CAR T Strategies for Multiple Myeloma

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- Advisory board: BMS, Johnson and Johnson, Pfizer, Regeneron, Takeda, Legend Biotech, Kite, Novartis, Sanofi, Abbvie, Genentech, Astra Zeneca
- Scientific Advisory Board: BMS, Oricell, Kite

Currently Approved T cell Redirecting Therapies in R/R MM

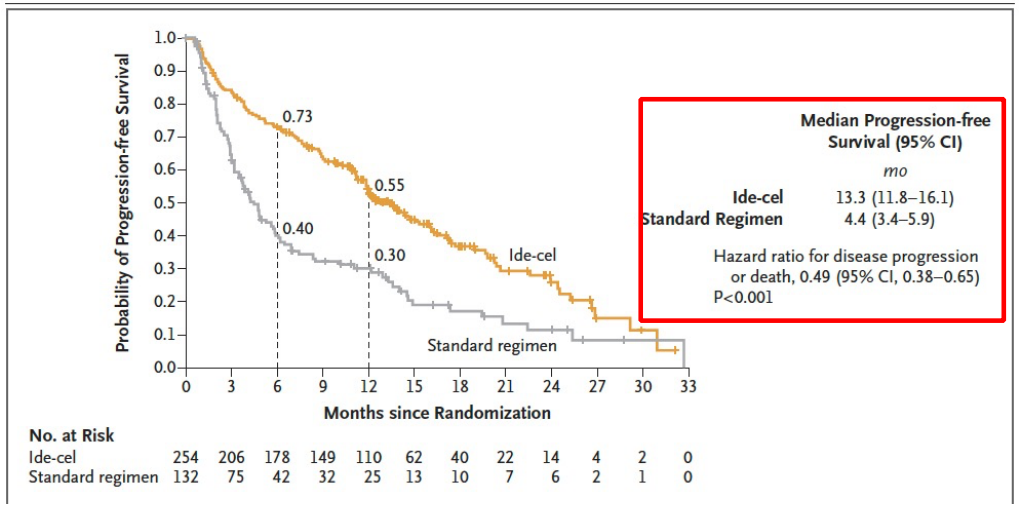
Agent	Category	Indication in R/RMM	Approval date
Idecabtagene vicleucel (BCMA)	CAR T-cell therapy	After >4 prior lines of therapy, including a PI, an IMiD, and an anti-CD38 mAb After ≥2 prior lines of therapy, including a PI, an IMiD, and an anti-CD38 mAb	March 2021 March 2024
Ciltacabtagene autoleucel (BCMA)	CAR T-cell therapy	After >4 prior lines of therapy, including a PI, an IMiD, and an anti-CD38 mAb After ≥ 1 prior line of therapy, including a PI and IMiD (refractory)	February 2022 March 2024
Teclistamab (BCMA)	Bispecific antibody	After >4 prior lines of therapy, including a PI, an IMiD, and an anti-CD38 mAb	October 2022
Talquetamab (GPRC5D)	Bispecific antibody	After >4 prior lines of therapy, including a PI, an IMiD, and an anti-CD38 mAb	August 2023
Elranatamab (BCMA)	Bispecific antibody	After >4 prior lines of therapy, including a PI, an IMiD, and an anti-CD38 mAb	August 2023

CAR, chimeric antigen receptor; IMiD, immunomodulatory agent; mAb, monoclonal antibody; MM, multiple myeloma; PI, proteosome inhibitor; R/R, relapsed/refractory; TCE, T-cell engager. FDA. Development & approval process | drugs. https://www.fda.gov/drugs/development-approval-process-drugs.

Randomized Phase 3 Data: Early Line Studies

KarMMa 3

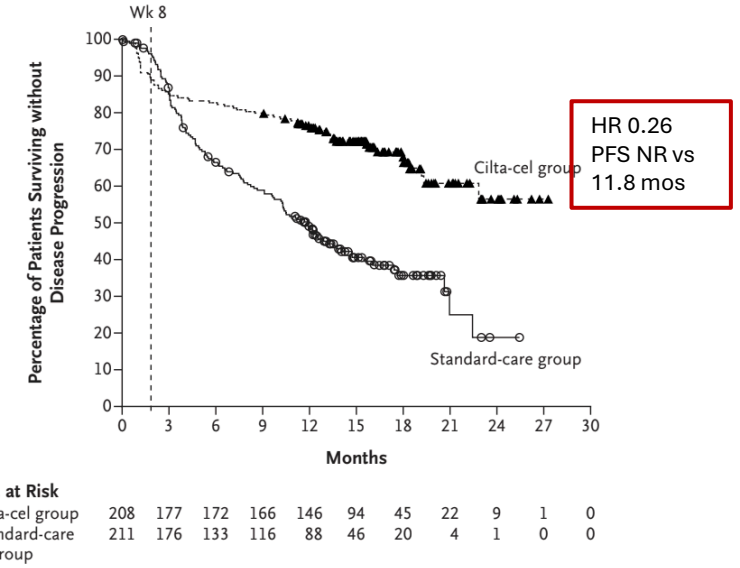
Rodriguez-Otero P, et al. NEJM 2023



- KarMMa 3: TCE, lines 3-5, vs DPD/DVD/KD/EPD/IRD
- >95% TCR

CARTITUDE 4

San Miguel J, et al. NEJM 2023



- CARTITUDE 4: lenalidomide refractory, lines 2-4, vs DPD/PVD
- 24% TCE/TCR

Quality of Life

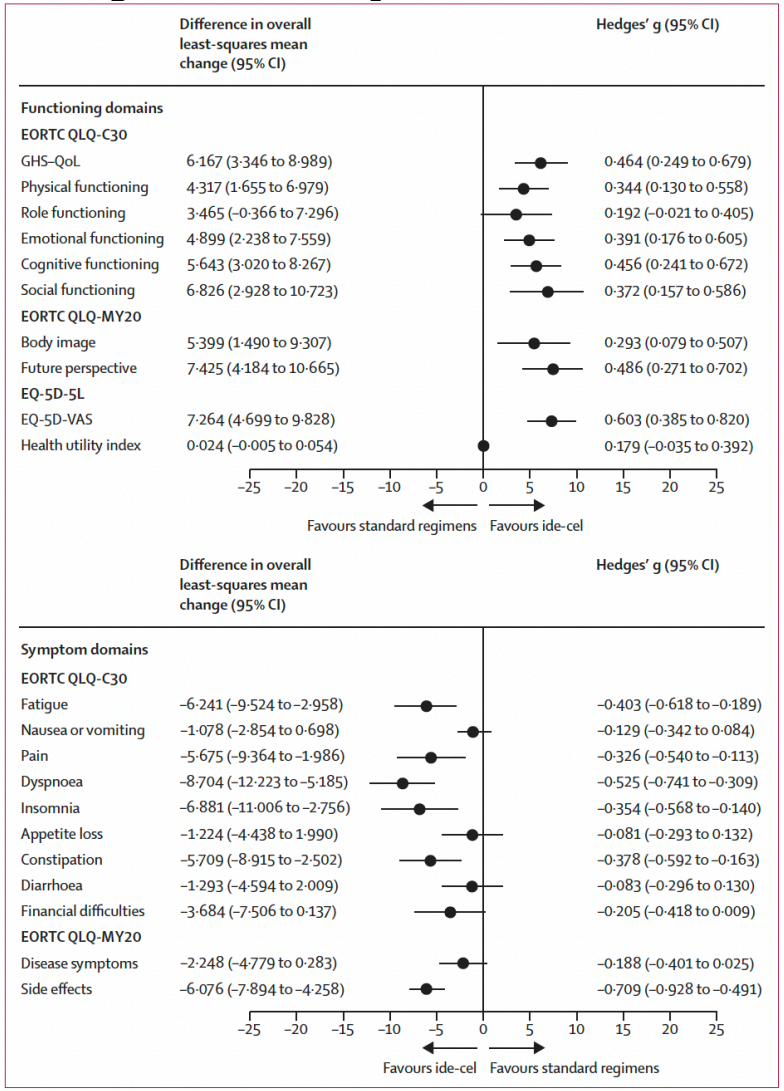


Figure 3: Differences in overall least-squares mean changes from baseline for ide-cel compared with standard regimens at month 20

”In this study, patients receiving ide-cel demonstrated statistically significant and clinically meaningful improvements across most domains, including fatigue, pain, and physical functioning.” [compared to SOC regimens]

Delforge, et al. Lancet Haematology2024

	Cilta-Cel (n = 99)	SOC (n = 66)
EORTC QLQ-C30, mean change (95% CI)		
Global health status/QoL		
Global health status	10.1 (7.0-13.1)	-1.5 (-5.3 to 2.3)
Functional scales		
Cognitive functioning	0.5 (-2.4 to 3.5)	-7.5 (-11.2 to -3.9)
Emotional functioning	9.5 (6.6-12.5)	2.2 (-1.3 to 5.7)
Physical functioning	6.5 (3.8-9.1)	-2.1 (-5.0 to 0.7)
Role functioning	7.7 (3.7-11.7)	-1.7 (-6.3 to 2.9)
Social functioning	6.1 (2.1-10.0)	-0.1 (-4.2 to 4.0)
Symptom scales/items		
Fatigue	-9.1 (-12.4 to -5.8)	2.8 (-1.4 to 7.0)
Nausea and vomiting	-1.2 (-3.1 to 0.7)	0.6 (-1.4 to 2.7)
Pain score	-10.2 (-14.0 to -6.5)	-3.9 (-7.9 to 0.2)
EQ-5D-5L, mean change (95% CI)		
Visual analogue scale	8 (5.2-10.7)	1.4 (-1.9 to 4.7)
MySIm-Q, mean change (95% CI)		
Total symptom subscale	-0.18 (-0.27 to -0.10)	0.17 (0.06-0.27)
Total impact subscale	-0.41 (-0.53 to -0.29)	0.01 (-0.13 to 0.14)

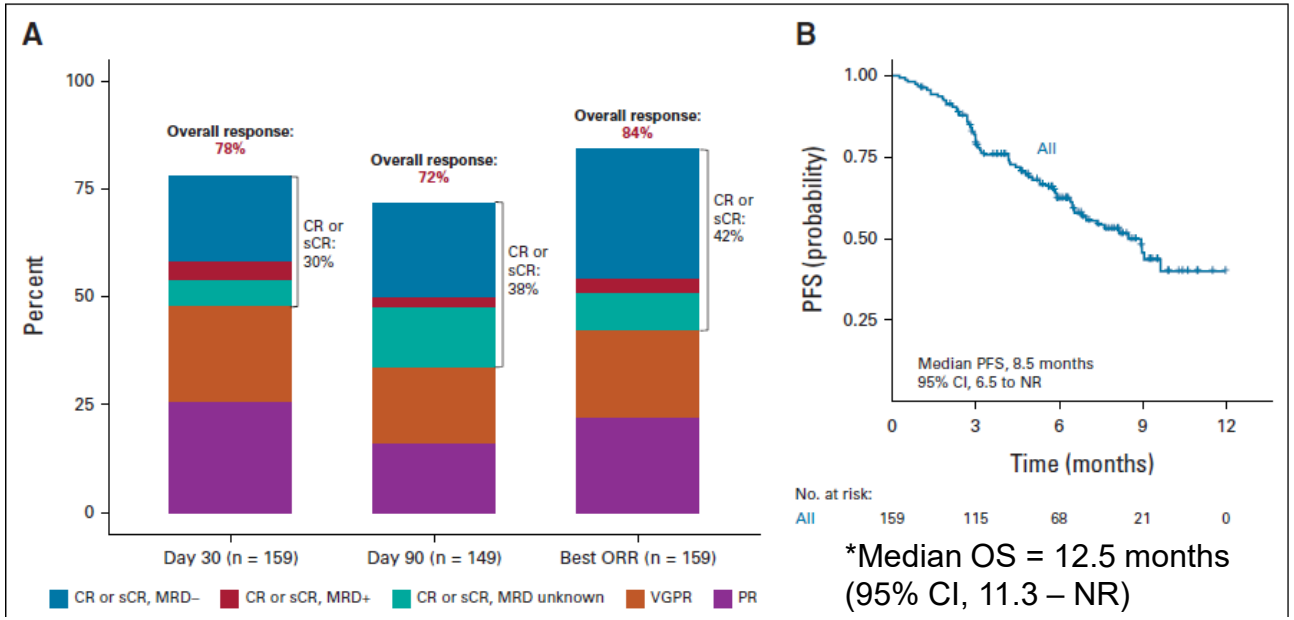
- Meaningful reductions in disease-specific symptoms on multiple PRO endpoints
- Improvements in health-related QoL were numerically greater with cilta-cel than with continuously administered SOC treatments across all scales

Mina R et al. ASH 2023. Abstract 1063.

RRMM CAR T RWE

Ide-Cel

75% pts ineligible for KarMMa

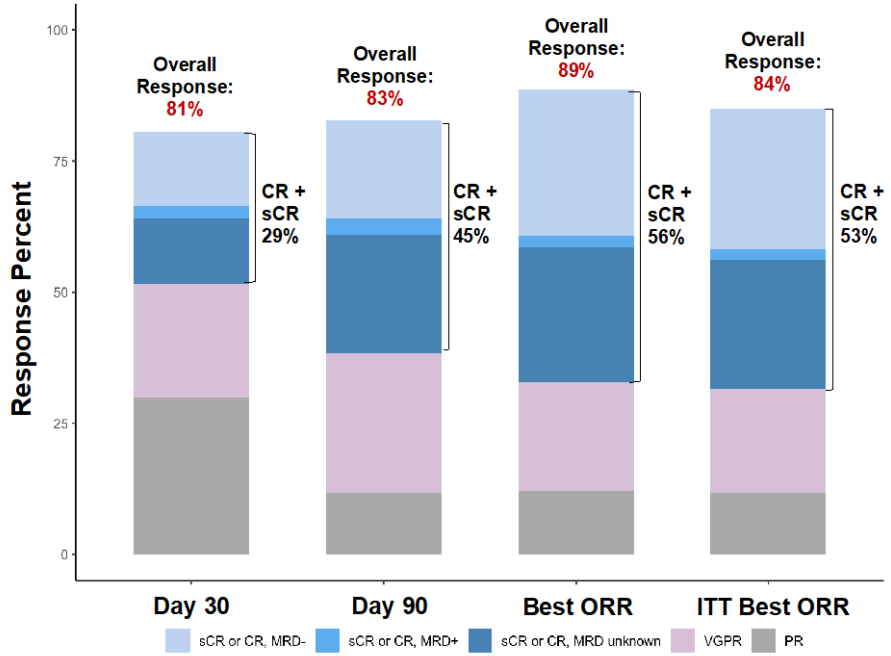


*Median OS = 12.5 months (95% CI, 11.3 – NR)

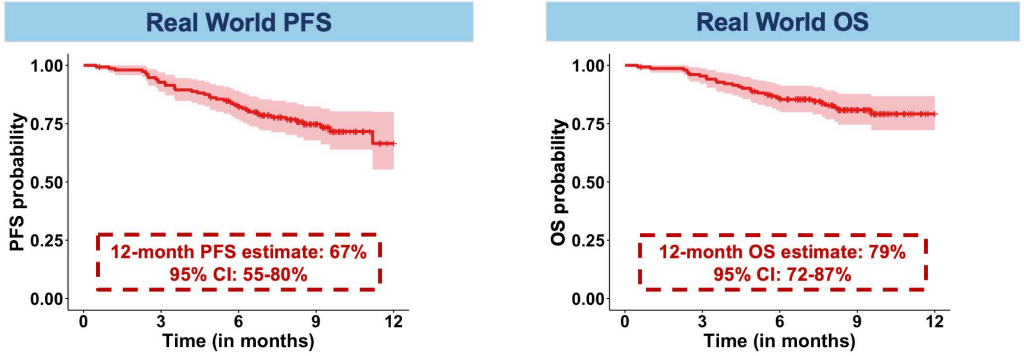
Hansen D, et al. JCO 2023

Cilta-cel

57% pts ineligible for CARTITIUDE



Real World PFS and OS, ITT: Median F/U 8.4 months



Sidana S, et. Al. Blood 2024

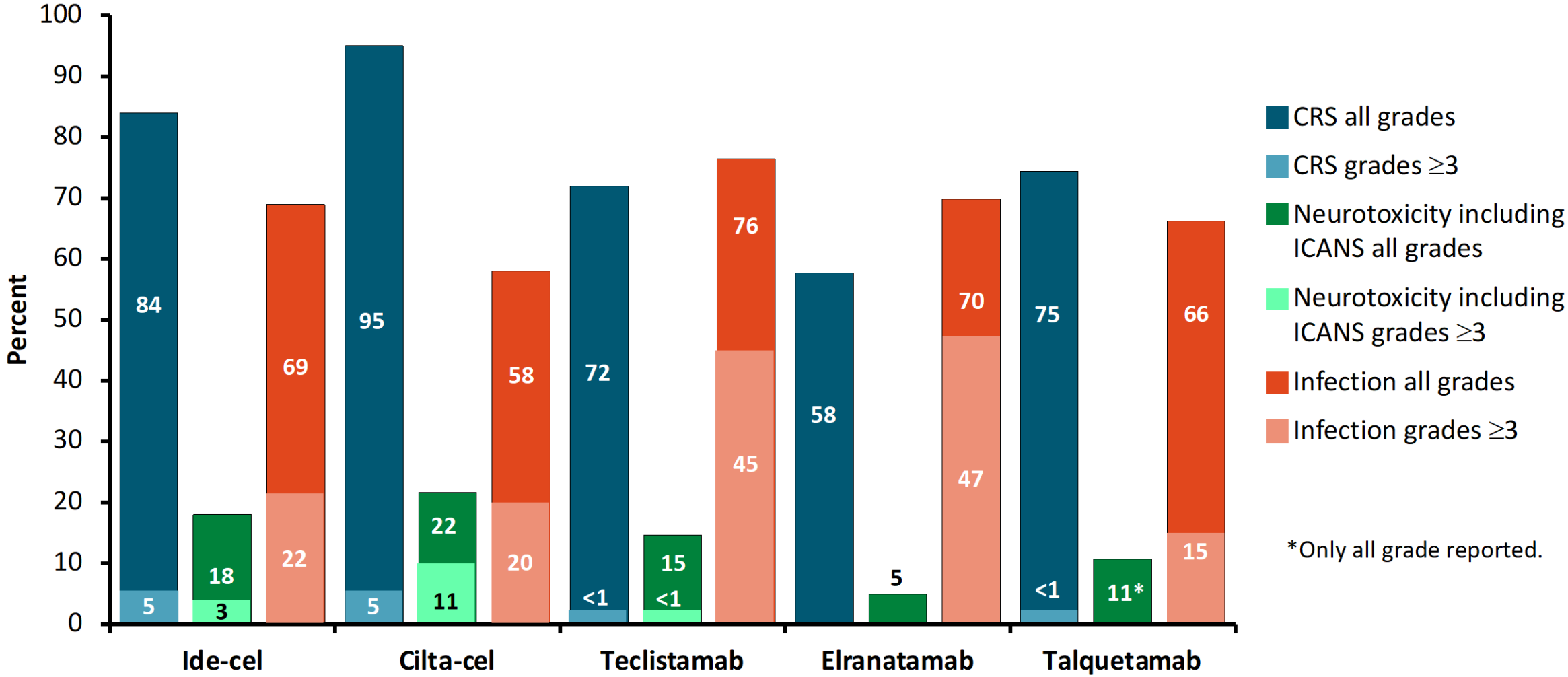
FDA-approved BCMA and GPRC5D Bispecifics

Bispecific antibody	Teclistamab[1]	Elranatamab[2]	Talquetamab[3] Phase 1/2 MonumenTAL-1 Study: GPRC x CD3		
Structure/function	Humanized antibody	Humanized antibody			
Treatment	QW SC	QW SC	0.4 mg/kg QW SC	0.8 mg/kg Q2W SC	Either dose
Patients	n = 165	n = 123	n = 143	n = 145	n = 51
Triple-class refractory	78%	97%	74%	69%	
ORR at RP2D	63%	61%	**74%**	**73%**	**63%** (prior CAR-T/bisp 72%/44%)
RP2D (n)	1.5 mg/kg SC **(n = 165)**	76 mg SC **(n = 123)**			
PFS	11.3 mo (8.8–17.1)	NE at 12 mo	**7.5 mo**	**11.9 mo**	**NR**
DoR	18.4 mo (14.9–NE)	NE at 12 mo	**9.3 mo**	**13.0 mo**	**12.7 + mo**
Median follow up	14.1 mo	14.7 mo			
AEs, all (Gr 3+)					
CRS	72% (0.6%)	58% (0%)	79% (2%)	72% (0.7%)	
Infections	76% (45%)	70% (40%)	57% (17%)	50% (12%)	
Neutropenia	71% (64%)	49% (49%)	34% (31%)	28% (22%)	
Anemia	52% (37%)	49% (37%)	45% (32%)	39% (25%)	
Thrombocytopenia	40% (21%)	31% (24%)	27% (20%)	27% (17%)	
Neurotoxicity	15% (0.1)	NR/NR	11% (1.6%)	10% (1.8%)	
Deaths	68 (41 due to PD)	55 (37 due to PD)	0 due to AEs	0 due to AEs	
Hypogamma/IVIg	75%/39%	NR/NR	NR/13%	NR/10%	
			Dysgeusia 48% (N/A)	Dysgeusia 46% (N/A)	
			Skin 56% (0%)	Skin 67% (0.7%)	
			Nail 52% (0%)	Nail 43% (0%)	

AE, adverse event; BCMA, B-cell maturation antigen; CRS, cytokine release syndrome; DoR, duration of response; FDA, Food and Drug Administration; GPRC5D, G protein–coupled receptor, class C group 5 member D; ICANS, immune effector cell-associated neurotoxicity syndrome; IV, intravenous; NE, not evaluable; NR, not reported; mo, month; ORR, overall response; PFS, progression-free survival; QW, every week; Q2W, every 2 weeks; RP2D, recommended phase II dose; SC, subcutaneous.

1. Moreau P, et al. *N Engl J Med*. 2022;387:495-505; 2. Lesohkin AM, et al. *Nat Med*. 2023;29:2259-2267; 3. Data provided by Lonial S.

Summary of Selected AE With CAR T-Cell Therapy and Bispecific Antibodies in R/R MM



- Results are from different clinical trials/populations and should not be used for cross-comparison

Ludwig. Lancet Oncol. 2023;24:e255. Munshi. NEJM. 2021;384:705. Martin. JCO. 2023;41:1265. Moreau. NEJM. 2022;387:495. Tomasson. ASH 2023. Abstr 3385. Schinke. ASCO 2023. Abstr 8036.

T Cell Redirection Toxicities

- Infections (target dependent?, anti-BMCA higher risk)
- Prolonged cytopenias
- Hypogammaglobulinemia (target dependent?, anti-BCMA higher risk)
- Delayed neurotoxicity (Parkinsonianism versus facial palsies)
- GPRC5D (TCE >>> CAR T): Dysgeusia/weight loss, skin/nail changes
- Worsening of comorbidities (delirium, heart failure, renal insufficiency, liver toxicity, lower GI, pulmonary toxicity)
- Secondary cancers (T cell, myeloid)

RW Problems: Sequencing different BCMA therapies

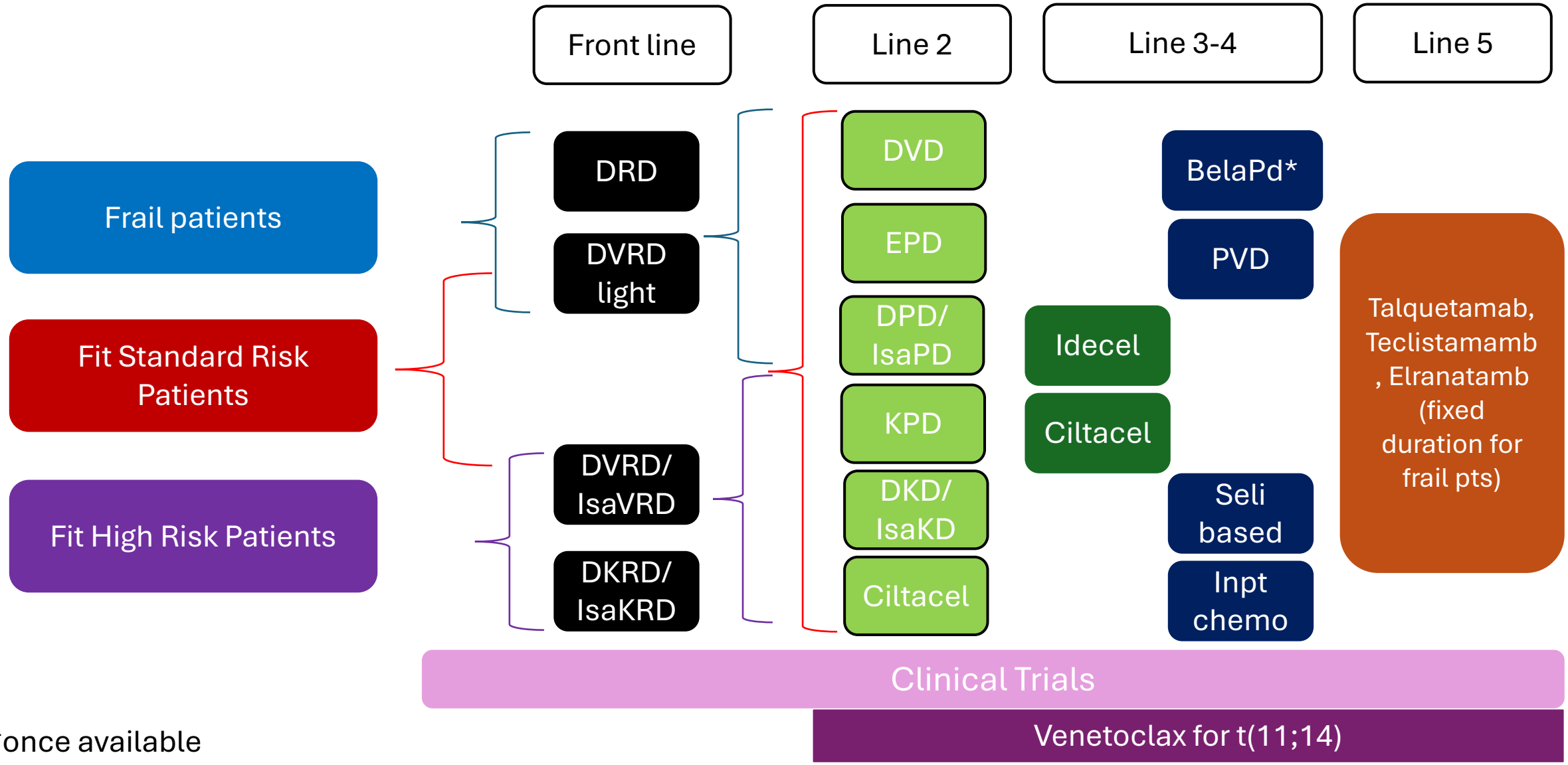
- Studies with BCMA/CD3 bispecific T cell engagers in patients with prior BCMA CAR T therapy (i.e. elranatamab, teclistamab) demonstrate approximately 10% lower ORR, DOR for elra NR @ 10 months

- Studies with BCMA CAR T therapy in patients with prior BCMA therapy reveal a significantly lower ORR/PFS for ciltacel (60%, 6 months) and lower PFS for idecel (3 months) in RWE.

- Each of these studies has a small n, however, in a hypothetical world that had no access issues, I would recommend CAR T first for eligible patients.

Cohen A, et al. Blood 2023
Ferreri et al. BCJ 2023

What I do today:



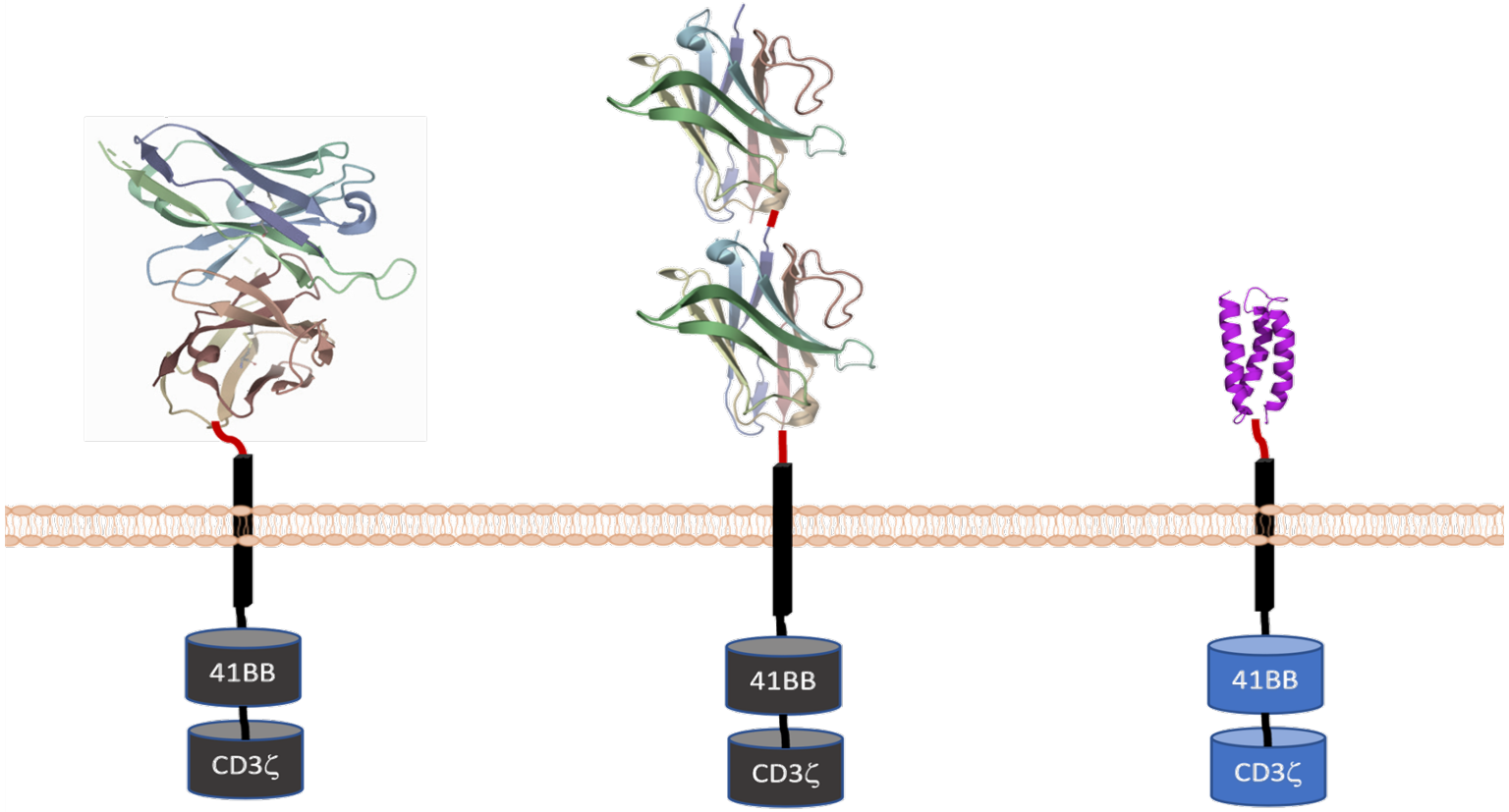
*once available

Current Research Trials in RRMM

- Next in line BCMA therapies
- New targets
- Combinations
- Improving on toxicity

Anitocabtagene autoleucel (anito-cel/CART-ddBCMA)

Autologous BCMA-directed CAR T-cell therapy using a novel, D-Domain binder[1]



scFv
(~25 kDa)

Bivalent camelid VHh
(~25 kDa)

D-Domain
(~8 kDa)

D-Domain Attributes:
Non-Antibody Derived Synthetic Protein[1,2]

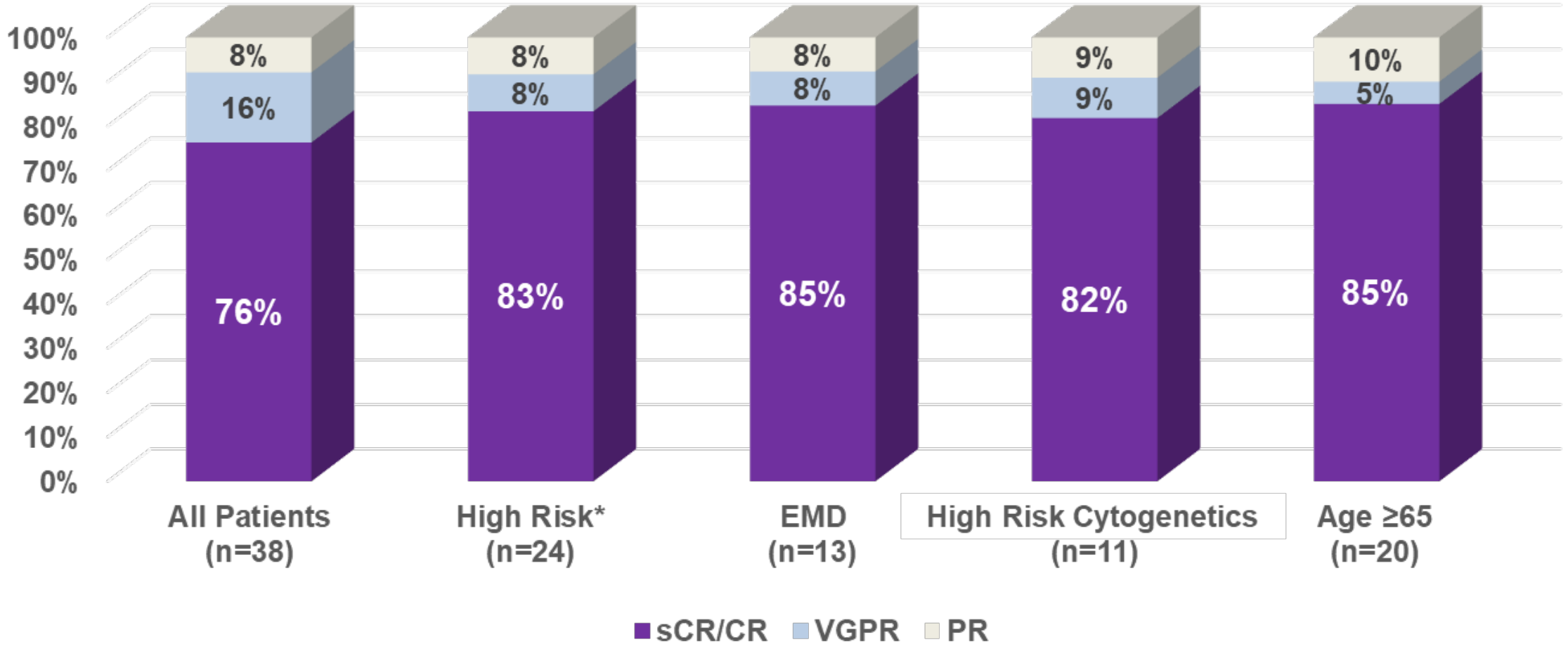
Size	**Small D-Domain construct facilitates high transduction efficiency, CAR positivity, and CAR density on the T-cell surface[2-4]**
Stability	**Rapid D-Domain folding, lack of disulfide bonds, and a hydrophobic core enables stability at and beyond physiologic conditions[5,6]**
Structure	**Due to small size and compact structure, D-Domain CARs have a low risk of tonic signaling[6]**

[1]Rotte, et al. *Immuno-Oncology Insights* 2022; 3(1), 13–24; [2]Frigault, et al. *Blood Adv*. 2023; 7(5):768-777; [3]Cante-Barrett, et al. *BMC Res. Notes* 2016; 9:13; [4]Buonato, et al. *Mol. Cancer Ther.* 2022; 21(7):1171-1183; [5]Zhu, et al. *Proc. Nat. Acad. Sci.* 2003; 100(26): 15486-15491; [6]Qin, et al. *Mol. Ther.* 2019; 27(7): 1262-1274.

Frigault M, et al. ASH 2023 Abstract 1023

Anito-cel Phase 1 Results: Best Overall Response

All Patients & High-Risk Sub-Groups

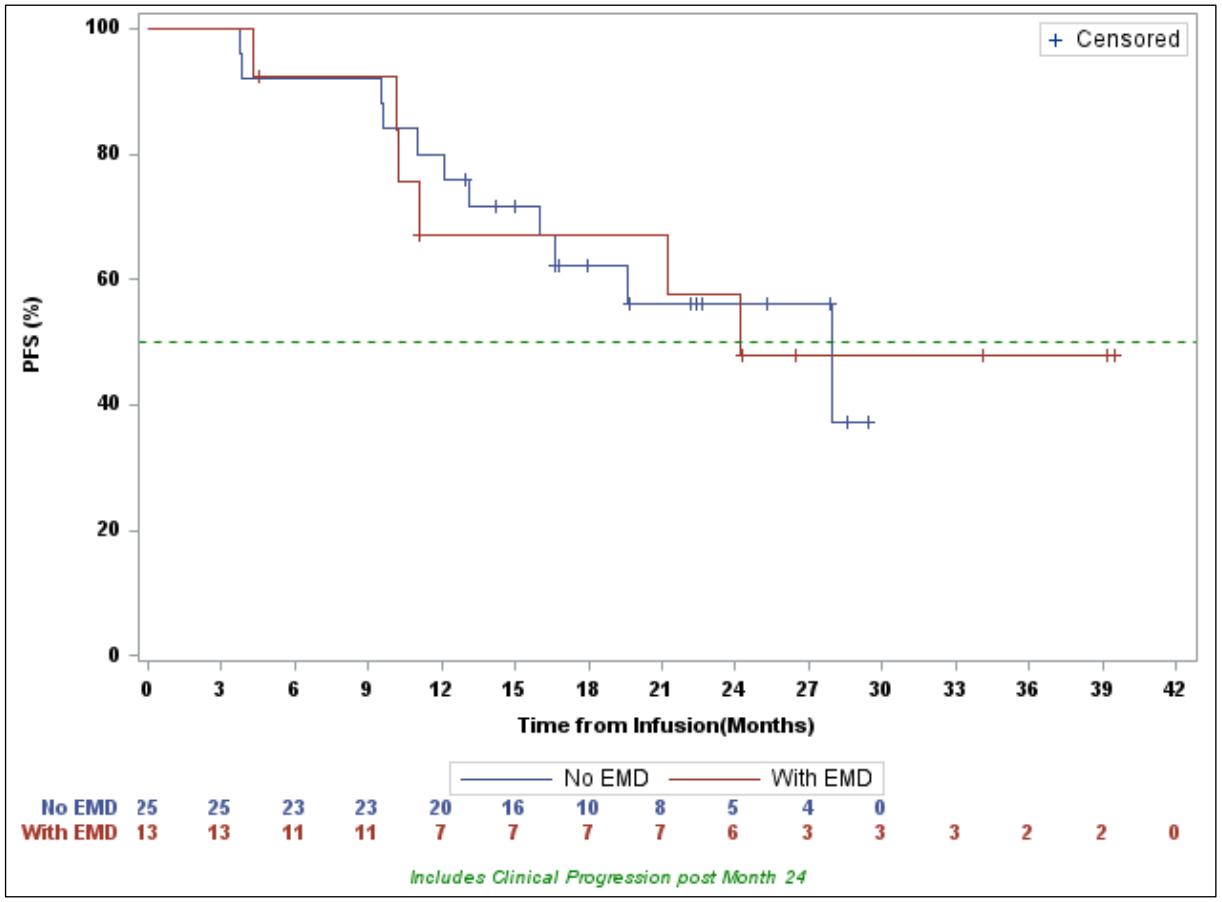


* High Risk defined as a patient with EMD, ISS Stage III (B2M ≥ 5.5), or BMPC ≥ 60%

Frigault M, et al. ASH 2023 Abstract 1023

Anito-cel Phase 1 Results: EMD, Non-EMD Patients

Median Follow-Up: EMD Patients ~33-mo. [14-44]; Non-EMD Patients ~25-mo. [15-40]



	Time (months)	PFS Estimate (%)	95% Confidence Interval (%)
With EMD (n = 13)	6	92.3	56.6, 98.9
	12	67.1	34.2, 86.2
	18	67.1	34.2, 86.2
	24	57.5	25.7, 79.9

- **Median PFS not reached for patients with EMD (n=13)**
- **Median PFS not reached for Non-EMD patients (n=25)**

Note: Data cut-off October 15, 2023

Frigault M, et al. ASH 2023 Abstract 1023

BCMAxCD3 Bispecifics in Research

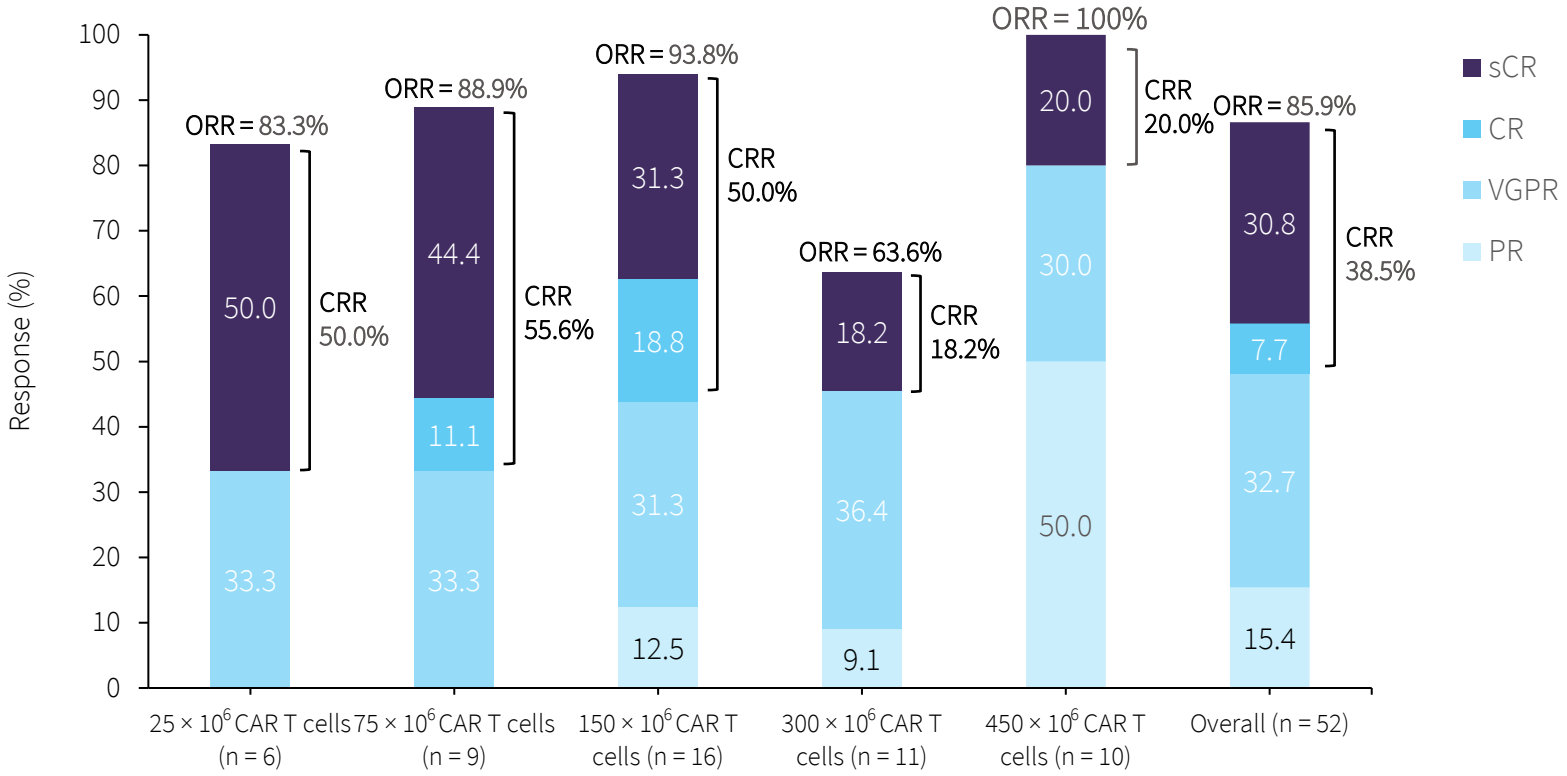
Bispecific antibody	Teclistamab[1,2] (JNJ-64007957)*	Elranatamab[3] (PF-06863135)*	Linvoseltamab[4] (REGN5458)	ABBV-383[6]	HPN217[7]
Structure/function	Humanized antibody	Humanized antibody	*Veloci-Bi*® platform fully human antibody	Low CD3 affinity fully human antibody	Trispecific 50kDa (albumin)
Treatment	QW SC	QW SC	QW IV	Q3W IV	Q2W IV
Patients	n = 165	n = 123	n = 252	n = 124	n = 97
Median prior lines	5	5	5	5	6
Triple-class refractory	78%	97%	81%	82%	70%
ORR at RP2D	63%	61%	64%	57%	63%
RP2D (n)	1.5 mg/kg SC (n = 165)	76 mg SC (n = 123)	200 mg IV (n = 58)	40 mg to 60 mg IV (n = 81 and n = 52)	12 mg (n = 19)
PFS	11.3 mo (8.8-17.1)	NE at 12 mo	NR	10.4 mo	NR
DoR	18.3 mo (15.1–NE)	NE at 12 mo	89% at 6 mo	NR	20.5 mo
Median follow up	14.1 mo/23 mo	10.4 mo	3.2 mo	10.4 mo	
AEs, all (Gr 3+)					
CRS	72% (0.6%)	58% (0%)	44% (1%)	57% (2%)	30 (2%)
Infections	80% (55%)	69% (39%)	54% (29%)	41% (22%)	59% (25%)
Neutropenia	72% (66%)	48% (48%)	25% (23%)	37% (34%)	40% (34%)
Anemia	52% (37%)	48% (37%)	36% (31%)	29% (16%)	44% (34%)
Thrombocytopenia	40% (21%)	30% (24%)	18% (6%)	23% (12%)	28 (18%)
Neurotoxicity	Neurotoxicity 15% (0.1)	NR/ PN	ICANS 2% (1%)	NE	22% (0%)
Deaths	68 (41 due to PD)	55 (37 due to PD)	NR	27	
Hypogamma/IVIg	72%/46%	75%/40%	NR	NE	

AE, adverse event; BCMA, B-cell maturation antigen; CRS, cytokine release syndrome; DoR, duration of response; ICANS, immune effector cell-associated neurotoxicity syndrome; IV, intravenous; IVIG. intravenous immunoglobulin; NE, not evaluable; NR, no response; mo, month; ORR, overall response; PFS, progression-free survival; QW, every week; Q2W, every 2 weeks; Q3W, every 3 weeks; Q4W, every 4 weeks; RP2D, recommended phase II dose; SC, subcutaneous. *Accelerated approval.

1. Moreau P, et al. *N Engl J Med*. 2022;387:495-505; 2. Van de Donk N. Abstract #OA-51. 20th IMS Annual Meeting; Sep 27–30, 2023; Athens, GR; 3. Lesohkin AM, et al. *Nature Med*. 2023;29:2259-2267; 4. Bumma N, et al. *Blood*. 2022;140(Suppl 1):10140-10141; 5. Voorhees PM, et al. *Blood*. 2022;140(Suppl 1):4401-4404; 6. D'Souza A, et al. *J Clin Oncol*. 2022;40(31):3576-3586; 7. Madan S, et al. Abstract

CC95266: GPRC5D CAR T-cells

Best overall response (efficacy-evaluable analysis set*)



Dose level	Median follow-up, months (range)
25 × 10^6 CAR T cells	18.0 (8.2–20.1)
75 × 10^6 CAR T cells	12.0 (6.5–16.0)
150 × 10^6 CAR T cells	6.0 (2.8–11.5)
300 × 10^6 CAR T cells	4.9 (1.0–8.8)
450 × 10^6 CAR T cells	2.3 (1.0–6.0)
Overall	6.0 (1.0–20.1)

300 × 10^6 cohort had the highest:

- Extramedullary disease (59%)
- Median baseline sBCMA (396.3 µg/L)

300 × 10^6 cohort had the lowest:

- Median time to progression on last prior anti-myeloma therapy (4.8 months)†

CAR, chimeric antigen receptor; CR, complete response; CRR, complete response rate; GPRC5D, G protein-coupled receptor class C group 5 member D; ORR, overall response rate; PR, partial response; sBCMA, soluble B-cell maturation antigen; sCR, stringent complete response; VGPR, very good partial response. Data cutoff: March 23, 2023. *The efficacy-evaluable analysis set includes all patients who received conforming BMS-986393 cell product, had measurable disease at the last disease assessment prior to BMS-986393 infusion, and had ≥ 1 post-infusion disease-response assessment. Responses were assessed per International Myeloma Working Group criteria. †Analysis conducted in the treated analysis set. Bal S, et al. Oral Abstract #S193 presented at the 28th Congress of the European Hematology Association, June 8-11, 2023, Frankfurt, DE.

GPRC5D CAR T-cells

TRAEs of interest

	All treated patients (N = 67)	
On-target/off-tumor, n (%)	Any grade	Grade ≥3
Skin*	14 (20.9)	0 (0)
Dysgeusia/taste disorder	12 (17.9)	0 (0)
Nails†	6 (9.0)	0 (0)
Dysphagia	1 (1.5)	0 (0)
Neurotoxicity, n (%)	Any grade	Grade 3‡
ICANS-type neurotoxicity§	7 (10.4)	2 (3.0)
Dizziness	7 (10.4)	1 (1.5)
Headache	7 (10.4)	0
Ataxia	2 (3.0)	0
Neurotoxicity‖	2 (3.0)	0
Gait disturbance	1 (1.5)	0
Dysarthria	1 (1.5)	0
Paresthesia	1 (1.5)	0

Most on-target/off-tumor skin, nail, and oral AEs (76.7%) did not require treatment.

ICANS-type neurotoxicity was reversible with or without intervention.

Non–ICANS-type neurotoxicity appeared to be dose-related; some cases showed evidence of reversibility.

AE, adverse event; ICANS, immune effector cell–associated neurotoxicity syndrome; TRAE, treatment-related adverse event.
Data cutoff: March 23, 2023.*Skin includes preferred terms of pruritis, maculo-papular rash, pain of skin, erythema, and vesicular rash. †Nails includes preferred terms of nail bed disorder and nail disorder. ‡No grade 4 or greater neurotoxicity TRAEs were observed. §One patient with Grade 5 CRS had ongoing Grade 1 ICANS at the time of death. ‖One patient experienced cerebellar toxicity that was coded to neurotoxicity and 1 patient experienced 'neurotoxicity/confusion' that was later updated post-data cut-off to 'ICANS'.
Bal S, et al. Oral abstract #S193 presented at the 28th Congress of the European Hematology Association, June 8-11, 2023, Frankfurt, DE.

Quintessential pivotal study

CA0881000 –Phase II study design

Study Population:

- R/R MM
- Quadruple class exposed
- 3+ PLT
- PD on / after last PLT
- Measurable disease
- ECOG ≤ 1

ICF signature + screening

Open label: GPRC5D-directed CAR T-cell therapy (BMS-986393)

150×10^6 CAR+T cells

Efficacy assessments (IMWG 2016)

Safety assessments

Endpoints:

Primary
- ORR in 4+ PLT

Secondary / exploratory
- CRR, ORR in 3+/4+ PLT
- MRD negativity
- TTR, DOR, PFS, OS
- Safety
- Cellular kinetics
- Anti-CAR Abs
- PROs, HCRU

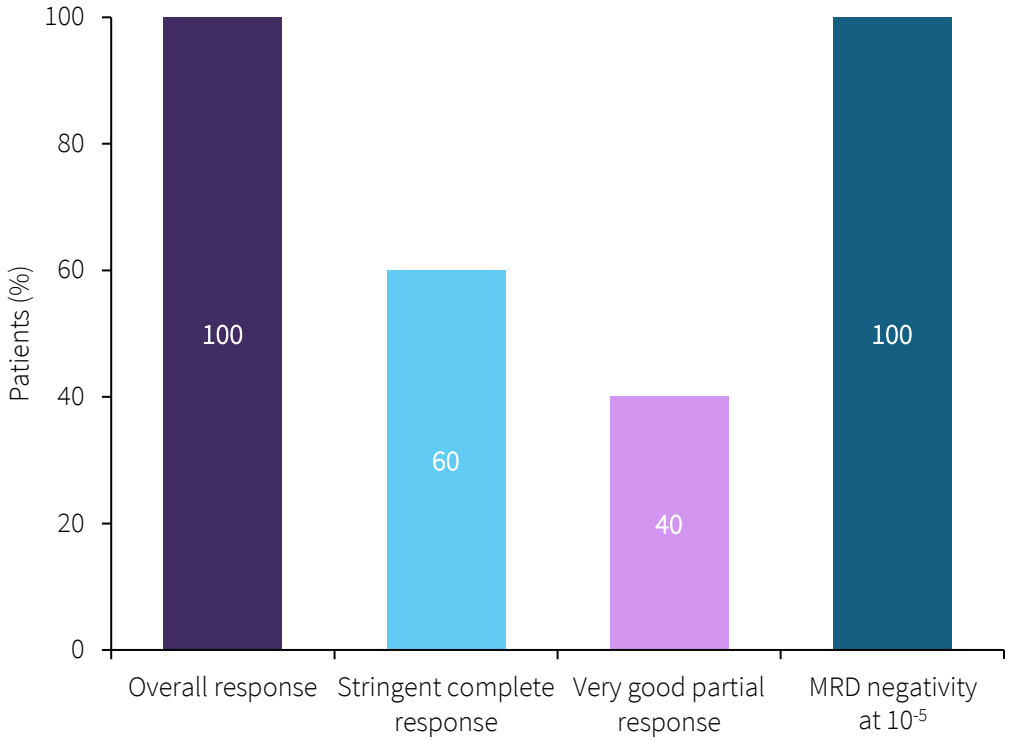
Ab, antibody; CAR, chimeric antigen receptor; CRR, complete response rate; DOR, duration of response; ECOG, East Cooperative Oncology Group; GPRC5D, G protein-coupled receptor class C group 5 member D; HCRU, health care resource utilization; ICF, informed consent form; IMWG, International Myeloma Working Group; LDC, lymphodepletion chemotherapy; MM, multiple myeloma; MRD, measurable residual disease; ORR, overall response rate; OS, overall survival; PD, progressive disease; PFS, progression-free survival; PLT, prior lines of therapy; PRO, patient-reported outcome; R/R, relapsed refractory; TTR, time to response.

Slide provided by Patel K.

OriCAR-017: Bi-epitope nanobody-based GPRC5D-targeted CAR T cells

POLARIS: First-in-human, single-center, single-arm, phase I study of GPRC5D-targeted CAR T cells in R/R MM

Patients' responses



All patients were MRD negative on Day 28. Serum M-protein concentrations decreased progressively, and clinical response in patients improved over time.

- Median time to **best response** was **3.1 months**.
- Median time to **complete response or better** was **4.1 months**.
- The median PFS time was not reached, but the 9-month estimated PFS was 87.5%.

CAR T-cell expansion was detected in all patients.

- C_{max} was 10.0 days.
- Median C_{max} was 7,930 copies per µL (5,494–16,486).
- C_{max} and AUC decreased during the first 28 days following CAR T-cell infusion as the infusion dose increased.

AUC, area under the curve; CAR, chimeric antigen receptor; Cmax, the median time to reach maximum CAR T-cell expansion; GPRC5D, G protein-coupled receptor class C group 5 member D; MM, multiple myeloma; MRD, measurable residual disease; PFS, progression-free survival; R/R, relapsed/refractory.

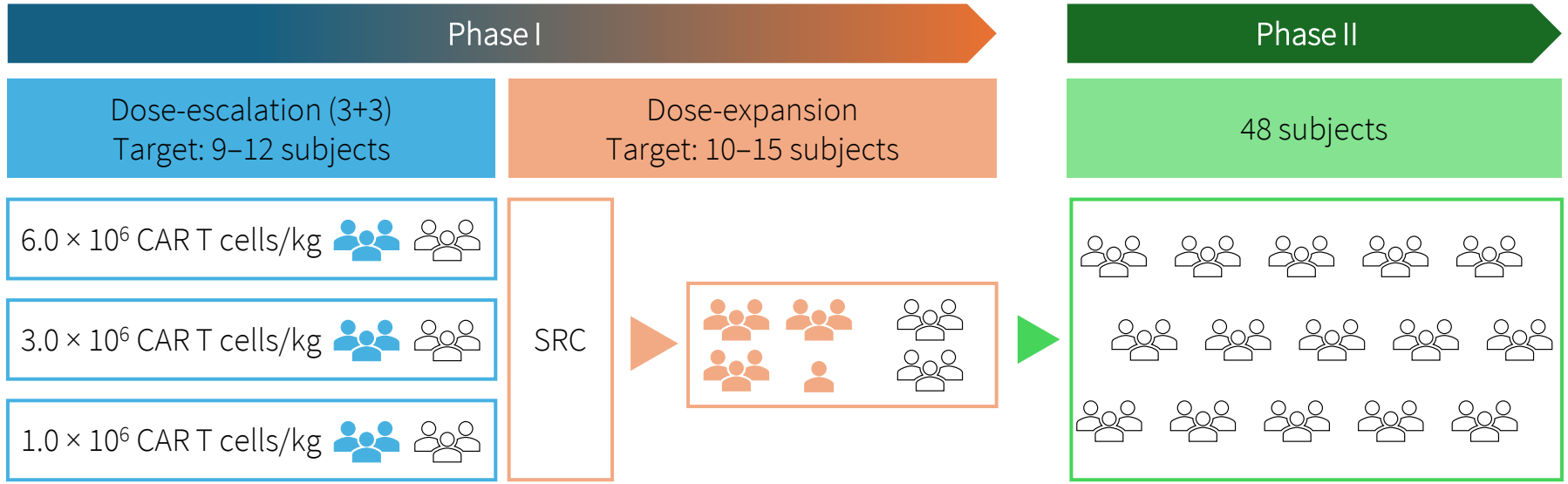
Zhang M, et al. *Lancet Haematol*. 2023;10(2):e107-e116

OriCAR-017-US-PI open-label, single-arm, multicenter phase I/II study

Inclusion criteria (protocol v1.3):
- Age 18–75 years
- ECOG PS ≤1
- Diagnosis of MM per IMWG criteria (2016 version)

Phase I (dose escalation):
- ≥3 lines of prior therapy, including anti-CD38 drugs, IMiDs, PIs, etc.
- Responded to ≥1 prior line of therapy
- Disease progression after last line of therapy
- Prior exposure to BCMA-directed therapies allowed

Phase I (dose expansion) + phase II:
- Previous exposure to BCMA-directed therapies required, including BCMA bispecific antibody, BCMA antibody-directed conjugate, and BCMA CAR T



	Phase I	Phase II
Primary endpoint	• DLT • MTD and/or RP2D or optimal biological dose • Incidence, characteristics, frequency, severity, and timing of AEs and SAEs	• IRC-assessed ORR per IMWG criteria • Incidence and characteristics of TEAEs
Secondary endpoints	• PK, PD • Investigator-assessed parameters per IMWG criteria: ORR, PFS, DoR, CBR, DCR • MRD negative rate • OS	• IRC-assessed ORR per IMWG criteria • IRC assessment of PFS, DoR, DCR, MRD negative rate, and OS • PK, PD • Incidence characteristics, frequency, severity, and timing of AEs and SAEs
Exploratory	• ADA against OriCAR-017, GPRC5D expression in bone marrow biopsy, and EMD and RCL	

AE, adverse event; BCMA, B-cell maturation antigen; CAR, chimeric antigen receptor; CBR, clinical benefit rate; DCR, disease control rate; DLT, dose-limiting toxicity; DoR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; EMD, extramedullary disease; GPRC5D, G protein-coupled receptor class C group 5 member D; IMiD, immunomodulatory drug; IMWG, International Myeloma Working Group; IRC, independent review committee; MM, multiple myeloma; MRD, measurable residual disease; MTD, maximum tolerated dose; ORR, overall response rate; OS, overall survival; PD, pharmacodynamics; PFS, progression-free survival; PI, proteasome inhibitor; PK, pharmacokinetics; RCL, replication-competent lentiviruse; RP2D, recommended phase II dose; SAE, serious adverse event; SRC, scientific review committee; TEAE, treatment-emergent adverse event.

Combination studies

- **NCT05850234[1]:** A phase Ib/II study of GC012F, a CAR T-cell therapy targeting CD19 and BCMA in subjects with relapsed/refractory multiple myeloma.

- **NCT05509530[2]:** Safety and efficacy of anti-BCMA/GPRC5D CAR T-cell therapy in treating relapsed and refractory multiple myeloma.

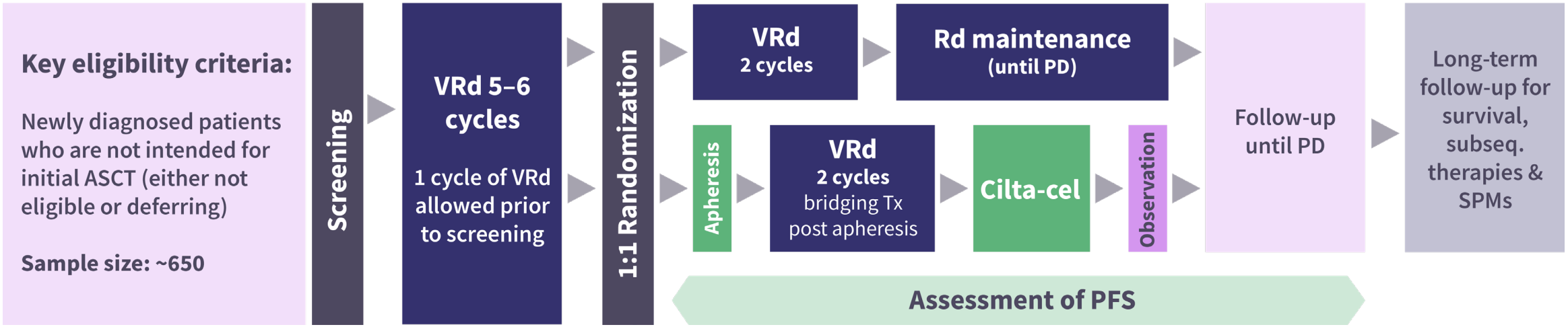
- **NCT06121843[3]:** A phase I, multicenter, open-label study to evaluate the safety and preliminary efficacy of BMS-986393 in novel combinations in participants with relapsed and/or refractory multiple myeloma and determine the recommended dose for each add-on investigational component drugs: alnuctamab, mezigdomide, or iberdomide.

BCMA, B-cell maturation antigen; CAR, chimeric antigen receptor; GPRC5D, G protein-coupled receptor class C group 5 member D.

1. Clinicaltrials.gov. NCT05850234. https://clinicaltrials.gov/study/NCT05850234. Accessed May 2024; 2. Clinicaltrials.gov. NCT05850234. https://clinicaltrials.gov/study/NCT05850234. Accessed May 2024; 3. Clinicaltrials.gov. NCT06121843. https://classic.clinicaltrials.gov/ct2/show/NCT06121843. Accessed May 2024.

CARTITUDE 5

Randomized phase III study in NDMM, not intended for initial transplant



Stratification factors:

a) R-ISS staging (I, II, III)
b) Age/transplant eligibility
   - Age ≥ 70 yrs
   - Age <70 yrs and transplant ineligible
   - Age < 70 yrs and transplant deferred
c) Response to VRd induction (≥VGPR; ≤PR)

Primary endpoint: PFS

ASCT, allogeneic stem cell transplant; cilta-cel, ciltacabtagene autoleucel; ND, newly diagnosed; MM, multiple myeloma; PD, progressive disease; PFS, progression-free survival; PR, partial response; Rd, lenalidomide and dexamethasone; R-ISS, revised International Staging System; SPM, subsequent primary malignancy; subseq, subsequent; Tx, treatment; VGPR, very good partial response; VRd, bortezomib, lenalidomide, and dexamethasone.

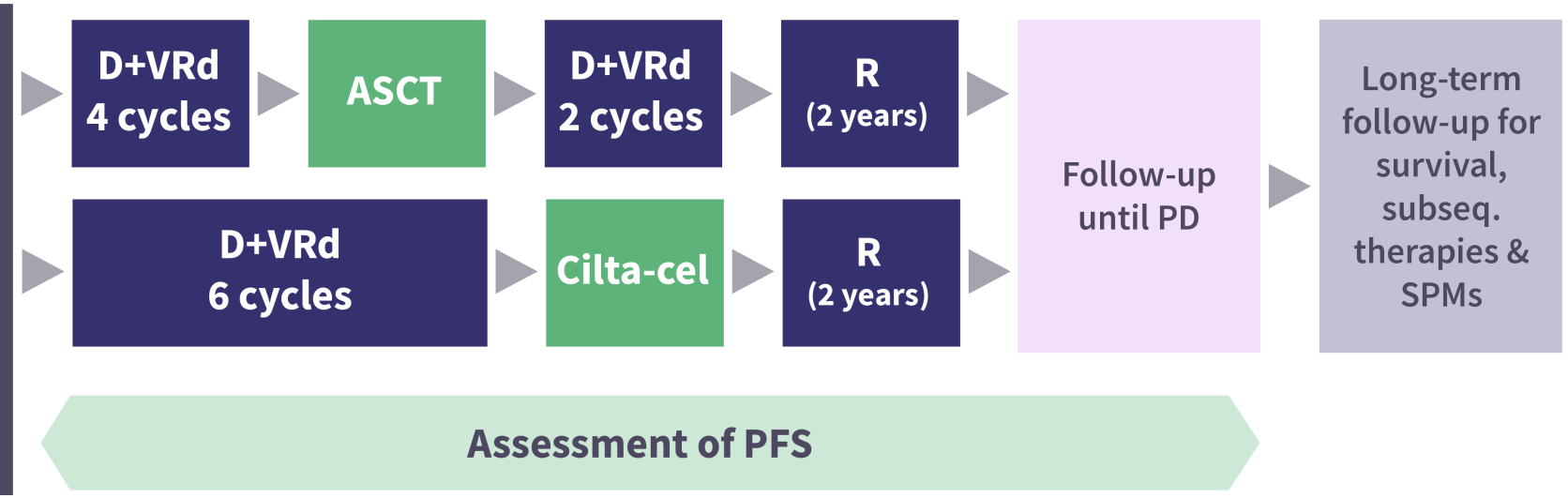
1. Clinicaltrials.gov. NCT04923893. https://www.clinicaltrials.gov/study/NCT04923893. Accessed May 2024. 2. Dytfeld D, et al. poster presented at the 63rd ASH Annual Meeting and Exposition; Dec 10-14, 2021, Atlanta, GA/Virtual.

CARTITUDE 6

Key eligibility criteria:

- **Newly diagnosed patients**
  - Age ≥18
  - Eligible for initial ASCT
- **All risk cytogenetics**

Sample size: ~750



Stratification factors:
a) ISS staging
b) Cytogenetics
c) Age

Dual primary endpoints:
PFS and sustained MRD-negative CR

ASCT, allogeneic stem cell transplant; cilta-cel, ciltacabtagene autoleucel; CR, complete response; D, dexamethasone; ISS, International Staging System; MRD, measurable residual disease; PD, progressive disease; PFS, progression-free survival; R, lenalidomide; SPM, subsequent primary malignancy; VRd, bortezomib, lenalidomide, and dexamethasone.

ClinicalTrials.gov. NCT05257083. https://classic.clinicaltrials.gov/ct2/show/NCT05257083. Accessed May 2024. 2. Boccadoro M, et al. oral abstract presented at the 64th ASH Annual Meeting and Exposition, Dec 10-13, 2022, New Orleans, LA/Virtual.

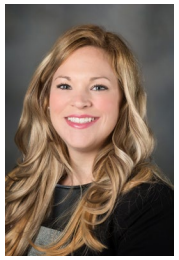
THE UNIVERSITY OF TEXAS MD Anderson Cancer Center

Key Takeaways

- BCMA targeting therapies have offered the highest response rates/PFS/DOR compared to any other myeloma therapies in the relapsed refractory setting (CAR T > bispecifics > ADC).
- Supportive care and preventive measures for infections, DVT, GI, and other toxicities must be optimized.
- New targets for both bispecifics and CAR T cells offer potentially better options post-BCMA therapy; however, more data are needed for long-term efficacy and toxicity regarding optimal sequencing vs combination.
- Mechanisms of resistance for these new-wave immunotherapies need to be further evaluated; biomarkers (immune and myeloma based) could really help make better decisions in clinic.

THANK YOU!

Special thanks to our patients/caregivers, clinical and research teams!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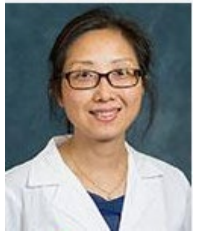
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