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UNIVERSITÀ DI BOLOGNA
DIPARTIMENTO DI
SCIENZE MEDICHE E CHIRURGICHE

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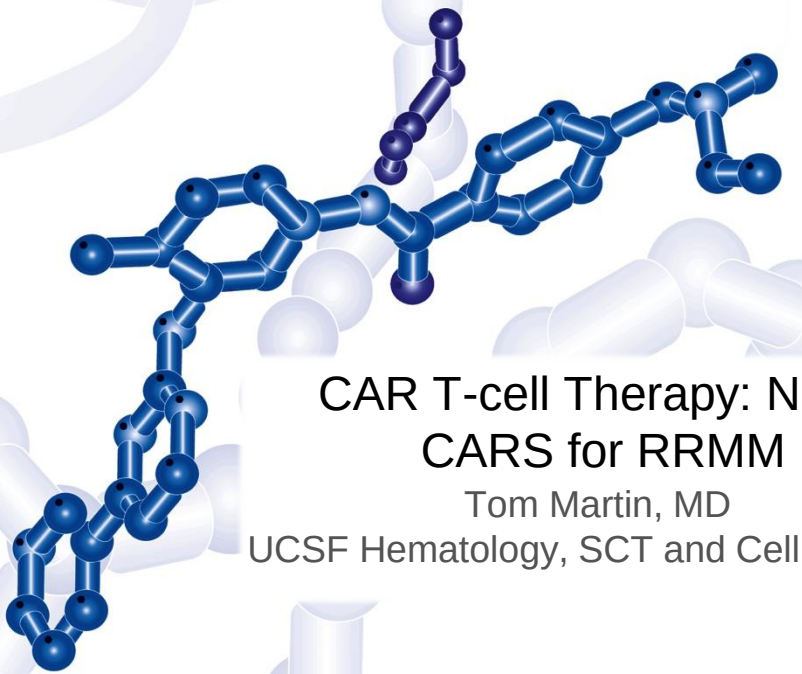


CAR T-cell Therapy: Novel CARS for RRMM

Tom Martin, MD
UCSF Hematology, SCT and Cell Therapy

New Drugs in Hematology

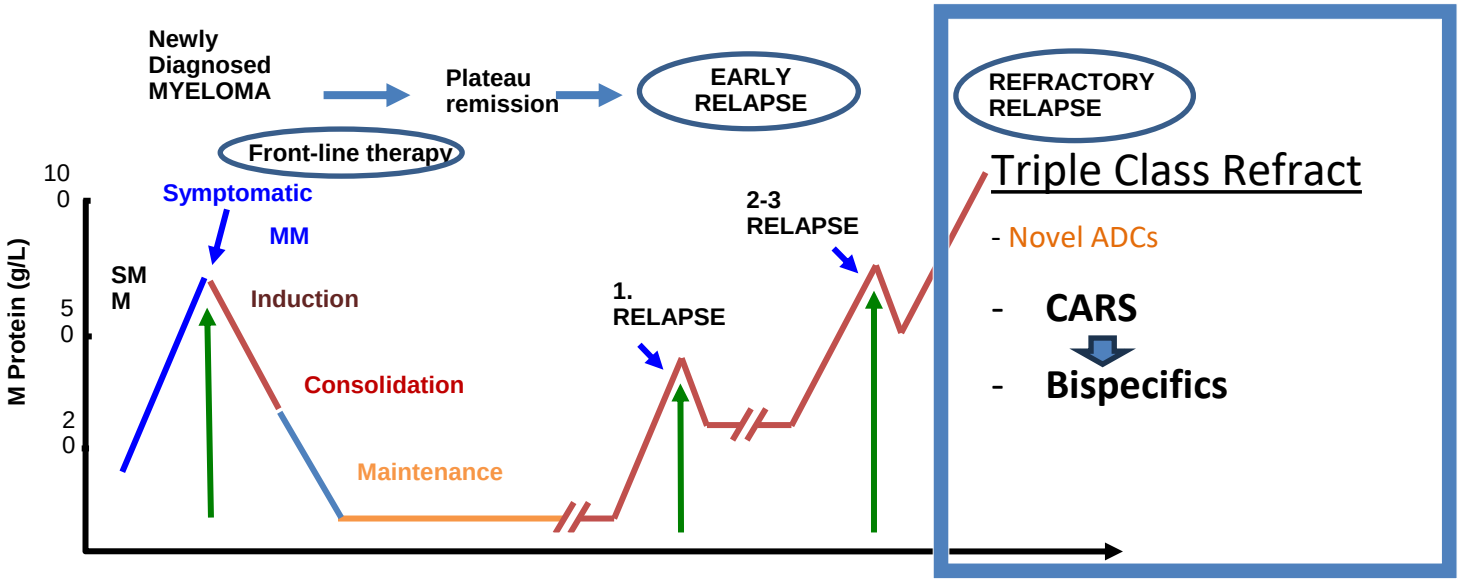
President: Pier Luigi Zinzani

Bologna,
Royal Hotel Carlton
May 18-19-20, 2026

Disclosures of Name Surname

Company name	Research support	Employee	Consultant	Stockholder	Speakers bureau	Advisory board	Other
Janssen	X						
Sanofi	X						
BMS	X						
GSK			X				
Pfizer			X				
Legend			X				
Lilly							DSMB
ABBVIE							DSMB

Immunotherapy in MM



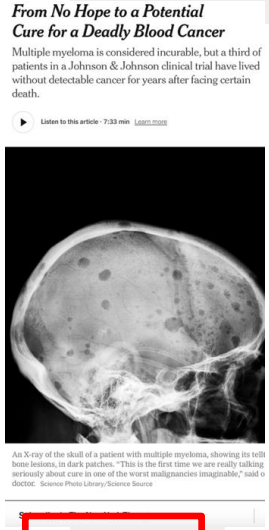
Frontline
Triplets/Quads
Survival >10 years

Early Relapse
(1-3 Prior Line): Triplets
Survival 3-7 years

Late Relapse
Recycle agents,
Survival <12 mos

UCSF

CARTITUDE-1 Long-Term Remission: 5-year follow-up
One-Third of Patients Were Progression-Free for ≥5 Years

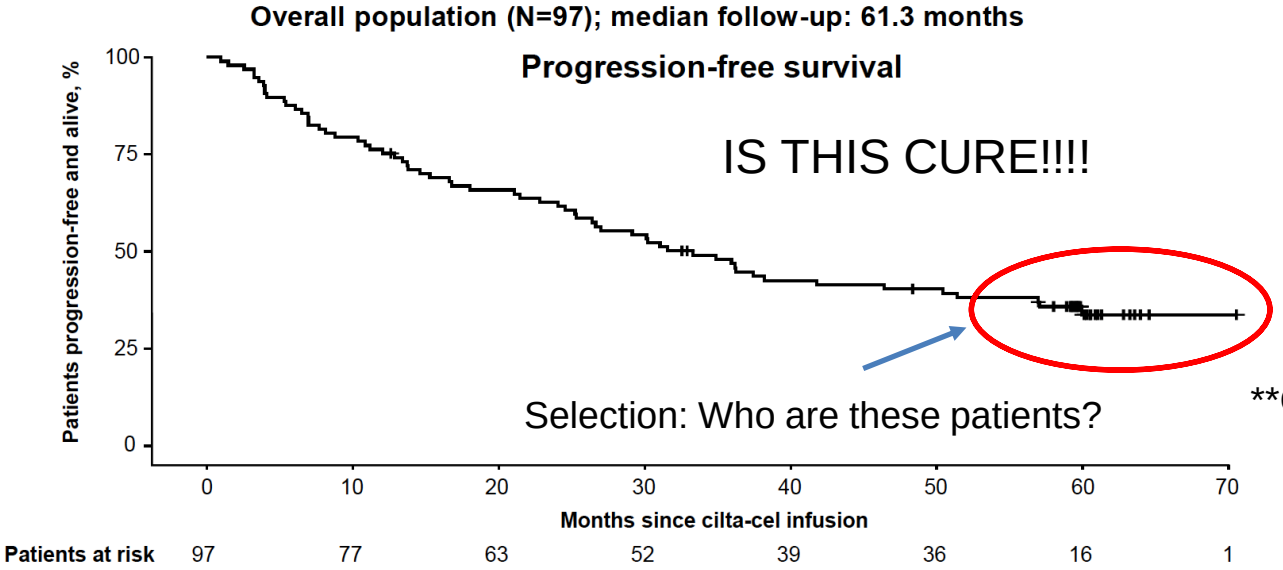

From No Hope to a Potential Cure for a Deadly Blood Cancer

Multiple myeloma is considered incurable, but a third of patients in a Johnson & Johnson clinical trial have lived without detectable cancer for years after facing certain death.

Listen to this article · 7:33 min Learn more

An X-ray of the skull of a patient with multiple myeloma, showing its telltale bone lesions, in dark patches. "This is the first time we are really talking seriously about cure in one of the worst malignancies imaginable," said one doctor. Science Photo Library/Science Source

NYT 2025



Selection: Who are these patients?

**Cost: for survivors ~ $9000/month

32 of 97 (33%) patients were treatment- and progression-free at ≥5 years

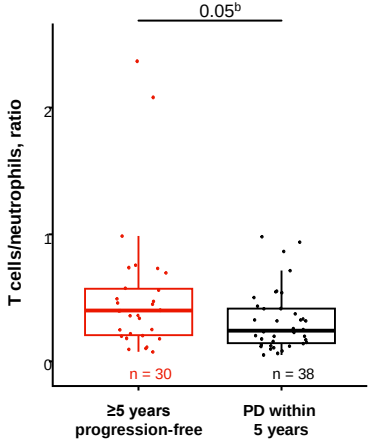
cilta-cel, ciltacabtagene autoleucel.

CARTITUDE-1 Long-Term Remission: Long-Term Disease Control Was Associated With Fitter Immune T Cells Before Infusion and Higher E:T Ratio After Infusion

Preinfusion

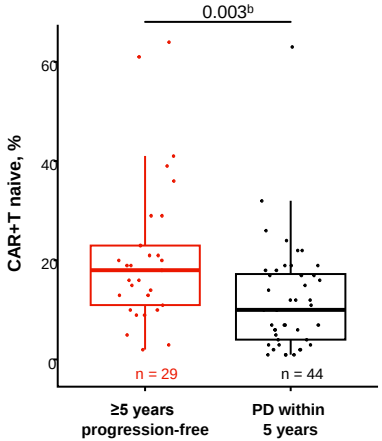
At apheresis

T cells/neutrophils



Drug product

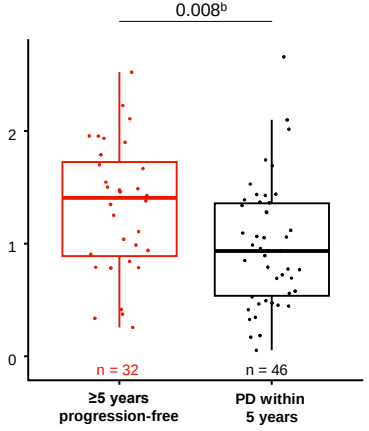
CAR+ T_{naive} cells[a]



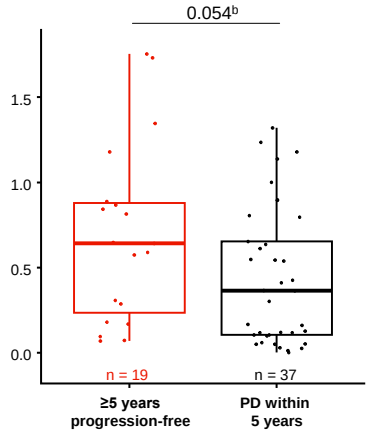
Postinfusion

E:T ratio at peak expansion[c]

CAR+ T cells



CAR+CD4+T_{cm}[1]



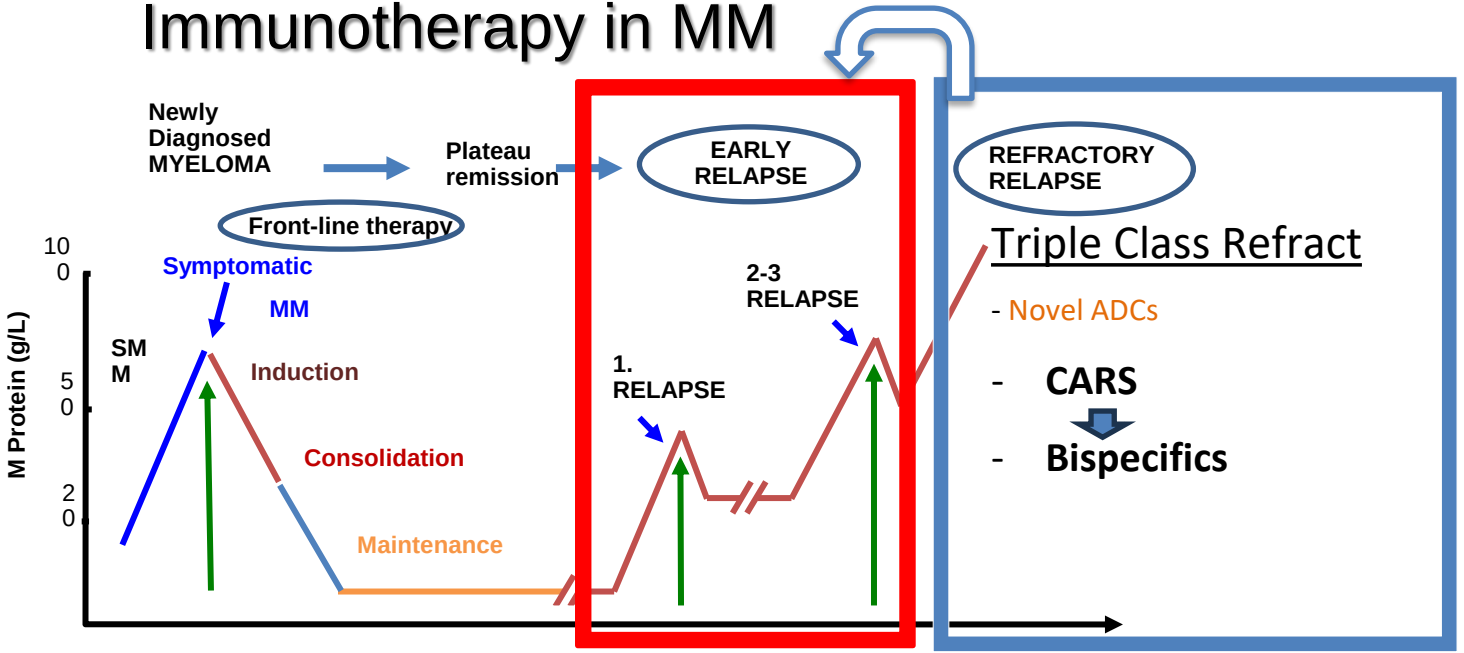
Long-term disease control was significantly associated with:

- Higher T cells over neutrophil ratio
- Fitter T_{naive} cells in the drug product
- Higher overall E:T ratio with either total CAR+ T cells or CAR+ CD4+ T cells with central memory phenotype at peak expansion

[a]CAR+ T_{naive} cells were defined as CD95-CD27+CD45RO-. [b]2-sided nominal *P* values unadjusted for multiplicity were provided for descriptive purposes. These analyses were exploratory in nature and utilized for hypothesis generation. [c]E:T ratio was defined as maximal CAR-positive T-cell levels normalized by preinfusion serum sBCMA levels.
CAR, chimeric antigen receptor; E:T, effector to target; PD, progressive disease; sBCMA, soluble B-cell maturation antigen; T_{cm}, central memory T cell; T_{naive}, naive T cell.

1. Ledergor G, et al. *Blood Adv* 2024;8:3562-75.

Immunotherapy in MM



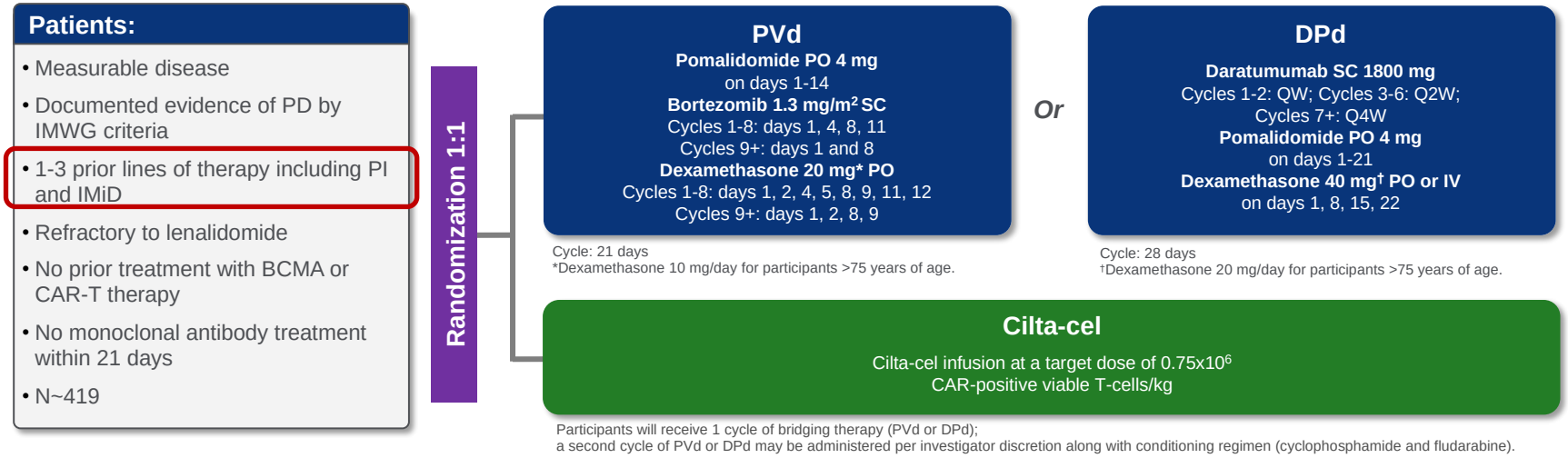
Frontline
Triplets/Quads
Survival >10 years

Early Relapse
(1-3 Prior Line): Triplets
Survival 3-7 years

Late Relapse
Recycle agents,
Survival <12 mos

UCSF

Cilta-cel: CARTITUDE-4 (MMY3002) Study Design



Primary Outcome:	Secondary Outcomes:	
• Progression-free survival	• CR or sCR • MRD negativity status • Sustained MRD negative rate	• HRQoL • OS, ORR, PFS2 • Safety

Approval in Early RRMM in April, 2024

1. https://clinicaltrials.gov/ct2/show/NCT04181827 2. https://www.prnewswire.com/news-releases/janssen-announces-unblinding-of-phase-3-cartitude-4-study-of-carvykti-cilta-cel-as-primary-endpoint-met-in-treatment-of-patients-with-relapsed-and-refractory-multiple-myeloma-301732398.html. San Miguel j. et al. NEJM 2023

CARTITUDE 4: Population and Results

- Results
  - **FIGURE1:** Primary Endpoint PFS

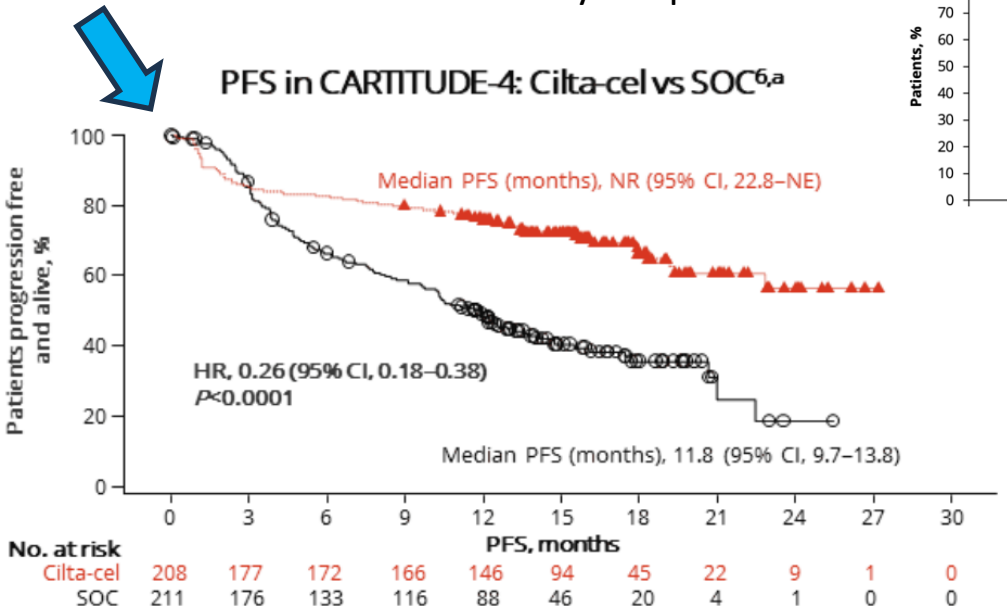
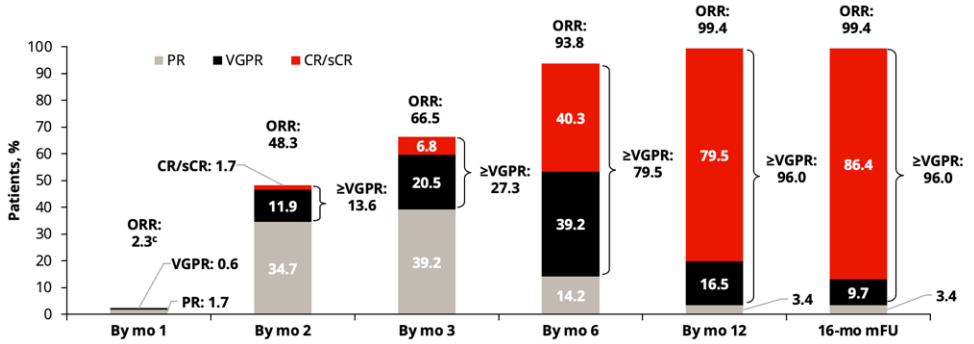


FIGURE 2: Responses deepened over time[a,b]



HR population: ~60% HR-fish

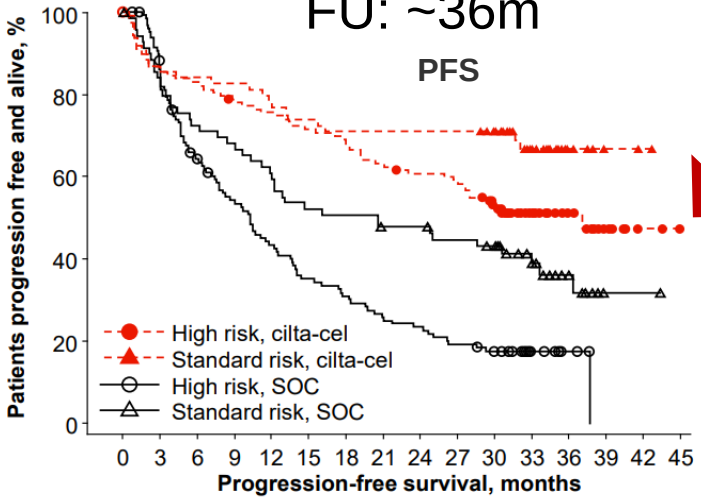
[a]Start of study treatment. [b]Physicians' choice. [c]Cyclophosphamide 300 mg/m^2 plus fludarabine 30 mg/m^2 daily for 3 days.
DPd, daratumumab, pomalidomide, and dexamethasone; PD, pharmacodynamics; PK, pharmacokinetics; PVd, pomalidomide, bortezomib, and dexamethasone.

Sidiqi MH et al. ASH 2023. Poster 4866

CARTITUDE-4: 1-3 PLoT

Efficacy by Standard and High-Risk[a] Status

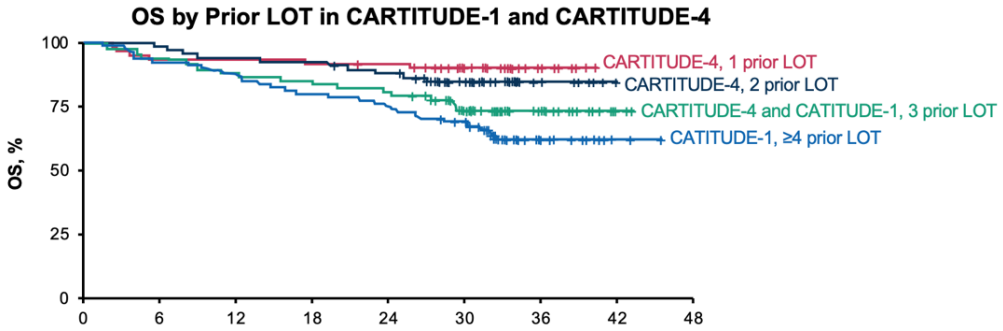
FU: ~36m



Patients at risk

High risk, SOC	132	111	79	65	52	42	37	31	28	23	20	7	3	0	0	0
High risk, cilta-cel	123	106	102	96	92	87	84	76	73	70	55	31	14	7	2	0
Standard risk, SOC	70	58	50	47	41	36	35	32	32	29	27	18	9	1	1	0
Standard risk, cilta-cel	69	59	58	57	53	51	49	49	49	49	46	27	9	2	1	0

Also impressive OS, by Prior LOT



Data Cut-off: May 1, 2024; Median Follow-up: 33.6 mo

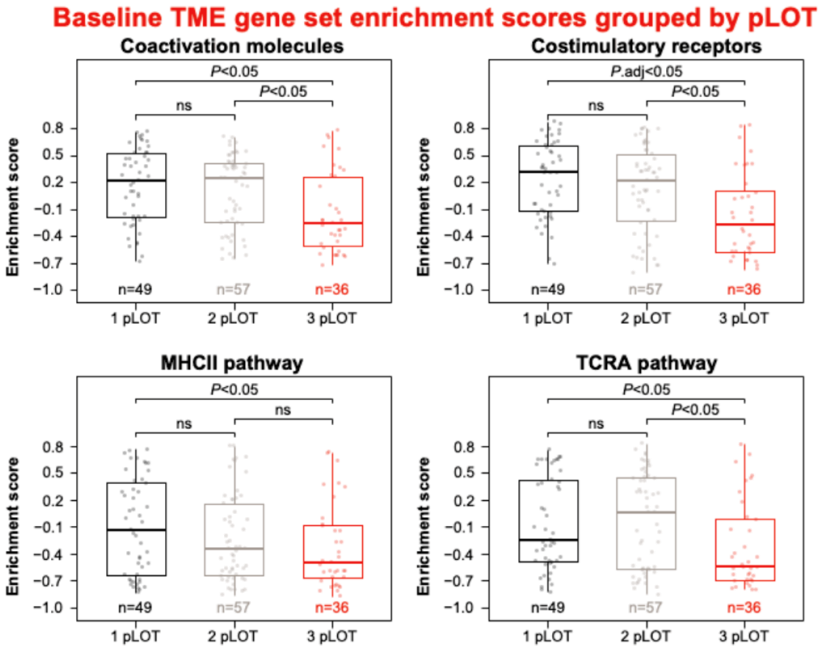
[a] High-risk cytogenetics was defined as del(17p), t(4;14), t(14;16), or gain/amp(1q) by FISH

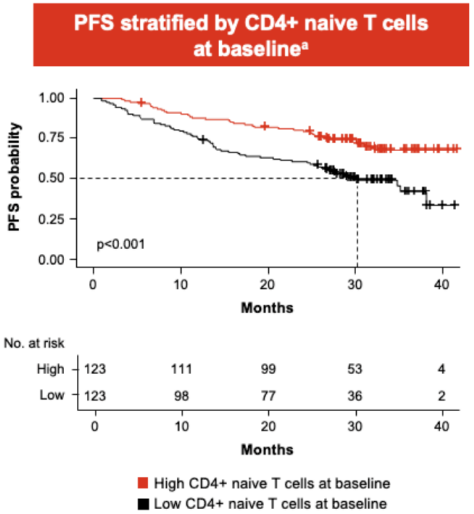
cilta-cel, ciltacabtagene autoleucel; FISH, fluorescence in situ hybridization; HR, hazard ratio; OS, overall survival; PFS, progression-free survival; SOC, standard of care.

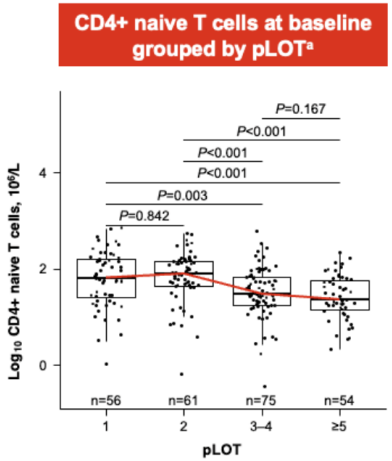
Sidana S, et al. ASCO 2025. Abstract 7539.

1. Parekh S et al. ASH 2025. Abstract 92.

Favorable T-cells in earlier lines = Improved PFS





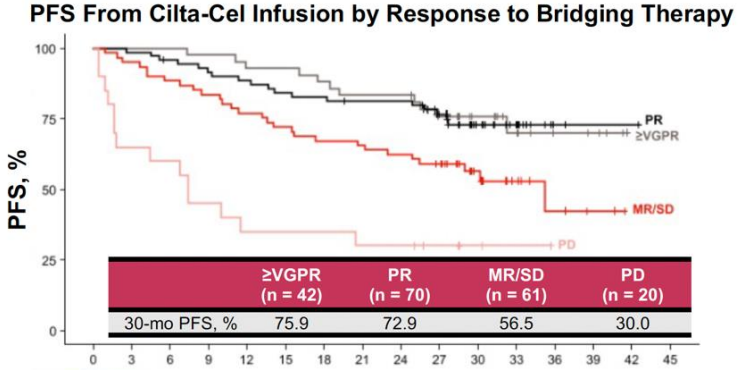


Samir Parekh, ASH 2025

Better Success with Effective Bridging Therapy

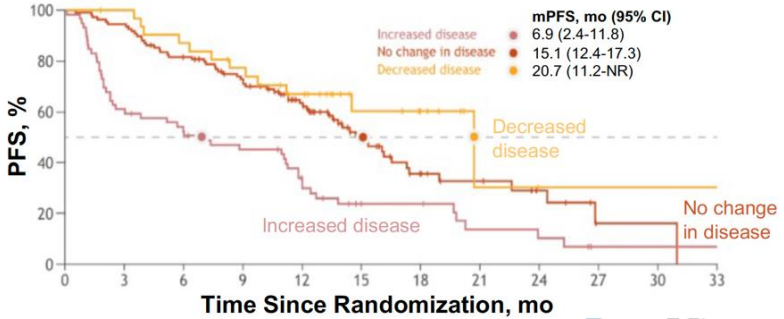
CARTITUDE4 – Cilta-cel 1-3 PLoT

CARTITUDE-4: Deeper response to bridging therapy is correlated with longer PFS and OS; lower incidence of fatal infections after cilta-cel[1,2]



KarMMa3 Ide-cel in 2-4 PLoT

KarMMa-3: Ide-cel resulted in longer mPFS and greater response in patients who had a decrease/no change versus increase in disease burden with bridging therapy[3]

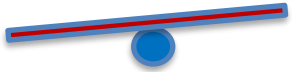


CART ➔ FIRST in RRMM?

1. Dhakal B et al. ASH 2025. Abstract 2215. 2. Dhakal B et al. Tandem 2026. Abstract 203. 3. Einsele H et al. IMS 2023. Abstract P-008.

Many considerations for CART use in RRMM

- Benefit vs Toxicity



- Sequencing/options
  - CAR ➔ Bispecific
  - Bispecific ➔ CAR
  - ADC ➔ CAR
  - BCMA ➔ GPRC5D
  - GPRC5D ➔ BCMA
- PFS1 + PFS2 +/- PFS3
  - Interim treatments
- Are patients cured with ITs?
- Should we use dual targets?
  - Trispecifics (multiple)
  - CARS (BCMA-GPRC5D CAR)
- Which dual targets are better
  - GPRC5D + BCMA
  - BCMA + CD19
- Preventing resistance
  - Greater after bsAb

Delayed CART Toxicity

Delayed Toxicities
▪ B-cell aplasia/hypogammaglobulinemia
▪ Prolonged cytopenias
▪ Late infections
▪ Long-term neurologic events
▪ Cranial neuropathies
▪ Peripheral neuropathy, Guillain barre
▪ Movement and neurocognitive
▪ Enterocolitis (IEC-EC)
▪ Transient cardiac toxicities
▪ Secondary malignancies?

May be recognized by primary oncologist
(Need collaboration with community MDs)

Management of Delayed Toxicities	
Prolonged cytopenias	Growth factors, Stem cells
Immunosuppression ‘‘B-cell aplasia’’	Prophylactic/preemptive IVIG for hypogammaglobulinemia
Infection (eg, HSV/VZV, encapsulated bacteria)	Vaccines, acyclovir, sulfamethoxazole/ trimethoprim, other
Delayed Neurotox	Corticosteroids, IVIG, chemotherapy (IV, IT)
Enterocolitis	Aggressive supportive care (TPN), Steroids, infliximab

Chakraborty. Transplant Cell Ther. 2021;27:222. Hill. Blood. 2020;136:925.
Munshi. NEJM. 2021;384:705. Berdeja. Lancet. 2021;398:10297. Cohen. Blood Cancer J. 2022;12:32.

Delayed Neurotox: ALC Elevation is Key

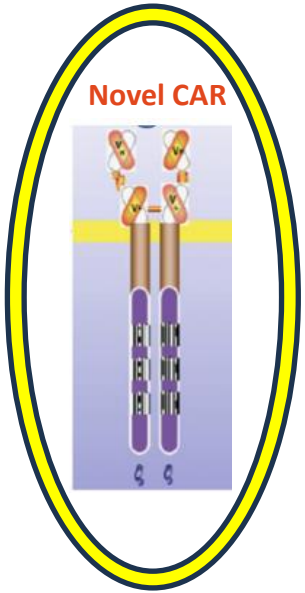
- Retrospective review of N=191 patients s/p CAR-T at UCSF from 2021-present
- Median ALC, through day 30: 1.96
  Ciltacel (n=147): 2.17 (0.21-39.04)
  Idecel (n=44): 1.13 (0.28-14.05)
- Timing of peak ALC elevation
  - Median ➔**day 13** (range 1-30d)
  - Median duration of ALC ≥3: 2d
- ALC ≥3: 66/191 (34.6%)
  Ciltacel: 38.8%
  Idecel: 13.3%

	ALC≥3 (n=66)	ALC<3 (n=125)
Neurotoxicity (n=20)	**16**	**4**
No Neurotoxicity (n=171)	**50**	**121**

24% chance of NT with ALC ≥3

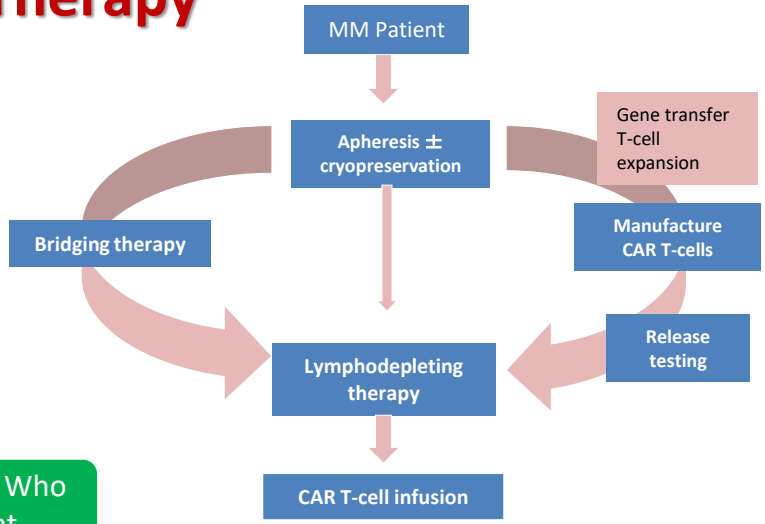
Response to Bridging ➔ Key for Toxicity

Innovation/New Drugs in CAR T-Cell Therapy



- TARGETS
- TECHNOLOGY
- **T**reated population: Identify best patients

3T's

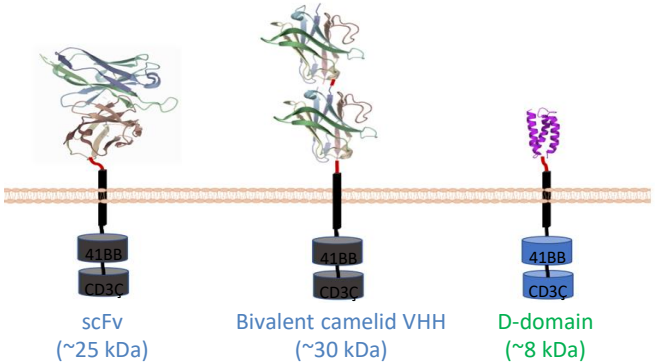


Improve targeting	**Improve Technology**	Improving Who to Treat
Human/Synthetic	CRISPR/Integrate	**NDMM**
Novel Antigens	Intracellular Signaling	**Healthy T's**
Dual targets	Switch tech	**Low-risk**
Intracellular Ag	*in vivo* CAR	

ACCESS, ACCESS, ACCESS
- Still requires academic center
- Still requires *"brain-to-vein"* time

Anitocabtagene Autoleucel: BCMA CART

- Anito-cel is an autologous BCMA-directed CAR T-cell therapy using a novel, D-domain binder[1,2]



D-Domain Attribute*	Description
Size	Small D-domain construct → high transduction efficiency/CAR positivity → low total cell dose[2-4]
Structure and stability	Stable, lack of tonic signaling because of rapid folding, hydrophobic core of the D-domain, and lack of disulfide bonds[4-6]
Binding	Fast off-rate and high CAR surface expression, which may allow optimal tumor cell killing in absence of prolonged inflammation

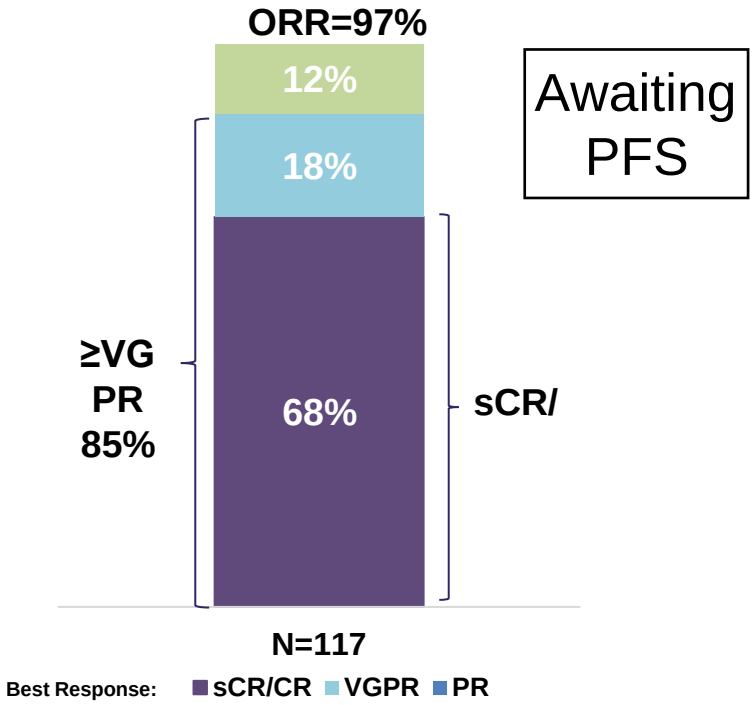
*A non–antibody-derived synthetic protein.

- In the phase I study in 38 patients with R/R MM after ≥3 prior LoT, anito-cel demonstrated[7-9]:
  - ORR: 100%; sCR/CR: 76%
  - 24-mo PFS: 56% (Median 30.2m)
- With high-risk features: 68%

1. Rotte. Immuno-Oncology Insights. 2022;3:13. 2. Frigault. Blood Adv. 2023;7:768. 3. Cante-Barrett. BMC Res. 2016;9.
4. Buonato. Mol Cancer Ther. 2022;21:1171. 5. Zhu. Proc Nat Acad Sci. 2003;100:15486. 6. Qin. Mol Ther. 2019;27:1262.
7. Frigault. ASH 2023. Abstr 1023. 8. Frigault. EHA 2024. Abstr S207. 9. Bishop. ASH 2024. Abstr 4825.

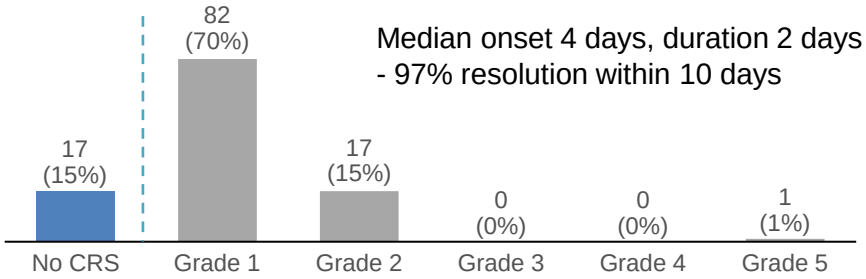
iMMagine-1: Anito-cel Efficacy and Safety

Efficacy Evaluable Patients, N=117



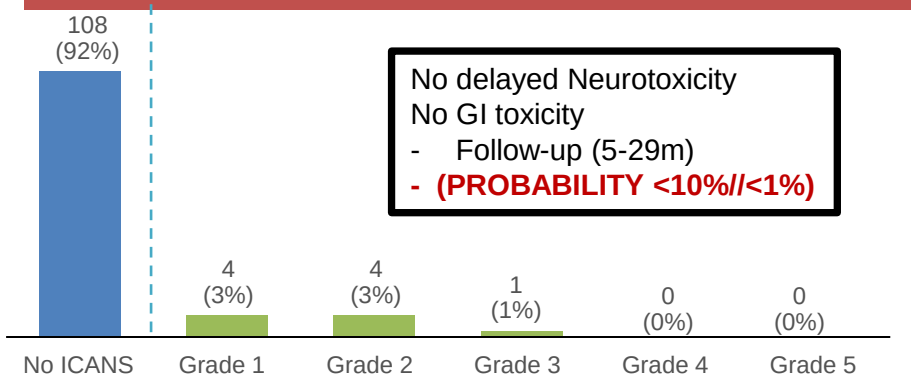
Awaiting PFS

Incidence and severity of CRS



Median onset 4 days, duration 2 days
- 97% resolution within 10 days

Incidence and severity of ICANS



No delayed Neurotoxicity
No GI toxicity
- Follow-up (5-29m)
- **(PROBABILITY <10%//<1%)**

Responses are investigator assessed per IMWG criteria, ORR defined as partial response or better; MRD evaluable patients had an identifiable malignant clone in the baseline bone marrow sample and had a post-treatment bone marrow sample sufficient to assess MRD negativity
CR, complete response; MRD, minimal residual disease; ORR, overall response rate; PR, partial response; sCR, stringent complete response; VGPR, very good partial response

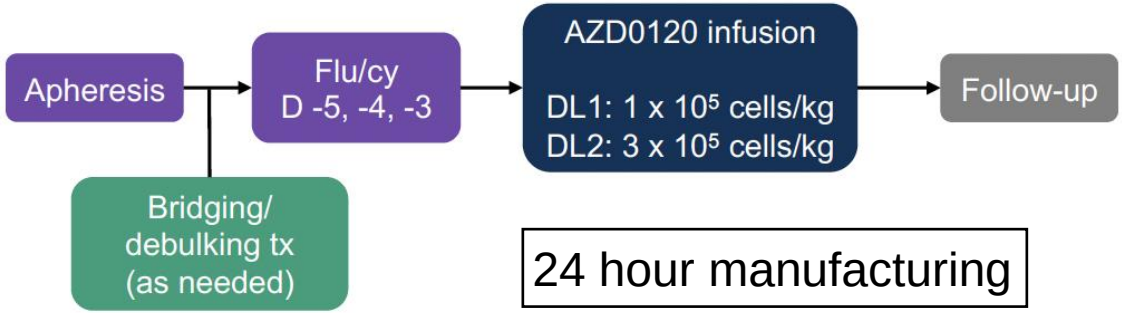
BCMA-CD19: Dual-targeted FasT CAR

DURGA -1 Assessed AZD0120 in RRMM[1]

Key Inclusion Criteria

- ≥3 prior LOT (exposure to PI, IMiD, and anti-CD38 Ab required)
- Documented evidence of PD with most recent LOT
- Prior exposure to BCMA-directed therapy permitted

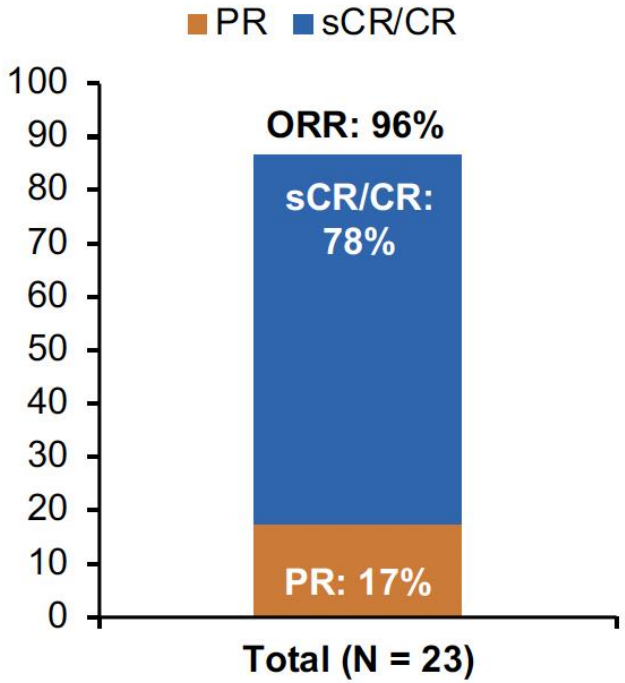
DURGA -1



Phase 1b primary objectives: safety/tolerability, RP2D determination

1. Richard S et al. ASH 2025. Abstract 269. 2. Richard S et al. Tandem 2026. Abstract 37.

DURGA -1: Early Evidence Showed Deep Responses With BCMA x CD19 Dual-Targeting CAR-T Therapy in RRMM[1,2]



- Median follow-up: 3.9 mo
- Median time to first response: 28 d
- Responses deepen over time

%	Total (N = 23)	BCMA CAR-T Exposed (n = 5)
ORR	96	100
sCR/CR	78	80

- 94% MRD negativity in 17 MRD-evaluable patients
- All patients achieved MRD negativity by month 1

No Delayed Tox

1. Richard S et al. ASH 2025. Abstract 269. 2. Richard S et al. Tandem 2026. Abstract 37.

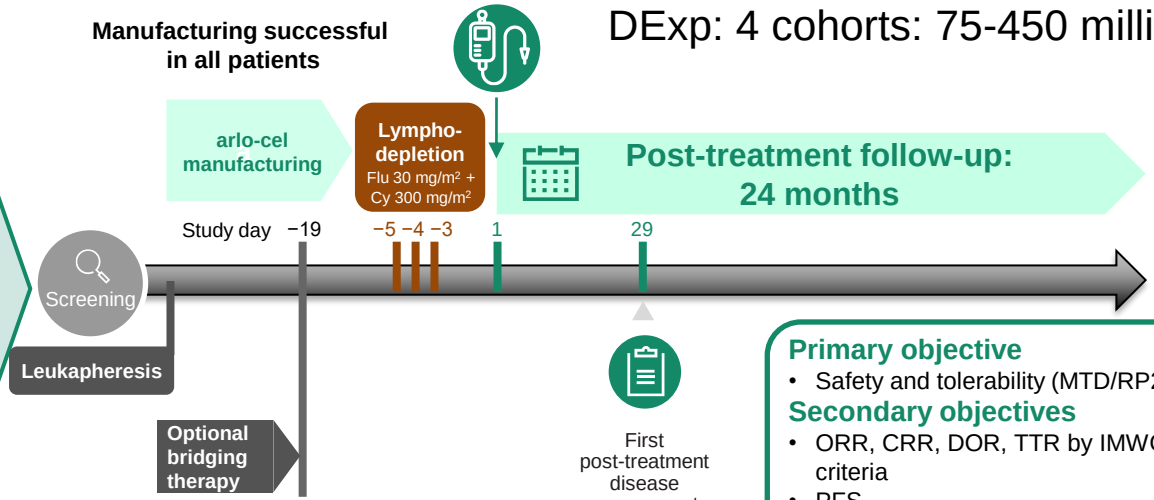
Arlo-cel: A GPRC5D Targeted CAR T-Cell Therapy

Phase 1 in patients with heavily pretreated (≥ 3 PLoT) RRMM

Part A and Part B, Cohort A: key eligibility criteria

- **Age ≥ 18 years**
- **RRMM that progressed ≤ 12 months of the most recent regimen per IMWG criteria[a]**
- **Previously exposed to ≥ 3 antimyeloma treatment regimens, including:**
  - **a PI**
  - **IMiD agent**
  - **Anti-CD38 therapy**
  - **ASCT (unless ineligible)**
- **Prior BCMA-directed therapies allowed, including CAR T cell therapies**
- **ECOG PS 0–1**

DEsc: 5 cohorts: 25-450 million
DExp: 4 cohorts: 75-450 million



Primary objective
- Safety and tolerability (MTD/RP2D)

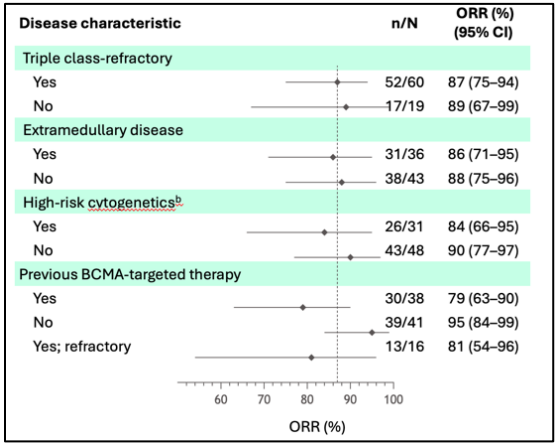
Secondary objectives
- ORR, CRR, DOR, TTR by IMWG criteria
- PFS
- OS

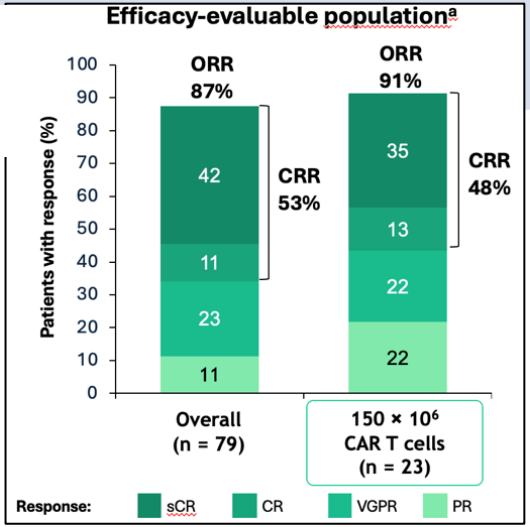
Exploratory objectives
- MRD-negative status
- Pharmacodynamics

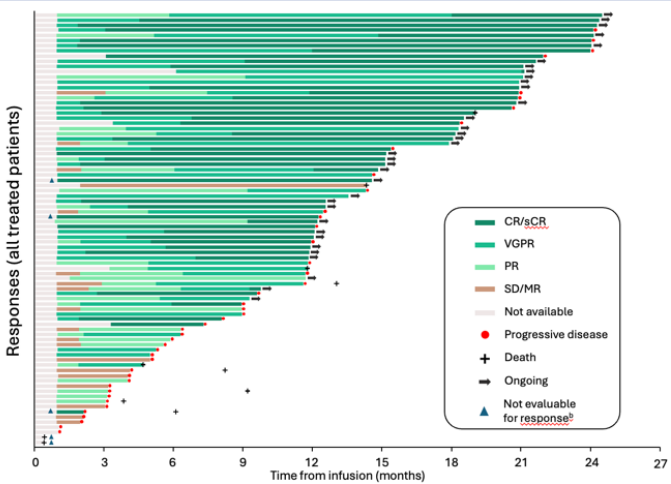
[a] Unless most recent therapy was CAR T-cell therapy, which could be ≥ 12 months prior. [b] Alternative bridging therapy was allowed after discussion with the medical monitor. arlo-cel, arlocabtagene autoleucel; ASCT, autologous stem cell transplant; BCMA, B-cell maturation antigen; CAR, chimeric antigen receptor; CRR, complete response rate; CVAD, cyclophosphamide, vincristine, doxorubicin, and dexamethasone; Cy, cyclophosphamide; DCEP, dexamethasone, cyclophosphamide, etoposide, and cisplatin; DEX, dexamethasone; DOR, duration of response; Flu, fludarabine; GPRC5D, G protein–coupled receptor class C group 5 member D; IMiD, immunomodulatory imide drug; IMWG, International Myeloma Working Group; MM, multiple myeloma; MRD, minimal residual disease; MTD, maximum tolerated dose; ORR, overall response rate; OS, overall survival; PFS, progression-free survival; PI, proteasome inhibitor; PLoT; prior lines of therapy; PS, performance status; RP2D, recommended phase 2 dose; RR, relapsed/refractory; TTR, time to response; VD PACE, bortezomib, dexamethasone, cisplatin, doxorubicin, cyclophosphamide, and etoposide. Bal S et al. ASH 2024. Abstract 922.

Arlo-cel in RRMM Results

Phase 1
- >79 treated
- 23 @ 150
- F/u 16m

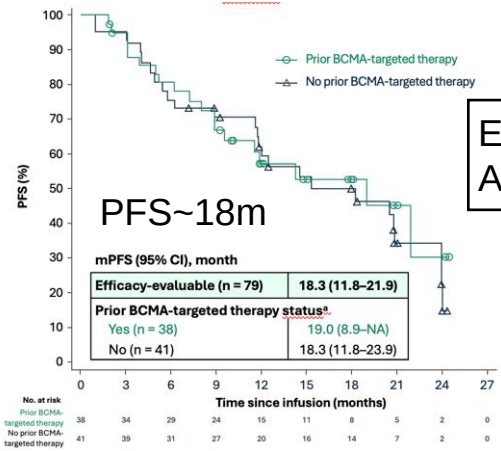






Results:

* ORR similar in prior BCMA Rx
* Overall - mPFS 18.3 m
  - Toxicity
    - Skin (30%)
    - Nails (19%)
    - Mouth (32%)
    - **Other Neuro (12%)**



Enrolling At 75 mill

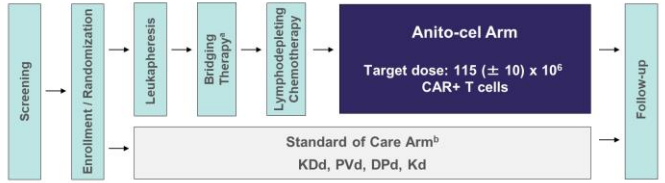
Data cutoff: August 23, 2024. [a] The efficacy-evaluable population includes all patients who received conforming arlo-cel, had measurable disease at the most recent disease assessment prior to arlo-cel infusion, had ≥ 1 post-infusion disease response assessment, and inclusion was irrespective to any possible response to bridging therapy. Five patients were not included in the efficacy-evaluable set; 2 died before the first post-infusion assessment, and 3 because their disease was no longer measurable after bridging therapy. [b] del(17p), t(4;14), and/or t(14;16). arlo-cel, arlocabtagene autoleucel; BCMA, B-cell maturation antigen; CAR, chimeric antigen receptor; CR, complete response; CRR, complete response rate; ORR, overall response rate; PR, partial response; sCR, stringent complete response; VGPR, very good partial response. Bal S et al. ASH 2024. Abstract 922.

Ongoing randomized trials of T-Cell in 2nd LOT and beyond

P3 BCMA CAR
- 12/23/26

iMMagine-3: Global Phase 3 Study

iMMagine-3 (NCT06413498) is a global, Phase 3 trial comparing anito-cel to standard of care therapy in patients with RRMM after 1-3 prior LoT, including an anti-CD38 monoclonal antibody and an iMiD

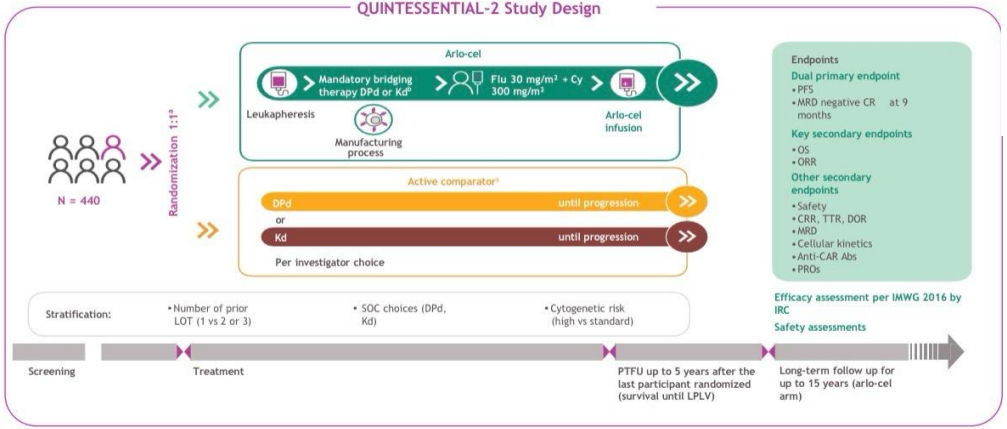


Study Design
- 1:1 Randomization
- n = Approximately 450, ~130 sites globally

Study Endpoints
- Primary Endpoint: PFS
- Key Secondary Endpoints: CR rate, MRD, OS, safety

[a] Bridging therapy will be the SOC regimen selected prior to randomization
[b] Cycles will continue until unacceptable toxicity, progression as per IMWG criteria, or patient withdrawal of consent

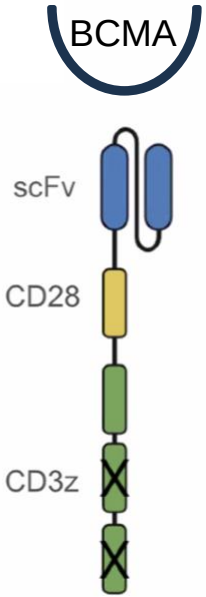
QUINTESSENTIAL-2

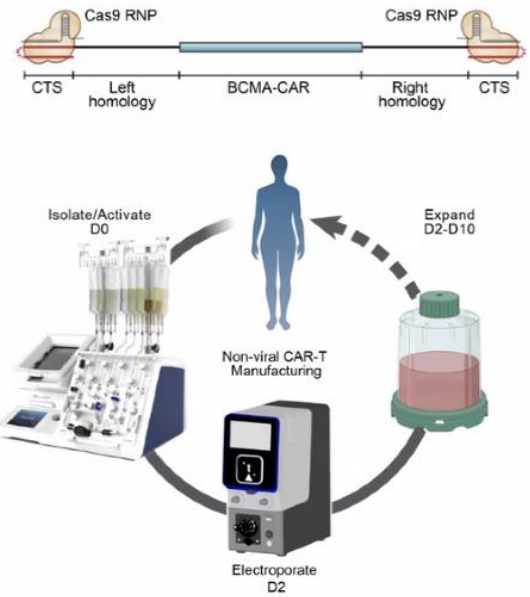


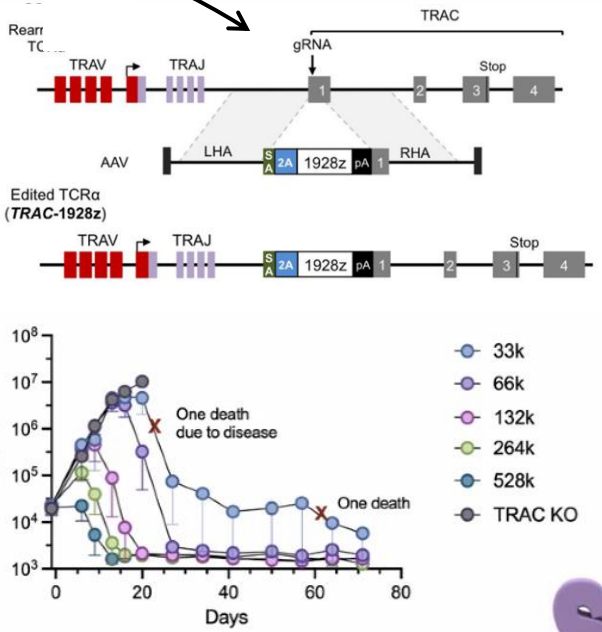
GPRC5D-CAR
- Phase 2 on-going

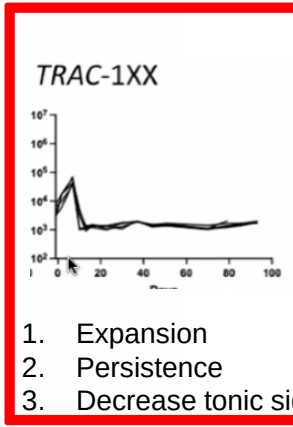
aLeukapheresis to occur within 3 days of randomization. bBridging Therapy to begin within 3 days of leukapheresis. cFirst active comparator dose to occur within 6 days of randomization; no crossover to receive arlo-cel is permitted. Abs, antibodies; CAR, chimeric antigen receptor; CR, complete response; Cy, cyclophosphamide; DOR, duration of response; DPd, daratumumab-pomalidomide-dexamethasone; Flu, fludarabine; IMWG, International Myeloma Working Group; Kd, carfilzomib plus dexamethasone; LOT, lines of therapy; LPLV, last patient last visit; MRD, minimal residual disease; ORR, overall response rate; OS, overall survival; PFS, progression-free survival; PROs, patient reported outcomes; PTFU, post treatment follow up; (RR)MM, (relapsed or refractory) multiple myeloma; SOC, standard of care; TTR, time to response.1. ClinicalTrials.gov. https://clinicaltrials.gov/study/NCT06615479. Accessed May 2025; 2. Bristol-Myers Squibb. Data on File 2025.

UCSF: 1XX-Enhanced and Fully Non-viral BCMA CAR for RRMM









1. Expansion
2. Persistence
3. Decrease tonic signal

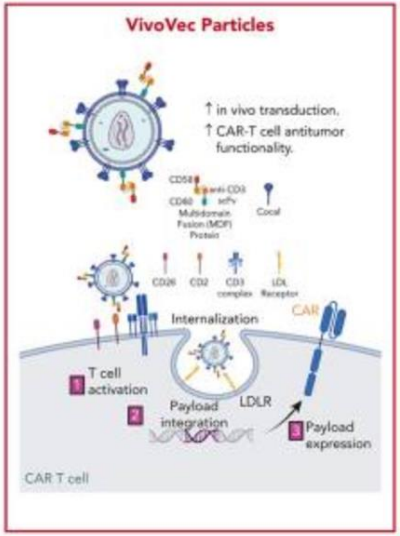
Jenny Lee, Ke Li, Niran Almudhfar, Shanshan Lang, Justin Eyquem

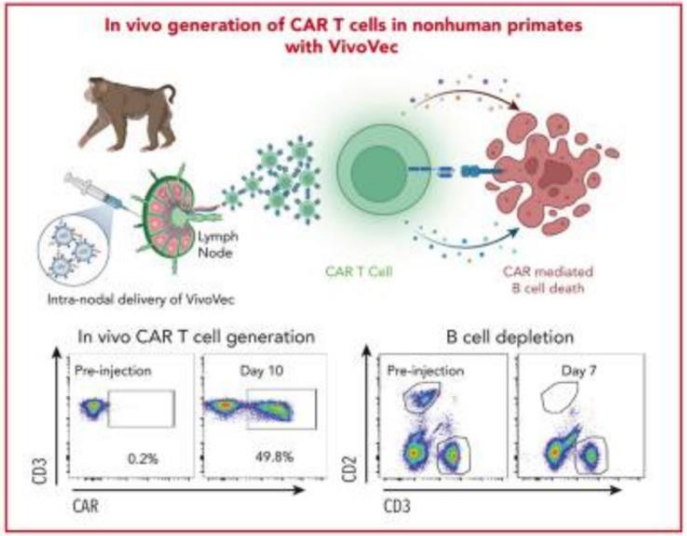
Novel CART Cell Designs

- ***In Vivo* CAR T-cell**
  - Apheresis-NO
  - Ex-vivo manufacturing-NO
  - Quality control testing – NO
  - LD Chemotherapy – NO
  - Reinfusion of CART-NO

  - Off-the shelf- YES
  - Delivery
    - Virus/viral particles
    - Nano-particles
  - Targeted to T-cells – Yes
  - *In vivo* T-Cell Expansion YES

In Vivo CAR T-Cell Generation in Nonhuman Primates Using Lentiviral Vectors Displaying a Multidomain Fusion Ligand





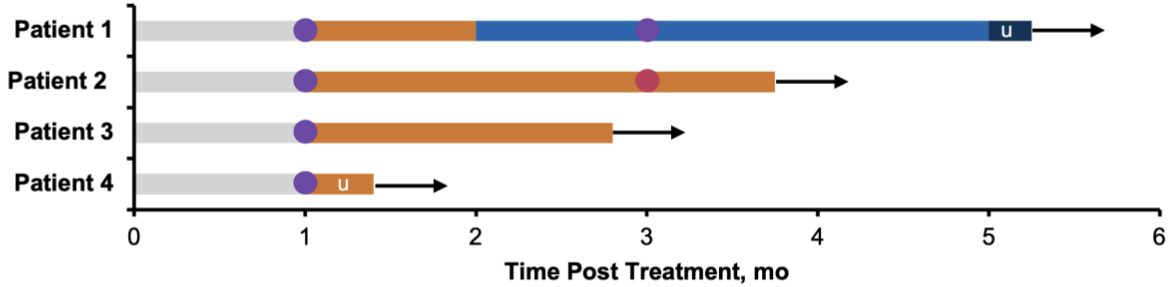
Conclusion: Administration of VivoVec particles into nonhuman primates in the absence of lymphodepleting chemotherapy resulted in a robust generation of anti-CD20 CAR T cells and complete depletion of B cells.

*Nicolai et al. DOI: 10.1182/**blood**.2024024523*

blood Visual Abstract

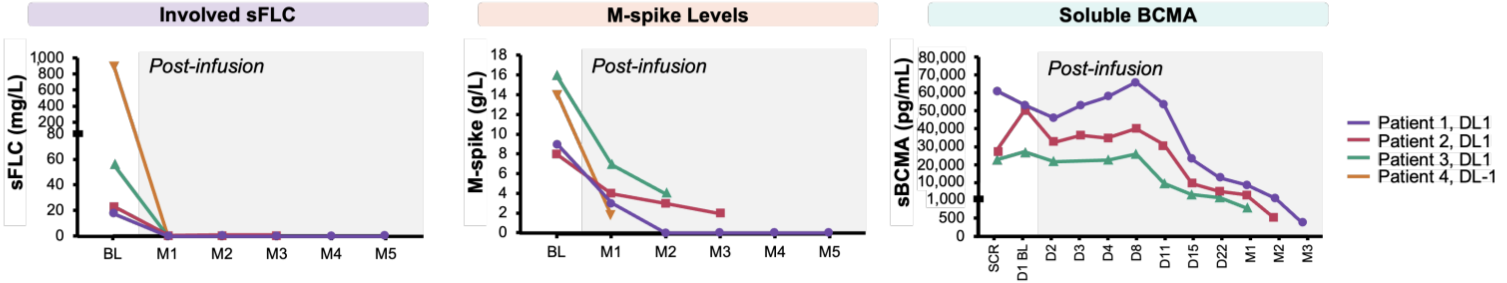
inMMyCAR: "Off-the-Shelf" In Vivo CAR-T Cell Generation Appears Feasible, Safe, and Effective[1]

KLN-1010 Is an Off-the-Shelf Gene Therapy Capable of Generating Anti-BCMA CAR-T Cells In Vivo for Patients With RRMM after ≥3 Prior Therapies



VGPR
PR
MRD negative 10^{-6}
MRD negative 10^{-5}

Most sensitive result from next generation flow cytometry or sequencing



- All instances of CRS were grade 1-2
- No ICANS or delayed neurotoxicity
- Cytopenias were limited (only one case of grade 4; transient neutropenia related to margination)
- Infusion-related reactions in 3/4 patients (two grade 2, one grade 3)–all received prophylactic tocilizumab after the first patient
- Persistent memory T cells in all patients; phenotypic evidence of memory CAR-T cell formation in blood after KLN-1010 treatment

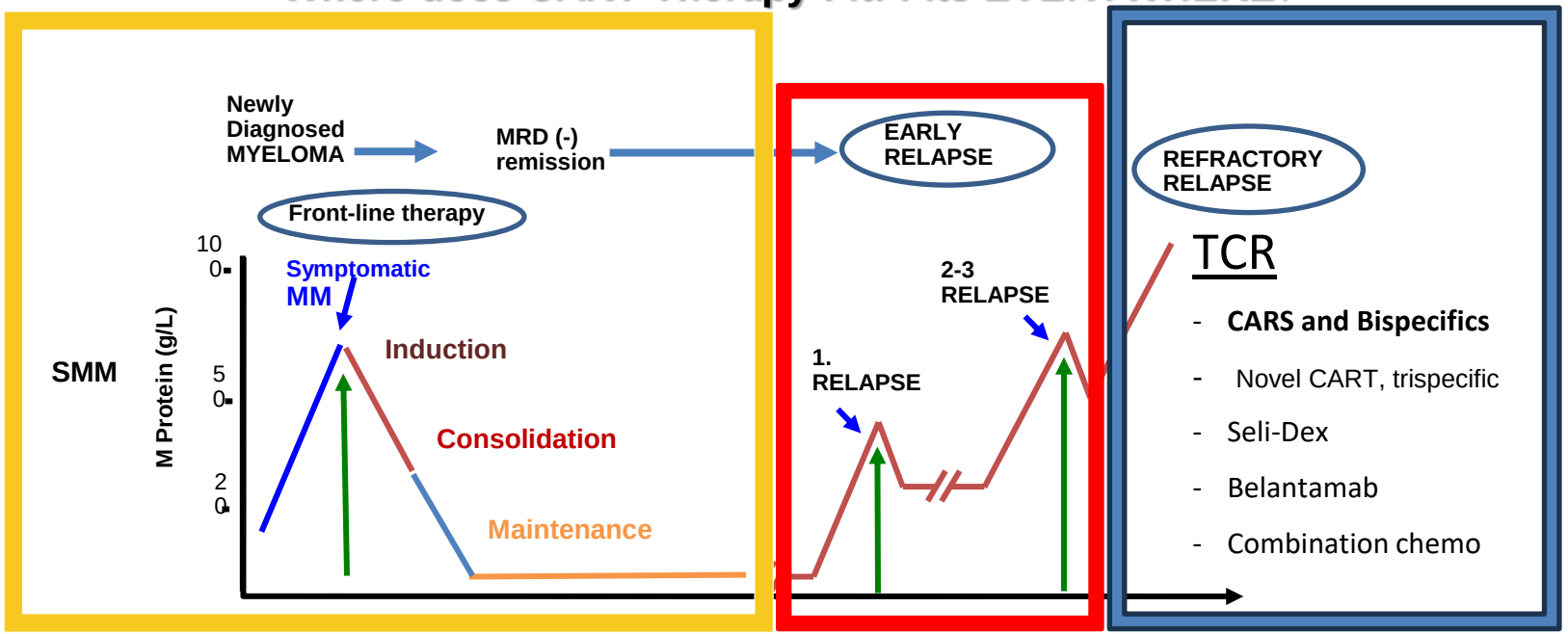
Harrison et al. ASH 2025

Summary

CART Therapy	Target/Binder	ORR	PFS	TRM*	Toxicity
Cilta-cel CART-4 *n*=208	BCMA (VHH)	84.6%	59.4% @33.6m	3-5%	Delayed Neuro-tox, IEC-EC (2-5%)
Ide-cel KarMM-3 *n*=254	BCMA (Murine scFv)	71% (≥CR = 44%)	13.8m (20.7m effective bridging)	2.7%	Low rates of delayed tox (<1%)
Zevo-CAR (approved - China) *n*=102	BCMA (Hum-scFv)	92.2 (%≥CR = 72%)	61.9% @18m	NR	No – IEC-EC, No-late Neurotox
AZD0120 Durga-1 *n*=29	BCMA/CD19 FasTCAR	100%	NR	NR	No – IEC-EC, No-late Neurotox
Anito-cel *n*=117	BCMA (D-domain)	>90%	30.2 months	NR	No – IEC-EC, No-late Neurotox
Arlo-cel	GPRC5D	87%	18.3m	NR	Non-ICANS neurotox 12%

*Need to report NRM or (RFS + IEC-Park + IEC-EC (N-GRFS))

Where does CART Therapy Fit: Fits EVERYWHERE?



Frontline
Induction Quads (CD38+PI/IMiD+Dex) **Consolid.** AutoSCTx. **Maint** R/DR

Early Relapse
(1-3 Prior Line): Triplets
Bela Triplets

Late Relapse
Recycle agents,
Survival <12 mos

Active therapy → **Time off therapy**

Conclusions

1. Cilta-cel remains the most potent CAR T-cell therapy
2. Cilta-cel is associated with >33% RFS @ 5 years in heavily pretreated
3. In early RRMM – perhaps >50% 5 year RFS, and less significant toxicity
4. Novel CARS may have lower potency but less toxicity (can they achieve plateau)
5. Can dual targeting get deeper remissions and exceed PFS1+PFS2.
6. In vivo CAR has generated significant enthusiasm ➔. *OFF THE SHELF*
7. Sequencing studies are needed!!!
8. “Cure” wins – whatever the platform

Future treatment paradigms.....

SCT eligible

QUAD Induction (4-6 cycles) → **CAR-T cell** → BsAb Maintenance (1, 2 yr)

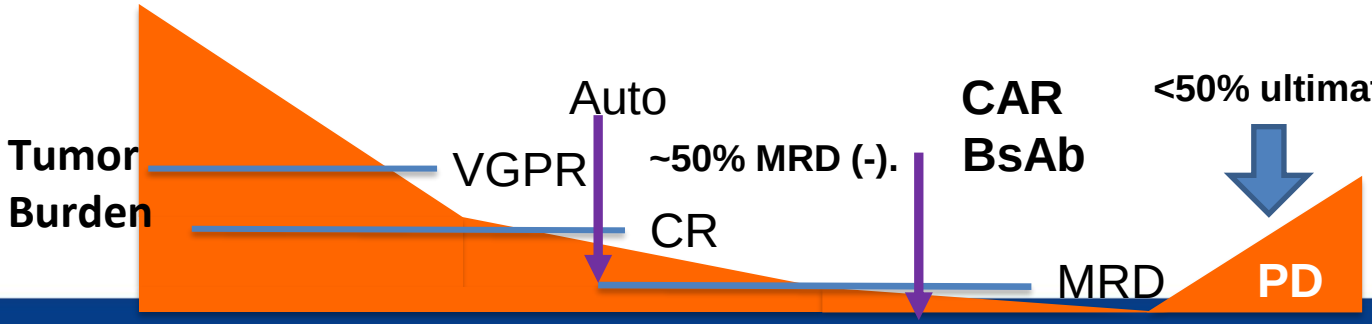
CAR eligible

Quad Induction (4-6 cycles) → **BsAb +/- partner** → Iber/BsAb Maintenance (1, 2 yr)

Frail

BsAb +/- partner(Cd38) → **BsAb (different target)**

Relapse



Many Other CAR Startegies being investigated

1. BCMA-GPRC5D dual targeted CART
2. BCMA-Taci dual targeted CART
3. CAR-Enhancers
4. TRUCKS
5. mRNA vaccines with CARs

Holding Therapy, Bridging Therapy, and Lymphodepletion Chemotherapy in MM

Holding therapy
- Definition: before apheresis
- Goal: control disease without jeopardizing feasibility of CAR T-cell therapy
- Not standardized
- Often used: PIs, IMiDs, anti-CD38 mAbs, dex
- Avoid use of alkylators, bendamustine, polychemotherapy, TCEs

Apheresis ←

→ **CAR T-Cell Infusion**

Bridging therapy
- Definition: after apheresis, waiting for CAR T-cell therapy
- Goal: avoid clinical deterioration, reduce disease burden
- Not standardized
- Often used: PIs, IMiDs, anti-CD38 mAbs, dex
- Acceptable: alkylators, bendamustine, polychemotherapy, TCEs

Lymphodepletion CT
- Standardized
- Timed with CAR T-cell infusion
- Goal: induce extreme lymphopenia and corresponding cytokine milieu
- Fludarabine + cyclophosphamide
- Limited data for bendamustine
- Dose adjustment/drug choice influenced by renal function

Adapted from Costa. Leukemia. 2025;39:543.