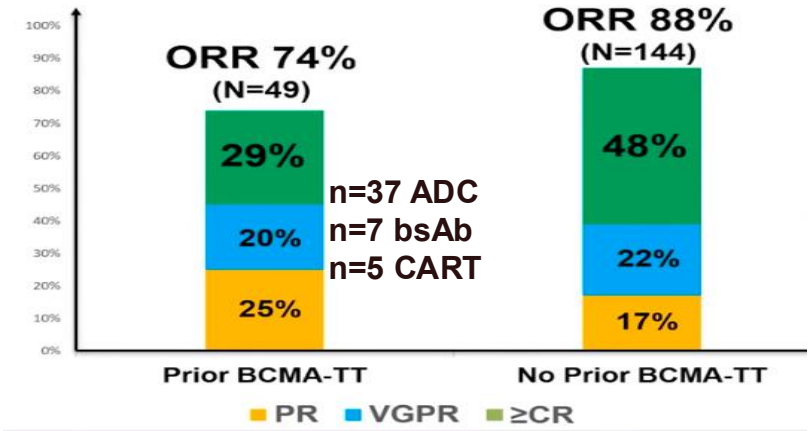


RRMM = relapsed/refractory multiple myeloma; LOT = line of therapy.

Mateos MV, et al. Presented at: 21st IMS Annual Meeting; 2024. Dhakal B, et al. *J Clin Oncol*. 2023;41(17 Suppl):LBA106.

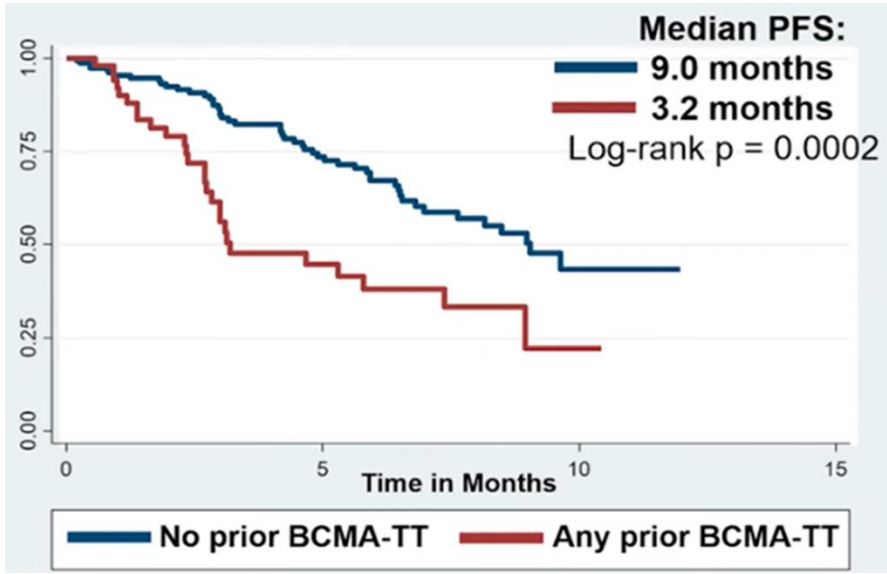
How to Use CAR T Cells for RRMM: Sequencing BCMA Therapies

Ide-cel



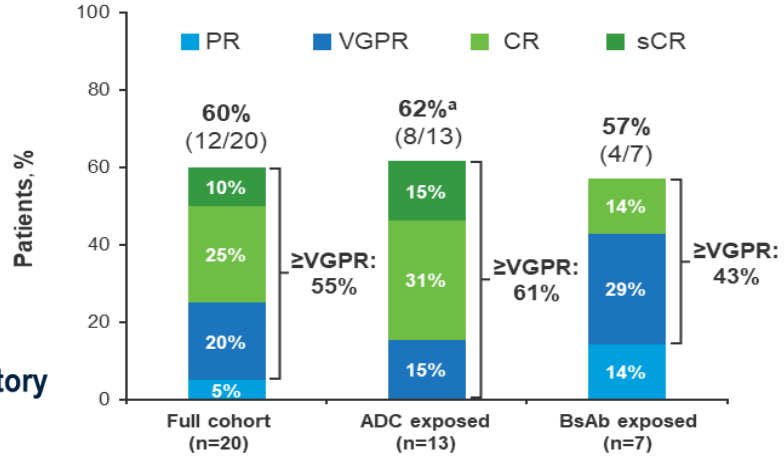
Med 9 priors
62% penta-ref

Med 6 priors
37% penta-ref



Cilta-cel

Median 8 priors
55% penta-refractory



Median DOR and PFS			
Estimate, months (95% CI)	Full cohort (N=20)	ADC exposed (N=13)	BsAb exposed (N=7)
DOR	12.3 (7.2–NE)	13.3 (7.2–NE)	8.2 (4.4–NE)
PFS	9.1 (1.5–13.2)	9.5 (1.0–15.2)	5.3 (0.6–NE)

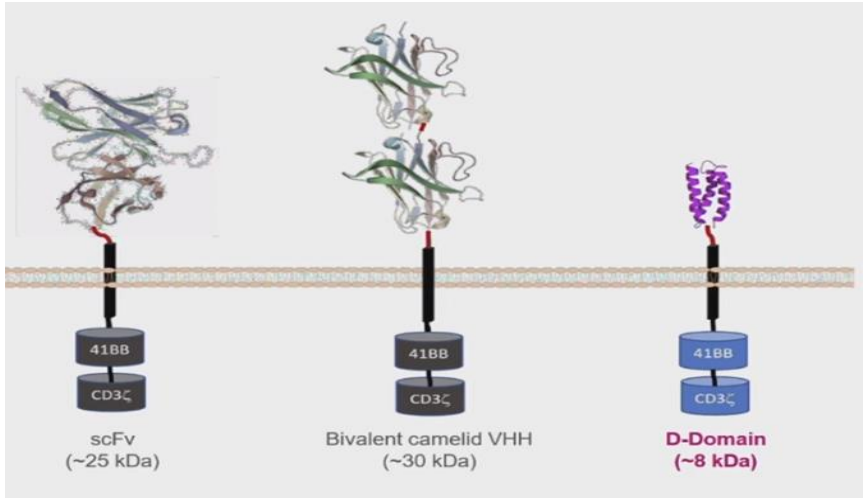
IMWG: if all else equal, give CART first
Costa et al, Leukemia 2025

TT = targeted therapy; ADC = antibody-drug conjugate; BsAb = bispecific antibody; DOR = duration of response; NE = not estimable.
Ferreri CJ, et al. *Blood*. 2022;140(Suppl 1):1856-1858. Cohen AD, et al. *Blood*. 2023;141(3):219-230. Costa LJ, et al. *Leukemia*. 2025;39(3):543-554.

Emerging CAR T Cell Therapies for RRMM

Anito-Cel (CART-ddBCMA) for Rel/Ref MM

Ide-cel **Cilta-cel** **Anito-cel**



Anito-cel phase 1 in RRMM

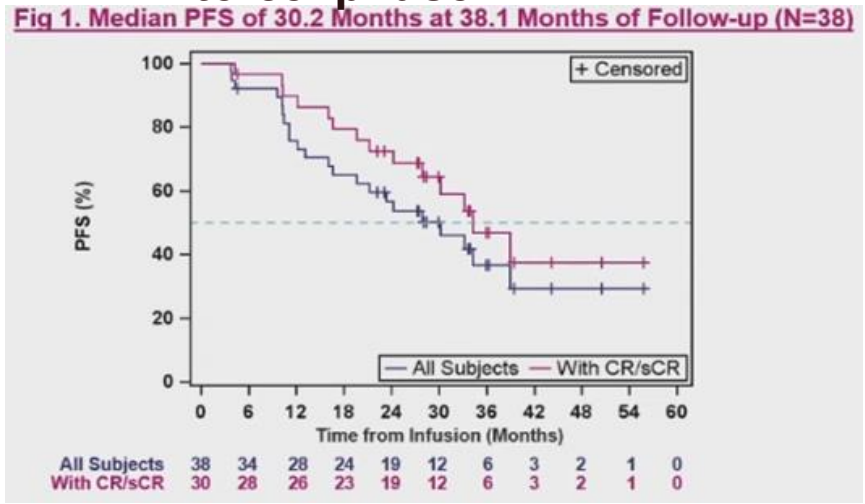
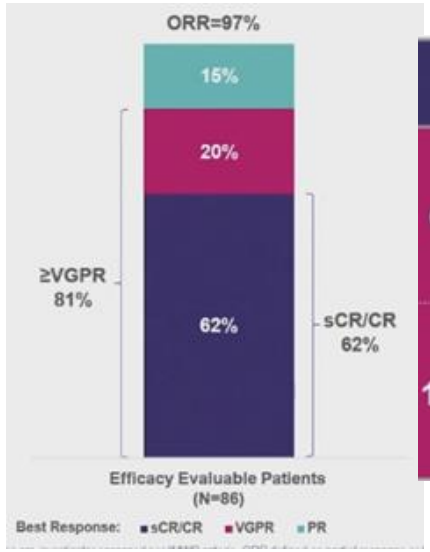


iMMagine-1 phase 2 registration study

Median 4 lines, 87% triple-class refractory, 0% BCMA tx

Median f/up = 9.5 months



	PFS Rate (%) (95% CI)	OS Rate (%) (95% CI)
6-Month	93.3% (84.4%, 97.2%)	96.5% (89.6%, 98.9%)
12-Month	78.5% (63.5%, 87.9%)	96.5% (89.6%, 98.9%)

No delayed neurotoxicity

CRS 83% (≥Gr3=1%)
ICANS 9% (≥Gr3=1%)
3 deaths
- HLH/hemorrhage, CRS, fungal infections

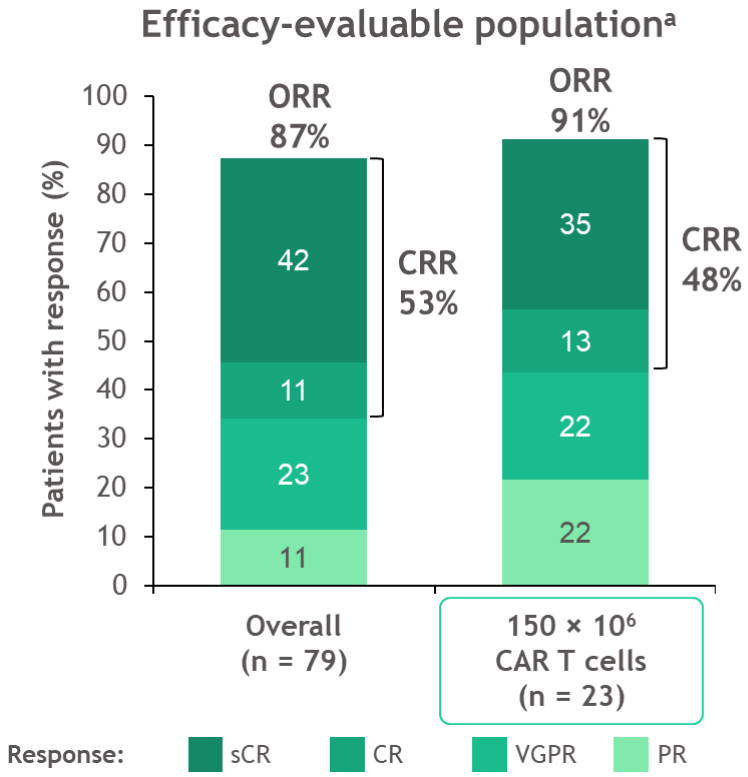
Phase 3 anito-cel vs SOC in 1-3 priors opened late 2024

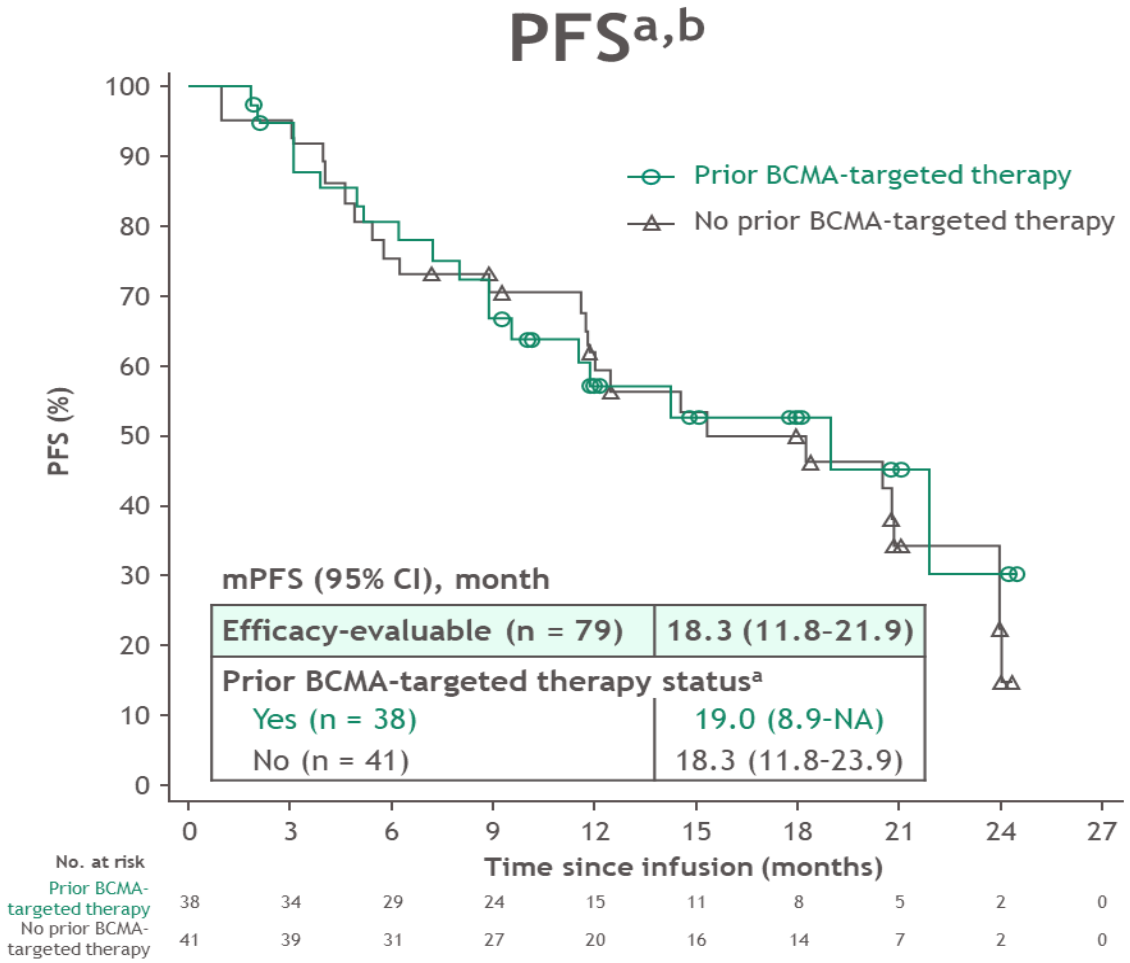
scFv = single-chain variable fragment; VHH = heavy-chain variable domain; HLH = hemophagocytic lymphohistiocytosis; dd = D-domain.

Bishop MR, et al. *Blood*. 2024;144(Suppl 1):4825. Freeman CL, et al. *Blood*. 2024;144(Suppl 1):1031.

Phase 1 of Arlocabtagene Autoleucel (Arlo-Cel, BMS-986393)

GPRCRD-targeted autologous CAR T cells
Median 5 lines, 76% triple-class refractory
49% prior BCMA tx





Bal S, et al. *Blood*. 2024;144(Suppl 1):922.

Phase 1 of Arlocabtagene Autoleucel (Arlo-Cel, BMS-986393)

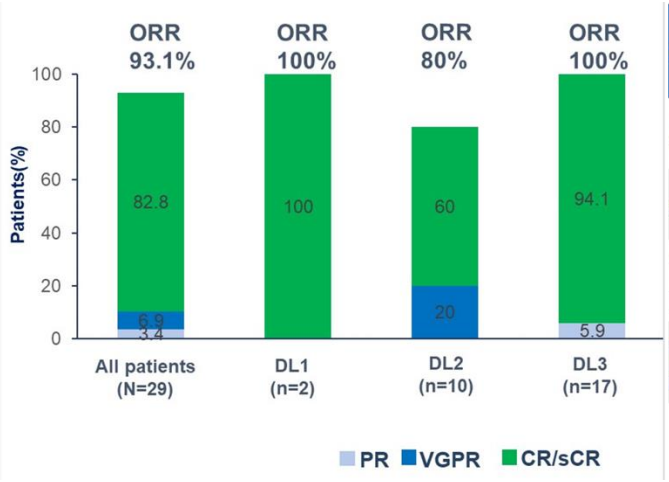
Select TRAEs	All treated patients (N = 84) Any grade	Grade 3/4
CRS, n (%)	69 (82)	3 (4)
ICANS, n (%)	8 (10)	2 (2)
Other select neurotoxicity,[a] n (%)	10 (12)	6 (7)
MAS/HLH, n (%)	0	3 (4)
On-target/off-tumor skin, nail, and/or oral event		
Skin		
Patients with an event, n (%)	25 (30)	0
Patients with resolved event(s), n (%)	22 (88)	
Median time to resolution[b]	26 days	
Nail		
Patients with an event, n (%)	16 (19)	0
Patients with resolved event(s), n (%)	12 (75)	
Median time to resolution[b]	98 days	
Oral, including dysgeusia and dysphagia		
Patients with an event, n (%)	27 (32)	0
Patients with resolved event(s), n (%)	19 (70)	
Median time to resolution[b]	66 days	

- CRS was predominantly grade 1 or 2
  - One patient had grade 5 CRS at the 450 × 10^6 DL
- Most patients with skin, nail, and/or oral on target off tumor toxicity did not require intervention (79%)
- Five patients experienced weight loss
- Other select neurotoxicity episodes occurred at the 150–450 × 10^6 DLs
  - Defined as dizziness, ataxia, neurotoxicity, dysarthria, and/or nystagmus
  - None were grade 4/5; median time to onset was 30.5 days
- No cases of parkinsonism, Guillain-Barré syndrome, or cranial nerve palsy

MAS = macrophage activation syndrome; DL = dose level.
Bal S, et al. *Blood*. 2024;144(Suppl 1):922.

Dual Antigen-Targeting CART Approaches

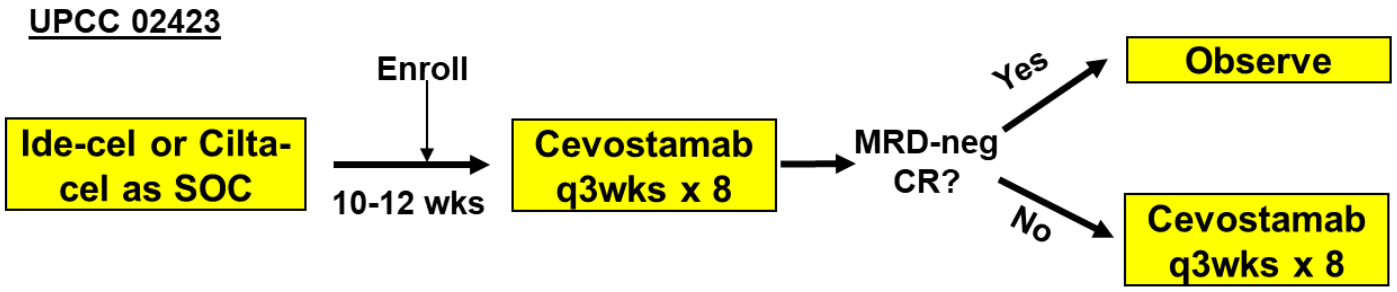
- Bispecific CARTs
  - CD19/BCMA (GC012F/AZD0120)
  - GPRC5D/BCMA
  - CD38/BCMA



Subgroup	n	PFS, Median (95% CI, mo)
All patients	29	38.0 (11.8, NE)
sCR	24	38.0 (13.7, NE)
12-month sustained MRD negativity	10	NE (38.0, NE)
12-month sustained MRD negative CR	10	NE (38.0, NE)

Du et al, J Clin Oncol 2023; 41:8005-8005

- CARTs + BsAbs
  - Talquetamab → BCMA CAR
  - Ide-cel → Talquetamab
  - Cilta-cel → Talquetamab
  - BCMA CAR → Cevostamab

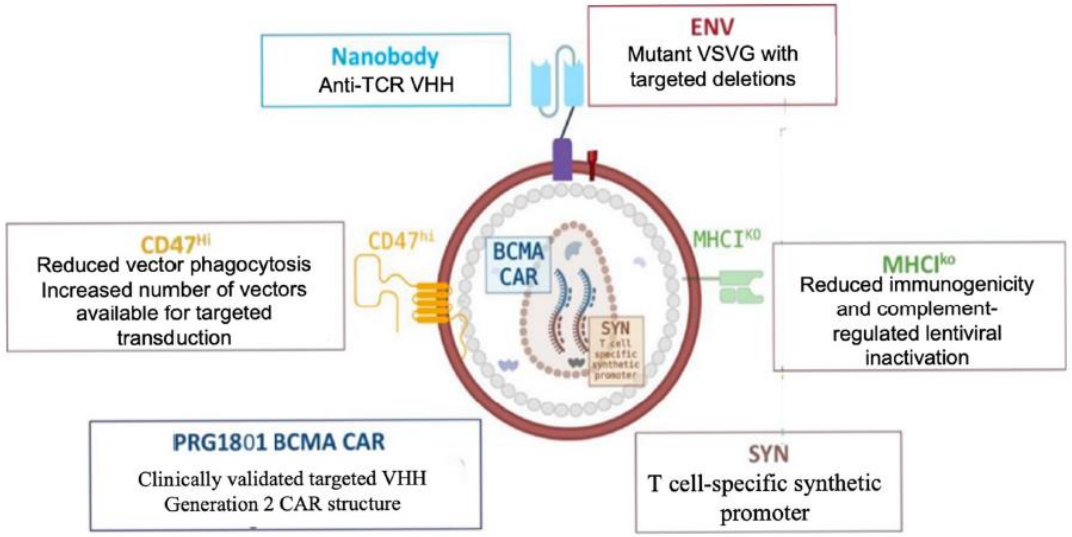


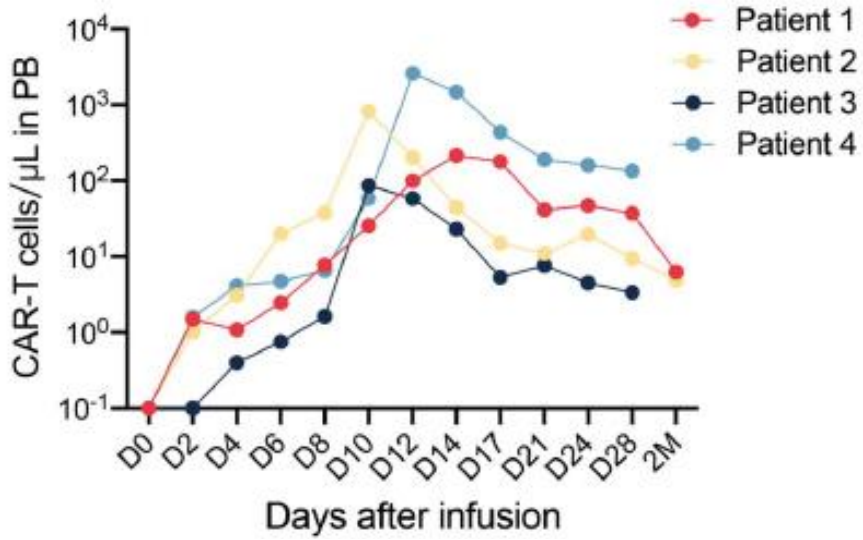
Cohen et al, Blood 2023;142(Suppl 1):3389

Du J, et al. *J Clin Oncol*. 2023;41(16 Suppl):8005. Cohen AD, et al. *Blood*. 2023;142(Suppl 1):3389.

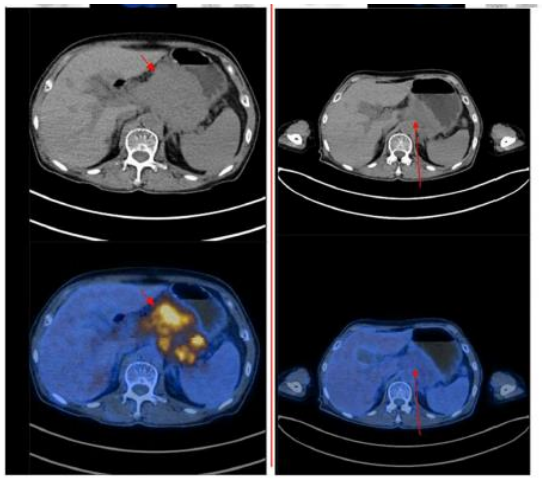
in vivo BCMA CAR T cells

ESO-T01: nanobody-targeted lentiviral vector

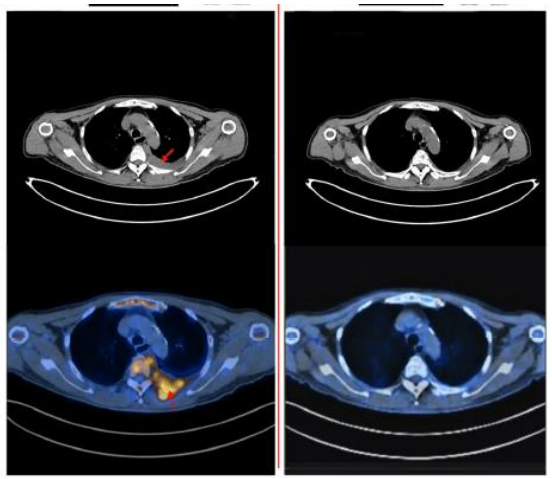




2 sCR, 2 PR



PET-CT of patient 3 at baseline and D28



PET-CT of patient 4 at baseline and D28

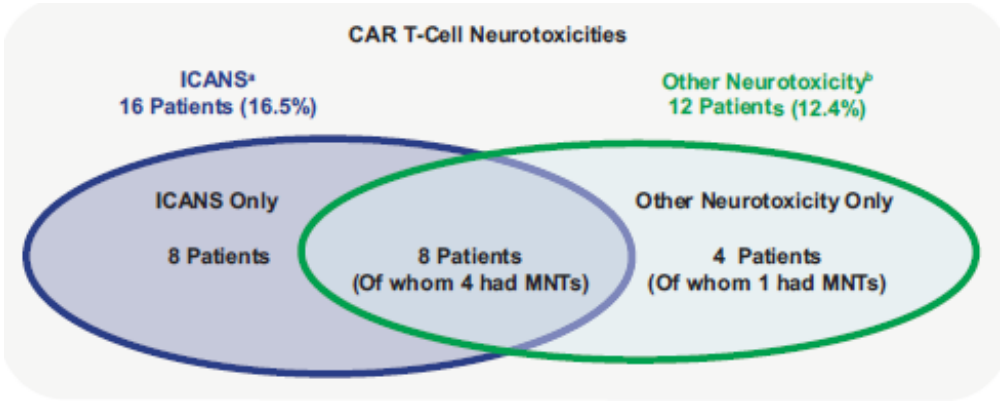
PET = positron emission tomography; CT = computed tomography.
Xu J, et al. *Lancet*. 2025;406(10500):228-231.

CAR T Cell Therapy-Associated Adverse Events

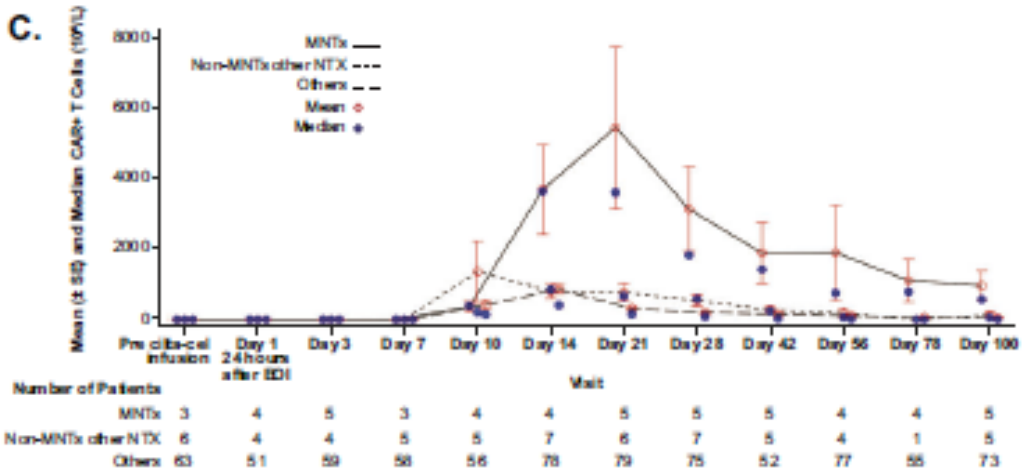
- CRS
- ICANS and other neurotoxicities
- HLH/MAS (IEC-HS)
- Cytopenias (ICAHT)
- Hypogammaglobulinemia and infections
- Second malignancies
- Enterocolitis

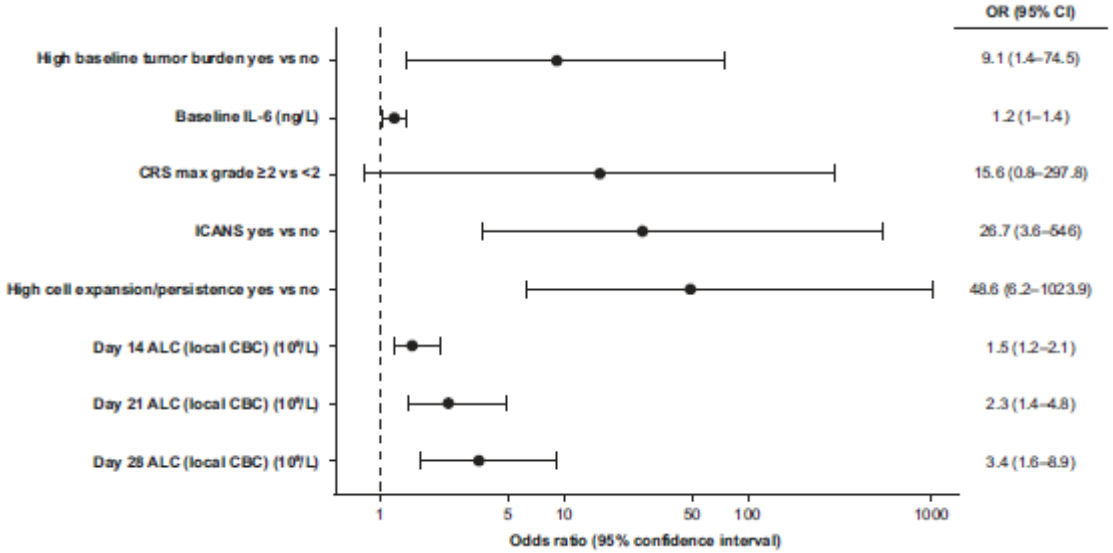
IEC-HS = immune effector cell-associated HLHs-like syndrome; ICAHT = immune effector cell-associated hematotoxicity.

Cilta-Cel: Delayed Neurotoxicity



MNTs (Parkinsonism) (n=5): median onset day 27 (14-108)





Mitigation strategies: minimize tumor burden pre-CART, aggressive tx of CRS/ICANS, aggressive monitoring

Optimal treatment of MNTs: unknown (steroids, IVIG, anakinra, IT chemo, cyclophosphamide, ruxolitinib)

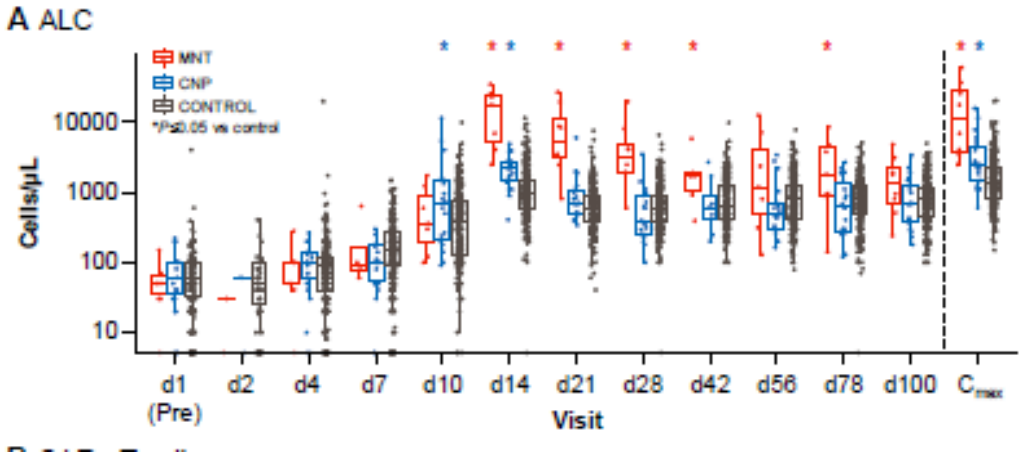
Update: 6th CARTITUDE-1 pt with MNT at day 914
Outcomes: n=3 deaths (1 from MNT, 2 infectious complications), n=1 recovered, n=2 stable/recovering (grade 1/2 symptoms)

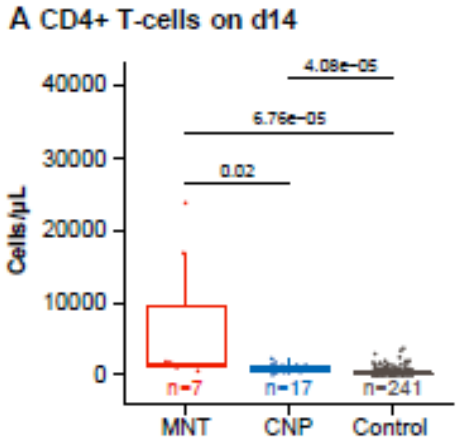
MNT incidence in subsequent cilta-cel studies: 0.66% (1/150)
MNT incidence in Chinese cilta-cel studies: 0% (0/122)
MNT incidence in real-world cilta-cel study: 2% (5/236)

MNT = movement and neurocognitive toxicity; IT = intrathecal; IVIG = intravenous immunoglobulin; NTX = neurotoxicity; ALC = absolute lymphocyte count; CBC = complete blood count.

Cohen AD, et al. *Blood Canc J*. 2022;12(2):32. Martin T, et al. *J Clin Oncol*. 2023;41(6):1265-1274. Zhao B, et al. *J Hematol Oncol*. 2022;15(1):153. Mi JQ, et al. *J Clin Oncol*. 2022;41(6):1275-1284. Sidana S, et al. Presented at: 21st IMS Annual Meeting; 2024.

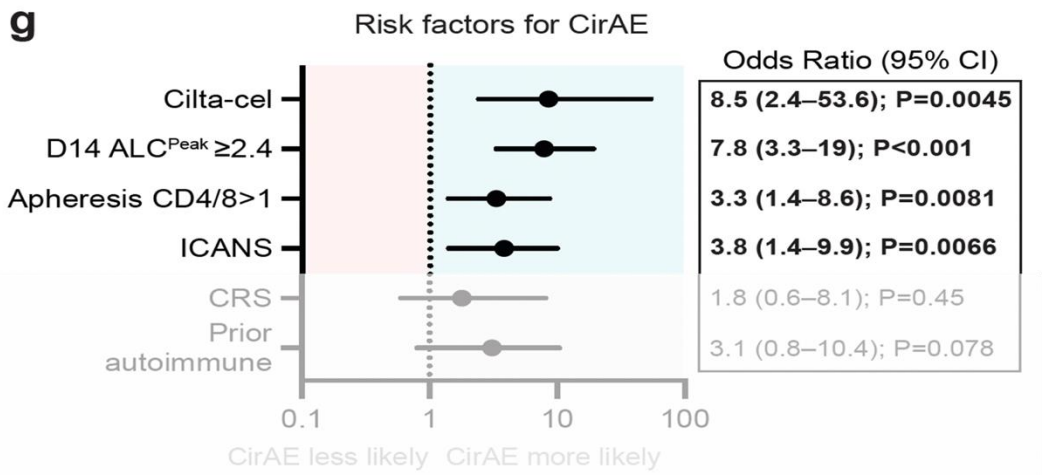
Delayed Neurotoxicity: High ALC and CD4 Skewing

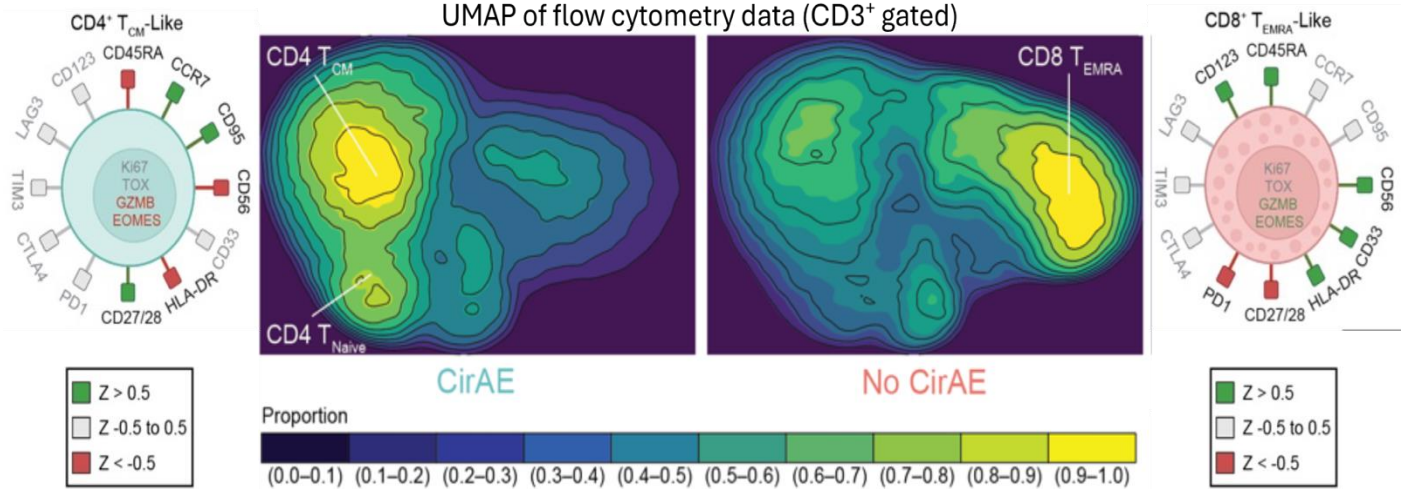




Can we intervene to prevent this?

- Lower tumor burden pre-CART
  - Better bridging
- Pre-emptive steroids?
  - Dex x 3 days for ALC >3.0?

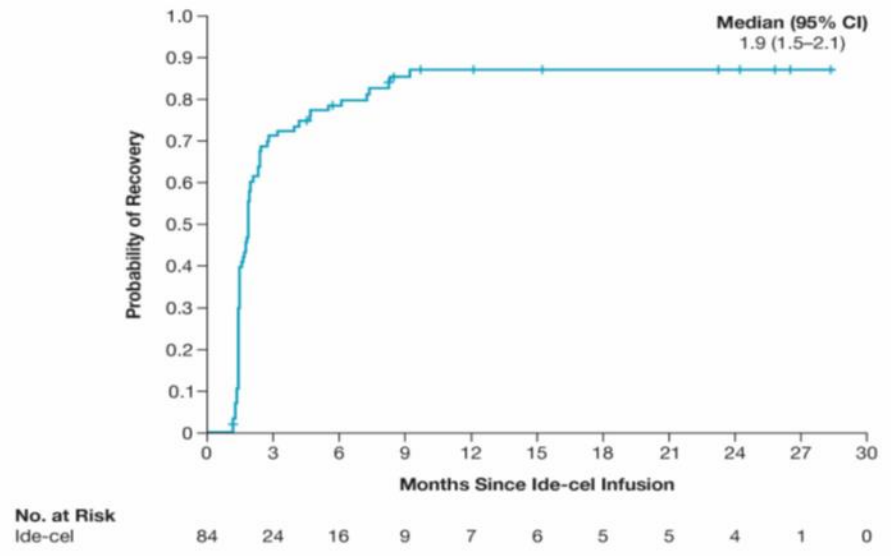


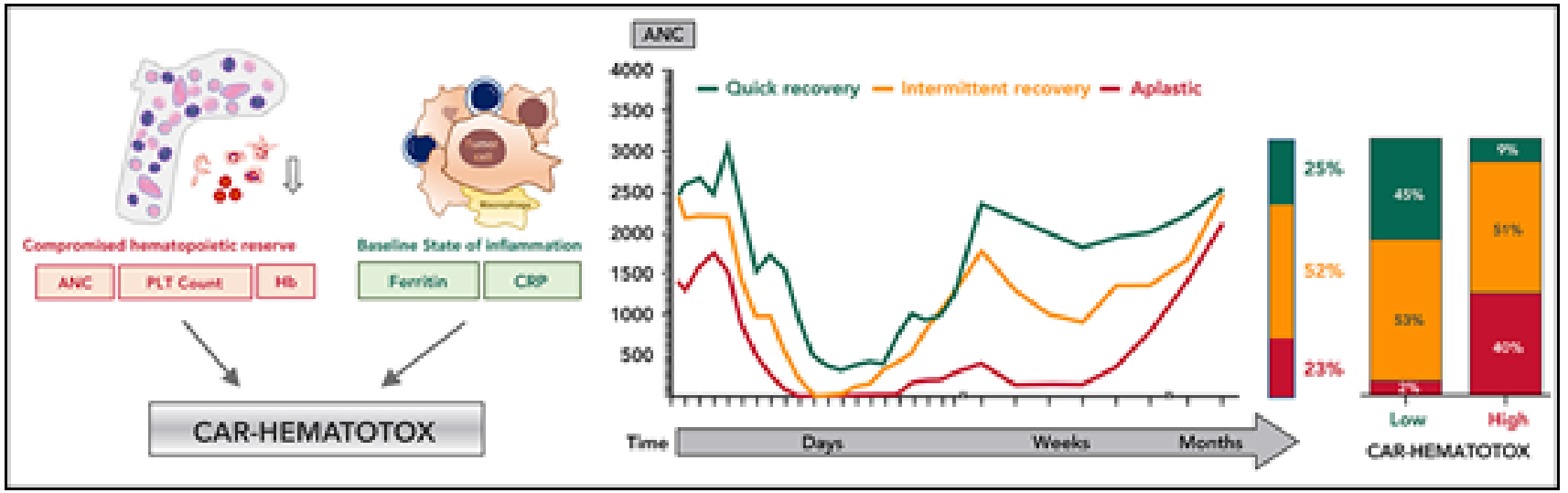


CNP = cranial nerve palsy; UMAP = uniform manifold approximation and projection; cirAE = cutaneous immune-related adverse event.
Lin Y, et al. Presented at: 22nd IMS Annual Meeting; 2025. Ho M, et al. Presented at: 22nd IMS Annual Meeting; 2025.

Late Toxicities

- Cytopenias (ICAHT)
  - 25-33% with gr 3/4 at 1 month
  - Growth factors, transfusions
    - Check for viruses (CMV, parvo)
    - Stem cell boost
  - CAR-HEMATOTOX score predictive





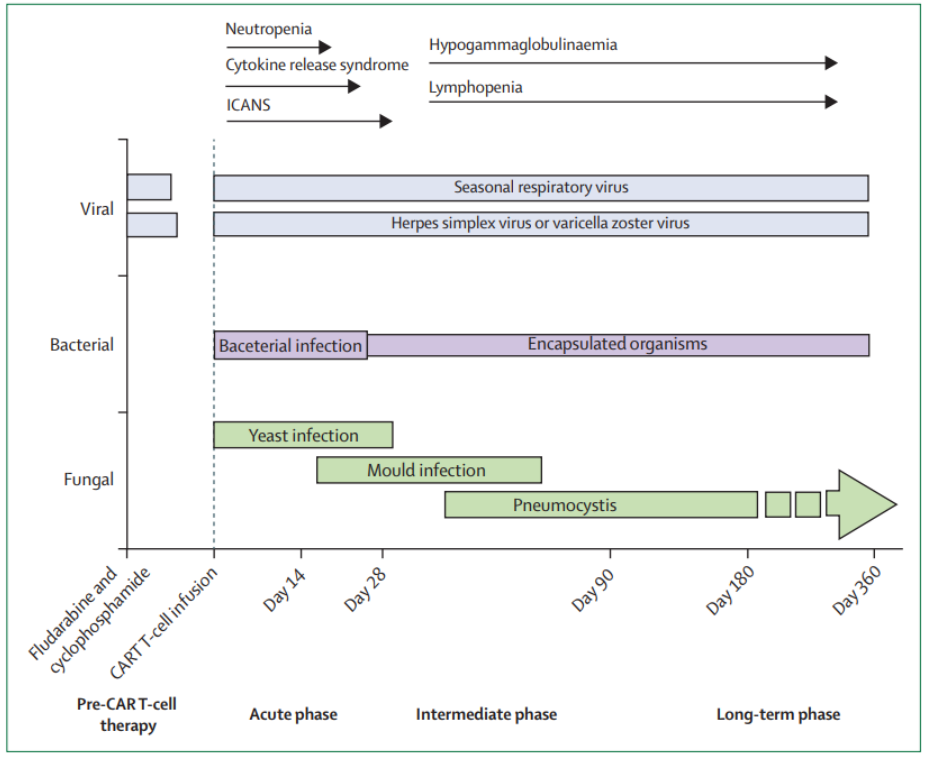
https://www.german-lymphoma-alliance.de/Scores.html

CMV = cytomegalovirus; ANC = absolute neutrophil count; Hb = hemoglobin.

Rodriguez-Otero P, et al. *N Engl J Med*. 2023;388(11):1002-1014. Rejeski K, et al. *Blood*. 2021;138(24):2499-2513. German Lymphoma Alliance [www.german-lymphoma-alliance.de]. https://www.german-lymphoma-alliance.de/Scores.html.

Late Toxicities

- Hypogammaglobulinemia and infections



	EBMT[75] recommendation	IMWG recommendation	Comments
Antiviral prophylaxis	Valacyclovir 500 mg twice a day and acyclovir 800 mg twice a day from lymphodepletion for 1 year post-CAR T-cell therapy	Valacyclovir 500 mg twice a day and acyclovir 400–800 mg twice a day from lymphodepletion for 1 year post-CAR T-cell therapy	Late varicella zoster virus has been described
Antibacterial prophylaxis	Not recommended	Levofloxacin 500 mg daily (or equivalent)	To start at neutropenia (ANC <500 per uL) or during high steroid or multiple immunosuppressive medication use
Antifungal prophylaxis	Not recommended	Fluconazole 400 mg daily (or equivalent); prophylaxis against mould (eg, aspergillus) should be considered in high-risk situations	To start at neutropenia (ANC <500 per uL) or during high steroid or multiple immunosuppressive medication use
Anti-pneumocystis prophylaxis	Co-trimoxazole 480 mg daily or 960 mg three times a week pre-lymphodepletion for 1 year post-CAR T-cell therapy	Sulfamethoxazole 800 mg and trimethoprim 160 mg three times a week pre-lymphodepletion until 6 months post-CAR T-cell therapy; alternatives could be considered in settings of cytopenia, allergy, or regional drug access; alternatives include monthly pentamidine nebuliser or atovaquone (1·5 g daily)	Late infections occur and continue therapy until CD4+ count >200 cells per uL
Intravenous gamma globulin	Consider in adults who have had encapsulated organism infections	Consider IgG replacement if IgG <400 mg/dL with 400–500 mg/kg intravenous immunoglobulin every 4–6 weeks	No formal studies, consider replacement if recurrent infections and IgG is 400–600 mg/dL*
G-CSF use	Consider G-CSF to shorten duration of neutropenia from 14 days after CAR T-cell infusion	Should be used to maintain ANC >1000 per uL in the first 3 months after CAR T-cell infusion	Avoid during cytokine release syndrome or ICANS, or if presenting with macrophage activation syndrome-like symptoms

ANC=absolute neutrophil count. EBMT=European Society for Blood and Marrow Transplantation. G-CSF=granulocyte-colony stimulating factor. ICANS=immune effector cell-associated neurotoxicity syndrome. IMWG=International Myeloma Working Group. *Correct IgG level for IgG paraprotein—eg, if a residual M-spike of 0·4 g/dL IgG-kappa exists and the total IgG level is 700 mg/dL, then the correct IgG would be estimated around 300 mg/dL.

Table 1: **Antimicrobial prophylaxis**

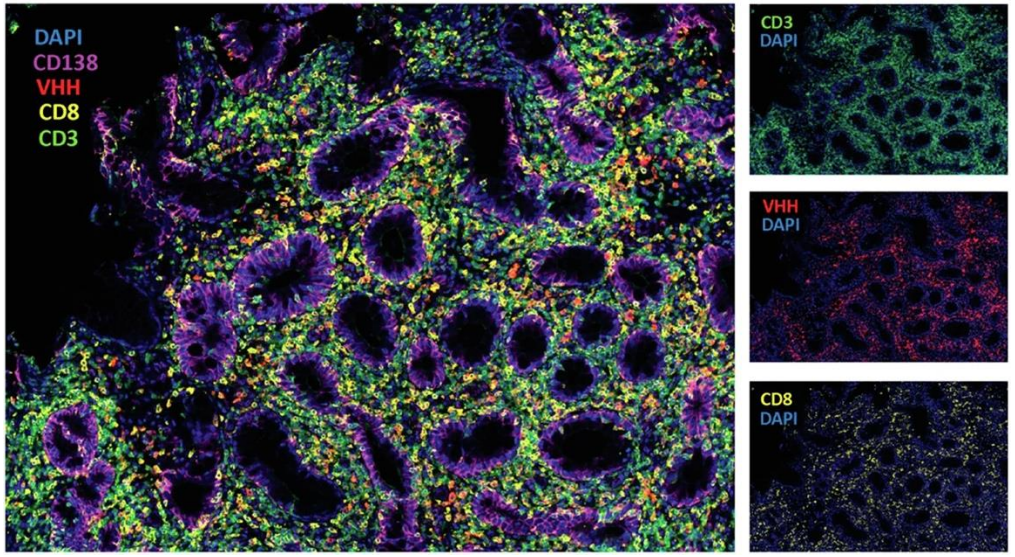
Lin Y, et al. *Lancet Oncol*. 2024;25(8):e374-e387.

Late Toxicities

- Second primary malignancies
  - MDS/AML
  - Lymphomas

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)

- Enterocolitis
  - Rare, case reports, small series
  - Incidence ~1-3%
  - Median onset—day 92



EBV = Epstein-Barr virus.
Mateos MV, et al. Presented at: 21st IMS Annual Meeting; 2024. Fortuna GG, et al. *Blood Cancer J. 2024*;14(1):180.

Key Learning Points

- Refractoriness to both an immunomodulatory agent and a proteasome inhibitor are critical factors to consider when initially evaluating a patient's eligibility for BCMA-directed CAR T-cell therapy in R/R MM
- A subset of late-line relapsed/refractory patients have durable remissions >5 years after current BCMA CAR T cell therapies
  - Need to better understand predictors of durable response
- Emerging guidance for managing aggressive R/R MM while awaiting CAR T-cell infusion calls for individualized bridging based on disease tempo and prior therapies
- Earlier use (1st or 2nd relapse) likely will improve proportion of durable remissions
  - Optimal timing remains unknown
  - Frontline use under investigation
- Late toxicities (delayed neurotox, enterocolitis, infections, second malignancies) remain an issue
  - Peak ALC may be predictor of delayed neurotox, GI tox → role for early steroid interventions?
  - What level of delayed severe toxicity and/or non-relapse mortality are we willing to accept?
- Many novel CAR T cell approaches in development
  - BCMA- and non-BCMA-targeted

GI = gastrointestinal.

Penn Myeloma Program

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NIH P01 CA214278-01

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Identifying and Addressing Barriers to T Cell Therapy

Joshua Richter, MD, FACP

Associate Professor of Medicine
Tisch Cancer Institute
Icahn School of Medicine at Mount Sinai
Director of Myeloma
The Blavatnik Family
Chelsea Medical Center at Mount Sinai
New York City, New York

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Agenda

- Identifying and addressing barriers to T Cell therapy
  - Interdisciplinary team approach
    - Earlier identification of patient candidates for CAR T cell therapy
    - Considerations for therapeutic bridging
    - Care coordination with CAR T cell therapy centers
  - Strategies for enhancing patient access to CAR T cell therapy
  - Patient education to optimize outcomes
  - Key learning points

Supportive Care Post-CAR T

- **Pancytopenia**
  - Could persist for months
  - Transfusions as needed
  - Hgb >7, plts >10 if asymptomatic
  - Filgrastim for ANC <1000
- **Hypogammaglobulinemia**
  - IVIG pre-lymphodepletion
  - Every month for 6 months and during winter months if recurrent infections, or continue beyond 6 months if severe hypogammaglobulinemia or HGG and infections
- **Infections (50-70%, 20-30% grade 3+)**
  - If neutropenic—then consider oral antibiotic prophylaxis and fungal prophylaxis
  - IV abx if febrile neutropenia
  - Acyclovir prophylaxis—400 mg BID for 1 year, then QD
  - Viral infections—CMV PCR monitoring weekly for 3 months, then monthly or at every visit
  - PJP prophylaxis for the first 6 months or for CD4 <200, whichever is later
  - Antifungal—consider mold active antifungals if h/o allo SCT, h/o invasive mold infection in the past, prolonged steroids or neutropenia
- **Vaccines schedule**—at 6 months post-CART
  - COVID vaccines start 3 months post-CART
- **Delayed toxicities** delayed neurotoxicities, MNTs, SPMs

Hgb = hemoglobin; plts = platelets; PCR = polymerase chain reaction; PJP = *Pneumocystis jiroveci* pneumonia; h/o = history of.

Engaging Patients in Shared Decision-Making

Steps

1. Invite patient to participate
2. Present options
3. Provide information on benefits and risks
4. Assist patient in evaluating options

Facilitate deliberation and decision-making

Assist with implementation

Topics to Discuss

- Medications
- Comorbidities
- Symptoms
- QoL
- Adherence to therapies

Shared decision-making has a substantial impact on the patient's psychological well-being, adherence, and confidence in the clinician.

QoL = quality of life.

Butterworth JE, Campbell JL. *Br J Gen Pract*. 2014;64:e709-e718. Center for Practice Innovations [www.practicinnovations.org]. Accessed May 12, 2025. https://practiceinnovations.org/resources/shared-decision-making.

Expanding Access to CAR T Cell Therapy

Challenges to Access: Logistics and Follow-Up

- CAR T in outpatient clinics can increase access to CAR T in the community setting

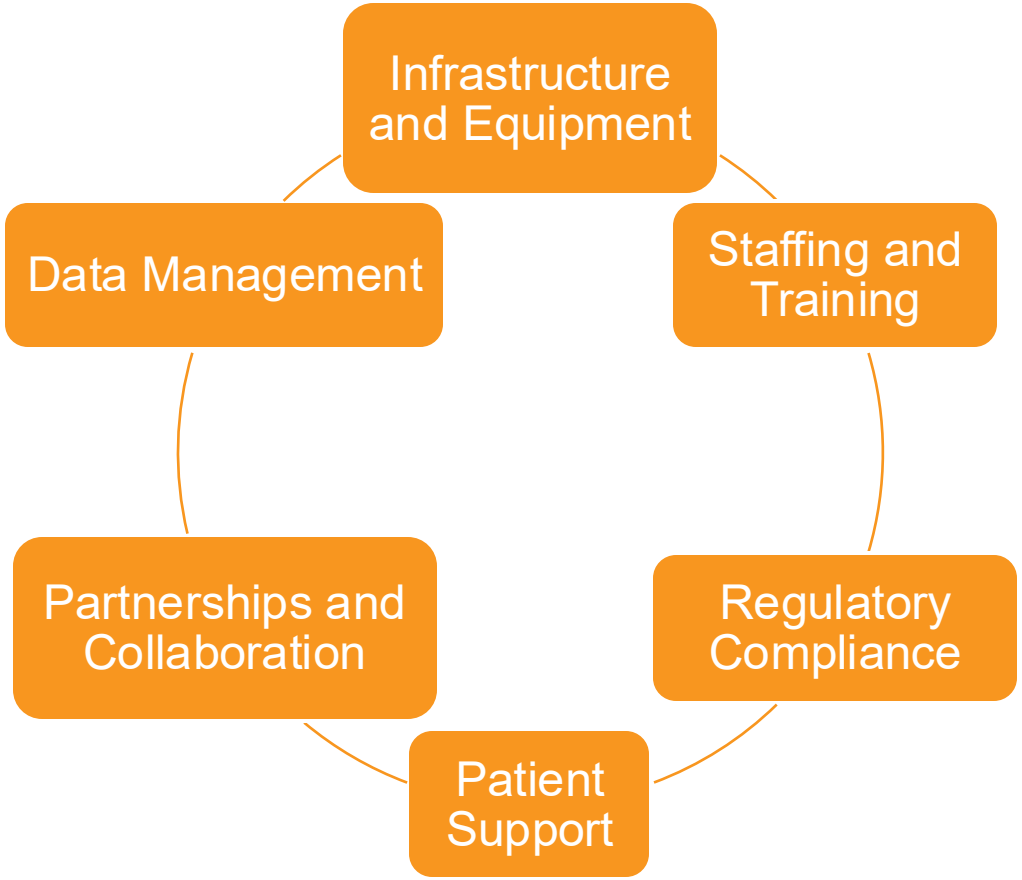
Management of Adverse Events

- Telemedicine/telemonitoring for follow-up
- Integration of EMR and engagement with emergency medicine

EMR = electronic medical record.

Perez A, et al. *Front Immunol*. 2024;15:1412002.

Expanding Access to MM Care in the Community



Perez A, et al. *Front Immunol*. 2024;15:1412002.

Timing Is a Key Determinant of Outcome

- **Factors influencing CAR T timing and outcomes**
  - **Disease biology** (aggressiveness, rate of progression)
  - **Refractoriness to lenalidomide and other agents**
  - **Depth and duration of prior responses**
  - **Overall patient fitness**
- **Advantages of earlier use**
  - Enables collection before frailty or organ dysfunction
  - Increases likelihood of successful apheresis
  - Minimizes risk of rapid progression during manufacturing

Time is T cell

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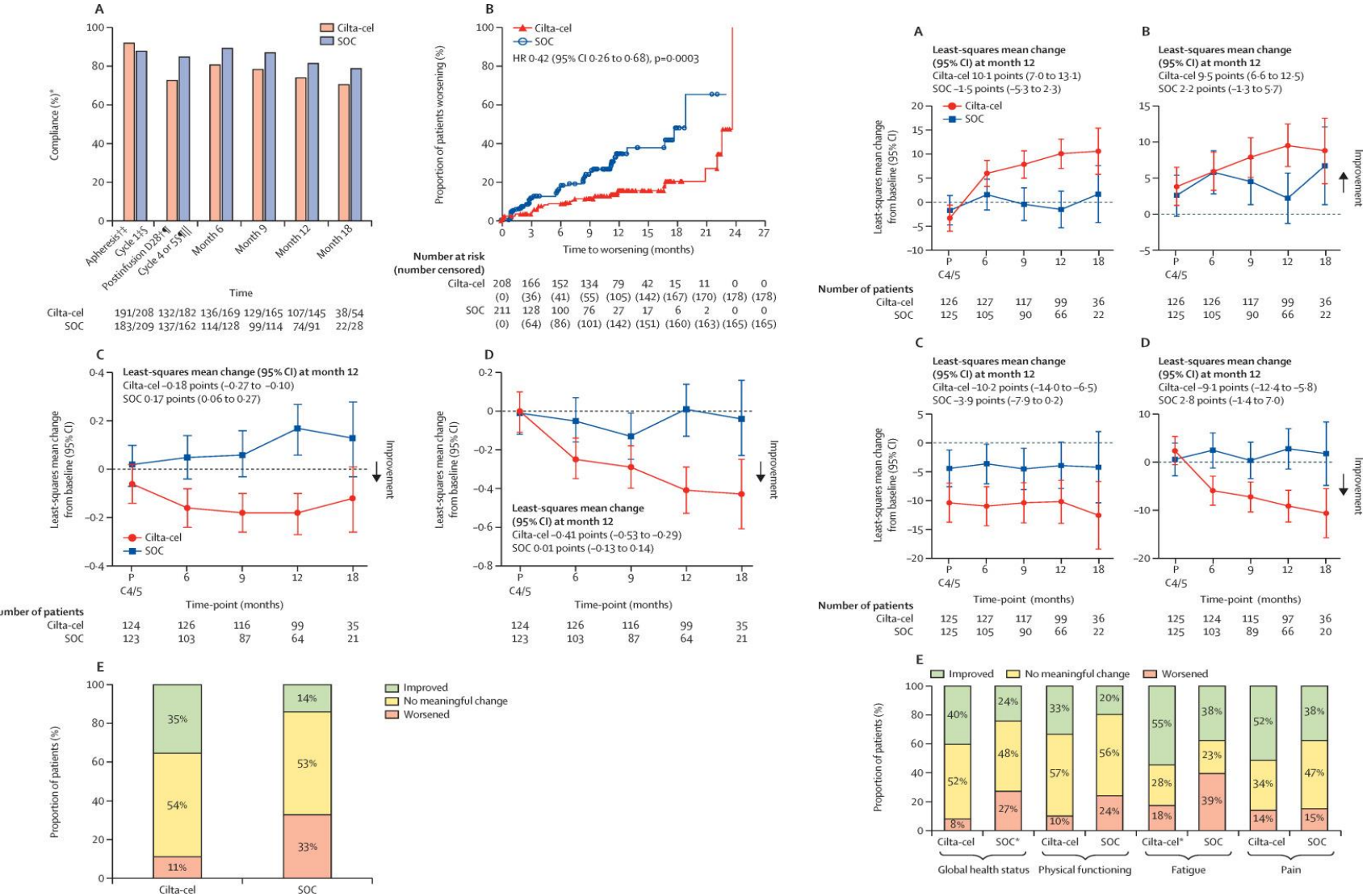
CAR T Improves Quality of QoL



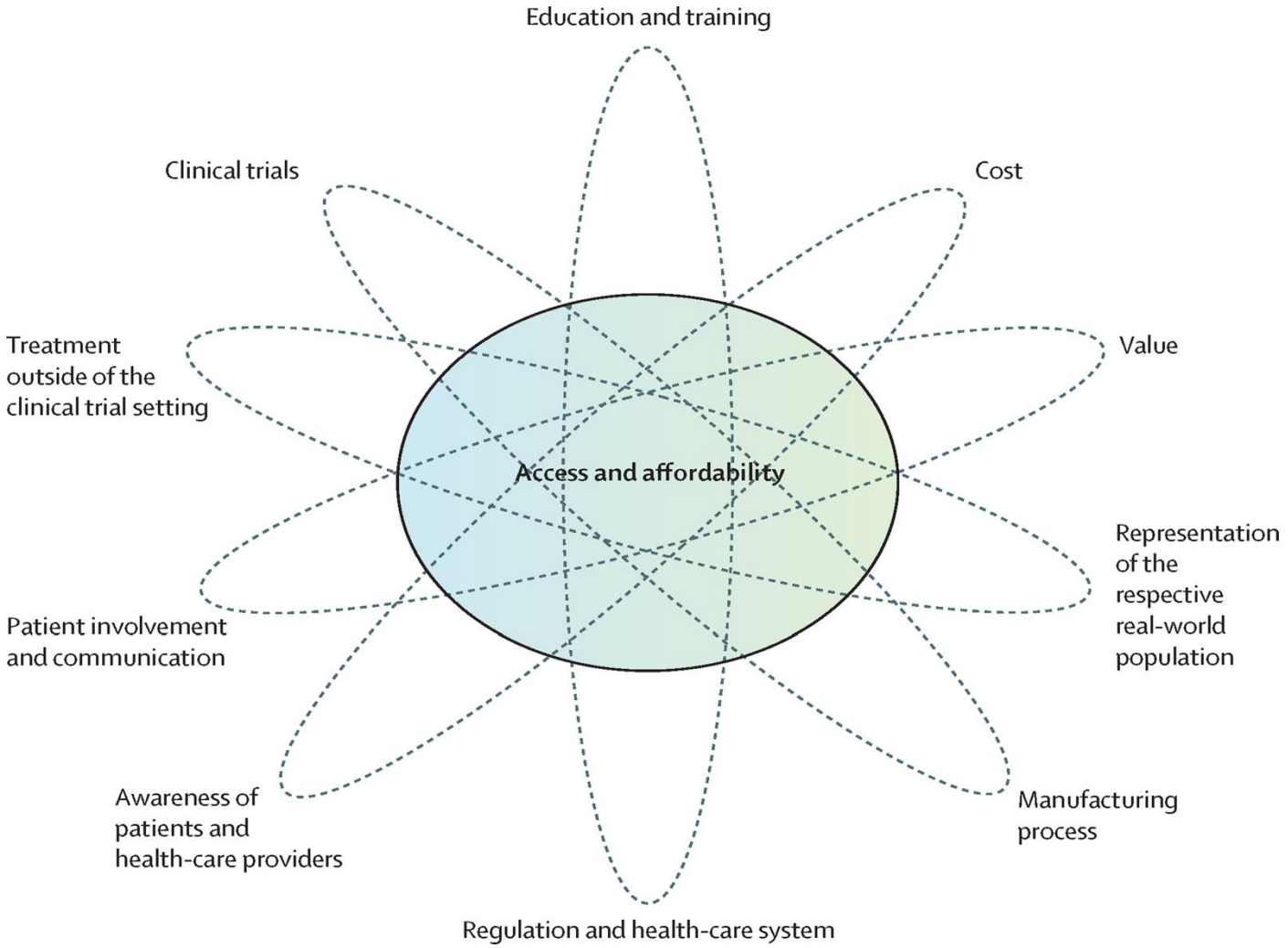
- CAR T therapies improved PROs and HRQoL vs SOC
- Cilta-cel showed numerically greater and more durable improvements in global health status and symptom control
- One-time CAR T infusion led to extended QoL benefit vs continuous SOC

PRO = patient-reported outcome; HRQoL = health-related quality of life;
Mina R, et al. *Lancet Haematol*. 2025;12(1):e45-e56.

The Promise of CAR T Therapy and Ground Reality—Access and Affordability Remain a Challenge

Central Issue:

⚠ **Access and affordability** sit at the intersection of clinical, regulatory, economic, and societal domains



Key interconnected factors:
Healthcare infrastructure: Regulation, education, provider/patient awareness
Systemic challenges: Cost, value, manufacturing complexity
Equity gaps: Clinical trial diversity, real-world representation
Patient-centered care: Involvement, communication, off-trial treatment access

Gagelmann N, et al. *Lancet*. 2022;9(10):E786-E795.

Patient Selection, Disease Control while Planning for CAR T Cell Therapy

Is this patient a candidate for CAR T cell therapy?

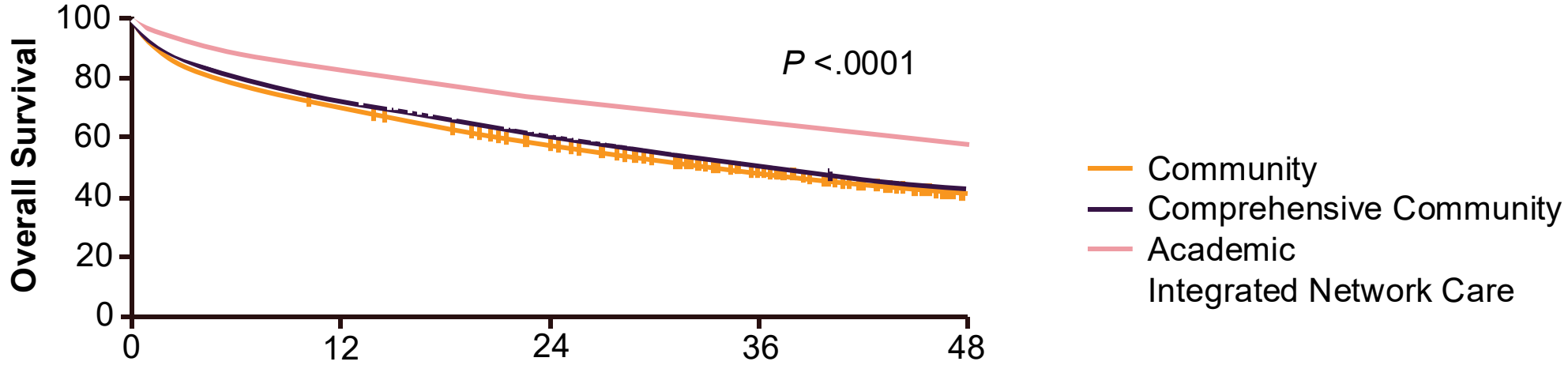
- Age, comorbidities, performance status, frailty—similar to evaluating candidacy for stem cell transplant
- **Real-world studies** show **older and sicker patients** with higher disease burden who received CAR T, yet they are often excluded
  - RW data from US MM immunotherapy consortium shows that 75% of patients treated with ide-cel and 55% of patients treated with cilta-cel would not have met eligibility criteria
- **TACTUM 23 survey: referral barriers for CAR T therapy:** Community oncologists cite financial toxicity as the primary barrier, while academic centers cite logistical issues
- QI survey of community oncology providers
  - 63% of providers reported difficulty in identifying patients eligible for CAR T
  - 24% of providers transferring patients to a CAR T center to be major hurdle
  - 22% providers had difficulty managing post-CAR T patients

<u>The primary challenge in CAR T access is the absence of standardized patient selection and timely referrals.</u>

RW = real-world.
Atallah R, et al. *Transplant Cell Ther.* 2024;30(9):925.e1-925.e6.

Treatment Location Impacts Survival in US Patients with MM

- Evaluation of 117,926 patients with MM diagnosed between 2005-2014 within the National Cancer Database
- Factors associated with improved survival included younger age, fewer comorbidities, living in a higher median income area, and treatment in academic centers



No. at Risk					
Community	10,639	7108	5314	3802	2636
Comprehensive Community	46,239	31,949	24,709	17,823	12,508
Academic	47,604	38,147	31,121	23,159	16,797
Integrated Network Care	11,866	8447	6584	4731	3444

Chamoun K, et al. *Cancers (Basel)*. 2021;13(4):590.

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Relative Proportion of Multiple Myeloma Treatment by Type in the US

Abbreviations: allo, allogeneic; auto, autologous; CAR-T, chimeric antigen receptor T cell.

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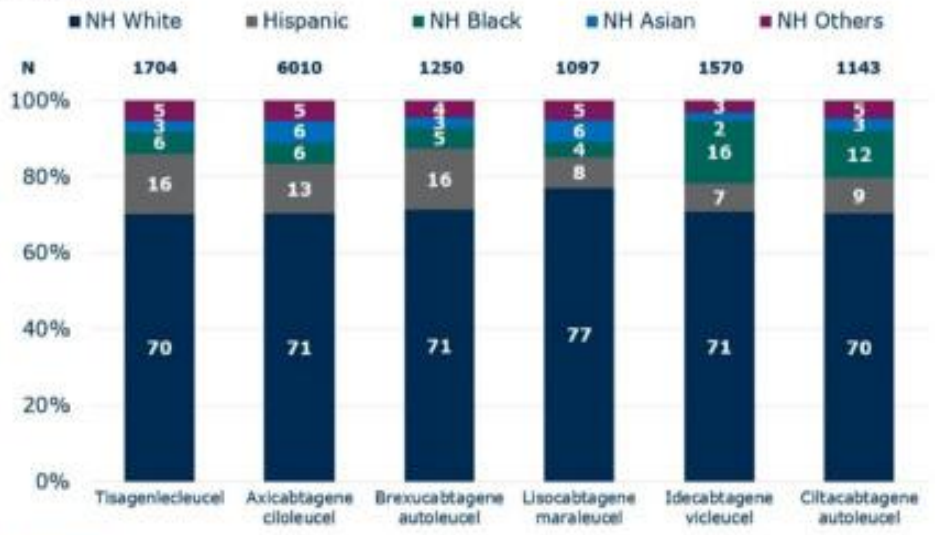
- **Persistent racial disparities**: NH White patients accounted for **64-75%** of ASCT and **70-77%** of CAR T recipients (2013-2023); NH Black and Hispanic patients comprised only **12-17%** and **5-13%**, respectively, despite a higher disease burden
- **Slow progress in equity**: Over a decade, NH Black representation in ASCT rose only **3%** (from **14% to 17%**); Hispanic and Asian groups remained largely unchanged at **3-5%**
- **CAR T adoption rising**: CAR T use in MM increased from **0% in 2018** to **16% in 2023**, while ASCT declined from **97% to 84%**—yet uptake remains disproportionately low in minority populations

ASCT = autologous stem cell transplantation.

Spellman SR, et al. *Transplant Cell Ther*. 2025;31(8):505-532.

CAR-T Infusion Product Type in the US by Race and Ethnicity, Adults 2016-2023



Abbreviation: NH, Not Hispanic or Latino. Note: Other includes: Native Hawaiian or other Pacific Islander (n=21); American Indian or Alaska Native (n=34); Other (n=53); and not a US resident (n=508).

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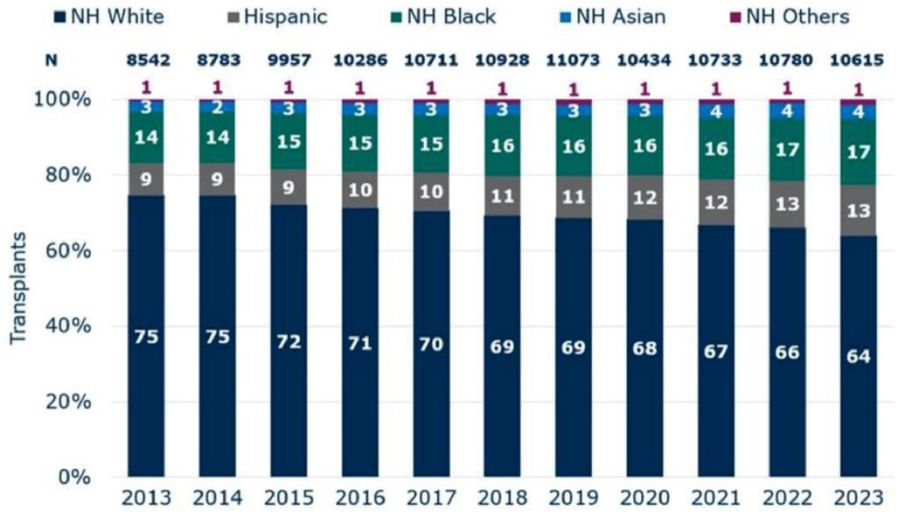
Autologous HCTs in the US by Race and Ethnicity, Adults



Abbreviation: NH, Not Hispanic or Latino. Note: Other includes: Native Hawaiian or other Pacific Islander (n=174); American Indian or Alaska Native (n=442); more than one race (n=349); and not a US resident (n=318).

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Socioeconomic and Racial Disparities Are Further Confirmed by Real-World Data

- Black and Hispanic patients, as well as those from lower-income neighborhoods, are underrepresented among CAR T recipients and trial participants
- In study of 1057 clinical trial participants of hematologic malignancies from 2017-2021, Black patients constituted 2-5% of the participants
- Patients with commercial insurance and higher socioeconomic status are more likely to receive CAR T, and travel burden is higher for those from higher SES backgrounds
- Only 7.3% of CAR T admissions were from neighborhoods with a median income below $40,000
- ***Despite these disparities, clinical outcomes with CAR T are similar across racial and ethnic groups,*** although Hispanic patients may have lower response rates, and Black patients may experience higher rates of cytokine release syndrome as evident by RW cohort of 207 RR patients in which **11% Hispanic, 17% non-Hispanic Black, and 72% non-Hispanic White**

SES = socioeconomic status.
Ahmed N, et al. *Transplant Cell Ther*. 2022;28(7):358-364. Al Hadidi S, et al. *JAMA Netw Open*. 2022;5(4):e228161. Peres LC, et al. *Blood Adv*. 2024;8(1):251-259.

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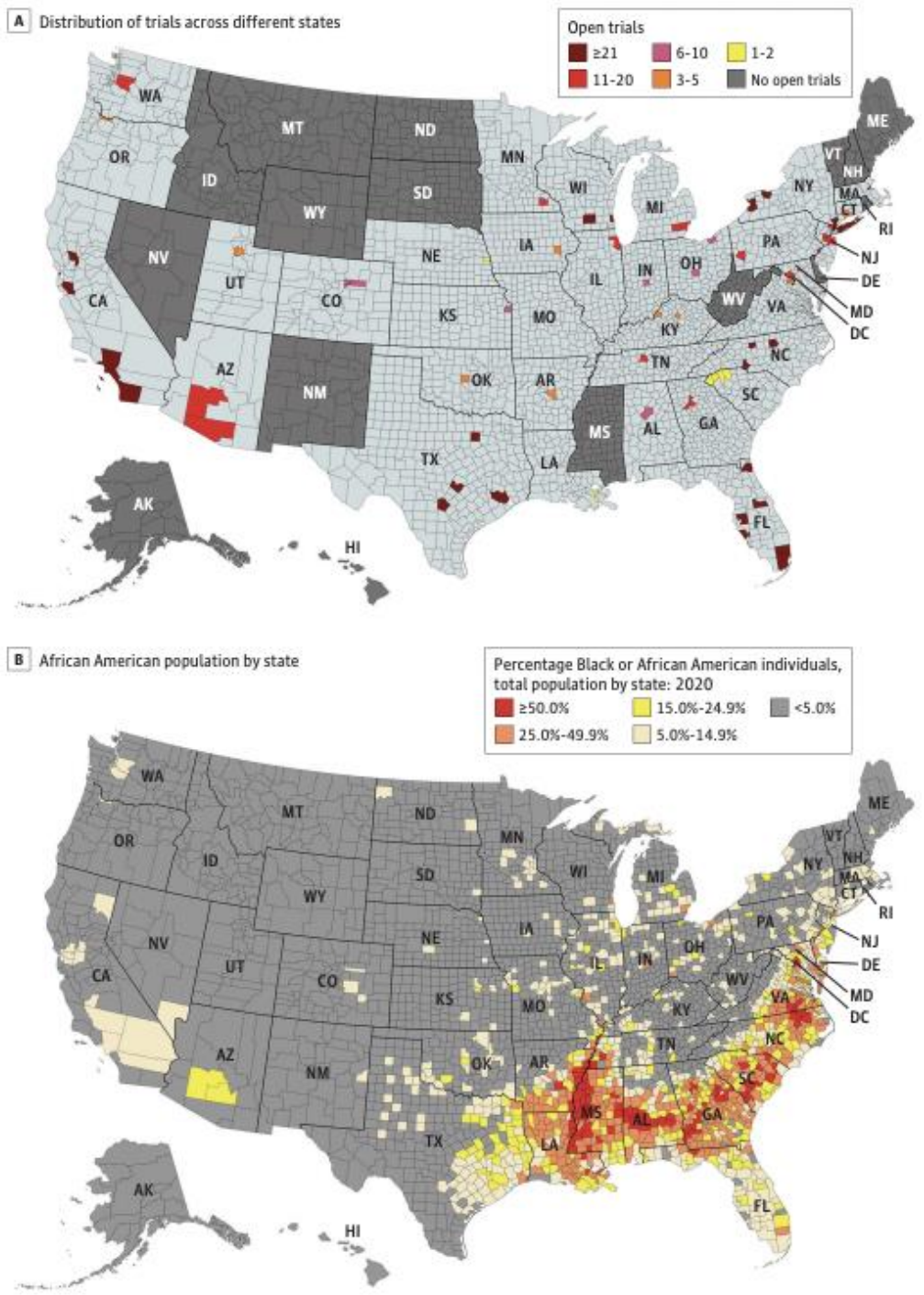
Distribution of Chimeric Antigen Receptor T Cells and Bispecific Antibodies Clinical Trials in the United States

- **Only 35.9%** of Black patients lived in a county with an open CAR T or bispecific trial
- In the **10 states** with the highest Black population, **60%** had ≤3 or **no open trials**
- Most trials are industry-sponsored and concentrated in urban academic centers, further limiting access for rural and minoritized populations
- **~33%** of CAR T recipients traveled >2 hours for treatment
  - These patients were more often from **higher socioeconomic groups**
  - **Fewer Medicare/uninsured** patients received CAR T

Impact of Distance on Outcomes

- **Longer travel time** linked to
  - Delayed supportive care
  - **Higher infection-related mortality**
  - Potentially **worse survival**



Alqazaqi R, et al. *JAMA Netw Open*. 2022;5(8):e2228877. Ahmed N, et al. *Transplant Cell Ther*. 2022;28(7):358-364.

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CAR-T vs Non-CAR T Treatment in Medicare Multiple Myeloma Patients

- Observational cohort analysis using Medicare fee-for-service data (2021-2023)
- **73 patients** in the CAR T intention-to-treat group (including 9 who underwent apheresis but did not receive CAR T)
- Matched to **219 non-CAR T** patients by line of therapy and index year

Key Differences in Treated Populations

- No significant differences were observed in **sex, region, or race/ethnicity**

Implications

- In the Medicare setting, CAR T therapy was more likely administered to **younger**, **less frail**, and **higher-SES** patients.
- Traditional disparities (by sex, race, or region) were not evident in this cohort—but barriers related to age, frailty, and financial resources appear to influence access

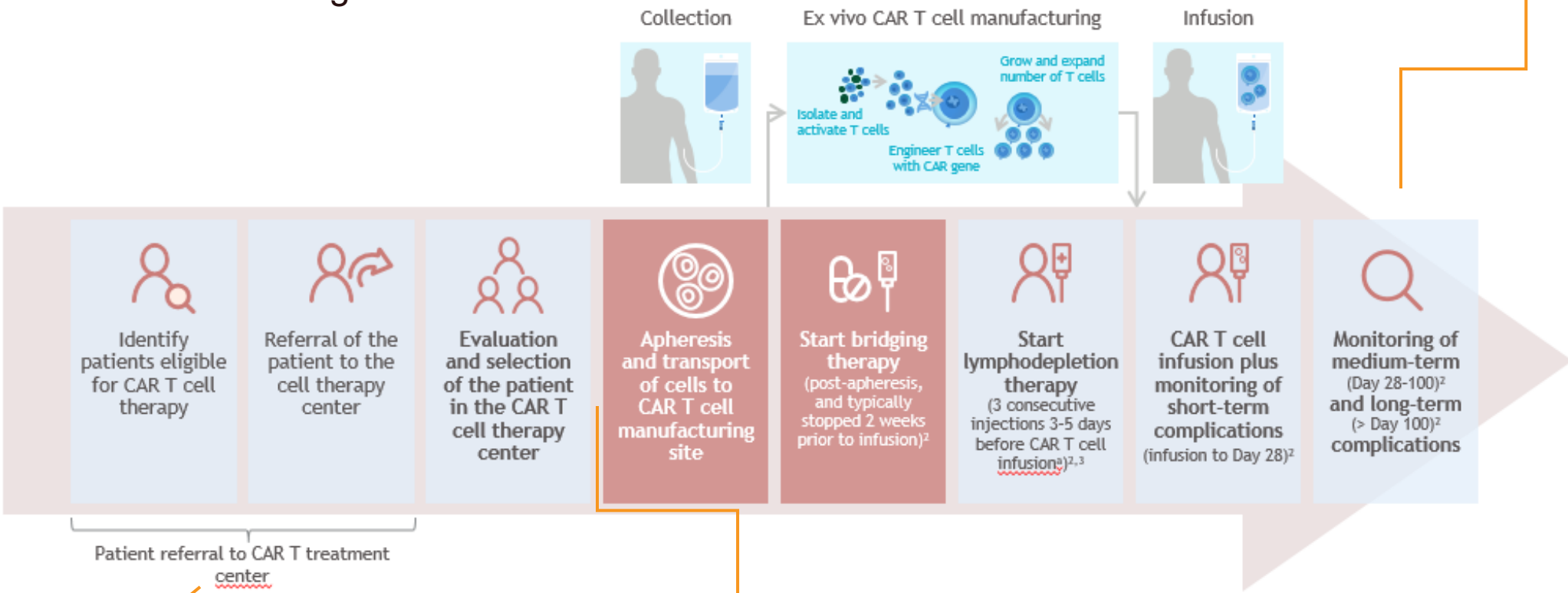
Patient Characteristic	CAR T Group (%)	Non-CAR T Group (%)	Odds Ratio (OR)
Age <75 years	59	36	0.29
Mean Frailty Index (CFI)	0.18	0.20	0.39
Dual Medicare/Medicaid	4	19	0.09
COPD	7	17	0.32
Other severe cancers	8	17	0.39

CFI = claims-based frailty index; COPD = chronic obstructive pulmonary disease.

Ailawadhi S, et al. *J Clin Oncol*. 2024;42(Suppl 16):e23310.

Complex Logistics

The **complex nature and delivery process of CAR T therapy** add additional challenges.



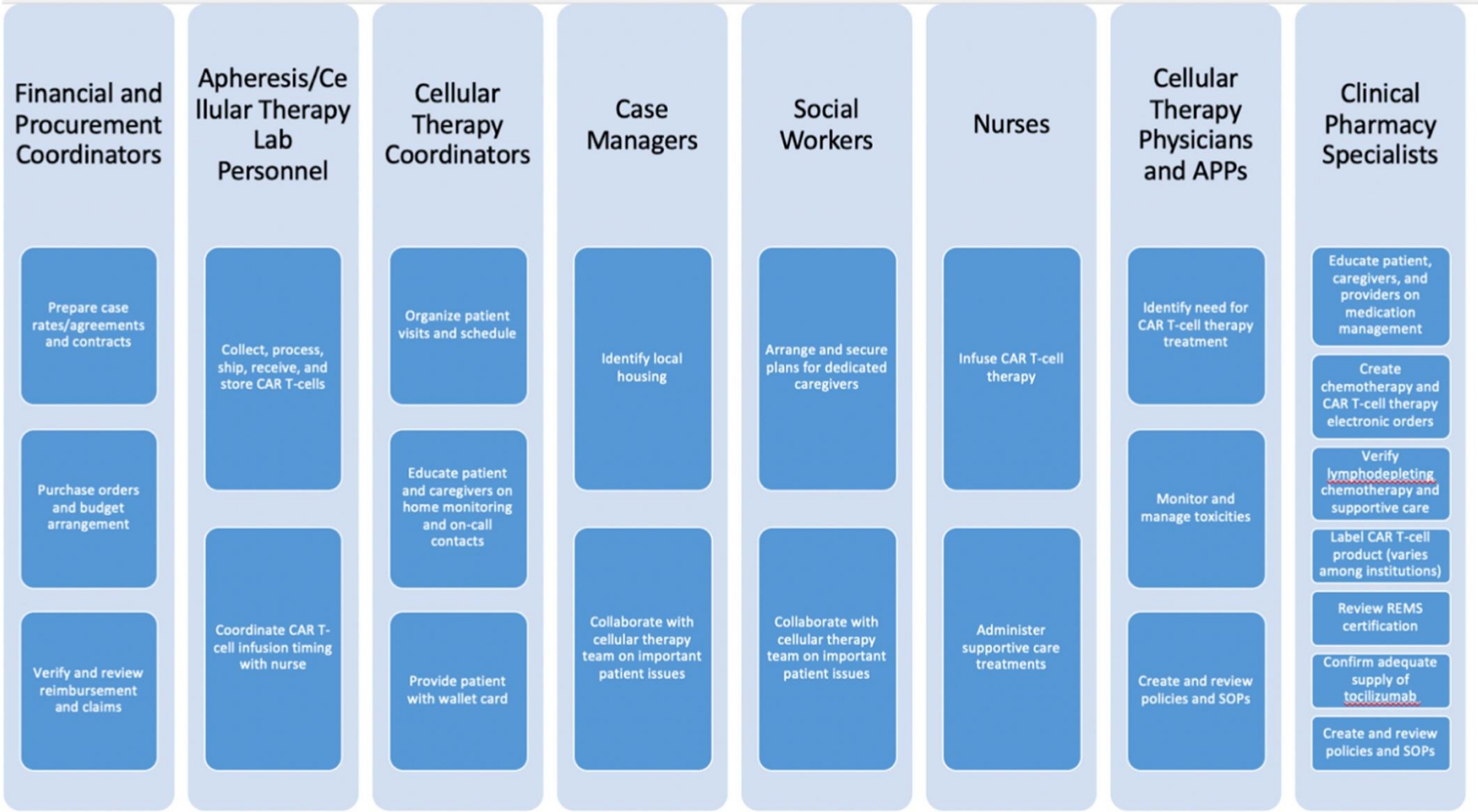
Caregiver burden, Driving restrictions

Insurance approval: Achilles' heel: 3-21 days; prior authorization.

Referral too late

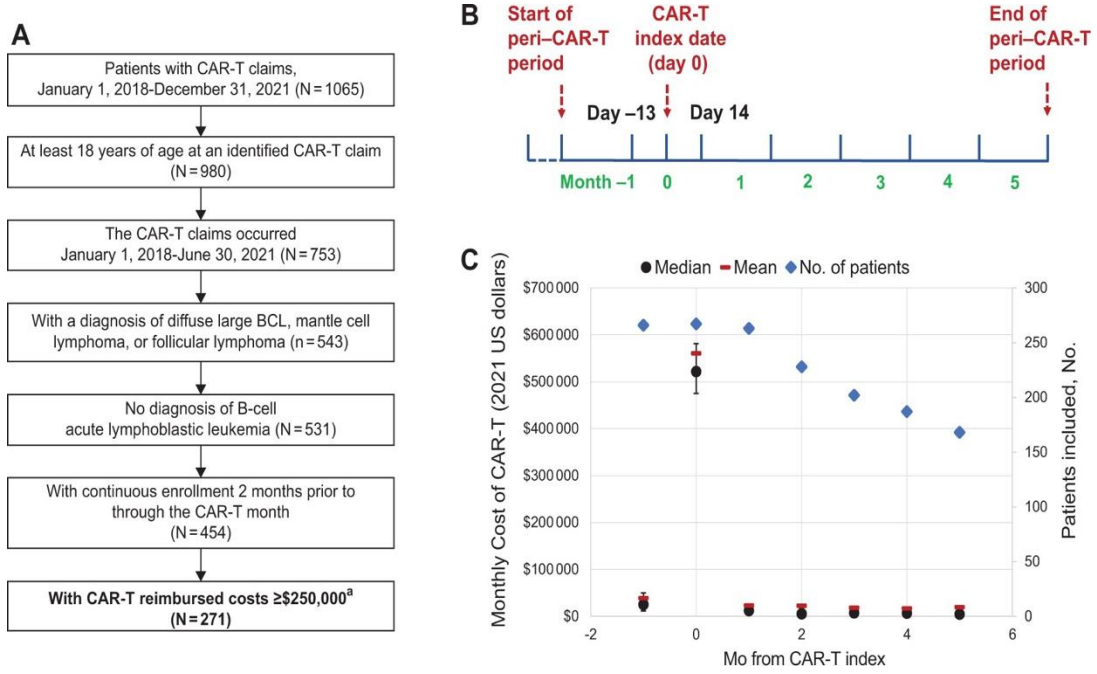
Adapted from slide courtesy Kaur G.

Personnel and Resources to Deliver CAR T Therapy



SOP = standard operating procedure; REMS = Risk Evaluation and Mitigation Strategy.
Oluwole OO, et al. *Transplant Cell Ther*. 2024;30(2):131-142.

Upfront Cost



N = 271, retrospective claims-based analysis
CAR T in lymphoma: High upfront cost burden
Median cost at infusion: ~$500,000
Post-infusion costs decline but remain substantial
Majority of spend concentrated in the **peri-CAR T window**

Long-Term Financial Toxicity

Study population

- 58 patients and 31 caregivers mostly remission
- Surveyed ≥12 months post-CAR T therapy

Key findings

- Financial toxicity was generally **low** among long-term responders
  - **25%** of patients: *mild-to-moderate* toxicity
  - **18%** of caregivers: *mild-to-severe* toxicity
- Median **annual household income** of participants: **$60,000**
- **Factors linked to higher financial burden**:
  - Lower income
  - Higher symptom burden
  - Poorer mental HRQoL
  - Younger caregivers
  - Retirement status

Di M, et al. JNCI Cancer Spectrum. 2024;8(4):pkae059. Andersen LP, et al. *Transplant Cell Ther*. 2025;31(8):592.E1-592.E13.

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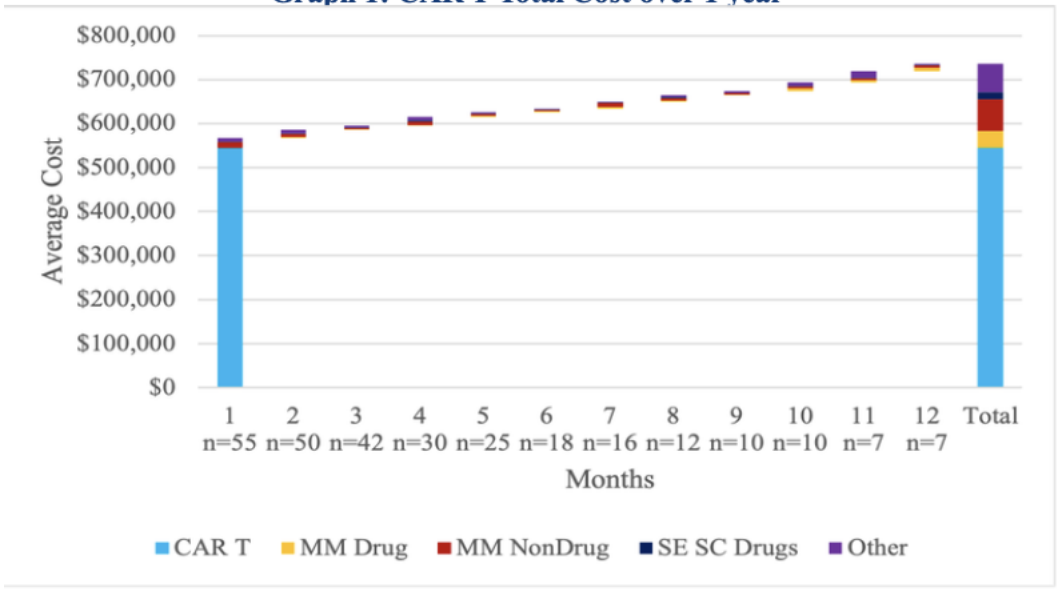
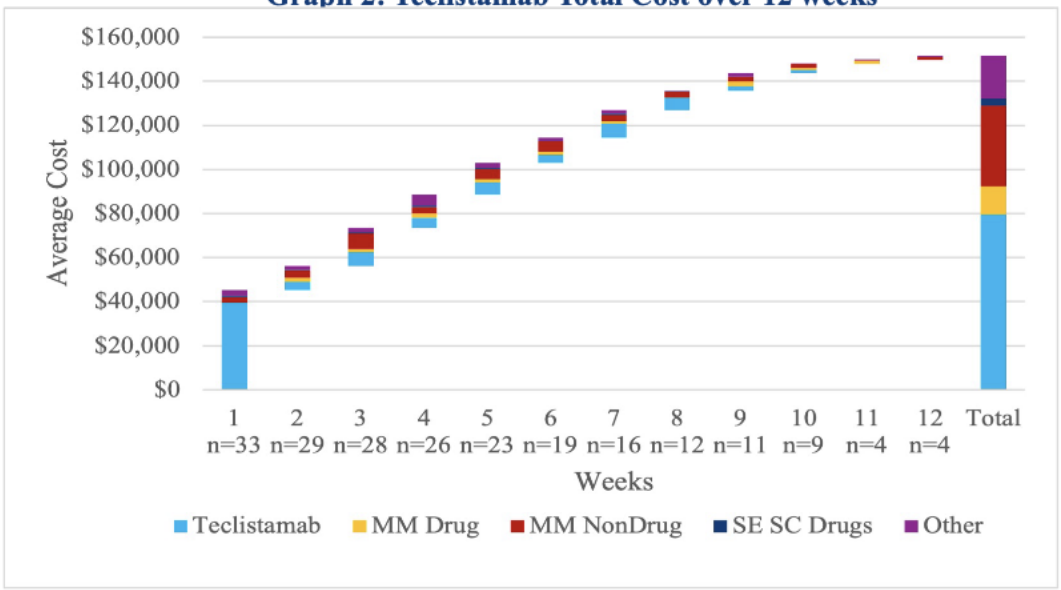
Cost of CAR T and Bispecifics

Graph 1: CAR T Total Cost over 1 year



'otal column reflects total average cost accumulated over 1 year for a patient after receiving CAR T. The n represents patients in continuous enrollment for the ıll month. 10 patients had less than 1 month of continuous enrollment data, so they were not included in the cost trend analysis. Baseline characteristics emained similar to Table 3. The total cost of care accumulated over 1 year is $736,231 and the cost of CAR T is $546,053, making up 74% of total cost of are.

Graph 2: Teclistamab Total Cost over 12 weeks



Total column reflects total average cost accumulated over 12 weeks for a patient receiving teclistamab. The n represents patients who were continuously enrolled for the full week. 4 patients had less than 7 days of continuous enrollment data, so they were not included in the cost trend analysis. Baseline characteristics remained similar to Table 3. The total cost of care accumulated over 12 weeks is $151,660 and the cost of teclistamab is $79,680, making up 53% of the total cost of care.

Cost Category	CAR T (ide-cel, cilta-cel)	Teclistamab (extrapolated to 8.5 months)
Drug Acquisition (Mean)	$557,698	$464,751
Drug Acquisition (Median)	$480,716	$388,251
Pre-Treatment Cost	$54,591 (includes bridging & LDC)	Not applicable
MM Treatment Cost	$42,807 (excluding CAR T)	N/A
Total Cost of Care	$736,231 over 12 months	$151,660 over 12 weeks
% of Cost from Drug	74%	53%

The study highlights that **CAR T cell therapy incurs a large up-front cost, while teclistamab's costs are distributed over the course of ongoing treatment.**

SE SC = side effect/supportive care.
Keohane N, et al. Presented at: Academy of Managed Care Pharmacy (AMCP) Nexus; 2023.

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Driving Restrictions Post-CAR T Therapy: A Barrier to Patient Independence

CAR T Physician Survey Findings N=41
73% of oncologists agree with driving restrictions during weeks 0-4
78% of oncologists disagree with restrictions beyond week 4
Only 14% of oncologists support restrictions in weeks 5-8
Significant difference in opinions between weeks 0-4 vs 5-8 ($P<0.01$)

RW Consortium Findings, N=553
<1% incidence of CRS or neurotoxicity in weeks 5-8
No de novo ICANS reported after day 28
10 deaths (2%) in weeks 5-8, primarily due to MM progression, not toxicity
3 cases of non-Parkinsonian neurotoxicity first diagnosed in weeks 5-8

Banerjee R, et al. Presented at: ASH Annual Meeting & Exposition; 2024.

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FDA-Approved Label Updates Reduce Monitoring Requirements for Ide-Cel and Cilta-Cel CAR T Cell Therapies

As of June 27, 2025, for treatment of MM

Outcome	Post label change	Pre label change
Driving restrictions	**2 weeks** after treatment	8 weeks after treatment
Proximity to healthcare facility requirement	**2 weeks** after treatment	4 weeks after treatment
REMS program enrollment	REMS program **removed**	REMS enrollment required

These updates are supported by new real-world data on ide-cel use that show most serious side effects occur within the first week after infusion[2]

Sidana, et al.
IMS Pos #PA-078

Most cases of CRS and neurotoxicity were low grade and occurred within 1 week of ide-cel infusion

For patients with onset >1 week after infusion, median time to resolution was ≤7 days

CRS, cytokine release syndrome; cilta-cel, ciltacabtagene autoleucel; FDA, Food And Drug Administration; ide-cel, idecabtagene vicleucel; MM, multiple myeloma; REMS, Risk Evaluation and Mitigation Strategies.

1. U.S. Food and Drug Administration. Released June 27, 2025. Accessed August 20, 2025. https://www.fda.gov/news-events/press-announcements/fda-eliminates-risk-evaluation-and-mitigation-strategies-rems-autologous-chimeric-antigen-receptor. **2.** Sidana S, et al. Presented at IMS; September 17-20, 2025; Toronto, Canada. Poster #PA-078.

Brain to Vein Time…And Beyond!

Indication	Leukapheresis	CAR T-cell manufacturing	Lymphodepletion	CAR T-cell infusion
Timely referral at the time of first sign of biochemical progression or insufficient response: • Discuss treatment options • Evaluate CAR T-cell therapy eligibility • Plan T-cell apheresis • Discuss optimal bridging therapy **Avoid agents with negative effect on T-cell function before T-cell apheresis (<6 months):** • T-cell redirecting bispecific antibodies • Belantamab mafodotin • Alkylating agents • Topoisomerase inhibitors	**Pre-apheresis CAR-HEMATOTOX score:** • Can be used to predict efficacy and safety • Helpful when counselling and selecting patients for CAR T-cell therapy	**Bridging therapy** • Often essential to help control multiple myeloma during CAR T-cell manufacturing **Reduction in tumour burden with bridging therapy improves efficacy and reduces risk of severe toxicities:** • Use drugs that have not been previously used • Avoid combinations that might lead to increased risk of severe cytopenias or infections • Avoid BCMA-directed therapies • GPRC5D-targeting bispecific antibodies can be effectively used, but treatment should be initiated after T-cell apheresis	**Lymphodepletion with fludarabine and cyclophosphamide:** • Routinely used before CAR T-cell therapy **Fludarabine dose:** • Should be reduced in patients with eGFR of 30–70 mL/min **Severe renal impairment:** • eGFR <30 mL/min • Use cyclophosphamide alone or bendamustine **MyCARe model and CAR-HEMATOTOX score:** • Can be used at time of lymphodepletion to predict outcomes	• Monitor for cytokine release syndrome and neurotoxicity • Timely initiation of infectious prophylaxis

eGFR = estimated glomerular filtration rate.
Adapted from slide courtesy Kaur G.

Key Learning Points

- Engaging patients in shared decision-making during CAR T therapy planning has a substantial impact on the patient's psychological well-being, adherence, and confidence in the clinician
- One-time CAR T infusion has been shown to lead to extended QoL benefit vs continuous SOC
- Access and affordability remain, with CAR T therapy as with all healthcare, areas of concern for patients with varying social determinants of health
- The primary challenge in CAR T access is the absence of standardized patient selection and timely referrals, and marked disparities persist based on race and socioeconomic status

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Thank You

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