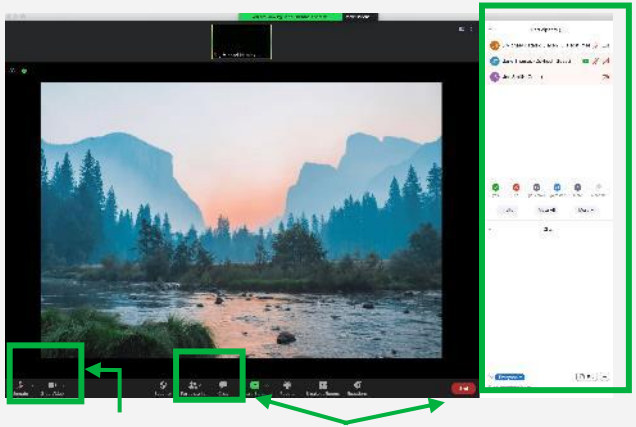
Housekeeping Notes for Faculty

To be announced prior to start of meeting

- To minimize the noise level, please turn cell phones to vibrate mode
- Mute your line if you are not speaking or presenting
- Keep your camera on at all times
- You have the ability to use the “raise your hand” option if you want to comment
- If you cannot comment at a certain moment, you can also use the chat function in Zoom
- Questions from the audience can be asked via the Q&A box
- The chair will manage the questions and address them during the Q&A sessions
- At the end of the meeting, please stay on the line for a quick debrief with the AH team
- Once the countdown has started, Aptitude Health will kick off and introduce the program and turn over the proceedings to the chair

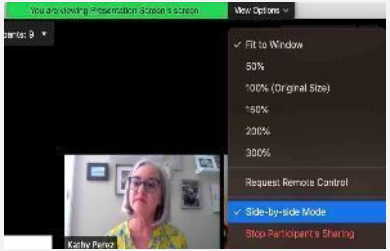
Functionality and Settings

To be announced prior to start of meeting

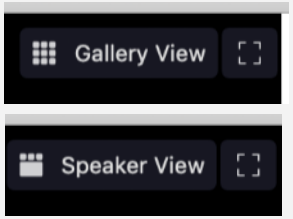


Microphone and Camera
Mute and unmute your camera/microphone by clicking the icons in the lower left-hand corner

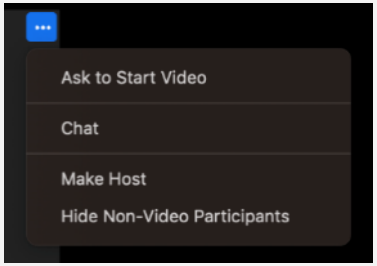
Participant and Chat Window
Reveal or hide the chat and participant window by selecting the corresponding icons in the bottom toolbar



Side-by-Side Mode
In the "View Options" tab (next to the green bar at top of screen), select "Side-by-Side Mode"



Gallery and Speaker View
In the upper right-hand corner, select "Gallery View" (Note: If button says "Speaker View," you are already seeing "Gallery View")



Hide Non-Video Participants
In any camera box, click the 3 white dots in the upper right-hand corner, and select "Hide Non-Video Participants"

Please remember to mute/unmute yourself by clicking the microphone icon in the lower left-hand corner of your screen.

Global Multiple Myeloma Academy

Get Ready

When not speaking

When presenting

Use chat

Ask/comment any time

APTITUDE HEALTH®

Global Multiple Myeloma Academy

Global Multiple Myeloma Academy

Emerging and Practical Concepts in Relapsed/Refractory Multiple Myeloma (RRMM)

April 29–30, 2026 – European Region

Pfizer

APTITUDE HEALTH®

Global Multiple Myeloma Academy

Welcome and Meeting Overview

Rafael Fonseca, MD

APTITUDE HEALTH®

Co-Chair

Rafael Fonseca, MD
Mayo Clinic Cancer Center, USA

Co-Chair

Philippe Moreau, MD
University Hospital of Nantes, France

Faculty

Hermann Einsele, MD, FRCP
Universitätsklinikum Würzburg, Germany

María-Victoria Mateos, MD, PhD
University of Salamanca, Spain

Xavier Leleu, MD, PhD
Hôpital La Milétrie, France

Katja Weisel, MD
University Medical Center Hamburg-Eppendorf

Objectives of the Program

- Present the current MM treatment landscape and discuss patient eligibility for CAR T-cell therapy, real-world evidence around earlier use of CAR T-cell therapy, and treatment options for non–CAR T-cell candidates
- Follow interactive presentations and case-based discussions with your peers on the latest updates for assessments and treatments for patients with multiple myeloma after initial therapy
- Share key data from recent conferences that could lead to improved treatment and management for patients with myeloma
- Engage with the faculty in panel discussions on therapeutic options for the later-line treatment setting in multiple myeloma
- Discuss regional case studies in late-stage RRMM with your colleagues
- Discuss the role of bispecific antibodies in RRMM and immunotherapy sequencing across the current and potential future treatment landscapes
- Discuss treatment strategies for RRMM
- Interact with faculty during a panel discussion on patient access and regional challenges for optimal patient care
- Explore regional challenges in the treatment of multiple myeloma across Europe

Agenda Day 2 – Europe

17.00 – 20.00 (Central European Summer Time)/8.00 AM – 11.00 AM (Pacific Standard Time)

Time (CEST)	Topic	Speaker
17.00 – 17.10 10 min	**Welcome and Meeting Overview**	Rafael Fonseca, MD, Philippe Moreau, MD
17.10 – 17.30 20 min	**Overview of RRMM Treatment: Early Lines of Therapy**	Philippe Moreau, MD
17.30 – 17.55 25 min	**CAR T-Cell Therapy in RRMM: Impact of Earlier Use and Real-World Data**	Xavier Leleu, MD, PhD
17.55 – 18.20 25 min	**Treatment Options for Non–CAR T-Cell Candidates** • Optimal use of treatment choices in RRMM (15-min presentation; 10-min Q&A)	María-Victoria Mateos, MD, PhD
18.20 – 18.30 10 min	**Break**	
18.30 – 19.25 55 min	**Patient Case Discussion: RRMM**	Regional case presentation All faculty
19.25 – 19.55 30 min	**Future Directions in Therapy for RRMM**	María-Victoria Mateos, MD, PhD
19.55 – 20.00 5 min	**Session Close** • ARS questions	Rafael Fonseca, MD

Question 1

In which country do you currently practice?

1. France
2. Germany
3. Italy
4. Spain
5. Portugal
6. UK
7. Scandinavia
8. Other European region/country
9. Middle East
10. North America
11. Other

Question 2

In the last 12 months, how many patients have you treated using CAR T-cell therapy?

1. ≤5
2. 6–15
3. 16–25
4. 26–35
5. ≥36

Question 3

True or False: BCMA is the most common antigen targeted by currently approved CAR T-cell therapies in multiple myeloma.

1. True
2. False

Question 4

What is the primary mechanism of action for CELMoDs?

1. Direct inhibition of the proteasome
2. Modulating cereblon E3 UL, leading to degradation of signaling proteins
3. Blockade of BCMA signaling
4. Activation of immune checkpoint pathways

Global Multiple Myeloma Academy

Overview of RRMM Treatment: Early Lines of Therapy

Philippe Moreau, MD

APTITUDE HEALTH®

Overview of RRMM Treatment
Early Lines of Therapy

Philippe Moreau
Nantes, France

DISCLOSURES

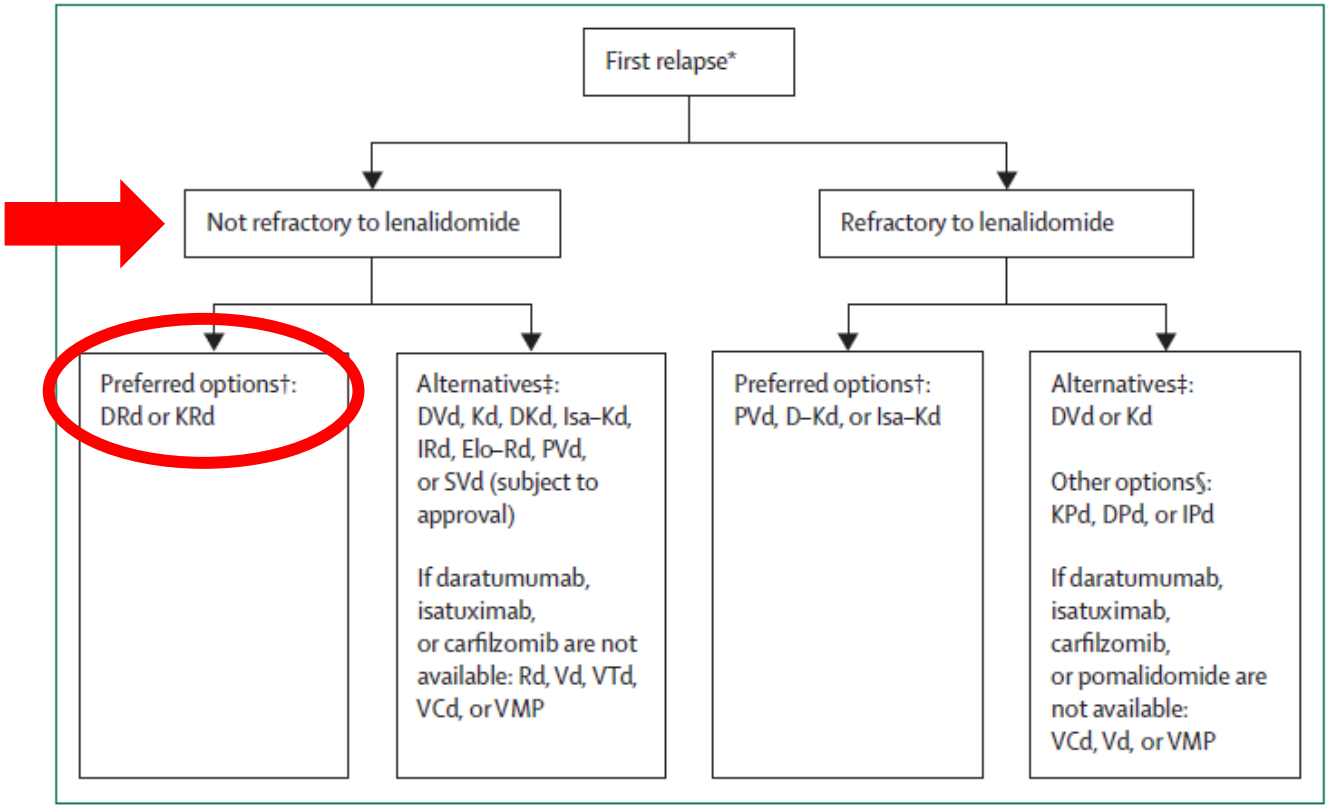
Honoraria & advisory boards:
Janssen, Celgene, Takeda, Amgen, Abbvie, Sanofi, GSK, Pfizer, BD

Treatment of relapsed and refractory multiple myeloma: recommendations from the International Myeloma Working Group

Philippe Moreau, Shaji K Kumar, Jesús San Miguel, Faith Davies, Elena Zamagni, Nizar Bahlis, Heinz Ludwig, Joseph Mikhael, Evangelos Terpos, Fredrik Schjesvold, Thomas Martin, Kwee Yong, Brian G M Durie, Thierry Facon, Artur Jurczyszyn, Surbhi Sidana, Noopur Raje, Niels van de Donk, Sagar Lonial, Michele Cavo, Sigurdur Y Kristinsson, Suzanne Lentzsch, Roman Hajek, Kenneth C Anderson, Cristina João, Hermann Einsele, Pieter Sonneveld, Monika Engelhardt, Rafael Fonseca, Annette Vangsted, Katja Weisel, Rachid Baz, Vania Hungria, Jesus G Berdeja, Fernando Leal da Costa, Angelo Maiolino, Anders Waage, David H Vesole, Enrique M Ocio, Hang Quach, Christoph Driessen, Joan Bladé, Xavier Leleu, Eloisa Riva, Peter Leif Bergsagel, Jian Hou, Wee Joo Chng, Ulf-Henrik Mellqvist, Dominik Dytfeld, Jean-Luc Harousseau, Hartmut Goldschmidt, Jacob Laubach, Nikhil C Munshi, Francesca Gay, Meral Beksac, Luciano J Costa, Martin Kaiser, Parameswaran Hari, Mario Boccadoro, Saad Z Usmani, Sonja Zweegman, Sarah Holstein, Orhan Sezer, Simon Harrison, Hareth Nahi, Gordon Cook, Maria-Victoria Mateos, S Vincent Rajkumar, Meletios A Dimopoulos, Paul G Richardson

Lancet Oncol. 2021;22(3):e105-e118.

First relapse

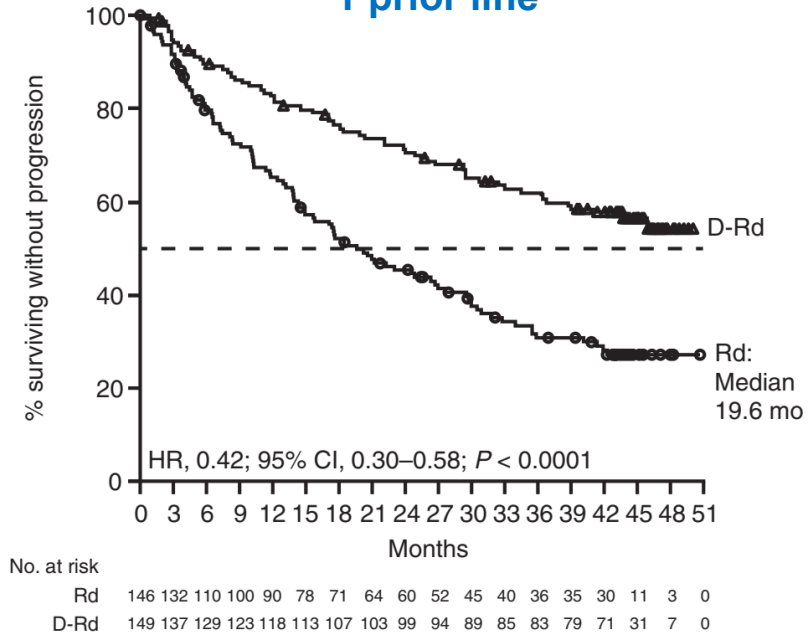


Moreau et al, IMWG guidelines, Lancet Oncol 2021

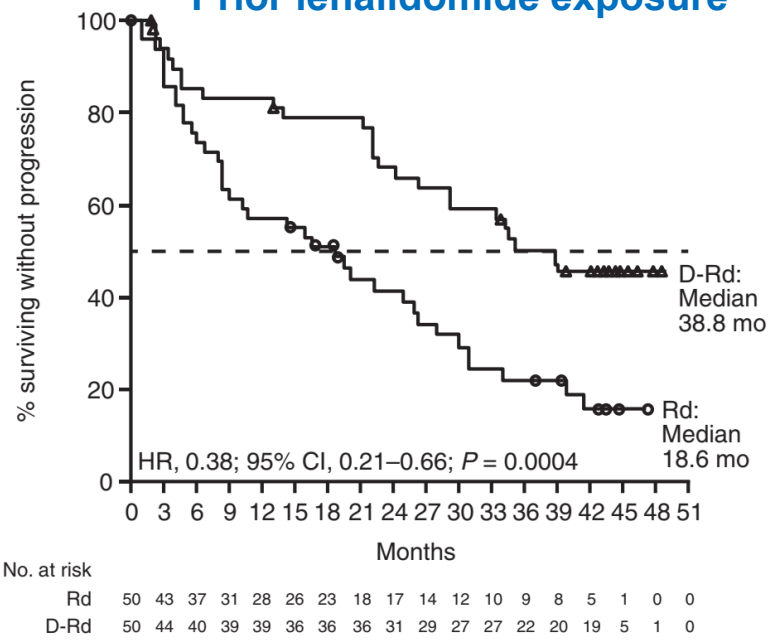
POLLUX: Rd vs Rd-Dara; updated PFS

Ongoing, randomized, open-label, multicenter, phase 3 study in patients with RRMM (ClinicalTrials.gov Identifier: NCT02076009); N=569

1 prior line



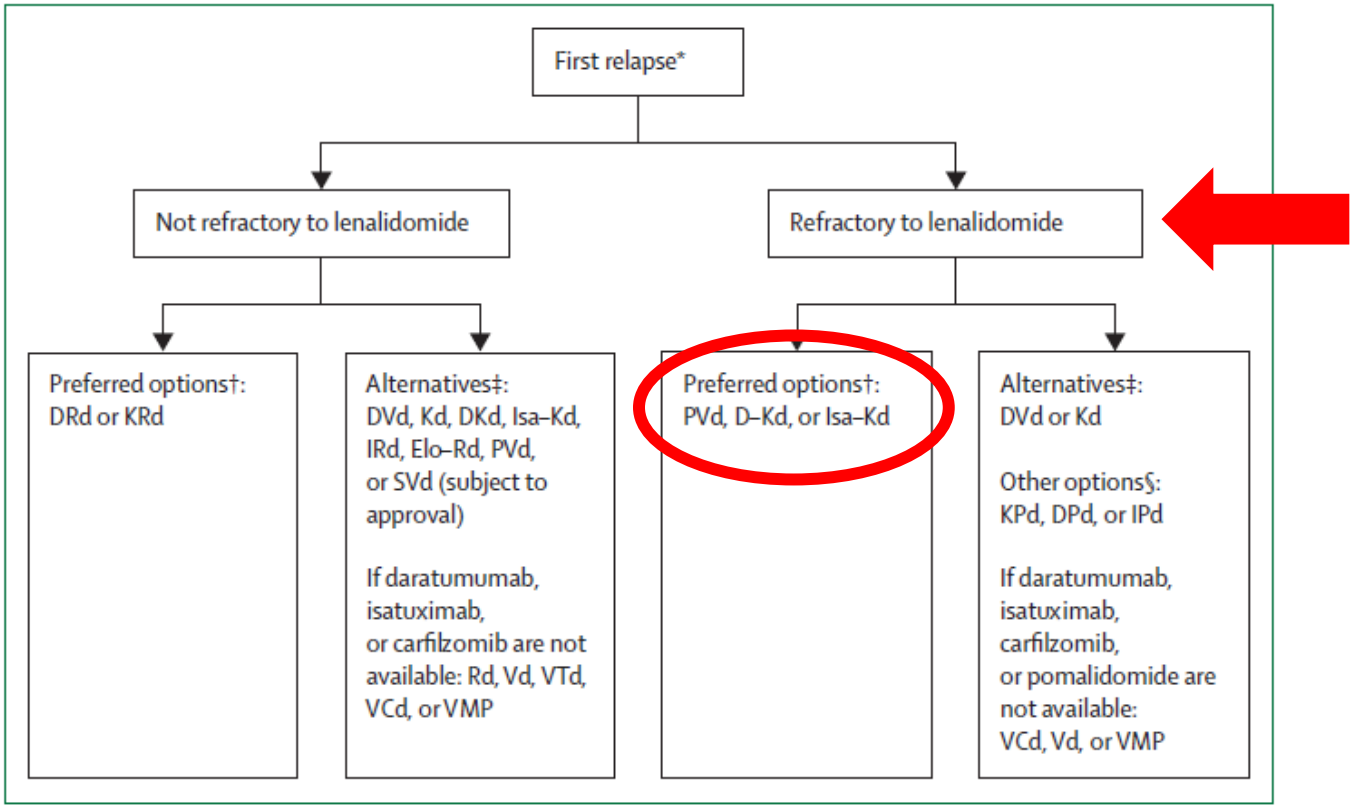
Prior lenalidomide exposure



DRd, daratumumab/lenalidomide/dexamethasone; PFS, progression-free survival; Rd, lenalidomide/dexamethasone; Std, standard

Bahlis NJ, *et al.* Leukemia. 2020;34(7):1875-1884.

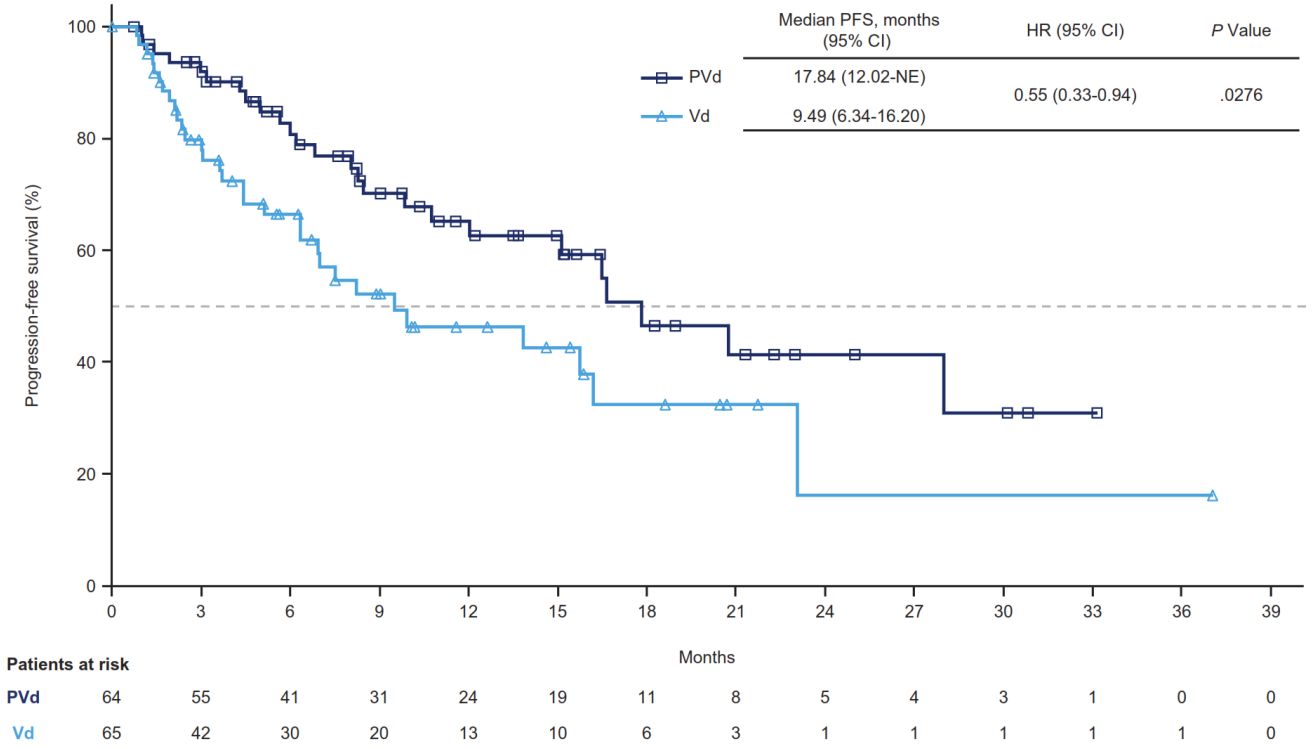
First relapse



Moreau et al, IMWG guidelines, Lancet Oncol 2021

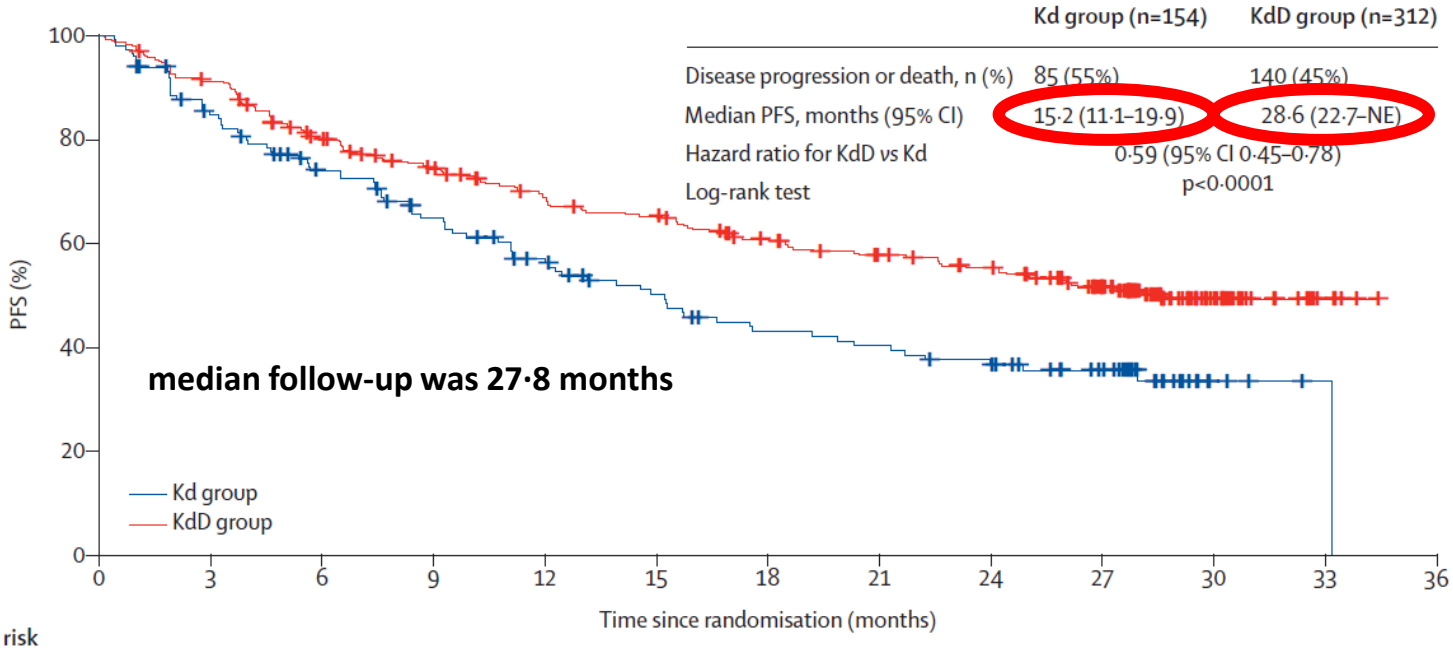
OPTIMISMM: PVD vs VD; 1st relapse, Len-refractory patients

A



Dimopoulos M, *et al*. Leukemia 2021;35:1722.

41% reduction in the risk of progression/death and a 13.4-month improvement in median PFS with KdD versus Kd



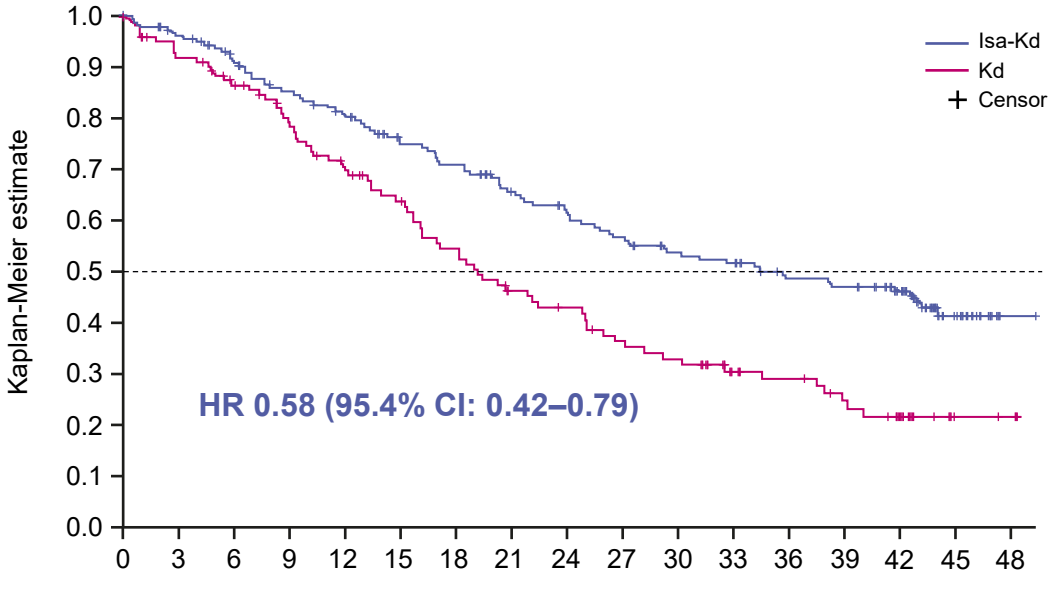
Number at risk (number censored)													
Kd group	154 (0)	120 (12)	99 (18)	83 (22)	69 (26)	57 (30)	47 (32)	44 (32)	39 (33)	28 (43)	4 (66)	1 (69)	0 (69)
KdD group	312 (0)	279 (6)	235 (16)	210 (25)	189 (31)	178 (32)	159 (39)	146 (44)	136 (48)	105 (70)	30 (143)	6 (166)	0 (172)

Usmani et al. Lancet Oncol. 2022 Jan;23(1):65-76

IKEMA

Moreau P, *et al.* Lancet 2021; updated COMY 2022,

Updated PFS (primary endpoint) – IRC assessment (ITT)



Number at Risk

Isa-Kd	179	164	151	136	127	114	108	95	88	81	75	72	64	62	50	18	1
Kd	123	108	99	85	73	63	53	43	39	32	29	23	21	16	10	3	2

Isa-Kd
mPFS: 35.7 months
(95% CI: 25.8–44.0)

Kd
mPFS: 19.2 months
(95% CI: 15.8–25.0)

With 2 additional years of follow-up, Isa-Kd showed the longest PFS on a PI-based backbone in the relapsed MM setting, with 42% reduction vs Kd in the risk of progression or death

CI, confidence interval; d, dexamethasone; HR, hazard ratio; IRC, Independent Review Committee; Isa, isatuximab; ITT, intent to treat; K, carfilzomib; m, median; MM, multiple myeloma; PFS, progression-free survival; PI, proteasome inhibitor

Myeloma: Second or higher relapse

Preferred Options

- Any first relapse options that have not been tried
- Isa-Pd; Dara-Kd, Isa-Kd, Dara-Pd (based on phase 3)
- Elo-Pd, KPd (based on phase 2)
- When dara / K / elo not available: PCD, PD

K or Pom as backbone + antiCD38 antibody

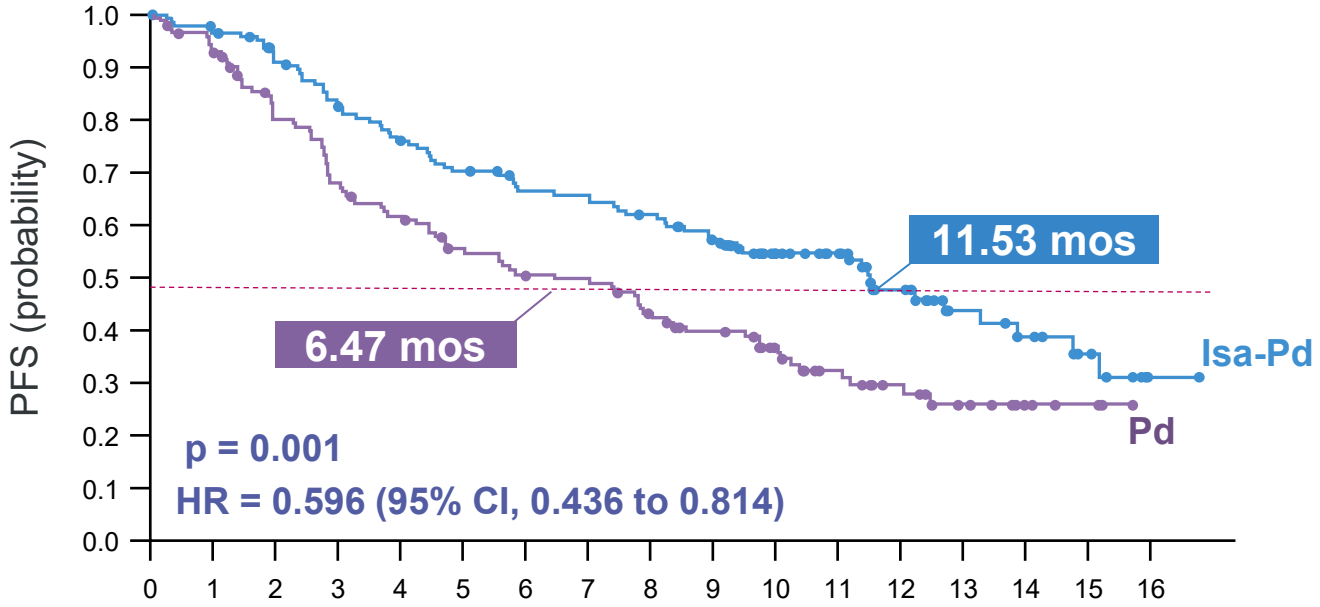
IKEMA and CANDOR

ICARIA and APPOLO

BCMA, B-cell maturation antigen; CAR, chimeric antigen receptor; DKd, daratumumab/carfilzomib/dexamethasone; DPd, daratumumab/pomalidomide/dexamethasone; Elo-Pd, elotuzumab/pomalidomide/dexamethasone; Isa-Kd, isatuximab/carfilzomib/dexamethasone; Isa-Pd, isatuximab/pomalidomide/dexamethasone; KPd, carfilzomib/pomalidomide/dexamethasone; PCd, pomalidomide/cyclophosphamide/dexamethasone; Pd, pomalidomide/Dexamethasone; VdT-PACE, bortezomib/dexamethasone/thalidomide/cisplatin/doxorubicin/cyclophosphamide/etoposide.

Moreau P, *et al*. IMWG Recommendations for RRMM. Lancet Oncol. 2021;22(3):e105-e118.

ICARIA : PFS primary endpoint – IRC assessment



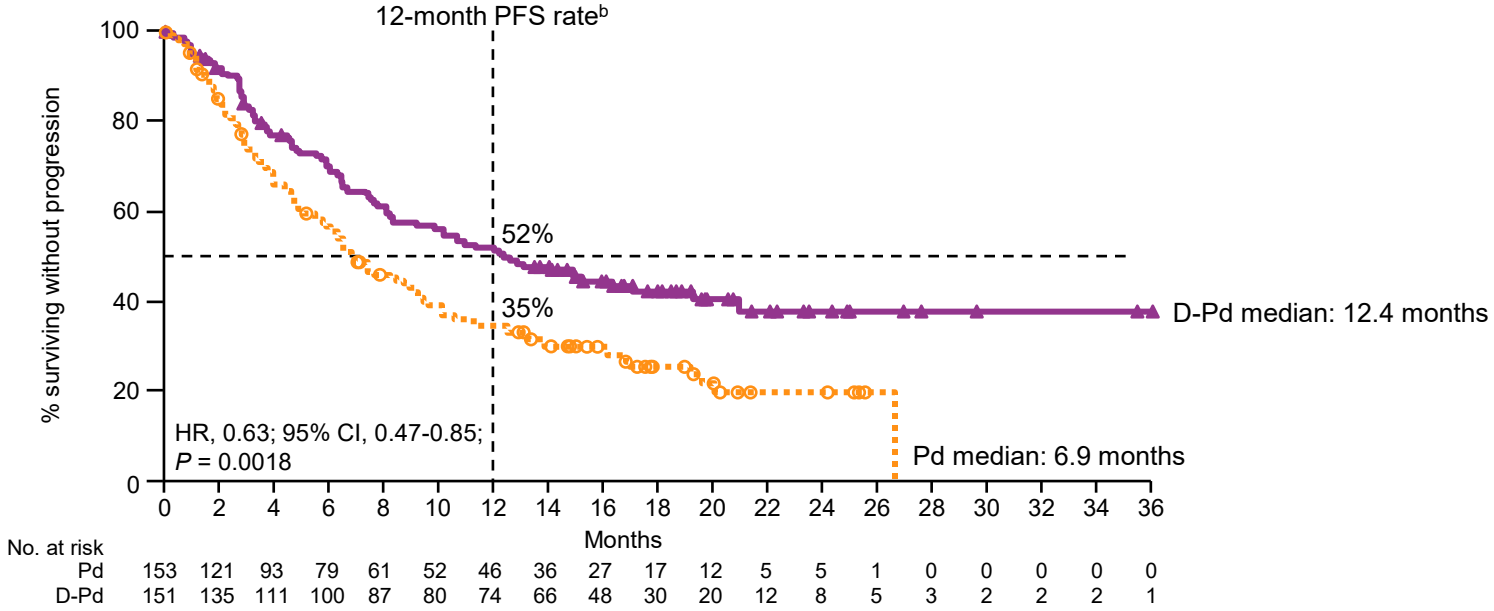
No. at risk									
Isa-Pd	154	129	106	89	81	52	30	14	1
Pd	153	105	80	63	51	33	17	5	0

Statistically significant and clinically meaningful improvement in PFS

The European Commission (EC) has approved isatuximab in combination with pomalidomide and dexamethasone (pom-dex) for the treatment of adult patients with relapsed and refractory multiple myeloma (MM) who have received at least two prior therapies including lenalidomide and a proteasome inhibitor and have demonstrated disease progression on the last therapy. Please consult your local label for the approved indication in your country.

Attal M, *et al.* Lancet. 2019;394(10214):2096-2107.

APOLLO: PFS at a median follow-up of 16.9 months[a]



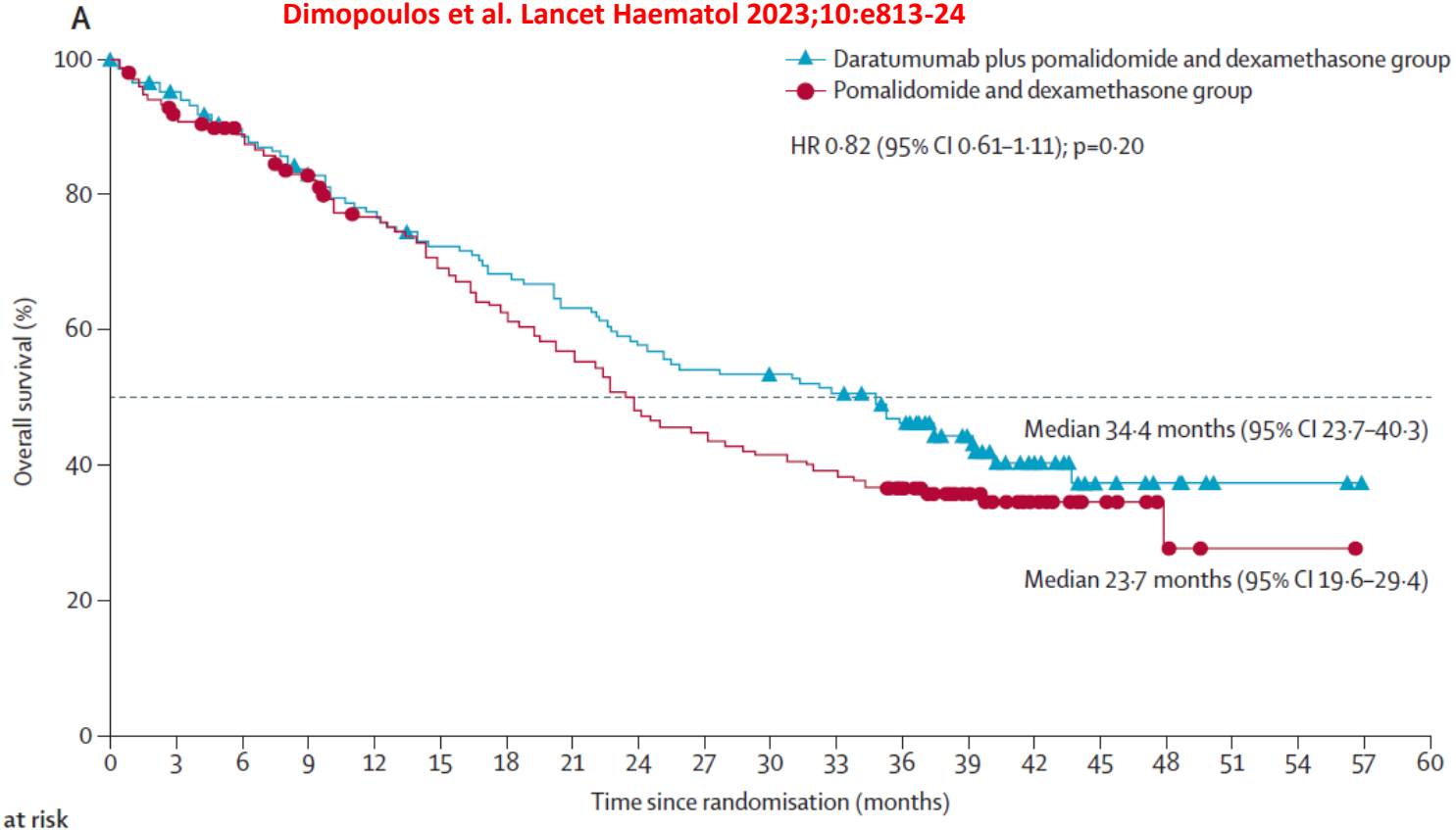
- Median PFS among patients refractory to lenalidomide was 9.9 months for D-Pd and 6.5 months for Pd

Addition of DARA SC to Pd improved PFS, with a 37% reduction in the risk of progression or death

HR, hazard ratio; CI, confidence interval. [a]Intent-to-treat population. [b]Kaplan–Meier estimate.

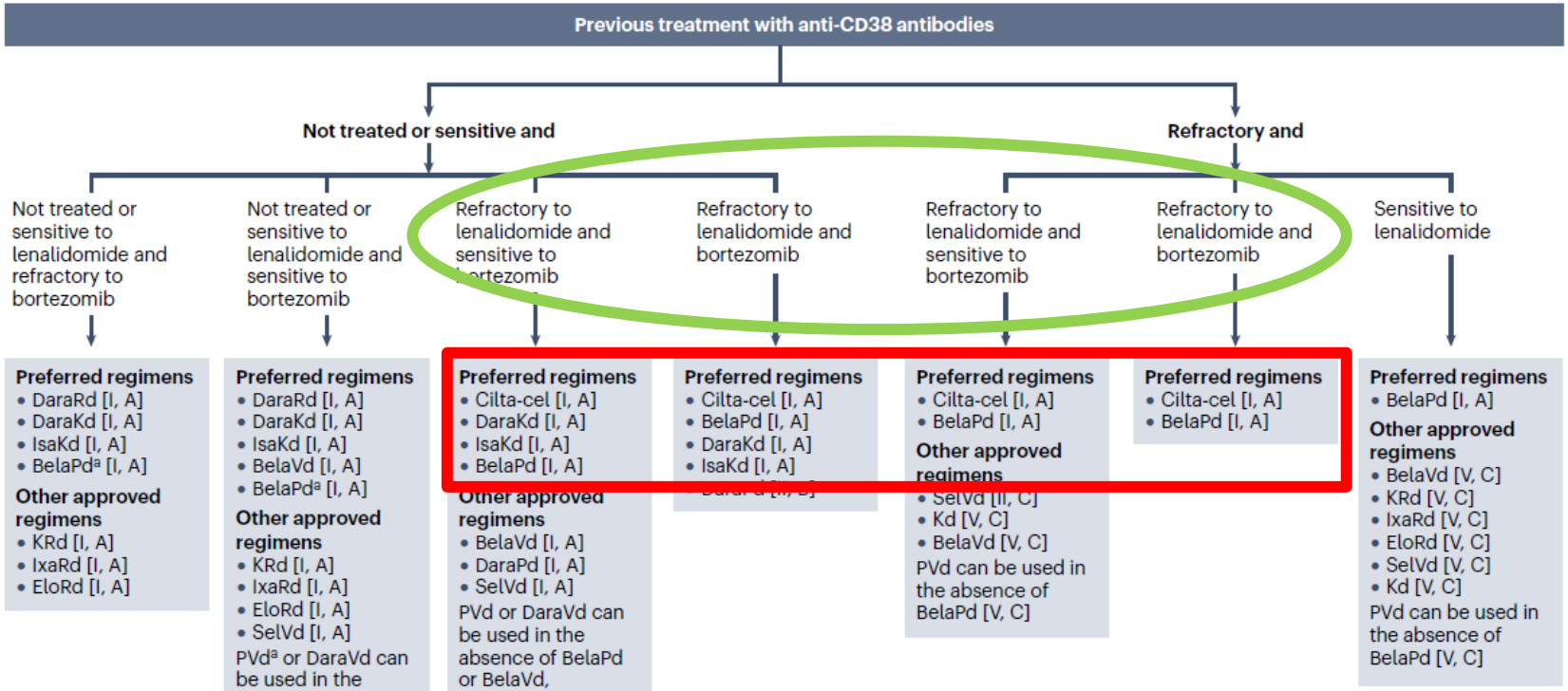
Dimopoulos MA, *et al*. ASH 2020 Abs 412.Oral presentation.

Dimopoulos et al. Lancet Haematol 2023;10:e813-24



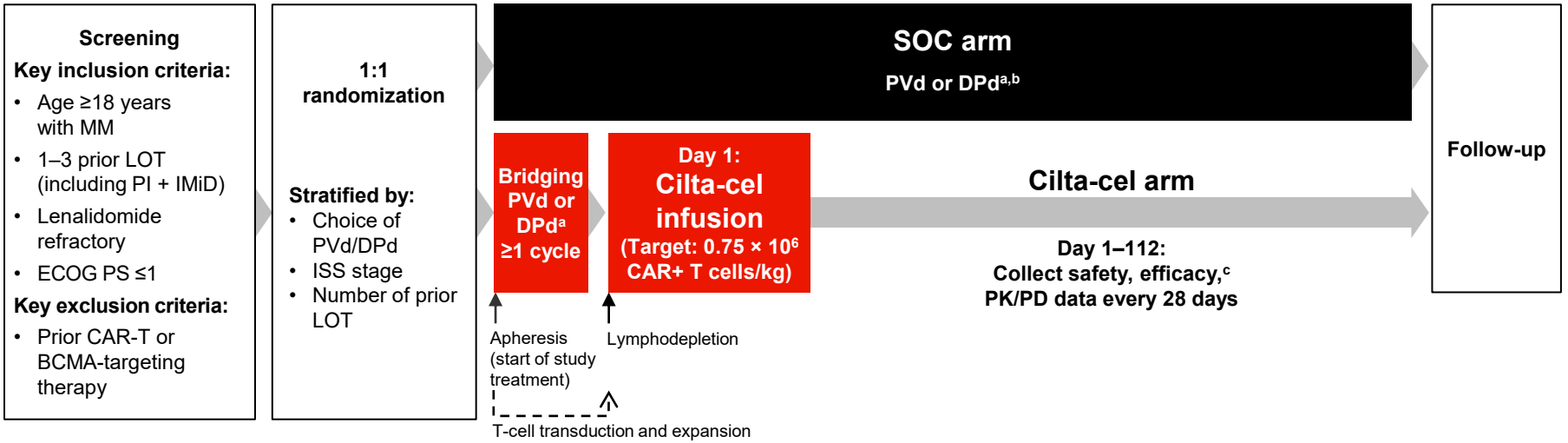
Number at risk (number censored)																				
Daratumumab plus pomalidomide and dexamethasone group	151 (0)	140 (3)	129 (6)	119 (7)	111 (7)	103 (8)	97 (8)	90 (8)	82 (8)	77 (8)	76 (8)	72 (9)	62 (13)	39 (33)	19 (50)	9 (59)	6 (62)	2 (66)	2 (66)	0 (68)	..
Pomalidomide and dexamethasone group	153 (0)	137 (3)	128 (8)	117 (11)	104 (15)	94 (15)	85 (15)	77 (15)	65 (15)	61 (15)	56 (15)	53 (15)	45 (20)	29 (35)	18 (45)	12 (51)	4 (48)	1 (61)	1 (61)	0 (62)	..

SECOND-LINE



Dimopoulos, Terpos et al. EHA / EMN guidelines. Nat Rev Clin Oncol. 2025 Sep;22(9):680-700

CARTITUDE-4: Study Design[1]



Primary endpoint

- PFS[d]

Secondary endpoints

- Efficacy: ≥CR, ORR, MRD negativity, OS
- Incidence and severity of AEs

[a]Physician's choice. [b]Administered until disease progression. [c]Efficacy data were collected after Day 112 every 28 days. [d]Time from randomization to disease progression/death. AE, adverse event; BCMA, B-cell maturation antigen; CAR, chimeric antigen receptor; CTCAE, Common Terminology Criteria for Adverse Events; DPd, daratumumab, pomalidomide, and dexamethasone; ECOG PS, Eastern Cooperative Oncology Group performance status; IMiD, immunomodulatory drug; ISS, International Staging System; ORR, overall response rate; PD, pharmacodynamics; PI, proteasome inhibitor; PK, pharmacokinetics; PVd, pomalidomide, bortezomib, and dexamethasone. 1. San-Miguel J, et al. *N Engl J Med* 2023;389:335-47.

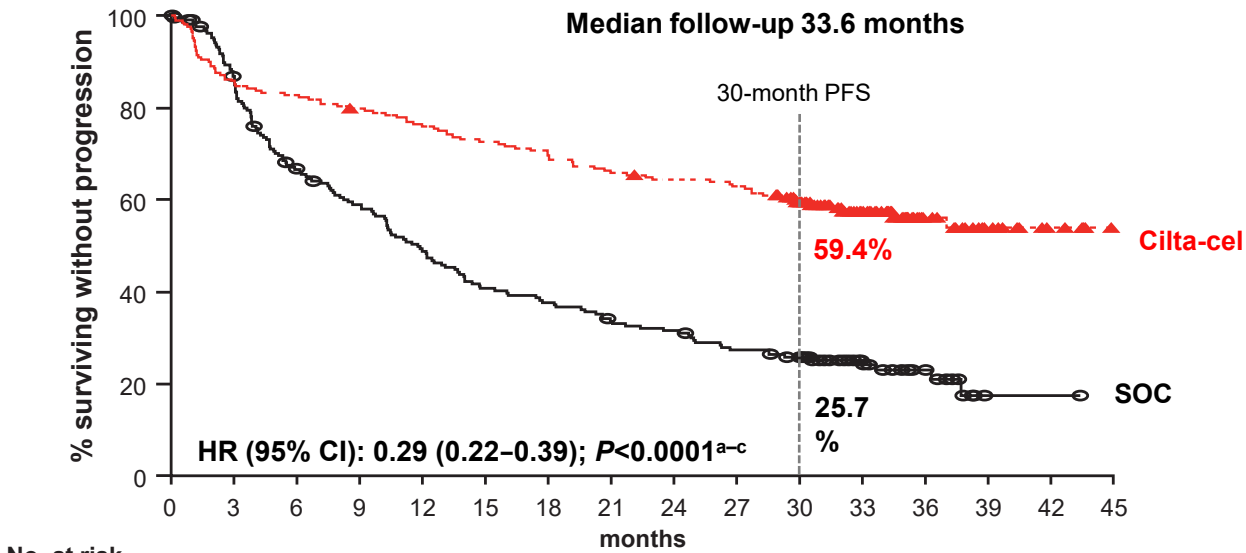
Presented by L Costa at the 67th American Society of Hematology (ASH) Annual Meeting; December 6–9, 2025; Orlando, FL, USA

CARTITUDE-4 : Baseline Demographics and Disease Characteristics

Baseline characteristic	ITT population	
	Cilta-cel (n=208)	SOC (n=211)
Age, median (range), years	61.5 (27–78)	61.0 (35–80)
Male, n (%)	116 (55.8)	124 (58.8)
White, n (%)	157 (75.5)	157 (74.4)
ECOG PS ≤1, n (%)[a,b]	207 (99.5)	210 (99.5)
ISS stage, n (%)		
I	136 (65.4)	132 (62.6)
II	60 (28.8)	65 (30.8)
III	12 (5.8)	14 (6.6)
Bone marrow plasma cells ≥60%,[c] n (%)	42 (20.4)	43 (20.7)
Presence of soft tissue plasmacytomas,[d] n (%)	44 (21.2)	35 (16.6)
Years since diagnosis, median (range)	3 (0.3–18.1)	3.4 (0.4–22.1)
Prior LOT, median (range)	2 (1–3)	2 (1–3)
1 prior LOT, n (%)	68 (32.7)	68 (32.2)
2 or 3 prior LOT, n (%)	140 (67.3)	143 (67.8)

Baseline characteristic	ITT population	
	Cilta-cel (n=208)	SOC (n=211)
Cytogenetic high risk, n (%)[e]	123 (59.4)	132 (62.9)
del(17p)	49 (23.7)	43 (20.5)
t(14;16)	3 (1.4)	7 (3.3)
t(4;14)	30 (14.5)	30 (14.3)
gain/amp(1q)	89 (43.0)	107 (51.0)
2 or more high-risk cytogenetic features	43 (20.8)	49 (23.3)
del(17p), t(14;16), or t(4;14)	73 (35.3)	69 (32.9)
Triple-class[f] exposed, n (%)	53 (25.5)	55 (26.1)
Penta-drug[g] exposed, n (%)	14 (6.7)	10 (4.7)
Refractory status, n (%)		
Triple-class refractory[f,h]	30 (14.4)	33 (15.6)
Bortezomib	55 (26.4)	48 (22.7)
Pomalidomide	8 (3.8)	9 (4.3)
Daratumumab	48 (23.1)	45 (21.3)
Any PI	103 (49.5)	96 (45.5)

Long-term CARTITUDE-4 Update (34 months): Cilta-cel Maintained Significant Improvement in Progression-free Survival



~70% reduction in the risk of progression or death in patients who received cilta-cel and mPFS has not been reached

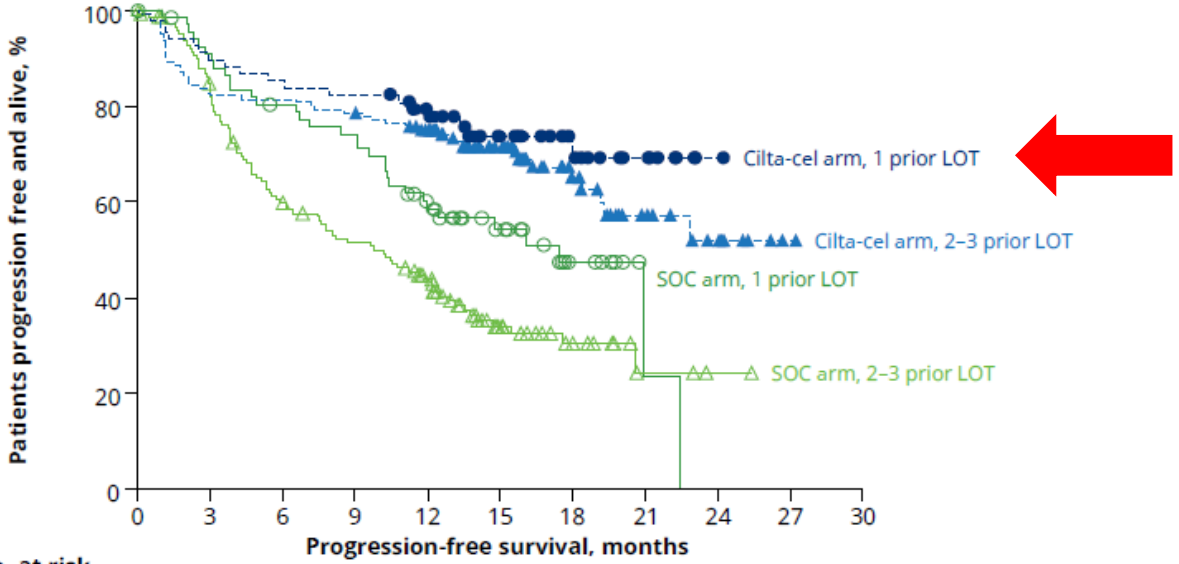
[a]Constant piecewise weighted log-rank test. [b]HR and 95% CI from a Cox proportional hazards model with treatment as the sole explanatory variable, including only PFS events that occurred >8 weeks post randomization. [c]Nominal *P*-value.
Cilta-cel, ciltacabtagene autoleucel; HR, hazard ratio; mPFS, median progression-free survival; SOC, standard of care.

Presented by M-V Mateos at the 21st International Myeloma Society (IMS) Annual Meeting; September 25–28, 2024; Rio de Janeiro, Brazil

CARTITUDE-4: PFS by Prior Line of Therapy

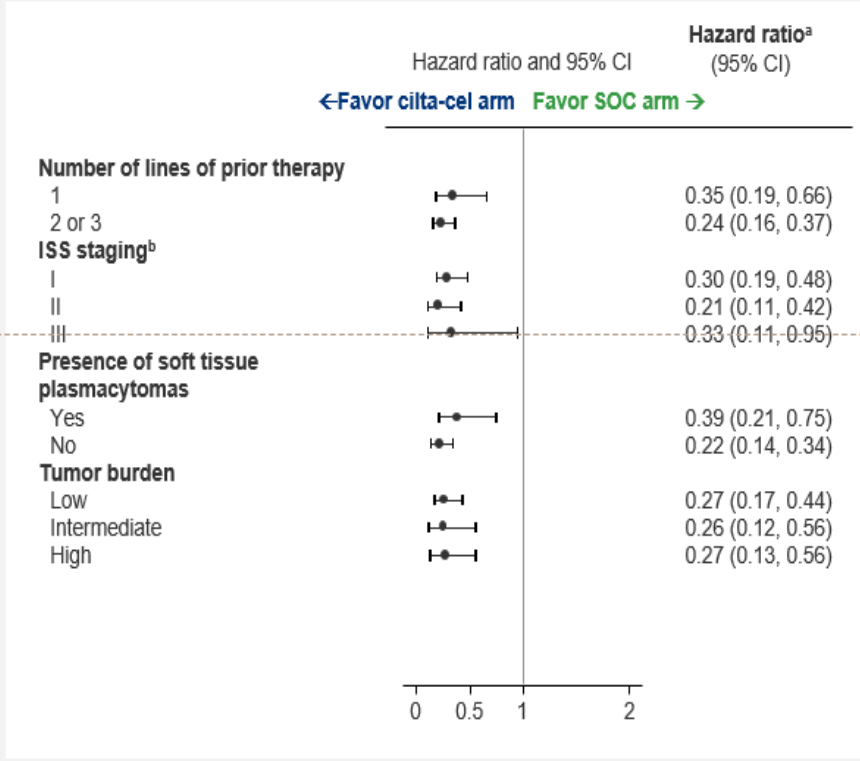
- Cilta-cel improved PFS vs SOC whether patients had 1 or 2–3 prior LOT

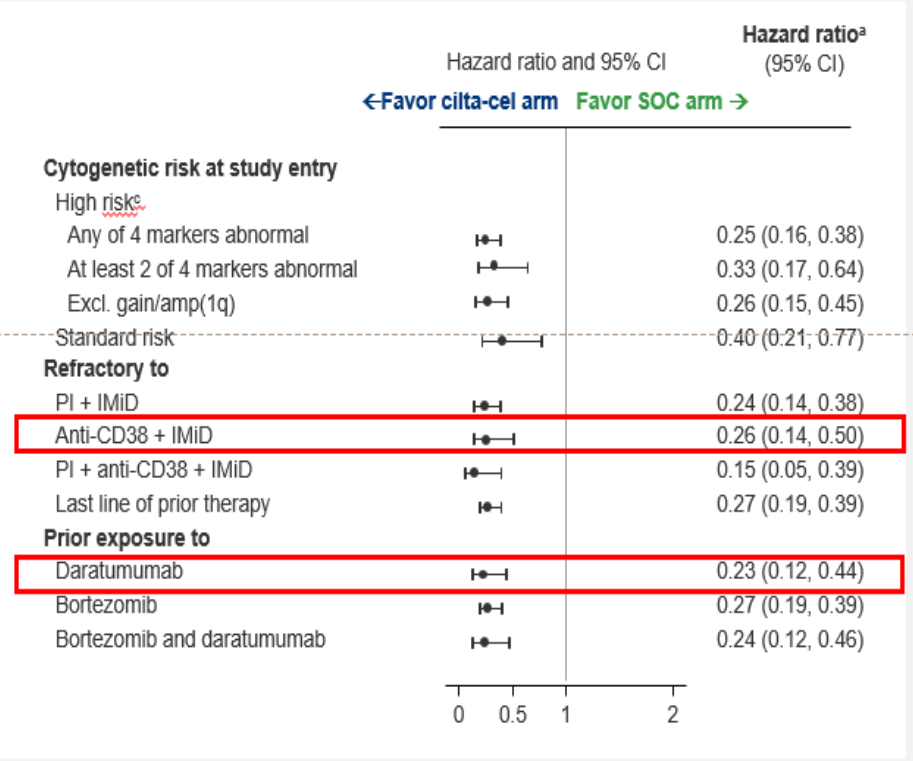
Progression-free survival by treatment and number of prior lines in the ITT set



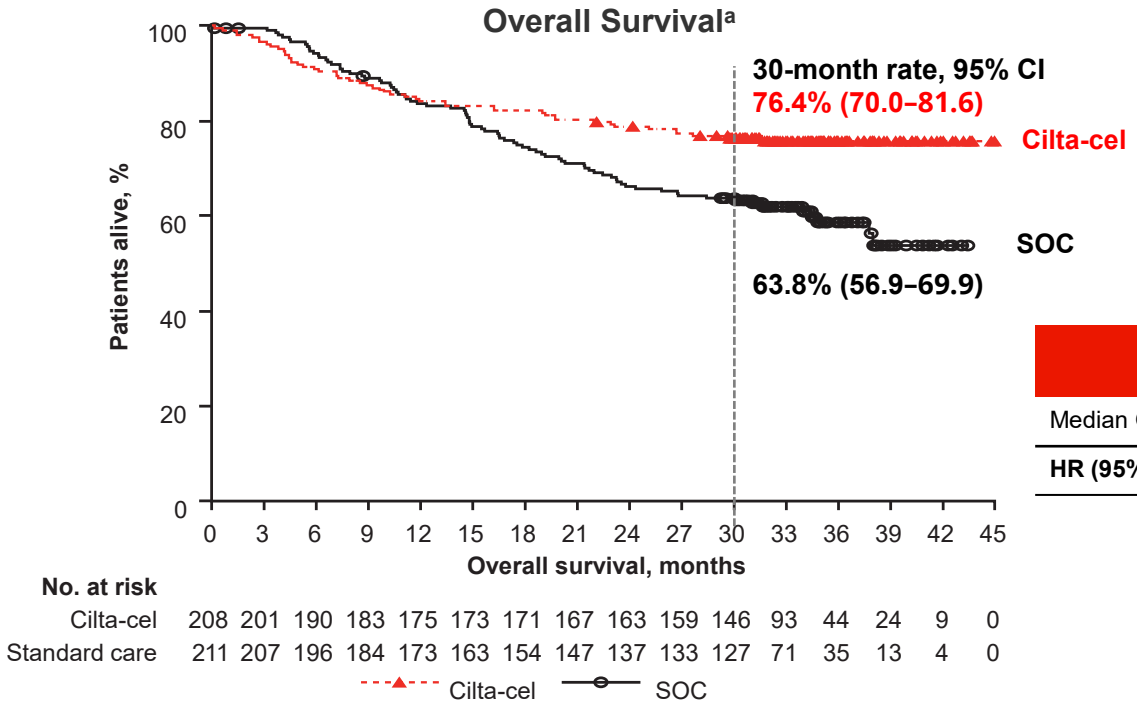
No. at risk											
Cilta-cel arm, 1 prior LOT	68	61	58	56	48	28	16	8	1	0	0
Cilta-cel arm, 2–3 prior LOT	140	116	114	110	98	66	29	14	8	1	0
SOC arm, 1 prior LOT	68	60	52	48	35	22	8	1	0	0	0
SOC arm, 2–3 prior LOT	143	116	81	68	53	24	12	3	1	0	0

CARTITUDE-4: Key Subgroup Analysis (ITT)





34-Month Update of CARTITUDE-4: OS Was Significantly Prolonged With Cilta-cel vs SOC

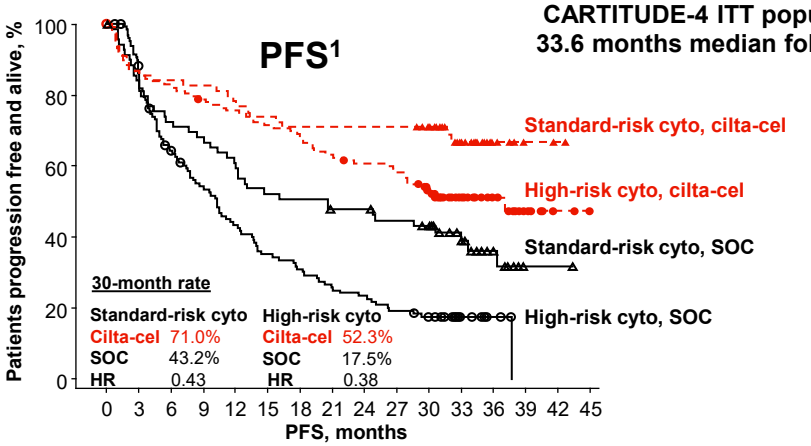


	Cilta-cel (N=208)	SOC (N=211)
Median OS (95% CI), months	NR (NE–NE)	NR (37.8–NE)
HR (95%CI); *P*-value[b]	**0.55 (0.39–0.79); 0.0009[b]**	

[a]Median follow-up, 33.6 months. [b]*P*-value, 0.0009, crossed the prespecified boundary of 0.0108 as implemented by the Kim-DeMets spending function with parameter=2.
Cilta-cel, ciltacabtagene autoleucel; HR, hazard ratio, mOS, median overall survival; NE, not estimable; NR, not reached; OS, overall survival; SOC, standard of care.

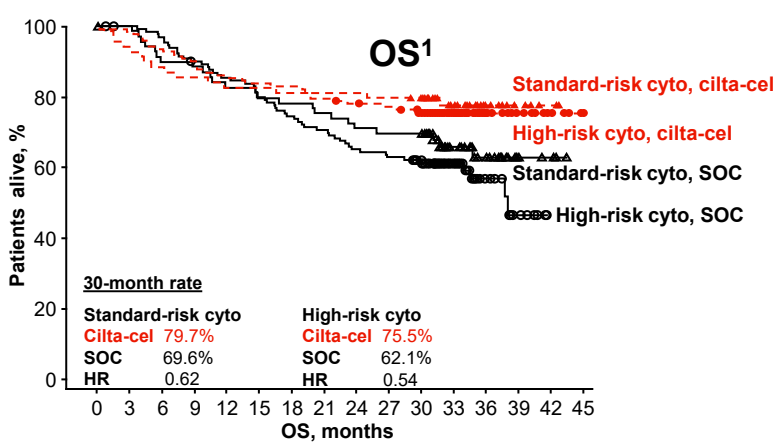
Presented by M-V Mateos at the 21st International Myeloma Society (IMS) Annual Meeting; September 25–28, 2024; Rio de Janeiro, Brazil

PFS and OS in Patients With High-Risk and Standard-Risk Cytogenetics (ITT)



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



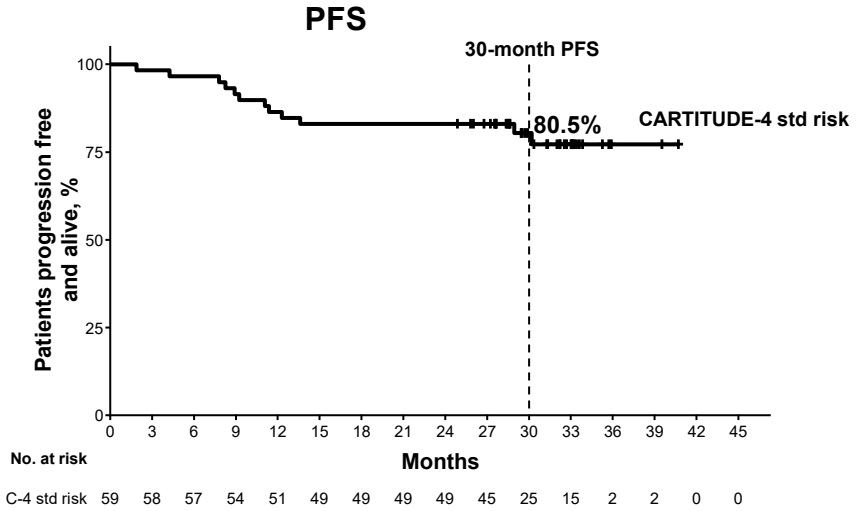
Patients at risk

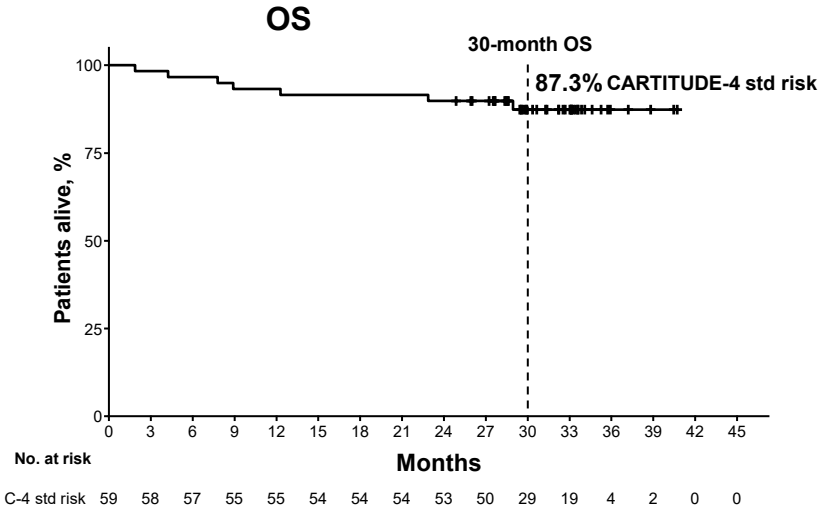
High risk, SOC	132	130	126	116	110	103	96	91	84	81	75	38	14	6	0	0
High risk, cilta-cel	123	121	115	111	105	103	102	98	95	93	83	50	23	14	5	0
Standard risk, SOC	70	69	62	61	57	55	54	52	49	48	48	29	18	5	3	0
Standard risk, cilta-cel	69	65	61	59	57	57	56	56	56	55	52	35	13	5	2	0

In CARTITUDE-4, cilta-cel improved PFS and OS in prespecified subgroups with standard- and high-risk cytogenetics[1]

1. Sidana S, et al. *J Clin Oncol* 2025;43:7539.

CARTITUDE-4: PFS and OS in Patients With Standard-Risk Cytogenetics (As-Treated)





80% of CARTITUDE-4 patients with standard-risk disease who received cilta-cel as study treatment remained progression free and off treatment at 30 months

Presented by L Costa at the 67th American Society of Hematology (ASH) Annual Meeting; December 6–9, 2025; Orlando, FL, USA

CARTITUDE-4: CRS and CAR-T Cell–Related Neurotoxicity

AEs, n, %	As-treated patients (n=176)				
	Any grade	Grade 3/4	Median time to onset, days	Median duration, days	Resolved, n
CRS	134 (76.1)	2 (1.1)	8	3	134
Neurotoxicity[a]	36 (20.5)	5 (2.8)			
ICANS	8 (4.5)	0[b]	10	2	8
Other[c]	30 (17.0)	4 (2.3)			
Cranial nerve palsy[d]	16 (9.1)	2 (1.1)	21	77	14
Peripheral neuropathy	5 (2.8)	1 (0.6)	63	201	3
MNT	1 (0.6)	0	85	-	0

In the cilta-cel as-treated population:

- 30 patients had non-ICANS neurotoxicities[c]
  - 16 cranial nerve palsies (14 recovered)
  - 5 peripheral neuropathies
  - 1 MNT (grade 1)
    - Patient was refractory to DPd bridging therapy and had grade 2 CRS after cilta-cel infusion (risk factors for MNTs)
- **Lower incidence and severity of CRS, ICANS, MNTs, and some cytopenias[e] observed with CARTITUDE-4 vs CARTITUDE-1**
  - Cilta-cel may be better tolerated when used earlier in treatment
  - Effective bridging therapy enables better control of tumor burden prior to CAR-T infusion
  - MNTs were lower likely related to patient management strategies implemented to mitigate this risk

Long-term CARTITUDE-4 Update (34 months): Safety Profile Consistent With Previous Analysis

Infections	Cilta-cel (n=208)	SOC (n=208)
Treatment-emergent infections, %		
All grade	63.5	76.4
Grade 3/4	28.4	29.8
Deaths due to TE- and non-TE infections, n	16	17
In first year, n	13	8
In second year, n	2	8

Cause of Death	Cilta-cel (n=208)	SOC (n=208)
Deaths, n	**50**	**82**
Due to progressive disease	**21**	**51**
Due to TEAE	12	8

- **Both arms had grade 3/4 TEAE around 97%; most frequently cytopenia**

SPM	Cilta-cel (n=208)	SOC (n=208)
SPMs, n (%)	**27 (13.0)**	**24 (11.5)**
Hematologic	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

- **New cases of SPM since previous report[a]**
  - Cilta-cel, n=18
  - SOC, n=10
- **No new cases of cranial nerve palsy or MNT for the cilta-cel arm since the previous report[a]**

[a]Includes 3 new cases of MDS and 1 new case of T-cell lymphoma for the cilta-cel arm and 1 new case of EBV-associated lymphoma for the SOC arm.
AE, adverse event; AML, acute myeloid lymphoma; cilta-cel, ciltacabtagene autoleucel; CNP, cranial nerve palsy; EBV, Epstein-Barr virus; MDS, myelodysplastic syndrome; MNT, movement and neurocognitive treatment-emergent adverse event; TE, treatment-emergent; TEAE, treatment-emergent adverse event; SOC, standard of care; SPM, second primary malignancy.

Presented by M-V Mateos at the 21st International Myeloma Society (IMS) Annual Meeting; September 25–28, 2024; Rio de Janeiro, Brazil

Phase 3 Randomized Study of Teclistamab Plus Daratumumab Versus Investigator's Choice of Daratumumab and Dexamethasone With Either Pomalidomide or Bortezomib (DPd/DVd) in Patients With Relapsed Refractory Multiple Myeloma (RRMM): Results of MajesTEC-3

Maria-Victoria Mateos,[1] Nizar J. Bahlis,[2] Aurore Perrot,[3] Ajay K. Nooka,[4] Jin Lu,[5] Charlotte Pawlyn,[6,7] Roberto Mina,[8] Gaston Caeiro,[9] Alain Kentos,[10] Vania Hungria,[11] Donna Reece,[12] Ting Niu,[13] Anne K. Mylin,[14] Charlotte Toftmann Hansen,[15] Raphael Teipel,[16] Britta Besemer,[17] Meletios A. Dimopoulos,[18,19] Elena Zamagni,[20,21] Satoshi Yoshihara,[22] Kihyun Kim,[23] Chang Ki Min,[24] Paul Geerts,[25] Elena Van Leeuwen-Segarceanu,[26] Agata Tyczynska,[27] Juan Luis Reguera Ortega,[28] Magnus Johansson,[29] Markus Hansson,[30] Mehmet Turgut,[31] Mark Grey,[32] Surbhi Sidana,[33] Paula Rodriguez-Otero,[34] Joaquin Martinez-Lopez,[35] Hamza Hashmi,[36] Robin Carson,[37] Rachel Kobos,[38] Weili Sun,[39] Kristen Lantz,[37] Anne Seifert,[40] Deborah Briseno-Toomey,[41] Lisa O'Rourke,[37] Maria Rubin,[38] Diego Vieyra,[37] Lijuan Kang,[39] Luciano J. Costa[42]

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Presented by M-V Mateos at the 67th American Society of Hematology (ASH) Annual Meeting and Exposition; December 6-9, 2025; Orlando, FL, USA.

https://www.congresshub.com/ASH2025/Oncology/Teclistamab/Mateos-LBA

MajesTEC-3: Phase 3 Study Design

Key inclusion criteria

- RRMM
- 1–3 prior LOTs including a PI and lenalidomide
  - Patients with only 1 prior LOT must have been lenalidomide refractory per IMWG criteria
- ECOG PS score of 0–2

Key exclusion criteria

- Prior BCMA-directed therapy
- Refractory to anti-CD38 mAbs[a]

1:1 randomization N=587

22 Oct 2021 to 29 Sept 2023[b]

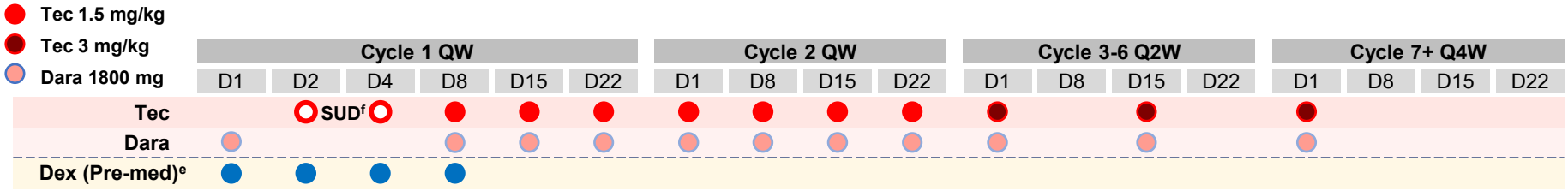
Tec-Dara
N=291
SC dosing following Dara schedule

DPd/DVd
N=296 (266/30)
by Investigator's choice[c]

Primary endpoint
- PFS per IRC

Key secondary endpoints
- ≥CR[d] and ORR[d]
- MRD negativity (10^{-5})
- OS
- MySIm-Q Total Symptom score

Other secondary endpoints
- Safety
- PK and immunogenicity



SC dosing aligned with Dara schedule, with monthly dosing after 6 cycles; steroid sparing after Cycle 1 Day 8

[a]Prior exposure to anti-CD38 mAbs was permitted. [b]During the COVID-19 pandemic. [c]DPd/DVd were administered per the approved schedules. [d]Response and disease progression were assessed by a blinded IRC per IMWG criteria. [e]Dexamethasone, acetaminophen, and diphenhydramine premedication was required for the first 2 weeks; subsequent dexamethasone was not required thereafter. [f]Patients received SUD of 0.06 mg/kg and 0.3 mg/kg on Days 2 and 4, respectively.

CR, complete response; DPd, daratumumab, pomalidomide, and dexamethasone; DVd, daratumumab, bortezomib, and dexamethasone; ECOG PS, Eastern Cooperative Oncology Group performance status; IMWG, International Myeloma Working Group; IRC, independent review committee; MRD, minimal residual disease; MySIm-Q, Multiple Myeloma Symptom and Impact Questionnaire; ORR, overall response rate; PI, proteasome inhibitor; PK, pharmacokinetics; QW, weekly; Q2W, every 2 weeks; Q4W, every 4 weeks; SC, subcutaneous; SUD, step-up dosing.

Presented by M-V Mateos at the 67th American Society of Hematology (ASH) Annual Meeting and Exposition; December 6-9, 2025; Orlando, FL, USA.

MajesTEC-3: Baseline Demographic and Disease Characteristics

Characteristic	Tec-Dara (n=291)	DPd/DVd (n=296)
Age		
Median (range), years	64 (36–88)	63 (25–84)
≥75 years, n (%)	31 (10.7)	25 (8.4)
Sex, n (%)		
Male	156 (53.6)	169 (57.1)
Female	135 (46.4)	127 (42.9)
Race, n (%)		
White	190 (65.3)	194 (65.5)
Asian	68 (23.4)	63 (21.3)
Black or African American	13 (4.5)	20 (6.8)
Other[a]	20 (6.9)	19 (6.4)

Characteristic	Tec-Dara (n=291)	DPd/DVd (n=296)
Baseline ECOG PS score, n (%)		
0	167 (57.4)	160 (54.1)
1	108 (37.1)	127 (42.9)
2	16 (5.5)	9 (3.0)
ISS stage, n/N (%)		
I	182 (62.5)	185 (62.5)
II	85 (29.2)	88 (29.7)
III	24 (8.2)	23 (7.8)
BMPCs ≥60%,[b] n/N (%)	28/286 (9.8)	24/293 (8.2)
Presence of soft-tissue plasmacytomas, n (%)	41 (14.1)	41 (13.9)
Extramedullary plasmacytomas	14 (4.8)	17 (5.7)
High-risk cytogenetics[c] n/N (%)	104/285 (36.5)	104/294 (35.4)

Baseline demographics well balanced and reflective of patients seen in real-world practice

[a]"Other" includes Native Hawaiian or Pacific Islander (Tec-Dara, n=1 [0.3%]; DPd/DVd, n=0; total, n=1 [0.2%]), American Indian or Alaska Native (Tec-Dara, n=0; DPd/DVd, n=1 [0.3%]; total, n=1 [0.2%]), not reported (Tec-Dara, n=14 [4.8%]; DPd/DVd, n=16 [5.4%]; total, n=30 [5.1%]), and unknown (Tec-Dara, n=5 [1.7%]; DPd/DVd, n=2 [0.7%]; total, n=7 [1.2%]). [b]Maximum value from bone marrow biopsy or bone marrow aspirate was selected if both results were available. [c]Presence of ≥1 of del(17p), t(4;14), or t(14;16).
BMPC, bone marrow plasma cell; ISS, International Staging System.

Presented by M-V Mateos at the 67th American Society of Hematology (ASH) Annual Meeting and Exposition; December 6-9, 2025; Orlando, FL, USA.

MajesTEC-3: Prior Lines of Therapy

Characteristic	Tec-Dara (n=291)	DPd/DVd (n=296)
Prior LOTs		
Median (range), n	2 (1–3)	2 (1–3)
1 prior LOT	108 (37.1)	114 (38.5)
2 prior LOTs	134 (46.0)	134 (45.3)
3 prior LOTs	49 (16.8)	48 (16.2)
Prior transplantation, n (%)	210 (72.2)	226 (76.4)

- 5% of patients were Dara exposed
- In real-world data sets, 70% of patients in 2L are Dara naïve or exposed

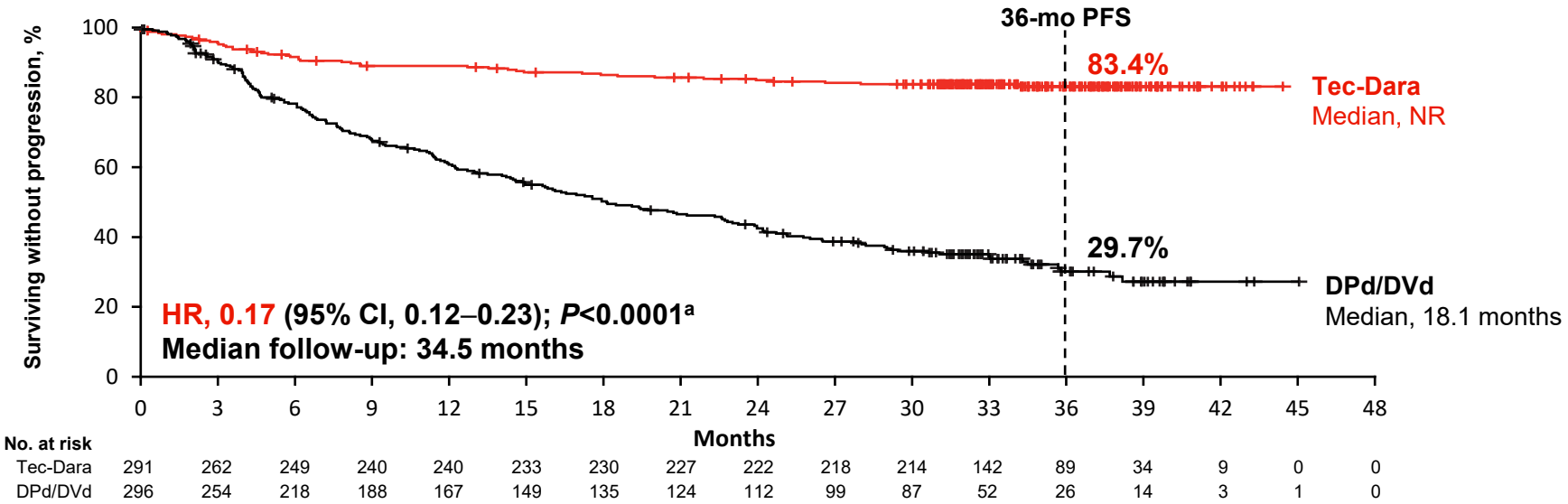
Characteristic	Tec-Dara (n=291)	DPd/DVd (n=296)
Prior therapy exposure, n (%)		
PI	290 (99.7)	296 (100)
IMiD	291 (100)	296 (100)
Anti-CD38, n (%)	15 (5.2)	16 (5.4)
Refractory status, n (%)		
To last prior LOT	250 (85.9)	251 (84.8)
Any PI	117 (40.2)	104 (35.1)
Any IMiD	247 (84.9)	253 (85.5)
Lenalidomide	240 (82.5)	251 (84.8)
Double (PI and IMiD)	99 (34.0)	88 (29.7)

Median of 2 prior LOTs and >85% of patients were refractory to an IMiD

2L, second-line; IMiD, immunomodulatory drug.

Presented by M-V Mateos at the 67th American Society of Hematology (ASH) Annual Meeting and Exposition; December 6-9, 2025; Orlando, FL, USA.

MajesTEC-3: PFS (Primary Endpoint)

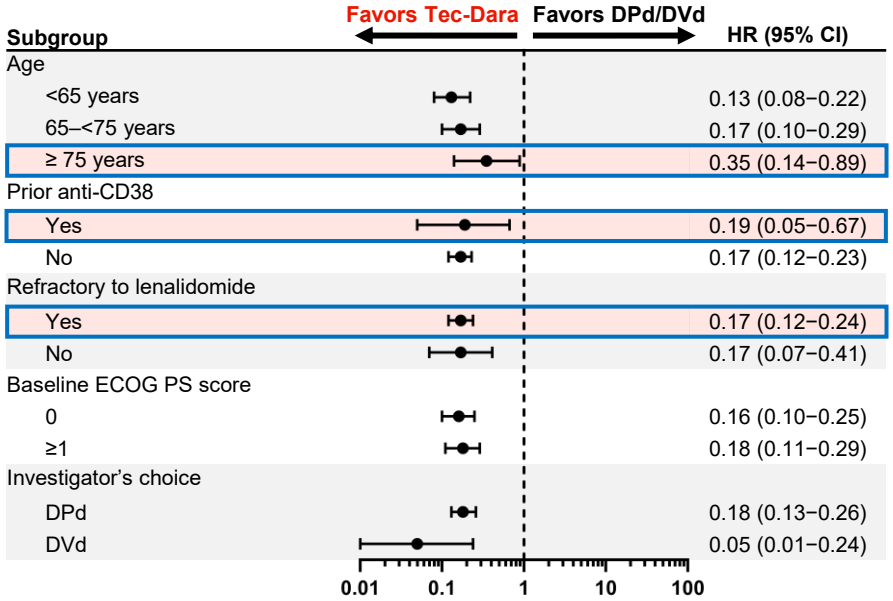


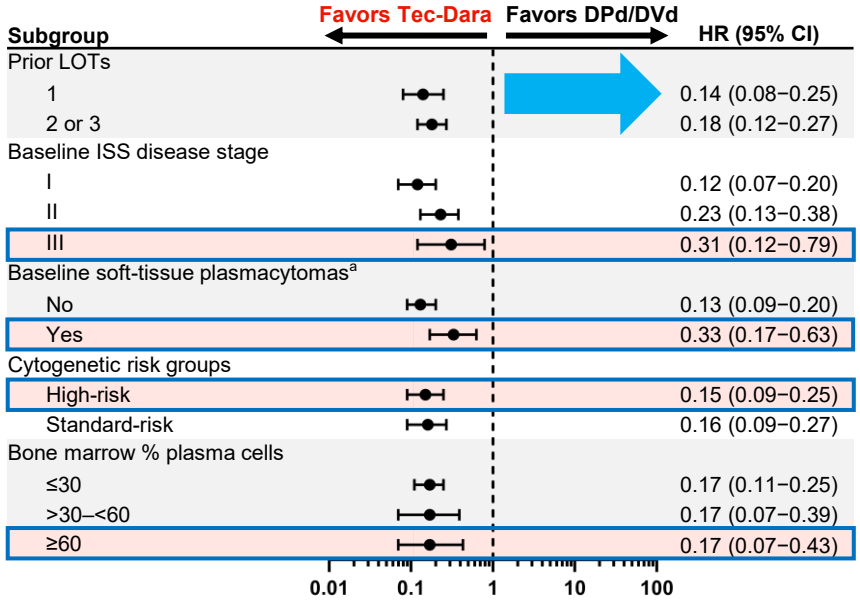
Tec-Dara significantly improved PFS, with a plateauing curve after ~6 months and >90% of patients progression-free at 6 months sustaining such a benefit at 3 years

[a]The *P* value crossed the prespecified stopping boundary for superiority for the first interim analysis (*P*=0.0139).
CI, confidence interval; HR, hazard ratio; NR, not reached.

Presented by M-V Mateos at the 67th American Society of Hematology (ASH) Annual Meeting and Exposition; December 6-9, 2025; Orlando, FL, USA.

MajesTEC-3: PFS Subgroup Analysis



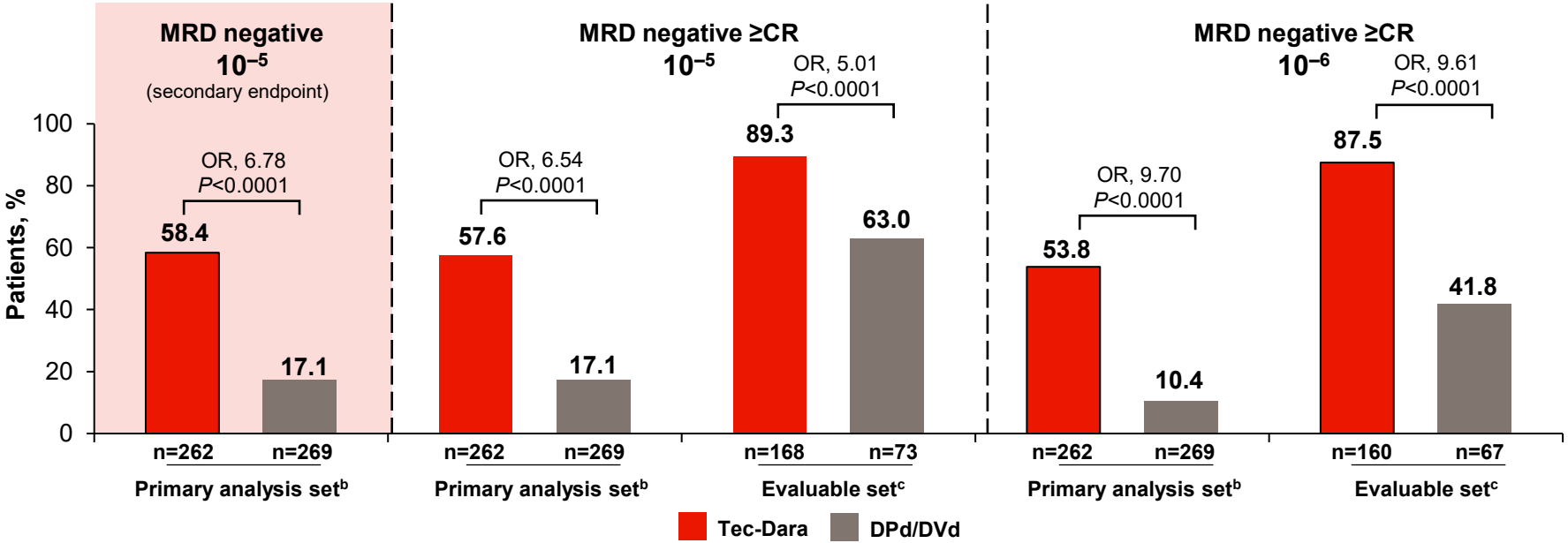


Superior PFS with Tec-Dara was consistent across all subgroups[b]

[a]Baseline soft-tissue plasmacytomas contain both extramedullary and paraskeletal plasmacytomas. [b]Not all clinically meaningful and prespecified subgroups that were assessed are shown; however, PFS was improved versus DPd/DVd across all subgroups.

Presented by M-V Mateos at the 67th American Society of Hematology (ASH) Annual Meeting and Exposition; December 6-9, 2025; Orlando, FL, USA.

MajesTEC-3: MRD Negativity[a]

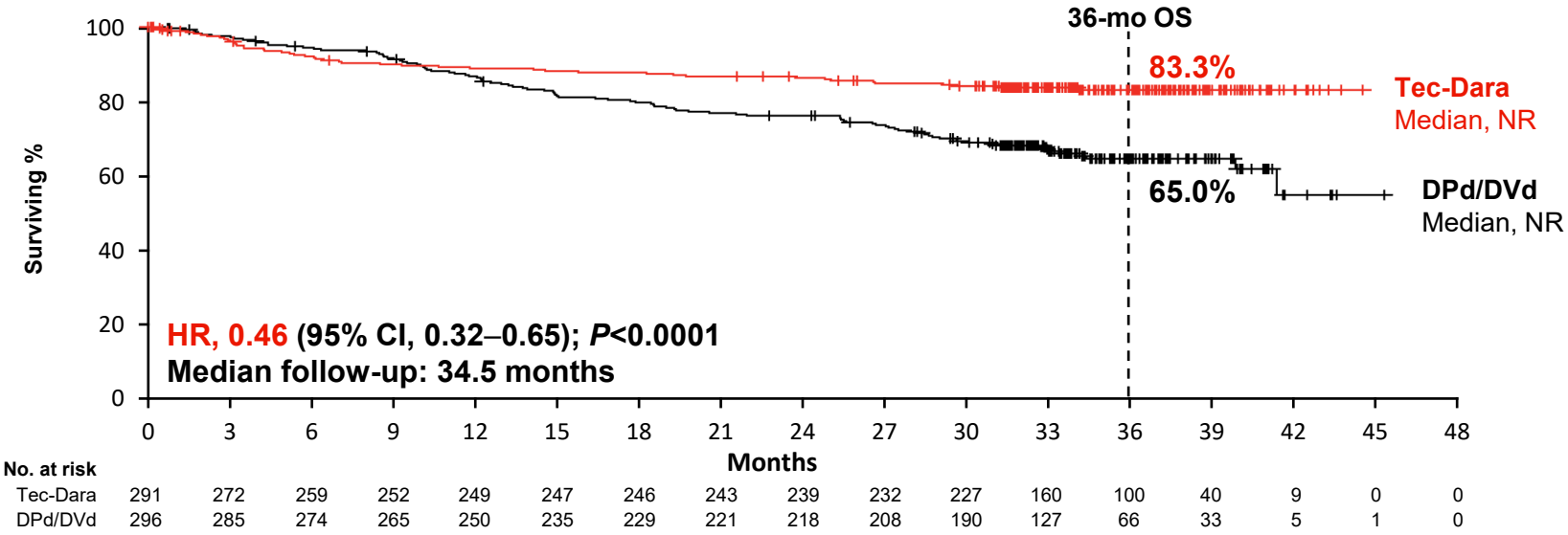


~90% MRD negativity with Tec-Dara in MRD evaluable patients

Median follow-up: 34.5 months.
[a]MRD was assessed in the bone marrow by NGS in accordance with International Myeloma Working Group guidelines. [b]The MRD NGS primary analysis set was defined as all randomized patients in the study except those recruited in China (due to China instead utilizing NGF for MRD assessment). [c]The MRD NGS evaluable set was defined as patients who achieved ≥CR, had a successful baseline calibration, and had ≥1 post-baseline MRD sample with a positive or negative result (per NGS) at the indicated threshold.
NGF, next-generation flow; NGS, next-generation sequencing.

Presented by M-V Mateos at the 67th American Society of Hematology (ASH) Annual Meeting and Exposition; December 6-9, 2025; Orlando, FL, USA.

MajesTEC-3: OS

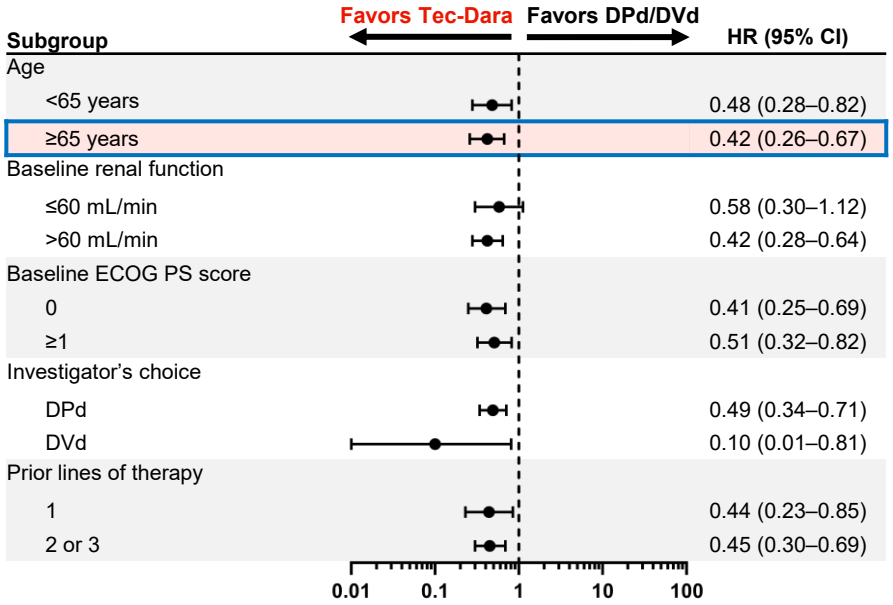


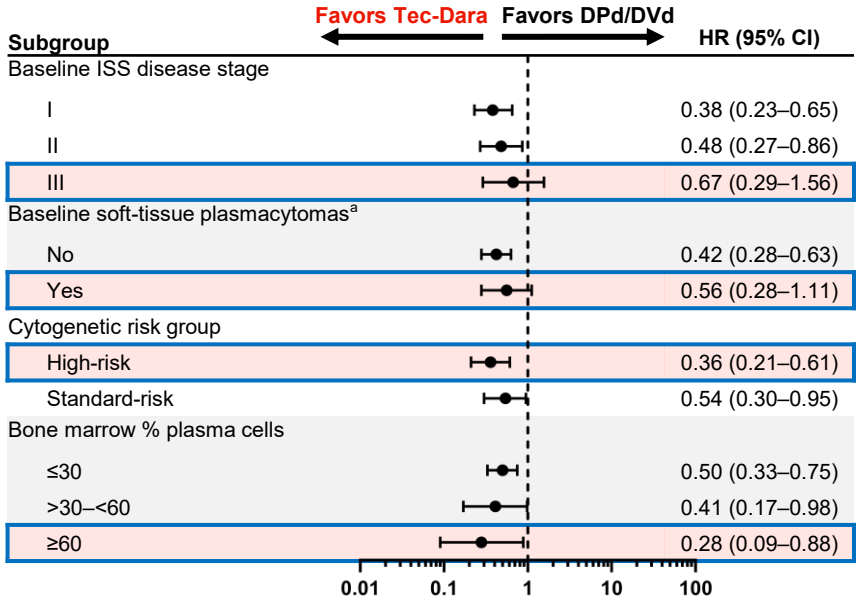
Tec-Dara significantly improved OS versus DPd/DVd, with 83% of patients alive at 3 years

Analysis of RMST demonstrated an OS benefit for Tec-Dara versus DPd/DVd (RMST difference, 2.15 months; *P*=0.0088).
RMST, restricted mean survival time.

Presented by M-V Mateos at the 67th American Society of Hematology (ASH) Annual Meeting and Exposition; December 6-9, 2025; Orlando, FL, USA.

MajesTEC-3: OS Subgroup Analysis





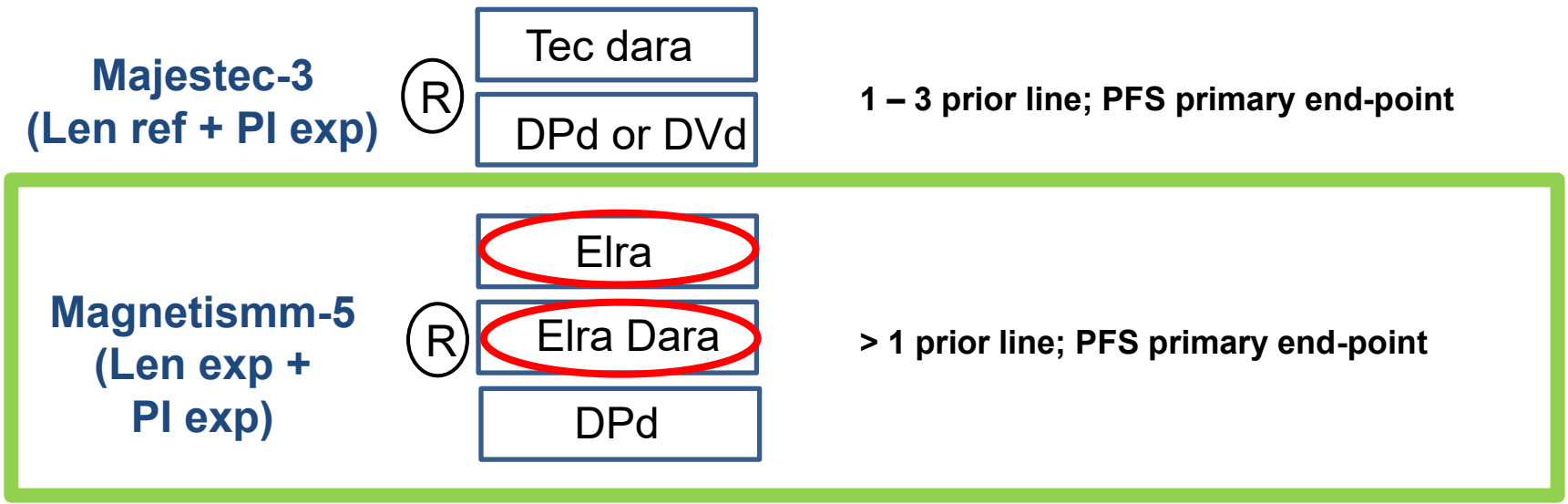
Superior OS with Tec-Dara across prespecified subgroups[b]

[a]Baseline soft-tissue plasmacytomas contain both extramedullary and paraskeletal plasmacytomas. [b]Not all prespecified subgroups that were assessed are shown; however, OS favored Tec-Dara versus DPd/DVd across all subgroups.

Presented by M-V Mateos at the 67th American Society of Hematology (ASH) Annual Meeting and Exposition; December 6-9, 2025; Orlando, FL, USA.

Patients at first relapse, len exp/ref

BCMA BispAbs



MajesTEC-9[1]

A study comparing teclistamab with investigator's choice of PVd or Kd in patients with RRMM who previously received 1-3 prior LOTs including an anti-CD38 mAb and lenalidomide[1,2]

Phase 3, randomized, open-label, multicenter study

Patients:

- Aged ≥18 years
- RRMM per IMWG criteria with evidence of PD or failure to achieve a response to last LOT
- ECOG PS of 0-2
- 1-3 prior LOT, including ≥2 consecutive cycles of an anti-CD38 mAb and lenalidomide
- Key exclusion criteria: prior BCMA targeted therapy

Primary Outcome:

- PFS
- CRS by severity

Secondary Outcomes:

- OR (≥ PR)
- ≥VGPR
- ≥CR
- OS
- PFS and depth of response in patients with high-risk molecular features
- TTNT
- Incidence and Severity of AEs; SAEs
- Change from baseline in HRQoL outcomes
- Time to worsening in symptoms, functioning, and overall HRQoL
- Proportion of patients with meaningful HRQoL improvement
- Teclistamab serum concentrations
- Presence of ADAs to teclistamab

results from the investigational Phase 3 MajesTEC-9 study of TECVAYLI® (teclistamab-cqyv) monotherapy, showing a 71% reduction in the risk of disease progression or death and a 40% reduction in the risk of death in a patient population that was predominantly refractory to anti-CD38 therapy and lenalidomide. Data confirm superior progression-free survival (PFS) and overall survival (OS) with TECVAYLI® compared to standard of care as early as second line.[1]

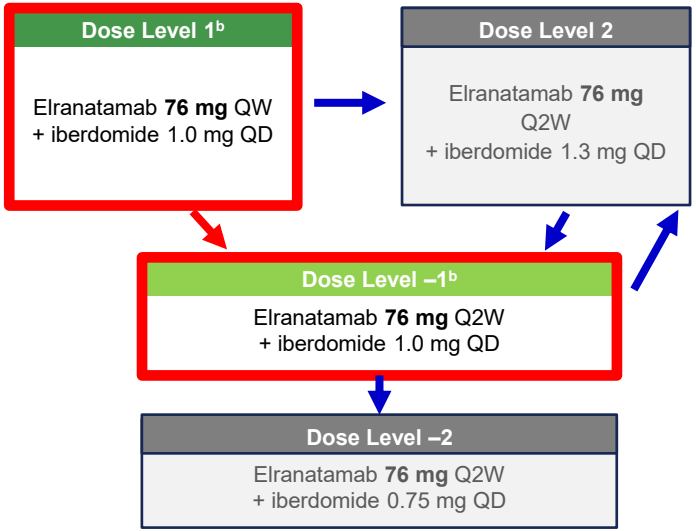
MagnetisMM-30 Study Design

- MagnetisMM-30 (NCT06215118) is a phase 1b, open-label, multicenter, prospective study
- **Part 1** (dose escalation) primary objective was to assess the tolerability and safety of elranatamab in combination with iberdomide to determine the recommended doses of the combination for evaluation in **Part 2** (randomized dose optimization)
  - A BOIN approach was used to guide dose escalation/de-escalation in **Part 1**

Patients with RRMM

Key inclusion criteria
- Age ≥18 years with MM per IMWG criteria
- ECOG PS 0-1
- 2-4 prior LOTs, including ≥1 IMiD and ≥1 PI[a]
- Relapsed or refractory to last LOT

Key exclusion criterion
- Stem cell transplant ≤12 weeks prior to enrollment or active GVHD
- Ongoing grade ≥2 peripheral sensory or motor neuropathy; history of grade ≥3 peripheral motor polyneuropathy



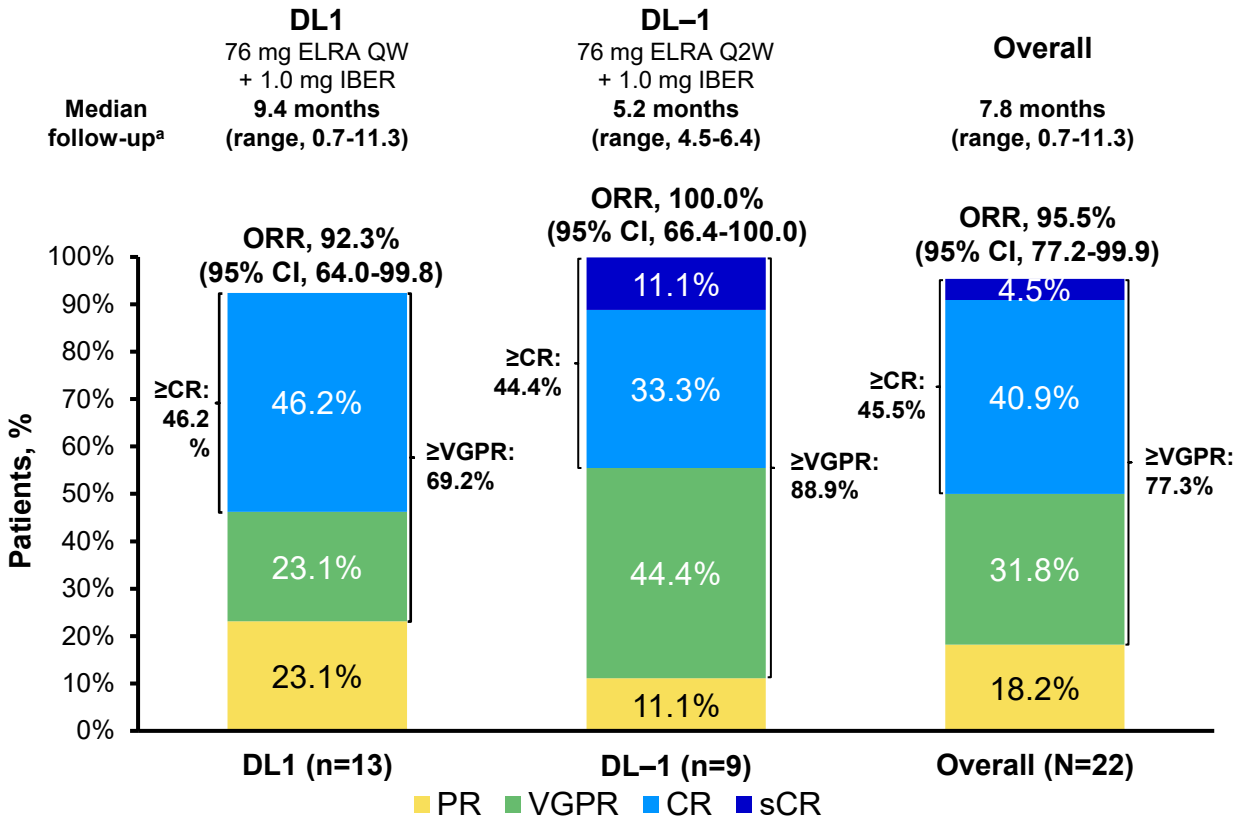
Primary endpoint
- DLTs during DLT observation period

Secondary endpoints
- AEs and laboratory abnormalities
- ORR[c]
- CR rate[c]
- Time-to-event endpoints[c]
- PK
- MRD negativity rate[c]
- Immunogenicity

[a] All patients must have received ≥2 consecutive cycles of an IMiD-containing regimen and ≥2 consecutive cycles of a PI or PI-containing regimen; [b] All patients received an initial 14-day cycle of elranatamab (12 mg on day 1, 32 mg on day 4, 76 mg on day 8) without iberdomide. Iberdomide was dosed at 21 out of 28 days for subsequent cycles; [c] Per IMWG criteria
AE=adverse event; BOIN=Bayesian Optimal Interval Design; CR=complete response; DLT=dose-limiting toxicity; ECOG PS=Eastern Cooperative Oncology Group performance status; GVHD=graft vs host disease; IMiD=immunomodulatory drug; IMWG=International Myeloma Working Group; LOT=line of therapy; MM=multiple myeloma; MRD=minimal residual disease; ORR=objective response rate; PI=proteasome inhibitor; PK=pharmacokinetics; QD=once daily; QW=once weekly; Q2W=once every 2 weeks

ORR

- Overall, the confirmed ORR by investigator was 95.5% (95% CI, 77.2-99.9)
- Responses occurred early
  - Median time to response was 1.4 months (range, 0.5-2.7)



[a] Simple median of observation times.
CR=complete response; DL=dose level; ELRA=elranatamab; IBER=iberdomide; ORR=objective response rate; PR=partial response; QW=once weekly; Q2W=every 2 weeks; sCR=stringent complete response; VGPR=very good partial response

2024 ASCO® ANNUAL MEETING

Results from the randomized phase 3 DREAMM-8 study of belantamab mafodotin plus pomalidomide and dexamethasone vs pomalidomide plus bortezomib and dexamethasone in relapsed/refractory multiple myeloma

Suzanne Trudel,[1] Meral Beksac,[2] Luděk Pour,[3] Sosana Delimpasi,[4] Hang Quach,[5] Vladimir I. Vorobyev,[6] Michele Cavo,[7] Kazuhito Suzuki,[8] Pawel Robak,[9] Kristin Morris,[10] Amy Phillips-Jones,[11] Xiaoou L. Zhou,[12] Giulia Fulci,[12] Neal Sule,[13] Brandon E. Kremer,[13] Joanna Opalinska,[13] Maria-Victoria Mateos Manteca,[14] Meletios A. Dimopoulos[15]

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Study Design

Recruitment period
October 2020 to December 2022

Treatment period
Until PD, death, unacceptable toxicity, end of study, or withdrawal of consent

Eligibility criteria

- Adults with MM
- ≥1 prior line of MM therapy including LEN
- Documented PD during or after their most recent therapy
- No prior treatment with anti-BCMA or pomalidomide; not refractory/intolerant to bortezomib

N=302

1:1 randomization

BPd (Q4W)

Belantamab mafodotin
2.5 mg/kg IV (cycle 1) then 1.9 mg/kg IV Q4W from cycle 2 onward
+
Pomalidomide 4 mg orally on days 1-21 (28-day cycles)
+
Dexamethasone 40 mg[a] on days 1, 8, 15, and 22

PVd (Q3W)

Bortezomib
1.3 mg/m^2 SC on days 1, 4, 8, and 11 of cycles 1-8 then days 1 and 8 (21-day cycles)
+
Pomalidomide 4 mg orally on days 1-14 (21-day cycles)
+
Dexamethasone 20 mg on the day of and day after bortezomib

End-of-treatment visit

Primary endpoint:
PFS (IRC assessed per IMWG)

Key secondary endpoints:
OS, MRD negativity, DOR

Additional secondary endpoints include:
ORR, CRR, ≥VGPR,TTBR, TTR, TTP, PFS2, AEs, ocular findings, HRQOL, and PROs

Stratification[b]:

- Prior lines of treatment (1 vs 2 or 3 vs ≥4)
- Prior bortezomib (yes vs no)
- Prior anti-CD38 therapy (yes vs no)

AE, adverse event; BCMA, B-cell maturation antigen; BPd, belamaf, pomalidomide, and dexamethasone; CD, cluster of differentiation; CRR, complete response rate; DOR, duration of response; HRQOL, health-related quality of life; IMWG, International Myeloma Working Group; IRC, independent review committee; ISS, International Staging System; IV, intravenous; LEN, lenalidomide; MM, multiple myeloma; MRD, minimal residual disease; ORR, objective response rate; OS, overall survival; PD, progressive disease; PFS, progression-free survival; PFS2, progression-free survival on subsequent line of therapy; PRO, patient-reported outcome; PVd, pomalidomide, bortezomib, and dexamethasone; Q3W, every 3 weeks; Q4W, every 4 weeks; SC, subcutaneous; TTBR, time to best response; TTP, time to progression; TTR, time to response; VGPR, very good partial response.
[a] Patients aged >75 years, with comorbidities, or intolerant to 40 mg received 20 mg per investigator discretion. [b] Some patients were stratified by ISS status (I vs II/III); the protocol was amended on 20 April 2021 to replace this randomization factor with prior anti-CD38 treatment (yes vs no).

Baseline Demographics and Clinical Characteristics Were Balanced

Baseline characteristics	ITT population	
	BPd (N=155)	PVd (N=147)
Age, median (range), years	67 (40-82)	68 (34-86)
<65, n (%)	64 (41)	53 (36)
65 to <75, n (%)	72 (46)	59 (40)
≥75, n (%)	19 (12)	35 (24)
Male/female, n (%)	99 (64)/56 (36)	82 (56)/65 (44)
White/Black/Asian/Mixed race, n (%)[a]	133 (86)/0/20 (13)/1 (<1)	127 (87)/0/17 (12)/0
ECOG PS ≤1, n (%)[b]	146 (97)	140 (97)
ISS stage at screening, n (%)		
I	93 (60)	85 (58)
II	39 (25)	40 (27)
III	22 (14)	22 (15)
Unknown	1 (<1)	0
Years since diagnosis, median (range)	4.04 (0.4-16.7)	3.43 (0.4-17.7)
Cytogenetic abnormalities, n (%)		
Standard risk[c]	72 (46)	75 (51)
High risk[d]	**52 (34)**	**47 (32)**
Missing or nonevaluable[e]	31 (20)	25 (17)
Time to relapse after initiation of 1L treatment		
≤12 months	**22 (14)**	**20 (14)**
>12 months	133 (86)	127 (86)
Extramedullary disease, n (%)	**20 (13)**	**11 (7)**

BPd, belantamab, pomalidomide, and dexamethasone; ECOG PS, Eastern Cooperative Oncology Group performance status; ISS, International Staging System; ITT, intent to treat; PVd, pomalidomide, bortezomib, and dexamethasone.

[a] Mixed race included a patient who was Native Hawaiian or Other Pacific Islander and White. [b] Evaluated in the safety population (BPd, N=150; PVd, N=145). [c] Standard-risk cytogenetics were defined as having negative results for all high-risk abnormalities: t(4;14), t(14;16), or del(17p13). [d] High-risk cytogenetics were defined as the presence of ≥1 of the following: t(4;14), t(14;16), or del(17p13). [e] Patients with considered missing or nonevaluable may not be high or standard risk.

Prior Treatments Were Generally Balanced

Prior treatments, n (%)	ITT population			
	BPd (N=155)		PVd (N=147)	
Prior LOT				
1 2 or 3 ≥4	82 (53) 54 (35) 19 (12)		77 (52) 48 (33) 22 (15)	
Prior ASCT	99 (64)		82 (56)	
Prior treatment	**Exposed**	**Refractory**	**Exposed**	**Refractory**
Prior proteasome inhibitor Bortezomib Carfilzomib Ixazomib	**140 (90)** 134 (86) 34 (22) 11 (7)	**40 (26)** 16 (10) 18 (12) 8 (5)	**136 (93)** 130 (88) 37 (25) 15 (10)	**35 (24)** 8 (5) 23 (16) 11 (7)
Prior immunomodulatory drug[a] **Lenalidomide** Thalidomide	155 (100) **155 (100)** 49 (32)	127 (82) **125 (81)** 9 (6)	147 (100) **147 (100)** 48 (33)	111 (76) **111 (76)** 6 (4)
Prior anti-CD38 monoclonal antibody[b] Daratumumab Isatuximab	**38 (25)** 36 (23) 2 (1)	**35 (23)** 33 (21) 2 (1)	**42 (29)** 39 (27) 3 (2)	**36 (24)** 34 (23) 2 (1)

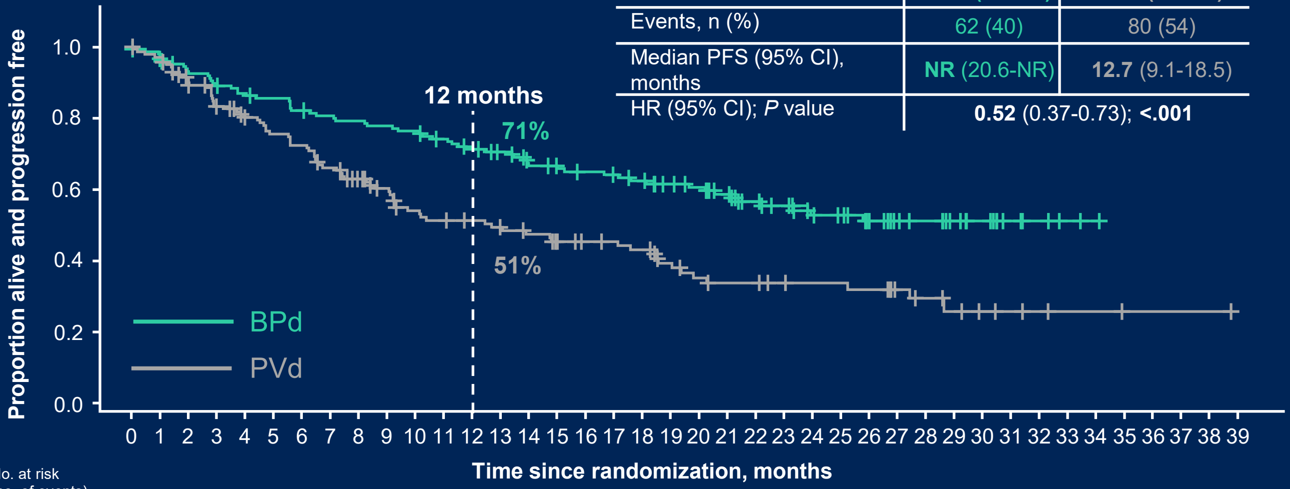
In the BPd group:

- 53% had received 1 prior LOT
- 90% received prior PI
- 81% were lenalidomide refractory
- 23% were anti-CD38 refractory

ASCT, autologous stem cell transplant; BPd, belamaf, pomalidomide, and dexamethasone; CD, cluster of differentiation; ITT, intent to treat; LOT, line of therapy; PI, proteosome inhibitor; PVd, pomalidomide, bortezomib, and dexamethasone.
[a] One patient in the PVd arm and no patients in the BPd arm received prior pomalidomide. [b] One patient in the PVd arm and no patients in the BPd arm received prior anti-CD38 inhibitors.

BPd Led to a Significant PFS Benefit vs PVd

PFS	BPd (N=155)	PVd (N=147)
Events, n (%)	62 (40)	80 (54)
Median PFS (95% CI), months	**NR** (20.6-NR)	**12.7** (9.1-18.5)
HR (95% CI); *P* value	**0.52** (0.37-0.73); **<.001**	



No. at risk (no. of events)

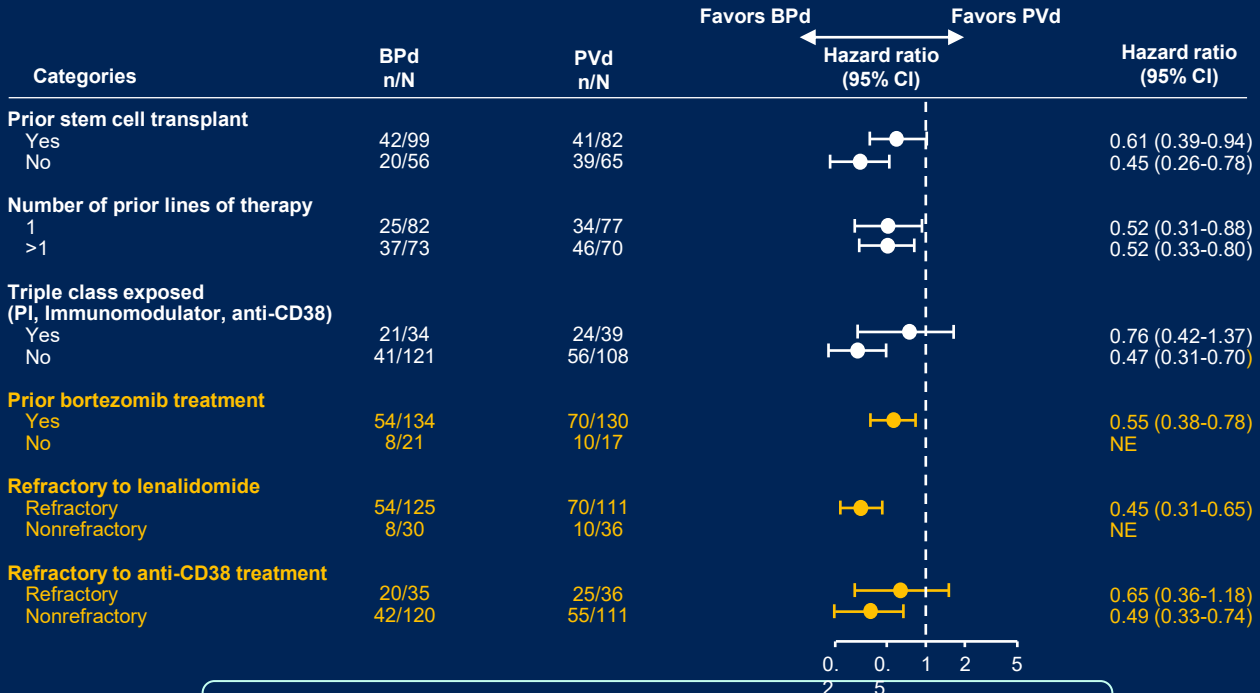
Month	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19
BPd	155 (0)	143 (5)	135 (10)	130 (15)	125 (19)	122 (21)	117 (26)	113 (28)	111 (30)	109 (32)	107 (34)	102 (37)	97 (41)	93 (42)	82 (47)	80 (47)	77 (49)	75 (50)	72 (52)	67 (53)
PVd	147 (0)	138 (4)	123 (14)	111 (23)	102 (27)	96 (33)	92 (37)	83 (45)	75 (49)	68 (52)	59 (59)	56 (62)	54 (62)	51 (64)	47 (66)	43 (68)	40 (68)	39 (68)	37 (70)	30 (73)

Month	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39
BPd	64 (54)	59 (56)	50 (58)	45 (59)	38 (61)	36 (61)	28 (62)	23 (62)	21 (62)	16 (62)	13 (62)	8 (62)	4 (62)	2 (62)	1 (62)	0 (62)	0 (62)	0 (62)	0 (62)	0 (62)
PVd	25 (76)	22 (77)	22 (77)	19 (77)	18 (77)	18 (77)	17 (78)	13 (78)	11 (79)	7 (80)	5 (80)	4 (80)	3 (80)	2 (80)	2 (80)	1 (80)	1 (80)	1 (80)	1 (80)	0 (80)

BPd led to a statistically significant and clinically meaningful reduction in risk of disease progression or death vs PVd (HR, 0.52; 95% CI, 0.37-0.73; *P*<.001)

Median follow-up, 21.8 months (range, 0.03-39.23 months)
The treatment effect (HR and corresponding 95% CIs) was estimated using the stratified Cox proportional hazards model, and the *P* value was produced based on the 1-sided stratified log-rank test. Stratified analyses were adjusted for number of prior lines of therapy and prior bortezomib use.
BPd, belamaf, pomalidomide, and dexamethasone; HR, hazard ratio; NR, not reported; PFS, progression-free survival; PVd, pomalidomide, bortezomib, and dexamethasone.

PFS Benefit Was Seen Consistently Across All Prespecified Subgroups



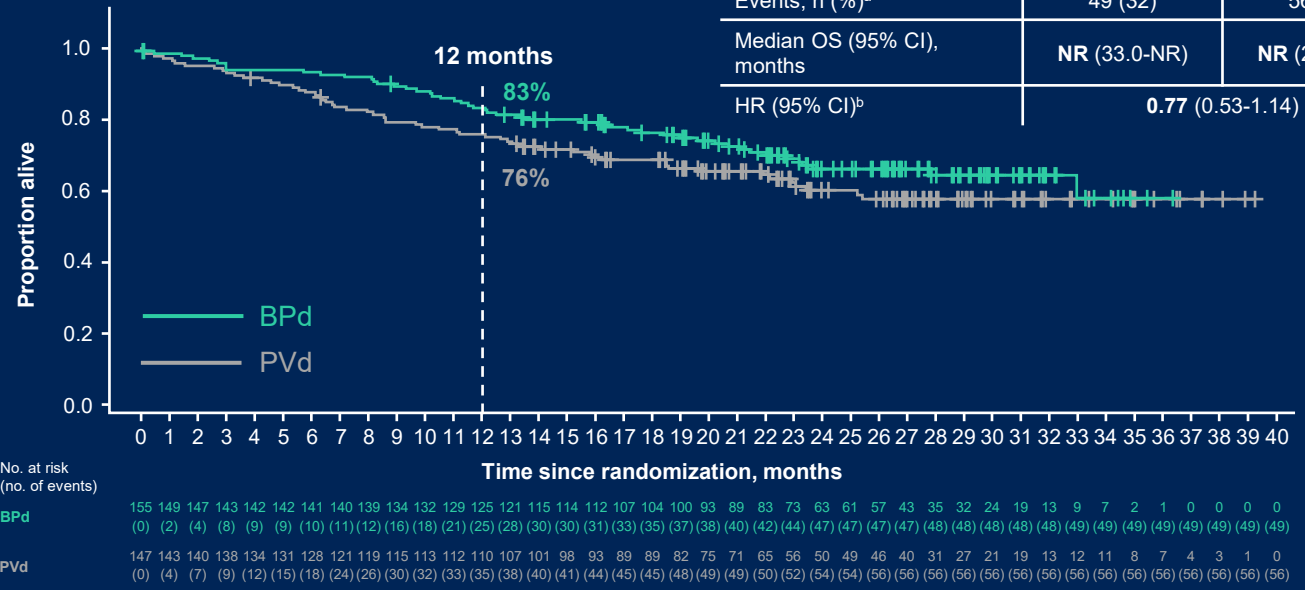
Categories	BPd n/N	PVd n/N	Hazard ratio (95% CI)
Prior stem cell transplant			
Yes	42/99	41/82	0.61 (0.39-0.94)
No	20/56	39/65	0.45 (0.26-0.78)
Number of prior lines of therapy			
1	25/82	34/77	0.52 (0.31-0.88)
>1	37/73	46/70	0.52 (0.33-0.80)
Triple class exposed (PI, Immunomodulator, anti-CD38)			
Yes	21/34	24/39	0.76 (0.42-1.37)
No	41/121	56/108	0.47 (0.31-0.70)
Prior bortezomib treatment			
Yes	54/134	70/130	0.55 (0.38-0.78)
No	8/21	10/17	NE
Refractory to lenalidomide			
Refractory	54/125	70/111	0.45 (0.31-0.65)
Nonrefractory	8/30	10/36	NE
Refractory to anti-CD38 treatment			
Refractory	20/35	25/36	0.65 (0.36-1.18)
Nonrefractory	42/120	55/111	0.49 (0.33-0.74)

PFS HR <1 was observed in difficult-to-treat subgroups

HRs for subgroups were only plotted if the number of events was ≥20 in total across both treatments and were estimated using Cox proportional hazards models, without adjustments for stratification variables. All patients were stratified by the number of prior LOT (1 vs 2 or 3 vs ≥4) and prior bortezomib (yes or no) according to an interactive voice response system stratum with a covariate of treatment. A patient was considered high risk if they had any of the following cytogenetics: t(4;14), t(14;16), or del(17p13) and considered standard risk if they had negative results for all high-risk cytogenetics listed above.
BPd, belamaf, pomalidomide, and dexamethasone; CD, cluster of differentiation; HR, hazard ratio; LOT, line of therapy; NE, not evaluable; PI, proteasome inhibitor; PFS, progression-free survival; PVd, pomalidomide, bortezomib, and dexamethasone.

Positive OS Trend Favoring BPd vs PVd

Interim OS	BPd (N=155)	PVd (N=147)
Events, n (%)[a]	49 (32)	56 (38)
Median OS (95% CI), months	**NR** (33.0-NR)	**NR** (25.2-NR)
HR (95% CI)[b]	**0.77** (0.53-1.14)	



Positive OS trend favoring BPd was seen despite the use of effective anti-MM therapies after progression with PVd; additional OS follow-up for future pre-specified analyses is ongoing

Median follow-up, 21.8 months (range, 0.03-39.23 months). Minimum ongoing follow-up, 12.8 months.
BPd, belamaf, pomalidomide, and dexamethasone; HR, hazard ratio; MM, multiple myeloma; NR, not reached; OS, overall survival; PVd, pomalidomide, bortezomib, and dexamethasone.
[a] Includes patients who died after study withdrawal when permitted per local laws. [b] The treatment effect (HR and corresponding 95% CIs) was estimated using the stratified Cox proportional hazards model. Stratified analyses were adjusted for number of prior lines of therapy and prior bortezomib use.

CONCLUSIONS

Immunotherapies are game changers

- CARTITUDE-4: cilta-cel

- BCMA bispecific-based therapy: TEC3, TEC9, Magnetism-5

- GPRC5D bispe: Monumental-3

Thank you

Global Multiple Myeloma Academy

Discussion

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CAR T-Cell Therapy in RRMM: Impact of Earlier Use and Real-World Data

Xavier Leleu, MD, PhD

APTITUDE HEALTH®

CAR T-Cell Therapy in RRMM: Impact of Earlier Use and Real-World Data

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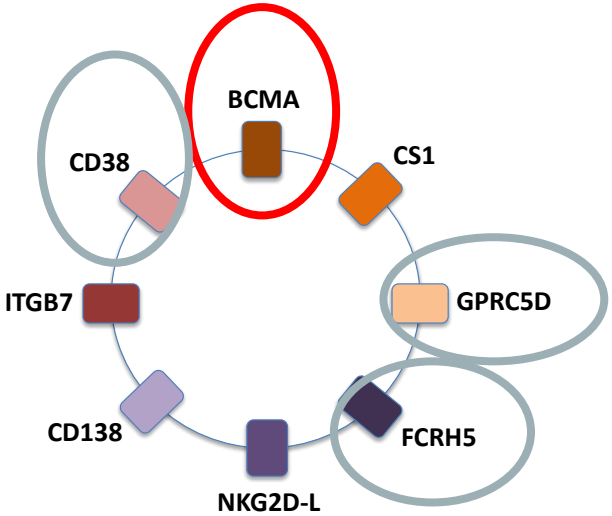
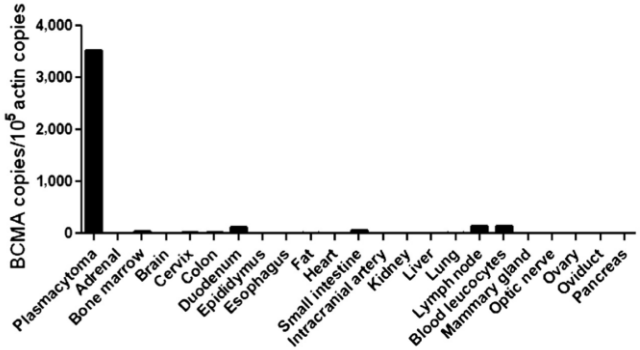
Dormance Tumorale Poitiers, France

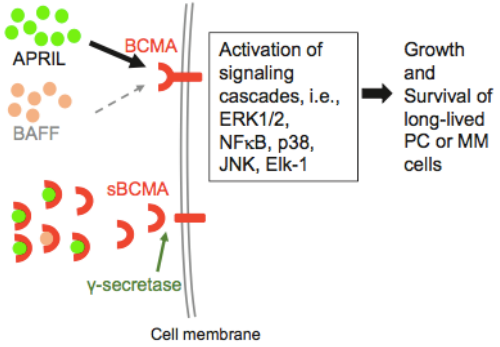
Honorarium, Grants/Research Support, and Consulting Fees:

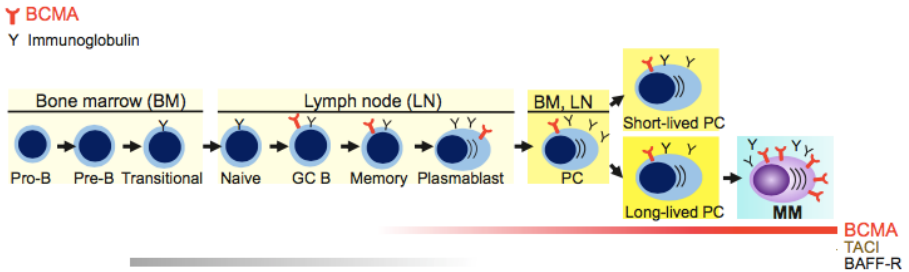
Amgen, Bristol Myers Squibb/Celgene, Janssen, Sanofi, Roche, AbbVie, Kite/Gilead, Pfizer, Regeneron, GSK, Ichnos, AstraZeneca

Targets for Immunotherapies in MM



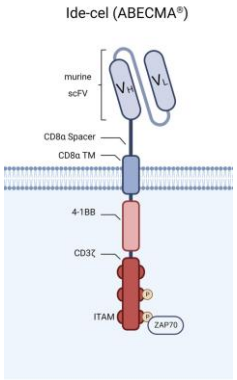




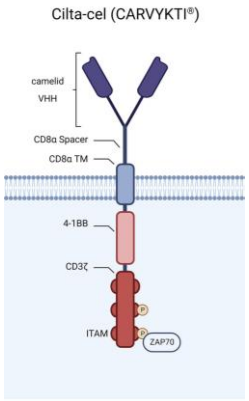


Carpenter RO, et al. *Clin Cancer Res*. 2013;19:2048-2060; Cho SF, et al. *Front Immunol*. 2018;9:1821.

FDA-Approved CAR T for Relapsed/Refractory (RR)MM



	Idecabtagene Vicleucel (ide-cel)	Ciltacabtagene Autoleucel (cilta-cel)
CAR type	**BCMA/4-1BB/CD3z**	**2-BCMA** epitope-binding domains/**4-1BB/CD3z**
Costimulatory domain	4-1BB	
Vector	Lentivirus	
LD (3 days)	Cyclophosphamide IV 300 mg/m^2 daily + fludarabine 30mg/m^2 IV daily	
Pivotal trial	**KarMMA-1 (RRMM)**	**CARTITUDE-1 (RRMM)**
Median time from apheresis to delivery	33 days	29 days



Initial approvals: patients with **RRMM after ≥4 prior LOT, including an IMiD, PI, and an anti-CD38 mAb.**

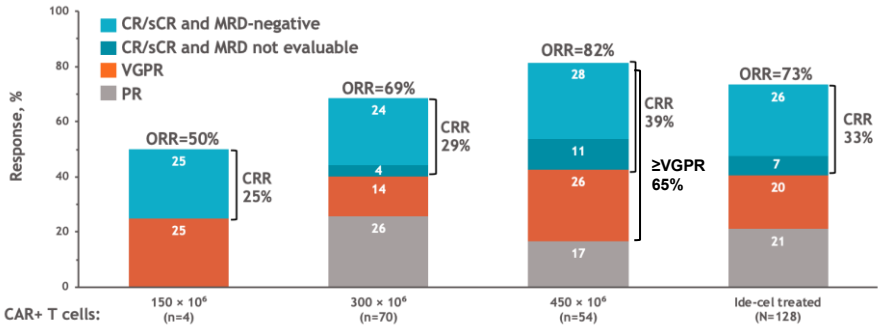
Berdeja JG, et al. *Lancet*. 2021;398:314-324.

Ide-Cel: The KarMMa Trial

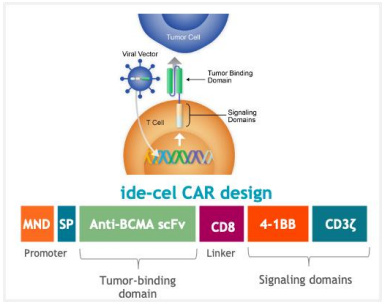
FDA approved in 2021
EMA approved in 2021

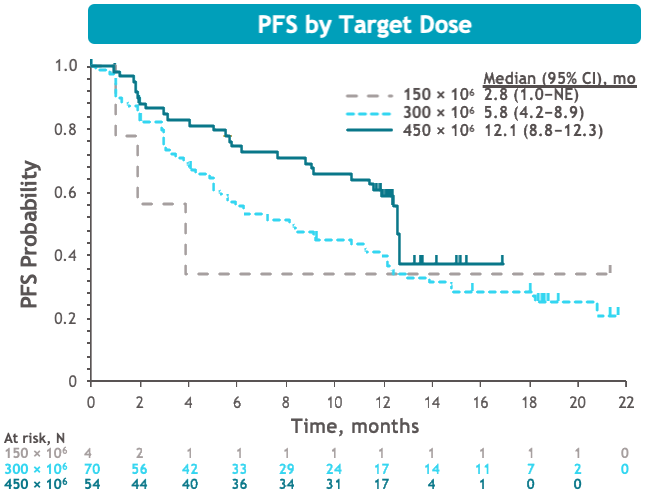
Second-generation CAR T cell, anti-BCMA murine scFv, 4-1BB costimulatory domain

KarMMa, Phase II Study (N = 128)		
Median prior lines: 6 (3−16)	84% of patients were triple-class refractory	Bridging possible Flu-Cy lymphodepletion



AE, n (%)	Ide-Cel–Treated (N = 128)	
	Any Grade	Grade ≥3
Hematologic		
Neutropenia	117 (91)	114 (89)
Anemia	89 (70)	77 (60)
Thrombocytopenia	81 (63)	67 (52)
CRS	107 (84)	7 (5)
Neurotoxicity	23 (18)	4 (3)





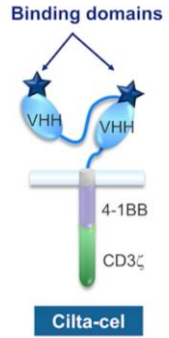
mOS = 19.4 mo

Munshi NC, et al. *N Engl J Med*. 2021;384:705-716.

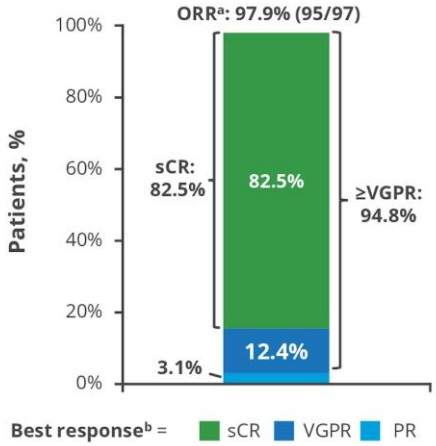
Cilta-Cel: The CARTITUDE-1 Trial

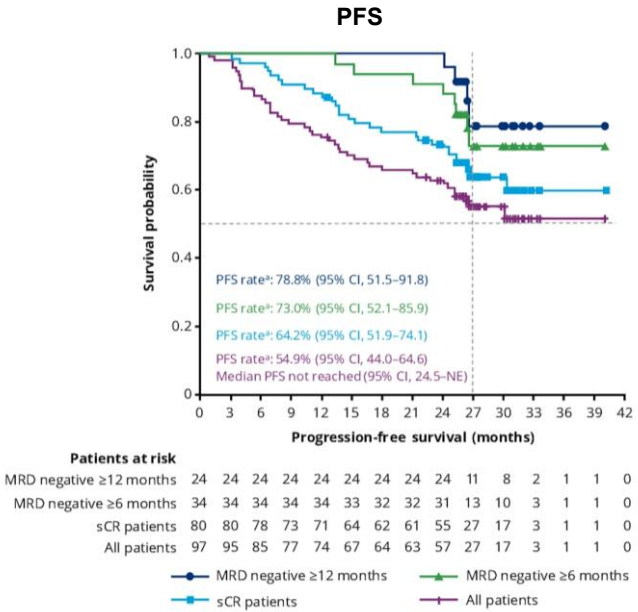
FDA approved in 2022
EMA approved in 2022

Second-generation CAR T cell, 2 anti-BCMA camelid VHH single domains, 4-1BB costimulatory domain



CARTITUDE-1, Phase II Study (N = 97)		
Median prior lines: 6 (3−18)	88% of patients were triple-class refractory	Bridging possible Flu-Cy lymphodepletion





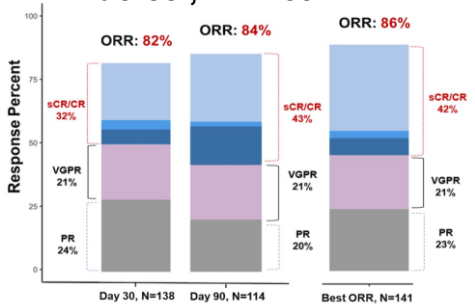
AE, n (%)	Cilta-Cel–Treated (N = 97)	
	Any Grade	Grade ≥3
Hematologic		
Neutropenia	93 (96)	92 (95)
Anemia	79 (81)	66 (68)
Thrombocytopenia	77 (80)	58 (60)
CRS	92 (95)	6 (5)
Neurotoxicity	20 (21)	10 (10)

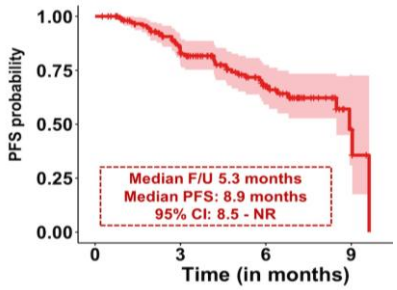
27-month OS rate = 70%

Berdeja JG, et al. *Lancet*. 2021;398:314-324.

Real-World Data (US consortium)

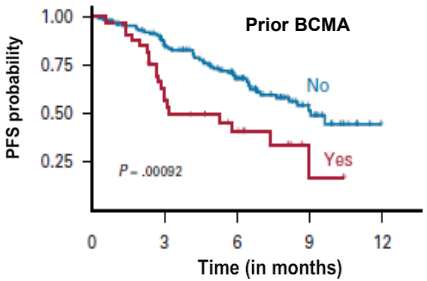
Ide-cel, n = 159





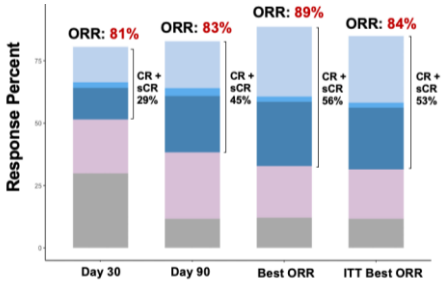
77% of patients (N=150) would have been ineligible for participation in the KarMMa trial

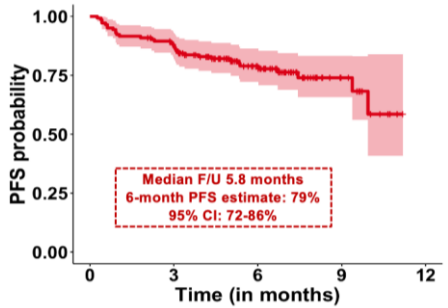
KarMMa-1 exclusion criteria at leukapheresis	No. (%)
Organ failure (renal, cardiac, hepatic)	60 (31)
Prior anti-BCMA therapy	43 (22)
Platelets < 50,000/μL	42 (21)
Hemoglobin < 8g/dL	33 (17)
ECOG PS ≥ 2	33 (17)
ANC < 1000/uL	29 (15)
PCL, POEMS, amyloidosis, non-secretory myeloma	26 (13)



Hansen DK, et al. ASCO 2022. Abstract 8042.; Hansen DK, et al. *J Clin Oncol.* 2023;41:2087-2097.

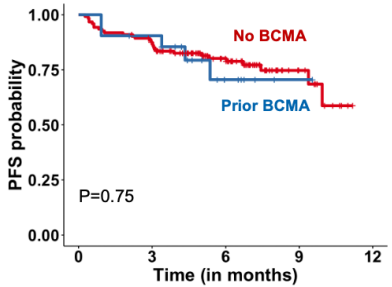
Cilta-cel, n = 143





57% of patients (N=81) would have been ineligible for participation in the CARTITUDE-1 trial

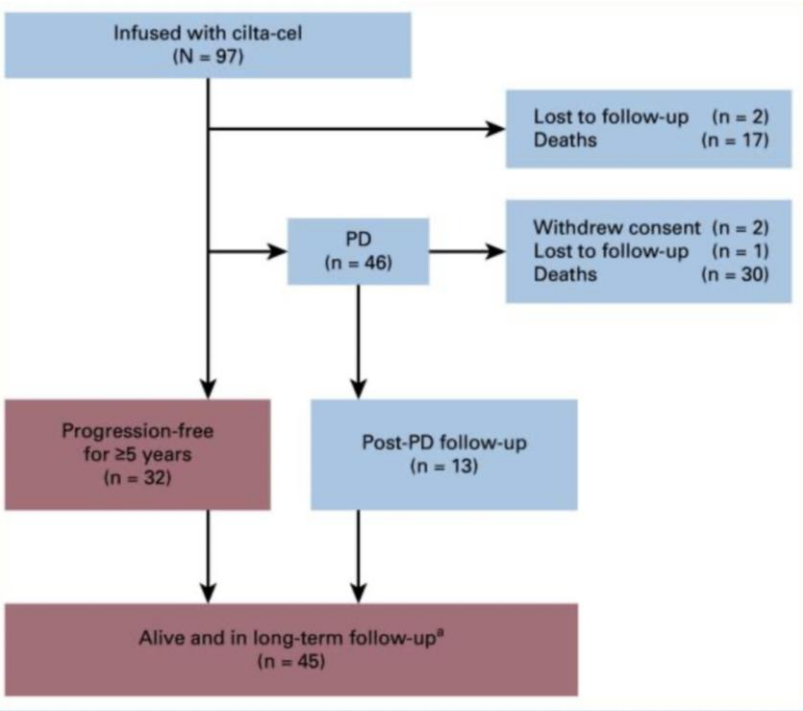
CARTITUDE-1 exclusion criteria at leukapheresis	No. (%)
Cytopenias	24 (17)
Oligosecretory/Non-secretory	23 (16)
Organ dysfunction	17 (12)
Prior anti-BCMA	17 (12)
ECOG PS ≥ 2	14 (10)
Plasma Cell Leukemia	10 (7)
History of CNS Pathology	9 (6)
Amyloid	4 (3)



Hansen DK, et al. ASCO 2023. Abstract 8012.

Cilta-Cel: The CARTITUDE-1 Trial – Survival Times With Long-Term Follow-Up (1/2)

Follow-up at 61.3-month (≥5 years after cilta-cel) median follow-up

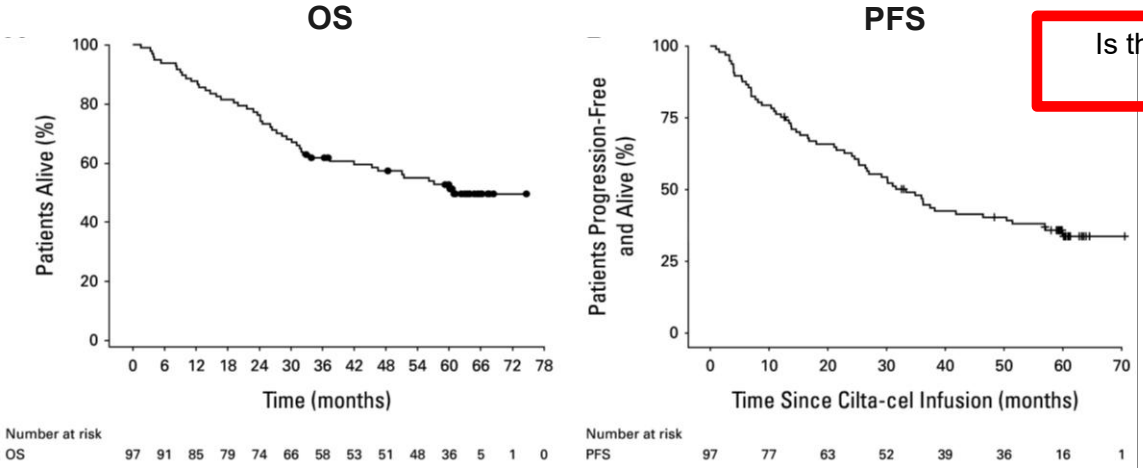


At data cutoff, of 97 patients receiving cilta-cel

- 45 (46.4%) are alive and in long-term follow-up
- 32 (33%) patients alive and progression free without further antimyeloma treatment
- 31 of 32 (96.9%) had stringent complete response (sCR) as their best response per independent review committee (IRC) assessments
- 1 patient with no measurable disease at baseline was not evaluable per IRC assessment but demonstrated sCR per investigator
- 46 (47%) had PD within 5 years; of the remaining 19, 17 died without PD and 2 were lost to follow-up

Jagannath S, et al. *J Clin Oncol*. 2025;2766-2771.

Cilta-Cel: The CARTITUDE-1 Trial – Survival Times With Long-Term Follow-Up (2/2)



Is this the definition of CURE?

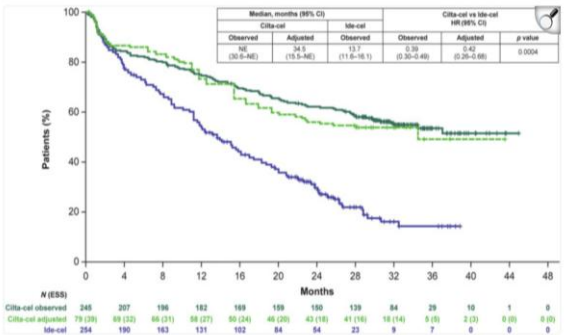
- mOS was 60.7 months (95% CI, 41.9 to not estimable)
- At a single center, 12 patients in sCR underwent serial minimal residual disease (MRD) and positron emission tomography-computed tomography assessments, and all (100%) were both MRD negative (at least 10^{-5} threshold) and imaging negative at year 5 or later after cilta-cel (data supplement)

Jagannath S, et al. *J Clin Oncol*. 2025;2766-2771.

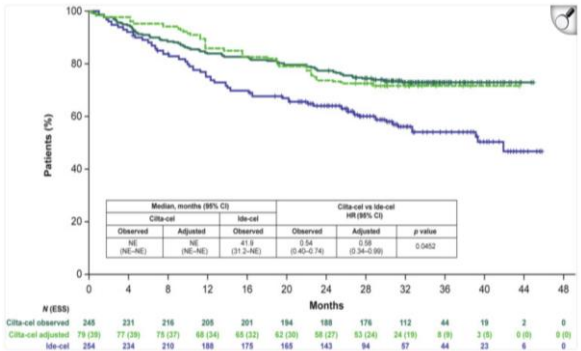
Cilta-Cel: The CARTITUDE-1, CARTITUDE-4, and KarMMa-3 Trials – Comparative Efficacy of PFS for Cilta-Cel vs Ide-Cel[1]

85 patients from CARTITUDE-4 and CARTITUDE-1 were included.
After adjustment, patients in the cilta-cel group (effective sample size = 39) had a 58% reduction in PFS risk (hazard ratio [HR] 0.42 [95% CI, 0.26–0.68]; *P* = .0004) and a 42% reduction in OS risk (HR 0.58 [0.34–0.99]; *P* = .0452) vs ide-cel.

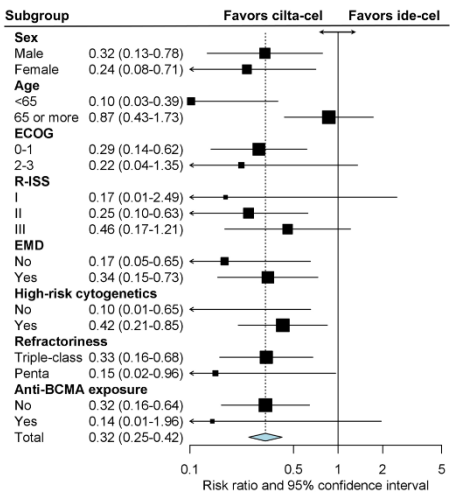
PFS



OS



Forest plot for PFS[2]

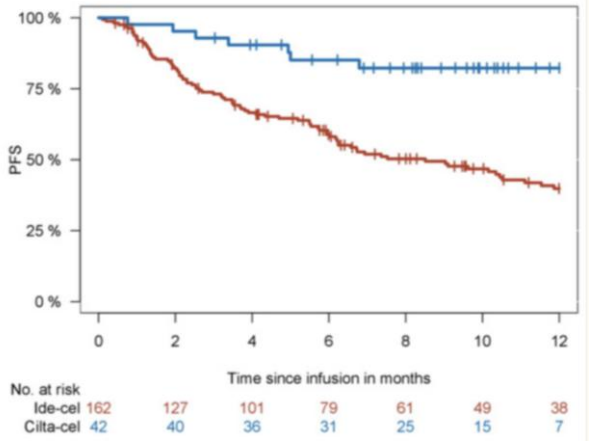


An unanchored MAIC was performed utilizing individual patient-level data (IPD) from CARTITUDE-4 (1–3 prior lines of therapy [LOT]; *n* = 208) and CARTITUDE-1 (3–4 prior LOT; *n* = 37). Patients fulfilling KarMMa-3 inclusion criteria (2–4 prior LOT, triple-class exposed) were selected, and outcomes were compared against published aggregate KarMMa-3 data. Cilta-cel IPD were weighted to match reported baseline characteristics of KarMMa-3 on key prognostic factors identified a priori.
HR <1 indicates favorable treatment effect for cilta-cel.
Comparative efficacy was estimated for progression-free survival (PFS) and OS.
Cilta-cel, ciltacabtagene autoleucel; HR, hazard ratio; ide-cel, idecabtagene vicleucel; NE, not estimable; PFS, progression-free survival; BCMA, B-cell maturation antigen; EMD, extramedullary disease; R-ISS, Revised International Staging System.
1. Lopez-Munoz N, et al. *Adv Ther*. 2026;43:1327-1340; 2. Merz M, et al. *HemaSphere*. 2025;9:e70070.

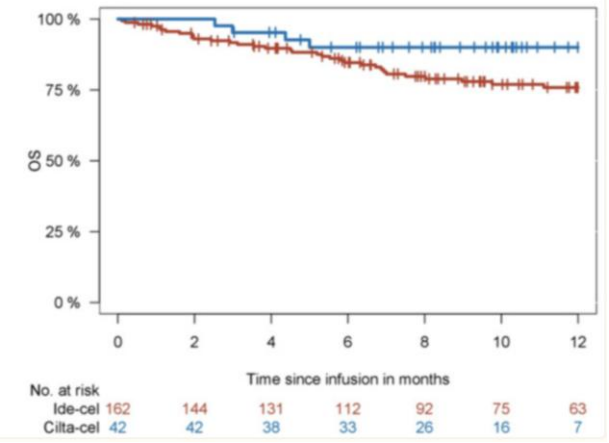
Ide-Cel or Cilta-Cel for RRMM: Real-Life Data – an International Multicenter Study

We compared the outcome of ide-cel (n = 162) vs cilta-cel (n = 42).
The median follow-up for survivors was 9.7 months in the cilta-cel group vs 12.1 months in the ide-cel group (*P* = .02)

PFS



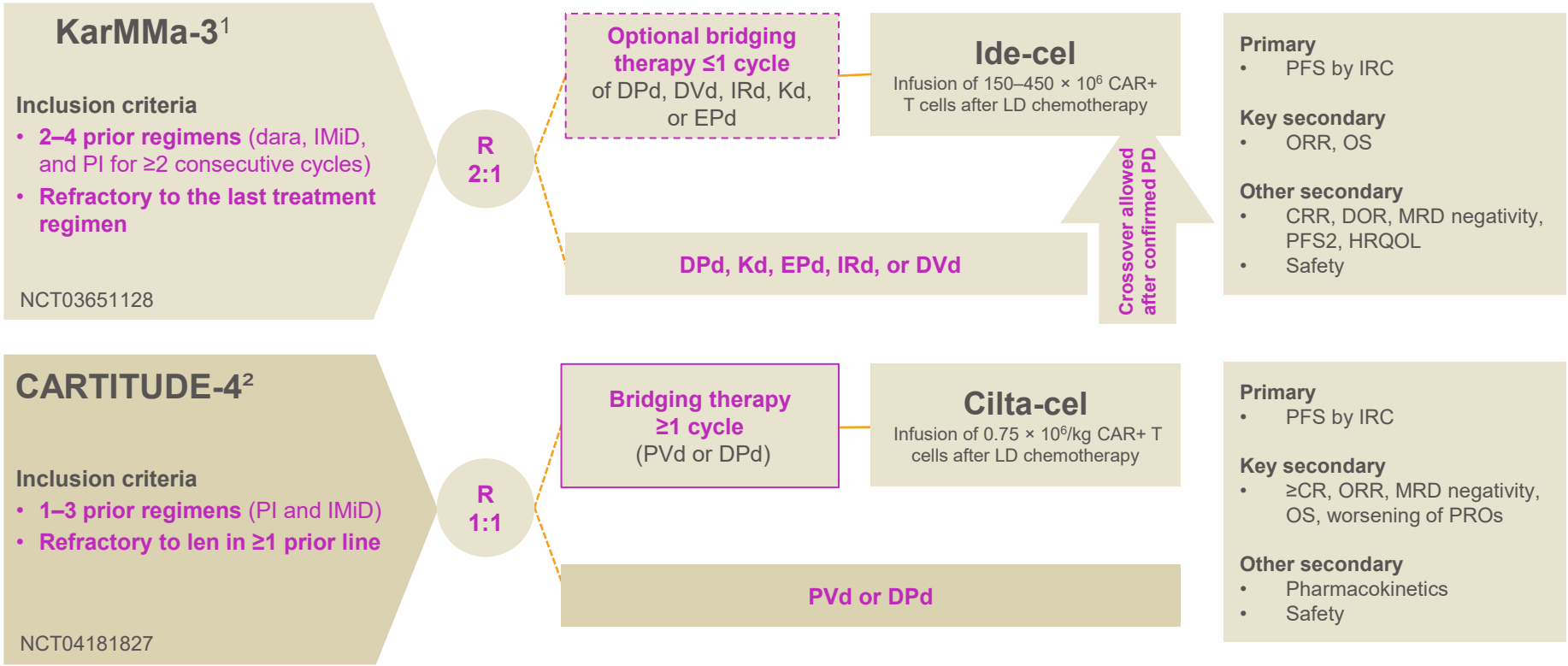
OS



Median age at the time of CAR T infusion was 61 years (range, 28–82 years) for ide-cel and 61 years (range, 24–84 years) for cilta-cel (*P* = .32).
Median time between diagnosis and CAR T infusion was 7.4 years for ide-cel vs 6.9 years for cilta-cel (*P* = .53).
Median number of prior lines of therapy was 6 for both groups.
Refractory status was triple-class for 64% in the ide-cel group and 67% in the cilta-cel group; 36% in the ide-cel group and 24% in the cilta-cel group were penta-refractory at the time of CAR T infusion.
11% in the ide-cel group and 10% in the cilta-cel group had a history of prior exposure to BCMA-directed therapy.
Median turnaround time between apheresis and infusion was 47 days for ide-cel vs 68 days for cilta-cel (*P* <.001). The 10-month PFS was 82% vs 47% (*P* <.001).
The 10-month OS was 90% for cilta-cel vs 77% ide-cel (*P* = .06).
Incidence of CRS and ICANS appeared similar (81% and 19% for cilta-cel vs 85% and 19% for ide-cel).
10% and 7% in the cilta-cel group vs 4% and 2% in the ide-cel group showed severe CRS and ICANS grade 3–4.
CRS occurred significantly earlier for ide-cel (median, 2 days vs 4 days; *P* <.001).
Nonrelapse mortality was 5% for cilta-cel vs 3% for ide-cel (*P* = .51).
Cilta-cel showed later peak of CAR T expansion at day 14 vs day 7 for ide-cel, while cilta-cel expansion was associated with ICANS.

Merz M, et al. *Hemasphere*. 2025;9:e70070.

Pivotal Clinical Trials for CAR T (1/2)

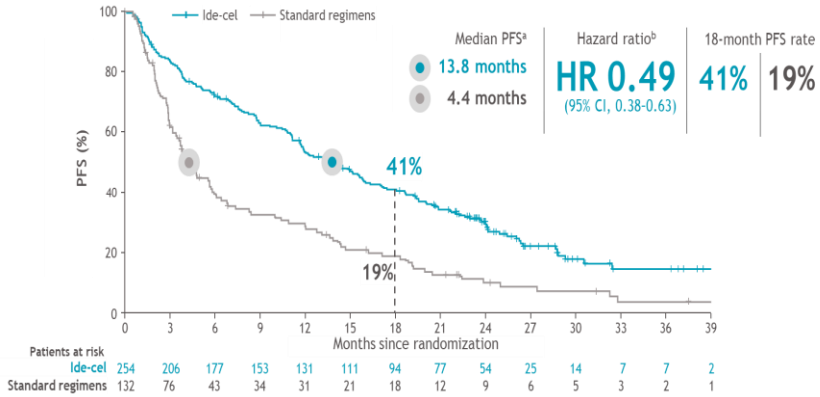


Ide-cel and cilta-cel have not been compared in a head-to-head clinical trial, and direct comparisons should not be made between studies due to differences in study design, treatments, and patient characteristics.

1. Rodriguez-Otero P, et al. *N Engl J Med.* 2023;388:1002-1014; 2. CARTITUDE-4 ClinicalTrials.gov number, NCT04181827.

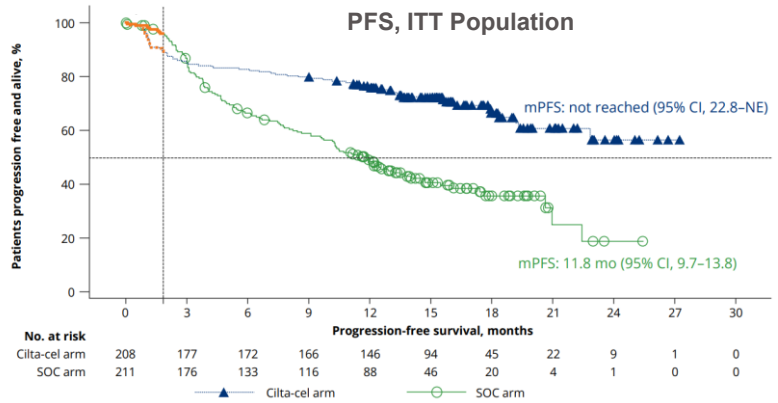
Pivotal Clinical Trials for CAR T (2/2)

KarMMa-3[1] — Median F/U 30.9 months



	Ide-Cel (n = 254)	Standard Regimen (n = 132)
Median PFS (95% CI)	**13.8**	**4.4**
HR (95% CI)	**0.49 (0.38–0.63); *P* <.0001**	

CARTITUDE-4[2] — Median F/U 15.9 months



	Cilta-Cel (n = 208)	Standard Regimen (n = 211)
Median PFS (95% CI)	**NE**	**11.79**
HR (95% CI)	**0.26 (95% CI, 0.18–0.38); *P* <.0001**	

Key trials

- *Idecabtagene vicleucel* – ORR ~73%
- *Ciltacabtagene autoleucel* – ORR ~98%

Advantages: deep, durable remissions; potential “one-shot” therapy

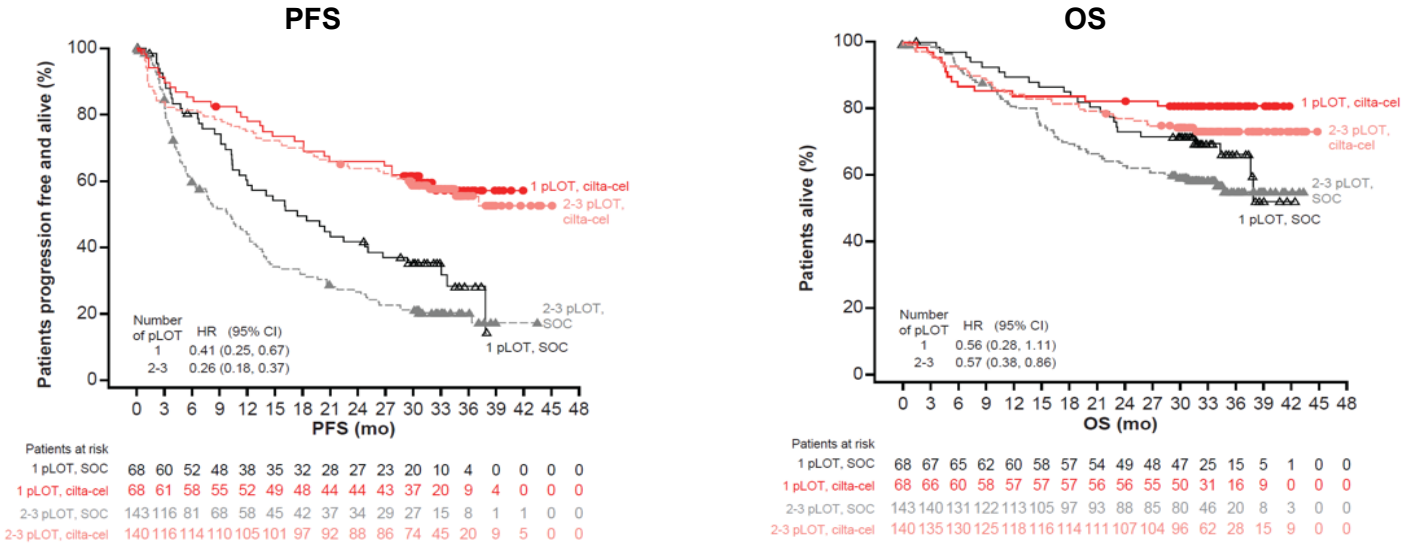
Limitations: manufacturing time, bridging therapy, CRS/ICANS, access, cost

Ide-cel and cilta-cel have not been compared in a head-to-head clinical trial, and direct comparisons should not be made between studies due to differences in study design, treatments, and patient characteristics.

1. Rodriguez-Otero P, et al. *N Engl J Med.* 2023;388:1002-1014; 2. San-Miguel J, et al. *N Engl J Med*. 2023;389:335-347.

Cilta-Cel: The CARTITUDE-4 Trial – Survival Times by Prior Lines

Kaplan-Meier Plot for PFS and OS by 1 and 2–3 pLOT Between Patients Treated With Cilta-Cel or SOC

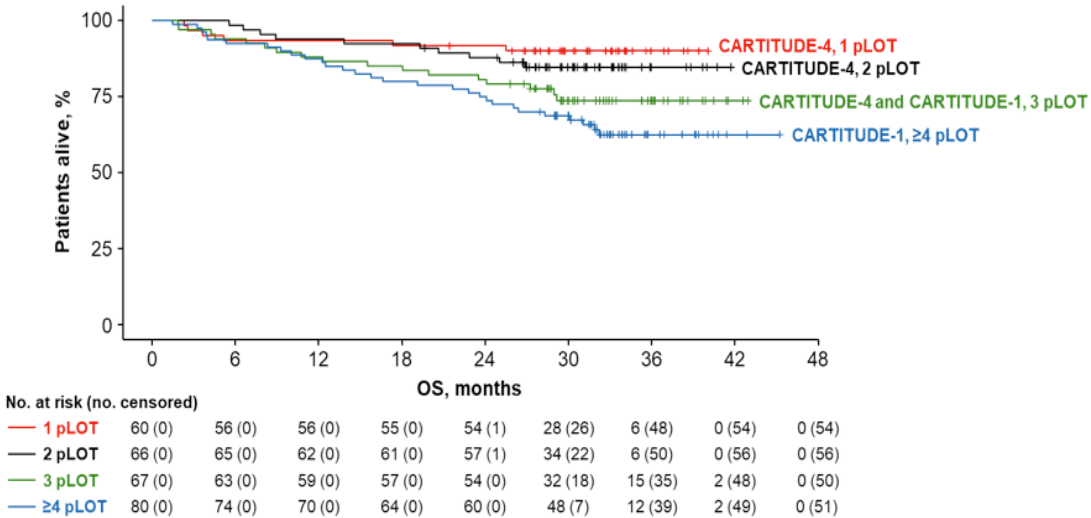


The 1 pLOT cohort in CARTITUDE-4 was enriched for patients with functional high-risk disease; 59% of patients had disease progression within 18 months after receiving autologous stem cell transplantation or initial therapy.

Note: PFS and OS measured starting from randomization. Hazard ratio and 95% CI from a Cox proportional hazards model with treatment as the sole explanatory variable, including only PFS events that occurred more than 8 weeks post-randomization. A hazard ratio <1 indicates an advantage for patients treated with cilta-cel. Intent-to-treat analysis set consists of patients who were randomized in the study.

Einsele H, et al. *Lancet Oncol*. 2026;27:254-268

Cilta-Cel: CARTITUDE-1 and CARTITUDE-4 – OS Based on Number of pLOT Across

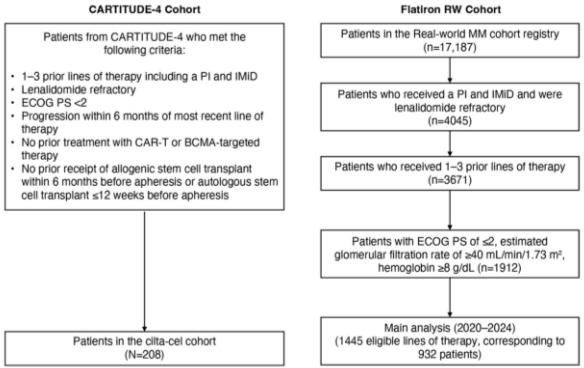


Patients with 1 and 2 pLOT were from the as-treated population in the CARTITUDE-4 trial (clinical cutoff of May 2024), patients with 3 pLOT were combined from the as-treated population in the CARTITUDE-4 (clinical cutoff of May 2024) and CARTITUDE-1 trials (clinical cutoff of October 2022), and patients with 4 or more LOT were from the CARTITUDE-1 trial (clinical cutoff of October 2022). OS starting from cilta-cel infusion.

Einsele H, et al. *Lancet Oncol*. 2026;27:254-268

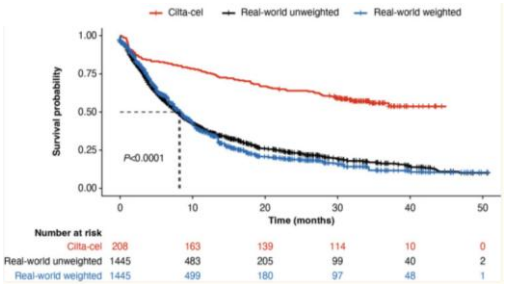
Cilta-Cel: The CARTITUDE-4 Trial

Comparative Effectiveness of Ciltacabtagene Autoleucel Versus Real-World Physician's Choice of Therapy from the Flatiron Registry in Lenalidomide-Refractory Multiple Myeloma



Treatment regimen, *n* (%)	*N* = 1445
Other drug combination[a]	256 (17.7)
DPd	231 (16.0)
Others	120 (8.3)
Daratumumab monotherapy	118 (8.2)
DKd	108 (7.5)
DVd	98 (6.8)
KPd	64 (4.4)
Pd	57 (3.9)
Kd	43 (3.0)
Clinical trial[b]	39 (2.7)
CyKd	39 (2.7)
Rd	34 (2.4)
EloPd	31 (2.1)
Vd	27 (1.9)
DRd	26 (1.8)
PVd	22 (1.5)
CyVd	21 (1.5)
IsaKd	21 (1.5)

PFS



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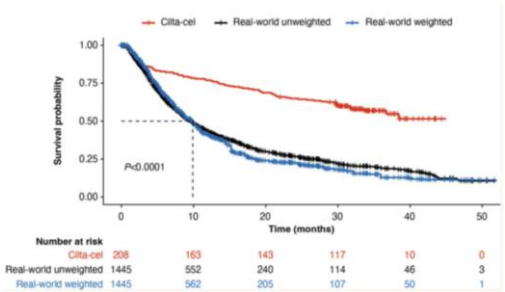
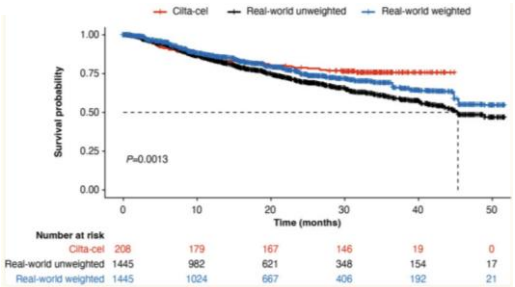
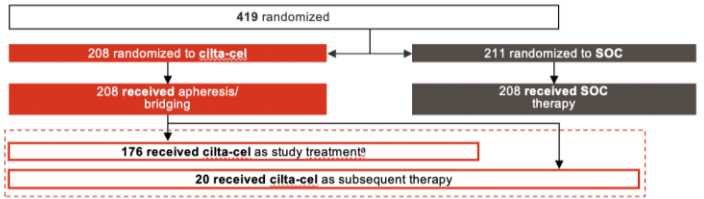


OS



Touzeau C, et al. *Adv Ther*. 2025;42:5023-5041.

Cilta-Cel: CARTITUDE-4 Bridging Therapy – Improved Response Correlates With Longer PFS



[a]32 had PD (n=30) or died (n=2) during bridging /lymphodepletion, before receiving cilta-cel as study treatment, of which 20 received cilta-cel as subsequent therapy. PD, disease progression.

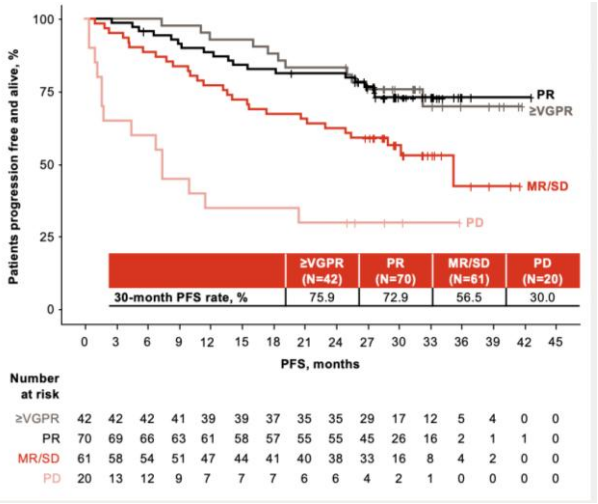
- PFS in this analysis was measured post hoc from cilta-cel infusion
  - Per protocol, pre–cilta-cel disease evaluations were to occur at apheresis, on day 1 ± 7 of each bridging cycle, starting cycle 2, and ≤7 days prior to start of lymphodepletion

AE, n (%)	≥VGPR (N=42)	PR (N=70)	MR/SD (N=61)	PD (N=20)
CRS[a]	28 (66.7)	53 (75.7)	51 (83.6)	17 (85.0)
ICANS	2 (4.8)	3 (4.3)	3 (4.9)	7 (35.0)
CNP[a]	5 (11.9)	5 (7.1)	5 (8.2)	1 (5.0)
IEC-parkinsonism	0	0	1 (1.6)*	1 (5.0)
Grade 3/4 infections[a]	17 (40.5)	25 (35.7)	25 (41.0)	6 (30.0)
Nonrelapse mortality[b]	3 (7.1)	6 (8.6)	11 (18.0)	6 (30.0)
Fatal infections	1 (2.4)	3 (4.3)	8 (13.1)	3 (15.0)
Prolonged grade 3/4[c] cytopenias				
Thrombocytopenia	4 (9.5)	8 (11.4)	7 (11.5)	10 (50.0)
Neutropenia	1 (2.4)	11 (15.7)	6 (9.8)	2 (10.0)
Anemia	0	1 (1.4)	1 (1.6)	3 (15.0)

*Occurred in a patient with unconfirmed PD at cilta-cel infusion. [a]Among 3 patients who were NE for response to bridging therapy, there were 2 CRS cases, 2 grade 3/4 infections, and 1 CNP case. [b]Deaths not due to PD were considered nonrelapse mortality at any time prior to clinical data cut-off. [c]Did not recover to grade 2 by day 60 post cilta-cel. CRS, cytokine release syndrome; ICANS, immune effector cell–associated neurotoxicity syndrome.

AE of special interest

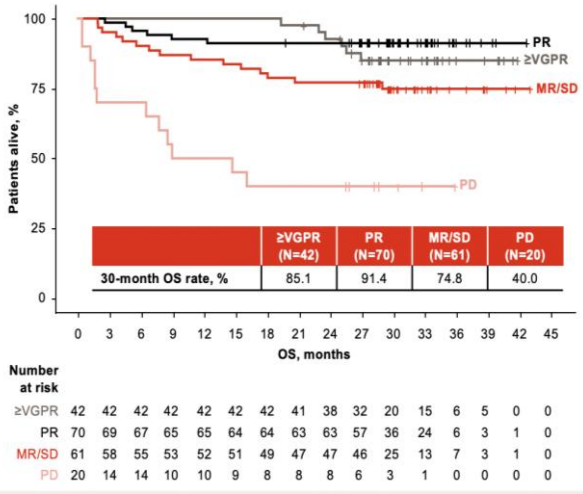
PFS and OS from cilta-cel infusion by response to bridging therapy



	≥VGPR (N=42)	PR (N=70)	MR/SD (N=61)	PD (N=20)
30-month PFS rate, %	75.9	72.9	56.5	30.0

Number at risk

≥VGPR	42	42	42	41	39	39	37	35	35	29	17	12	5	4	0	0
PR	70	69	66	63	61	58	57	55	55	45	26	16	2	1	1	0
MR/SD	61	58	54	51	47	44	41	40	38	33	16	8	4	2	0	0
PD	20	13	12	9	7	7	7	6	6	4	2	1	0	0	0	0



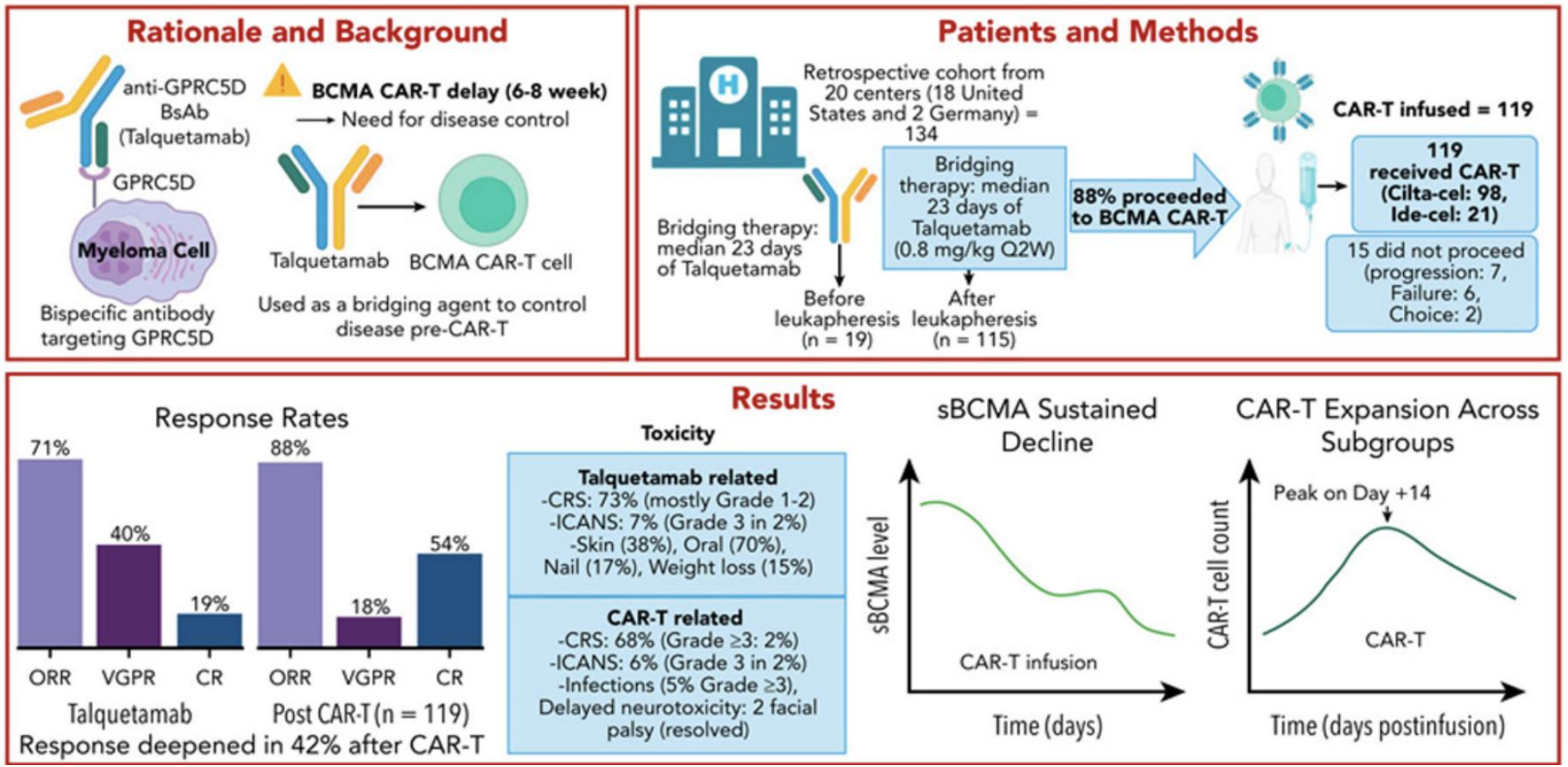
	≥VGPR (N=42)	PR (N=70)	MR/SD (N=61)	PD (N=20)
30-month OS rate, %	85.1	91.4	74.8	40.0

Number at risk

≥VGPR	42	42	42	42	42	42	42	41	38	32	20	15	6	5	0	0
PR	70	69	67	65	65	64	64	63	63	57	36	24	6	3	1	0
MR/SD	61	58	55	53	52	51	49	47	47	46	25	13	7	3	1	0
PD	20	14	14	10	10	9	8	8	8	6	3	1	0	0	0	0

Dhakal B, et al. ASH 2025. Abstract 2215.

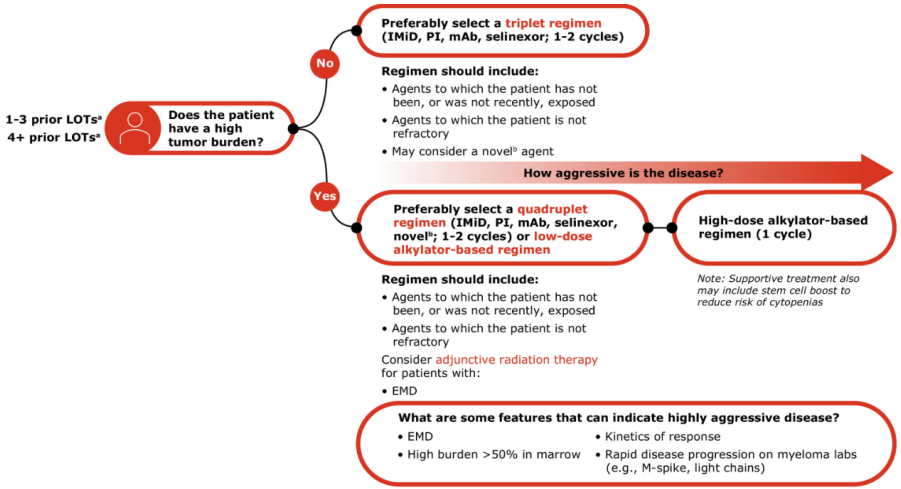
Sequential Targeting in Multiple Myeloma: Talquetamab as a Bridge to BCMA CAR T Therapy

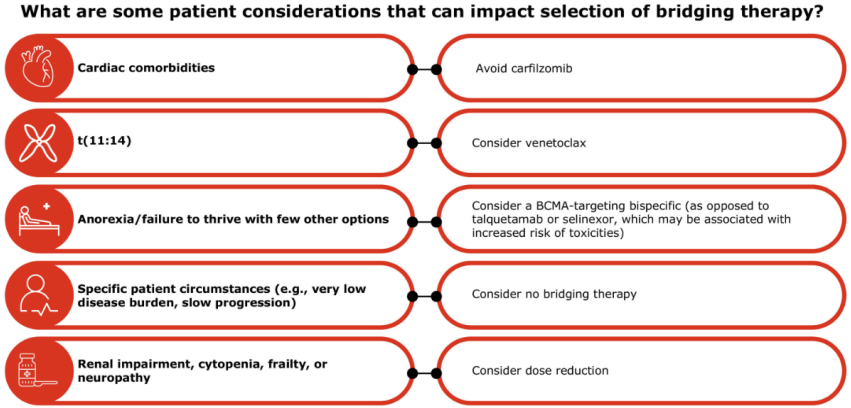


Dhakal B, et al. *Blood.* 2025;146:2063-2072.

Functional Algorithm for Selection of Bridging Therapy

[a]The algorithm is the same regardless of the number of prior LOT; however, additional options will be available for patients in earlier lines who have had less exposure to bridging agents. Furthermore, bridging may be needed less commonly in earlier lines; [b]Novel agents include venetoclax for patients with t(11:14) and BsAbs (BCMA- and GPRC5D-targeting) that may require longer washout. Avoid agents that might compromise patients' participation in a future clinical trial.





BCMA, B-cell maturation antigen; EMD, extramedullary disease; GPRC5D, G protein–coupled receptor class C group 5 member D; IMiD, immunomodulatory drug; LOT, line of therapy; mAb, monoclonal antibody; PI, proteosome inhibitor. [a]The algorithm is the same regardless of the number of prior LOTs; however, additional options will be available for patients in earlier lines who have had less exposure to bridging agents. Furthermore, bridging may be needed less commonly in earlier lines. [b]Novel agents include venetoclax for patients with t(11:14) and bispecifics (BCMA- and GPRC5D-targeting) that may require longer washout. Avoid agents that might compromise patients' participation in a future clinical trial.

BCMA, B-cell maturation antigen; EMD, extramedullary disease; GPRC5D, G protein-coupled receptor class C group 5 member D; IMiD, immunomodulatory drug; LOT, lines of therapy; mAb, monoclonal antibody; PI, proteasome inhibitor.

Ailawadhi S, et al. *Clin Lymphoma Myeloma Leuk*. 2026;26:85-93.

Incidence of CRS, ICANS, and Infections in CAR T Cells and BsAbs

	Ide-Cel KarMMa[1] (n = 128)	Cilta-Cel CARTITUDE-1[2-4] (n = 97)	Teclistamab MajesTec-1[5,6] (n = 165)	Elranatamab MagnetisMM-3[7] (n = 55)
Median FU	13 months	12 months	23 months	14 months
CRS (%)	84	95	72	58
CRS grade ≥3 (%)	6	4	0.6	0
Median onset CRS (day)	1 (1–12)	7 (1–12)	2 (1–6)	NR
ICANS (%)	18	16.5*	3	3
ICANS grade ≥3 (%)	4	2.1	0	0
Median onset ICANS (day)	2 (1–10)	8	2.5 (1–7)	NR
Infections (%)	69	58	80	70
Infection grade ≥3 (%)	22	20	55	40
COVID (%)	NR	NR	29	29
CMV (%)	NR	NR	NR	6
PJP (%)	NR	NR	4	5
Hypogammaglobulinemia (%)	21	NR	20	NR

*Total neurotoxicity 20.6%, non-ICANS neurotoxicity 12%. ICANS and non-ICANS neurotoxicities were not mutually exclusive, as 8 patients (8.2%) experienced both.[3,4]

1. Anderson LD, et al. ASCO 2021. Abstract 8061; 2. Usmani S, et al. ASCO 2021. Abstract 8005; 3. Martin T, et al. *J Clin Oncol.* 2022;41:1265-1274; 4. Cohen AD, et al. *Blood Cancer J.* 2022;12:32; 5. Moreau P, et al. *N Engl J Med.* 2022;387:1722-1723; Moreau P, et al. ASH 2021. Abstract 2744; 7. Sebag M, et al. ASH 2021. Abstract 653.

Late-Onset Neurotoxicity

nature medicine
BRIEF COMMUNICATION
https://doi.org/10.1038/s41591-021-01564-7
Check for updates

Neurocognitive and hypokinetic movement disorder with features of parkinsonism after BCMA-targeting CAR-T cell therapy

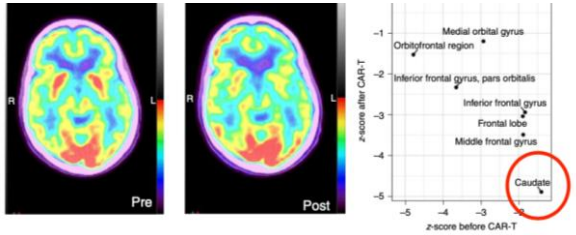
Patient management strategies for neurologic AEs in CARTITUDE

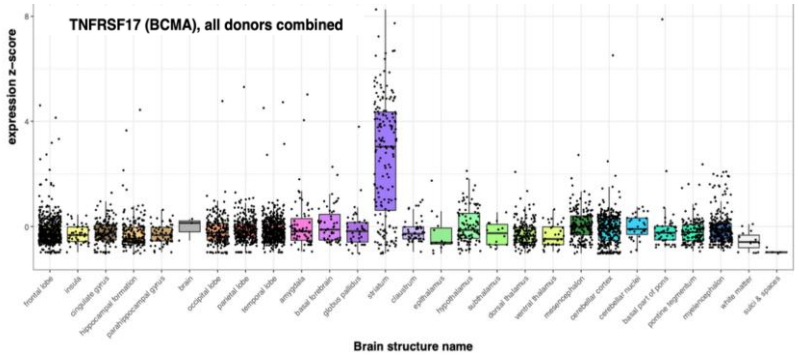
Movement and neurocognitive TEAEs risk factors (2 or more)
- High tumor burden[a]
- Grade ≥2 CRS
- ICANS
- High CAR T-cell expansion and persistence

Implementation of patient management strategies
- More effective bridging therapy to reduce tumor burden
- Early and aggressive treatment of CRS and ICANS
- Handwriting assessments and extended monitoring

DNT: delayed neurotoxicity
NINT: non-ICANS neurotoxicity

Alteration of caudate nucleus

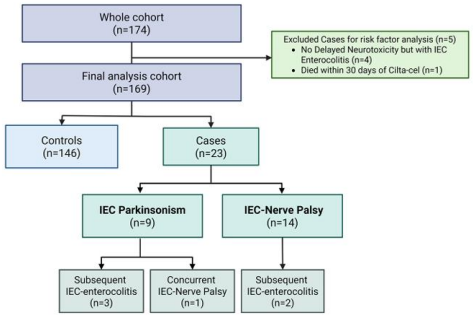


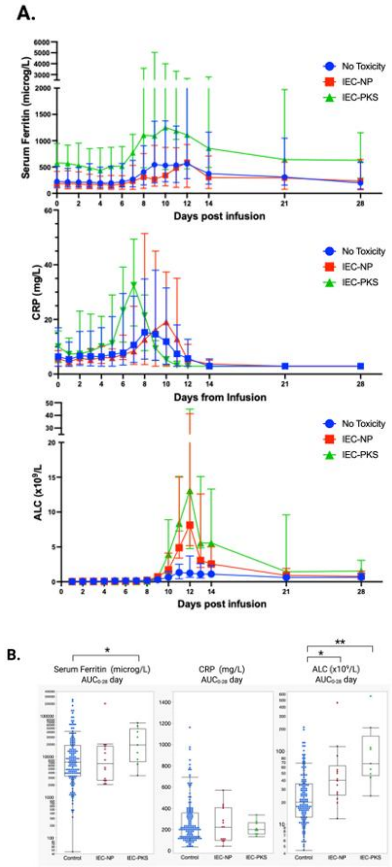


- Cranial nerve palsies
- Parkinson disease and parkinsonism
- Acute and chronic polyneuropathies
- Guillain-Barré syndrome
- Intracranial hemorrhage
- Cerebrovascular accidents
- Meningoencephalitis

Madduri D, et al. ASH 2020. Abstract 177; Van Oekelen O, et al. *Nat Med.* 2021;27:2099-2103.

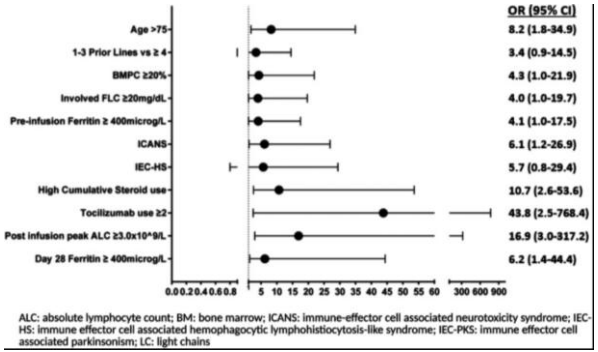
Cilta-Cel: Clinical Course, Risk Factors, and Mitigating Strategies for Immune Effector Cell-Associated Late-Onset Neurotoxicities (1/2)





Serum ferritin, CRP, and ALC (median, interquartile range) expansion from cilta-cel infusion to 28 days of the controls; IEC-NP and IEC-PKS groups are plotted in (A) and calculated as area under the curve for 28 days (AUC_{28}) and shown in (B).

Forrest plot of potential factors associated with IEC-PKS



ALC: absolute lymphocyte count; BM: bone marrow; ICANS: immune-effector cell associated neurotoxicity syndrome; IEC-HS: immune effector cell associated hemophagocytic lymphohistiocytosis-like syndrome; IEC-PKS: immune effector cell associated parkinsonism; LC: light chains

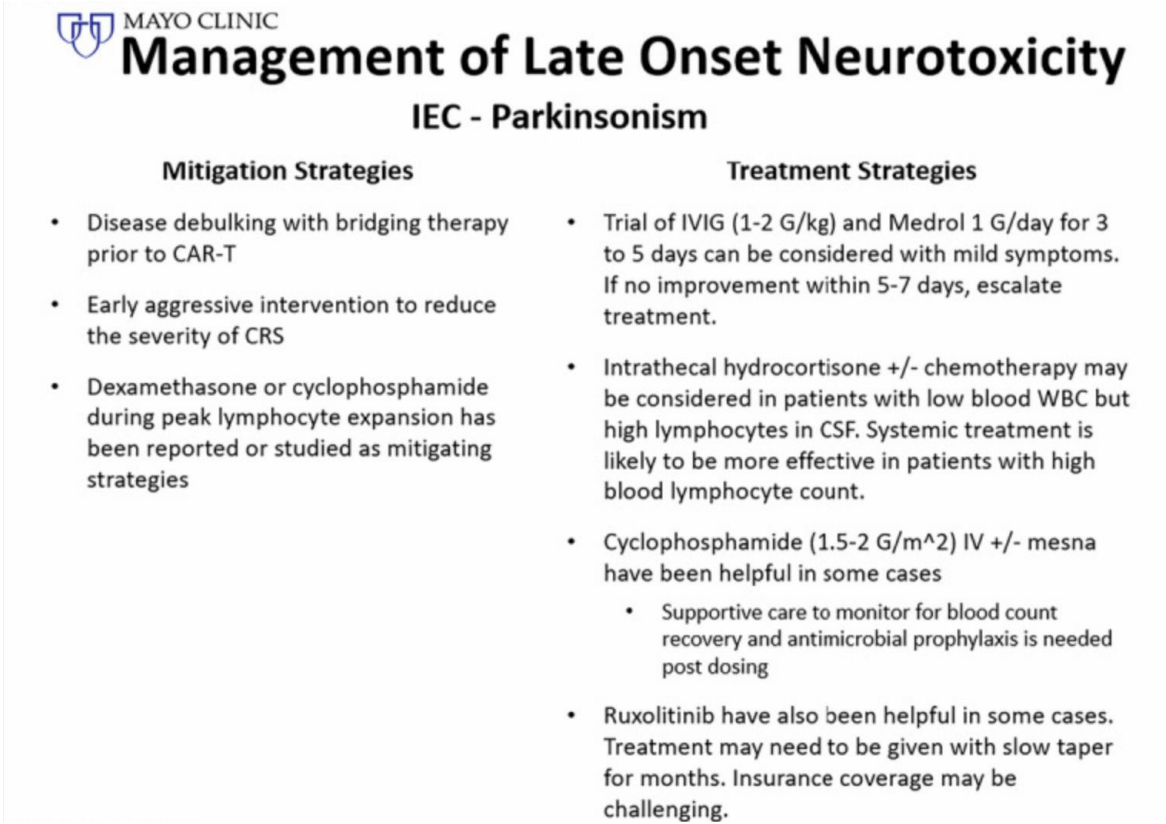
Contingency table of ALC peak for IEC-neurotoxicity

A. Delayed Neurotoxicity			
ALC peak	**No Toxicity**	**Delayed Neurotoxicity**	**Total**
$<3 \times 10^9$/L	99	2	101
$\geq 3 \times 10^9$/L	47	21	68
Total	146	23	169
B. Nerve Palsy			
ALC peak	**No IEC-NP**	**IEC-NP**	**Total**
$<3 \times 10^9$/L	100	1	101
$\geq 3 \times 10^9$/L	54	14	68
Total	154	15	169
C. Parkinsonism			
ALC peak	**No IEC-PKS**	**IEC-PKS**	**Total**
$<3 \times 10^9$/L	100	1	101
$\geq 3 \times 10^9$/L	60	8	68
Total	160	9	169

Negative predictive value of ALCpeak $<3 \times 10^9$/L = 98%.
Positive predictive value of ALCpeak $\geq 3 \times 10^9$/L = 31%.
Negative predictive value of ALCpeak $<3 \times 10^9$/L = 99%.
Positive predictive value of ALCpeak $\geq 3 \times 10^9$/L = 21%.
Negative predictive value of ALCpeak $<3 \times 10^9$/L = 99%.
Positive predictive value of ALCpeak $\geq 3 \times 10^9$/L = 12%.

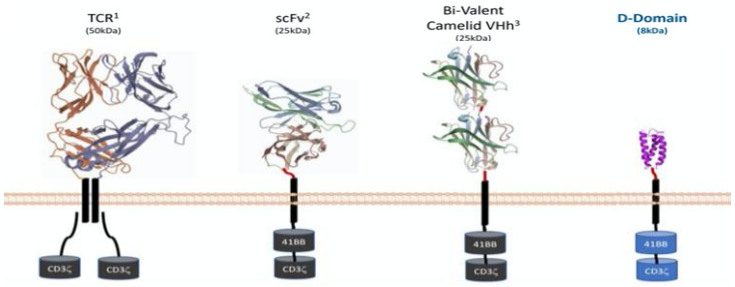
Lim KJC, et al. *Blood Cancer J*. 2025;16:18.

Cilta-Cel: Clinical Course, Risk Factors, and Mitigating Strategies for Immune Effector Cell-Associated Late-Onset Neurotoxicities (2/2)



Lim KJC, et al. *Blood Cancer J*. 2025;16:18.

Alternative Construct: CART-ddBCMA



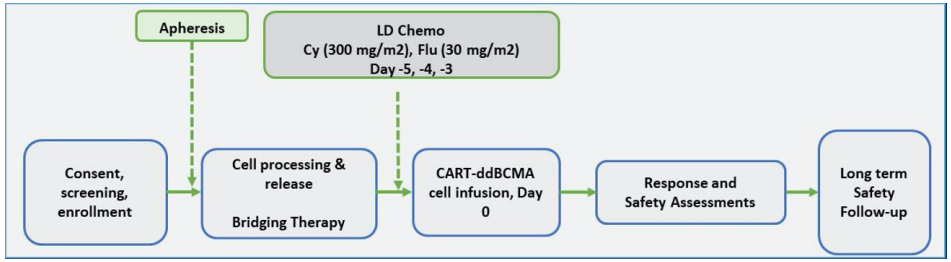
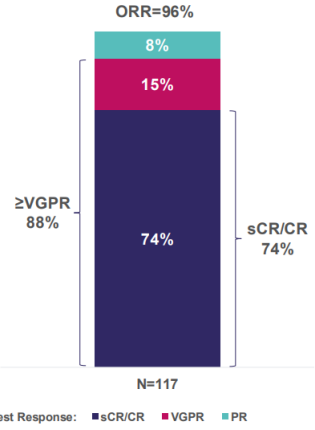


iMMagine-1: Overall Response Rate and Depth of Response

Efficacy Evaluable Patients, N=117



- Responses continue to deepen over time
- At a median follow-up of 15.9 months, IRC-assessed ORR was 96% and sCR/CR rate was 74%

	Median (months)	Interquartile Range	Min, Max
Time to first response	1.0	1.0, 1.9	0.9, 13.8
Time to best response	4.8	2.1, 9.0	0.9, 23.8
Time to sCR/CR	3.2	2.0, 9.2	0.9, 23.8

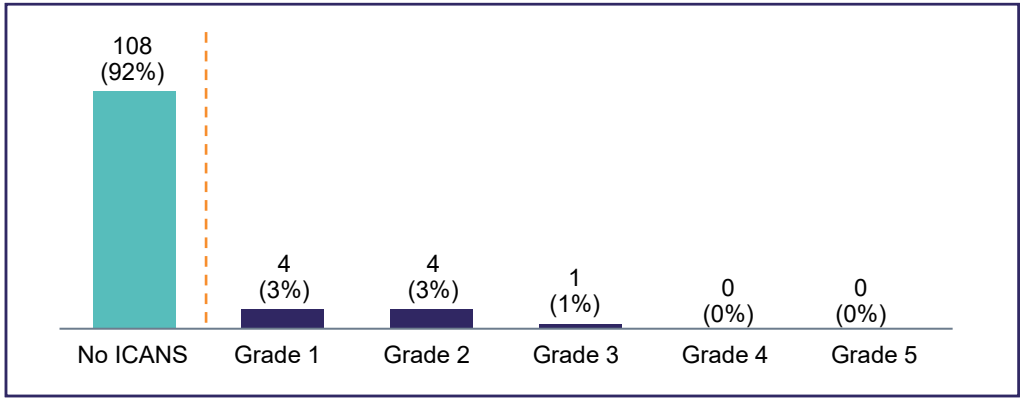
Responses are per IMWG criteria and are IRC assessed; ORR defined as partial response or better.
CR, complete response; IRC, independent review committee; ORR, overall response rate; PR, partial response;sCR, stringent complete response; VGPR, very good partial response

Patel K, et al. ASH 2025. Abstract 256;
Frigault MJ, et al. ASCO 2022. Abstract 8003.

Late-Onset Neurotoxicity Cilta-Cel

- Cranial nerve palsies
- Parkinson disease and parkinsonism
- Acute and chronic polyneuropathies
- Guillain-Barré syndrome
- Intracranial hemorrhage
- Cerebrovascular accidents
- Meningoencephalitis

iMMagine-1: Immune Effector Cell-Associated Neurotoxicity Syndrome (ICANS)



- 8% (9/117) of patients had ICANS of any grade; all cases resolved
- No delayed or non-ICANS neurotoxicities were observed, including no incidence of parkinsonism, no cranial nerve palsies, and no Guillain-Barré syndrome (n = 117; median follow-up of 12.6 months, range: 5–29 months)
- Similarly, no delayed or non-ICANS neurotoxicities have been observed in the phase I study[1] (n = 38; median follow-up of 38.1 months, range: 25–56 months)

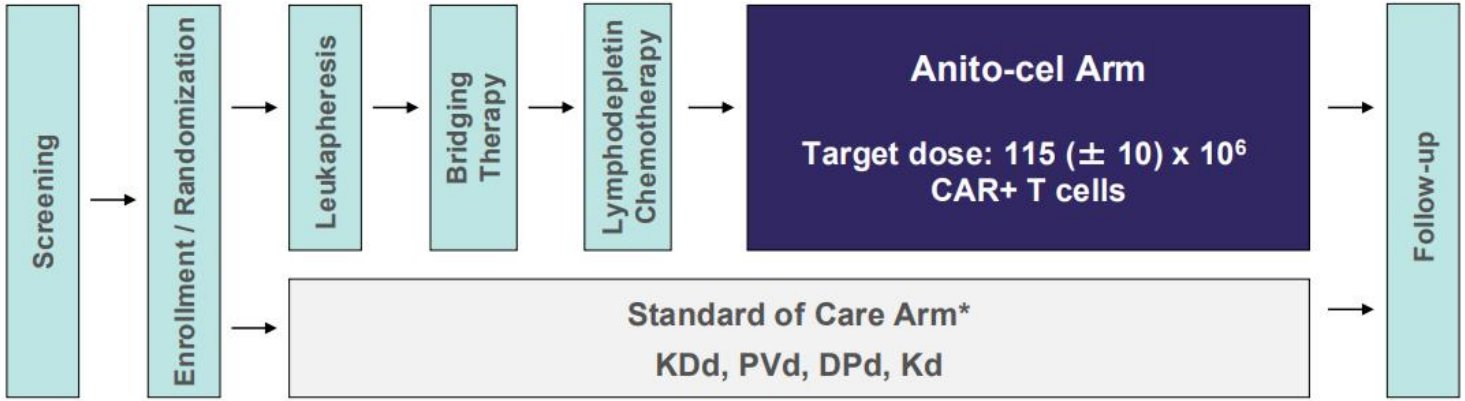
Anito-cel demonstrated deep, durable responses in 4L+ RRMM with a manageable safety profile, including no delayed or non-ICANS neurotoxicities and no immune effector cell-associated enterocolitis

Madduri D, et al. ASH 2020. Abstract 177; Van Oekelen O, et al. *Nat Med.* 2021;27:2099-2103. Bishop MR, et al. *Blood*. 2024;144:4825, as presented in poster 4825 at ASH 2024.

iMMagine-3 Design, Global Phase 3 Study – Now Enrolling

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

Anito-cel is being co-developed by Arcellx and Kite, and is being manufactured by Kite for iMMagine-3



Study Design

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

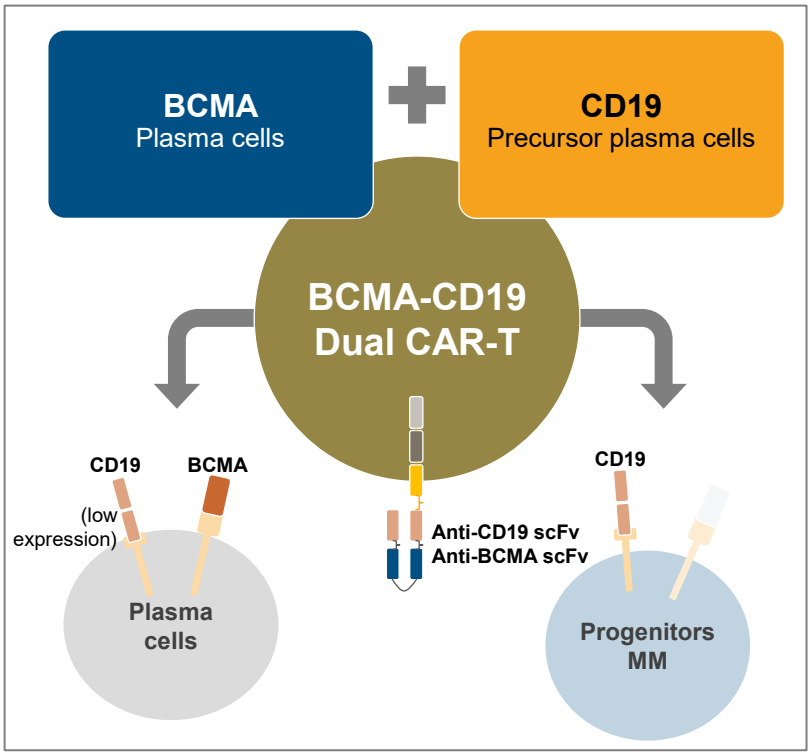
Study Endpoints

- Primary Endpoints:
  - PFS
  - MRD-negative CR rate at 9 months
- Key Secondary Endpoints: CR rate, MRD, OS, safety

**Cycles will continue until unacceptable toxicity, progression as per IMWG criteria, orpatient withdrawal of consent*

GC012F/AZD0120

Dual CAR T and FasTCAR

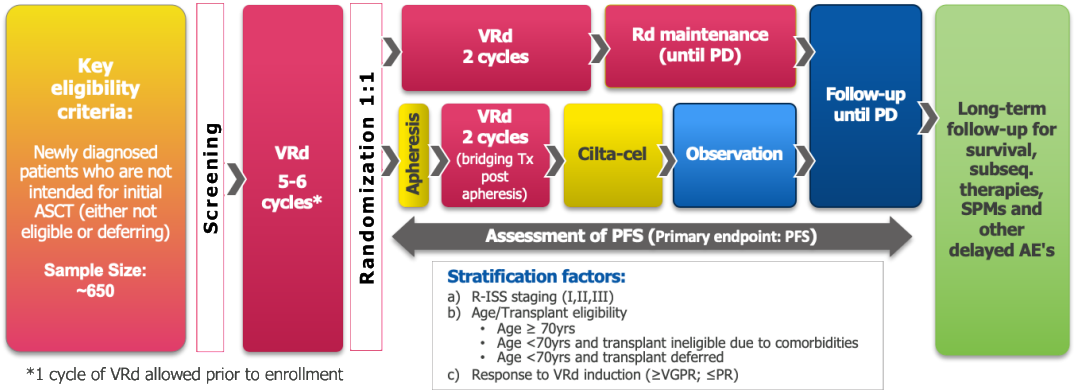


DURGA program

Du J, et al. ASH 2025. Abstract 258.

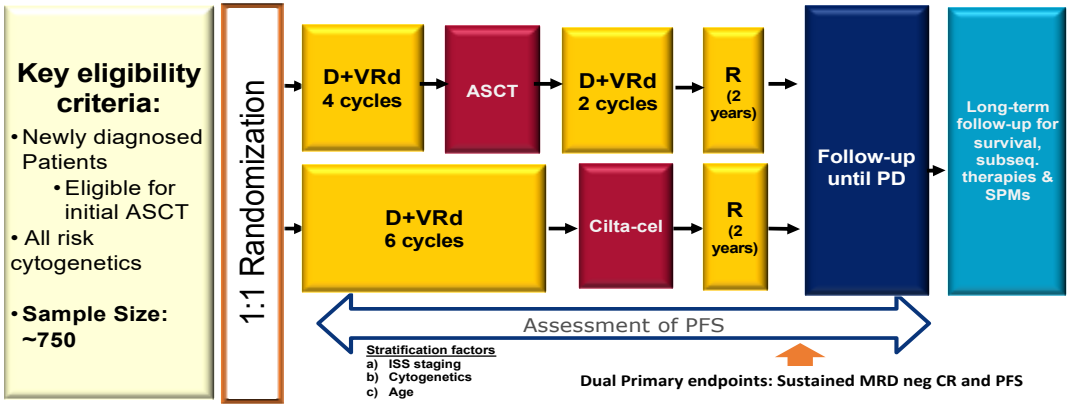
Future Directions

CARTITUDE-5 (transplant nonintended)



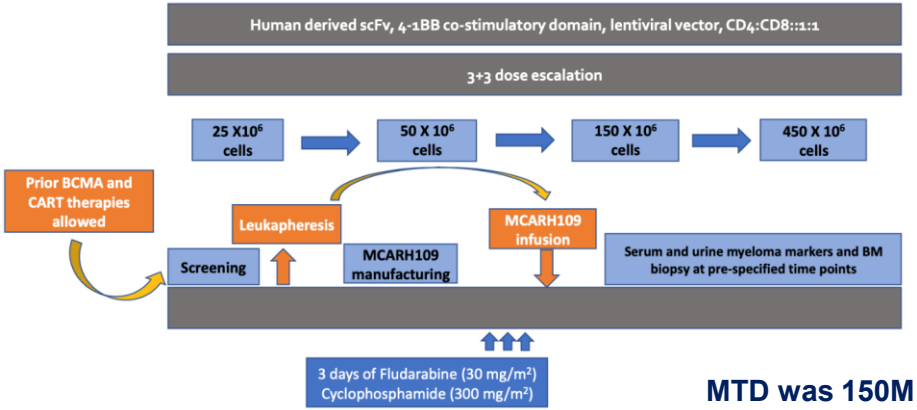
NCT04923893

CARTITUDE-6 (transplant eligible)



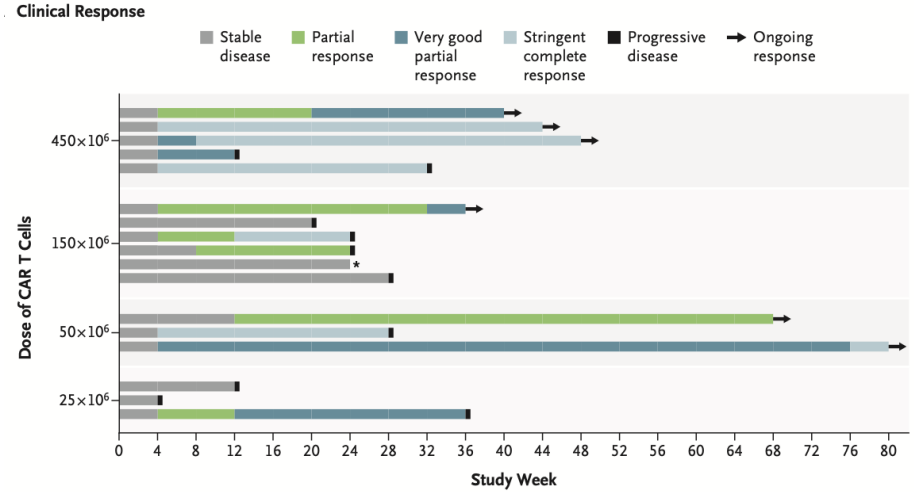
NCT05257083

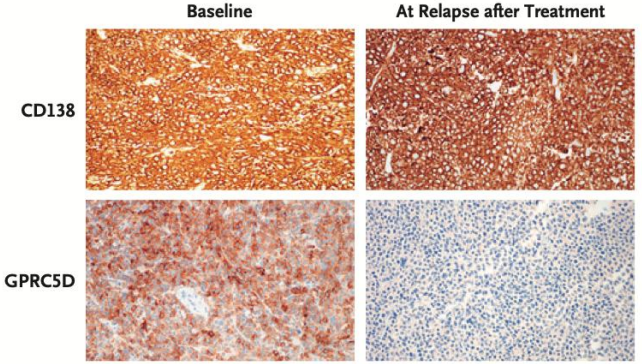
Alternative Target: GPRC5D, the MCARH109 Trial



MTD was 150M cells

	Total (N=16)
Cytokine Release Syndrome (CRS), n (%)	14 (93)
Grade 3 or higher	1 (6)
Median time to onset, days (range)	2 (1-11)
Median duration, days (range)	3 (1-19)
Neurologic Toxicity (ICANS), n (%)	1 (6)
Grade 3 or higher	1 (6)
Median time to onset, days (range)	1 (NA)
Median duration, days (range)	46 (NA)
Grade 1 Nail changes, n (%)	6 (38)
Grade 1 Maculo-papular rash, n (%)	2 (13)
Grade 1 Dysgeusia, n (%)	1 (6)





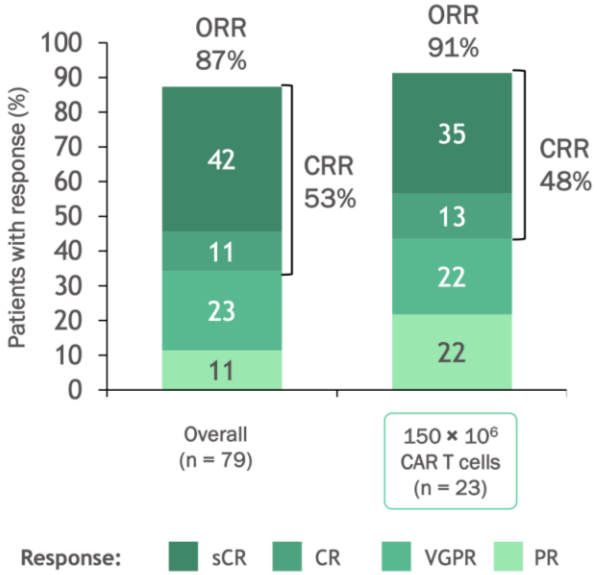
What could also happen in case of BCMA Failure (or even in its absence!) ? Arlo-cel (Anti-GPRC5D CAR T) after ≥ 3 pLOT

≥ 3 Prior regimens

Patient characteristics

Baseline characteristics	All treated patients (N = 84)
Median age (range), years	63 (39-80)
Male sex, n (%)	43 (51)
High-risk cytogenetics, del (17p), n (%)	26 (31)
EMP, n (%)	39 (46)
Median time since diagnosis (range), years	6.1 (0.7-17.1)
Median of prior regimens (range)	5 (3-15)
Prior BCMA-TT, n (%)	41 (49)
Refractory status to prior therapy, n (%)	
BCMA-TT	17 (20)
Triple-class	64 (76)
Penta drug	29 (33)
Most recent antimyeloma regimen	70 (83)

ORR



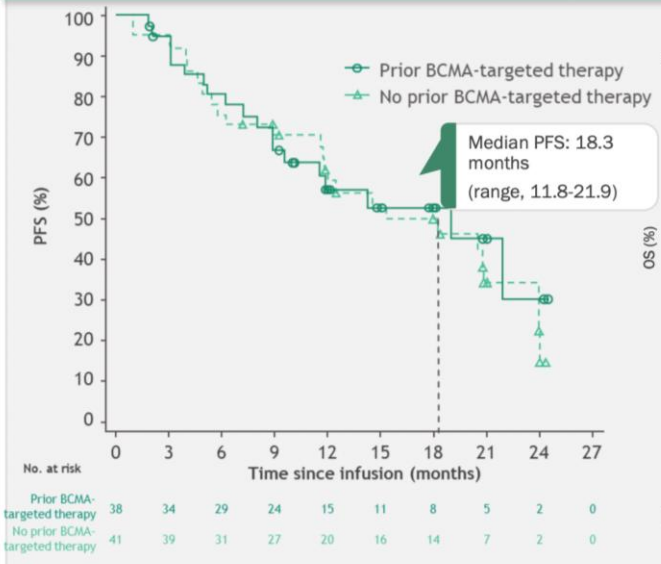
❖ Prior BCMA therapy: 49%, 42% pts had high-risk cytogenetics, and 46% EMD

Arlo-cel is an investigational product, currently not approved by any regulatory agency. Bal et al, abstract #922, ASH 2024

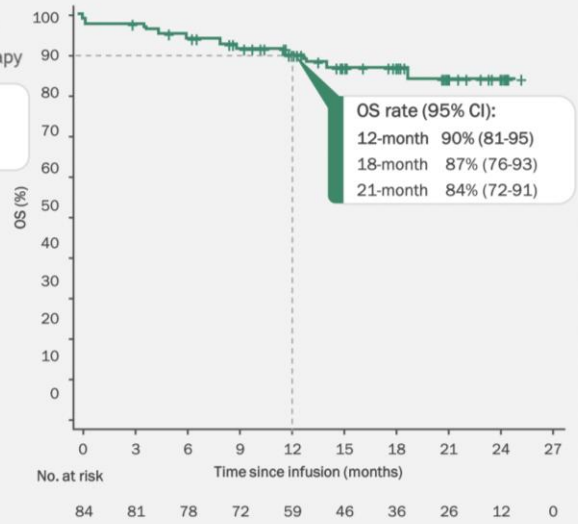
Arlo-cel: arlocabtagene autoleucel , BCMA: B Cell Membrane Antigen, CRR: Complete Response Rate, EMD: Extramedullary disease , M: median, PLOT: Previous Lines of Treatment, OS: Overall Survival, ORR: Overall Response Rate, pLOT: previous lines of treatment, PFS: Progression Free Survival, PR: Partial response, Pts : patients, sCR: stringent Complete Response, VGPR: Very good PR

Arlo-cel Phase 1 Cohort A: Efficacy and Safety in RRMM (≥ 3 prior regimens)

PFS in the efficacy-evaluable population[a,b]



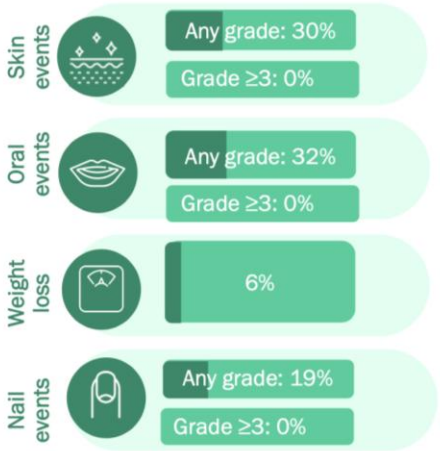
OS in all treated patients



Median PFS in the efficacy-evaluable heavily pre-treated population was 18.3 months, and the 12-month OS rate was 90%

Safety Profile

All treated patients (N=84)



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)

Median follow-up in the efficacy-evaluable population: 16.1 months. Data cutoff: August 23, 2024. PFS and OS were estimated by Kaplan–Meier methods. Symbols show censored patients. [a]The efficacy-evaluable population includes all 79 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]mPFS in all treated patients was 15.3 months (95% CI 11.8–20.8). arlo-cel, arlocabtagene autoleucel; BCMA, B-cell maturation antigen; CRS, Cytokine Release Syndrome; ICANS: Immune effector cell-associated neurotoxicity syndrome; m, median; NA, not applicable; OS, overall survival; PFS, progression-free survival. 4L, fourth-line; BsAB, bispecific antibody; CAR T, chimeric antigen receptor T cell; GPRC5D, G protein–coupled receptor class C group 5 member D; RRMM, relapsed/refractory multiple myeloma; TRAE, treatment-related adverse event

Arlo-cel is an investigational product, currently not approved by any regulatory agency. Bal S et al. Oral presentation at ASH 2024. Abstract 922.

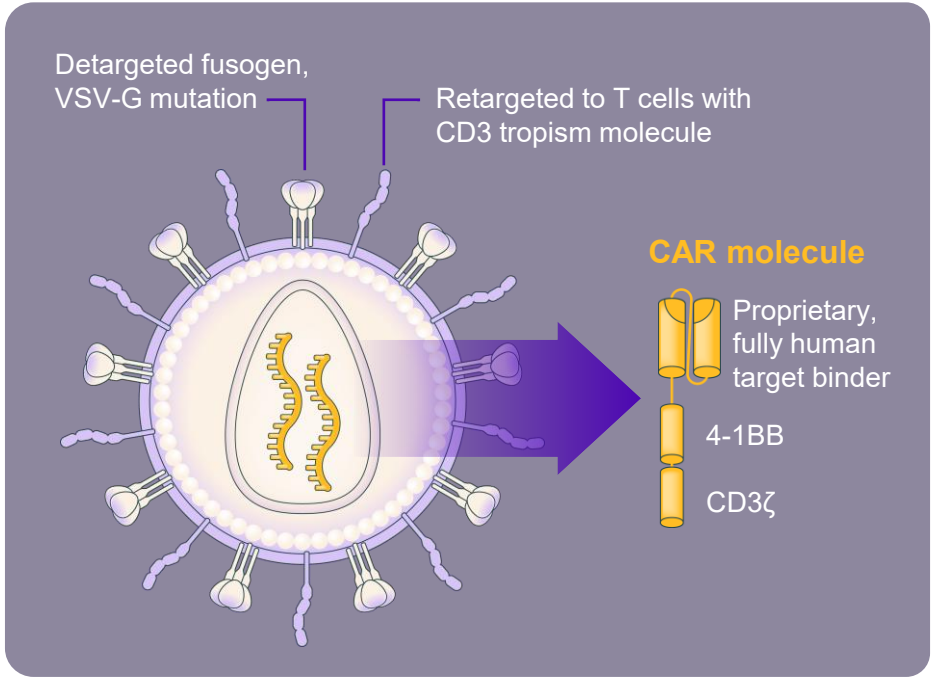
KLN-1010: Modified LVV-Generating Anti-BCMA CAR T Cells In Vivo

- Envelope-modified, replication-incompetent, self-inactivating lentiviral vector
- Detargeted VSV-g fusogen avoids delivery to LDL-expressing cells while maintaining high transduction efficiency
- Precise targeting to T cells with a CD3 scFv
- Delivers fully human anti-BCMA CAR

Preclinical studies in animal models

KLN-1010 led to

- More profound killing of tumor compared with similarly manufactured cilta-cel–like CAR Ts
- Increased persistence and memory CAR T composition
- High T-cell specificity with no germ cell transduction



2020–2030

Merci de votre attention

Global Multiple Myeloma Academy

Discussion

APTITUDE HEALTH®

Global Multiple Myeloma Academy

Treatment Options for Non–CAR T-Cell Candidates

María-Victoria Mateos, MD, PhD

APTITUDE HEALTH®

Treatment Options for Non-CAR T-Cell Candidates
Optimal Use of Treatment Choices in RRMM

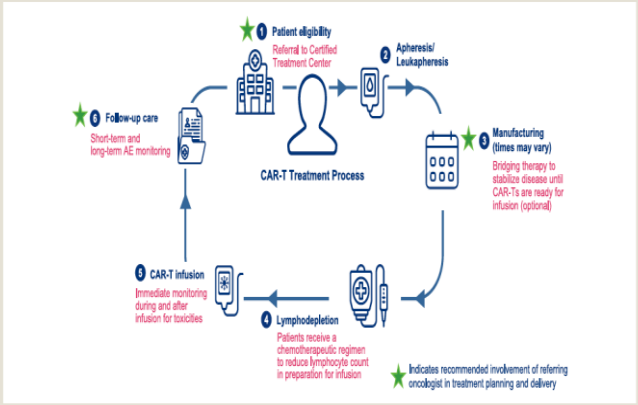
María-Victoria Mateos
Salamanca, Spain

Disclosures

- Honoraria derived from lectures and participation in advisory boards from Janssen, Bristol Myers Squibb, Amgen, GSK, AbbVie, Pfizer, Regeneron, Roche, Sanofi, Stemline, Kite

Who Is Not Eligible for CAR T-Cell Therapy?

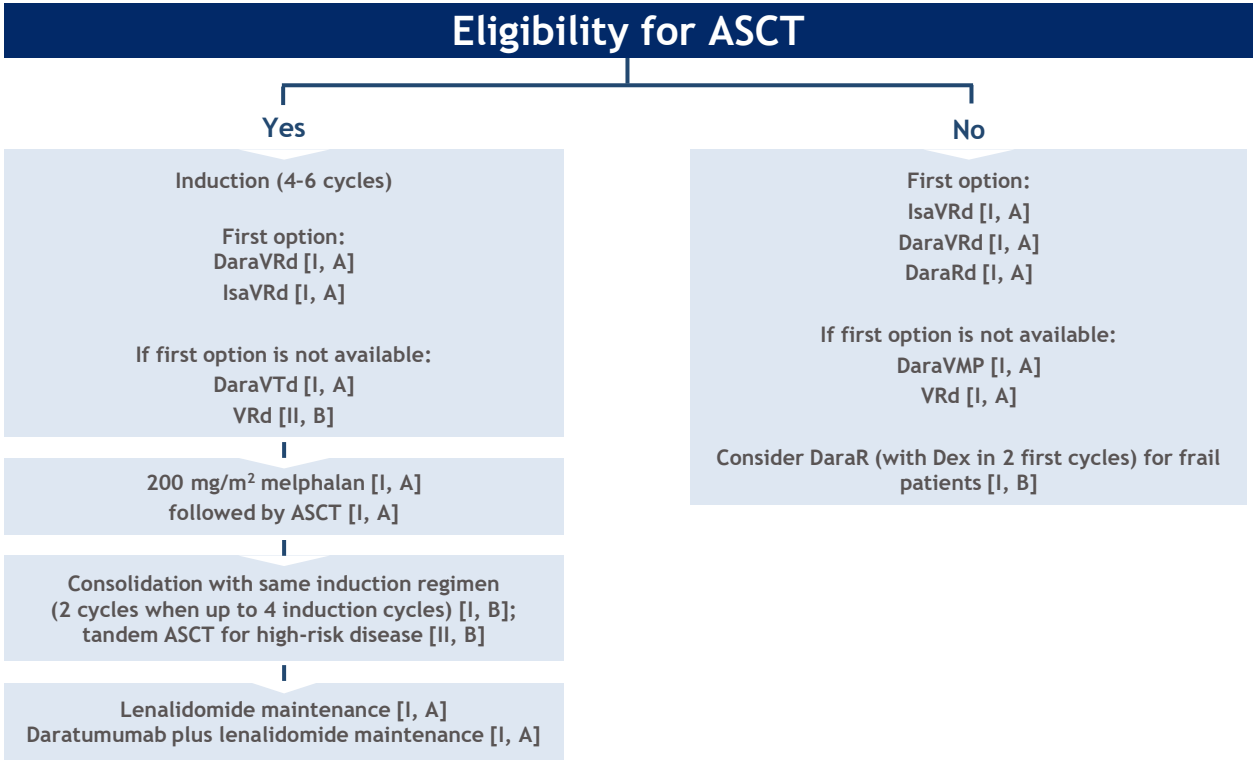
Figure 1 Overview of the CAR-T treatment process. Depiction of the treatment process from patient eligibility through follow-up care.



Treatment Stage	Key Considerations
Patient selection and referrals	• Differences from eligibility criteria used in pivotal trials (eg, performance status, comorbidities)[3,4] • Performance status, rate of disease progression, organ function, patient willingness, and logistical or supportive requirements (eg, insurance, caregiver availability) • Initiation of conversations regarding potential referrals of patients for CAR-T therapy prior to eligibility • Consider referrals for CAR-T therapy at least 1 LOT prior to CAR-T eligibility (eg, after exposure to 3 treatment classes with current indications for CAR-T therapy in MM) • Consider early conversations regarding referral for historically underserved patients (eg, older adults, rural, lower socioeconomic status, racial/ethnic minorities). Consider early conversations regarding referrals for patients with high-risk MM at diagnosis
Apheresis	• Adhere to recommended treatment washout times prior to apheresis • Consider impact of prior therapies (eg, alkylator therapies) on T-cell fitness and CAR-T manufacturing/patient outcomes • Consider delaying apheresis for a minimum of 30 days after discontinuation of high-dose alkylator therapy
Bridging therapy	• Tailor bridging therapy to patient needs (eg, treatment history, disease status, comorbidities, anticipated toxicities of bridging therapy, anticipated manufacturing time) • Consider logistical factors (eg, use of oral bridging therapies if administered at a different center from the CAR-T center) • Halt bridging therapy ≥ 1 week (or 5 times the agent half-life, if shorter) prior to CAR-T infusion
Lymphodepletion	• May adjust dosing of lymphodepleting chemotherapy for patients with renal insufficiency • Delay lymphodepletion for patients with active infection or other toxicities related to bridging therapy/disease progression
CAR-T infusion and monitoring	• Collaborate with other specialists (eg, cardiology, neurology, infectious disease) • Review product-specific guidance for infusion and monitoring requirements • Maintain communication between treating and referring healthcare providers following CAR-T administration

Advanced ECOG PS, aggressive disease, comorbidities, no caregiver, renal impairment, patient availability for being referred to a CAR T-cell center . . .

EHA-EMN 2025 Guidelines

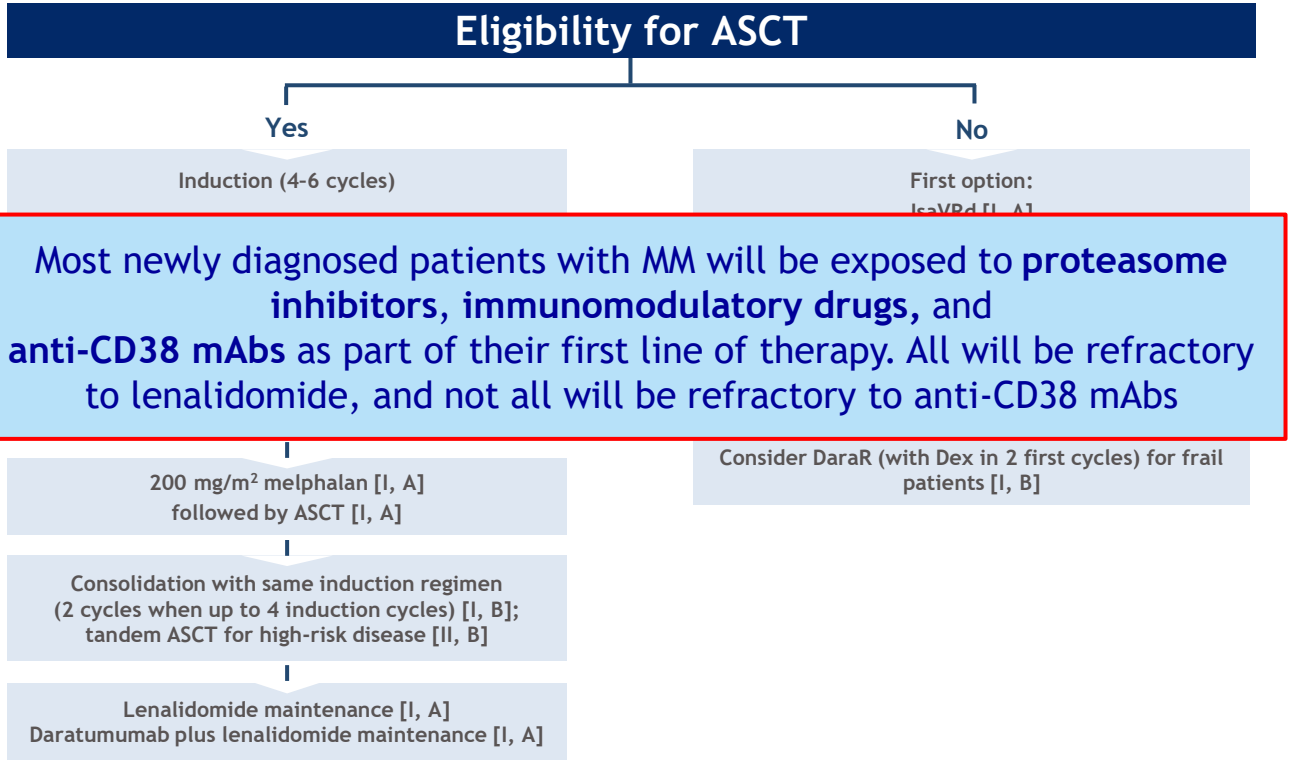


ASCT, autologous stem cell transplantation; Dara, daratumumab; Dex, dexamethasone; EHA, European Hematology Association; EMN, European Myeloma Network; Isa, isatuximab; mAb, monoclonal antibody; MM, multiple myeloma; R, lenalidomide; Rd, lenalidomide-dexamethasone; VMP, bortezomib-melphalan-prednisone; VRd, bortezomib-lenalidomide-dexamethasone; VTd, bortezomib-thalidomide-dexamethasone.

Dimopoulos MA, et al. *Nat Rev Clin Oncol*. 2025;22:680-700. (under minor revision)

EHA-EMN 2025 Guidelines

Newly diagnosed MM: Exposure to proteasome inhibitors, immunomodulatory drugs, and anti-CD38 mAbs



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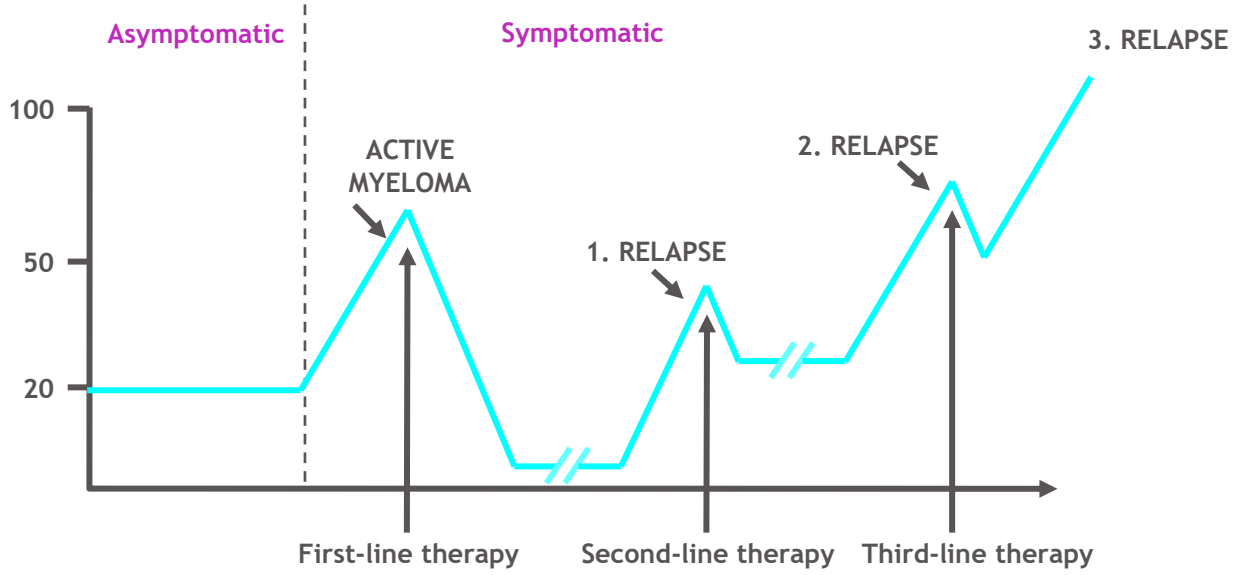
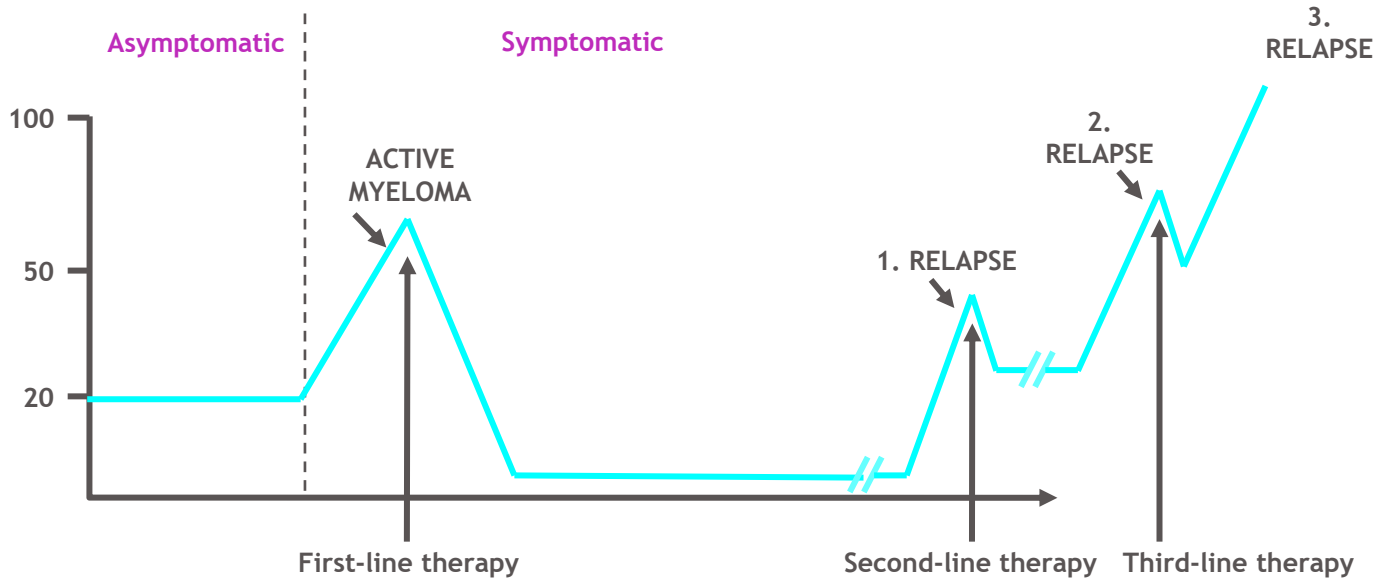
Natural History of Multiple Myeloma

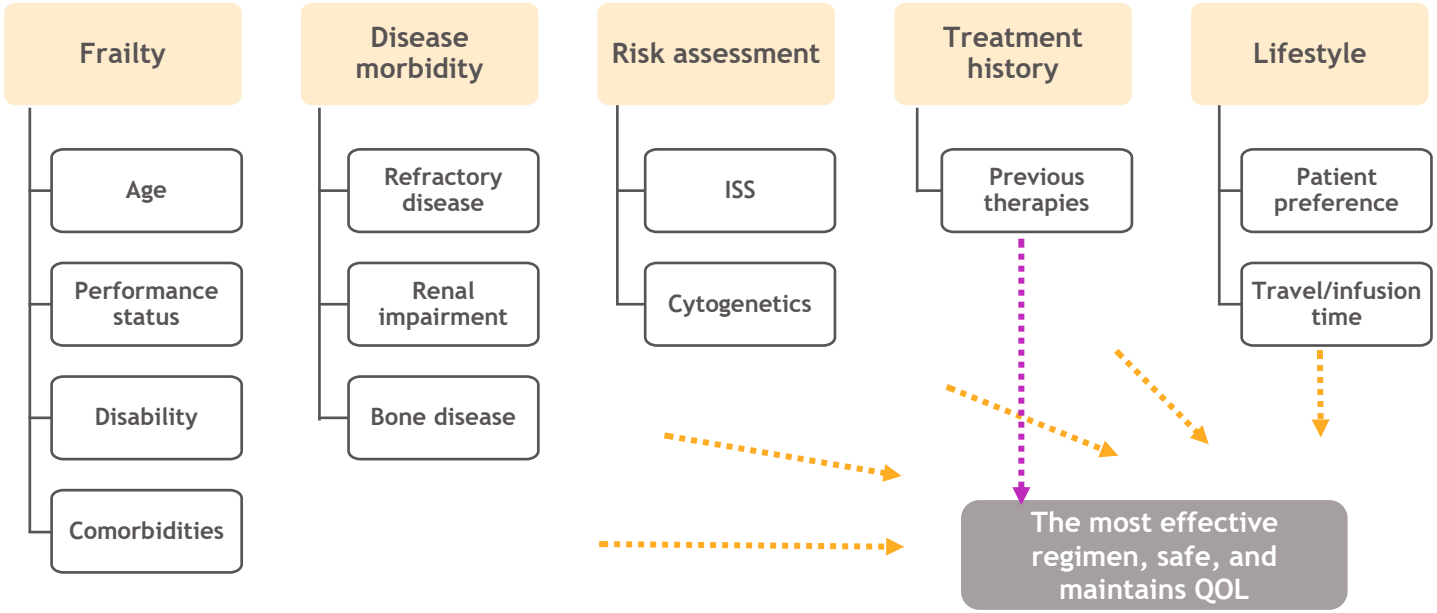


Natural History of Multiple Myeloma



Patients will present later at first relapse
Most patients will be triple-class exposed or Len-Dara exposed, and all will be refractory to lenalidomide

Disease and Patient-Based Factors Influencing Treatment Decision-Making in the Relapse Setting



Treatment history is a crucial factor
Other factors to take into consideration in the relapse setting

Treatment Landscape in Multiple Myeloma

First line

ASCT eligible

Anti-CD38 + PI + IMiD + Dex

ASCT

Len/Dara-Len

ASCT ineligible

Dara-Len-Dex

Dara-VMP/RVd

Anti-CD38 + PI + IMiD + Dex

Second line

Based on sensitivity/refractoriness to daratumumab and lenalidomide

Anti-CD38 + carfilzomib-Dex

Anti-CD38 + pomalidomide-Dex

Pomalidomide-bortezomib-Dex

Selinexor-bortezomib-Dex

Carfilzomib-Dex

Cilta-cel

New combinations

Teclistamab-Dara/Elra-Dara/Elra monotherapy

Talquetamab-Dara

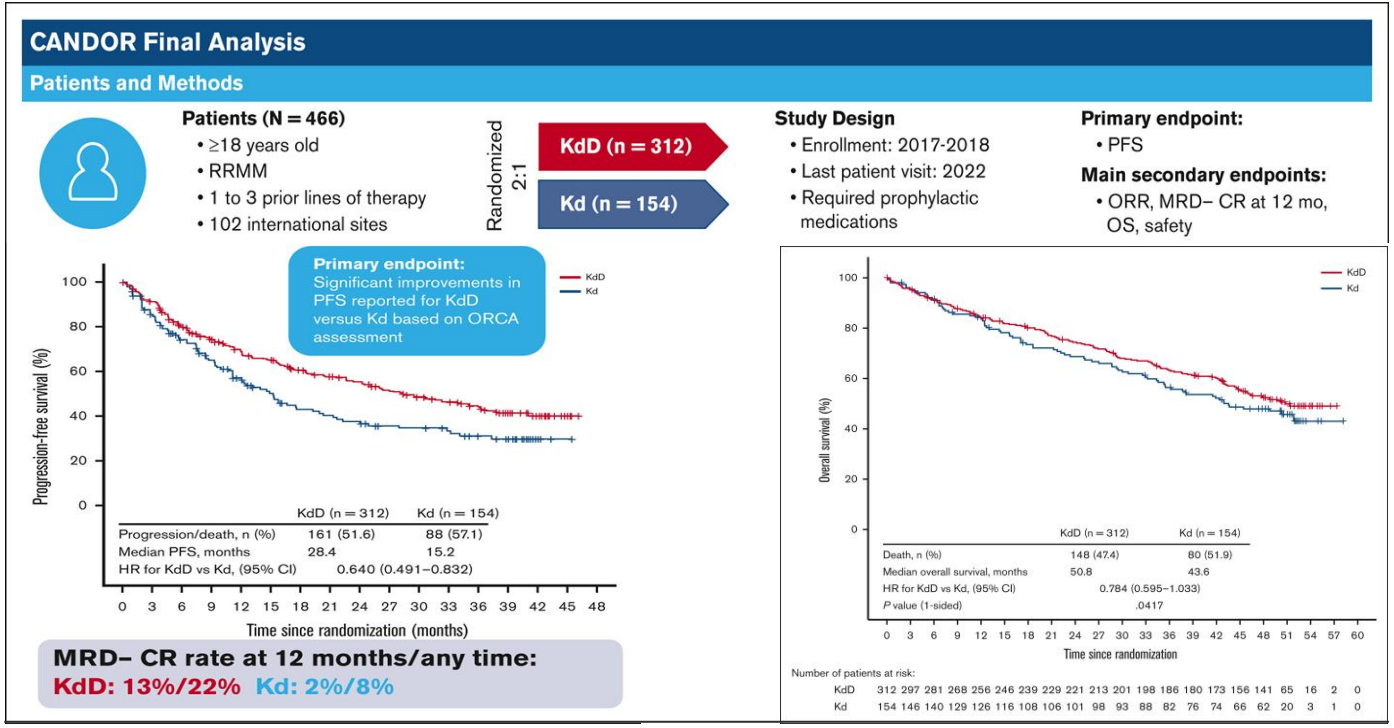
Belantamab-Vd (DREAMM-7)

Belantamab-Pd (DREAMM-8)

How to select the right combination in the near future???

Mateos MV, personal communication; Dimopoulos MA, et al. *Ann Oncol*. 2021;32:309-322.

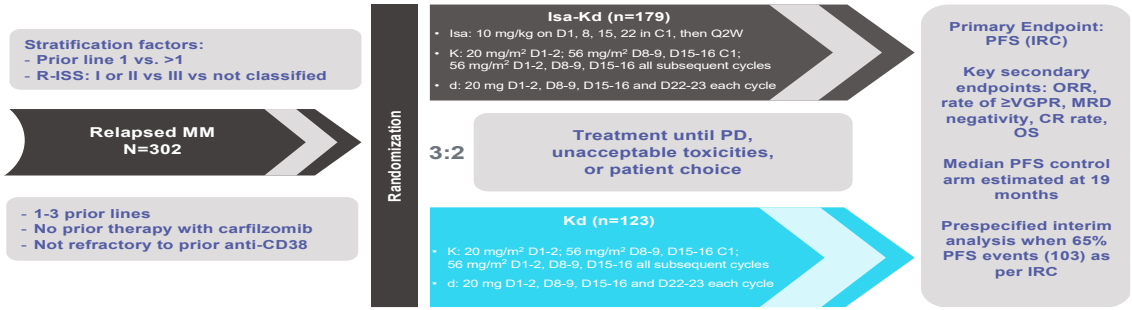
CANDOR: Study Design

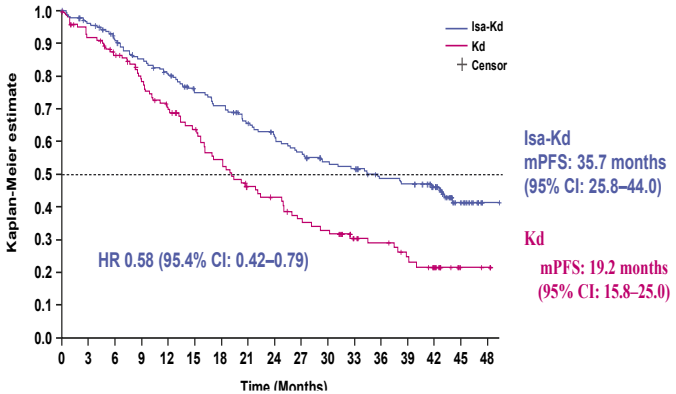


- Hazard ratio for PFS is sustained across all subgroups of patients, including those refractory to lenalidomide (30%) after 1 or more prior lines of therapy
- Safety profile acceptable

Usmani SZ, et al. *Blood Adv*. 2023;7:3739-3748.

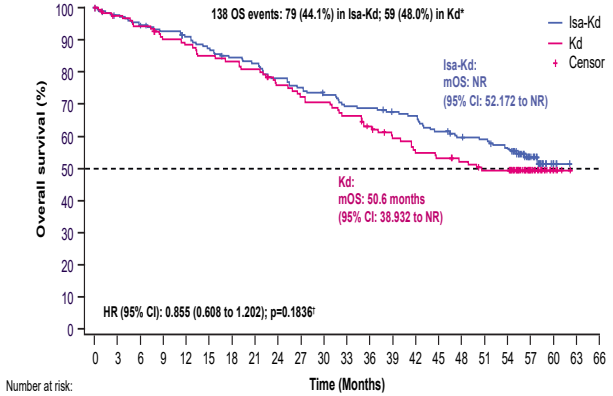
IKEMA: Study Design – Isa-Kd vs Kd in Relapsed Multiple Myeloma





Isa-Kd
mPFS: 35.7 months
(95% CI: 25.8–44.0)

Kd
mPFS: 19.2 months
(95% CI: 15.8–25.0)



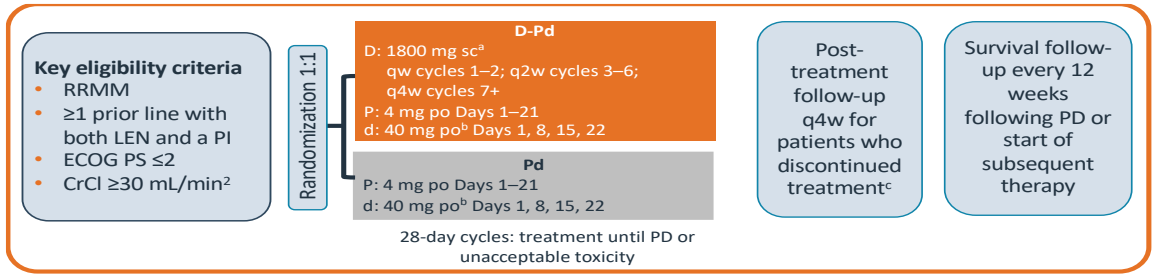
Extrapolating the current observed trend for an additional 12 months of follow-up, the mOS estimate for Isa-Kd arm is **63 months** (95% CI: 59–69)

This corresponds to an estimated 1-year difference in mOS

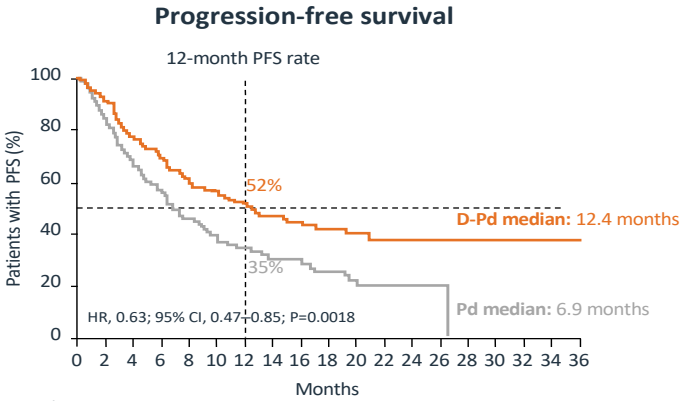
- Hazard ratio for PFS is sustained across all subgroups of patients, including those refractory to lenalidomide (30%) after 1 or more prior lines of therapy
- Safety profile acceptable

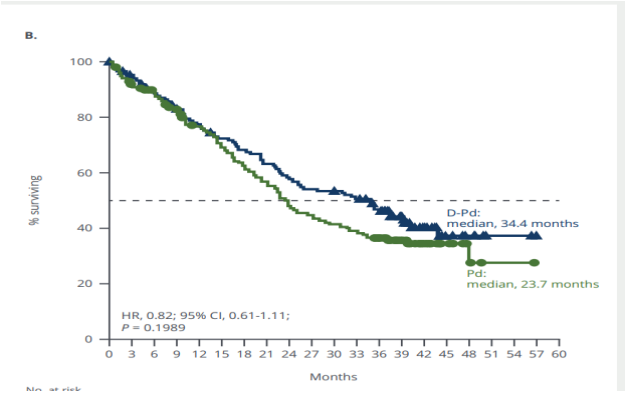
Yong K, et al. *Lancet Haematol*. 2024;11:e741-e750.

APOLLO: Subcutaneous Dara Plus Pom-Dex vs Pom-Dex in RRMM



- **Primary endpoint:** PFS
- **Secondary endpoints:** ORR, ≥VGPR, ≥CR, MRD, OS, time to response, DoR, time to next therapy, safety, HRQoL





- The number of patients included after 1 PL is rather small (11% of patients)
- 80% of patients were Len refractory, and the median PFS in Len-refractory patients is 9.9 months for Dara-Pd and 6.5 months for Pd
- Safety profile acceptable

Treatment Landscape in Multiple Myeloma

First line

ASCT eligible

Anti-CD38 + PI + IMiD + Dex

ASCT

Len/Dara-Len

ASCT ineligible

Dara-Len-Dex

Dara-VMP/RVd

Anti-CD38 + PI + IMiD + Dex

Second line

Based on sensitivity/refractoriness to daratumumab and lenalidomide

Anti-CD38 + carfilzomib-Dex

Anti-CD38 + pomalidomide-Dex

Pomalidomide-bortezomib-Dex

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Teclistamab-Dara/Elra-Dara/Elra monotherapy

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Belantamab-Vd (DREAMM-7)

Belantamab-Pd (DREAMM-8)

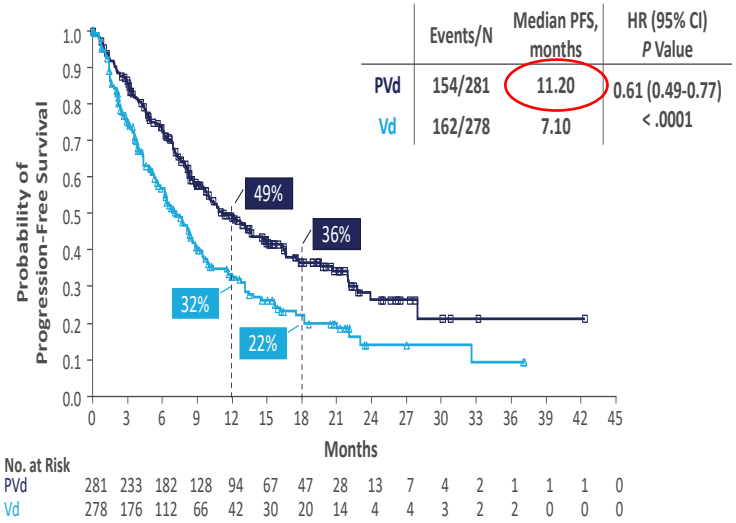
How to select the right combination in the near future???

Mateos MV, personal communication; Dimopoulos MA, et al. *Ann Oncol*. 2021;32:309-322.

OPTIMISMM: PVd vs Vd in Patients With RRMM

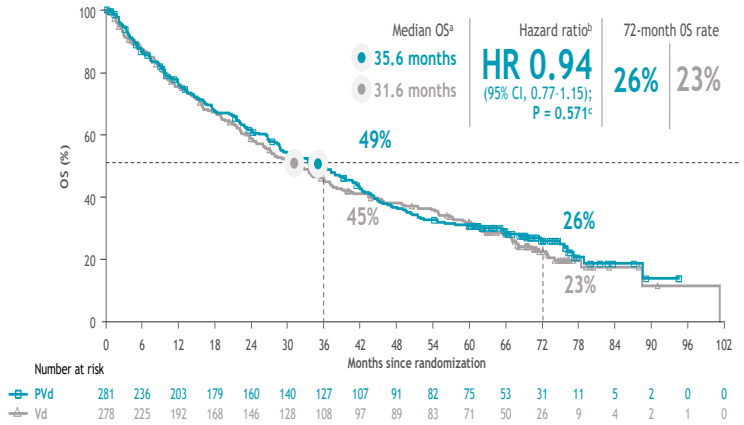
559 patients; median 2 prior lines of therapy; 100% Len exposed; 70% Len refractory; 63% Len refractory as part of the last line of therapy

PVd reduced the risk of progression and death by 39% compared with Vd



	Events/N	Median PFS, months	HR (95% CI) *P* Value
PVd	154/281	11.20	0.61 (0.49-0.77)
Vd	162/278	7.10	< .0001

OS: ITT population



Median OS was numerically longer for PVd versus Vd, but this difference was not statistically significant

- Median PFS for PVd in patients refractory to Len after the first line of therapy was 17.8 months
- Safety profile acceptable

Richardson P, et al. *J Clin Oncol*. 2018;36:2492-2503. Abstract 8001.

BOSTON: Selinexor Vd vs Vd in Patients With RRMM

- Median age: 66 years (SVd) vs 67 years (Vd)
- 2 prior lines: 33% vs 31%; 3 prior lines: 16% vs 21%
- High-risk cytogenetics: 50% vs 46%
- Lenalidomide exposed: 39.5% vs 37.2%

	SVd arm (n = 195)	Vd arm (n = 207)
Median PFS, months (95% CI)*	13.93 (11.73, NE)	9.46 (8.11, 10.78)
HR=0.70 (95% CI: 0.53, 0.93); one-sided *P* = .0075		

Kaplan-Meier estimates of progression-free survival among patients in the ITT population

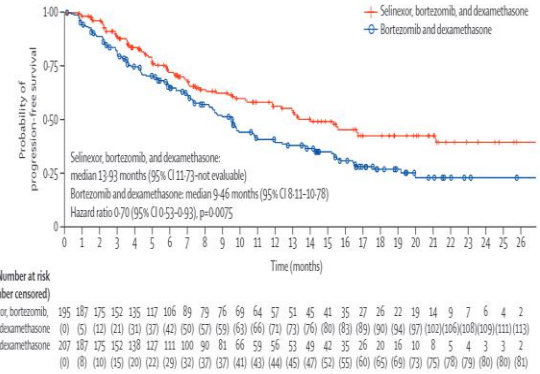
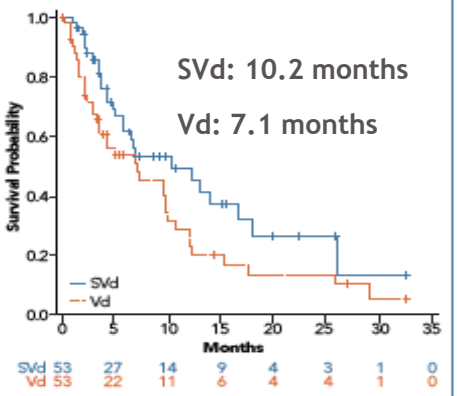
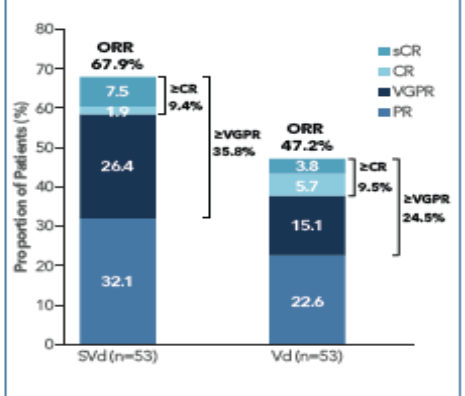


Figure 1. PFS in Lenalidomide-Refractory Patients



*ITTNT was calculated from the date of randomization to the start of next anti-MM treatment or death, whichever occurred first. Patients without an event were censored at the date of discontinuation from the study or last participating visit or database cut-off date, whichever occurred first.

Figure 2. Response in Lenalidomide-Refractory Patients



CR, complete response; ORR, overall response rate; PR, partial response; sCR, stringent complete response; SVd, selinexor + bortezomib + dexamethasone; Vd, bortezomib + selinexor; VGPR, very good partial response.

- 106 patients in the BOSTON trial were Len refractory, and the majority of them were after 2 or 3 PL

- Safety profile was acceptable, and for those patients in whom the dose was modified, the outcome was better
- No significant benefit reported in overall survival

Grosicki S, et al. *Lancet*. 2020;396:1563-1573.

Treatment Landscape in Multiple Myeloma

First line

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ASCT

Len/Dara-Len

ASCT ineligible

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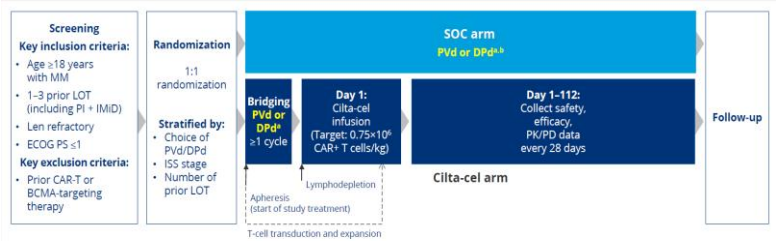
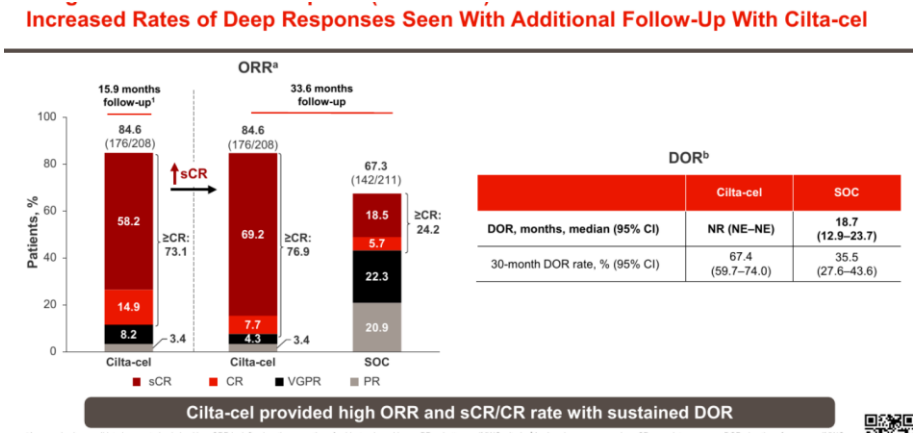
CARTITUDE-4: Phase III Trial of Cilta-Cel vs PVd/DPd in Len-Refractory MM After 1-3 PL

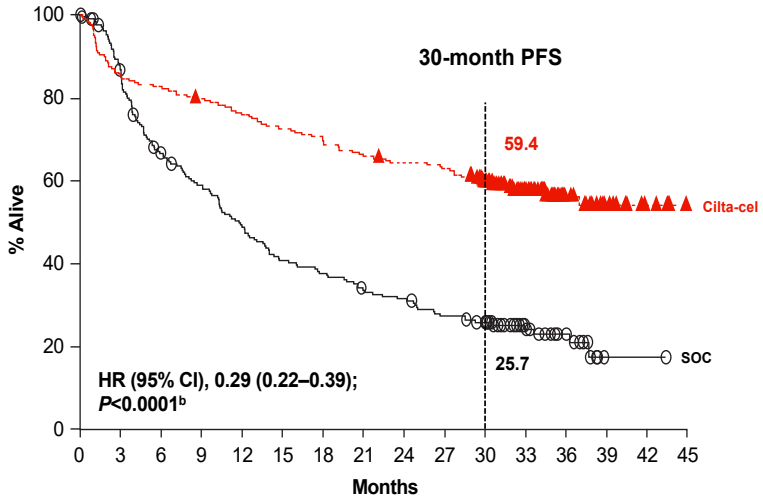


- Median number of PL: 2
- 33% of patients with HRCA and 21% double hit
- 25% TC exposed and 14% TC refractory
- 100% Len refractory

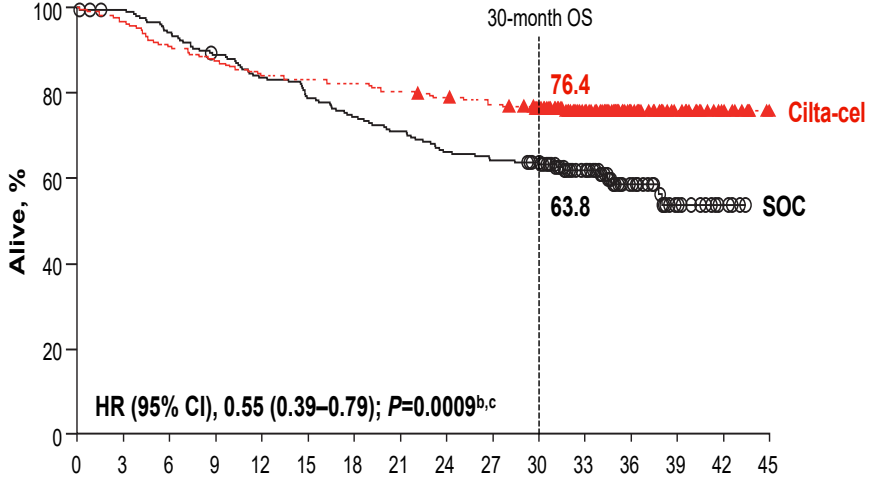


Phase III CARTITUDE-4 Trial: Efficacy

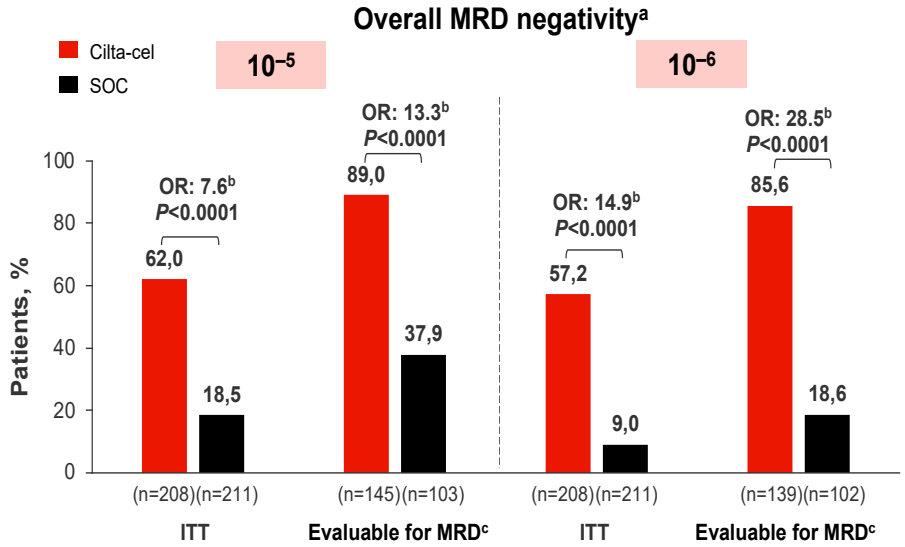
PFS (ITT; 33.6-mo median follow-up)

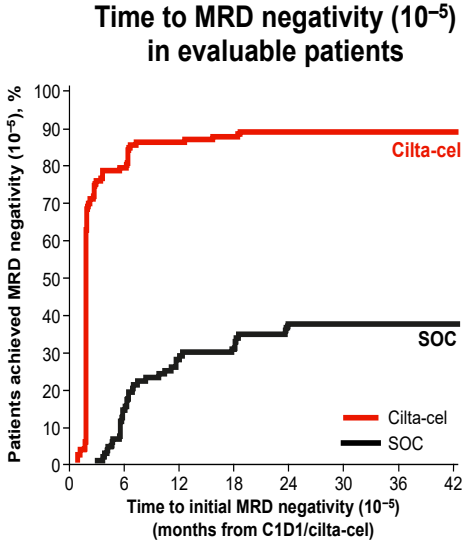


OS (ITT; 33.6-mo median follow-up)



Phase III CARTITUDE-4 Trial: MRD-Negativity Analysis



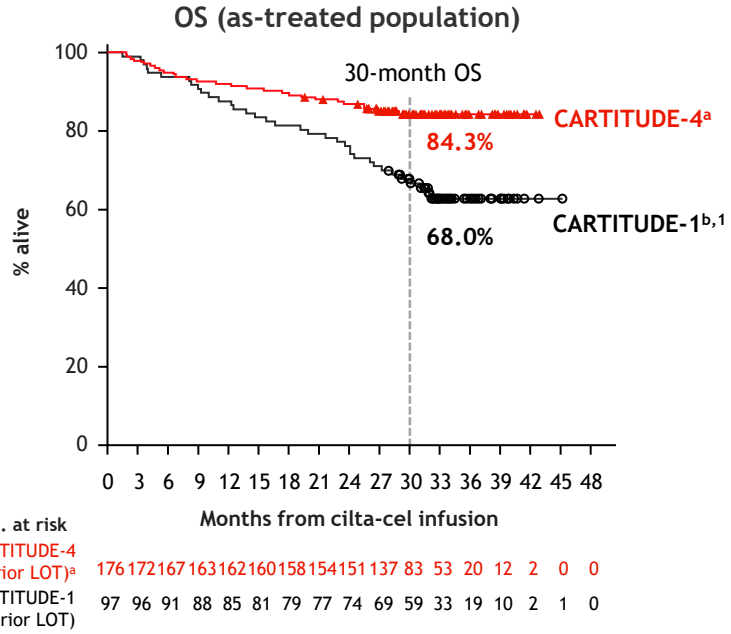


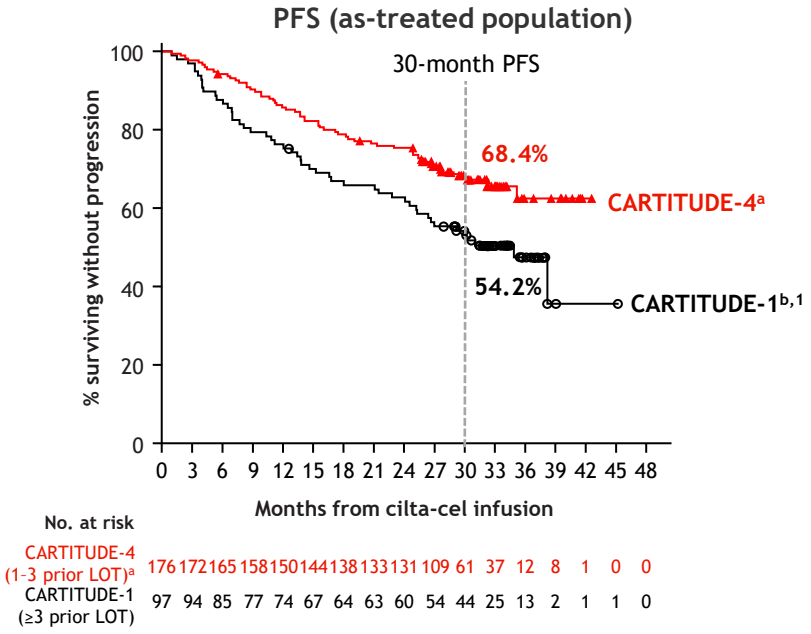
- 69% of evaluable patients achieved MRD negativity (10^{-5}) by day 56 (ITT, 48%), rising to 86% (ITT, 60%) by 6 months post cilta-cel infusion

- **High rates of overall MRD negativity are rapidly achieved with Cilta-cel**, and almost all patients receiving Cilta-cel negative at 10^{-5} **were also negative at** 10^{-6}
- Across subgroups, Cilta-cel **increased overall MRD-negativity rates** at the 10^{-5} threshold vs SOC

Popat R, et al. ASH 2024. Abstract 1032.

Long-Term CARTITUDE-4 Update (34 months): Numerically Higher OS and PFS Rates vs CARTITUDE-1



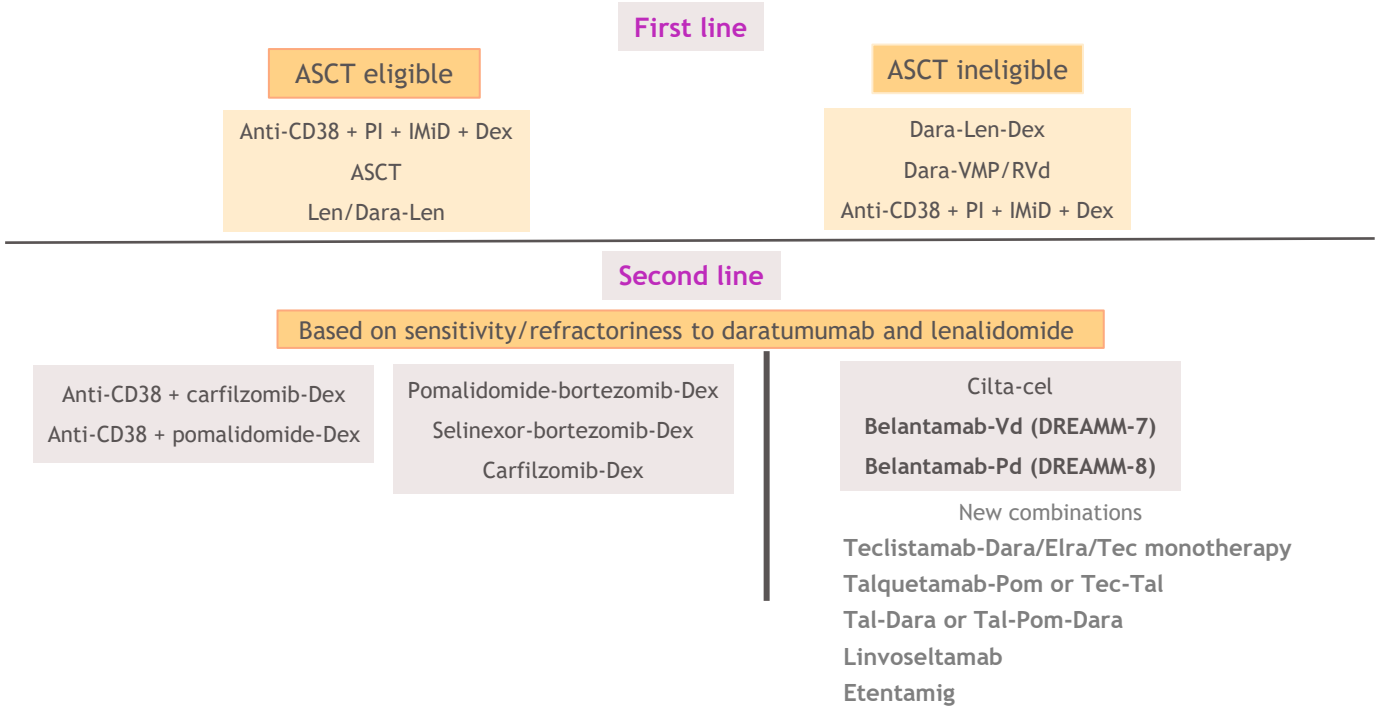


Cilta-cel use in earlier lines demonstrated numerically higher rates of overall and progression-free survival

[a]Re-baselined to begin at time of cilta-cel infusion for patients who received cilta-cel as study treatment, with median follow-up of 30.5 months; [b]33.4-month median follow-up.
Cilta-cel, ciltacabtagene autoleucel; LOT, line of therapy; OS, overall survival; PFS, progression-free survival; SOC, standard of care.

1. Lin Y, et al. ASCO 2023.Abstract 8009.

Treatment Landscape in Multiple Myeloma

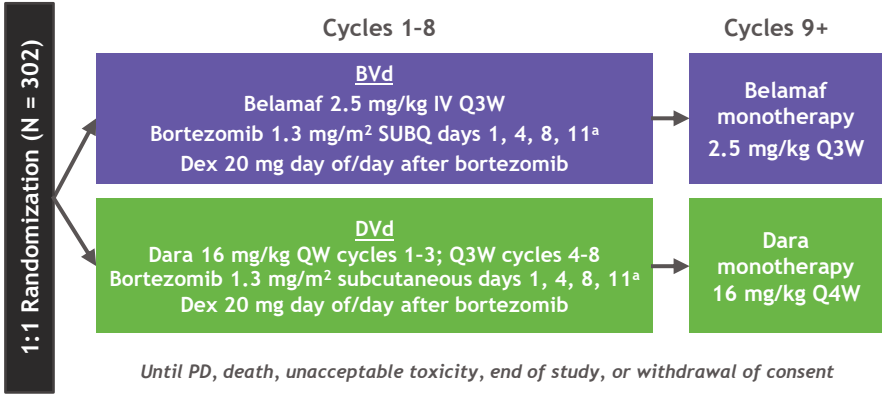


Mateos MV, personal communication; Dimopoulos MA, et al. *Ann Oncol*. 2021;32:309-322.

DREAMM-7: Phase III Trial of BVd vs DVd in RRMM – Study Design and Patients

Key Eligibility Criteria

- ≥1 prior LOT and PD during or after most recent therapy
- **No prior anti-BCMA**
- **Not refractory to or intolerant of daratumumab or bortezomib**



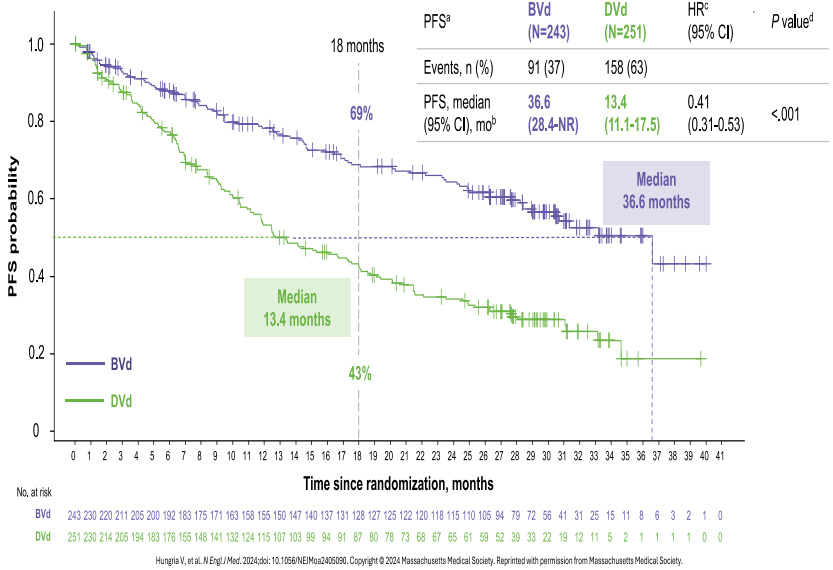
Primary endpoint: PFS (IRC)
Key secondary endpoints: OS, DOR, MRD

Patient Characteristics		BVd (n = 243)	DVd (n = 251)
Median age (range), years		65.0 (34-86)	64.0 (32-89)
ECOG PS ≤1, n (%)		232 (96)	235 (96)
R-ISS stage I at screening, n (%)		102 (42)	103 (41)
High-risk cytogenetics, n (%)		67 (28)	69 (27)
t(4;14)		41 (61)	42 (61)
t(14;16)		8 (12)	6 (9)
del(17p13)		30 (45)	33 (51)
Prior LOT, n (%)	1	125 (51)	125 (50)
	2 or 3	88 (36)	99 (39)
	≥4	30 (12)	27 (11)
Prior treatment, n (%)	Bortezomib	210 (86)	211 (84)
	Daratumumab	3 (1)	4 (2)
	Lenalidomide	127 (52)	130 (52)
Refractory to Len, n (%)		79 (33)	87 (35)
Refractory (n = 79/87) or not (n = 164/164) by prior LOT, n (%)	1	22 (28)/103 (63)	27 (31)/98 (60)
	2	24 (30)/30 (18)	21 (24)/42 (26)
	3+	33 (42)/31 (19)	39 (45)/24 (15)

[a]21-day cycles.

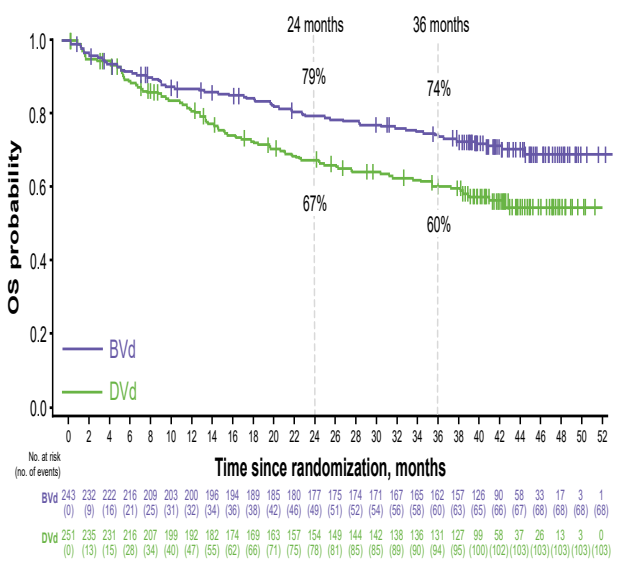
DREAMM-7: Phase III Trial of BVd vs DVd in RRMM – PFS/OS in All Patients

PFS



PFS[a]	BVd (N=243)	DVd (N=251)	HR[c] (95% CI)	*P* value[d]
Events, n (%)	91 (37)	158 (63)		
PFS, median (95% CI), mo[b]	36.6 (28.4-NR)	13.4 (11.1-17.5)	0.41 (0.31-0.53)	<.001

OS



OS[a]	BVd (N=243)	DVd (N=251)
Events, n (%)	68 (28)	103 (41)
OS, median (95% CI), months[b]	NR (NR-NR)	NR (41.0-NR)
HR (95% CI)[c]	**0.58 (0.43-0.79)**	
P value[d]	**.00023**	
24-Month survival (95% CI), %	79 (73-84)	67 (61-73)
36-Month survival (95% CI), %	74 (68-79)	60 (54-66)

- **BVd demonstrated statistically significant and clinically meaningful PFS benefit (HR, 0.41; 95% CI, 0.31-0.53; *P* <.001), with a median PFS that was 23 months longer than that with DVd (36.6 months vs 13.4 months)**
- **Median OS was not reached. Predicted median OS based on modeling is 84 months with BVd and 51 months with DVd**

Hungria V, et al. *N Engl J Med*. 2024;393-407; Hungria V, et al. ASH 2024. Abstract 772.

Non-Ocular AEs Associated With BVd Were Manageable, Enabling Patients to Continue Treatment[1-3]

DREAMM-7 update (39.4-month median follow-up)

n (%)	BVd (n = 242)		DVd (n = 246)	
Blood and lymphatic system disorders	All grades	Grade ≥3	All grades	Grade ≥3
Thrombocytopenia[b]	169 (70)	135 (56)	122 (50)	87 (35)
Anemia[c]	48 (20)	21 (9)	65 (26)	25 (10)
Neutropenia[d]	45 (19)	34 (14)	44 (18)	24 (10)
Infections and infestations	176 (73)	80 (33)	167 (68)	49 (20)
Pneumonia	48 (20)	30 (12)	23 (9)	10 (4)

Exposure-adjusted rate (per 100 person-years)[e]	BVd (n = 242)		DVd (n = 246)	
Blood and lymphatic system disorders	All grades	Grade ≥3	All grades	Grade ≥3
Thrombocytopenia	42.01	33.56	35.58	25.37
Neutropenia	11.19	8.45	12.83	7.00
Infections and infestations	43.75	19.89	48.71	14.29
Pneumonia	11.93	7.46	6.71	2.92

The safety and tolerability of the BVd regimen was **consistent with the known safety profile of the individual agents**

In the BVd and DVd arms, **exposure-adjusted rates of infections** were **43.75 and 48.71 (all grades)** and **19.89 and 14.29 (grade ≥3),** respectively

There was **low usage of immunoglobulin replacement in both arms (BVd, 8%; DVd, 4%)[3]**

[a]Graded using CTCAE version 5.0; [b]If platelet count decrease is also included, the percentage of thrombocytopenia events for all grades was 88% and 65% with BVd and DVd, respectively, and for grade 3/4 was 73% and 46% with BVd and DVd, respectively; [c]Red blood cell decrease was not reported; [d]Neutropenia includes preferred terms febrile neutropenia, neutropenia, and neutrophil count decrease; [e]Exposure-adjusted event rates were calculated as the total number of patients with an event divided by the total exposure time in person-years (per 100 person-years).
AE, adverse event; AR, adverse reaction; BVd, belantamab mafodotin, bortezomib, and dexamethasone; DVd, daratumumab, bortezomib, and dexamethasone; SAE, serious adverse event.

1. Hungria V, et al. ASH 2024. Abstract 772; 2. Hungria V, et al. *N Engl J Med*. 2024;391(5):393-407; 3. Robak P, et al. EHA 2025. Poster PS1762.

Ocular AEs Occurred More Frequently With BVd Compared With DVd; However, Some Patients in the DVd Arm Also Experienced Ocular Events[1]

Grade ≥3 ocular events (CTCAE) in ≥5% of patients in either treatment group by preferred term and maximum grade

Ocular AESIs (by CTCAE) preferred terms, n (%)[1]	BVd (n = 242)		DVd (n = 246)	
	All grades	Grade ≥3	All grades	Grade ≥3
Any event	191 (79)	82 (34)	72 (29)	7 (3)
Blurred vision	160 (66)	53 (22)	26 (11)	2 (<1)
Dry eye	123 (51)	17 (7)	17 (7)	0
Eye irritation	103 (43)	12 (5)	13 (5)	0
Visual impairment	26 (11)	13 (5)	4 (2)	1 (<1)

Ocular exams for patients in the BVd arm were assessed at screening/baseline and then every 3 weeks prior to dosing, up to at least the sixth dose of belantamab mafodotin and then every 3 months if there were no significant ocular findings. For patients in the DVd arm, ocular exams were performed at screening/baseline with on-treatment ocular exams performed at cycle 6 and then decreased to every 6 months.

Low incidence of BCVA worsening and discontinuations due to ocular events
In Europe, there were no discontinuations due to ocular events[2]

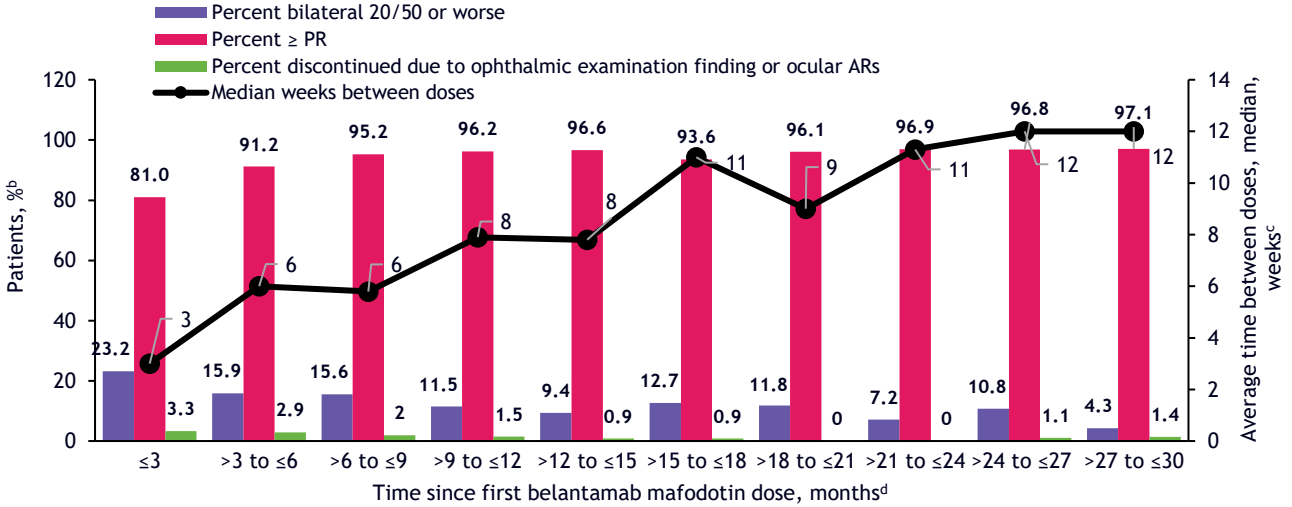
BCVA changes were **reversible**[3]

Blurred vision was experienced for only ~11% of time on treatment[4]

AESI, adverse event of special interest; CTCAE, Common Terminology Criteria for Adverse Events.

1. Mateos MV, et al. ASCO 2024. Abstract 439572; 2. Oriol A, et al. LXVI SEHH 2024; 3. Trudel S, et al. ASCO 2024. Abstract LBA105; 4. Hajek R, et al. EHA 2025. Abstract PS1761.

DREAMM-7: Median Dosing Interval, Response Rates, and Ocular Events[1,a]

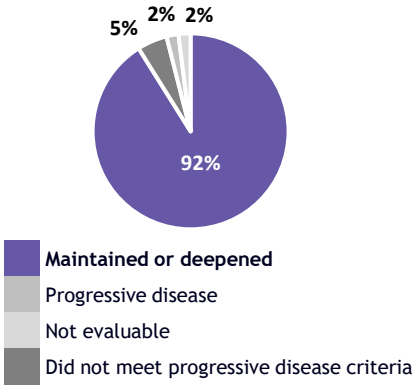


	≤3	>3 to ≤6	>6 to ≤9	>9 to ≤12	>12 to ≤15	>15 to ≤18	>18 to ≤21	>21 to ≤24	>24 to ≤27	>27 to ≤30
No. of patients on treatment[b]	211	170	147	131	117	110	102	97	93	69
No. of patients with bilateral 20/50 or worse[b]	49	27	23	15	11	14	12	7	10	3
Median days between doses[b]	21	42	41	55	54	77	63	79	84	84
No. of patients who discontinued due to ocular event[b]	7	5	3	2	1	1	0	0	1	1
No. of patients with ≥ PR	171	155	140	126	113	103	98	94	90	67

- **Median time between doses was** 5.7 weeks during all treatment and 9.5 weeks beyond 12 months[2]
- **Prevalence of 20/50 or worse** events generally **decreased during treatment**

DREAMM-7[3]

(n = 127)

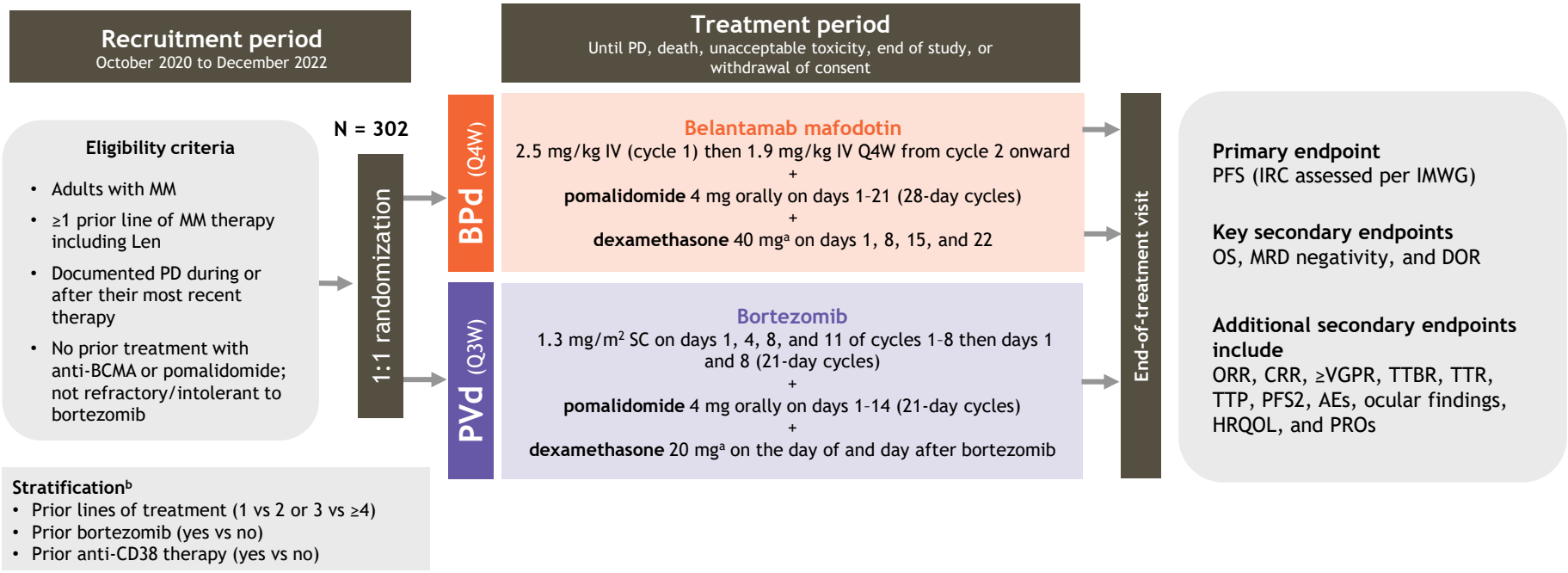


High response rates were maintained despite longer dosing intervals. Most patients (92%) maintained or deepened their response during their first extended dose delay.[2] Median BVd dosing interval was 5.7 weeks[3]

[a]Only the belantamab mafodotin treatment period was considered in these post hoc analyses; [b]Only patients with 20/25 or better in ≥1 eye at baseline are considered; [c]Mean of days between doses for each patient per interval is used; [d]Graph is truncated at 30 months because data beyond 30 months represented a low number of patients on treatment (>30 to ≤33 months, n = 42; >33 to ≤36 months, n = 20; >36 to ≤39 months, n = 8; >39 to ≤42 months, n = 3).
AR, adverse reaction; BCVA, best-corrected visual acuity; PR, partial response.

1. Mateos MV, et al. *Blood Adv*. 2025;9:5708-5719; 2. Hungria V, et al. IMS 2024. Poster P-396. *Clin Lymphoma Myeloma Leuk*. 2024;24:S262-S263; 3. Hajek R, et al. EHA 2025. Poster PS1761.

DREAMM-8: Phase III Study Examining a Belantamab Mafodotin-Based Combination in 2L+ RRMM (NCT04484623)



[a]Patients aged >75 years, with comorbidities, or intolerant to 40 mg dose in Arm A or 20 mg dose in Arm B could have dose level reduced to half per investigator discretion; [b]Some patients were stratified by ISS status (I vs II/III); the protocol was amended on April 20, 2021, to replace this randomization factor with prior anti-CD38 treatment (yes vs no).

2L, second line: AE, adverse event; BCMA, B-cell maturation antigen; BPd, belamaf, pomalidomide, and dexamethasone; CD, cluster of differentiation; CRR, complete response rate; DOR, duration of response; HRQOL, health-related quality of life; IMWG, International Myeloma Working Group; IRC, independent review committee; ISS, International Staging System; IV, intravenous; LEN, lenalidomide; MM, multiple myeloma; MRD, minimal residual disease; ORR, objective response rate; OS, overall survival; PD, progressive disease; PFS, progression-free survival; PFS2, progression-free survival on subsequent line of therapy; PRO, patient-reported outcome; PVd, pomalidomide, bortezomib, and dexamethasone; Q3W, every 3 weeks; Q4W, every 4 weeks; RRMM, relapsed or refractory multiple myeloma; SC, subcutaneous; TTBR, time to best response; TTP, time to progression; TTR, time to response; VGPR, very good partial response.

DREAMM-8: Baseline Disease Characteristics and Clinical Characteristics

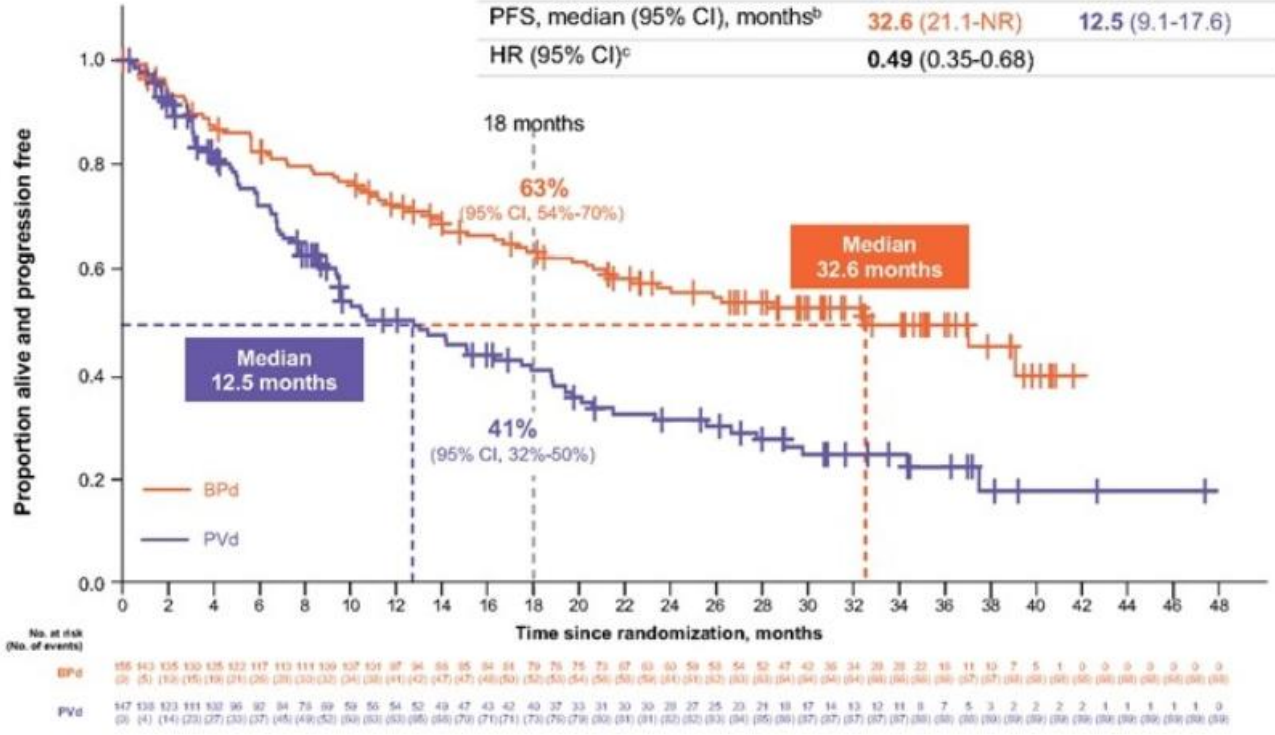
Baseline Characteristics	ITT Population	
	BPd (n = 155)	PVd (n = 147)
Age, median (range), years	67 (40-82)	68 (34-86)
<65, n (%)	64 (41)	53 (36)
65 to <75, n (%)	72 (46)	59 (40)
≥75, n (%)	19 (12)	35 (24)
Male/female, n (%)	99 (64)/56 (36)	82 (56)/65 (44)
White/Black/Asian/Mixed race, n (%)[a]	133 (86)/0/20 (13)/1 (<1)	127 (87)/0/17 (12)/0
ECOG PS ≤1, n (%)[b]	146 (97)	140 (97)
ISS stage at screening, n (%)		
I	93 (60)	85 (58)
II	39 (25)	40 (27)
III	22 (14)	22 (15)
Unknown	1 (<1)	0
Years since diagnosis, median (range)	4.04 (0.4-16.7)	3.43 (0.4-17.7)
Cytogenetic abnormalities, n (%)		
Standard risk[c]	72 (46)	75 (51)
High risk[d]	52 (34)	47 (32)
Missing or nonevaluable[e]	31 (20)	25 (17)
Time to relapse after initiation of 1L treatment		
≤12 months	22 (14)	20 (14)
>12 months	133 (86)	127 (86)
Extramedullary disease, n (%)	20 (13)	11 (7)

Prior Treatments, n (%)	ITT Population			
	BPd (n = 155)		PVd (n = 147)	
Prior LOT				
1	82 (53)		77 (52)	
2 or 3	54 (35)		48 (33)	
≥4	19 (12)		22 (15)	
Prior ASCT	99 (64)		82 (56)	
Prior treatment	**Exposed**	**Refractory**	**Exposed**	**Refractory**
Prior proteasome inhibitor	140 (90)	40 (26)	136 (93)	35 (24)
Bortezomib	134 (86)	16 (10)	130 (88)	8 (5)
Carfilzomib	34 (22)	18 (12)	37 (25)	23 (16)
Ixazomib	11 (7)	8 (5)	15 (10)	11 (7)
Prior immunomodulatory drug[a]	155 (100)	127 (82)	147 (100)	111 (76)
Lenalidomide	155 (100)	125 (81)	147 (100)	111 (76)
Thalidomide	49 (32)	9 (6)	48 (33)	6 (4)
Prior anti-CD38 monoclonal antibody[b]	38 (25)	35 (23)	42 (29)	36 (24)
Daratumumab	36 (23)	33 (21)	39 (27)	34 (23)
Isatuximab	2 (1)	2 (1)	3 (2)	2 (1)

[a]Mixed race included a patient who was Native Hawaiian or Other Pacific Islander and White; [b]Evaluated in the safety population (BPd, N=150; PVd, N=145). [c]Standard-risk cytogenetics were defined as having negative results for all high-risk abnormalities: t(4;14), t(14;16), or del(17p13); [d]High-risk cytogenetics were defined as the presence of ≥1 of the following: t(4;14), t(14;16), or del(17p13); [e]Patients with considered missing or nonevaluable may not be high or standard risk. Pd, belamaf, pomalidomide, and dexamethasone; ECOG PS, Eastern Cooperative Oncology Group performance status; ISS, International Staging System; ITT, intent to treat; PVd, pomalidomide, bortezomib, and dexamethasone.

DREAMM-8: PFS

PFS[a]	BPd (N=155)	PVd (N=147)
Events, n (%)	68 (44)	89 (61)
PFS, median (95% CI), months[b]	**32.6** (21.1-NR)	**12.5** (9.1-17.6)
HR (95% CI)[c]	**0.49** (0.35-0.68)	

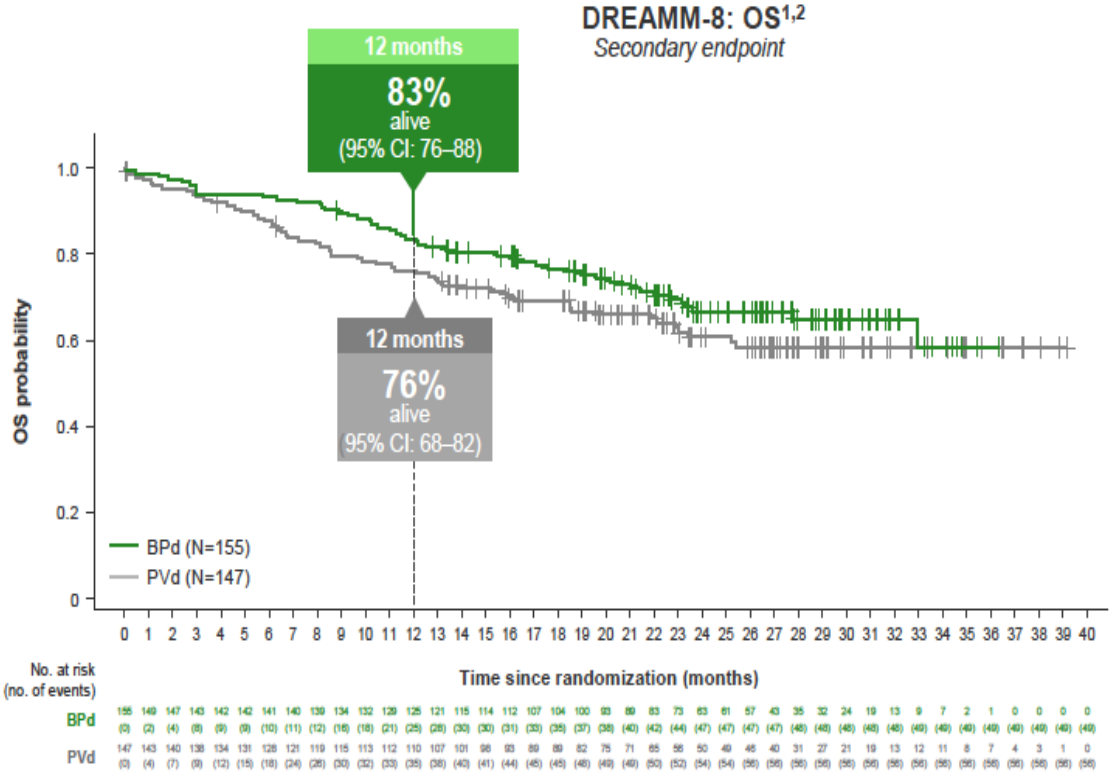


PFS benefit was observed across all prespecified subgroups, including

- **High-risk cytogenetics: HR 0.57 (95% CI, 0.34-0.95)**
- Bortezomib refractory: HR 0.45 (95% CI, 0.3–0.65)

Dimopoulos M, et al. EHA 2025. Abstract PF728.

A Trend Toward Early and Sustained OS Has Been Observed; mOS Has Not Yet Been Reached[1-3a,b]



mOS[c,d] not reached at time of primary analysis[1,2]

- Median follow-up: **21.8 months**[1,2]
- Events, n (%): **BPd, 49 (32)**; **PVd, 56 (38)**[1,2]

Adapted from Dimopoulos MA, et al. *N Engl J Med*. 2024;391:408-421.

DREAMM-8: General Safety Profile

Event	Safety Population	
	BPd (n = 150)	PVd (n = 145)
Any AE, n (%)	149 (>99)	140 (97)
Grade 3/4 AE, n (%)[a]	136 (91)	108 (74)
Exposure adjusted, patients/100 person-years[b]	55	70
AEs leading to interruption/delay, n (%)	137 (91)	110 (76)
Exposure adjusted, patients/100 person-years[b]	55	72
AEs leading to dose reduction, n (%)	94 (63)	88 (61)
Exposure adjusted, patients/100 person-years[b]	38	57
AEs leading to permanent discontinuation of any study treatment, n (%)	28 (19)	21 (14)
Exposure adjusted, patients/100 person-years[b]	11	14
Any SAE, n (%)	101 (67)	68 (47)
Exposure adjusted, patients/100 person-years[b]	41	44
Fatal SAEs, n (%)	19 (13)[c]	18 (12)

[a]Includes any patient with a grade 3 or 4 AE; [b]Exposure-adjusted incident rates were calculated as the total number of patients with an event divided by the total exposure time in person-years (per 100 person-years). Total person-years is the sum of all patient exposure calculated as (last dose − first dose + 1) / 365.25; [c]Fatal SAEs of pneumonia, meningoencephalitis herpetic, and metastatic gastrointestinal cancer were considered related to treatment in 1 patient each in the BPd group.
AE, adverse event; BPd, belantamab mafodotin, pomalidomide, and dexamethasone; PVd, pomalidomide, bortezomib, and dexamethasone; SAE, serious adverse event.

AEs of Clinical Interest[1]

Grouped Term	Safety Population			
	BPd (n = 150)		PVd (n = 145)	
	n (%)	Patients/100 PYs	n (%)	Patients/100 PYs
Thrombocytopenia[a]				
Any event	81 (54)	33	60 (41)	39
Grade ≥3	57 (38)	23	42 (29)	27
Neutropenia[b]				
Any event	97 (65)	39	69 (48)	45
Grade ≥3	87 (58)	35	60 (41)	39
Infections[c]				
Any event	124 (83)	50	101 (70)	66
Grade ≥3	78 (52)	31	39 (27)	25
Ocular AESIs (by CTCAE) preferred terms, n (%) ≥30% of patients in either treatment group				
	Any grade	**Grade ≥3**	**Any grade**	**Grade ≥3**
Any event	133 (89)	66 (44)	46 (32)	3 (2)
Blurred vision	120 (80)	26 (17)	23 (16)	0
Dry eye	92 (61)	13 (9)	14 (10)	0
Foreign body sensation in eye	91 (61)	9 (6)	11 (8)	0
Eye irritation	77 (51)	6 (4)	14 (10)	0
Photophobia	69 (46)	5 (3)	6 (4)	0
Eye pain	49 (33)	3 (2)	8 (6)	0

In the BPd and PVd arms, **exposure-adjusted rates of infections** were **50 and 66 (all grades)** and **31 and 25 (grade ≥3),** respectively

There was **low usage of immunoglobulin replacement in both arms (BPd, 18%; PVd, 9%)**[2]

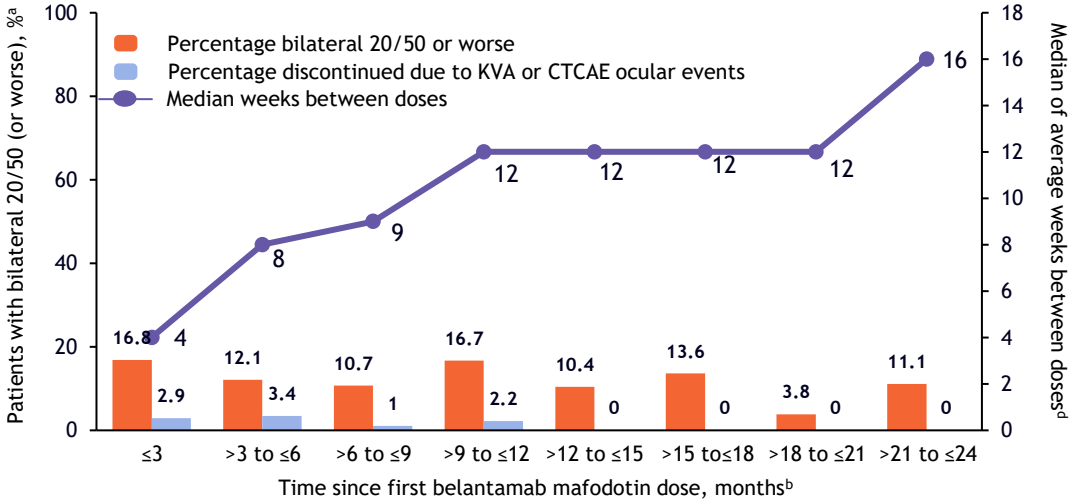
BCVA changes were **reversible**[3]

Blurred vision was experienced for only ~14% of time on treatment[4]

[a]Post hoc analysis; [b]Thrombocytopenia includes events identified by site or preferred terms thrombocytopenia or platelet count decreased; [c]Neutropenia includes preferred terms febrile neutropenia, neutropenia, and neutrophil count decreased; [d]Infections are based on all preferred terms included in the system organ class of infections and infestations.
AE, adverse event; AESI, adverse event of special interest; BPd, belamaf, pomalidomide, and dexamethasone; CTCAE, Common Terminology Criteria for Adverse Events; PVd, pomalidomide, bortezomib, and dexamethasone.

1. Dimopoulos MA, et al. EHA 2025. Poster PF728; 2. Robak P, et al. EHA 2025. Poster PS1762; 3. Trudel S, et al. ASCO 2024. Abstract LBA105; 4. Hajek R, et al. EHA 2025. Abstract PS1761.

Dose Modifications Optimize Efficacy vs Ocular Safety[1a]

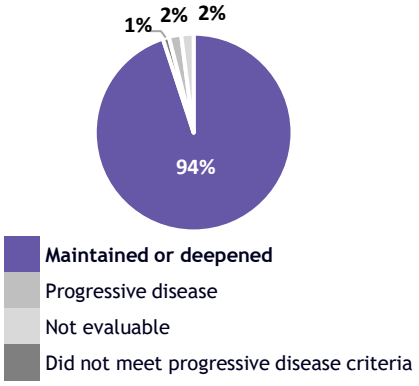


	≤3	>3 to ≤6	>6 to ≤9	>9 to ≤12	>12 to ≤15	>15 to≤18	>18 to ≤21	>21 to ≤24
No. of patients on treatment[c]	137	116	103	90	77	59	52	45
No. of patients with bilateral 20/50 or worse[c]	23	14	11	15	8	8	2	5
Median days between doses[c]	28.5	56	63.5	84	84	86	84	111
No. of patients who discontinued due to KVA or ocular CTCAE event[c]	4	4	1	2	0	0	0	0
No. of patients with ≥ PR	98	97	91	84	69	54	48	40

- **Median time between doses** was 8.7 weeks during all treatment and 14.1 weeks beyond 12 months[3]
- **Prevalence of 20/50 or worse** events generally **decreased during treatment**

DREAMM-8[3]

(n = 82)



Median BPd dosing interval was 8.7 weeks.[2] Most patients (94%) maintained or deepened their response during their first extended dose delay

[a]Only the belantamab mafodotin treatment period was considered in these post hoc analyses; [b]First 2 years of treatment shown due to limited patients at risk beyond his time point; [c]Only patients with 20/25 or better in either or both eyes at baseline are considered; [d]Mean of days between doses, for each patient, per interval is used; [e]Only patients receiving ≥6 months of treatment were included in the analysis to exclude early discontinuations (eg, rapid PD). BPd, belamaf, pomalidomide, and dexamethasone; CTCAE, Common Terminology Criteria for Adverse Events; KVA, Keratopathy and Visual Acuity; PD, progressive disease; PFS, progression-free survival.

1. Mateos MV, et al. *Blood Adv*. 2025;9:5708-5719; 2. Quach H, et al. IMS 2024. Poster P-413; 3. Hajek R, et al. EHA 2025. Poster PS1761.

Treatment Landscape in Multiple Myeloma

First line

ASCT eligible

Anti-CD38 + PI + IMiD + Dex

ASCT

Len/Dara-Len

ASCT ineligible

Dara-Len-Dex

Dara-VMP/RVd

Anti-CD38 + PI + IMiD + Dex

Second line

Based on sensitivity/refractoriness to daratumumab and lenalidomide

Anti-CD38 + carfilzomib-Dex

Anti-CD38 + pomalidomide-Dex

Pomalidomide-bortezomib-Dex

Selinexor-bortezomib-Dex

Carfilzomib-Dex

Cilta-cel

Belantamab-Vd (DREAMM-7)

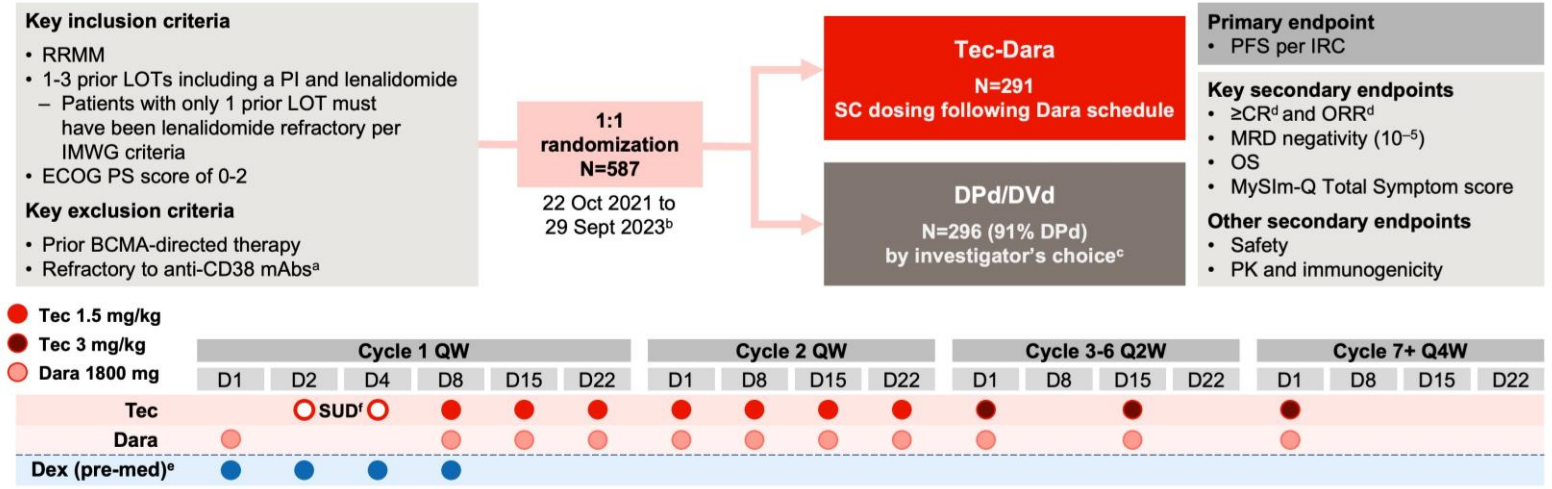
Belantamab-Pd (DREAMM-8)

Teclistamab-daratumumab

What information do we have about BsAbs in earlier lines?

Mateos MV, personal communication; Dimopoulos MA, et al. *Ann Oncol*. 2021;32:309-322.

MajesTEC-3: Phase III Randomized Trial in RRMM Comparing Tec-Dara With DaraPd or DaraVd – Study Design



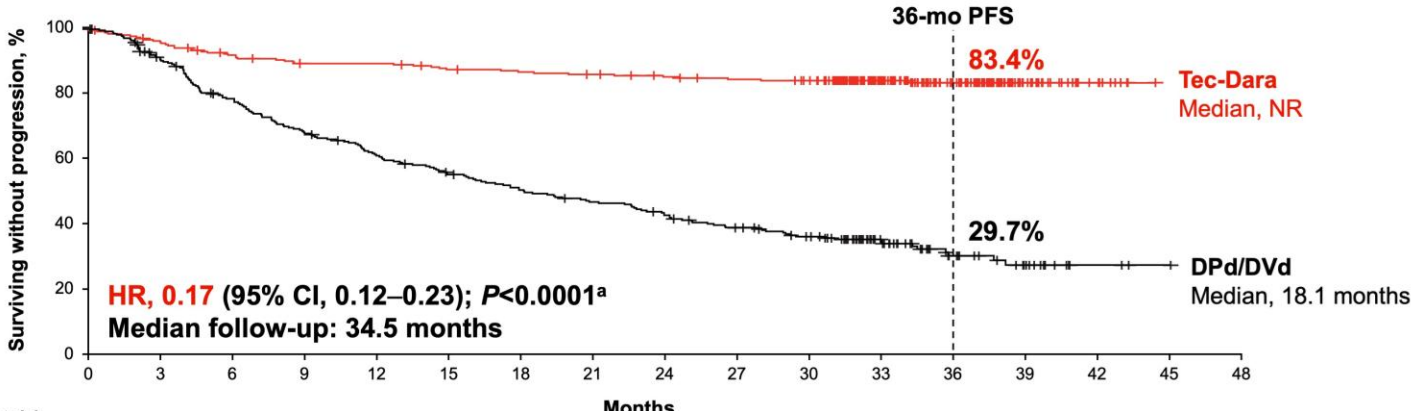
[a]Prior exposure to anti-CD38 mAbs was permitted. [b]During the COVID-19 pandemic. [c]DPd/DVd were administered per the approved schedules. [d]Response and disease progression were assessed by a blinded IRC per IMWG criteria. [e]Dexamethasone, acetaminophen, and diphenhydramine pre-medication was required for the first 2 weeks; subsequent dexamethasone was not required thereafter. [f]Patients received SUD of 0.06 mg/kg and 0.3 mg/kg on Days 2 and 4, respectively.

CR, complete response; D, day; Dex, dexamethasone; DPd, daratumumab, pomalidomide, and dexamethasone; DVd, daratumumab, bortezomib, and dexamethasone; ECOG PS, Eastern Cooperative Oncology Group performance status; IMWG, International Myeloma Working Group; IRC, independent review committee; MRD, minimal residual disease; MySIm-Q, Multiple Myeloma Symptom and Impact Questionnaire; ORR, overall response rate; PFS, progression-free survival; PI, proteasome inhibitor; PK, pharmacokinetics; pre-med, pre-medication; QW, weekly; Q2W, every 2 weeks; Q4W, every 4 weeks; SC, subcutaneous; SUD, step-up dosing.

Presented by M-V Mateos at the 67th American Society of Hematology (ASH) Annual Meeting and Exposition; December 6-9, 2025; Orlando, FL, USA.

Mateos MV, et al. ASH 2025. Abstract LBA-6.

MajesTEC-3: PFS (primary endpoint)



Tec-Dara significantly improved PFS, with a plateauing curve after ~6 months and >90% of patients progression-free at 6 months sustaining such a benefit at 3 years

[a]The *P* value crossed the prespecified stopping boundary for superiority for the first interim analysis (*P*=0.0139).
CI, confidence interval; HR, hazard ratio; NR, not reached.
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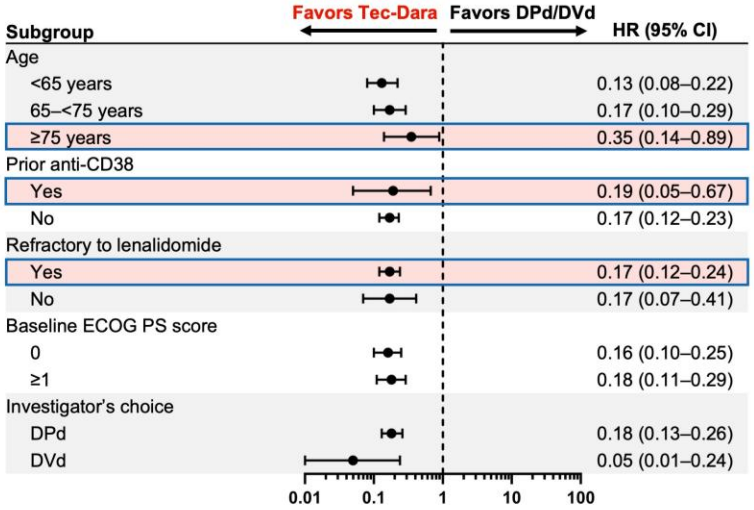
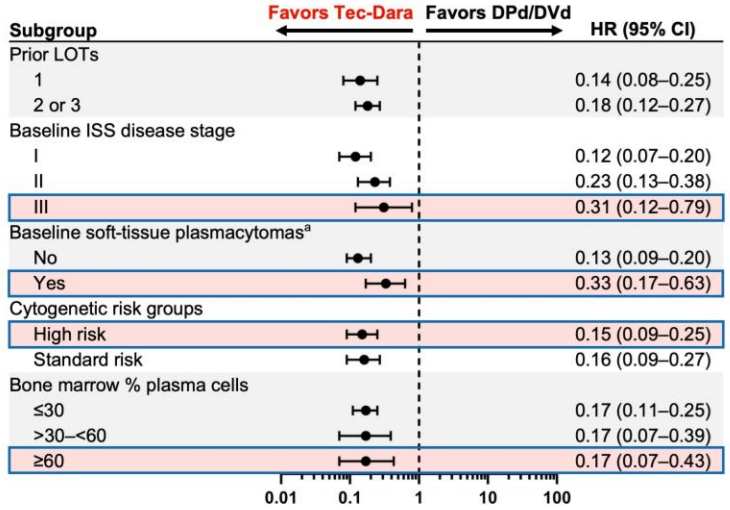
Presented by M-V Mateos at the 67th American Society of Hematology (ASH) Annual Meeting and Exposition; December 6-9, 2025; Orlando, FL, USA.

Mateos MV, et al. ASH 2025. Abstract LBA-6.

MajesTEC-3: PFS Subgroup Analysis





Superior PFS with Tec-Dara was consistent across all subgroups[b]

[a]Baseline soft-tissue plasmacytomas contain both extramedullary and paraskeletal plasmacytomas. [b]Not all clinically meaningful and prespecified subgroups that were assessed are shown; however, PFS was improved versus DPd/DVd across all subgroups.

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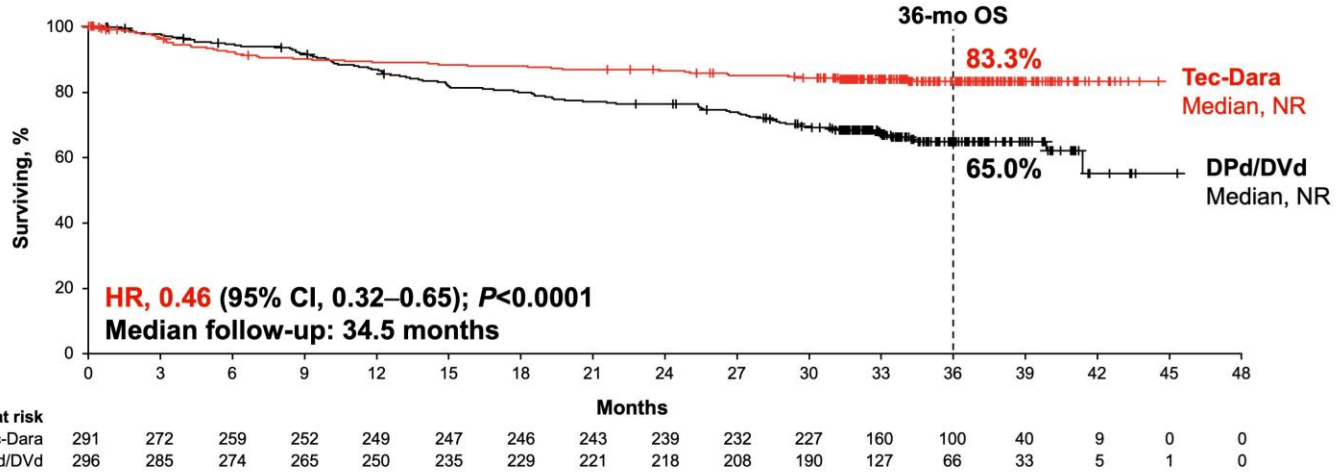
Presented by M-V Mateos at the 67th American Society of Hematology (ASH) Annual Meeting and Exposition; December 6-9, 2025; Orlando, FL, USA.

MajesTEC-3: OS



Tec-Dara significantly improved OS versus DPd/DVd, with 83% of patients alive at 3 years

Analysis of RMST demonstrated an OS benefit for Tec-Dara versus DPd/DVd (RMST difference, 2.15 months; *P*=0.0088).
RMST, restricted mean survival time.
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Presented by M-V Mateos at the 67th American Society of Hematology (ASH) Annual Meeting and Exposition; December 6-9, 2025; Orlando, FL, USA.

MajesTEC-3: Summary of Infections

- Study started during the COVID-19 pandemic and prior to bispecific treatment guidelines
- Hypogammaglobulinemia[a]: 84.5% with Tec-Dara
- 13 (4.6%) deaths due to infection with Tec-Dara[b]
  - 12 occurred within 6 months of treatment (3 due to COVID-19); 9 of 12 patients did not receive IgRT
  - Protocol was subsequently amended in Feb 2023 to reinforce IgRT supplementation and antimicrobial prophylaxis[c]
    - 87.3% received ≥1 dose of Ig[d]
    - 1 infectious death occurred post amendment

TEAE, n (%)	Tec-Dara (n=283)		DPd/DVd (n=290)	
	Any grade	Grade 3/4	Any grade	Grade 3/4
Any infection	273 (96.5)	153 (54.1)	244 (84.1)	126 (43.4)
Treatment-emergent infection or infestation[e]				
COVID-19	124 (43.8)	17 (6.0)	97 (33.4)	6 (2.1)
URTI	115 (40.6)	12 (4.2)	88 (30.3)	7 (2.4)
Pneumonia	65 (23.0)	47 (16.6)	53 (18.3)	43 (14.8)
Nasopharyngitis	62 (21.9)	0	57 (19.7)	0
Sinusitis	52 (18.4)	5 (1.8)	17 (5.9)	3 (1.0)
Rhinovirus infection	44 (15.5)	5 (1.8)	10 (3.4)	1 (0.3)
Bronchitis	40 (14.1)	2 (0.7)	31 (10.7)	6 (2.1)
Influenza	38 (13.4)	8 (2.8)	43 (14.8)	10 (3.4)
COVID-19 pneumonia	34 (12.0)	32 (11.3)	12 (4.1)	7 (2.4)
UTI	29 (10.2)	4 (1.4)	27 (9.3)	1 (0.3)

Infections with Tec-Dara require diligent use of established IgRT and prophylaxis protocols

[a]Hypogammaglobulinemia was defined as patients with ≥1 TEAE of hypogammaglobulinemia or a post-baseline IgG value <400 mg/dL. Rate of hypogammaglobulinemia in the DPd/DVd arm was 60.3%. [b]In the DPd/DVd group, 4 patients had a fatal infection, 2 of which occurred after the implementation of protocol amendment #6. [c]Protocol amendment #6 affirmed the importance of medical monitoring of IgG levels and adherence to protocol-specified Ig supplementation guidance. [d]Percentage at clinical cutoff. [e]Most common defined as occurring in ≥10% of patients in either treatment group; shown with percent occurrence of respective grade 3/4 infection.
Ig, immunoglobulin; IgG, immunoglobulin G; IgRT, immunoglobulin replacement therapy; UTI, urinary tract infection.

Presented by M-V Mateos at the 67th American Society of Hematology (ASH) Annual Meeting and Exposition; December 6-9, 2025; Orlando, FL, USA.

MajesTEC-3: Conclusions

Synergistic[1] immunotherapy combination of Tec-Dara versus DPd/DVd in 1-3 prior LOTs in RRMM:

- Greatest PFS treatment effect to date (HR, 0.17),[2-6] with plateauing curve after ~6 months suggesting potential for functional cure
  - Benchmark 83.4% PFS rate at 3 years, with clear benefit in patients with high-risk cytogenetics, EMD, ISS stage III, and prior anti-CD38 exposure
- Superior OS (HR, 0.46)
- Grade ≥3 infections were highest in the first 6 months, then declined over time; patients should be supported with infection prophylaxis, monitoring, and established IgRT supplementation protocols
- CRS profile and combinability of Tec with Dara on approved Dara schedule support potential for community adoption

Tec-Dara showed unprecedented efficacy, supporting a new 2L+ SOC with broad potential across academic and community settings

1. Vishwamitra D, et al. Presented at: ASH Annual Meeting and Exposition; December 7-10, 2024; San Diego, CA, USA. Oral 594. 2. San-Miguel J, et al. *N Engl J Med*. 2023;389:335-347. 3. Usmani SZ, et al. *Blood Adv*. 2023;7:3737-3748. 4. Hungria V, et al. *N Engl J Med*. 2024;391:393-407. 5. Dimopoulos MA, et al. *N Engl J Med*. 2024;391:408-421. 6. Martin T, et al. *Blood Cancer J*. 2023;13:72.
EMD, extramedullary disease.

Presented by M-V Mateos at the 67th American Society of Hematology (ASH) Annual Meeting and Exposition; December 6-9, 2025; Orlando, FL, USA.

This combination has just been approved by the FDA

Phase III Clinical Trials With BsAbs in Earlier Lines of Therapy

Clinical Trial	Bispecific Antibodies	Control Arm	N	Key Criteria
MajesTEC-3	Teclistamab-Dara	DPd or DVd	587	Patients exposed to PI and IMiD after 1-3 PL Patients refractory to anti-CD38 not allowed
MagnetisMM-5	Elranatamab	DPd	450	Patients exposed to PI and IMiD after at least 1 PL Patients exposed to anti-CD38 and anti-BCMA allowed, but after a washout period of at least 6 months
MajesTEC-9	Teclistamab	Kd or PVd	590	Patients exposed to anti-CD38 and Len after 1-3 PL
MagnetisMM-32	Elranatamab	Kd, PVd, or EloPd	492	Patients exposed to anti-CD38 and Len after 1-4 PL
MonumenTAL-3	Teclistamab-Talquetamab Talquetamab-Pom	EloPd or PVd	795	Patients exposed to anti-CD38 and Len after 1-4 PL
MonumenTAL-1	Talquetamab-Dara Talquetamab-Pom-Dara	DaraPd	810	Patients exposed to PI and IMiD after at least 1 PL Patients after 1 PL must be Len refractory
LinkerMM-3	Linvoseltamab	EloPd	300	Patients exposed to PI and IMiD after 1-4 PL
CERVINO	Etentamig	EloPd, SVd, or Kd	380	Patients triple-class exposed after at least 2 PL

These trials are recruiting, and some have already finalized their recruitment

Information on the trials is from clinicaltrials.gov.

MajesTEC-9: Tec Monotherapy vs PVd or Kd in Patients With RRMM - Press Release

TECVAYLI® monotherapy demonstrates superior progression-free and overall survival versus standard of care as early as first relapse in patients with multiple myeloma predominantly refractory to anti-CD38 therapy and lenalidomide

TECVAYLI® alone reduced risk of disease progression or death by 71% in a high unmet need population

MajesTEC-9 is the second positive Phase 3 study to support TECVAYLI® regimens as a potential new standard of care as early as first relapse

- HR for PFS: 0.29
- HR for OS: 0.60
- Safety profile of Tec was clinically manageable using established protocols and consistent with its known safety profile, with no new safety concerns identified

MonumenTAL-3	Teclistamab-Talquetamab Talquetamab-Pom	EloPd or PVd	795	Patients exposed to anti-CD38 and Len after 1-4 PL

This study will report data soon

Treatment Landscape in Multiple Myeloma

First line

ASCT eligible

Anti-CD38 + PI + IMiD + Dex

ASCT

Len/Dara-Len

ASCT ineligible

Dara-Len-Dex

Dara-VMP/RVd

Anti-CD38 + PI + IMiD + Dex

Second line

Based on sensitivity/refractoriness to daratumumab and lenalidomide

Anti-CD38 + carfilzomib-Dex

Anti-CD38 + pomalidomide-Dex

Pomalidomide-bortezomib-Dex

Selinexor-bortezomib-Dex

Carfilzomib-Dex

Cilta-cel

Belantamab-Vd (DREAMM-7)

Belantamab-Pd (DREAMM-8)

Teclistamab-daratumumab

Teclistamab s/a

Elranatamab s/a

Tal-Dara-Pom and Tal-Dara

Tal-Tec

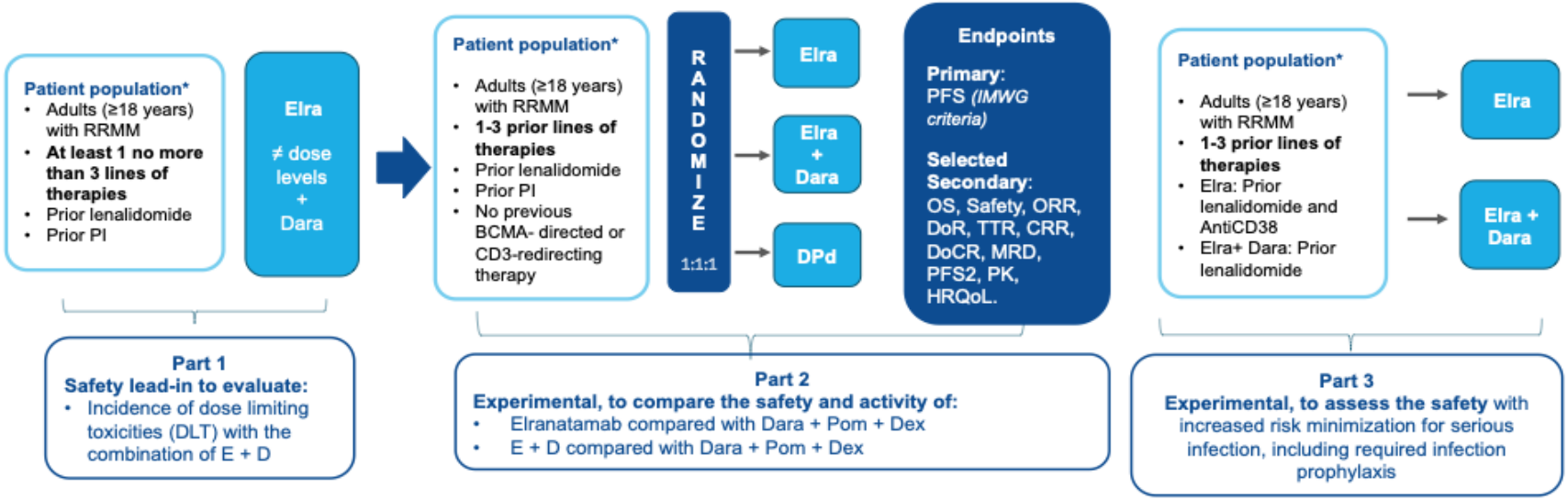
Mateos MV, personal communication; Dimopoulos MA, et al. *Ann Oncol*. 2021;32:309-322.

MagnetisMM-5

RRMM

Phase III trial (NCT05020236) – *Recruiting*

Open-label, 3-arm, multicenter, randomized trial to evaluate **efficacy** and **safety** of **elranatamab monotherapy** and **elranatamab + daratumumab** vs. *daratumumab + pomalidomide + dexamethasone* in adults patients with **RRMM**



*RRMM: Relapsed/refractory multiple mieloma; PI: proteasome inhibitor; E: elranatamab; D: daratumumab; P: pomalidomide; d: dexamethasone; PFS: progression-free survival; OS: overall survival; ORR: overall response ratio; DoR: Duration of Response; TTR: time to response; CRR: complete response ratio; DOCR: duration of complete response; MRD: minimal residual disease; PK: pharmacokinetics; HRQoL: health-related quality of life.; RP3D; Recommended Phase 3 dose. *based on main eligibility criteria*

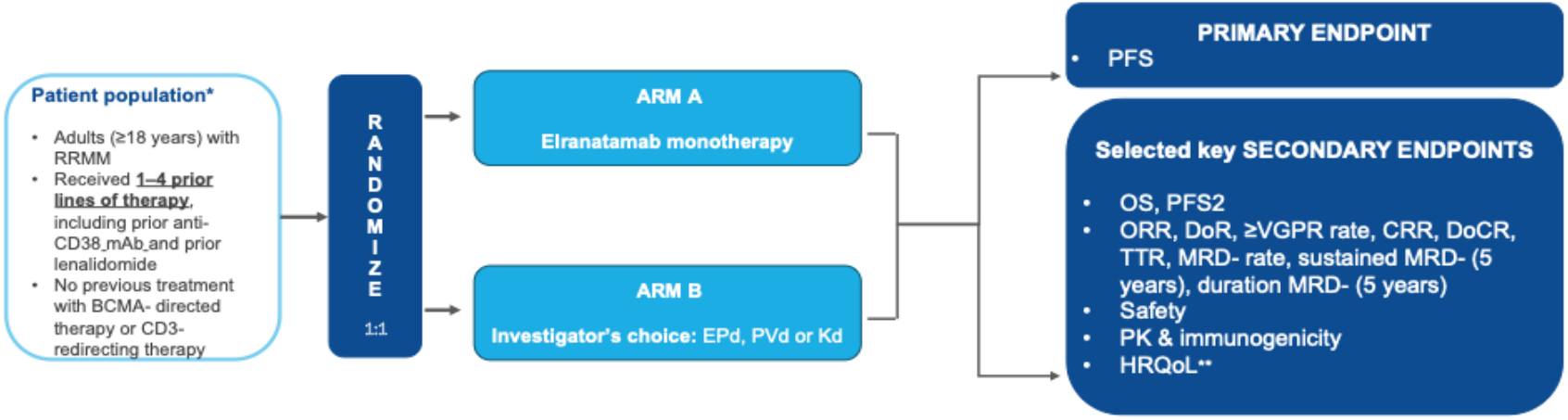
Created from REEC (REEC - MagnetisMM-5) and Clinicaltrials.gov data (NCT05020236: NCT05020236 | ClinicalTrials.gov) Last access: Mar 2026.

MagnetisMM-32

RRMM

Phase III trial (NCT06152575) – *Recruiting*

Open-label, multicenter, randomized trial to evaluate **efficacy** and **safety** of **elranatamab monotherapy** vs. *elotuzumab + pomalidomide + dexamethasone or pomalidomide + bortezomib + dexamethasone or carfilzomib + dexamethasone* in adults patients with **RRMM**



***By EORTC QLQ – Myeloma 20 and EORTC QLQ – Core 30*

*RRMM: relapsed/refractory multiple myeloma; PFS: progression free survival; OS: overall survival; ORR: objective response ratio; DoR: duration of response; VGPR: very Good partial response; CRR: complete response ratio;DoCR: duration of CR; TTR: time to response; MRD-: minimal residual disease negativity; PK: pharmacokinetic; HRQoL: health related quality of life. *based on main eligibility criteria*

Created from REEC (REEC - MagnetisMM-32) Clinicaltrials.gov data (NCT06152575: NCT06152575 | MagnetisMM-32 | ClinicalTrials.gov) Last access: Feb 2026.

Treatment Landscape in Multiple Myeloma

First line

ASCT eligible

Anti-CD38 + PI + IMiD + Dex

ASCT

Len/Dara-Len

ASCT ineligible

Dara-Len-Dex

Dara-VMP/RVd

Anti-CD38 + PI + IMiD + Dex

Second line

Based on sensitivity/refractoriness to daratumumab and lenalidomide

Anti-CD38 + carfilzomib-Dex

Anti-CD38 + pomalidomide-Dex

Pomalidomide-bortezomib-Dex

Selinexor-bortezomib-Dex

Carfilzomib-Dex

Iberdomide-Dara-Dex

Mezigdomide-Kd

Cilta-cel

Belantamab-Vd (DREAMM-7)

Belantamab-Pd (DREAMM-8)

Teclistamab-daratumumab

Teclistamab s/a

Elranatamab s/a

Tal-Dara-Pom and Tal-Dara

Tal-Tec

What about CELMoDs in early lines of therapy?

Mateos MV, personal communication; Dimopoulos MA, et al. *Ann Oncol*. 2021;32:309-322.

EXCALIBER-RRMM: Phase III Study

EXCALIBER 1-2 priors RRMM

Phase III, 2-stage seamless adaptive inferential design

Objective: Evaluate the efficacy and safety of treatment with iberdomide, daratumumab and dexamethasone (IberDd) vs daratumumab, bortezomib and dexamethasone (DVd) in patients with relapsed or refractory multiple myeloma

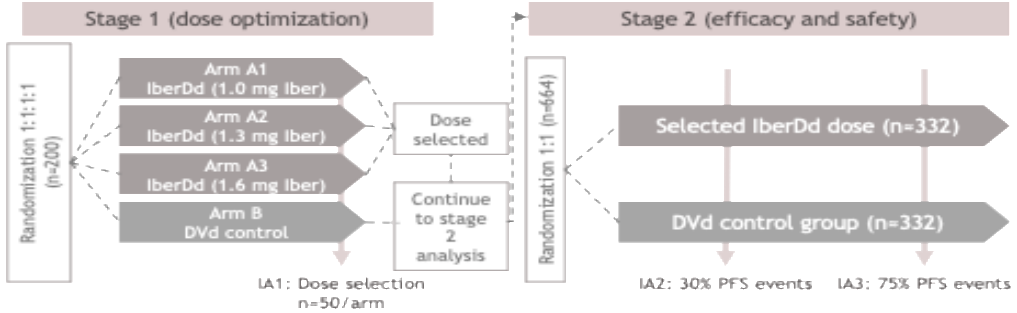
RRMM with 1-2 priors (N=864)

Inclusion Criteria

- Adult patients who received 1 to 2 prior lines of anti-myeloma therapy and progressive disease

Exclusion Criteria

- Patients who are refractory to bortezomib or an anti-CD38 therapy
- Patients with prior anti-CD38 exposure. Some exceptions apply in stage 2



Primary Endpoint: PFS
Secondary Endpoints: OS, MRD negativity rate, ORR, TTR, DoR, TTP, TTNT, PFS2, Safety, HR-QoL and PK

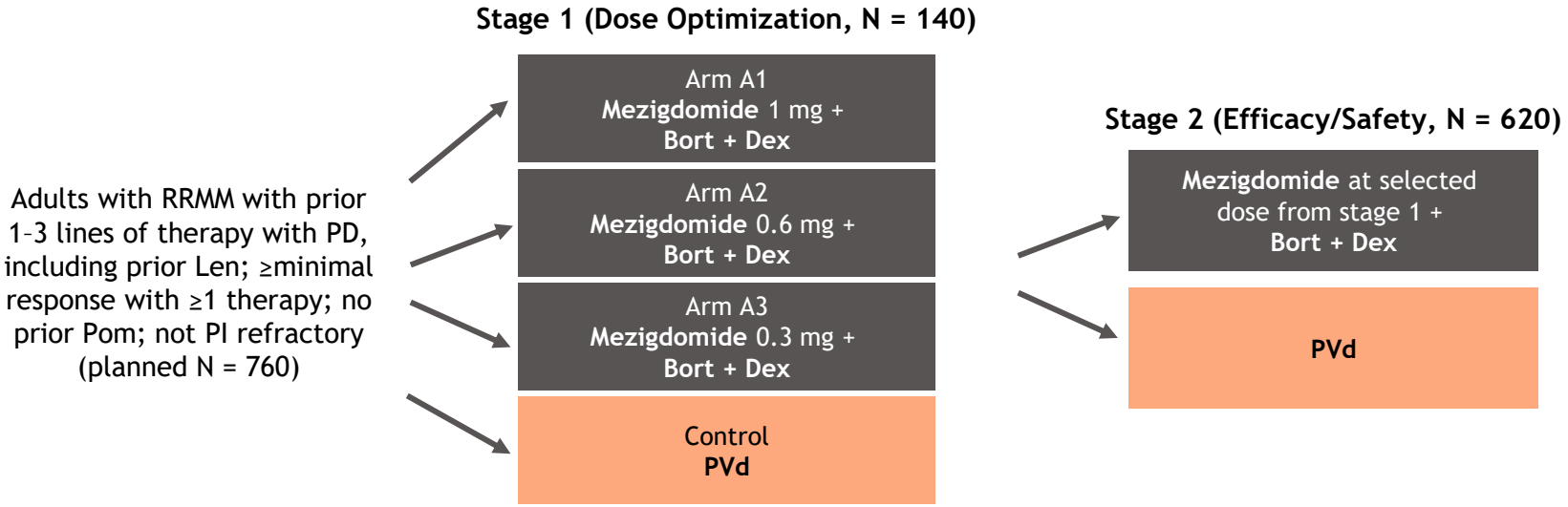
Target PFS HR 0.75, 458 PFS events, 84% power	
Analysis	HR Boundary
Interim 75% PFS	≤ 0.777
Final Analysis	≤ 0.829

Bristol Myers Squibb announces phase III EXCALIBER-RRMM study evaluating iberdomide in combination with standard therapies demonstrated a significant improvement in minimal residual disease negativity rates in relapsed or refractory multiple myeloma

D, Darzalex (daratumumab); d, dexamethasone; DOR, duration of response; iber, iberdomide; HR-QOL, health-related quality of life; IA, interim analysis; MRD, minimal residual disease; ORR, overall response rate; OS, overall survival; PFS, progression-free survival; TTNT, time to next treatment; TTP, time to progression; TTR, time to response; V, Velcade (bortezomib)

SUCCESSOR-1: Mezigdomide + Bortezomib + Dex vs PVd for RRMM (1-3 LOT)

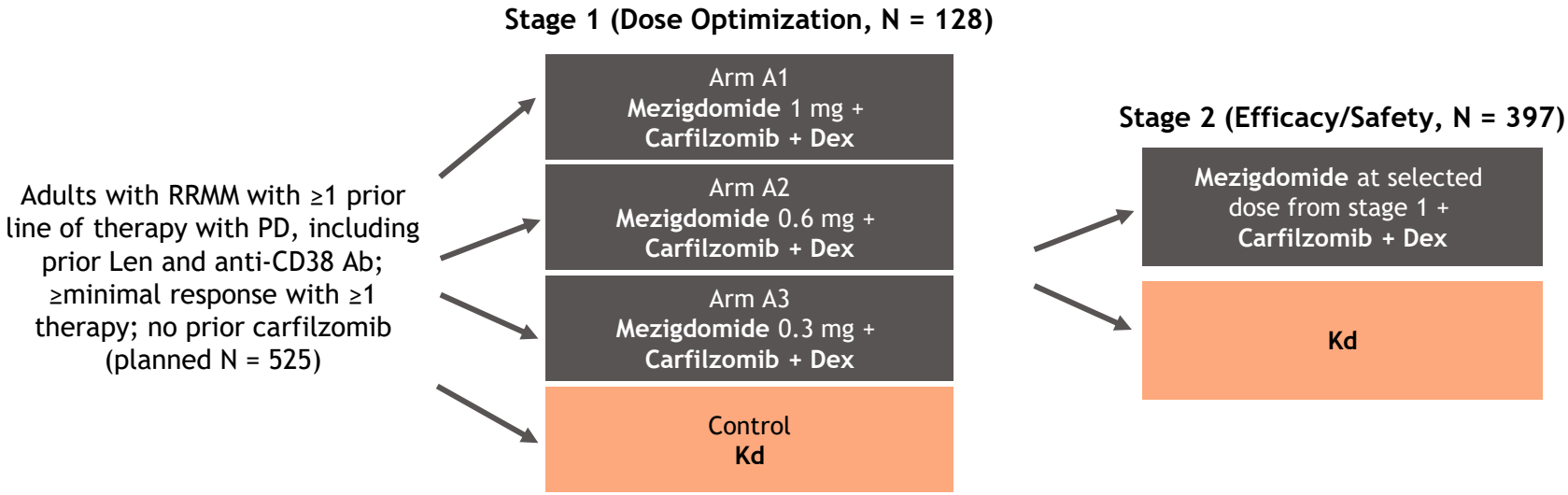
- 2-stage, randomized phase III trial



- Primary endpoints: PFS
- Secondary endpoints: OS, ORR, TTR, DOR, TTP, TTNT PFS2, MRD-negative rate, safety, HRQOL, biomarker analysis, PK

SUCCESSOR-2: Mezigdomide + Carfilzomib + Dex vs Kd for RRMM (≥1 LOT)

- 2-stage, randomized phase III trial



- Primary endpoints: PFS
- Secondary endpoints: OS, ORR, VGPRR, CR, MRD-negative rate, TTR, DOR, TTP, TTNT, PFS2, safety, HRQOL

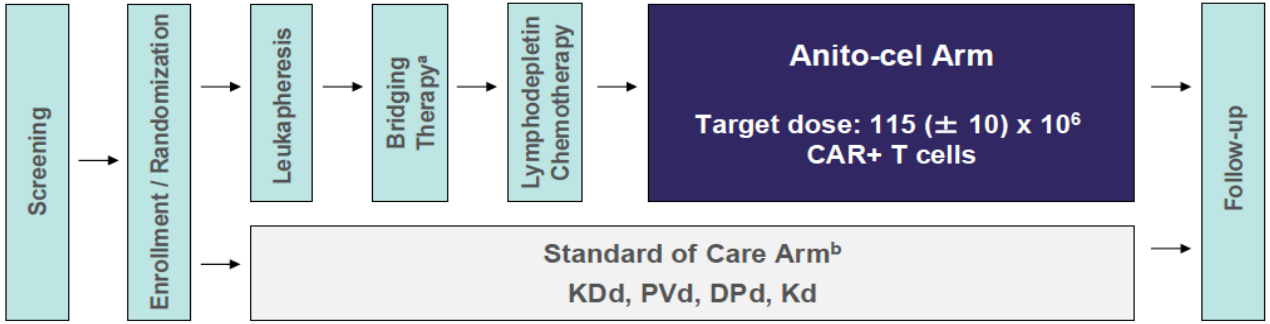
More Innovation in Early Lines of Therapy in the Future?

iMMagine-3: Phase III Clinical Trial

iMMagine-3 Design, Global Phase 3 Study – Now Enrolling

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

Anito-cel is being co-developed by Arcellx and Kite, and is being manufactured by Kite for iMMagine-3



Study Design

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

Study Endpoints

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

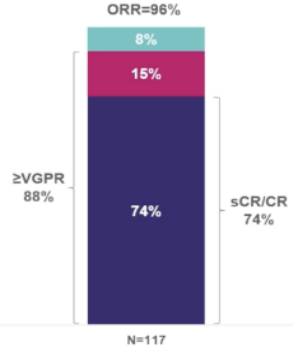
[a] *Optional Bridging therapy will be the SOC regimen selected prior to randomization*
[b] *Cycles will continue until unacceptable toxicity, progression as per IMWG criteria, or patient withdrawal of consent*

iMMagine-1: Phase II Study of Anito-Cel – Preliminary Results (n = 129, median FU 15.9 months)[1]

Key inclusion: RRMM TCE 3 or more PL
Median age 65y (38–78). Median number of PL 4 (3–18), EMD 16%
TCR 86%, Bridging therapy 71%

Target dose: 115 x 10^6 CAR+ T cell
129 pt lymphoapheresis > 118 pt lymphodepletion > total dosed 117 pts
Safety evaluable: 98 pts // Efficacy evaluable 86 pts

Overall response rate
Efficacy evaluable (n=117)



PFS and OS
Efficacy evaluable (n=117)

N=117	PFS Rate (%) (95% CI)	OS Rate (%) (95% CI)
6-Month	93.1 (86.7, 96.5)	95.7 (90.0, 98.2)
12-Month	82.1 (73.6, 88.1)	94.0 (87.8, 97.1)
18-Month	67.4 (55.4, 76.8)	88.0 (78.8, 93.4)
24-Month	61.7 (48.0, 72.8)	83.0 (70.7, 90.5)

Key safety data
Safety evaluable (n=98)

Key AEs	All grade	G3-4
CRS	95% (G1 68%, G2 16%)	1 grade 5
Median time to onset 4 days		
ICANS	9% (3% G1/4% G2)	1% grade 3
Infections	56%	9%
Neutropenia	71%	70%

3 deaths: 1 CRS, 1 retroperitoneal haemorraghe, 1 fungal infection. No new deaths since last cut-off

No delayed or non-ICANS neurotoxicities
No incidence of Parkinsonism, no cranial nerve palsy, no Guillen-Barré Sd

MRD Negativity at 10^{-5} Sensitivity Level	
Overall MRD negativity, % (n/N)	95% (91/96)
Median time to MRD negativity, months (min – max)	1.0 (0.9 – 6.4)
MRD negativity sustained for ≥ 6 months, % (n/N)	83% (54/65)
MRD Negativity at 10^{-6} Sensitivity Level	
Overall MRD negativity, % (n/N)	78% (68/87)

AEs, adverse events; BT, bridging therapy; CI, confidence interval; CR, complete response; CRS, cytokine release syndrome; EMD, extramedullary disease; FUP, follow-up; IMD, immunomodulatory drug; MRD, minimal residual disease; OS, overall survival; PD, progressive disease; PFS, progression-free survival; PL, prior lines; pt, patient; RRMM, relapsed or refractory multiple myeloma; SCR, stringent complete response; TCE, t-cell engager; TCR, t-cell receptor.

1. Patel K, et al. Poster presented at ASH 2025.

QUINTESSENTIAL-2: Phase III Clinical Trial

The QUINTESSENTIAL-2 study (NCT06615479) is investigating the efficacy and safety of arlo-cel (a GPRC5D-directed CAR T-cell therapy requiring only 1 infusion) vs standard of care in adults with RRMM exposed to lenalidomide

STUDY SNAPSHOT

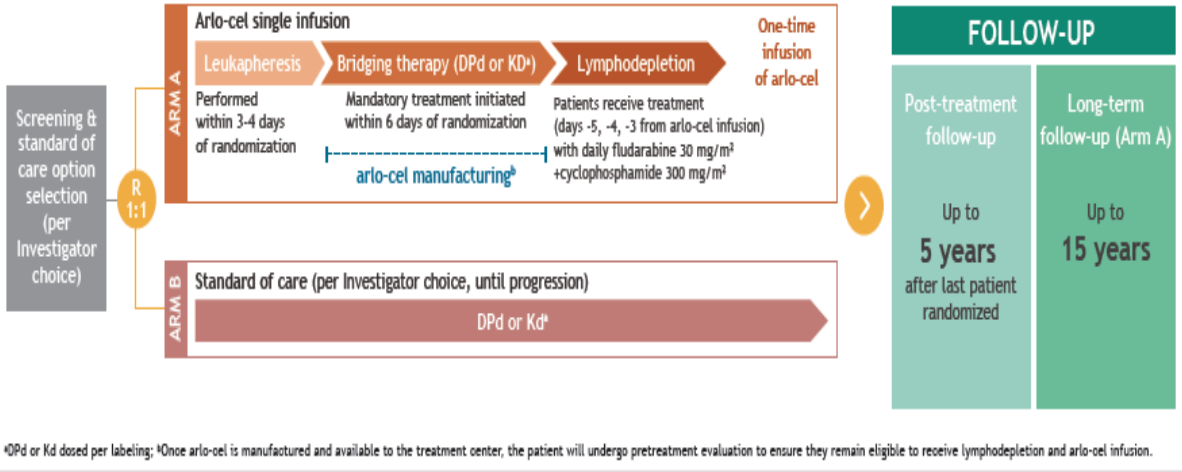
Phase 3
Ongoing trial

RRMM exposed to lenalidomide
N ~ 440 (planned)

Randomized, open label

Multicenter
~125 sites in 31 countries

Figure 1. Study design overview



[a]DPd or Kd dosed per labeling; [b]Once arlo-cel is manufactured and available to the treatment center, the patient will undergo pretreatment evaluation to ensure they remain eligible to receive lymphodepletion and arlo-cel infusion.

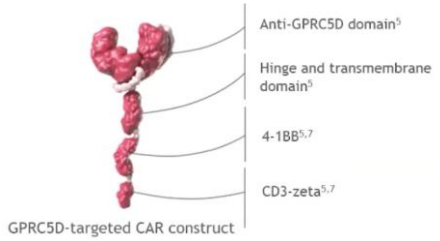
arlo-cel, arlocabtagene autoleucel; DPd, daratumumab, pomalidomide, and dexamethasone; GPRC5D, G protein-coupled receptor class C group 5 member D; Kd, carfilzomib and dexamethasone; R, randomization; RRMM, relapsed and refractory multiple myeloma.

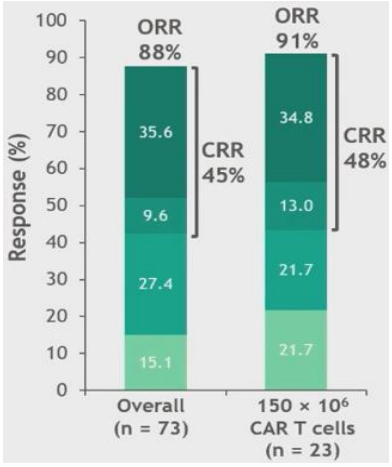
BMS-986393 (CC-95266), a GPRC5D CAR T for RRMM: Updated Results From a Phase I Study

84 patients with RRMM with ≥3 PL including PI, IMiD, and anti-CD38 antibody, and progression within <12 months of last regimen

Median 5PL; 74% were TCR. 44% EMD, 40% HRCA. 26 patients had received 150 × 10^6 CAR Ts

Prior BCMA allowed → 39 patients (46%) prior exposed to BCMA-TT and 30 BCMA CAR T



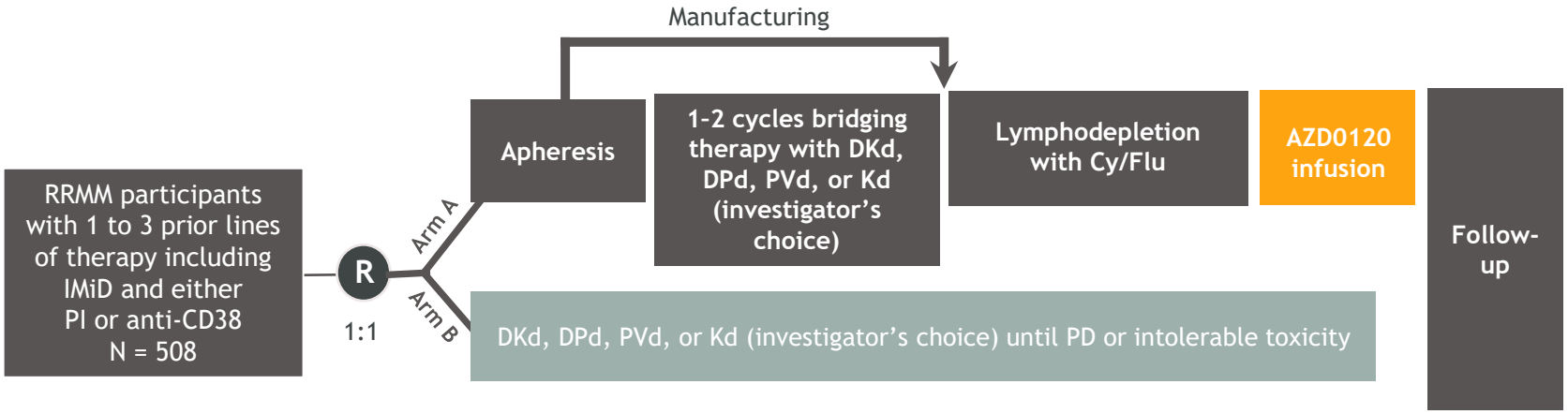


ORR in subgroups of interest (all dose levels)

Disease characteristic, % (n/N)	Present	Absent
Prior BCMA treatment	78% 25/32	95% 39/41
Extramedullary disease	84% 26/31	91% 38/42
High-risk cytogenetics[b]	83% 24/29	91% 40/44
Triple-class refractory	88% 50/57	88% 14/16

Promising efficacy and safety data even in patients previously exposed to BCMA-TT

DURGA-4: Study Design



Stratification

- Investigator's choice for the control arm (DKd vs PVd/DPd/Kd)
- High-risk status (R-ISS III or per IMS-IMWG Consensus Genomic Staging vs all others)
- Number of prior lines of therapy (1 vs 2 or 3)

Dual Primary Endpoints
PFS MRD-negative CR rate at 9 months
Key Secondary Endpoints
OS, CR/sCR rate, ORR

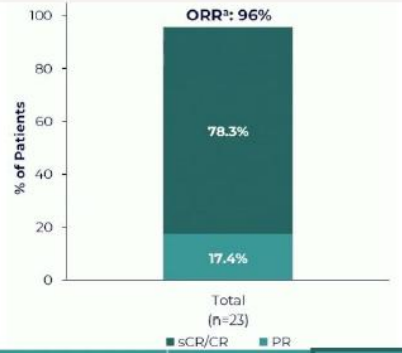
DURGA-4

DURGA-1: AZD0120 – BCMA-CD19 Dual CAR T in Patients With TCE RRMM

Key inclusion: ≥3PL, triple-class-exposed.
Median age: 63 y (44-78); Triple-class refractory 69%; 27% received BT
6 patients had prior BCMA-therapy: 5 prior CAR (median time since last CAR T 2.6 years) and 1 prior BsAbs (Teclistamab), median time of 0.6 years
N=32 enrolled, n=26 LD chemo, n=26 infused [n=12 at DL1 (1x10e5 cells/kg) and n=14 at DL2 (3x10e5cells/kg)]

ORR (n=23)

N=17 MRD evaluable > MRDneg in 94% (NGS)



	Total (n=23)	BCMA CAR T Exposed (n=5)
ORR	96%	100%
sCR/CR	78%	80%
Follow-up, median (range), months	3.9 (0.9–19.7)	3.9 (3.0–4.0)

Overall Safety

n=26

CRS	DL1 (n=12)	DL2 (n=14)	Total (n=26)
CRS, overall	**9 (75%)**	**7 (50%)**	**16 (62%)**
Grade 1	9 (75%)	6 (43%)	15 (58%)
Grade 2	0	1 (7%)	1 (4%)
Grade 3+	0	0	0
Onset time, median (range), days	9 (2–11)	9 (8–10)	9 (2–11)*
Duration, median (range), days	1 (1–4)	2 (1-2)	1.5 (1–4)
CRS management			
Tocilizumab	7 (58%)	5 (36%)	12 (46%)
Dexamethasone	1 (8%)	2 (14%)	3 (12%)
Anakinra	0	1 (7%)	1 (4%)

- No grade 3+ CRS reported
- *CRS onset on day 8–11 for 15 of 16 patients

ICANS	DL1 (n=12)	DL2 (n=14)
ICANS, overall	**0**	**1 (7%)**
Grade 1	0	1 (7%)
Grade 2	0	0
Grade 3+	0	0
Onset time, days	NA	10
Duration, day	NA	1

- **No delayed neurotoxicities, including no Parkinsonism, no cranial nerve palsies, and no Guillain-Barré syndrome reported**
- **No IEC-associated colitis reported**
- **Only one grade 1 ICANS event**
- **One patient with IEC-HS (DL1, grade 2); resolved within 7 days**

- **Neutropenia** grade 3–4, overall 81%, 83% at DL1 and 79% at DL2
- **Infections** 8% grade 3–4 overall, and 8% at DL1 and 7% at DL2
- **No DLTs**
- **Similar toxicity profiles between DL1 and DL2**

BCMA, b-cell maturation antigen; BT, bridging therapy; CAR, chimeric antigen receptor; CR, complete response; CRS, cytokine release syndrome; DLT, dose-limiting toxicity; EMD, extramedullary disease; FUP, follow-up; ICANS, immune effector cell–associated neurotoxicity syndrome; IEC-HS, immune effector cell-associated hemophagocytic syndrome; MRD, minimal residual disease; ORR, overall response rate; PL, three prior lines; PR, partial response; RRMM, relapsed/refractory multiple myeloma; sCR, stringent complete response; SPL, single prior line.

1. Richard S, et al. Oral presentation at ASH 2025. Presentation no. 704.

Treatment Landscape in Multiple Myeloma: First Take-Home Message

First line

ASCT eligible

Anti-CD38 + PI + IMiD + Dex

ASCT

Len/Dara-Len

ASCT ineligible

Anti-CD38 + PI + IMiD + Dex

Dara-Len-Dex

Dara-VMP/RVd

Second line

BCMA is a novel target that may help address the unmet need at first relapse[1]

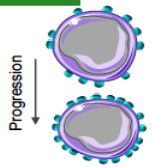
BCMA presents a clinically meaningful and well-validated target in MM

Cell specificity

- Expressed almost **exclusively on plasma cells** and overexpressed on malignant plasma cells in MM[1,2]
- Minimal expression on other essential cells, **increasing target specificity**[1,3,4]

Expression level

- High expression across most MM cases, correlating with disease progression[2,4]
- Reliable marker for targeting malignant cells[4]

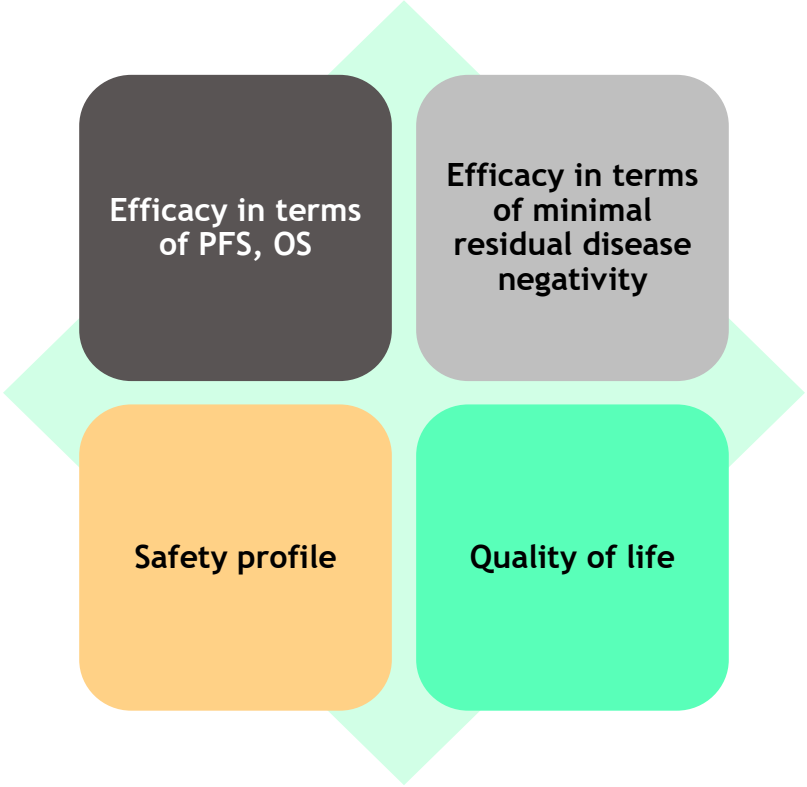


Mateos MV, personal communication; Dimopoulos MA, et al. *Ann Oncol*. 2021;32:309-322.

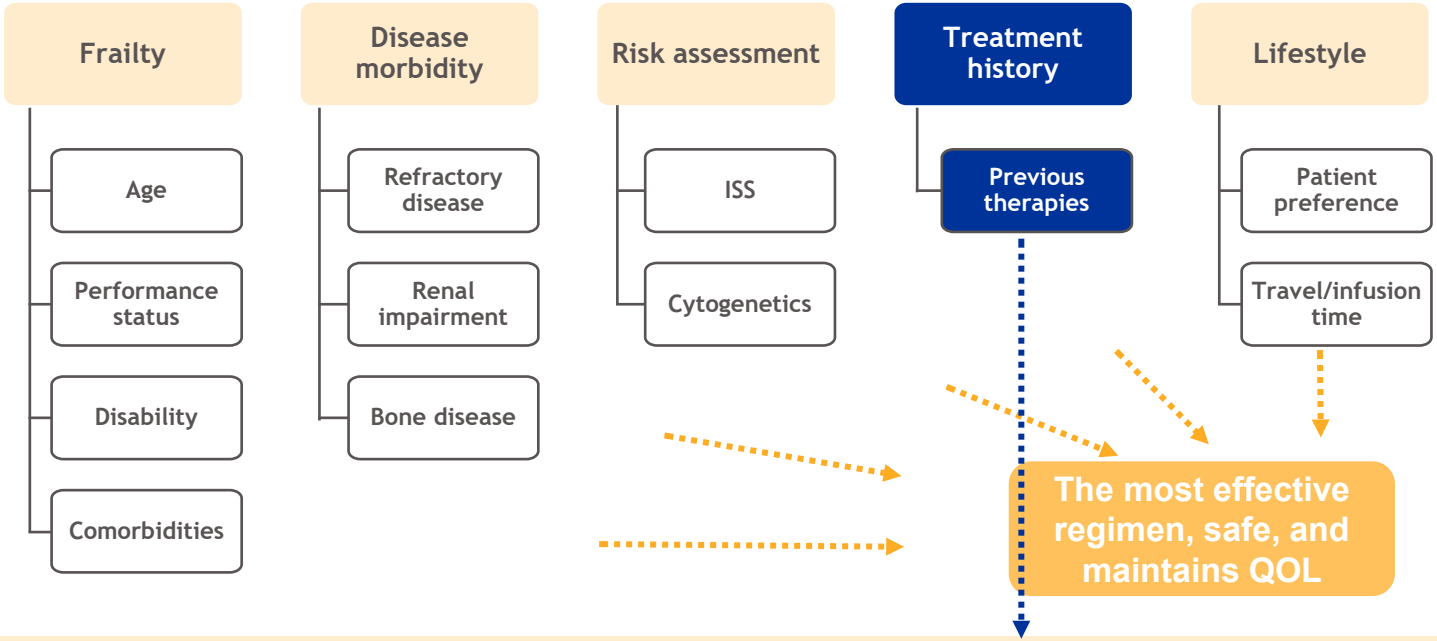
What Are the Key Administration Considerations for Anti-BCMA Therapies?

Aspect	ADC (belantamab)	CAR T (cilta-cel)	BCMA BsAb
Indication	RRMM after ≥1 prior LOT (PI + IMiD exposed)	RRMM after ≥1 prior LOT (PI + IMiD; often lenalidomide-refractory)	RRMM after ≥1 prior LOT (PI + IMiD)
Efficacy	Improved outcomes vs DVd/PVd	Marked efficacy benefit vs standard of care	Clinically meaningful efficacy benefit vs standard of care with the best HR so far reported
Key safety	Ocular toxicity, thrombocytopenia, infections	CRS, ICANS, serious infections, delayed neurotoxicity	Infections requiring prophylaxis and IVIG
Eligibility	Few formal contraindications	Required normal function of vital organs	Few formal contraindications
Treatment burden	Regular ophthalmologic assessments	Lymphodepletion and close post-infusion monitoring	Clinical monitoring focused on infectious risk
Administration	Intravenous, short infusion time	Single infusion at certified centers	Subcutaneous; monthly admin in the f/u for most of them

What Is Relevant for Treatment Decision-Making?



Disease and Patient-Based Factors Influencing Treatment Decision-Making in the Relapse Setting



Many patients might be equally eligible for CAR T-cell therapy, antibody-drug conjugates, or bispecific antibodies. In these situations, patient preference—based on toxicity concerns, family and personal circumstances, and the patient's geographic location—will play an important role in treatment selection.

Treatment Landscape in Multiple Myeloma

First line

ASCT eligible

Anti-CD38 + PI + IMiD + Dex

ASCT

Len/Dara-Len

ASCT ineligible

Dara-Len-Dex

Dara-VMP/RVd

Anti-CD38 + PI + IMiD + Dex

Second line

Based on sensitivity/refractoriness to daratumumab and lenalidomide

Anti-CD38 + carfilzomib-Dex

Anti-CD38 + pomalidomide-Dex

Pomalidomide-bortezomib-Dex

Selinexor-bortezomib-Dex

Carfilzomib-Dex

Belantamab-Vd (DREAMM-7)

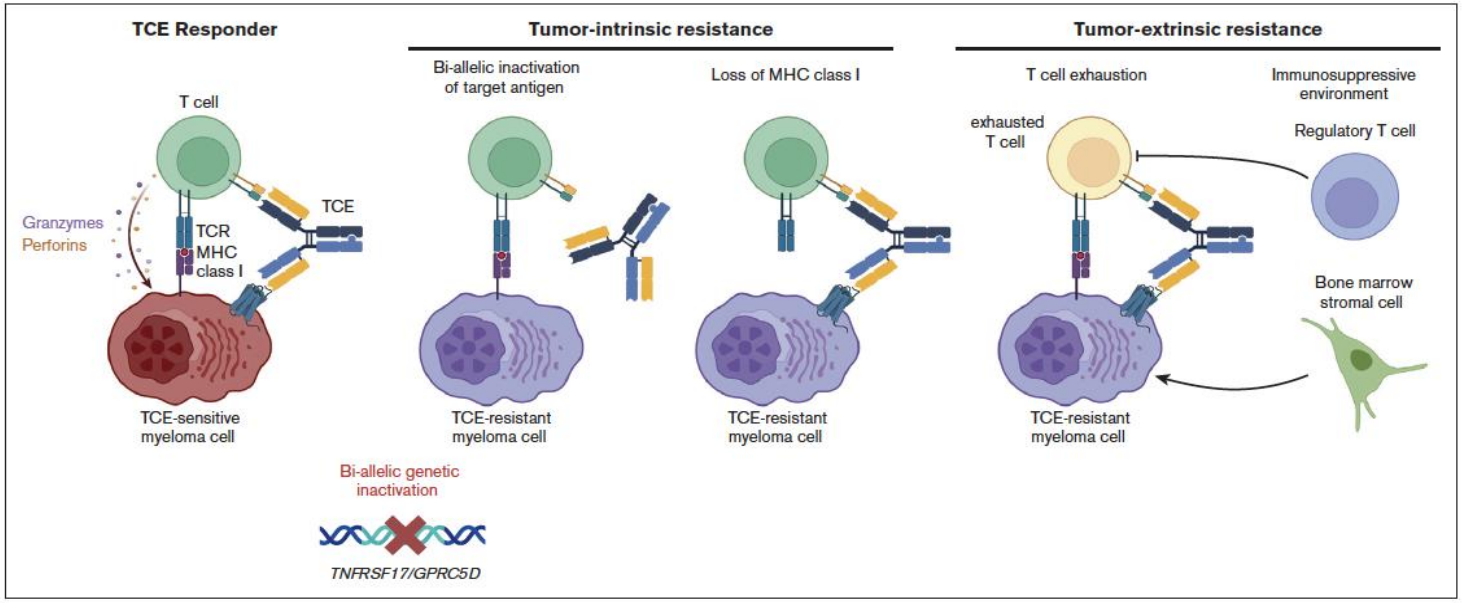
Belantamab-Pd (DREAMM-8)

Teclistamab-daratumumab

- **BCMA as first option at the first relapse**
- **Elderly patients treated with continuous therapy with DRd → Belamaf-based combos**
- **Patients naive or sensitive to anti-CD38 → Tec-Dara is an option because of the efficacy**
- **We also have to incorporate toxicity**
  - **High risk of infections → Bela-based combinations**
  - **Severe ocular problems → Tec-Dara if possible**

Mateos MV, personal communication; Dimopoulos MA, et al. *Ann Oncol*. 2021;32:309-322.

Mechanisms of Resistance and Clinical Implications for BCMA-TT Are Crucial in Terms of Sequencing



After the use of BCMA-targeted therapy at first relapse, would it be possible to sequence BCMA-TT in subsequent relapses?

MHC, major histocompatibility complex; TCE, trichloroethylene; TCR, talquetamab crossover regimen.

Figure adapted from Letouzé E, et al. *Blood Adv*. 2024;8:2952-2959.

Mechanisms of Resistance and Clinical Implications

Table 1. Clinical impact of resistance mechanisms

	Alteration	Disease stage	Frequency	Detection technique*	Clinical impact	R
BCMA	16p loss (*TNFRSF17*)	Pretreatment screening	3%-4% of TCE-naive MM	WGS	May facilitate biallelic target inactivation by second hit	
	TNFRSF17 mutation	Pretreatment screening	1.1% (somatic) and 0.7% (germ line) of TCE-naive MM	WGS	May facilitate biallelic target inactivation by second hit	
	Abundance of exhausted T-cell clones	Pretreatment screening	TBD	scRNA/VDJ-seq	Predicts response failure to BCMA-targeting TCE	
BCMA	*TNFRSF17* homozygous deletion	At relapse	1/14 relapses after BCMA-targeting TCE	WGS	Precludes response to other BCMA-targeting therapy	
	TNFRSF17 p.Arg27Pro	At relapse	1/14 relapses after BCMA-targeting TCE	WGS	Confers resistance to teclistamab and elranatanab	
	TNFRSF17 p.Pro34del	At relapse	3/14 relapses after BCMA-targeting TCE	WGS	Confers resistance to teclistamab and elranatanab	
	TNFRSF17 p.Ser30del	At relapse	2/14 relapses after BCMA-targeting TCE	WGS	Confers resistance to teclistamab	

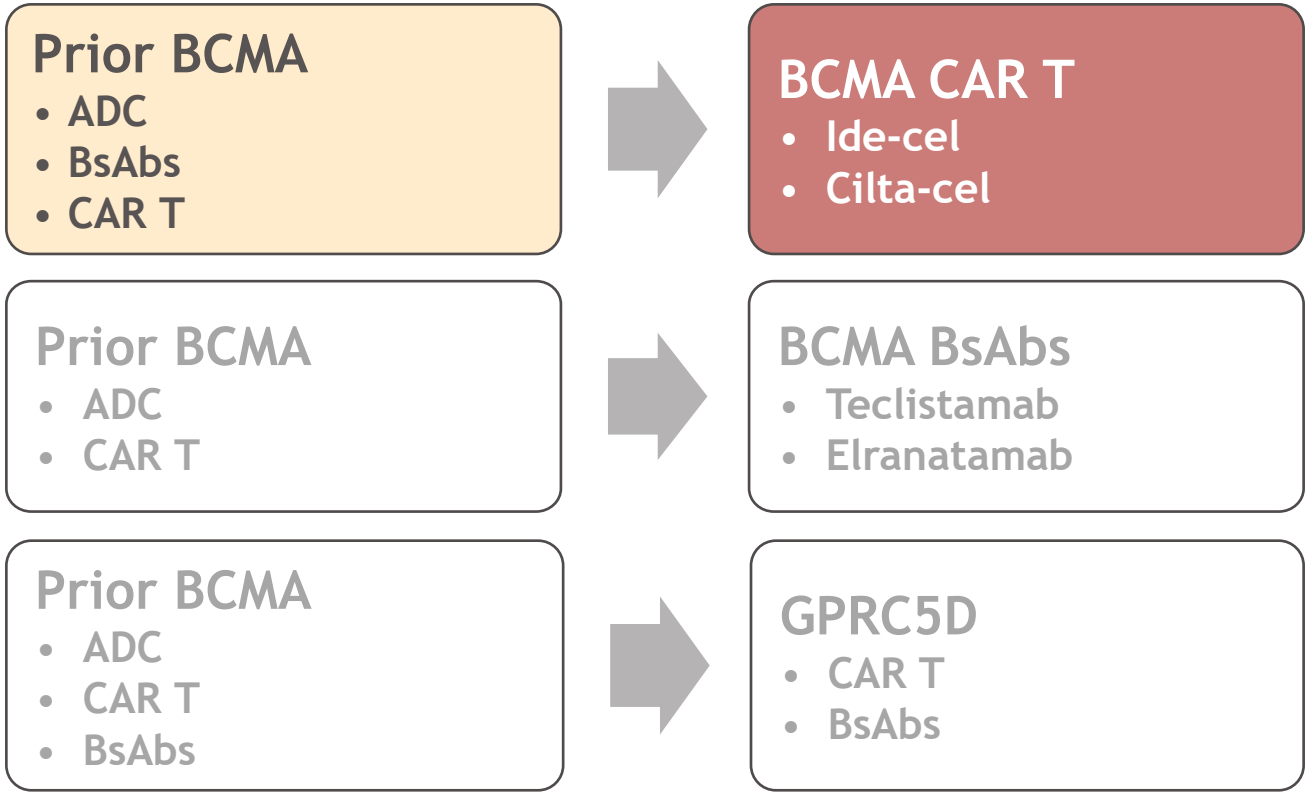
BCMA antigen escape via biallelic TNFRSF17 loss has been observed at relapse after BCMA-directed therapies in up to 14%-15% of the patients

T-cell exhaustion is another mechanism of resistance, applicable mainly to continuous treatment with bispecific antibodies

ATAC-seq, Assay for Transposase-Accessible Chromatin using sequencing; BCMA, B cell maturation antigen; MM, multiple myeloma; RNA-seq, RNA sequencing; TBD, to be determined; TCE, Trichloroethylene; WGS, whole-genome sequencing.

Letouzé E, et al. *Blood Adv*. 2024;8:2952-2959; Lee H, et al. *Nat Med*. 2023;29:2295-2306.

Would It Be Possible to Sequence Both Approaches?

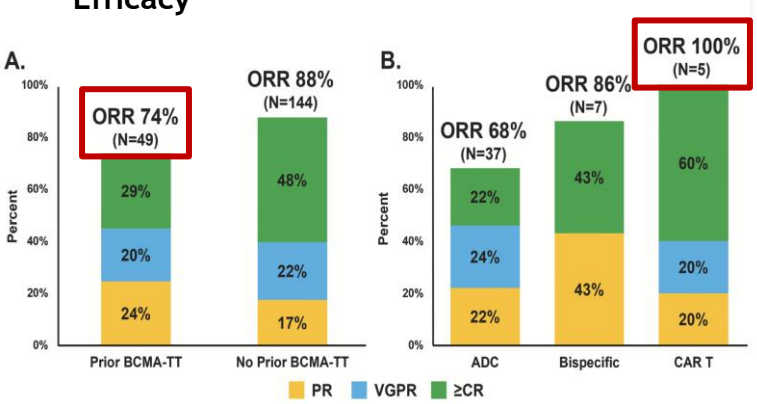


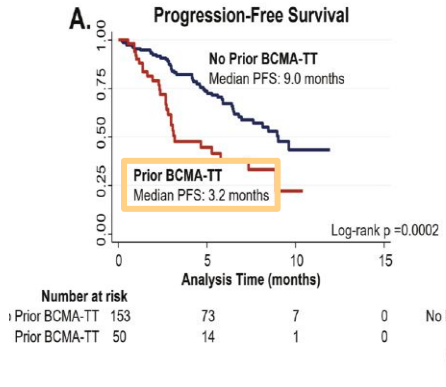
Ide-Cel for RRMM: Real-World Experience in Patients Previously Exposed to BCMA-Targeted Therapy

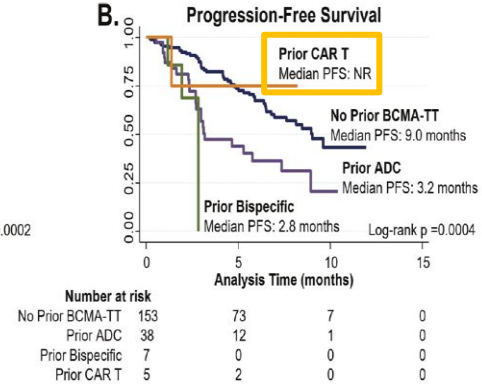
50 patients treated with Ide-cel after prior BCMA-TT (ADC 76%/BsAbs 14%/CAR T 10%); timing of prior BCMA TT: 40% <6 months

153 patients treated with Ide-cel and no prior BCMA-TT. Median follow-up duration of 4.5 months and 6 months, respectively

Efficacy







Ide-cel administered to patients previously exposed to BCMA-targeted therapy

The achievement of ≥PR after the BCMA-targeted therapy was predicted to reach CR

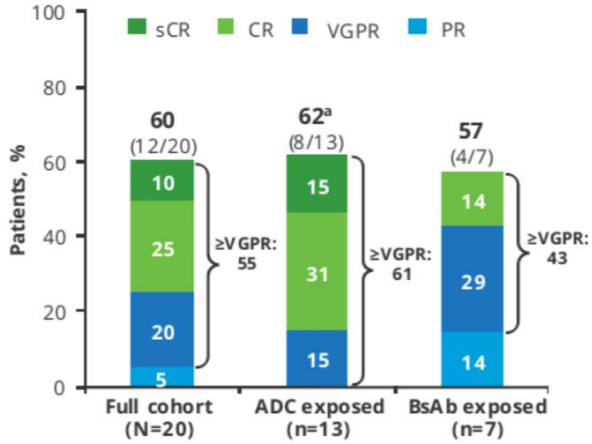
Shorter PFS in prior BCMA-TT than that observed in BCMA-naive patients

The shorter duration of prior BCMA-TT (<6 months) and the longer interval between BCMA-TT and Ide-cel predicted response

Ferreri C, et al. *Blood Cancer J.* 2023;13:117

Cilta-Cel for RRMM: CARTITUDE-2 Cohort C Patients Previously Exposed to BCMA-Targeted Therapy (n = 20)

FIGURE 2: Overall response rate



[a]Percentages may not sum appropriately due to rounding.
PR, partial response; sCR, stringent complete response.

ADC: 1 out of 4 patients who received anti-BCMA ADC as immediate pretreatment responded to Cilta-cel (vs 7 out of 9 patients who received intermediate treatments).[1,2]

BsAb: 2 out of 2 patients who received BsAb anti-BCMA as an immediate pretreatment against BCMA responded to Cilta-cel (vs 2 out of 5 patients who received intermediate treatments).[1,2]

TABLE: Median DOR, PFS, and OS

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)
OS	16.0 (8.3–NE)	21.0 (9.4–NE)	13.2 (0.6–NE)

NE, not estimable.

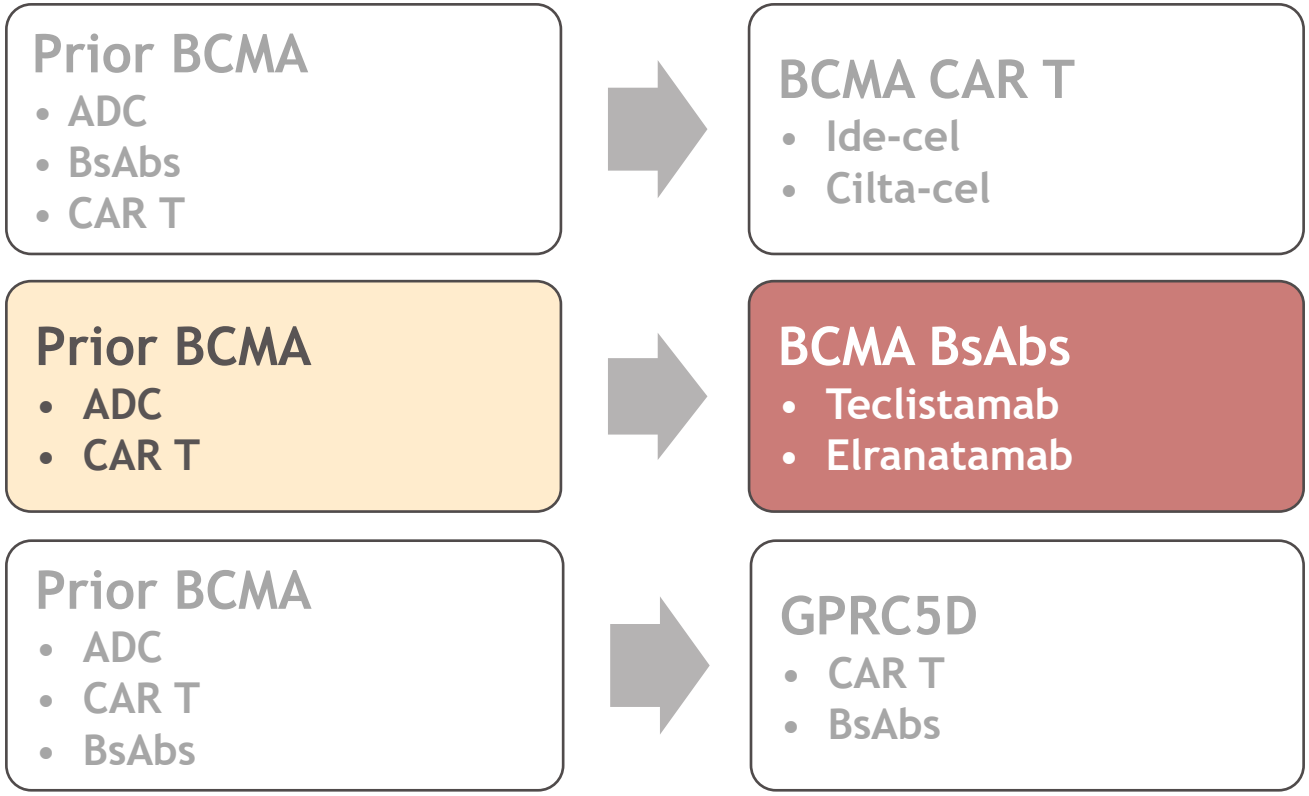
Cilta-cel induced favorable responses in highly pretreated patients with MM with prior exposure to anti-BCMAs[1,2]

The efficacy of Cilta-cel in patients enrolled in CARTITUDE-1 appears to be higher than in this cohort of patients, but the sample size is very small[1,2]

ADC, antibody-drug conjugate; BCMA, B-cell maturation antigen; Cilta-cel, ciltacabtagene autoleucel; MM, multiple myeloma.

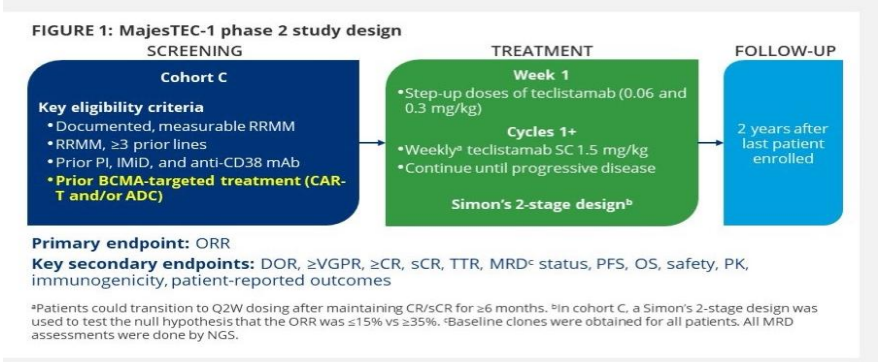
1. Cohen AD, et al. *Blood*. 2023;141:219-230; 2. Cohen AD, et al. IMS 2023. Abstract P-240.

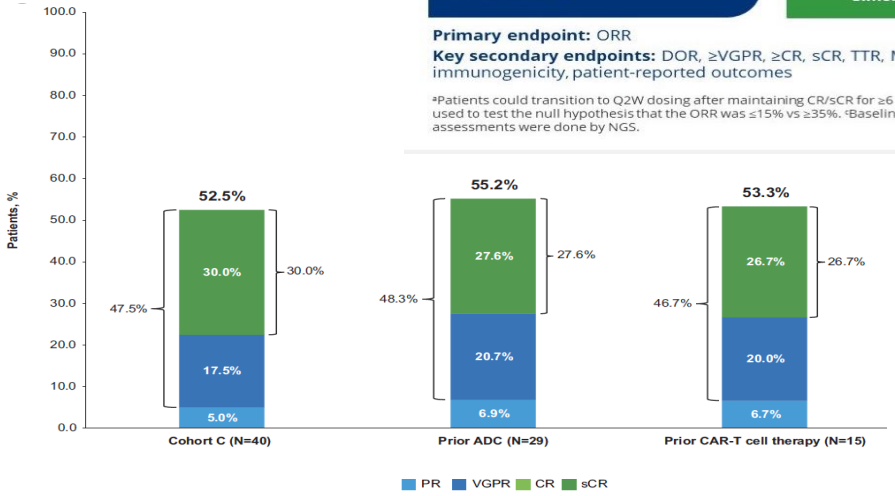
Would It Be Possible to Sequence Both Approaches?



Teclistamab: BCMA Plus CD3 Bispecific mAb – Update of MajesTEC-1 in Patients Previously Exposed to BCMA-Targeted Therapy

40 patients previously exposed to BCMA-TT/Median of 6 PL/72.5% ADC/37.5% CAR T





	Cohort C	Prior CAR T	Prior ADC
Median PFS, months	4.5	4.4	7.6
Median OS, months	15.5	14.9	16

Touzeau C, et al. *Blood*. 2024;144:2375-2388.

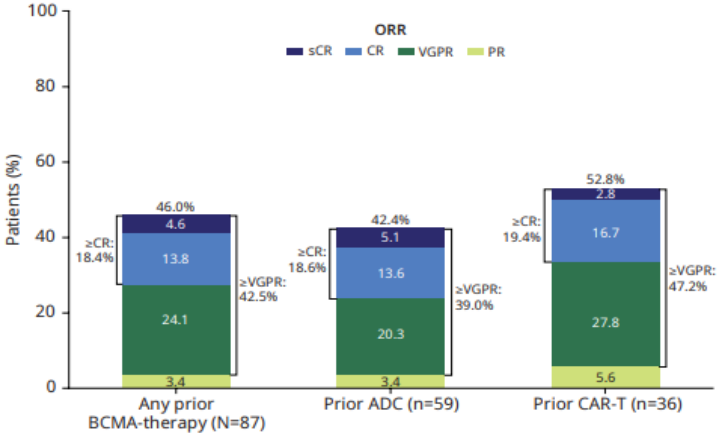
Elranatamab: Outcomes in RRMM With Prior BCMA-Directed Therapy

87 patients previously exposed to BCMA-TT from pooled analysis of MagnetisMM trials (at least 3 PL)

Median of 7 PL/68% ADC/41% CAR T/9% CAR + ADC

Median follow-up of 11.3 months (range, 0.3–32.3)

Primary endpoint: ORR



PFS

Median Survival, months (95% CI)	Prior BCMA (n = 87)	Prior ADC (n = 59)	Prior CAR T (n = 36)
PFS	5.5 (2.2–10.0)	3.9 (1.9–6.6)	10.0 (1.9–NE)
OS	12.1 (7.5–NE)	12.1 (6.4–NE)	12.1 (6.5–NE)

Manier S, et al. *HemaSphere*. 2023;7(suppl):e26808c7.

Elranatamab: Outcomes in RRMM With Prior BCMA-Directed Therapy

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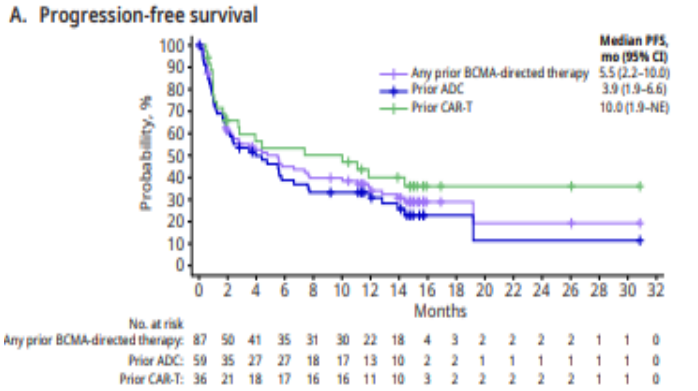
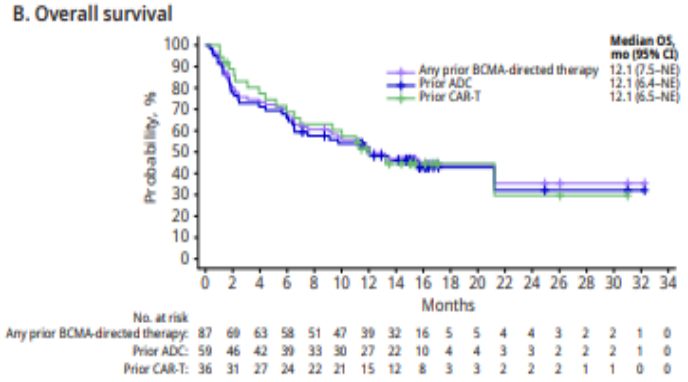
PFS



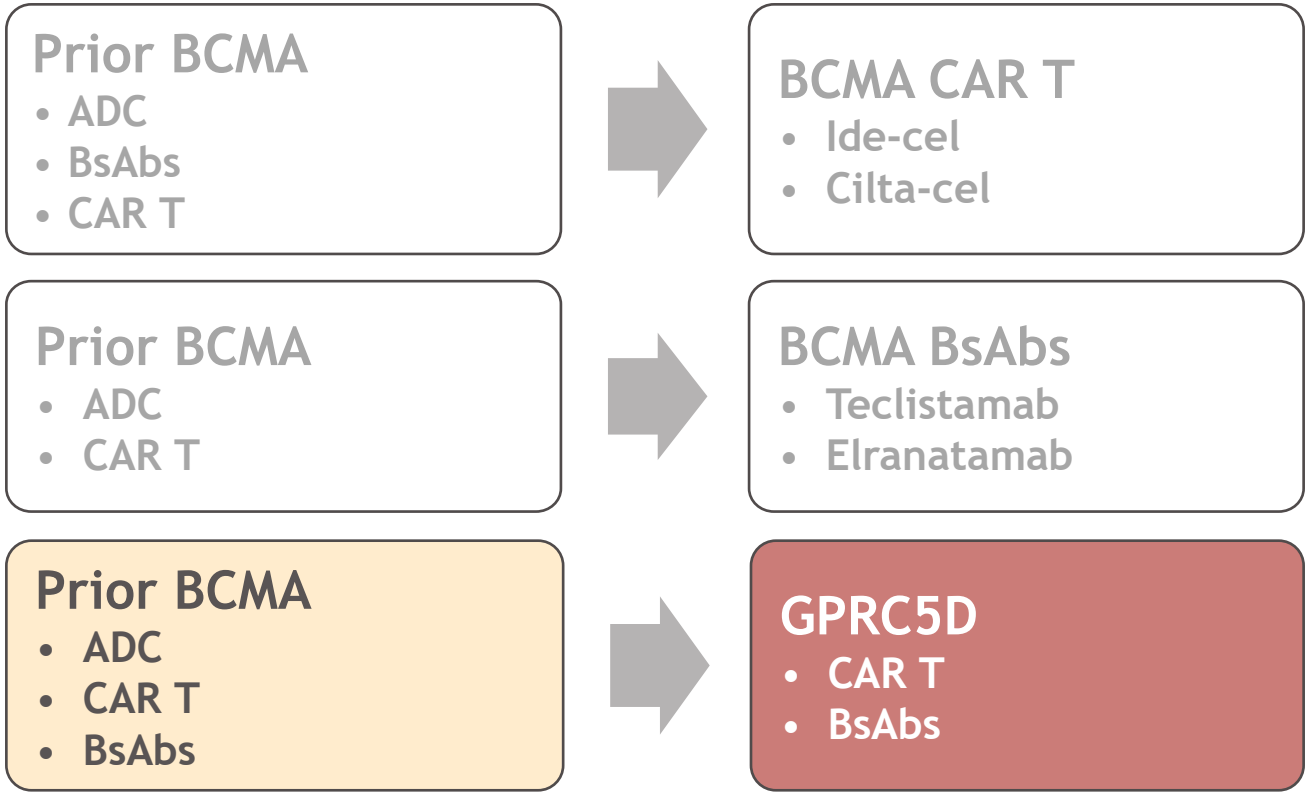
OS



Median PFS and median OS were 5.5 (95% CI, 2.2–10.0) months and 12.1 (7.5–NE) months, respectively

Manier S, et al. *HemaSphere*. 2023;7(suppl):e26808c7.

Would It Be Possible to Sequence Both Approaches?

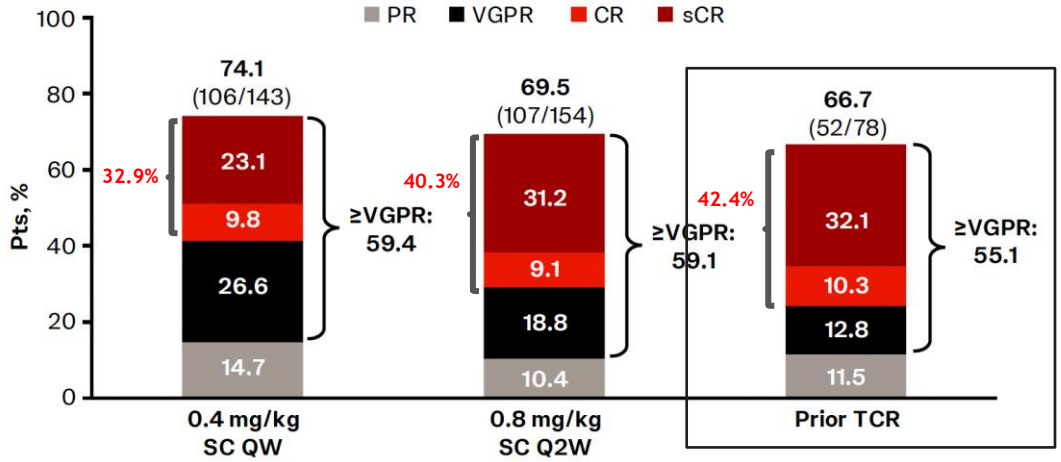


MonumenTAL-1 First-in-Human Phase I Trial: Talquetamab (GPRC5D/CD3 duo Ab) for RRMM – Efficacy With Longer FU

Cohort 0.4 mg/kg SC QW → PL: 5/TCE 100%/TCR 74%/Penta-ref: 29%/EMD 23%/HR CTG 31%/Prior ADC BCMA 15%

Cohort 0.8 mg/kg Q2W→ PL: 5/ TCE 100%/TCR 69%/Penta-ref: 23%/EMD 25%/HR CTG 29%/Prior ADC BCMA **11%**

Prior TCR (n = 78) → PL: 6/TCE 100%/TCR 84%/Penta-ref: 41%/EMD 31%/HR CTG 41%/**Prior ADC BCMA 12%/Prior BCMA BsAbs 31%/Prior BCMA CAR T 67%**



prior BCMA CAR T therapy
- ORR → 71% (n = 40/56)
- mPFS 12 months

prior BCMA bispecific mAbs
- ORR → **58%** (n = 15/26)
- mPFS 4.1 months

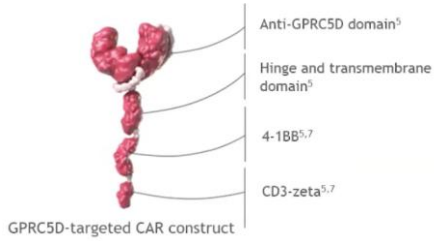
ORR 67% in the prior TCR cohort at the approved Tal doses
mPFS when previously treated with BCMA CAR T 12 months as compared with 4 months when treated with prior BCMA BsAbs

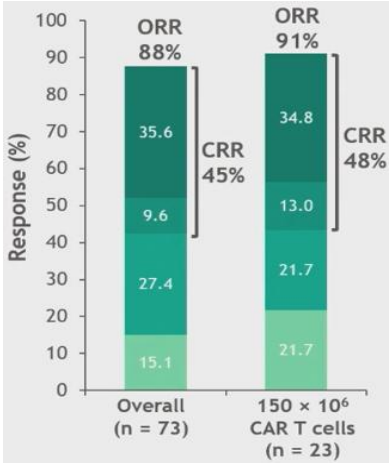
BMS-986393 (CC-95266), a GPRC5D CAR T for RRMM: Updated Results From a Phase I Study

84 patients with RRMM with ≥3 PL including PI, IMiD, and anti-CD38 antibody, and progression within <12 months of last regimen

Median 5PL; 74% were TCR. 44% EMD, 40% HRCA. 26 patients had received 150 × 10^6 CAR Ts

Prior BCMA allowed → 39 patients (46%) prior exposed to BCMA-TT and 30 BCMA CAR T





ORR in subgroups of interest (all dose levels)

Disease characteristic, % (n/N)	Present	Absent
Prior BCMA treatment	78% 25/32	95% 39/41
Extramedullary disease	84% 26/31	91% 38/42
High-risk cytogenetics[b]	83% 24/29	91% 40/44
Triple-class refractory	88% 50/57	88% 14/16

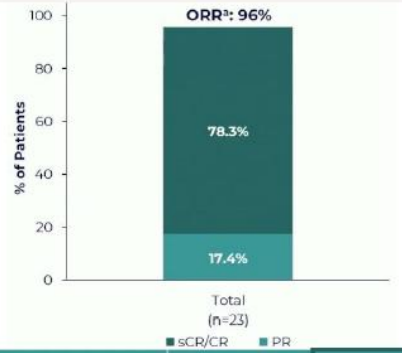
Promising efficacy and safety data even in patients previously exposed to BCMA-TT

DURGA-1: AZD0120 – BCMA-CD19 Dual CAR T in Patients With TCE RRMM

Key inclusion: ≥3PL, triple-class-exposed.
Median age: 63 y (44-78); Triple-class refractory 69%; 27% received BT
6 patients had prior BCMA-therapy: 5 prior CAR (median time since last CAR T 2.6 years) and 1 prior BsAbs (Teclistamab), median time of 0.6 years
N=32 enrolled, n=26 LD chemo, n=26 infused [n=12 at DL1 (1x10e5 cells/kg) and n=14 at DL2 (3x10e5cells/kg)]

ORR (n=23)

N=17 MRD evaluable > MRDneg in 94% (NGS)



	Total (n=23)	BCMA CAR T Exposed (n=5)
ORR	96%	100%
sCR/CR	78%	80%
Follow-up, median (range), months	3.9 (0.9–19.7)	3.9 (3.0–4.0)

Overall Safety

n=26

CRS	DL1 (n=12)	DL2 (n=14)	Total (n=26)
CRS, overall	**9 (75%)**	**7 (50%)**	**16 (62%)**
Grade 1	9 (75%)	6 (43%)	15 (58%)
Grade 2	0	1 (7%)	1 (4%)
Grade 3+	0	0	0
Onset time, median (range), days	9 (2–11)	9 (8–10)	9 (2–11)*
Duration, median (range), days	1 (1–4)	2 (1-2)	1.5 (1–4)
CRS management			
Tocilizumab	7 (58%)	5 (36%)	12 (46%)
Dexamethasone	1 (8%)	2 (14%)	3 (12%)
Anakinra	0	1 (7%)	1 (4%)

- No grade 3+ CRS reported
- *CRS onset on day 8–11 for 15 of 16 patients

ICANS	DL1 (n=12)	DL2 (n=14)
ICANS, overall	**0**	**1 (7%)**
Grade 1	0	1 (7%)
Grade 2	0	0
Grade 3+	0	0
Onset time, days	NA	10
Duration, day	NA	1

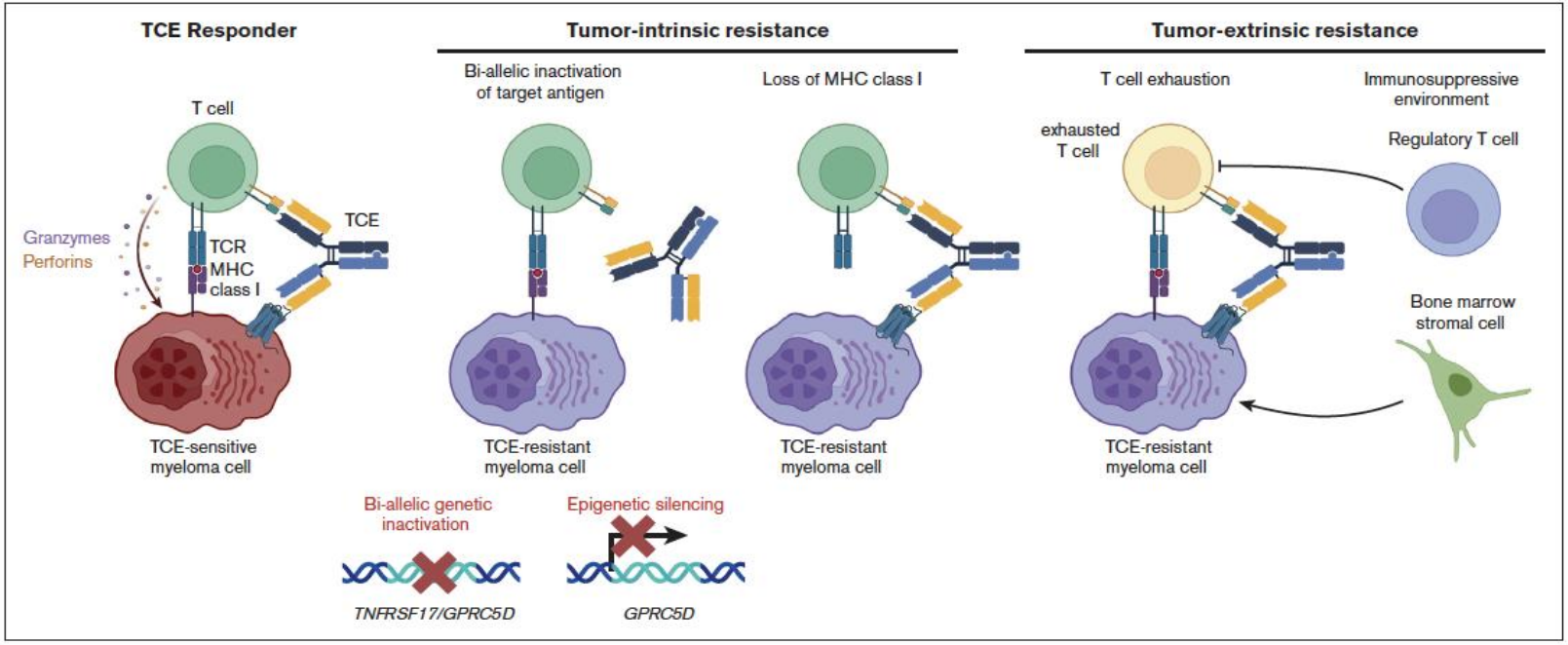
- **No delayed neurotoxicities, including no Parkinsonism, no cranial nerve palsies, and no Guillain-Barré syndrome reported**
- **No IEC-associated colitis reported**
- **Only one grade 1 ICANS event**
- **One patient with IEC-HS (DL1, grade 2); resolved within 7 days**

- **Neutropenia** grade 3–4, overall 81%, 83% at DL1 and 79% at DL2
- **Infections** 8% grade 3–4 overall, and 8% at DL1 and 7% at DL2
- **No DLTs**
- **Similar toxicity profiles between DL1 and DL2**

BCMA, b-cell maturation antigen; BT, bridging therapy; CAR, chimeric antigen receptor; CR, complete response; CRS, cytokine release syndrome; DLT, dose-limiting toxicity; EMD, extramedullary disease; FUP, follow-up; ICANS, immune effector cell–associated neurotoxicity syndrome; IEC-HS, immune effector cell-associated hemophagocytic syndrome; MRD, minimal residual disease; ORR, overall response rate; PL, three prior lines; PR, partial response; RRMM, relapsed/refractory multiple myeloma; sCR, stringent complete response; SPL, single prior line.

1. Richard S, et al. Oral presentation at ASH 2025. Presentation no. 704.

Mechanisms of Resistance and Clinical Implications for BCMA-TT



MHC, major histocompatibility complex; TCE, trichloroethylene; TCR, talquetamab crossover regimen.

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	TNFRSF17 mutation	Pretreatment screening	1.1% (somatic) and 0.7% (germ line) of TCE-naive MM	WGS	May facilitate biallelic target inactivation by second hit	
GPRC5D	12p loss (*GPRC5D*)	Pretreatment screening	13%-15% of TCE-naive MM	WGS	May facilitate biallelic target inactivation by second hit	
	GPRC5D mutation	Pretreatment screening	4% TCE-naive MM	WGS	May facilitate biallelic target inactivation by second hit	
	Low GPRC5D expression	Pretreatment screening	TBD	RNA-seq	Associated with reduced talquetamab efficacy in vitro. May facilitate epigenetic inactivation of the target	
	Abundance of exhausted T-cell clones	Pretreatment screening	TBD	scRNA/VDJ-seq	Predicts response failure to BCMA-targeting TCE	
BCMA	*TNFRSF17* homozygous deletion	At relapse	1/14 relapses after BCMA-targeting TCE	WGS	Precludes response to other BCMA-targeting therapy	
	TNFRSF17 p.Arg27Pro	At relapse	1/14 relapses after BCMA-targeting TCE	WGS	Confers resistance to teclistamab and elranatanab	
	TNFRSF17 p.Pro34del	At relapse	3/14 relapses after BCMA-targeting TCE	WGS	Confers resistance to teclistamab and elranatanab	
	TNFRSF17 p.Ser30del	At relapse	2/14 relapses after BCMA-targeting TCE	WGS	Confers resistance to teclistamab	
GPRC5D	Bi-allelic genetic GPRC5D inactivation	At relapse	5/7 post-talquetamab relapses	WGS	Likely precludes response to other GPRC5D-targeting therapy	
	Epigenetic GPRC5D inactivation	At relapse	2/3 post-talquetamab relapses	scMultiome (RNA-seq + ATAC-seq)	Likely precludes response to other GPRC5D-targeting therapy	

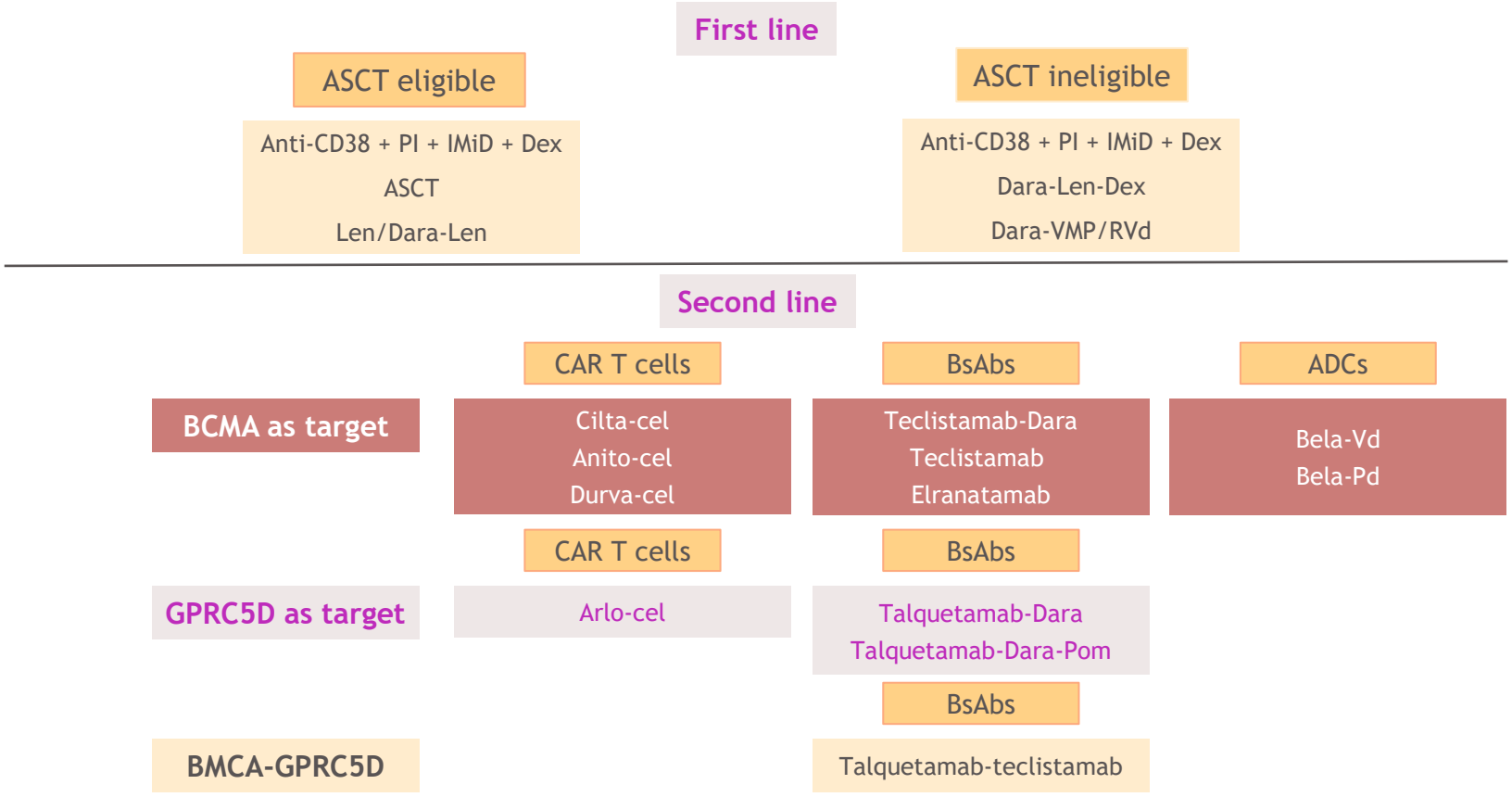
GPRC5D antigen escape via mutations has been observed at relapse after GPRC5D-directed therapies in up to 50% of the patients

T-cell exhaustion is another mechanism of resistance applicable mainly to continuous treatment with bispecific antibodies

ATAC-seq, Assay for Transposase-Accessible Chromatin using sequencing; BCMA, B cell maturation antigen; MM, multiple myeloma; RNA-seq, RNA sequencing; TBD, to be determined; TCE, Trichloroethylene; WGS, whole-genome sequencing.

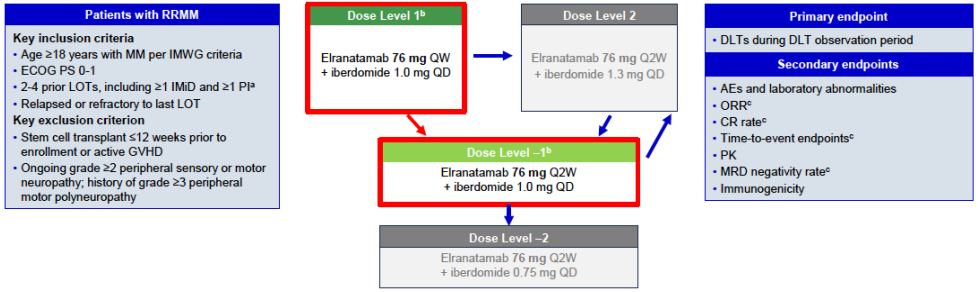
Letouzé E, et al. *Blood Adv*. 2024;8:2952-2959; Lee H, et al. *Nat Med*. 2023;29:2295-2306.

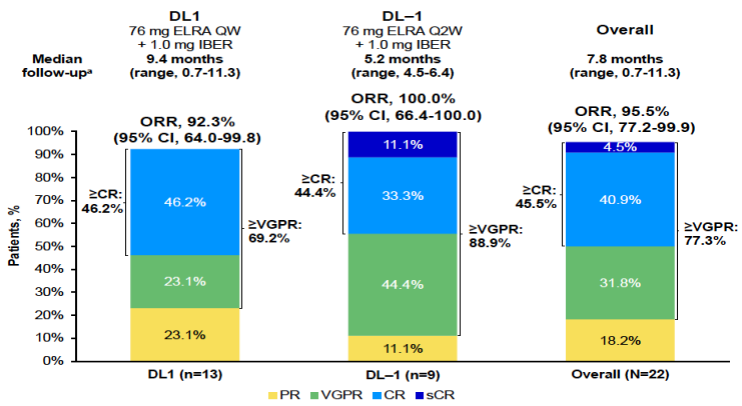
Treatment Landscape in Multiple Myeloma in Early Relapse in the Future



Mateos MV, personal communication; Dimopoulos MA, et al. *Ann Oncol*. 2021;32:309-322.

Other Combinations Are Ongoing but in the Early Phase of Clinical Trials: MagnetisMM-30





Responses are expected to deepen with further follow-up

- 22 patients with RRMM after a median number of 2.5 PL
- 50% triple-class refractory
- 100% triple-class exposed

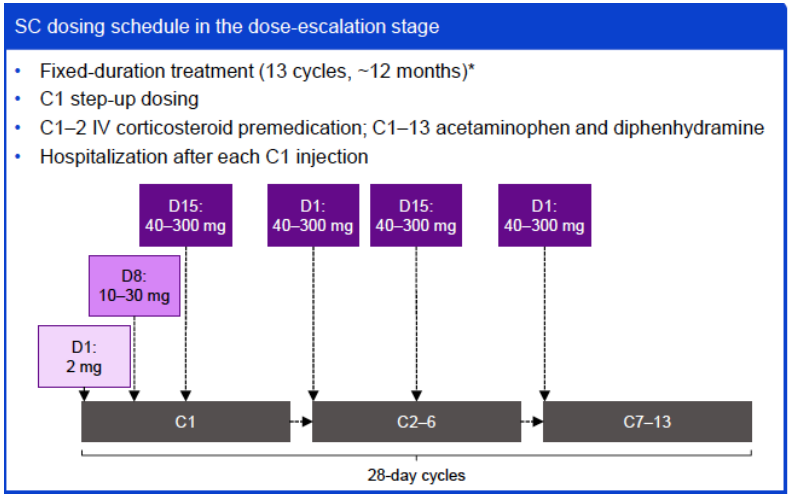
	N=22	
TEAE, n (%)[a]	**Any grade**	**Grade 3/4**
Any	22 (100.0)	19 (86.4)
Hematologic		
Neutropenia	17 (77.3)	16 (72.7)
Anemia	7 (31.8)	3 (13.6)
Lymphopenia	4 (18.2)	4 (18.2)
Nonhematologic		
CRS	15 (68.2)	0
Fatigue	14 (63.6)	0
Diarrhea	11 (50.0)	0
Headache	10 (45.5)	0
Cough	10 (45.5)	0
Nausea	9 (40.9)	1 (4.5)
Injection site reaction	9 (40.9)	0
Decreased appetite	8 (36.4)	1 (4.5)

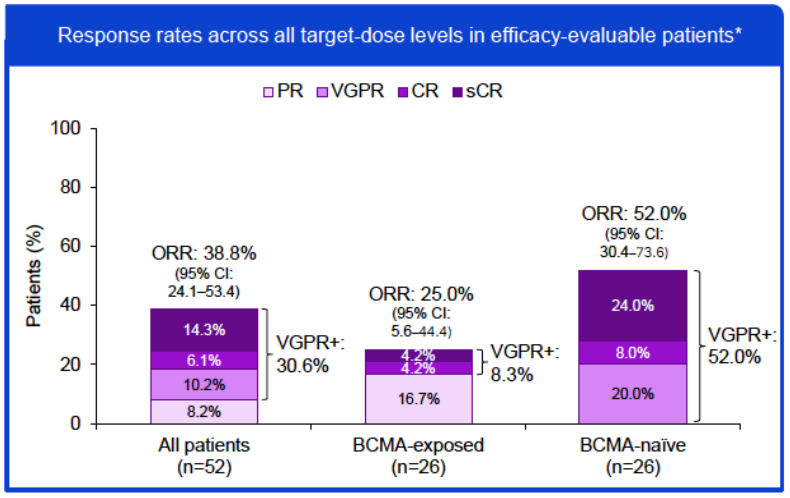
Infections occurring in >5% of patients	**N=22**	
TEAE, n (%)[a]	**Any grade**	**Grade 3**
Infections[b]	9 (40.9)	2 (9.1)
Upper respiratory tract infection	6 (27.3)	0
Candida infection	3 (13.6)	0
Urinary tract infection	2 (9.1)	0

IVIG prophylaxis was administered approximately every 4 weeks to maintain IgG levels above 400 mg/dL

Cevostamab, Subcutaneous FcRH5 Bispecific mAb: Results of the Phase Ib CAMMA Study

- 58 patients with RRMM were included in the trial. Median number of PL: 5 (64% triple-class refractory and 48% prior anti-BCMA therapy, including CAR T, ADC, and bispecific monoclonal antibodies)





- Median DOR was 12 months, NR in BCMA-naive, and 8.3 months in BCMA-exposed patients
- CRS in 69% (G3 in 1 patient); infections in 45% (G3–5 in 15%); IVIG administration in 41% of patients

Cevostamab Plus Pomalidomide-Dex in Patients With RRMM

Adults with RRMM with ≥1 prior LoT including an IMiD and a PI; not refractory to pomalidomide; ECOG PS 0/1
(N = 64)

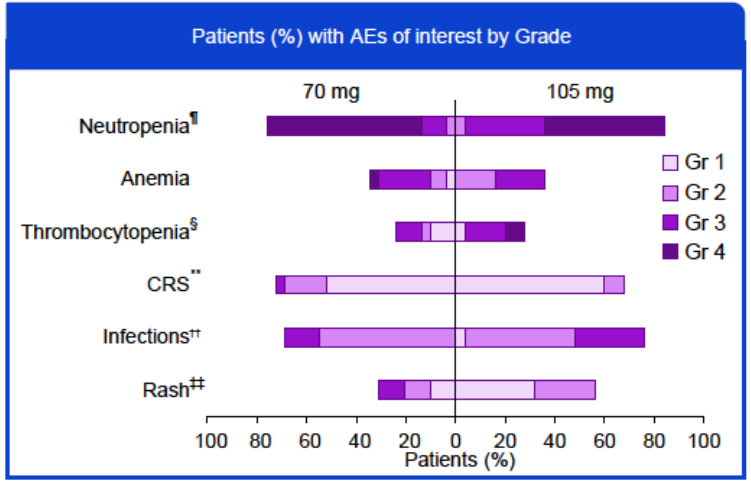
Cevostamab* 70 mg IV Q2W in cycles 1-6 of 28-day cycles then Q4W (D1) in cycles 7+
+ Pomalidomide 2 mg PO on D1-21 from cycle 1+
+ Dexamethasone 20 mg IV/PO on D1, 8, 15, 22 from cycle 1+
(n = 29 BCMA naive)

Cevostamab* 105 mg IV Q2W in cycles 1-6 of 28-day cycles then Q4W in cycles 7+
+ Pomalidomide 2 mg PO on D1-21 from cycle 1+
+ Dexamethasone 20 mg IV/PO on D1, 8, 15, 22 from cycle 1+
(n = 25 BCMA naive)

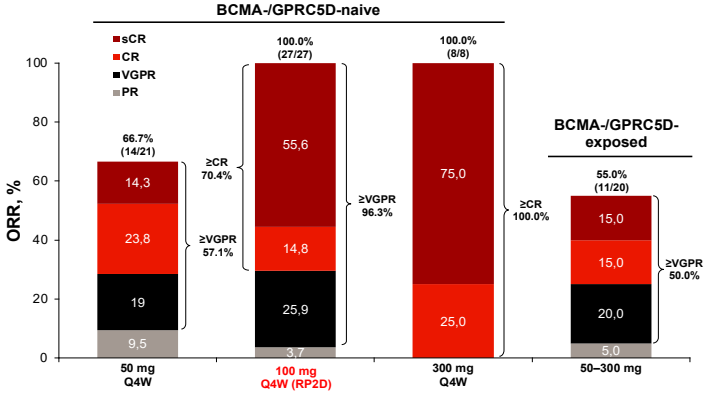
*Prephase dosing of cevostamab: double-step up dosing (0.3/3.3 mg) in a 14-day prephase or triple step-up (0.3/1.2/3.6 mg) in a 21-day prephase. Patients hospitalized after prephase cevostamab infusions for ≥48 hr.

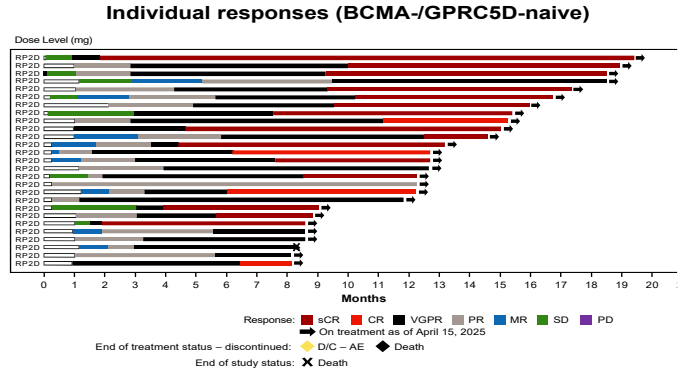
Parameter, %	Cevo 70 mg/ Pom/Dex (n = 29)	Cevo 105 mg/ Pom/Dex (n = 25)
ORR, % (95% CI)	86.2 (71.9–100)	88.0 (73.3–100)
sCR, %	34.5	44.0
CR, %	10.3	16.0
VGPR, %	27.6	16.0
PR, %	13.8	12.0
≥ CR, %	44.8	60.0
≥ VGPR, %	72.4	76.0
Responders with ongoing response at DCO, n/N (%)	20/25 (80.0)	18/22 (81.8)
6-mo DoR, % (95% CI)	96.0 (88.3–100)	90.9 (78.9–100)
MRD− CR in MRD-evaluable CR+ patients, n/N (%)		
• MRD− CR at 10^{-5}	10/11 (90.9)	11/12 (91.7)
• MRD− CR at 10^{-6}	8/11 (72.7)	10/12 (83.3)
MRD− CR at 10^{-5} in all patients, n/N (%)	10/29 (34.5)	11/25 (44.0)

- 29 patients included in this cohort, after a median of 2L of therapy; 72.4% TCE and 31% TCR
- 25 patients included in this cohort, after a median of 2L of therapy; 56% TCE and 24% TCR

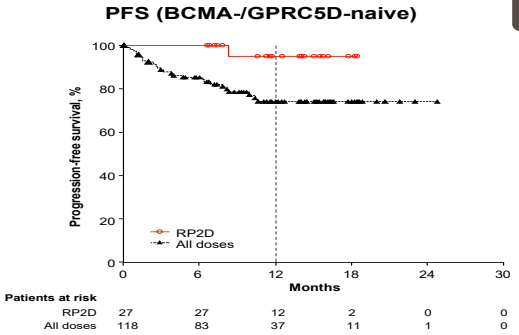


First-in-Human Study of JNJ-79635322 (JNJ-5322): Ramantamig, a BCMA-GPRC5D-CD3 mAb and Novel Next-Generation Trispecific Antibody, in Patients With RRMM – Initial Phase I Results





Only one discontinuation to date at the RP2D



12-month PFS 95.0% at the RP2D (74.1% across all doses) PFS data support the RP2D

AE, adverse event; BCMA, B cell maturation antigen; CR, complete response; D/C, discontinued; ORR, overall response rate; MR, minimal response; PD, progressive disease; PFS, progression free survival; Q4W, every 4 weeks; RP2D, recommended phase II dose; RRMM, relapsed/refractory multiple myeloma; SD, stable disease; vGPR, very good partial response.

Figures adapted from Popat R, et al. EHA 2025. Abstract S100.

TRIgnite-1 ISB 2001 (BCMA × CD38 × CD3): First TREAT TM Trispecific Antibody for RRMM

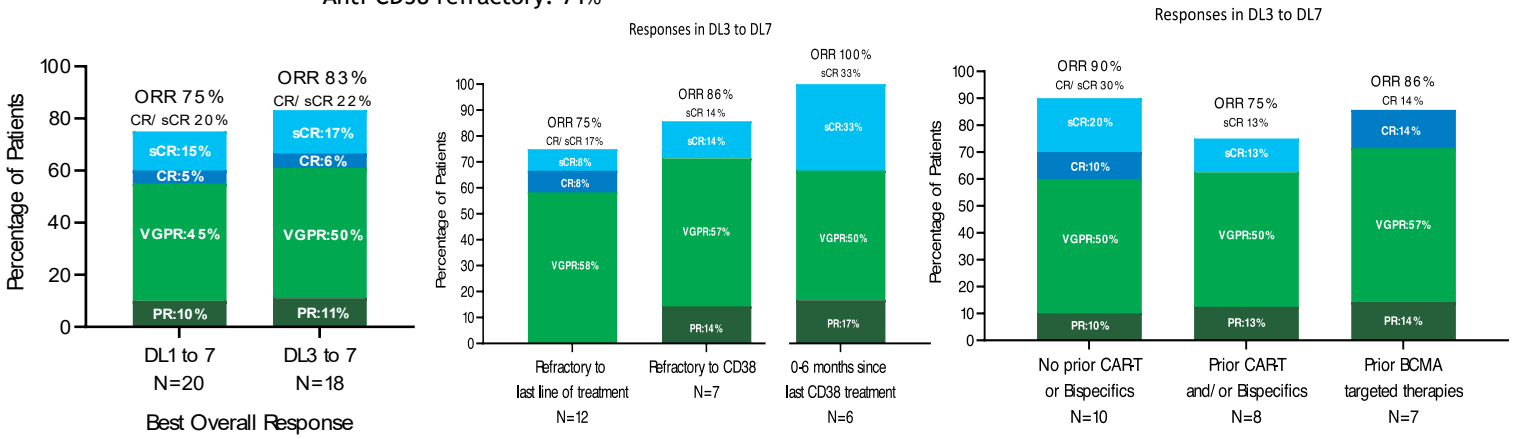
Dose escalation/expansion study in dose escalation. ISB 2001 is administered SC QW in 28-day cycles, starting with 2 step-up doses on days 1 and 4, followed by the full target dose from day 8 onward

Population (n = 40)

Median number of 6 PL. 100% TCE and 25% TCR

Prior BCMA therapy: 46%; Prior BCMA CAR T: 10%; Prior BCMA BsAbs: 20%; Prior BCMA ADC: 25%

Anti-CD38 refractory: 71%



Safety profile: G3–4 neutropenia in 30%, and G3–4 infections in 15%; CRS in 75%, but G1–2; median time to onset was 3 days and duration of 2 days

Trial is ongoing to define the RP2D

TREAT ™, Trispecific Engagement by Antibodies based on the TCR; BEAT®, Bispecific Engagement by Antibodies based on the TCR.

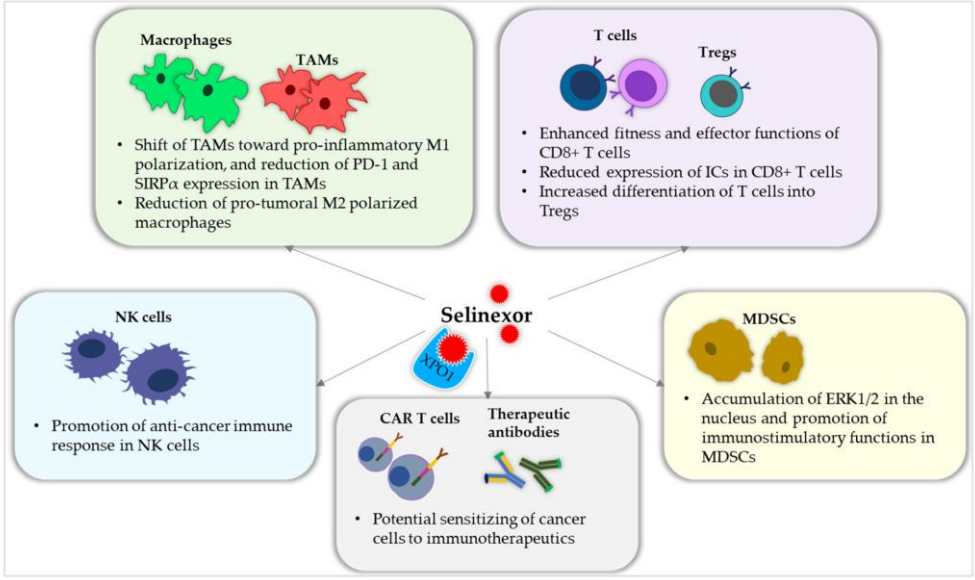
Carretero-Iglesia L, et al. *Nat Cancer*. 2024;5:1494-1514; Quach H, et al. ASH 2024. Abstract P898.

And Beyond the T-Cell Redirecting Therapies . . .

- We have to implement the use of therapies to enhance the immune system to facilitate adequate sequencing

Selinexor Influences Multiple Immune Cells Pathways

Schematic illustration of selinexor's influence on immune cells and immunotherapy



Selinexor is suggested to **impact macrophages** and **tumor-associated macrophages** (TAMs), **myeloid-derived suppressor cells** (MDSCs), **natural killer** (NK) **cells**, and T cells in the **tumor microenvironment**

Selinexor potentially **sensitizes cancer cells** to **CAR T cells** and therapeutic **antibodies**[a]

[a]Selinexor SmPC does not specify guidance on its use in sequence with CAR T cells.
CAR-T, chimeric antigen receptor T cell; ERK1/2, extracellular-signal regulated kinases 1/2; IC, immune checkpoint; MDSC, myeloid-derived suppressor cell; NK, natural killer; PD-1, programmed death 1; SIRPα, signal regulatory protein alpha; TAM, tumor-associated macrophage; Treg, regulatory T cell.

UPREGULATION OF BCMA EXPRESSION BY SELINEXOR

Christina Verbruggen[1], Umair Munawar[1], Seungbin Han[1], Julia Mersi[1], Emma Besant[1], Shilpa Kurian[1], Silvia Nerreter[1], Nina Rein[1], Johanna Lehmann[1], Max Koeppel[1], Hermann Einsele[1], Johannes Waldschmidt[1], Martin Kortüm[1]

1. University Hospital Wuerzburg, Department of Internal Medicine II, Wuerzburg, Germany

Abstract # 6102

INTRODUCTION

- Selinexor is a selective inhibitor of nuclear export that targets XPO1
- XPO1 exports tumor suppressor proteins and oncogenic factors from nucleus to cytoplasm.
- Selinexor + bortezomib + dexamethasone (SVd) is FDA-approved (BOSTON trial) for ≥1 prior-line multiple myeloma.
- Prior work reports Selinexor increases BCMA expression (Wang et al., 2023), but solely based on flow cytometry, no functional assays.
- Flow cytometry is limited in sensitivity and cannot quantify receptor density on a single-cell level.

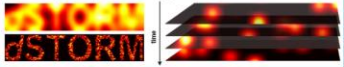
AIM

Provide first insights into BCMA receptor density changes after Selinexor treatment using *d*STORM.

METHOD

Treatment of MM cell models (OPM-2, AMO1) with Selinexor for 1, 2 and 5 days at 10 nM and 50 nM concentration followed by:

- Gene expression analysis via qPCR
- Receptor expression analysis via *d*STORM



RESULTS

1. BCMA GENE EXPRESSION INCREASED BY SELINEXOR TREATMENT

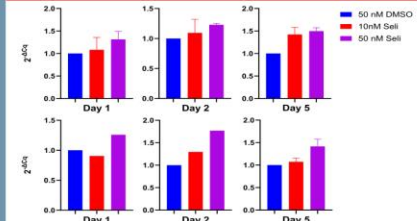


Figure 1. qPCR quantification of BCMA gene expression in OPM-2 (top) and AMO1 (bottom) cells treated with 50 nM DMSO (blue), 10 nM Selinexor (red) or 50 nM Selinexor (magenta) for 1, 2 and 5 days. OPM-2 cells showed a 1.2- and 1.5-fold increase and AMO1 cells revealed a 1.8- and 1.5-fold increase in BCMA gene expression on days 2 and day 5, respectively.

2. SELINEXOR CONCENTRATIONS DO NOT IMPACT CELL VIABILITY

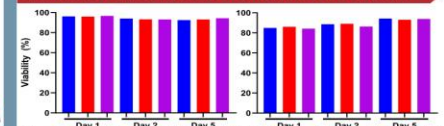


Figure 2. Cell viability of OPM-2 (left) and AMO1 (right) cells when treated with 50 nM DMSO (blue), 10 nM Seli (red) or 50 nM Seli (magenta). Viability of OPM-2 cells remained above 90% and AMO1 cell viability even improved from 84% to 93% by day 5

3. BCMA RECEPTOR EXPRESSION INCREASED BY SELINEXOR TREATMENT

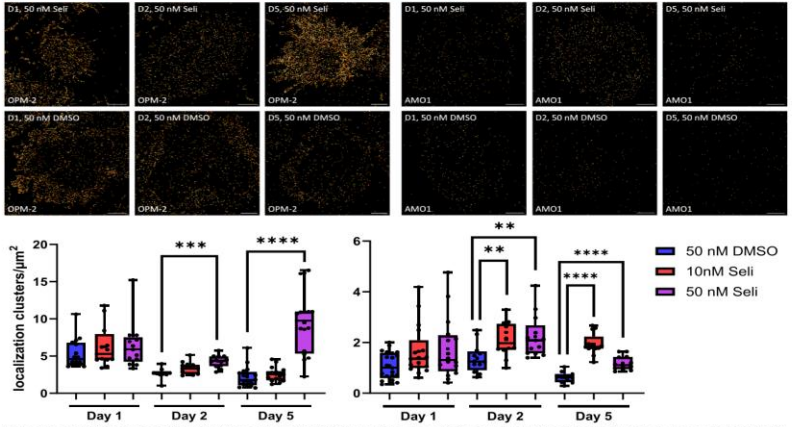


Figure 3. Top: *d*STORM images of OPM-2 (first three columns) and AMO1 (last three columns) after respectively 1, 2 and 5 days of treatment. Top panels show 50 nM Selinexor treated cells, bottom panel 50 nM DMSO. Scale bars, 3 µm. Each yellow dot corresponds to one BCMA receptor, an increase in signal can be seen in the Selinexor treated samples compared to DMSO treated cells. Bottom: Corresponding quantifications of BCMA receptor density from *d*STORM measurements plotted in a box plot. Here, each dot respresents the BCMA expression in one cell and the line in the middle corresponds to the median receptor density. Significant increases in BCMA receptor density corresponding to a 1.6- and 4.2-fold increase in OPM-2 cells and 1.9- and 1.6-fold increase in AMO1 cells on day 2 and 5, respectively.

CONCLUSIONS

Selinexor may enhance target antigen availability on the cell surface, potentially improving the efficacy of BCMA-directed immunotherapies.

- BCMA gene and receptor expression are significantly increased in AMO1 and OPM-2 cell lines by Selinexor in a time- and dose- dependent fashion
- Cell viability is not impacted by the chosen Selinexor concentrations

OUTLOOK

- Verify BCMA upregulation by Selinexor in patient samples
- Correlate receptor expression with therapeutic efficacy (BiSpecs, BCMA CAR-T cells, ADCs)
- Study impact of Selinexor on T cell fitness
- Study Selinexor modulation of other immunotherapy targets (CD38, FcRH5, GPRC5D)

CONTACT INFORMATION

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Summary

- Treatment is rapidly evolving
- The first line of therapy seems to be now well established with PIs, IMiDs, and anti-CD38 mAbs
- BCMA-targeted therapies are options at early relapse: If patients are not eligible for CAR T, belamaf-based combinations and BCMA BsABs have been approved (bela by the EMA and Tec-Dara by the FDA)

- The availability of all these options may allow for a more individualized therapy based on the disease and patient-based characteristics

- The selection should be based on multiple factors, including patients' preferences

Global Multiple Myeloma Academy

Discussion

APTITUDE HEALTH®

Global Multiple Myeloma Academy

Break

APTITUDE HEALTH®

Global Multiple Myeloma Academy

Patient Case Discussion: RRMM

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Global Multiple Myeloma Academy

Patient Case 1: RRMM

María-Victoria Mateos, MD, PhD

APTITUDE HEALTH®

Francisco

75-year-old
Spanish man
BCMA naive

Diagnosed with MM in October 2016

INITIAL PRESENTATION AND HISTORY

Presentation	Asthenia, bone pain
Performance status	ECOG PS 2
Radiographic findings	PET scan showed multiple lytic lesions with no extramedullary disease
Laboratory values	M-protein no detectable in serum. sFLC lambda of 9587 mg/L anemia (Hb 7.9 g/dL); renal impairment (CrCl 30 mL/min); hypercalcemia (total serum calcium 9.6 mg/dL)
Bone marrow biopsy findings	80% monoclonal plasma cells with 3% of PC in peripheral blood
Cytogenetic findings	FISH results showed +1q amp and t(11;14)
Staging	ISS 3 and R-ISS II
Transplant eligibility	Transplant eligible due to age and fitness

This patient profile is hypothetical and represents the type of patient typically seen in clinical practice.

BCMA, B-cell maturation antigen; CrCl, creatinine clearance; ECOG PS, Eastern Cooperative Oncology Group performance status; FISH, fluorescence in situ hybridization; Hb, hemoglobin; ISS, International Staging System; MM, multiple myeloma; PET, positron emission tomography; R-ISS, Revised International Staging System.

Francisco

75-year-old Spanish man BCMA naive

TREATMENT HISTORY

42 months	60 months	12 months
1L October 2016	**2L March 2020**	**3L**
• Induction: VTd (4 cycles) → VRd because of PN • Consolidation: ASCT • Consolidation: KRd until the patient reaches MRD negative • Maintenance: Lenalidomide • **Best response:** CR, with DOR 42 months	• DKd followed by D monotherapy until progression • **Best response:** sCR, MRD negative • DOR 60 months	• ???????

Comorbidities

- Diabetes
- Hypertension
- Renal impairment

Key AEs/toxicities

- Well tolerated
- No significant toxicities

[a]Carfilzomib was discontinued after 2 cycles due to cardiotoxicity.
1L, first line; 2L, second line; 3L, third line; 4L, fourth line; AE, adverse event; ASCT, autologous stem cell transplant; BCMA, B-cell maturation antigen; CR, complete response; d, dexamethasone; D, daratumumab; DOR, duration of response; E, elotuzumab; K, carfilzomib; mo, months; P, pomalidomide; PR, partial response; R, lenalidomide; V, bortezomib.

Francisco

75-year-old
Spanish man
BCMA naive

CURRENT TREATMENT CONSIDERATIONS

Current Presentation

- On routine follow-up, patient presented with positive urine IF with slow increase of FLC. Within 1 month, FLC had increased, and we planned to start a new line of therapy because of its presentation at diagnosis

Clinical Factors

- This is not a rapid-progression disease in principle
- Triple-class exposed
- BCMA-directed therapy naive
- Hypertension, diabetes, and CrCl of 32 mL/min
- No extramedullary disease per repeated PET scans

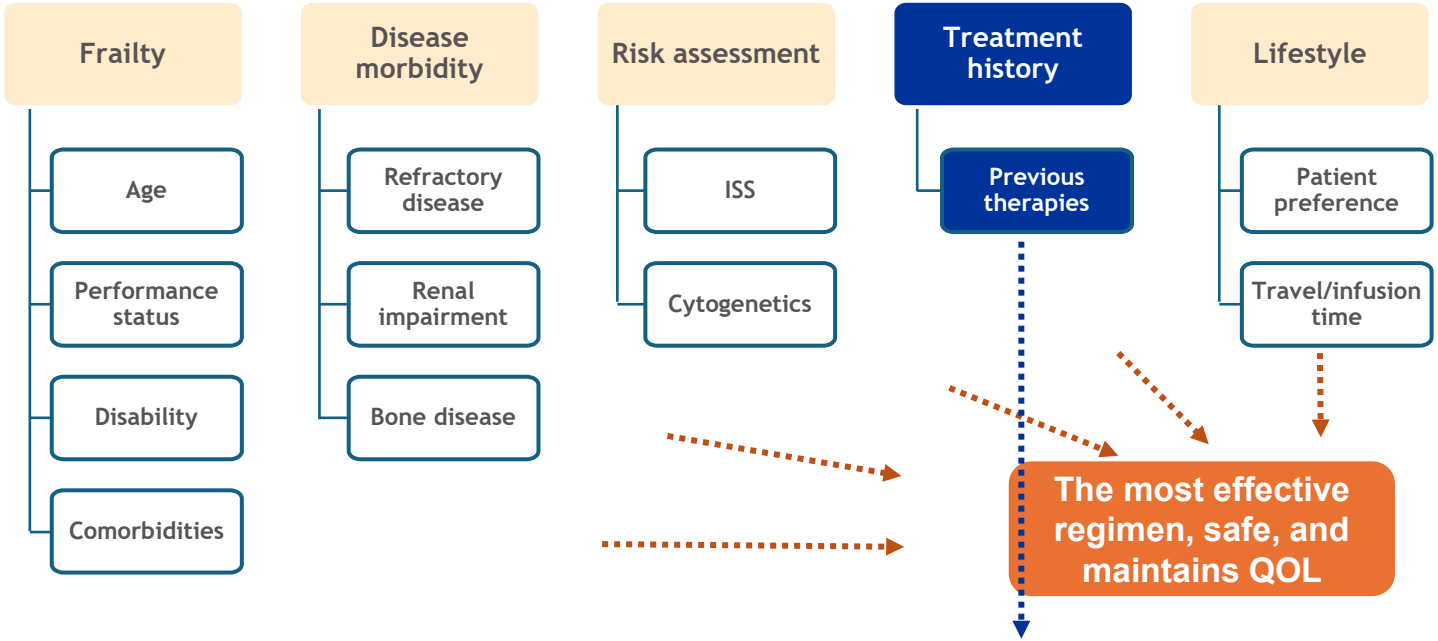
Patient Preferences

- No preferences
  He asked me about my best choice for him

IS THE PATIENT ELIGIBLE FOR CAR T?

BCMA, B-cell maturation antigen; CAR, chimeric antigen receptor; PET, positron emission tomography.

Disease and Patient-Based Factors Influencing the Treatment Decision-Making in the Relapse Setting



The problem for this patient was the renal impairment, because the CrCl is 32 mL/min, and cilta-cel, which is approved in Spain, requires from a CrCl of at least 45 mL/min

RRMM: Phase II GEM-RANTAB

In active recruitment

- **GEM-RANTAB** is an open-label, multicenter, nonrandomized, phase II study
- To evaluate the efficacy and safety of **elranatamab** monotherapy at the dose of 76 mg subcutaneously in participants with **RRMM after 1 or 2 prior lines of therapy** who have received prior treatment with immunomodulatory drugs, protease inhibitors, and anti-CD38 therapy and were refractory to the last line of therapy
- **Ideal rescue for patients enrolled in the GEM-2017Fit trial** (triple-class exposed)

Patients with RRMM

Key inclusion criteria

- **RRMM after 1 or 2 prior lines**
- **Prior exposure to proteasome inhibitor, immunomodulatory drug, and anti-CD38 antibody**
- **Disease relapsed or refractory to their last antimyeloma regimen**
- **ECOG 0–1**
- **Creatinine clearance ≥30 mL/min**
- **Platelets ≥25 × 10^9/L**
- ANC ≥1.0 × 10^9/L
- Hemoglobin ≥8 g/dL

Cohort (n = 50)

No prior BCMA-directed treatment is allowed

Elranatamab 76 mg SC QW on a 28-day cycle

Primary endpoint

- **MRD at 6 and 12 months**

Secondary endpoints

- Sustained MRD
- CR rate
- ORR
- ORR by baseline extramedullary disease status
- Duration of CR
- Time to response
- PFS
- OS
- Safety (CRS, ICANS, etc)
- Biological studies

For patients receiving ≥6 cycles and achieving partial response or better with responses persisting for ≥2 months, the dosing interval will be changed to Q2W, and from Q2W to Q4W after at least 6 Q2W cycles (C13 onward)

Francisco

75-year-old Spanish man BCMA naive

- FLC lambda baseline of 2344
- Bence-Jones proteinuria in 24-hour urine: 190 mg

TREATMENT HISTORY

10 April 2025	13 April 2025	17 April 2025	24 hours later
Step-up dose 1 12 mg	**Step-up dose 2 36 mg**	**Full dose 76 mg SC**	
• Fever after SUD1 with no hypotension and no hypoxia • Cultures, empiric Ab with cefepime • Symptomatic treatment • **CRS G1**	• Asymptomatic	• Asymptomatic	• Discharge from the hospital 48 hours later

Cultures results

- Staphylococcus epidermidis

Key AEs/toxicities

- Well tolerated
- No significant toxicities

[a]Carfilzomib was discontinued after 2 cycles due to cardiotoxicity.
1L, first line; 2L, second line; 3L, third line; 4L, fourth line; AE, adverse event; ASCT, autologous stem cell transplant; BCMA, B-cell maturation antigen; CR, complete response; d, dexamethasone; D, daratumumab; DOR, duration of response; E, elotuzumab; K, carfilzomib; mo, months; P, pomalidomide; PR, partial response; R, lenalidomide; V, bortezomib.

Francisco

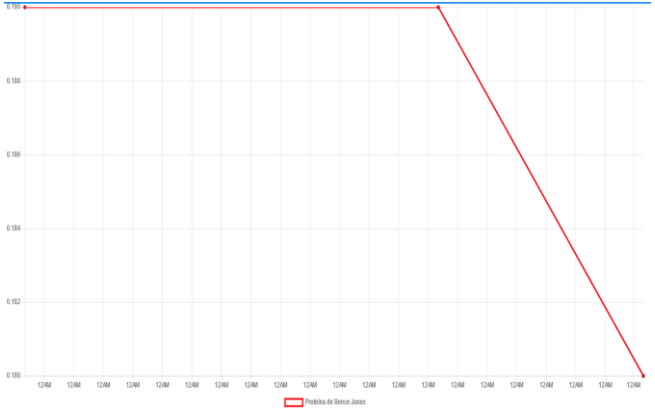
75-year-old
Spanish man
BCMA naive

CURRENT TREATMENT CONSIDERATIONS

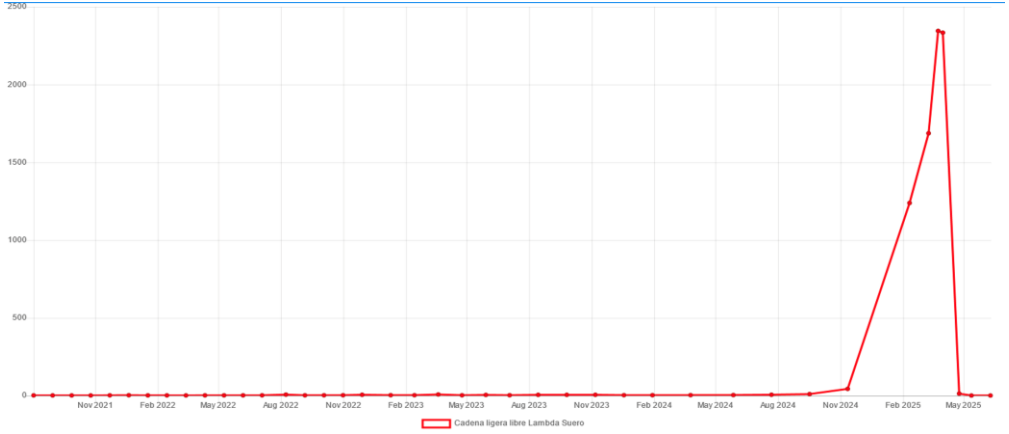
Current Presentation

- Patient continues receiving elranatamab monthly now from C7
  Patient is in sCR, MRD negative, PET-CT negative, and mass spectrometry negative

Bence-Jones proteinuria



Lambda FLC



PATIENT IS NOW AT HIS CYCLE 14

BCMA, B-cell maturation antigen; CAR, chimeric antigen receptor; PET, positron emission tomography.

Francisco

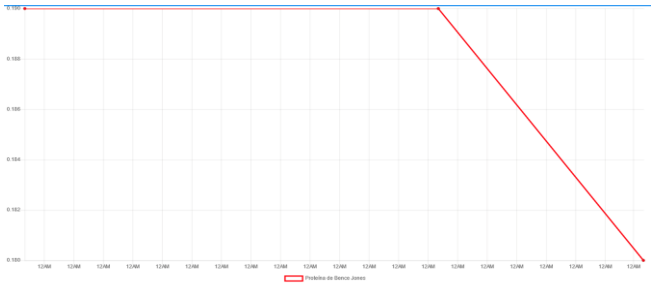
75-year-old
Spanish man
BCMA naive

CURRENT TREATMENT CONSIDERATIONS

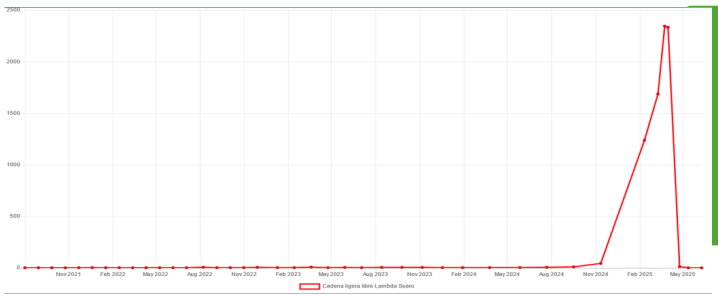
Current Presentation

- Patient continues receiving elranatamab monthly now from C7

Bence-Jones proteinuria after C1



Lambda FLC after C1



PATIENT IS NOW AT HIS CYCLE 14
Patient is in sCR, MRD negative, PET-CT negative, and mass spectrometry negative

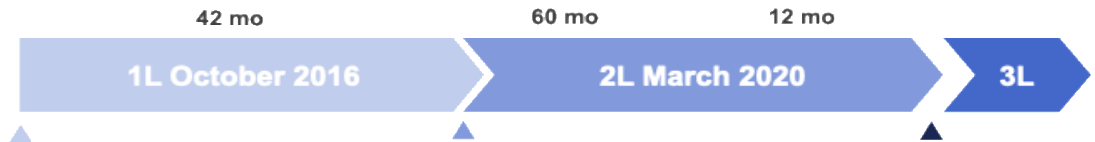
JANUARY 2025: CUTANEOUS SQUAMOUS CELL CARCINOMA OF THE SCALP, 25 MM IN SIZE.
HE HAS JUST RECEIVED 25 SESSIONS OF RADIOTHERAPY

BCMA, B-cell maturation antigen; CAR, chimeric antigen receptor; PET, positron emission tomography.

Francisco

75-year-old
Spanish man
BCMA naive

TREATMENT HISTORY



- Induction: VTd (4 cycles) → VRd because of PN
- Consolidation: ASCT
- Consolidation: KRd until the patient reaches MRD -ve
- Maintenance: Lenalidomide
- **Best response**: CR, with DOR 42 mo

- DKd followed by D monotherapy until progression
- **Best response**: sCR, MRD –ve
- DOR 60 mo

- ???????

Comorbidities

- Diabetes
- Hypertension
- Renal impairment

Key AEs/toxicities

- Well tolerated
- No significant toxicities

What else we can learn from this patient?

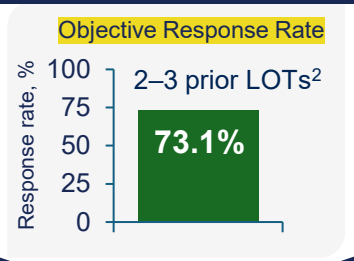
- What is his expected outcome based on his baseline characteristics?
  - This patient had received only 2 prior lines

[a]Carfilzomib was discontinued after 2 cycles due to cardiotoxicity.
1L, first line; 2L, second line; 3L, third line; 4L, fourth line; AE, adverse event; ASCT, autologous stem cell transplant; BCMA, B-cell maturation antigen; CR, complete response; d, dexamethasone; D, daratumumab; DOR, duration of response; E, elotuzumab; K, carfilzomib; mo, months; P, pomalidomide; PR, partial response; R, lenalidomide; V, bortezomib.

Select Patient Populations

In C demonstrated **61% ORR** at median follow-up of 28.4 months (95% CI: 28.0–29.0)[1]

Earlier Lines



ta have been generated
ons in MagnetisMM-3

MM-3 Cohort A Subpopulations

- 2–3 Prior LOTs[2]
- Elderly[3]
- High-risk Cytogenetics[4,a]

Elranatamab was also evaluated following BCMA-directed therapy in a separate pooled analysis

POOLED ANALYSIS
BCMA-Directed Therapy–Exposed Patients

- Prior BCMA-Directed Therapy[5]

These data represent prespecified subgroup analyses that were not powered to detect statistical significance. Small patient numbers and lack of multiplicity adjustments can be limitations of these analyses. No conclusion about efficacy in subgroups can be drawn from these data.

[a]Includes t(4;14), t(14;16), and del(17p) chromosomal abnormalities.[4]
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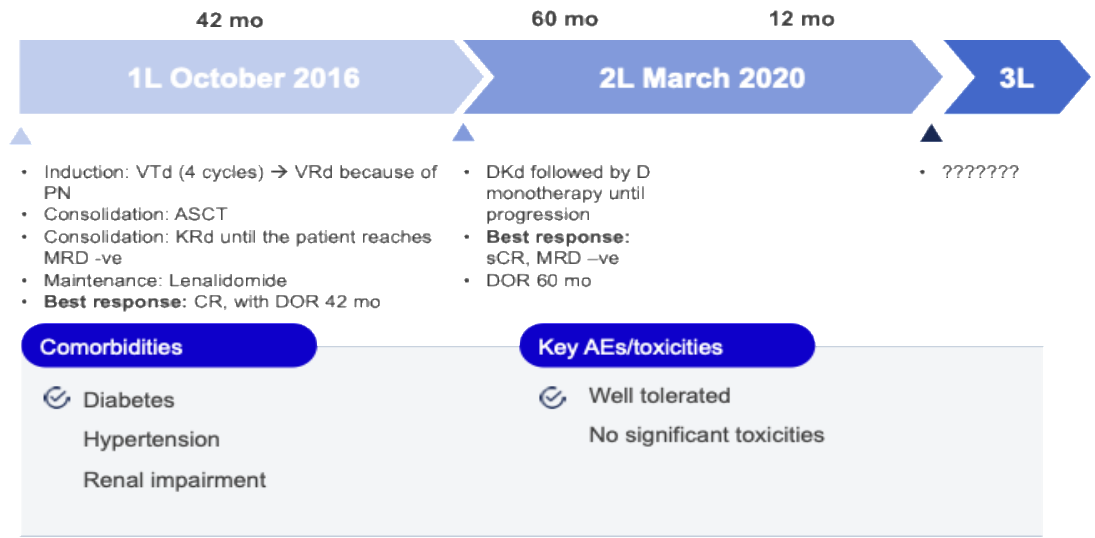
Francisco

75-year-old
Spanish man
BCMA naive

TREATMENT HISTORY



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  - This patient had received only 2 prior lines
  - This patient was older than 65 years

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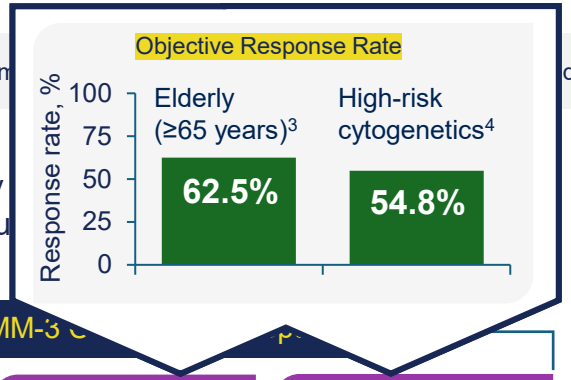
1L, first line; 2L, second line; 3L, third line; 4L, fourth line; AE, adverse event; ASCT, autologous stem cell transplant; BCMA, B-cell maturation antigen; CR, complete response; d, dexamethasone; D, daratumumab; DOR, duration of response; E, elotuzumab; K, carfilzomib; mo, months; P, pomalidomide; PR, partial response; R, lenalidomide; V, bortezomib.

Select Patient Populations

In Cohort A of MagnetisMM-3, elranatam… …dian follow-up of 28.4 months (95% CI: 28.0–29.0)[1]

Exploratory … for subpopu…



Elranatamab was also evaluated following BCMA-directed therapy in a separate pooled analysis

MagnetisMM-3 C… P…

2–3 Prior LOTs[2]

Elderly[3]

High-risk Cytogenetics[4,a]

POOLED ANALYSIS
BCMA-Directed Therapy–Exposed Patients

Prior BCMA-Directed Therapy[5]

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Efficacy and Safety of Elranatamab by Age and Frailty in Patients With RRMM: A Subgroup Analysis From MagnetisMM-3

Frailty was evaluated according to the modified-IMWG frailty score including chronologic age, ECOG PS, and Charlson Comorbidity Index

Table 1: Baseline demographics and characteristics and prior treatments

	<65 y n=43	≥65 y n=80	Non-frail n=84	Frail n=39
Age, median (range), y	58.0 (36–64)	71.0 (65–89	65.0 (36–79)	75.0 (47–89)
Male, n (%)	26 (60.5)	42 (52.5)	44 (52.4)	24 (61.5)
Race				
White	25 (58.1)	47 (58.8)	49 (58.3)	23 (59.0)
Asian	7 (16.3)	9 (11.3)	15 (17.9)	1 (2.6)
Black or African American	5 (11.6)	4 (5.0)	5 (6.0)	4 (10.3)
Not reported or unknown	6 (14.0)	20 (25.0)	15 (17.9)	11 (28.2)
ECOG performance status, n (%)				
0	23 (53.5)	22 (27.5)	41 (48.8)	4 (10.3)
1	19 (44.2)	52 (65.0)	43 (51.2)	28 (71.8)
2	1 (2.3)	6 (7.5)	0	7 (17.9)
R-ISS disease stage, n (%)				
I	11 (25.6)	17 (21.3)	24 (28.6)	4 (10.3)
II	24 (55.8)	44 (55.0)	47 (56.0)	21 (53.8)
III	6 (14.0)	13 (16.3)	8 (9.5)	11 (28.2)
Unknown	2 (4.7)	6 (7.5)	5 (6.0)	3 (7.7)
Extramedullary disease by BICR, n (%)[a]	14 (32.6)	25 (31.3)	26 (31.0)	13 (33.3)
Bone marrow plasma cells, n (%)				
<50%	30 (69.8)	59 (73.8)	60 (71.4)	29 (74.4)
≥50%	9 (20.9)	17 (21.3)	18 (21.4)	8 (20.5)
Missing	4 (9.3)	4 (5.0)	6 (7.1)	2 (5.1)
Prior lines of anti-myeloma therapy, median (range)	5.0 (2–22)	5.0 (2–12)	5.0 (2–22)	5.0 (2–12)
Refractory status, n (%)				
Triple-class[b]	41 (95.3)	78 (97.5)	84 (100.0)	35 (89.7)
Penta-drug[c]	19 (44.2)	33 (41.3)	38 (45.2)	14 (35.9)
Refractory to last line of therapy	43 (100.0)	75 (93.8)	80 (95.2)	38 (97.4)

[a] Extramedullary disease was defined as presence of any p… medullary and/or paramedullary with a soft tissue component; [b] Triple-class refers to at least 1 proteosome inhibitor, 1 immunomodulatory drug, and 1 anti-CD38 antibody; [c] Penta-drug refers to at least 2 proteosome inhibitors, 2 immunomodulatory drugs, and 1 anti-CD38 antibody

BICR=blinded independent central review; ECOG=Eastern Cooperative Oncology Group; R-ISS=Revised Multiple Myeloma International Staging System

Our patient would qualify as **frail** because

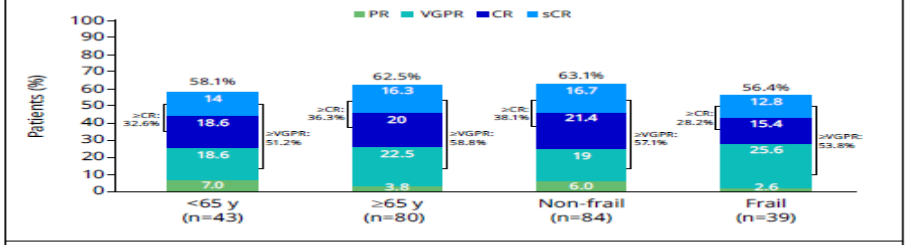
- Age: 75 years old
- PS ECOG: 1
- Comorbidities: Renal insufficiency
  Diabetes
  Hypertension

Raje Net al. ASCO 2023. Abstract P8040.

Efficacy and Safety of Elranatamab by Age and Frailty in Patients With RRMM: A Subgroup Analysis From MagnetisMM-3

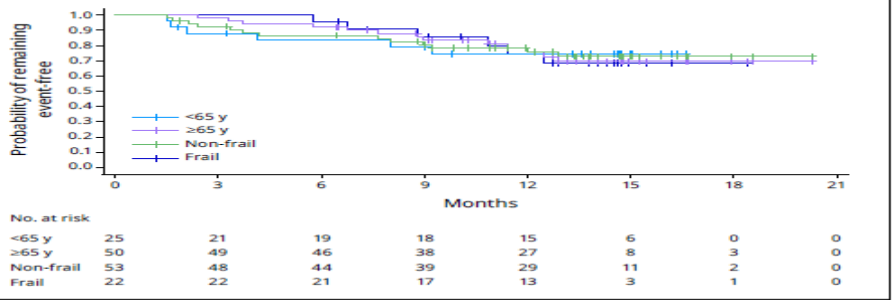
Frailty was evaluated according to the modified-IMWG frailty score including chronologic age, ECOG PS, and Charlson Comorbidity Index

Figure 2: Best overall response and objective response rate



Objective response defined as sCR+CR+VGPR+PR
CR=complete response; PR=partial response; sCR=stringent complete response; VGPR=very good partial response

Figure 3: Duration of response



The probability of remaining event-free for patients in each subgroup is plotted over time

Raje Net al. ASCO 2023. Abstract P8040.

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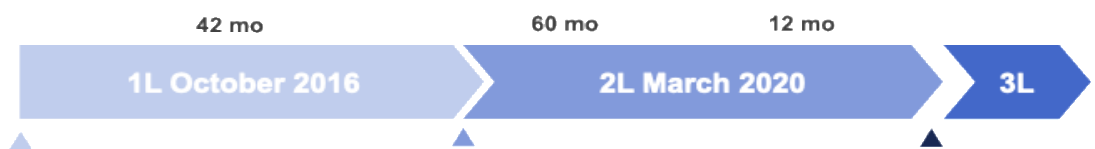
TREATMENT HISTORY



- Induction: VTd (4 cycles) → VRd because of PN
- Consolidation: ASCT
- Consolidation: KRd until the patient reaches MRD -ve
- Maintenance: Lenalidomide
- **Best response**: CR, with DOR 42 mo

- DKd followed by D monotherapy until progression
- **Best response**: sCR, MRD –ve
- DOR 60 mo

- ???????

Comorbidities

- Diabetes
- Hypertension
- Renal impairment

Key AEs/toxicities

- Well tolerated
- No significant toxicities

What else we can learn from this patient?

- What is his expected outcome based on his baseline characteristics?
  - This patient had received only 2 prior lines
  - This patient was older than 65 years
  - This patient presented with amp 1q

[a]Carfilzomib was discontinued after 2 cycles due to cardiotoxicity.
1L, first line; 2L, second line; 3L, third line; 4L, fourth line; AE, adverse event; ASCT, autologous stem cell transplant; BCMA, B-cell maturation antigen; CR, complete response; d, dexamethasone; D, daratumumab; DOR, duration of response; E, elotuzumab; K, carfilzomib; mo, months; P, pomalidomide; PR, partial response; R, lenalidomide; V, bortezomib.

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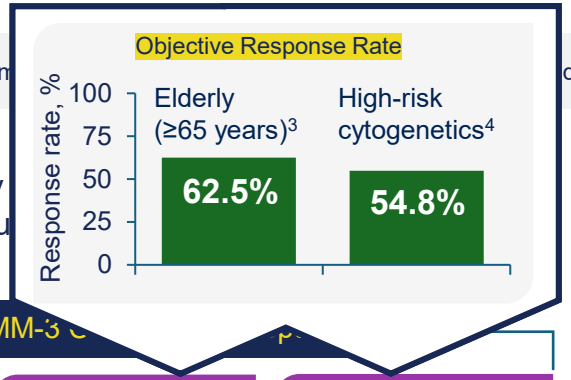

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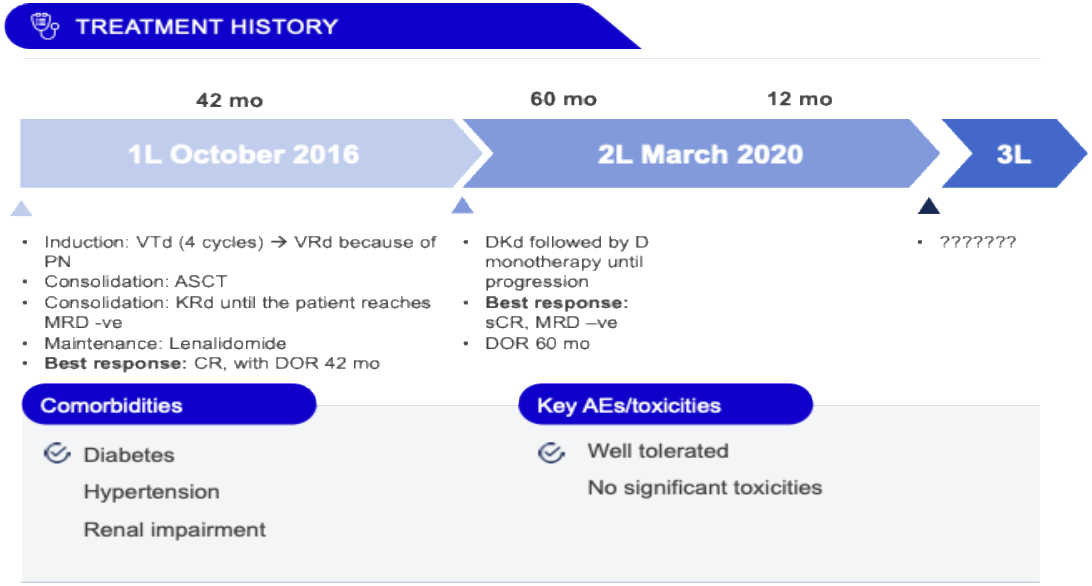

What else we can learn from this patient?

- What is his expected outcome based on his baseline characteristics??
  - This patient had received only 2 prior lines
  - This patient was older than 65 years
  - This patient presented with amp 1q
  - This patient presented with renal impairment but CrCL 32 mL/min and met the inclusion criteria

[a]Carfilzomib was discontinued after 2 cycles due to cardiotoxicity.
1L, first line; 2L, second line; 3L, third line; 4L, fourth line; AE, adverse event; ASCT, autologous stem cell transplant; BCMA, B-cell maturation antigen; CR, complete response; d, dexamethasone; D, daratumumab; DOR, duration of response; E, elotuzumab; K, carfilzomib; mo, months; P, pomalidomide; PR, partial response; R, lenalidomide; V, bortezomib.

Global Multiple Myeloma Academy

Discussion

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Patient Case 2: RRMM

Hermann Einsele, MD, FRCP

APTITUDE HEALTH®

Patient Case 2

Uniklinikum Würzburg

♂ **62 yo, MM lambda light chain, Dx 02/2011, ISS 3, sFLC lambda: 35.575 mg/L, acute renal failure, dialysis dependent initially**

02/11	Initial diagnosed with dialysis-dependent acute kidney injury
02 – 04/11	3 cycles of PAD → acute renal failure
04/11	Stem cell mobilization from cyclophosphamide-etoposide
05/11	First high-dose melphalan + ASCT
10/11	Second high-dose melphalan + ASCT → CR
	Relapse
03 – 10/14	6 cycles of bRAD → PD
12/15 – 12/16	16 cycles of panobinostat-bortezomib-dexamethasone → VGPR
05 – 11/17	6 cycles of ixazomib-thalidomide-dexamethasone (AGMT MM-1 study)
11/17	Switch to Rd → PD
01/18	**MM-Bite study AMG 420 → CR**

Patient Case 2

Uniklinikum Würzburg

♂ **62 yo, MM lambda light chain, Dx 02/2011, ISS 3, sFLC lambda: 35.575 mg/L, acute renal failure, dialysis dependent initially**

03/19 – 7/20	18 cycles of KRd → PD
08 – 12/20	2 cycles of DVd → PD
12/20	**2 cycles of belantamab mono → PD → Biallelic BCMA loss**
04/21	2 cycles of VDT-PACE → SD
06/21	**Talquetamab → CR**
12/22	PD → Carf-Pom-Dex → SD
01/23	3. High-dose chemotherapy + ASCT
05/23	→ Documented loss of BCMA and GPRC5D
12/25	**Currently: selinexor-bortezomib**
	→ VGPR

Global Multiple Myeloma Academy

Patient Case 3: RRMM

Hermann Einsele, MD, FRCP

APTITUDE HEALTH®

Patient Case 3

Uniklinikum Würzburg

♂ **71 yo, MM type IgA kappa, ISS II, Dx 01/14**

01/14	3× VCD
05/14	Stem cell mobilization
05/14	High-dose melphalan + autoSCT
04-8/17	2. LOT: 7× KRd
04/18	Switch to Ixa-Len-Dex
04/19	3. LOT: 22 cycles of Dara-Pom-Dex
05/22	26 cycles of Dara-Pom-Dex
10/22	Leukapheresis
	Bridging with Dara-Pom-Dex

Patient Case 3

Uniklinikum Würzburg

♂ **71 yo, MM type IgA kappa, ISS II, Dx 01/14**

12/22	4. LOT: **CAR T-cell therapy (ide-cel)**
	→ CRS grade II → CR
03/24	5. LOT: Dara-Pom-Dex (3 cycles)
06/24	6. LOT: DaraVCd (9 cycles)
01/25	7. LOT: KDT-P(A)CE
03/25	Leukapheresis
	Bridging therapy (talquetamab)
07/25	**CAR T-cell therapy (cilta-cel)**
07/25	MRD-negative CR
04/26	MRD-negative CR

Global Multiple Myeloma Academy

Discussion

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Future Directions in Early Lines of Therapy for RRMM

María-Victoria Mateos, MD, PhD

APTITUDE HEALTH®

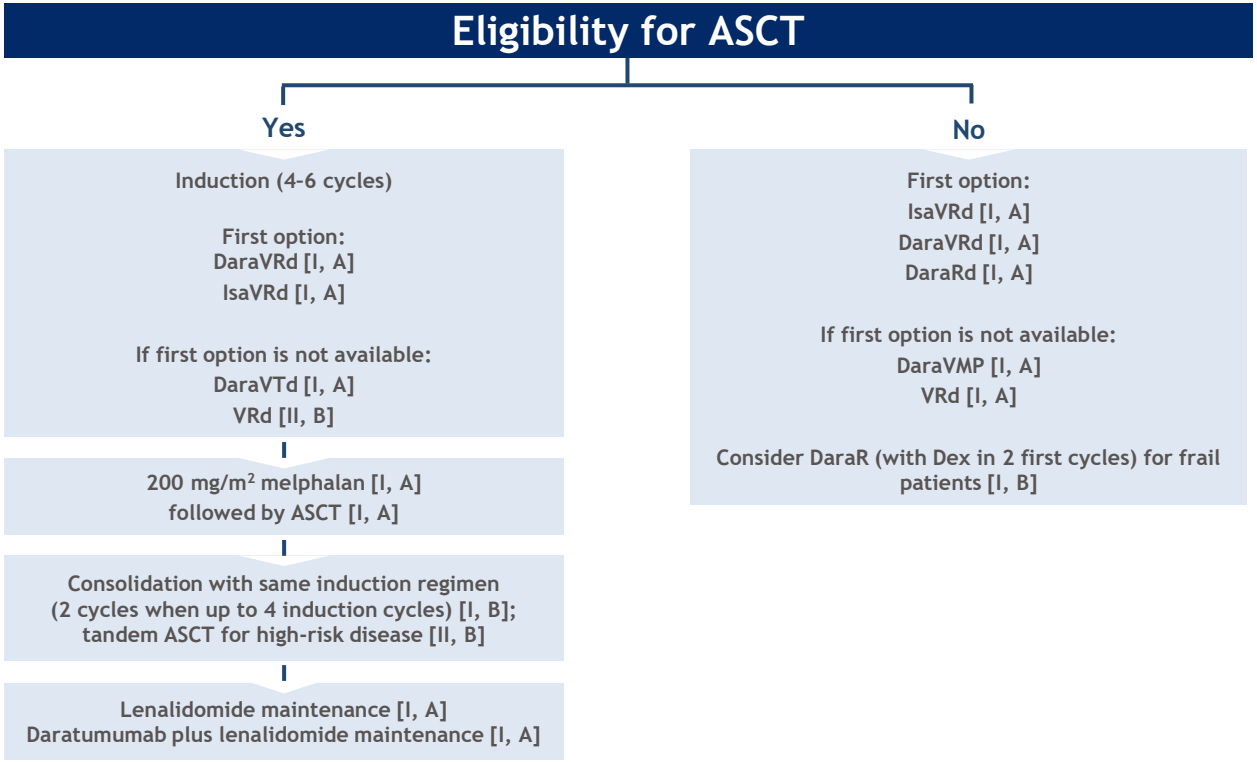
Future Directions in Early Lines of Therapy for Patients With RRMM

María-Victoria Mateos
Salamanca, Spain

Disclosures

- Honoraria derived from lectures and participation in advisory boards from Janssen, Bristol Myers Squibb, Amgen, GSK, AbbVie, Pfizer, Regeneron, Roche, Sanofi, Stemline, Kite

EHA-EMN 2025 Guidelines

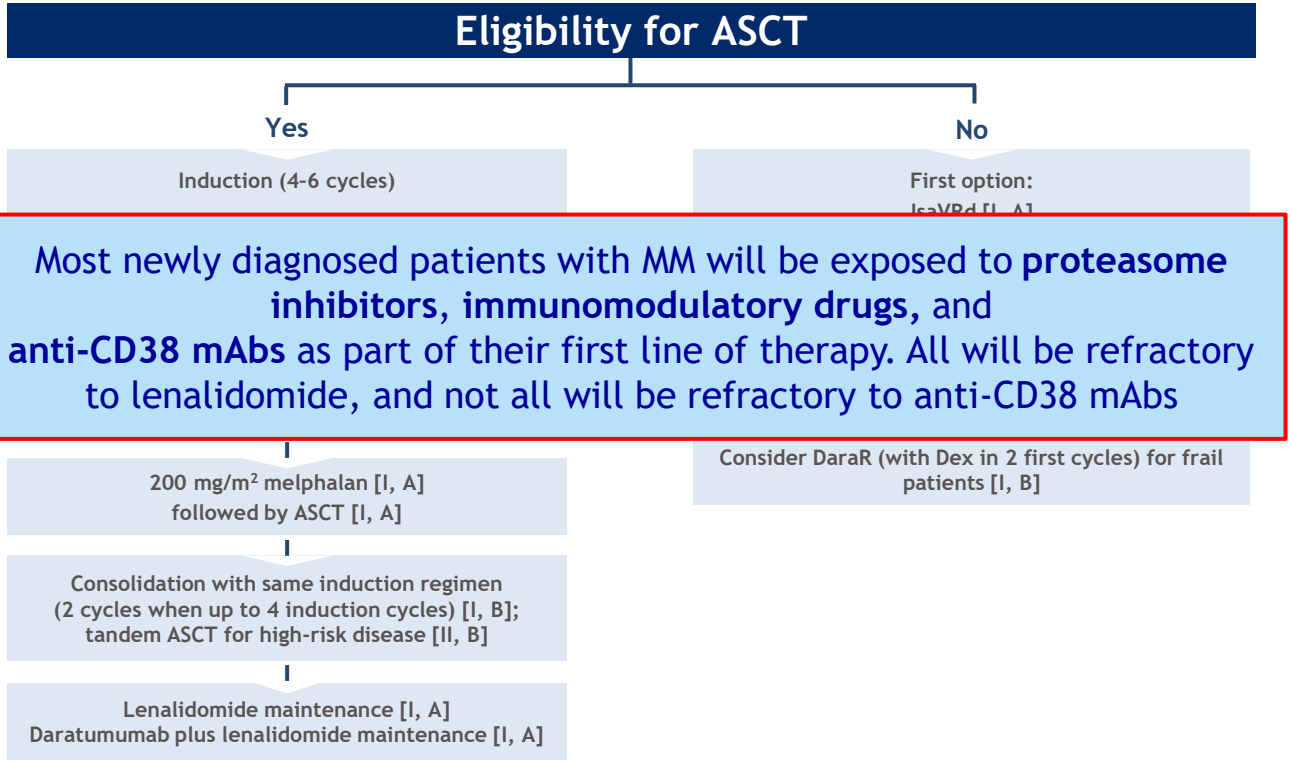


ASCT, autologous stem cell transplantation; Dara, daratumumab; Dex, dexamethasone; EHA, European Hematology Association; EMN, European Myeloma Network; Isa, isatuximab; mAb, monoclonal antibody; MM, multiple myeloma; R, lenalidomide; Rd, lenalidomide-dexamethasone; VMP, bortezomib-melphalan-prednisone; VRd, bortezomib-lenalidomide-dexamethasone; VTd, bortezomib-thalidomide-dexamethasone.

Dimopoulos MA, et al. *Nat Rev Clin Oncol*. 2025;22:680-700. (under minor revision)

EHA-EMN 2025 Guidelines

Newly diagnosed MM: Exposure to proteasome inhibitors, immunomodulatory drugs, and anti-CD38 mAbs



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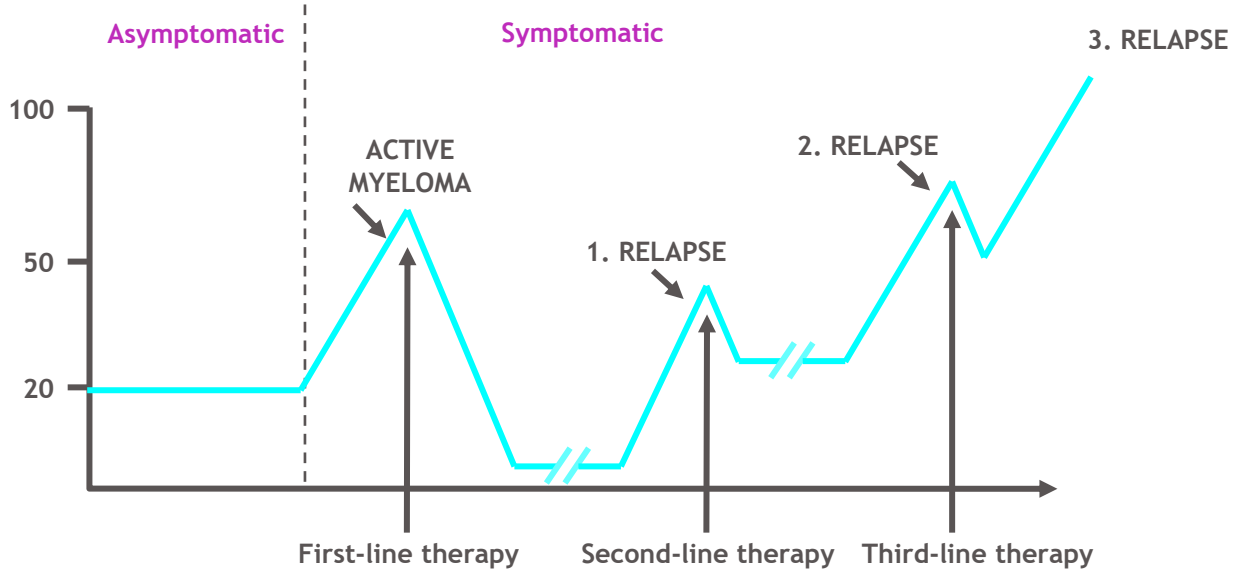
Natural History of Multiple Myeloma



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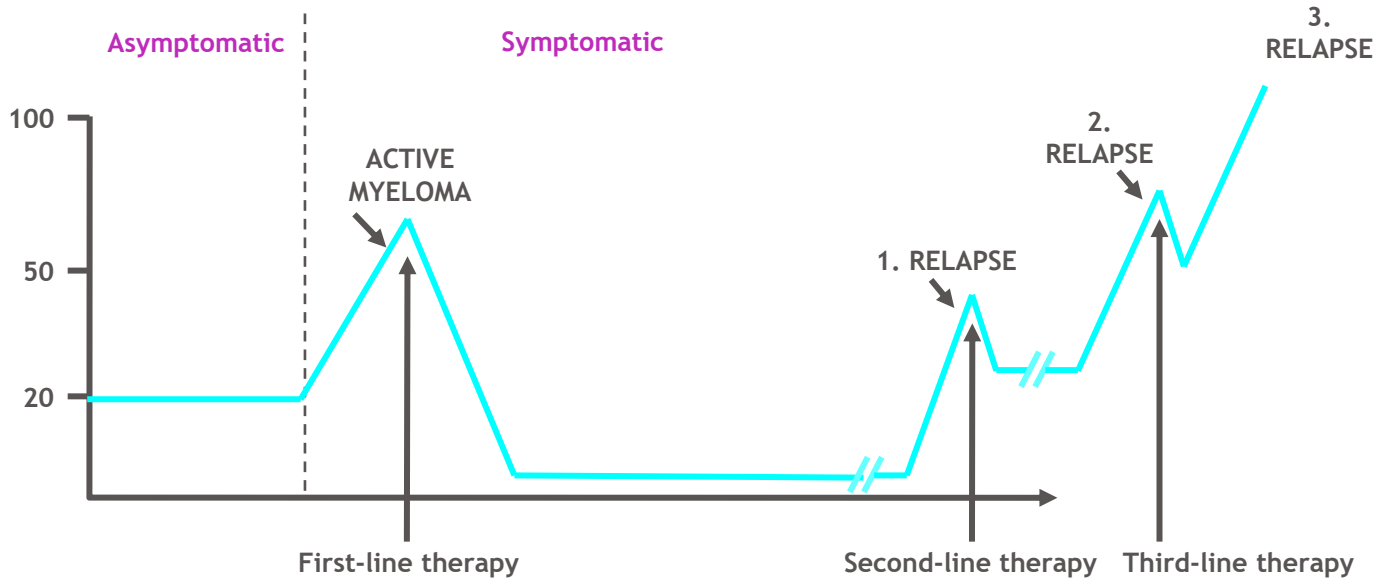
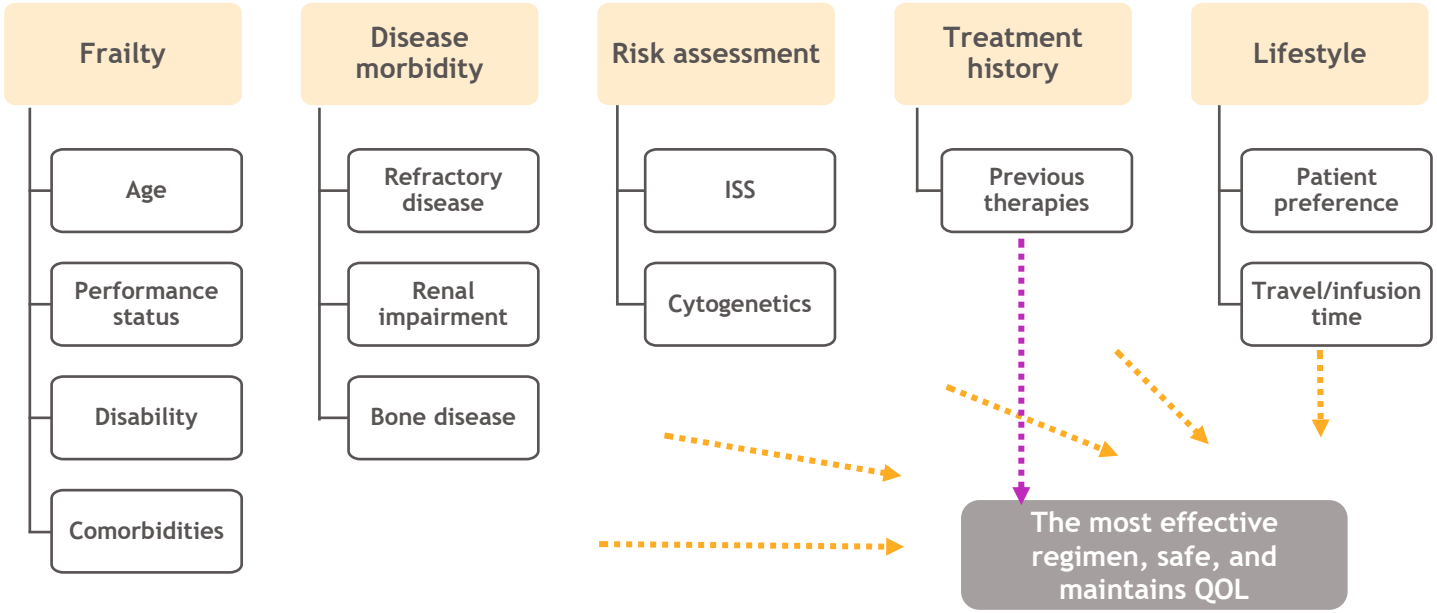


Patients will present later at first relapse
Most patients will be triple-class exposed or Len-Dara exposed, and all will be refractory to lenalidomide

Disease and Patient-Based Factors Influencing Treatment Decision-Making in the Relapse Setting



Treatment history is a crucial factor
Other factors to take into consideration in the relapse setting

Treatment Landscape in Multiple Myeloma

First line

ASCT eligible

Anti-CD38 + PI + IMiD + Dex

ASCT

Len/Dara-Len

ASCT ineligible

Dara-Len-Dex

Dara-VMP/RVd

Anti-CD38 + PI + IMiD + Dex

Second line

Based on sensitivity/refractoriness to daratumumab and lenalidomide

Anti-CD38 + carfilzomib-Dex

Anti-CD38 + pomalidomide-Dex

Pomalidomide-bortezomib-Dex

Selinexor-bortezomib-Dex

Carfilzomib-Dex

Cilta-cel

New combinations

Teclistamab-Dara/Elra-Dara/Elra monotherapy

Talquetamab-Dara

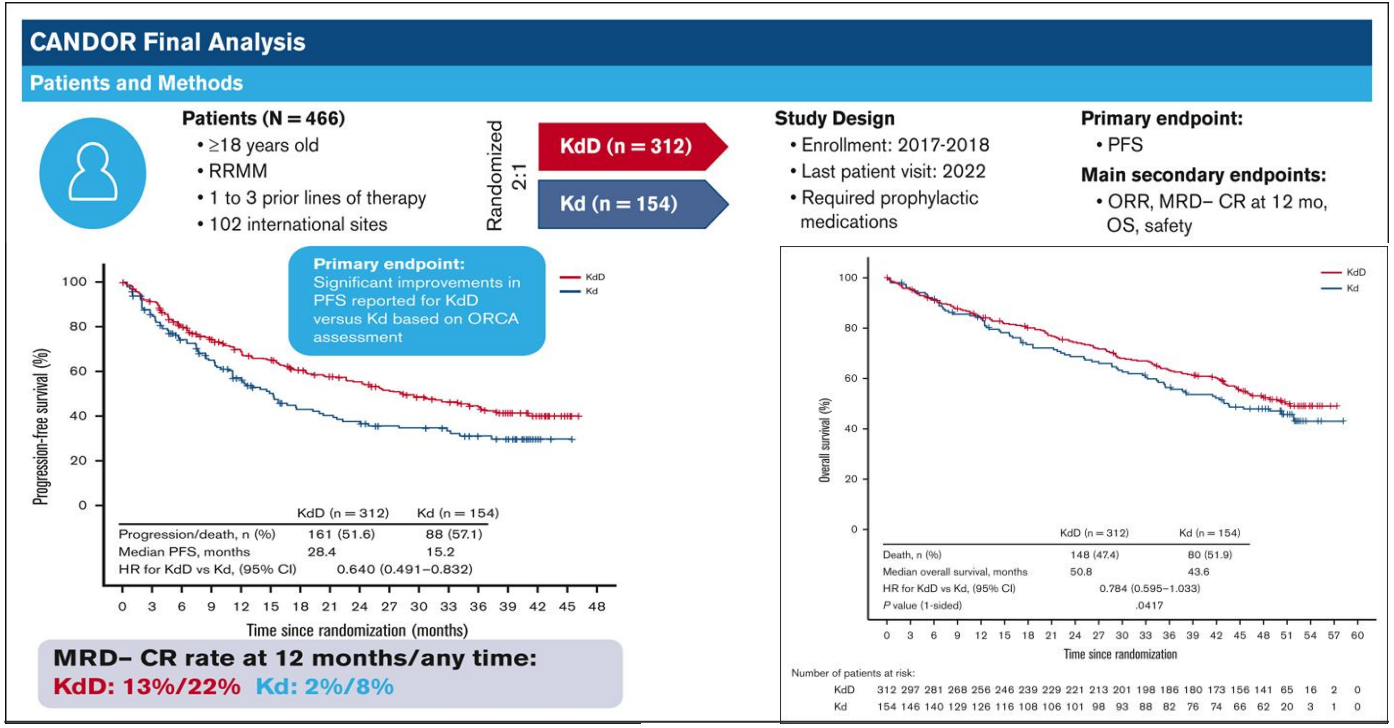
Belantamab-Vd (DREAMM-7)

Belantamab-Pd (DREAMM-8)

How to select the right combination in the near future???

Mateos MV, personal communication; Dimopoulos MA, et al. *Ann Oncol*. 2021;32:309-322.

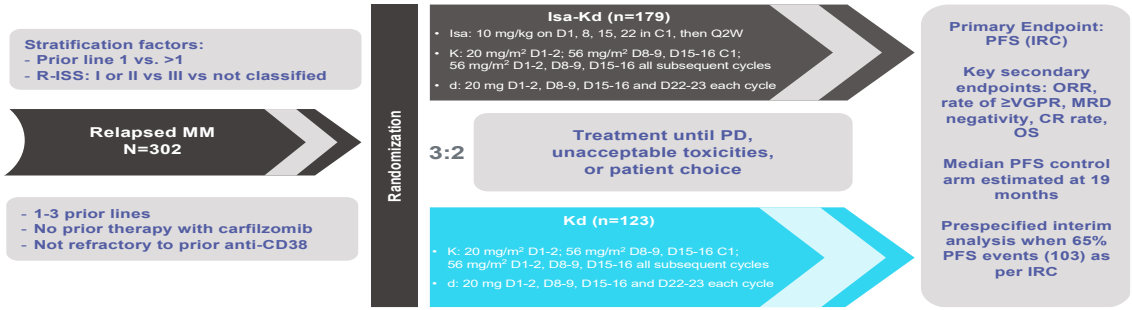
CANDOR: Study Design

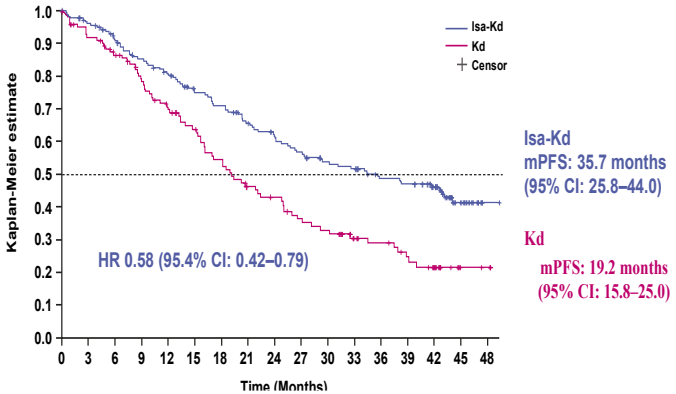


- Hazard ratio for PFS is sustained across all subgroups of patients, including those refractory to lenalidomide (30%) after 1 or more prior lines of therapy
- Safety profile acceptable

Usmani SZ, et al. *Blood Adv*. 2023;7:3739-3748.

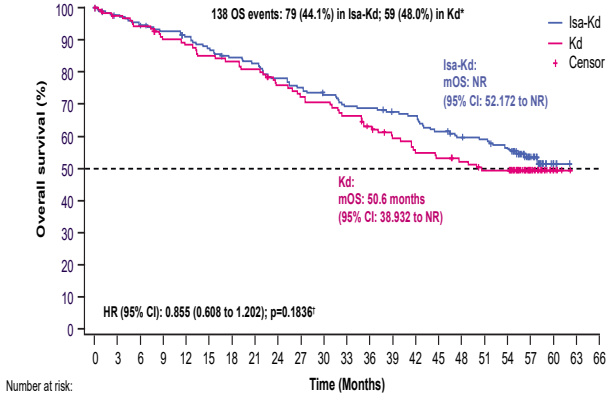
IKEMA: Study Design – Isa-Kd vs Kd in Relapsed Multiple Myeloma





Isa-Kd
mPFS: 35.7 months
(95% CI: 25.8–44.0)

Kd
mPFS: 19.2 months
(95% CI: 15.8–25.0)



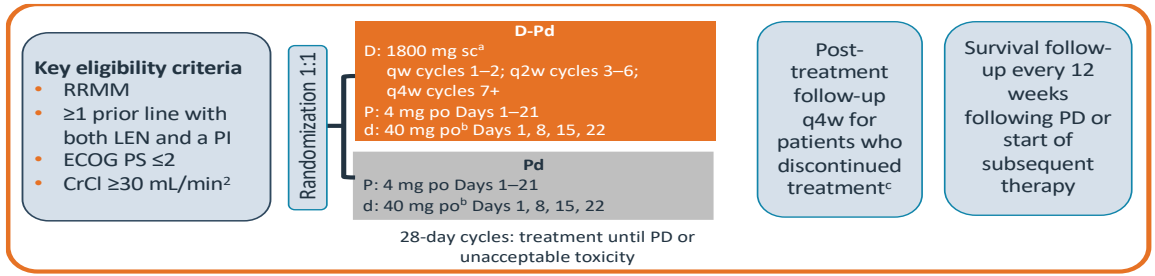
Extrapolating the current observed trend for an additional 12 months of follow-up, the mOS estimate for Isa-Kd arm is **63 months** (95% CI: 59–69)

This corresponds to an estimated 1-year difference in mOS

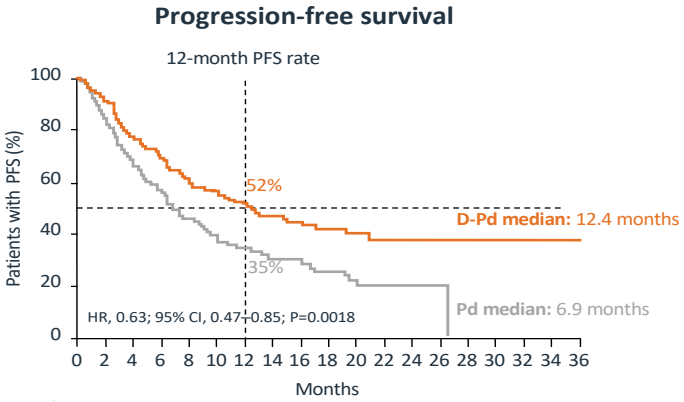
- Hazard ratio for PFS is sustained across all subgroups of patients, including those refractory to lenalidomide (30%) after 1 or more prior lines of therapy
- Safety profile acceptable

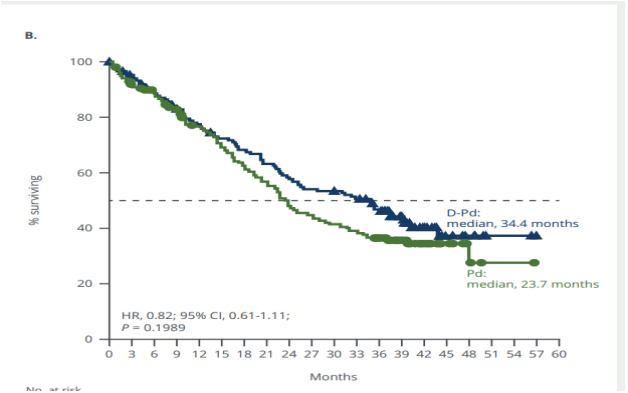
Yong K, et al. *Lancet Haematol*. 2024;11:e741-e750.

APOLLO: Subcutaneous Dara Plus Pom-Dex vs Pom-Dex in RRMM



- **Primary endpoint:** PFS
- **Secondary endpoints:** ORR, ≥VGPR, ≥CR, MRD, OS, time to response, DoR, time to next therapy, safety, HRQoL





- The number of patients included after 1 PL is rather small (11% of patients)
- 80% of patients were Len refractory, and the median PFS in Len-refractory patients is 9.9 months for Dara-Pd and 6.5 months for Pd
- Safety profile acceptable

Treatment Landscape in Multiple Myeloma

First line

ASCT eligible

Anti-CD38 + PI + IMiD + Dex

ASCT

Len/Dara-Len

ASCT ineligible

Dara-Len-Dex

Dara-VMP/RVd

Anti-CD38 + PI + IMiD + Dex

Second line

Based on sensitivity/refractoriness to daratumumab and lenalidomide

Anti-CD38 + carfilzomib-Dex

Anti-CD38 + pomalidomide-Dex

Pomalidomide-bortezomib-Dex

Selinexor-bortezomib-Dex

Carfilzomib-Dex

Cilta-cel

New combinations

Teclistamab-Dara/Elra-Dara/Elra monotherapy

Talquetamab-Dara

Belantamab-Vd (DREAMM-7)

Belantamab-Pd (DREAMM-8)

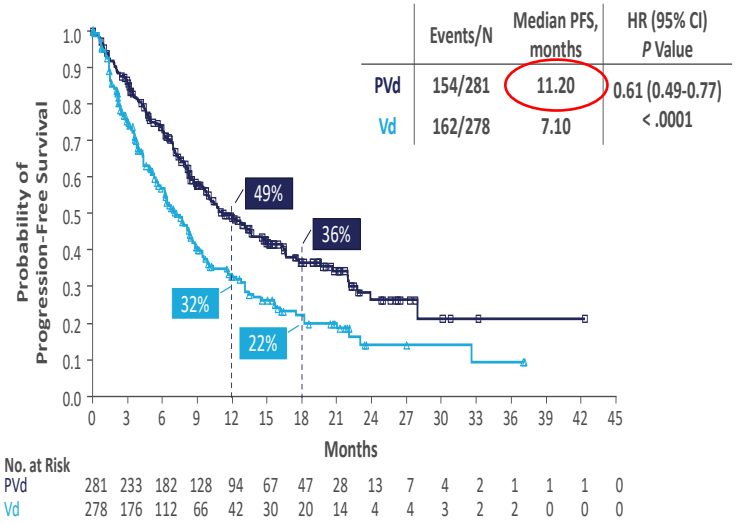
How to select the right combination in the near future???

Mateos MV, personal communication; Dimopoulos MA, et al. *Ann Oncol*. 2021;32:309-322.

OPTIMISMM: PVd vs Vd in Patients With RRMM

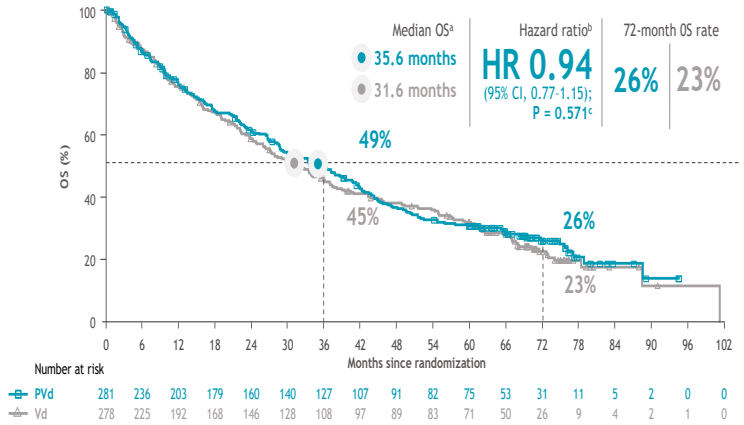
559 patients; median 2 prior lines of therapy; 100% Len exposed; 70% Len refractory; 63% Len refractory as part of the last line of therapy

PVd reduced the risk of progression and death by 39% compared with Vd



	Events/N	Median PFS, months	HR (95% CI) *P* Value
PVd	154/281	11.20	0.61 (0.49-0.77)
Vd	162/278	7.10	< .0001

OS: ITT population



Median OS was numerically longer for PVd versus Vd, but this difference was not statistically significant

- Median PFS for PVd in patients refractory to Len after the first line of therapy was 17.8 months
- Safety profile acceptable

Richardson P, et al. *J Clin Oncol*. 2018;36:2492-2503. Abstract 8001.

BOSTON: Selinexor Vd vs Vd in Patients With RRMM

- Median age: 66 years (SVd) vs 67 years (Vd)
- 2 prior lines: 33% vs 31%; 3 prior lines: 16% vs 21%
- High-risk cytogenetics: 50% vs 46%
- Lenalidomide exposed: 39.5% vs 37.2%

	SVd arm (n = 195)	Vd arm (n = 207)
Median PFS, months (95% CI)*	13.93 (11.73, NE)	9.46 (8.11, 10.78)
HR=0.70 (95% CI: 0.53, 0.93); one-sided *P* = .0075		

Kaplan-Meier estimates of progression-free survival among patients in the ITT population

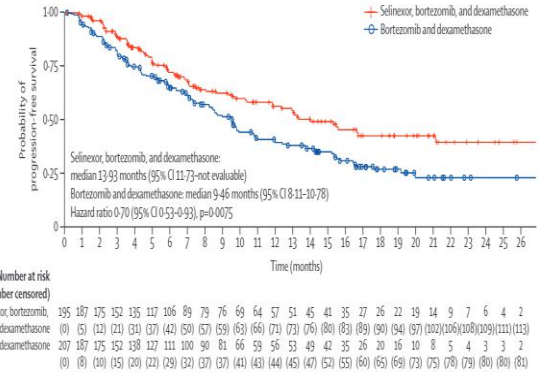
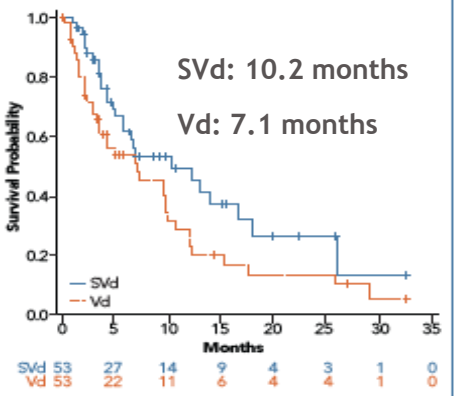
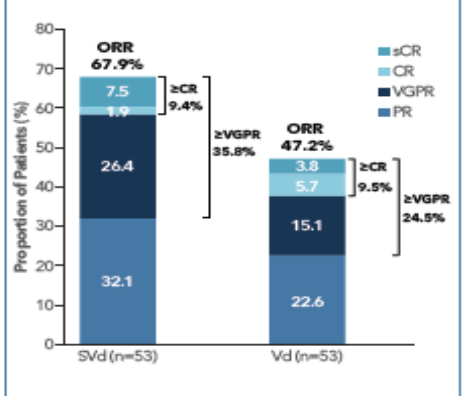


Figure 1. PFS in Lenalidomide-Refractory Patients



*ITTNT was calculated from the date of randomization to the start of next anti-MM treatment or death, whichever occurred first. Patients without an event were censored at the date of discontinuation from the study or last participating visit or database cut-off date, whichever occurred first.

Figure 2. Response in Lenalidomide-Refractory Patients



CR, complete response; ORR, overall response rate; PR, partial response; sCR, stringent complete response; SVd, selinexor + bortezomib + dexamethasone; Vd, bortezomib + selinexor; VGPR, very good partial response.

- 106 patients in the BOSTON trial were Len refractory, and the majority of them were after 2 or 3 PL

- Safety profile was acceptable, and for those patients in whom the dose was modified, the outcome was better
- No significant benefit reported in overall survival

Grosicki S, et al. *Lancet*. 2020;396:1563-1573.

Treatment Landscape in Multiple Myeloma

First line

ASCT eligible

Anti-CD38 + PI + IMiD + Dex

ASCT

Len/Dara-Len

ASCT ineligible

Dara-Len-Dex

Dara-VMP/RVd

Anti-CD38 + PI + IMiD + Dex

Second line

Based on sensitivity/refractoriness to daratumumab and lenalidomide

Anti-CD38 + carfilzomib-Dex

Anti-CD38 + pomalidomide-Dex

Pomalidomide-bortezomib-Dex

Selinexor-bortezomib-Dex

Cilta-cel

New combinations

Teclistamab-Dara/Elra-Dara/Elra monotherapy

Talquetamab-Dara

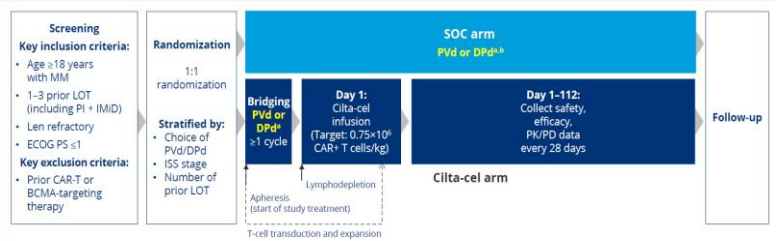
Belantamab-Vd (DREAMM-7)

Belantamab-Pd (DREAMM-8)

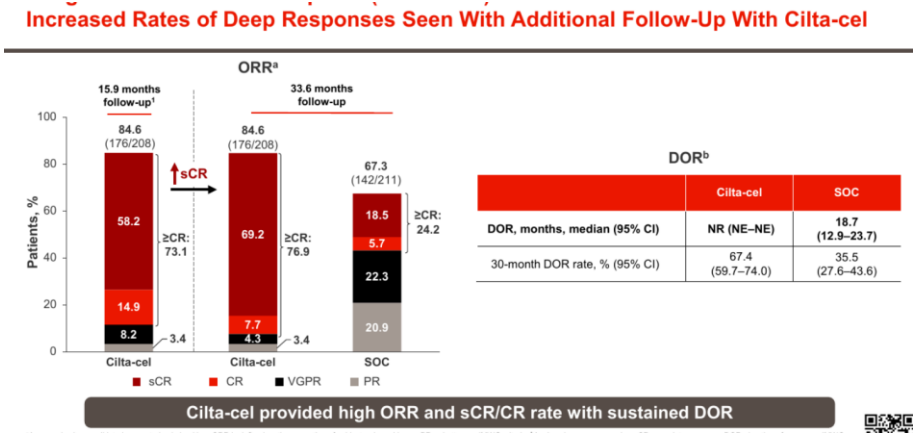
How to select the right combination in the near future???

Mateos MV, personal communication; Dimopoulos MA, et al. *Ann Oncol*. 2021;32:309-322.

CARTITUDE-4: Phase III Trial of Cilta-Cel vs PVd/DPd in Len-Refractory MM After 1-3 PL

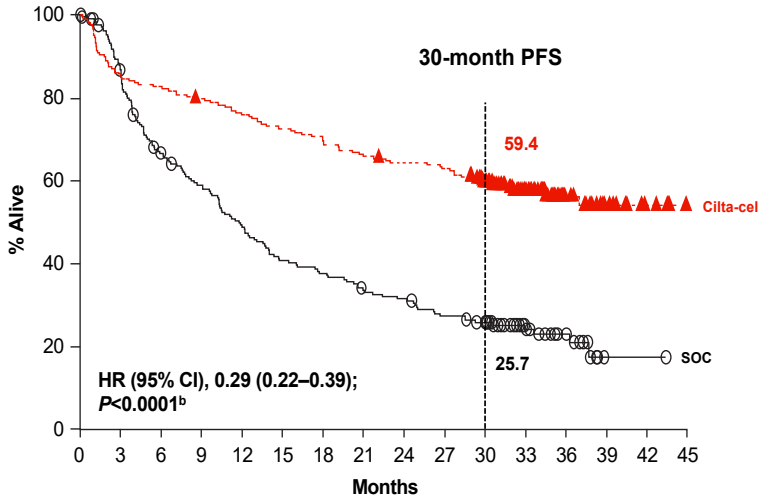


- Median number of PL: 2
- 33% of patients with HRCA and 21% double hit
- 25% TC exposed and 14% TC refractory
- 100% Len refractory

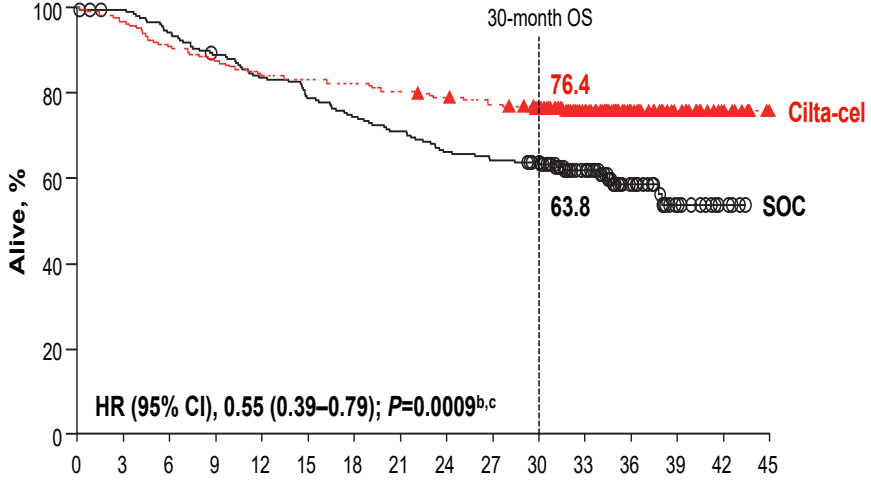


Phase III CARTITUDE-4 Trial: Efficacy

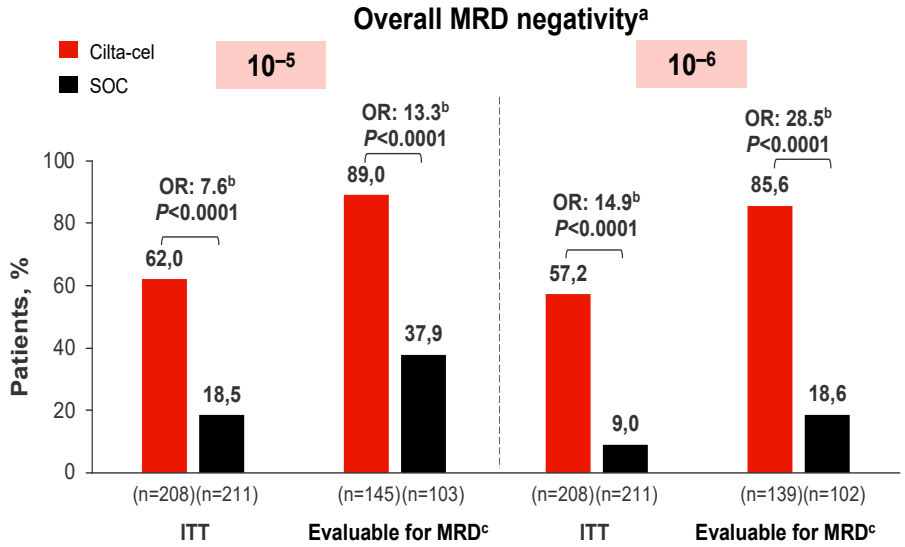
PFS (ITT; 33.6-mo median follow-up)

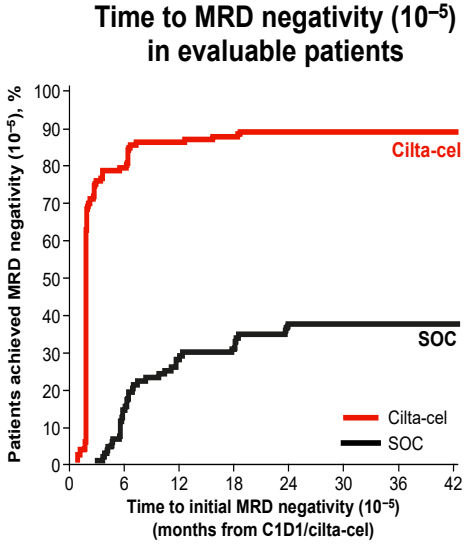


OS (ITT; 33.6-mo median follow-up)



Phase III CARTITUDE-4 Trial: MRD-Negativity Analysis



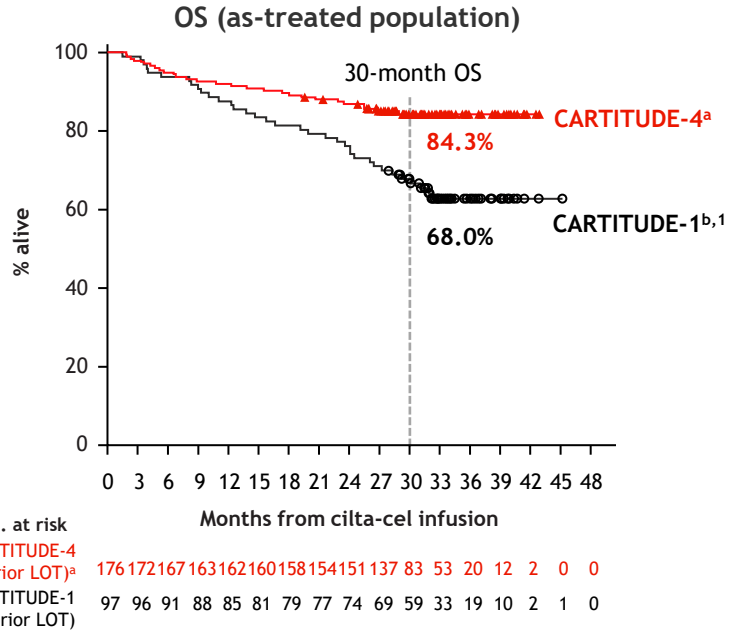


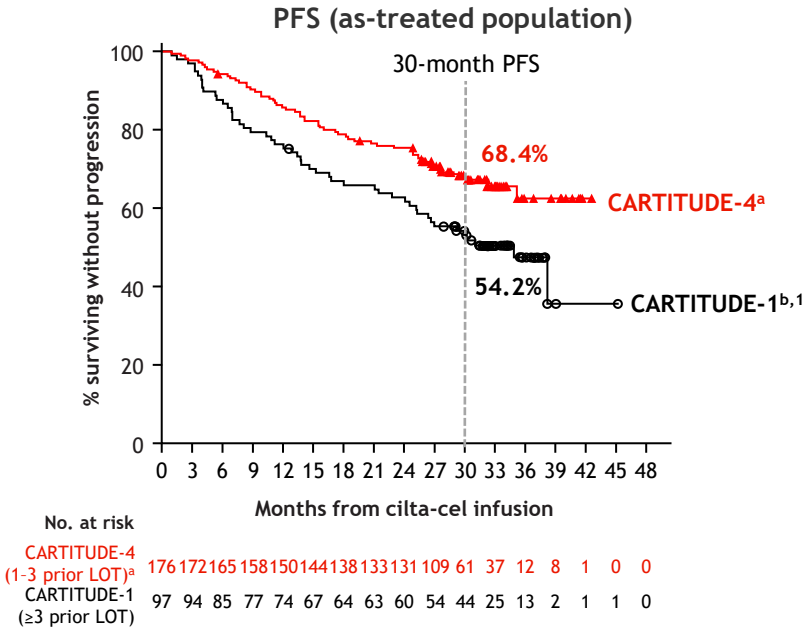
- 69% of evaluable patients achieved MRD negativity (10^{-5}) by day 56 (ITT, 48%), rising to 86% (ITT, 60%) by 6 months post cilta-cel infusion

- **High rates of overall MRD negativity are rapidly achieved with Cilta-cel**, and almost all patients receiving Cilta-cel negative at 10^{-5} **were also negative at** 10^{-6}
- Across subgroups, Cilta-cel **increased overall MRD-negativity rates** at the 10^{-5} threshold vs SOC

Popat R, et al. ASH 2024. Abstract 1032.

Long-Term CARTITUDE-4 Update (34 months): Numerically Higher OS and PFS Rates vs CARTITUDE-1





Cilta-cel use in earlier lines demonstrated numerically higher rates of overall and progression-free survival

[a]Re-baselined to begin at time of cilta-cel infusion for patients who received cilta-cel as study treatment, with median follow-up of 30.5 months; [b]33.4-month median follow-up.
Cilta-cel, ciltacabtagene autoleucel; LOT, line of therapy; OS, overall survival; PFS, progression-free survival; SOC, standard of care.

1. Lin Y, et al. ASCO 2023.Abstract 8009.

Treatment Landscape in Multiple Myeloma

First line

ASCT eligible

Anti-CD38 + PI + IMiD + Dex

ASCT

Len/Dara-Len

ASCT ineligible

Dara-Len-Dex

Dara-VMP/RVd

Anti-CD38 + PI + IMiD + Dex

Second line

Based on sensitivity/refractoriness to daratumumab and lenalidomide

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Anti-CD38 + pomalidomide-Dex

Pomalidomide-bortezomib-Dex

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Carfilzomib-Dex

Cilta-cel

Belantamab-Vd (DREAMM-7)

Belantamab-Pd (DREAMM-8)

New combinations

Teclistamab-Dara/Elra/Tec monotherapy

Talquetamab-Pom or Tec-Tal

Tal-Dara or Tal-Pom-Dara

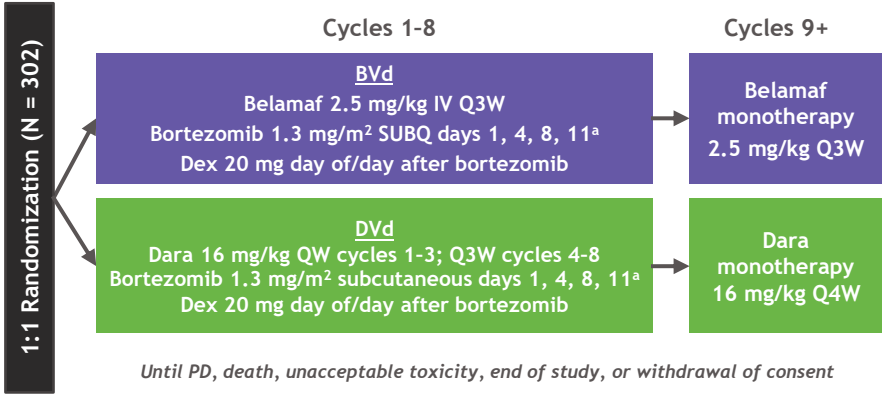
Linvoseltamab

Etentamig

Mateos MV, personal communication; Dimopoulos MA, et al. *Ann Oncol*. 2021;32:309-322.

DREAMM-7: Phase III Trial of BVd vs DVd in RRMM – Study Design and Patients

Key Eligibility Criteria
- ≥1 prior LOT and PD during or after most recent therapy
- **No prior anti-BCMA**
- **Not refractory to or intolerant of daratumumab or bortezomib**



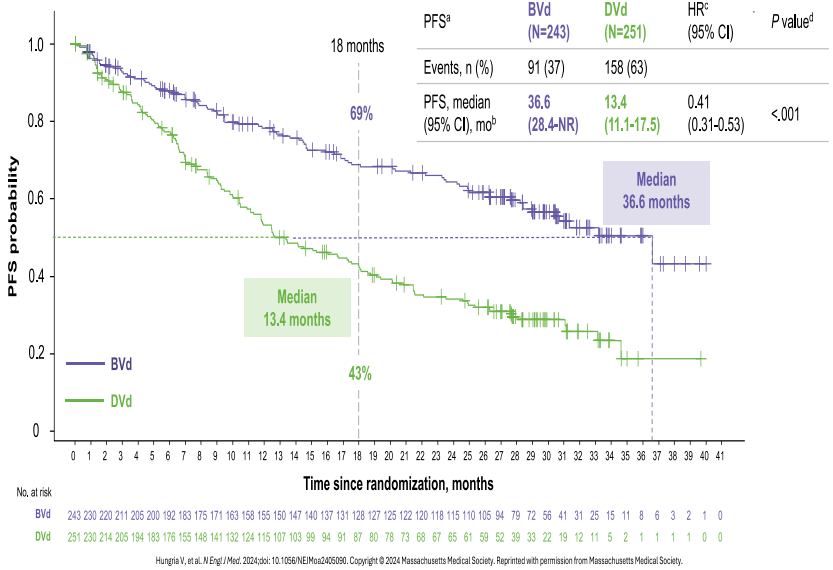
Primary endpoint: PFS (IRC)
Key secondary endpoints: OS, DOR, MRD

Patient Characteristics[b]		BVd (n = 243)	DVd (n = 251)
Median age (range), years		65.0 (34-86)	64.0 (32-89)
ECOG PS ≤1, n (%)		232 (96)	235 (96)
R-ISS stage I at screening, n (%)		102 (42)	103 (41)
High-risk cytogenetics, n (%)		67 (28)	69 (27)
t(4;14)		41 (61)	42 (61)
t(14;16)		8 (12)	6 (9)
del(17p13)		30 (45)	33 (51)
Prior LOT, n (%)	1	125 (51)	125 (50)
	2 or 3	88 (36)	99 (39)
	≥4	30 (12)	27 (11)
Prior treatment, n (%)	Bortezomib	210 (86)	211 (84)
	Daratumumab	3 (1)	4 (2)
	Lenalidomide	127 (52)	130 (52)
Refractory to Len, n (%)		79 (33)	87 (35)
Refractory (n = 79/87) or not (n = 164/164) by prior LOT, n (%)[b]	1	22 (28)/103 (63)	27 (31)/98 (60)
	2	24 (30)/30 (18)	21 (24)/42 (26)
	3+	33 (42)/31 (19)	39 (45)/24 (15)

[a]21-day cycles; [b]Subgroup analyses by high- vs standard-risk cytogenetics and Len refractory vs not Len refractory are noted by the blue shading; [c]Post hoc analysis.

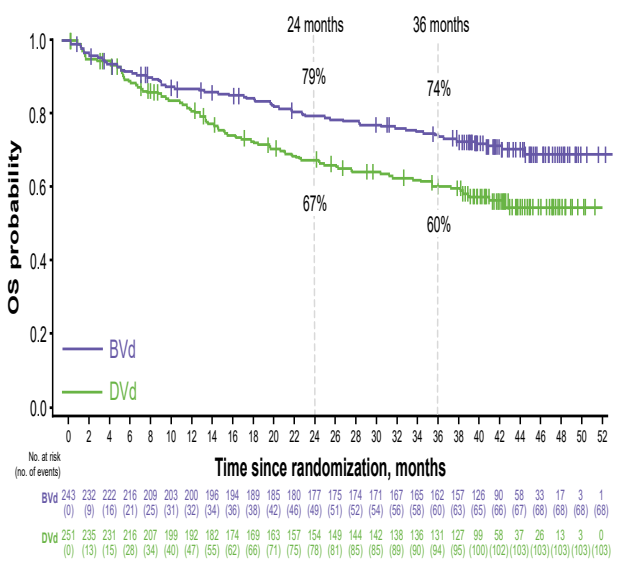
DREAMM-7: Phase III Trial of BVd vs DVd in RRMM – PFS/OS in All Patients

PFS



PFS[a]	BVd (N=243)	DVd (N=251)	HR[c] (95% CI)	*P* value[d]
Events, n (%)	91 (37)	158 (63)		
PFS, median (95% CI), mo[b]	36.6 (28.4-NR)	13.4 (11.1-17.5)	0.41 (0.31-0.53)	<.001

OS

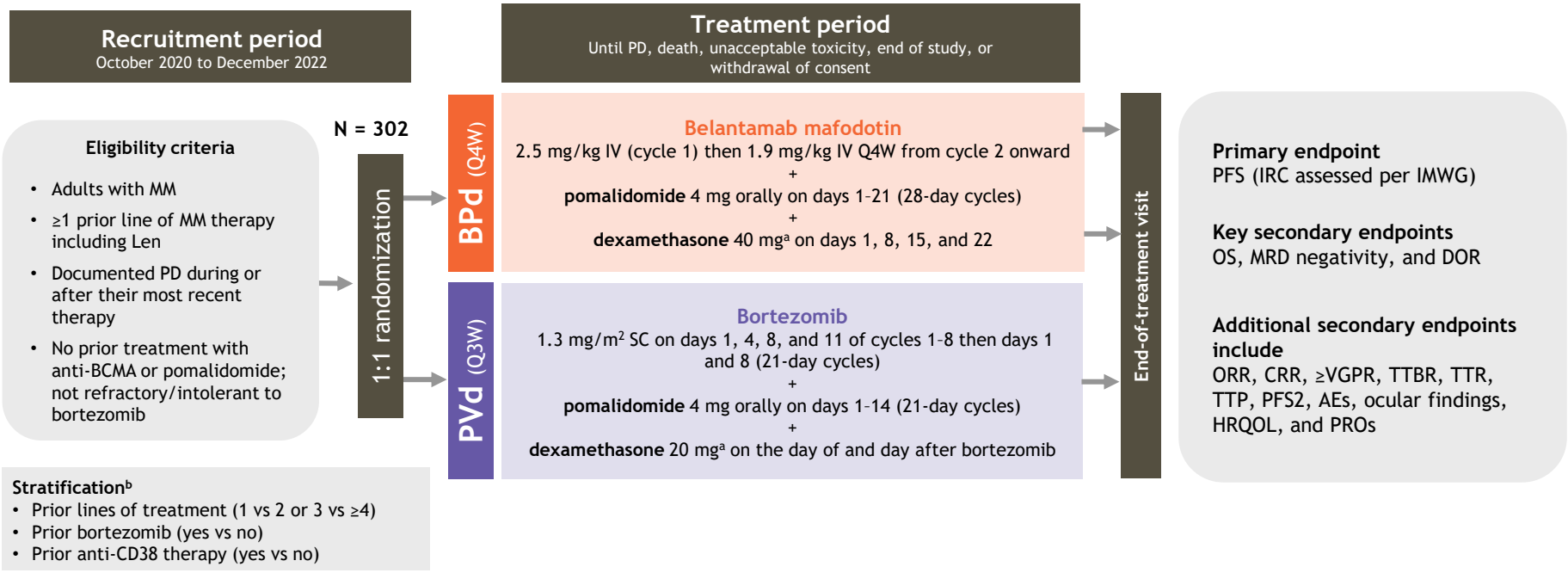


OS[a]	BVd (N=243)	DVd (N=251)
Events, n (%)	68 (28)	103 (41)
OS, median (95% CI), months[b]	NR (NR-NR)	NR (41.0-NR)
HR (95% CI)[c]	**0.58 (0.43-0.79)**	
P value[d]	**.00023**	
24-Month survival (95% CI), %	79 (73-84)	67 (61-73)
36-Month survival (95% CI), %	74 (68-79)	60 (54-66)

- **BVd demonstrated statistically significant and clinically meaningful PFS benefit (HR, 0.41; 95% CI, 0.31-0.53; *P* <.001), with a median PFS that was 23 months longer than that with DVd (36.6 months vs 13.4 months)**
- **Median OS was not reached. Predicted median OS based on modeling is 84 months with BVd and 51 months with DVd**

Hungria V, et al. *N Engl J Med*. 2024;393-407; Hungria V, et al. ASH 2024. Abstract 772.

DREAMM-8: Phase III Study Examining a Belantamab Mafodotin-Based Combination in 2L+ RRMM (NCT04484623)



[a]Patients aged >75 years, with comorbidities, or intolerant to 40 mg dose in Arm A or 20 mg dose in Arm B could have dose level reduced to half per investigator discretion; [b]Some patients were stratified by ISS status (I vs II/III); the protocol was amended on April 20, 2021, to replace this randomization factor with prior anti-CD38 treatment (yes vs no).

2L, second line: AE, adverse event; BCMA, B-cell maturation antigen; BPd, belamaf, pomalidomide, and dexamethasone; CD, cluster of differentiation; CRR, complete response rate; DOR, duration of response; HRQOL, health-related quality of life; IMWG, International Myeloma Working Group; IRC, independent review committee; ISS, International Staging System; IV, intravenous; LEN, lenalidomide; MM, multiple myeloma; MRD, minimal residual disease; ORR, objective response rate; OS, overall survival; PD, progressive disease; PFS, progression-free survival; PFS2, progression-free survival on subsequent line of therapy; PRO, patient-reported outcome; PVd, pomalidomide, bortezomib, and dexamethasone; Q3W, every 3 weeks; Q4W, every 4 weeks; RRMM, relapsed or refractory multiple myeloma; SC, subcutaneous; TTBR, time to best response; TTP, time to progression; TTR, time to response; VGPR, very good partial response.

DREAMM-8: Baseline Disease Characteristics and Clinical Characteristics

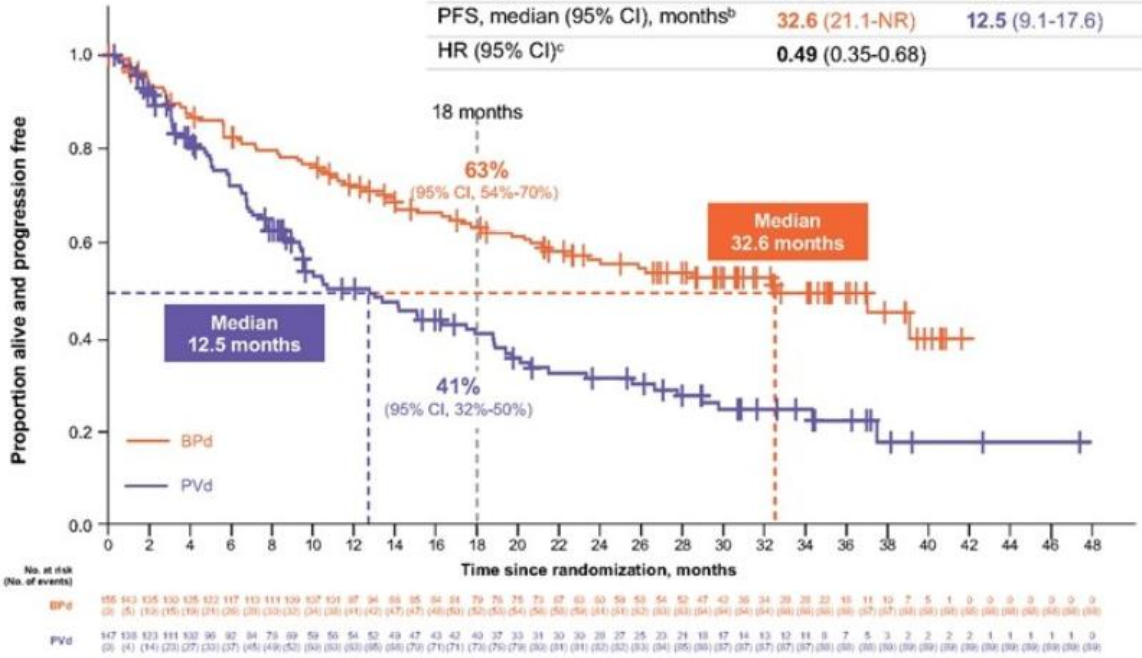
Baseline Characteristics	ITT Population	
	BPd (n = 155)	PVd (n = 147)
Age, median (range), years	67 (40-82)	68 (34-86)
<65, n (%)	64 (41)	53 (36)
65 to <75, n (%)	72 (46)	59 (40)
≥75, n (%)	19 (12)	35 (24)
Male/female, n (%)	99 (64)/56 (36)	82 (56)/65 (44)
White/Black/Asian/Mixed race, n (%)[a]	133 (86)/0/20 (13)/1 (<1)	127 (87)/0/17 (12)/0
ECOG PS ≤1, n (%)[b]	146 (97)	140 (97)
ISS stage at screening, n (%)		
I	93 (60)	85 (58)
II	39 (25)	40 (27)
III	22 (14)	22 (15)
Unknown	1 (<1)	0
Years since diagnosis, median (range)	4.04 (0.4-16.7)	3.43 (0.4-17.7)
Cytogenetic abnormalities, n (%)		
Standard risk[c]	72 (46)	75 (51)
High risk[d]	52 (34)	47 (32)
Missing or nonevaluable[e]	31 (20)	25 (17)
Time to relapse after initiation of 1L treatment		
≤12 months	22 (14)	20 (14)
>12 months	133 (86)	127 (86)
Extramedullary disease, n (%)	20 (13)	11 (7)

Prior Treatments, n (%)	ITT Population			
	BPd (n = 155)		PVd (n = 147)	
Prior LOT				
1	82 (53)		77 (52)	
2 or 3	54 (35)		48 (33)	
≥4	19 (12)		22 (15)	
Prior ASCT	99 (64)		82 (56)	
Prior treatment	Exposed	Refractory	Exposed	Refractory
Prior proteasome inhibitor	140 (90)	40 (26)	136 (93)	35 (24)
Bortezomib	134 (86)	16 (10)	130 (88)	8 (5)
Carfilzomib	34 (22)	18 (12)	37 (25)	23 (16)
Ixazomib	11 (7)	8 (5)	15 (10)	11 (7)
Prior immunomodulatory drug[a]	155 (100)	127 (82)	147 (100)	111 (76)
Lenalidomide	155 (100)	125 (81)	147 (100)	111 (76)
Thalidomide	49 (32)	9 (6)	48 (33)	6 (4)
Prior anti-CD38 monoclonal antibody[b]	38 (25)	35 (23)	42 (29)	36 (24)
Daratumumab	36 (23)	33 (21)	39 (27)	34 (23)
Isatuximab	2 (1)	2 (1)	3 (2)	2 (1)

[a]Mixed race included a patient who was Native Hawaiian or Other Pacific Islander and White; [b]Evaluated in the safety population (BPd, N=150; PVd, N=145). [c]Standard-risk cytogenetics were defined as having negative results for all high-risk abnormalities: t(4;14), t(14;16), or del(17p13); [d]High-risk cytogenetics were defined as the presence of ≥1 of the following: t(4;14), t(14;16), or del(17p13); [e]Patients with considered missing or nonevaluable may not be high or standard risk. Pd, belamaf, pomalidomide, and dexamethasone; ECOG PS, Eastern Cooperative Oncology Group performance status; ISS, International Staging System; ITT, intent to treat; PVd, pomalidomide, bortezomib, and dexamethasone.

DREAMM-8: PFS

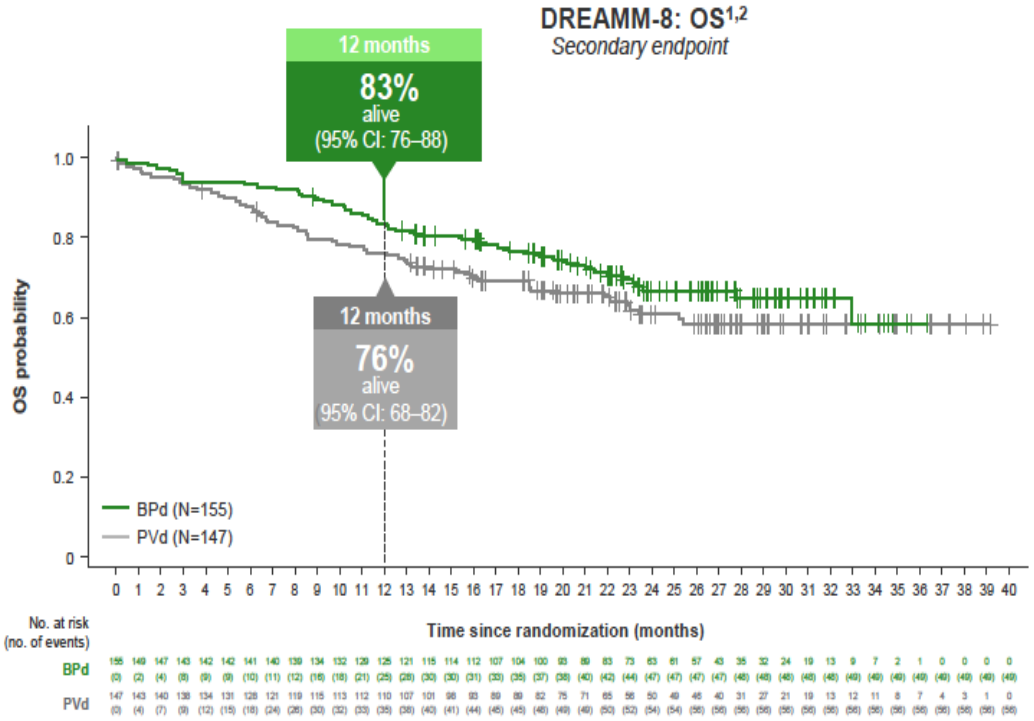
PFS[a]	BPd (N=155)	PVd (N=147)
Events, n (%)	68 (44)	89 (61)
PFS, median (95% CI), months[b]	32.6 (21.1-NR)	12.5 (9.1-17.6)
HR (95% CI)[c]	0.49 (0.35-0.68)	



PFS benefit was observed across all prespecified subgroups, including

- **High-risk cytogenetics: HR 0.57 (95% CI, 0.34-0.95)**
- Bortezomib refractory: HR 0.45 (95% CI, 0.3–0.65)

A Trend Toward Early and Sustained OS Has Been Observed; mOS Has Not Yet Been Reached[1-3a,b]



mOS[c,d] not reached at time of primary analysis[1,2]

- Median follow-up: **21.8 months**[1,2]
- Events, n (%): **BPd, 49 (32); PVd, 56 (38)**[1,2]

Adapted from Dimopoulos MA, et al. *N Engl J Med*. 2024;391:408-421.

Treatment Landscape in Multiple Myeloma

First line

ASCT eligible

Anti-CD38 + PI + IMiD + Dex

ASCT

Len/Dara-Len

ASCT ineligible

Dara-Len-Dex

Dara-VMP/RVd

Anti-CD38 + PI + IMiD + Dex

Second line

Based on sensitivity/refractoriness to daratumumab and lenalidomide

Anti-CD38 + carfilzomib-Dex

Anti-CD38 + pomalidomide-Dex

Pomalidomide-bortezomib-Dex

Selinexor-bortezomib-Dex

Carfilzomib-Dex

Cilta-cel

Belantamab-Vd (DREAMM-7)

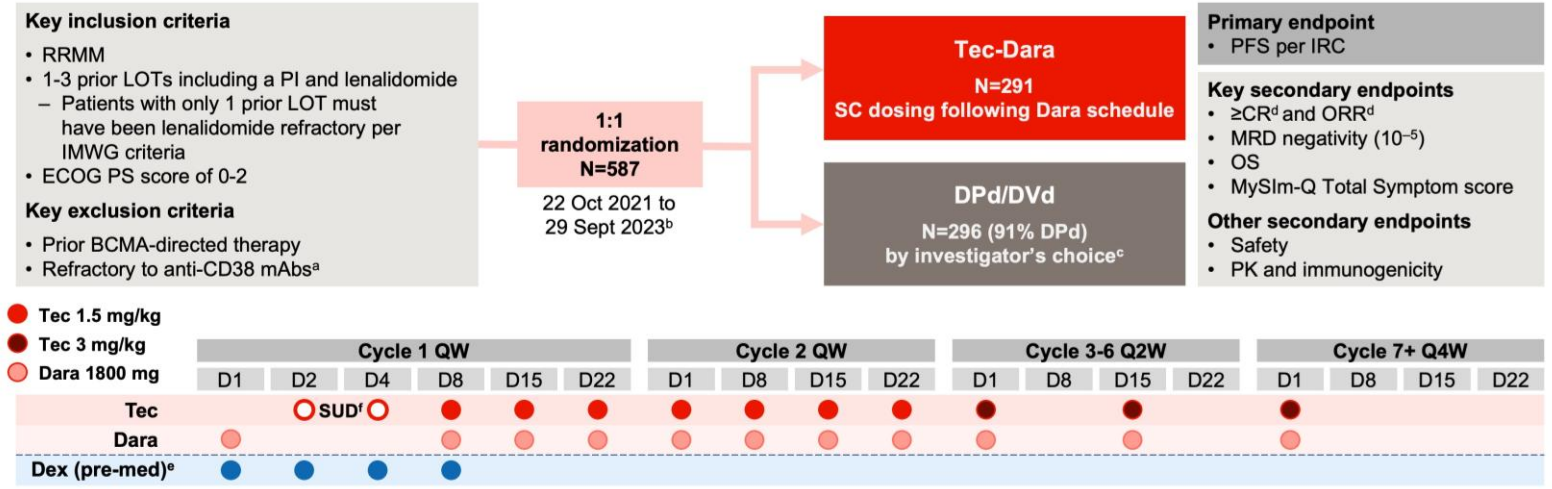
Belantamab-Pd (DREAMM-8)

Teclistamab-daratumumab

What information do we have about BsAbs in earlier lines?

Mateos MV, personal communication; Dimopoulos MA, et al. *Ann Oncol*. 2021;32:309-322.

MajesTEC-3: Phase III Randomized Trial in RRMM Comparing Tec-Dara With DaraPd or DaraVd – Study Design



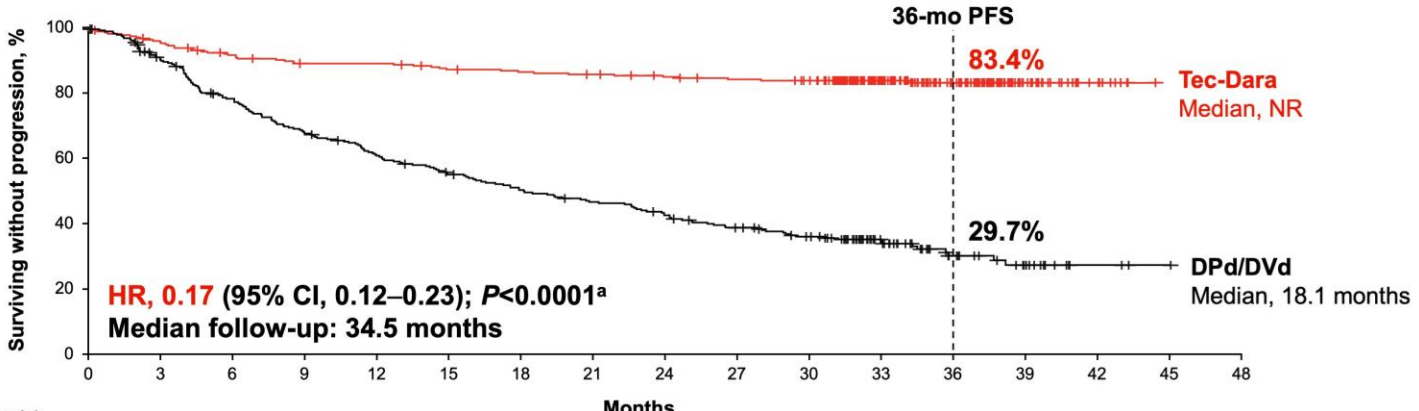
[a]Prior exposure to anti-CD38 mAbs was permitted. [b]During the COVID-19 pandemic. [c]DPd/DVd were administered per the approved schedules. [d]Response and disease progression were assessed by a blinded IRC per IMWG criteria. [e]Dexamethasone, acetaminophen, and diphenhydramine pre-medication was required for the first 2 weeks; subsequent dexamethasone was not required thereafter. [f]Patients received SUD of 0.06 mg/kg and 0.3 mg/kg on Days 2 and 4, respectively.

CR, complete response; D, day; Dex, dexamethasone; DPd, daratumumab, pomalidomide, and dexamethasone; DVd, daratumumab, bortezomib, and dexamethasone; ECOG PS, Eastern Cooperative Oncology Group performance status; IMWG, International Myeloma Working Group; IRC, independent review committee; MRD, minimal residual disease; MySIm-Q, Multiple Myeloma Symptom and Impact Questionnaire; ORR, overall response rate; PFS, progression-free survival; PI, proteasome inhibitor; PK, pharmacokinetics; pre-med, pre-medication; QW, weekly; Q2W, every 2 weeks; Q4W, every 4 weeks; SC, subcutaneous; SUD, step-up dosing.

Presented by M-V Mateos at the 67th American Society of Hematology (ASH) Annual Meeting and Exposition; December 6-9, 2025; Orlando, FL, USA.

Mateos MV, et al. ASH 2025. Abstract LBA-6.

MajesTEC-3: PFS (primary endpoint)



Tec-Dara significantly improved PFS, with a plateauing curve after ~6 months and >90% of patients progression-free at 6 months sustaining such a benefit at 3 years

[a]The *P* value crossed the prespecified stopping boundary for superiority for the first interim analysis (*P*=0.0139).
CI, confidence interval; HR, hazard ratio; NR, not reached.
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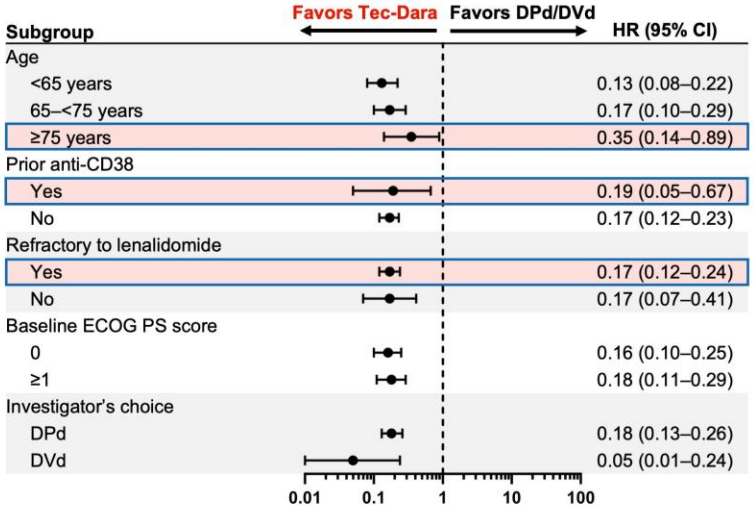
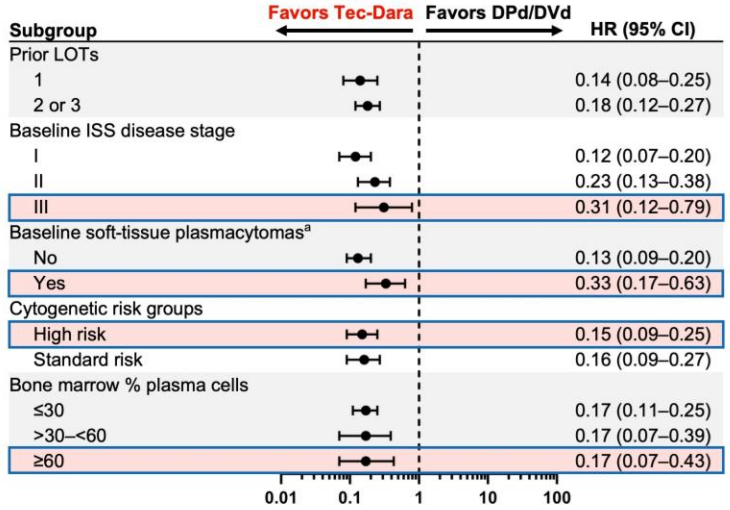
Mateos MV, et al. ASH 2025. Abstract LBA-6.

MajesTEC-3: PFS Subgroup Analysis





Superior PFS with Tec-Dara was consistent across all subgroups[b]

[a]Baseline soft-tissue plasmacytomas contain both extramedullary and paraskeletal plasmacytomas. [b]Not all clinically meaningful and prespecified subgroups that were assessed are shown; however, PFS was improved versus DPd/DVd across all subgroups.

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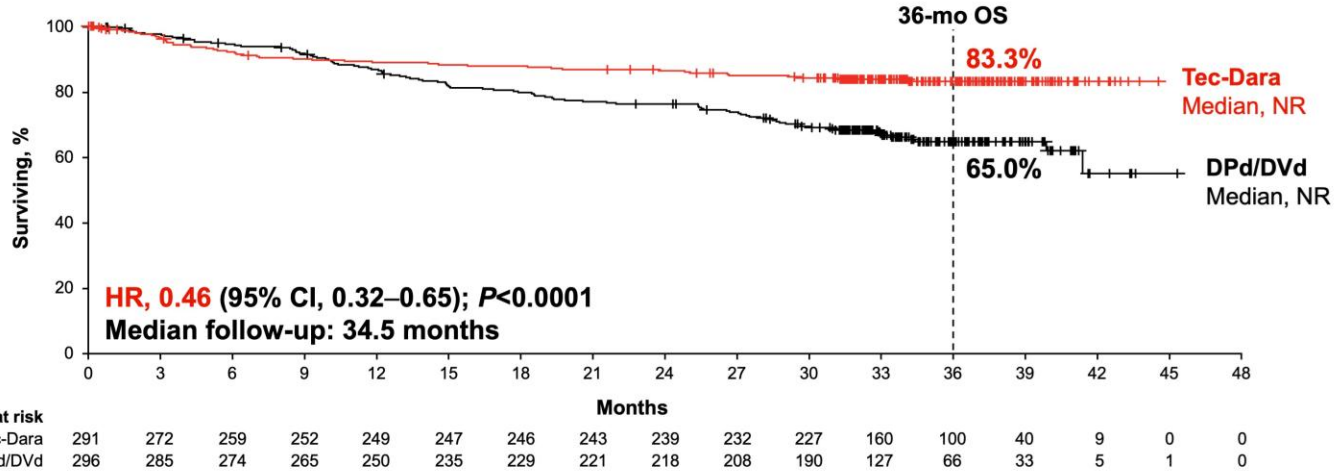
Presented by M-V Mateos at the 67th American Society of Hematology (ASH) Annual Meeting and Exposition; December 6-9, 2025; Orlando, FL, USA.

MajesTEC-3: OS



Tec-Dara significantly improved OS versus DPd/DVd, with 83% of patients alive at 3 years

Analysis of RMST demonstrated an OS benefit for Tec-Dara versus DPd/DVd (RMST difference, 2.15 months; *P*=0.0088).
RMST, restricted mean survival time.
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Presented by M-V Mateos at the 67th American Society of Hematology (ASH) Annual Meeting and Exposition; December 6-9, 2025; Orlando, FL, USA.

MajesTEC-3: Summary of Infections

- Study started during the COVID-19 pandemic and prior to bispecific treatment guidelines
- Hypogammaglobulinemia[a]: 84.5% with Tec-Dara
- 13 (4.6%) deaths due to infection with Tec-Dara[b]
  - 12 occurred within 6 months of treatment (3 due to COVID-19); 9 of 12 patients did not receive IgRT
  - Protocol was subsequently amended in Feb 2023 to reinforce IgRT supplementation and antimicrobial prophylaxis[c]
    - 87.3% received ≥1 dose of Ig[d]
    - 1 infectious death occurred post amendment

TEAE, n (%)	Tec-Dara (n=283)		DPd/DVd (n=290)	
	Any grade	Grade 3/4	Any grade	Grade 3/4
Any infection	273 (96.5)	153 (54.1)	244 (84.1)	126 (43.4)
Treatment-emergent infection or infestation[e]				
COVID-19	124 (43.8)	17 (6.0)	97 (33.4)	6 (2.1)
URTI	115 (40.6)	12 (4.2)	88 (30.3)	7 (2.4)
Pneumonia	65 (23.0)	47 (16.6)	53 (18.3)	43 (14.8)
Nasopharyngitis	62 (21.9)	0	57 (19.7)	0
Sinusitis	52 (18.4)	5 (1.8)	17 (5.9)	3 (1.0)
Rhinovirus infection	44 (15.5)	5 (1.8)	10 (3.4)	1 (0.3)
Bronchitis	40 (14.1)	2 (0.7)	31 (10.7)	6 (2.1)
Influenza	38 (13.4)	8 (2.8)	43 (14.8)	10 (3.4)
COVID-19 pneumonia	34 (12.0)	32 (11.3)	12 (4.1)	7 (2.4)
UTI	29 (10.2)	4 (1.4)	27 (9.3)	1 (0.3)

Infections with Tec-Dara require diligent use of established IgRT and prophylaxis protocols

[a]Hypogammaglobulinemia was defined as patients with ≥1 TEAE of hypogammaglobulinemia or a post-baseline IgG value <400 mg/dL. Rate of hypogammaglobulinemia in the DPd/DVd arm was 60.3%. [b]In the DPd/DVd group, 4 patients had a fatal infection, 2 of which occurred after the implementation of protocol amendment #6. [c]Protocol amendment #6 affirmed the importance of medical monitoring of IgG levels and adherence to protocol-specified Ig supplementation guidance. [d]Percentage at clinical cutoff. [e]Most common defined as occurring in ≥10% of patients in either treatment group; shown with percent occurrence of respective grade 3/4 infection.
Ig, immunoglobulin; IgG, immunoglobulin G; IgRT, immunoglobulin replacement therapy; UTI, urinary tract infection.

Presented by M-V Mateos at the 67th American Society of Hematology (ASH) Annual Meeting and Exposition; December 6-9, 2025; Orlando, FL, USA.

MajesTEC-3: Conclusions

Synergistic[1] immunotherapy combination of Tec-Dara versus DPd/DVd in 1-3 prior LOTs in RRMM:

- Greatest PFS treatment effect to date (HR, 0.17),[2-6] with plateauing curve after ~6 months suggesting potential for functional cure
  - Benchmark 83.4% PFS rate at 3 years, with clear benefit in patients with high-risk cytogenetics, EMD, ISS stage III, and prior anti-CD38 exposure
- Superior OS (HR, 0.46)
- Grade ≥3 infections were highest in the first 6 months, then declined over time; patients should be supported with infection prophylaxis, monitoring, and established IgRT supplementation protocols
- CRS profile and combinability of Tec with Dara on approved Dara schedule support potential for community adoption

Tec-Dara showed unprecedented efficacy, supporting a new 2L+ SOC with broad potential across academic and community settings

1. Vishwamitra D, et al. Presented at: ASH Annual Meeting and Exposition; December 7-10, 2024; San Diego, CA, USA. Oral 594. 2. San-Miguel J, et al. *N Engl J Med*. 2023;389:335-347. 3. Usmani SZ, et al. *Blood Adv*. 2023;7:3737-3748. 4. Hungria V, et al. *N Engl J Med*. 2024;391:393-407. 5. Dimopoulos MA, et al. *N Engl J Med*. 2024;391:408-421. 6. Martin T, et al. *Blood Cancer J*. 2023;13:72.
EMD, extramedullary disease.

Presented by M-V Mateos at the 67th American Society of Hematology (ASH) Annual Meeting and Exposition; December 6-9, 2025; Orlando, FL, USA.

This combination has just been approved by the FDA

Phase III Clinical Trials With BsAbs in Earlier Lines of Therapy

Clinical Trial	Bispecific Antibodies	Control Arm	N	Key Criteria
MajesTEC-3	Teclistamab-Dara	DPd or DVd	587	Patients exposed to PI and IMiD after 1-3 PL Patients refractory to anti-CD38 not allowed
MagnetisMM-5	Elranatamab	DPd	450	Patients exposed to PI and IMiD after at least 1 PL Patients exposed to anti-CD38 and anti-BCMA allowed, but after a washout period of at least 6 months
MajesTEC-9	Teclistamab	Kd or PVd	590	Patients exposed to anti-CD38 and Len after 1-3 PL
MagnetisMM-32	Elranatamab	Kd, PVd, or EloPd	492	Patients exposed to anti-CD38 and Len after 1-4 PL
MonumenTAL-3	Teclistamab-Talquetamab Talquetamab-Pom	EloPd or PVd	795	Patients exposed to anti-CD38 and Len after 1-4 PL
MonumenTAL-1	Talquetamab-Dara Talquetamab-Pom-Dara	DaraPd	810	Patients exposed to PI and IMiD after at least 1 PL Patients after 1 PL must be Len refractory
LinkerMM-3	Linvoseltamab	EloPd	300	Patients exposed to PI and IMiD after 1-4 PL
CERVINO	Etentamig	EloPd, SVd, or Kd	380	Patients triple-class exposed after at least 2 PL

These trials are recruiting, and some have already finalized their recruitment

Information on the trials is from clinicaltrials.gov.

MajesTEC-9: Tec Monotherapy vs PVd or Kd in Patients With RRMM - Press Release

TECVAYLI® monotherapy demonstrates superior progression-free and overall survival versus standard of care as early as first relapse in patients with multiple myeloma predominantly refractory to anti-CD38 therapy and lenalidomide

TECVAYLI® alone reduced risk of disease progression or death by 71% in a high unmet need population

MajesTEC-9 is the second positive Phase 3 study to support TECVAYLI® regimens as a potential new standard of care as early as first relapse

- HR for PFS: 0.29
- HR for OS: 0.60
- Safety profile of Tec was clinically manageable using established protocols and consistent with its known safety profile, with no new safety concerns identified

MonumenTAL-3	Teclistamab-Talquetamab Talquetamab-Pom	EloPd or PVd	795	Patients exposed to anti-CD38 and Len after 1-4 PL

This study will report data soon

Treatment Landscape in Multiple Myeloma

First line

ASCT eligible

Anti-CD38 + PI + IMiD + Dex

ASCT

Len/Dara-Len

ASCT ineligible

Dara-Len-Dex

Dara-VMP/RVd

Anti-CD38 + PI + IMiD + Dex

Second line

Based on sensitivity/refractoriness to daratumumab and lenalidomide

Anti-CD38 + carfilzomib-Dex

Anti-CD38 + pomalidomide-Dex

Pomalidomide-bortezomib-Dex

Selinexor-bortezomib-Dex

Carfilzomib-Dex

Cilta-cel

Belantamab-Vd (DREAMM-7)

Belantamab-Pd (DREAMM-8)

Teclistamab-daratumumab

Teclistamab s/a

Elranatamab s/a

Tal-Dara-Pom and Tal-Dara

Tal-Tec

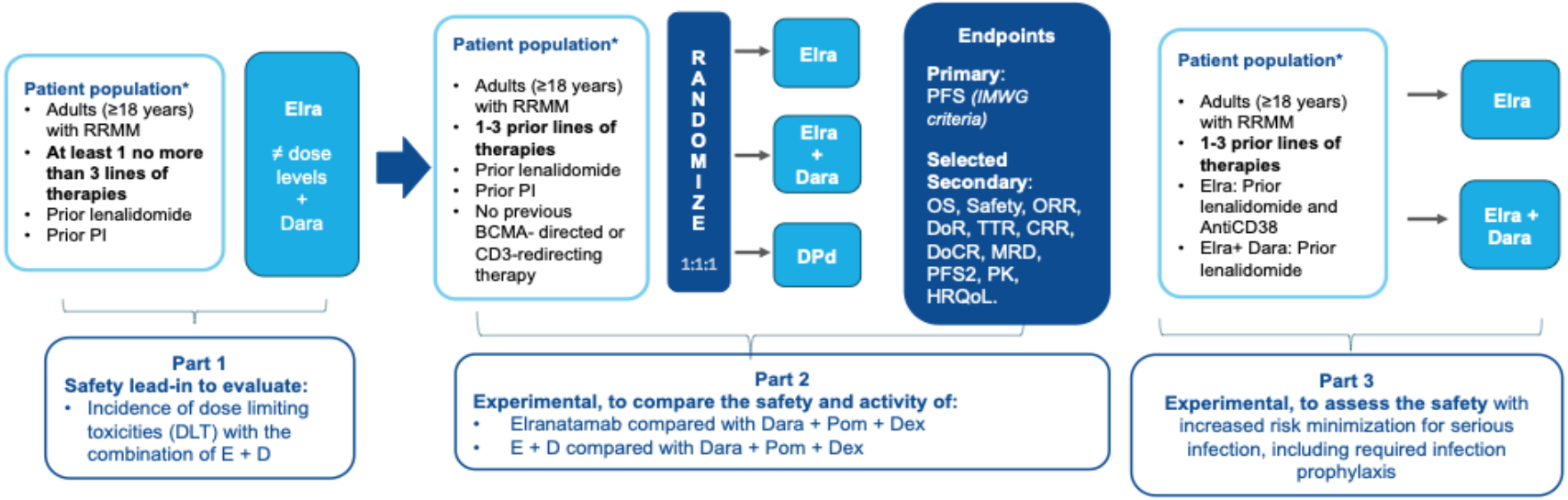
Mateos MV, personal communication; Dimopoulos MA, et al. *Ann Oncol*. 2021;32:309-322.

MagnetisMM-5

RRMM

Phase III trial (NCT05020236) – *Recruiting*

Open-label, 3-arm, multicenter, randomized trial to evaluate **efficacy** and **safety** of **elranatamab monotherapy** and **elranatamab + daratumumab** vs. *daratumumab + pomalidomide + dexamethasone* in adults patients with **RRMM**



*RRMM: Relapsed/refractory multiple mieloma; PI: proteasome inhibitor; E: elranatamab; D: daratumumab; P: pomalidomide; d: dexamethasone; PFS: progression-free survival; OS: overall survival; ORR: overall response ratio; DoR: Duration of Response; TTR: time to response; CRR: complete response ratio; DOCR: duration of complete response; MRD: minimal residual disease; PK: pharmacokinetics; HRQoL: health-related quality of life.; RP3D; Recommended Phase 3 dose. *based on main eligibility criteria*

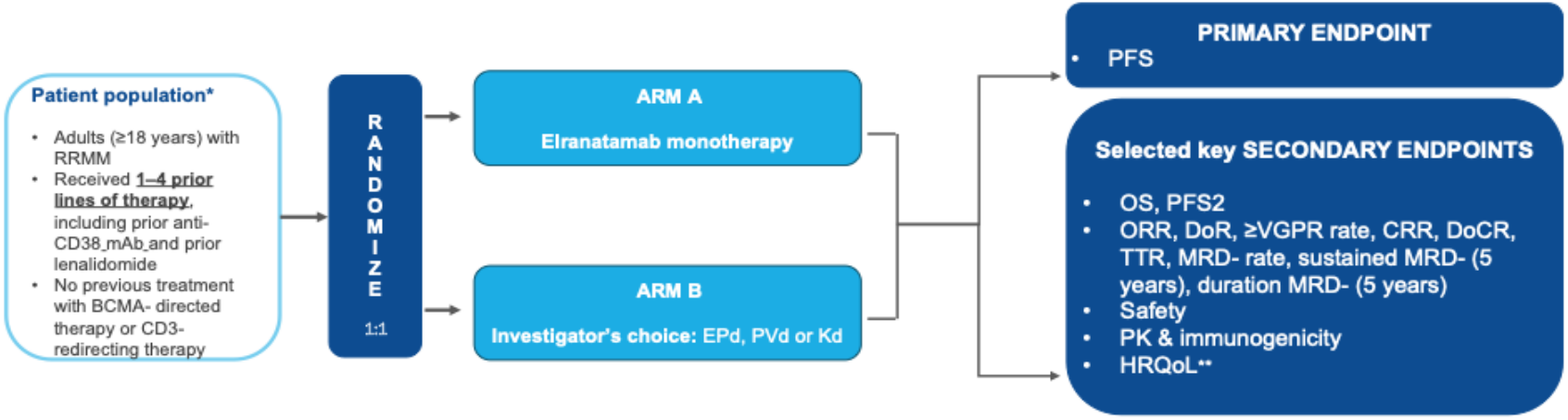
Created from REEC (REEC - MagnetisMM-5) and Clinicaltrials.gov data (NCT05020236: NCT05020236 | ClinicalTrials.gov) Last access: Mar 2026.

MagnetisMM-32

RRMM

Phase III trial (NCT06152575) – *Recruiting*

Open-label, multicenter, randomized trial to evaluate **efficacy** and **safety** of **elranatamab monotherapy** vs. *elotuzumab + pomalidomide + dexamethasone or pomalidomide + bortezomib + dexamethasone or carfilzomib + dexamethasone* in adults patients with **RRMM**



***By EORTC QLQ – Myeloma 20 and EORTC QLQ – Core 30*

*RRMM: relapsed/refractory multiple myeloma; PFS: progression free survival; OS: overall survival; ORR: objective response ratio; DoR: duration of response; VGPR: very Good partial response; CRR: complete response ratio;DoCR: duration of CR; TTR: time to response; MRD-: minimal residual disease negativity; PK: pharmacokinetic; HRQoL: health related quality of life. *based on main eligibility criteria*

Created from REEC (REEC - MagnetisMM-32) Clinicaltrials.gov data (NCT06152575: NCT06152575 | MagnetisMM-32 | ClinicalTrials.gov) Last access: Feb 2026.

Treatment Landscape in Multiple Myeloma

First line

ASCT eligible

Anti-CD38 + PI + IMiD + Dex

ASCT

Len/Dara-Len

ASCT ineligible

Dara-Len-Dex

Dara-VMP/RVd

Anti-CD38 + PI + IMiD + Dex

Second line

Based on sensitivity/refractoriness to daratumumab and lenalidomide

Anti-CD38 + carfilzomib-Dex

Anti-CD38 + pomalidomide-Dex

Pomalidomide-bortezomib-Dex

Selinexor-bortezomib-Dex

Carfilzomib-Dex

Iberdomide-Dara-Dex

Mezigdomide-Kd

Cilta-cel

Belantamab-Vd (DREAMM-7)

Belantamab-Pd (DREAMM-8)

Teclistamab-daratumumab

Teclistamab s/a

Elranatamab s/a

Tal-Dara-Pom and Tal-Dara

Tal-Tec

What about CELMoDs in early lines of therapy?

Mateos MV, personal communication; Dimopoulos MA, et al. *Ann Oncol*. 2021;32:309-322.

EXCALIBER-RRMM: Phase III Study

EXCALIBER 1-2 priors RRMM

Phase III, 2-stage seamless adaptive inferential design

Objective: Evaluate the efficacy and safety of treatment with iberdomide, daratumumab and dexamethasone (IberDd) vs daratumumab, bortezomib and dexamethasone (DVd) in patients with relapsed or refractory multiple myeloma

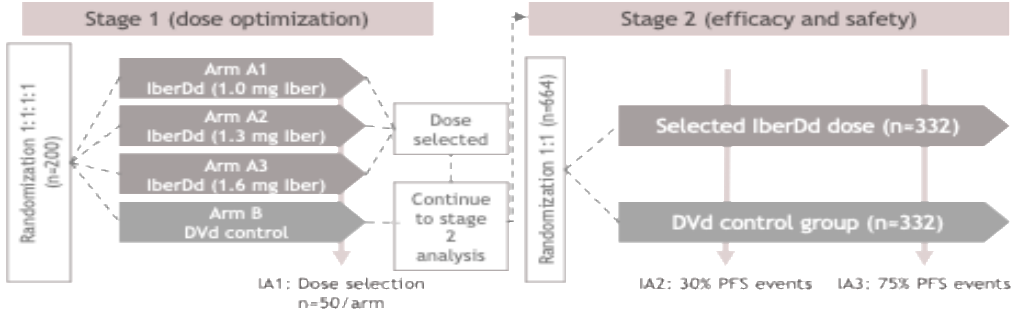
RRMM with 1-2 priors (N=864)

Inclusion Criteria

- Adult patients who received 1 to 2 prior lines of anti-myeloma therapy and progressive disease

Exclusion Criteria

- Patients who are refractory to bortezomib or an anti-CD38 therapy
- Patients with prior anti-CD38 exposure. Some exceptions apply in stage 2



Primary Endpoint: PFS
Secondary Endpoints: OS, MRD negativity rate, ORR, TTR, DoR, TTP, TTNT, PFS2, Safety, HR-QoL and PK

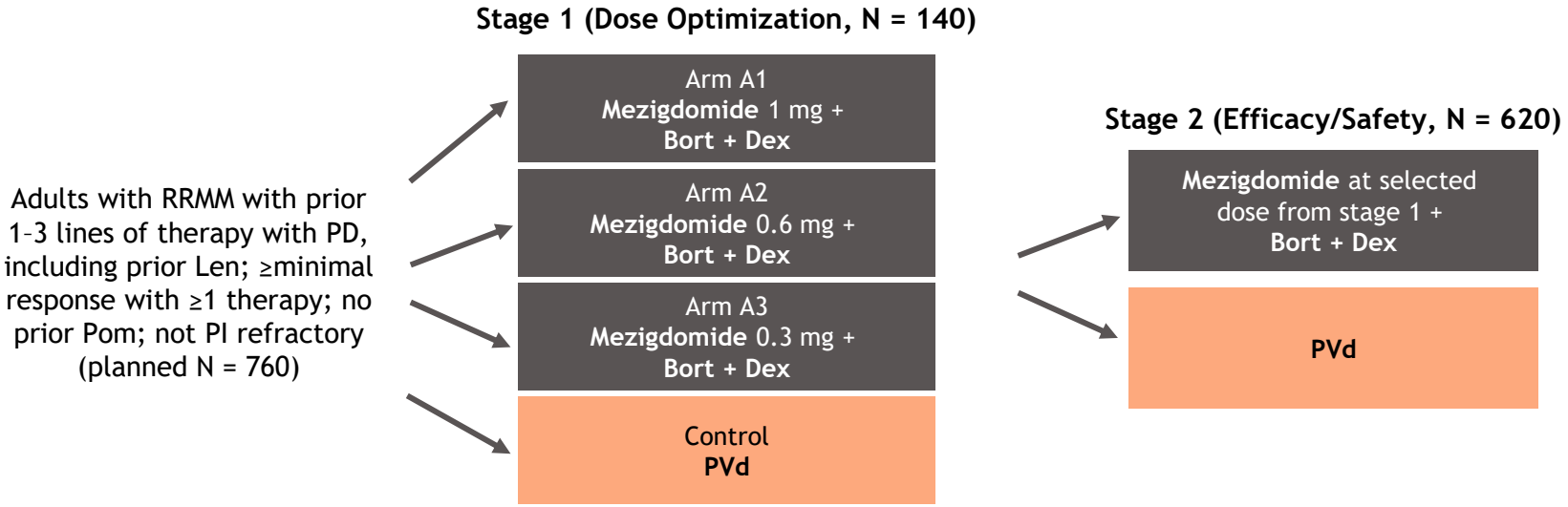
Target PFS HR 0.75, 458 PFS events, 84% power	
Analysis	HR Boundary
Interim 75% PFS	≤ 0.777
Final Analysis	≤ 0.829

Bristol Myers Squibb announces phase III EXCALIBER-RRMM study evaluating iberdomide in combination with standard therapies demonstrated a significant improvement in minimal residual disease negativity rates in relapsed or refractory multiple myeloma

D, Darzalex (daratumumab); d, dexamethasone; DOR, duration of response; iber, iberdomide; HR-QOL, health-related quality of life; IA, interim analysis; MRD, minimal residual disease; ORR, overall response rate; OS, overall survival; PFS, progression-free survival; TTNT, time to next treatment; TTP, time to progression; TTR, time to response; V, Velcade (bortezomib)

SUCCESSOR-1: Mezigdomide + Bortezomib + Dex vs PVd for RRMM (1-3 LOT)

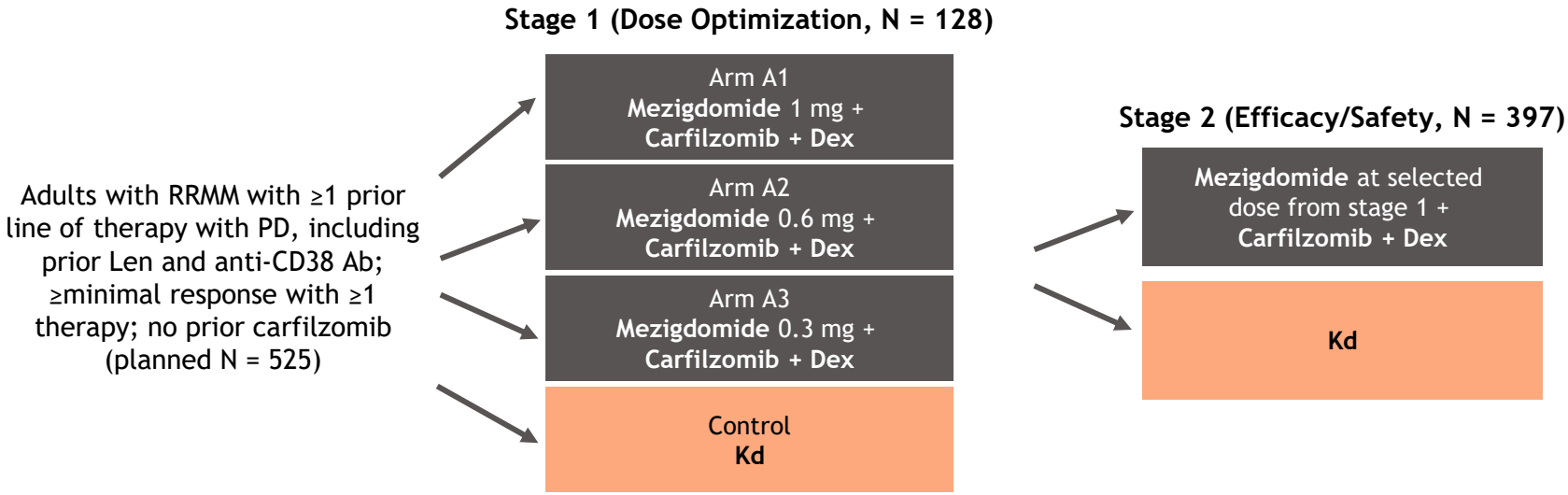
- 2-stage, randomized phase III trial



- Primary endpoints: PFS
- Secondary endpoints: OS, ORR, TTR, DOR, TTP, TTNT PFS2, MRD-negative rate, safety, HRQOL, biomarker analysis, PK

SUCCESSOR-2: Mezigdomide + Carfilzomib + Dex vs Kd for RRMM (≥1 LOT)

- 2-stage, randomized phase III trial



- Primary endpoints: PFS
- Secondary endpoints: OS, ORR, VGPRR, CR, MRD-negative rate, TTR, DOR, TTP, TTNT, PFS2, safety, HRQOL

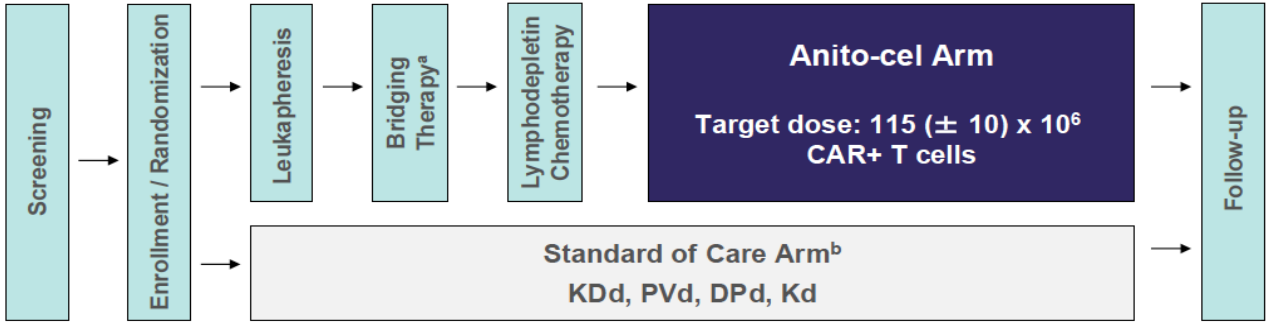
More Innovation in Early Lines of Therapy in the Future?

iMMagine-3: Phase III Clinical Trial

iMMagine-3 Design, Global Phase 3 Study – Now Enrolling

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

Anito-cel is being co-developed by Arcellx and Kite, and is being manufactured by Kite for iMMagine-3



Study Design

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

Study Endpoints

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

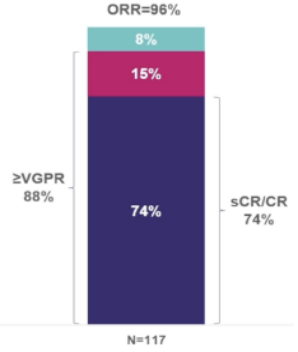
[a] *Optional Bridging therapy will be the SOC regimen selected prior to randomization*
[b] *Cycles will continue until unacceptable toxicity, progression as per IMWG criteria, or patient withdrawal of consent*

iMMagine-1: Phase II Study of Anito-Cel – Preliminary Results (n = 129, median FU 15.9 months)[1]

Key inclusion: RRMM TCE 3 or more PL
Median age 65y (38–78). Median number of PL 4 (3–18), EMD 16%
TCR 86%, Bridging therapy 71%

Target dose: 115 x 10^6 CAR+ T cell
129 pt lymphoapheresis > 118 pt lymphodepletion > total dosed 117 pts
Safety evaluable: 98 pts // Efficacy evaluable 86 pts

Overall response rate
Efficacy evaluable (n=117)



PFS and OS
Efficacy evaluable (n=117)

N=117	PFS Rate (%) (95% CI)	OS Rate (%) (95% CI)
6-Month	93.1 (86.7, 96.5)	95.7 (90.0, 98.2)
12-Month	82.1 (73.6, 88.1)	94.0 (87.8, 97.1)
18-Month	67.4 (55.4, 76.8)	88.0 (78.8, 93.4)
24-Month	61.7 (48.0, 72.8)	83.0 (70.7, 90.5)

Key safety data
Safety evaluable (n=98)

Key AEs	All grade	G3-4
CRS	95% (G1 68%, G2 16%)	1 grade 5
Median time to onset 4 days		
ICANS	9% (3% G1/4% G2)	1% grade 3
Infections	56%	9%
Neutropenia	71%	70%

3 deaths: 1 CRS, 1 retroperitoneal haemorraghe, 1 fungal infection. No new deaths since last cut-off

No delayed or non-ICANS neurotoxicities
No incidence of Parkinsonism, no cranial nerve palsy, no Guillen-Barré Sd

MRD Negativity at 10^{-5} Sensitivity Level	
Overall MRD negativity, % (n/N)	95% (91/96)
Median time to MRD negativity, months (min – max)	1.0 (0.9 – 6.4)
MRD negativity sustained for ≥ 6 months, % (n/N)	83% (54/65)
MRD Negativity at 10^{-6} Sensitivity Level	
Overall MRD negativity, % (n/N)	78% (68/87)

AEs, adverse events; BT, bridging therapy; CI, confidence interval; CR, complete response; CRS, cytokine release syndrome; EMD, extramedullary disease; FUP, follow-up; IMD, immunomodulatory drug; MRD, minimal residual disease; OS, overall survival; PD, progressive disease; PFS, progression-free survival; PL, prior lines; pt, patient; RRMM, relapsed or refractory multiple myeloma; SCR, stringent complete response; TCE, t-cell engager; TCR, t-cell receptor.

1. Patel K, et al. Poster presented at ASH 2025.

QUINTESSENTIAL-2: Phase III Clinical Trial

The QUINTESSENTIAL-2 study (NCT06615479) is investigating the efficacy and safety of arlo-cel (a GPRC5D-directed CAR T-cell therapy requiring only 1 infusion) vs standard of care in adults with RRMM exposed to lenalidomide

STUDY SNAPSHOT

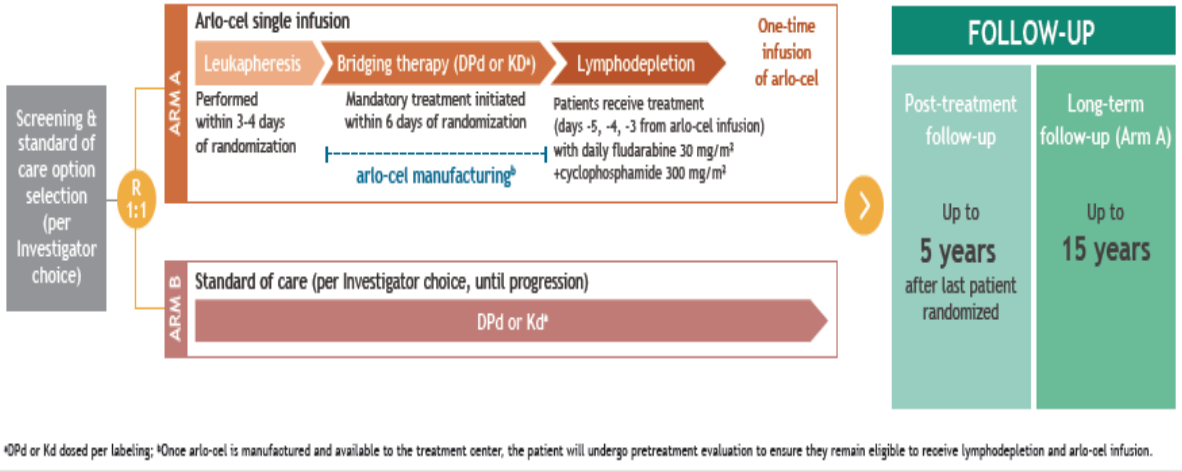
Phase 3
Ongoing trial

RRMM exposed to lenalidomide
N ~ 440 (planned)

Randomized, open label

Multicenter
~125 sites in 31 countries

Figure 1. Study design overview



[a]DPd or Kd dosed per labeling; [b]Once arlo-cel is manufactured and available to the treatment center, the patient will undergo pretreatment evaluation to ensure they remain eligible to receive lymphodepletion and arlo-cel infusion.

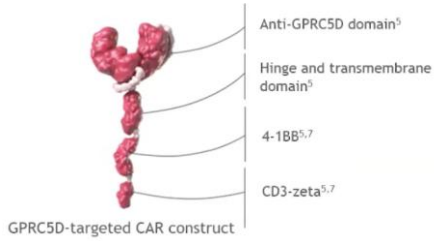
arlo-cel, arlocabtagene autoleucel; DPd, daratumumab, pomalidomide, and dexamethasone; GPRC5D, G protein-coupled receptor class C group 5 member D; Kd, carfilzomib and dexamethasone; R, randomization; RRMM, relapsed and refractory multiple myeloma.

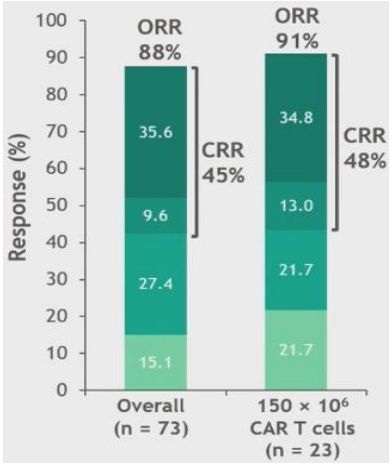
BMS-986393 (CC-95266), a GPRC5D CAR T for RRMM: Updated Results From a Phase I Study

84 patients with RRMM with ≥3 PL including PI, IMiD, and anti-CD38 antibody, and progression within <12 months of last regimen

Median 5PL; 74% were TCR. 44% EMD, 40% HRCA. 26 patients had received 150 × 10^6 CAR Ts

Prior BCMA allowed → 39 patients (46%) prior exposed to BCMA-TT and 30 BCMA CAR T



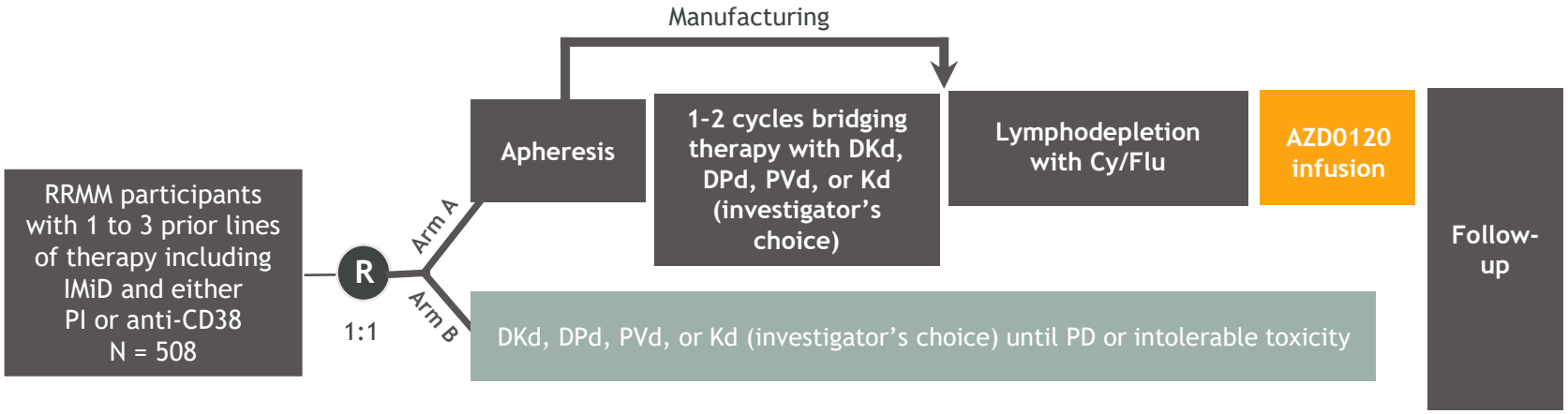


ORR in subgroups of interest (all dose levels)

Disease characteristic, % (n/N)	Present	Absent
Prior BCMA treatment	78% 25/32	95% 39/41
Extramedullary disease	84% 26/31	91% 38/42
High-risk cytogenetics[b]	83% 24/29	91% 40/44
Triple-class refractory	88% 50/57	88% 14/16

Promising efficacy and safety data even in patients previously exposed to BCMA-TT

DURGA-4: Study Design



Stratification

- Investigator's choice for the control arm (DKd vs PVd/DPd/Kd)
- High-risk status (R-ISS III or per IMS-IMWG Consensus Genomic Staging vs all others)
- Number of prior lines of therapy (1 vs 2 or 3)

Dual Primary Endpoints
PFS MRD-negative CR rate at 9 months
Key Secondary Endpoints
OS, CR/sCR rate, ORR

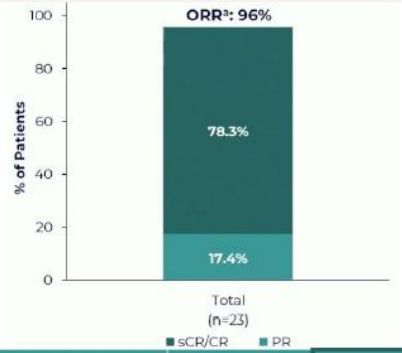
DURGA-4

DURGA-1: AZD0120 – BCMA-CD19 Dual CAR T in Patients With TCE RRMM

Key inclusion: ≥3PL, triple-class-exposed.
Median age: 63 y (44-78); Triple-class refractory 69%; 27% received BT
6 patients had prior BCMA-therapy: 5 prior CAR (median time since last CAR T 2.6 years) and 1 prior BsAbs (Teclistamab), median time of 0.6 years
N=32 enrolled, n=26 LD chemo, n=26 infused [n=12 at DL1 (1x10e5 cells/kg) and n=14 at DL2 (3x10e5cells/kg)]

ORR (n=23)

N=17 MRD evaluable > MRDneg in 94% (NGS)



	Total (n=23)	BCMA CAR T Exposed (n=5)
ORR	96%	100%
sCR/CR	78%	80%
Follow-up, median (range), months	3.9 (0.9–19.7)	3.9 (3.0–4.0)

Overall Safety

n=26

CRS	DL1 (n=12)	DL2 (n=14)	Total (n=26)
CRS, overall	**9 (75%)**	**7 (50%)**	**16 (62%)**
Grade 1	9 (75%)	6 (43%)	15 (58%)
Grade 2	0	1 (7%)	1 (4%)
Grade 3+	0	0	0
Onset time, median (range), days	9 (2–11)	9 (8–10)	9 (2–11)*
Duration, median (range), days	1 (1–4)	2 (1-2)	1.5 (1–4)
CRS management			
Tocilizumab	7 (58%)	5 (36%)	12 (46%)
Dexamethasone	1 (8%)	2 (14%)	3 (12%)
Anakinra	0	1 (7%)	1 (4%)

- No grade 3+ CRS reported
- *CRS onset on day 8–11 for 15 of 16 patients

ICANS	DL1 (n=12)	DL2 (n=14)
ICANS, overall	**0**	**1 (7%)**
Grade 1	0	1 (7%)
Grade 2	0	0
Grade 3+	0	0
Onset time, days	NA	10
Duration, day	NA	1

- **No delayed neurotoxicities, including no Parkinsonism, no cranial nerve palsies, and no Guillain-Barré syndrome reported**
- **No IEC-associated colitis reported**
- **Only one grade 1 ICANS event**
- **One patient with IEC-HS (DL1, grade 2); resolved within 7 days**

- **Neutropenia** grade 3–4, overall 81%, 83% at DL1 and 79% at DL2
- **Infections** 8% grade 3–4 overall, and 8% at DL1 and 7% at DL2
- **No DLTs**
- **Similar toxicity profiles between DL1 and DL2**

BCMA, b-cell maturation antigen; BT, bridging therapy; CAR, chimeric antigen receptor; CR, complete response; CRS, cytokine release syndrome; DLT, dose-limiting toxicity; EMD, extramedullary disease; FUP, follow-up; ICANS, immune effector cell–associated neurotoxicity syndrome; IEC-HS, immune effector cell-associated hemophagocytic syndrome; MRD, minimal residual disease; ORR, overall response rate; PL, three prior lines; PR, partial response; RRMM, relapsed/refractory multiple myeloma; sCR, stringent complete response; SPL, single prior line.

1. Richard S, et al. Oral presentation at ASH 2025. Presentation no. 704.

Treatment Landscape in Multiple Myeloma: First Take-Home Message

First line

ASCT eligible

Anti-CD38 + PI + IMiD + Dex

ASCT

Len/Dara-Len

ASCT ineligible

Anti-CD38 + PI + IMiD + Dex

Dara-Len-Dex

Dara-VMP/RVd

Second line

BCMA is a novel target that may help address the unmet need at first relapse[1]

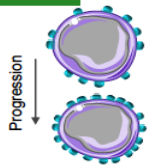
BCMA presents a clinically meaningful and well-validated target in MM

Cell specificity

- Expressed almost **exclusively on plasma cells** and overexpressed on malignant plasma cells in MM[1,2]
- Minimal expression on other essential cells, **increasing target specificity**[1,3,4]

Expression level

- High expression across most MM cases, correlating with disease progression[2,4]
- Reliable marker for targeting malignant cells[4]

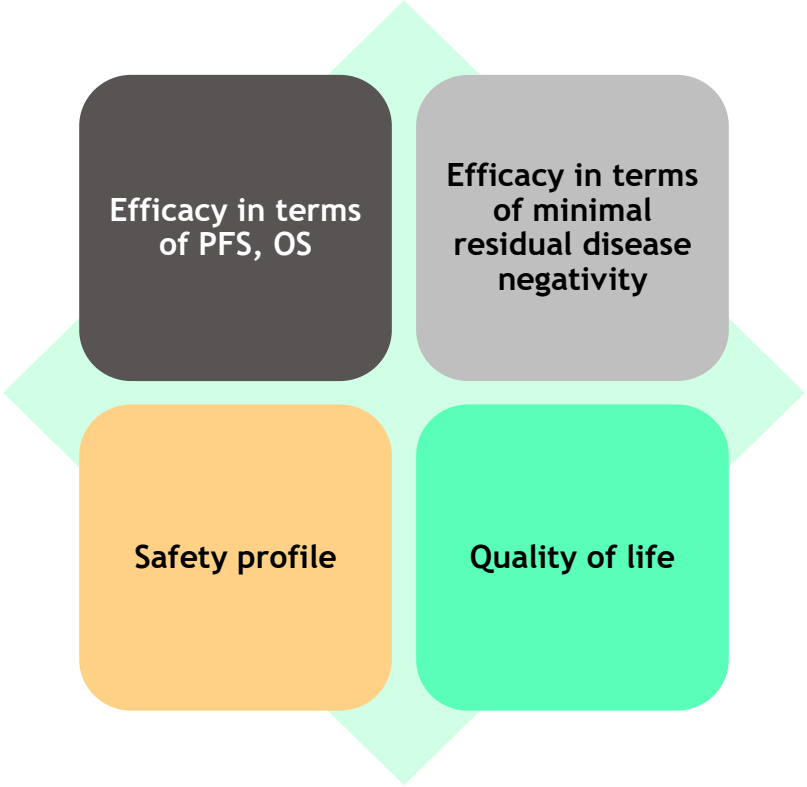


Mateos MV, personal communication; Dimopoulos MA, et al. *Ann Oncol*. 2021;32:309-322.

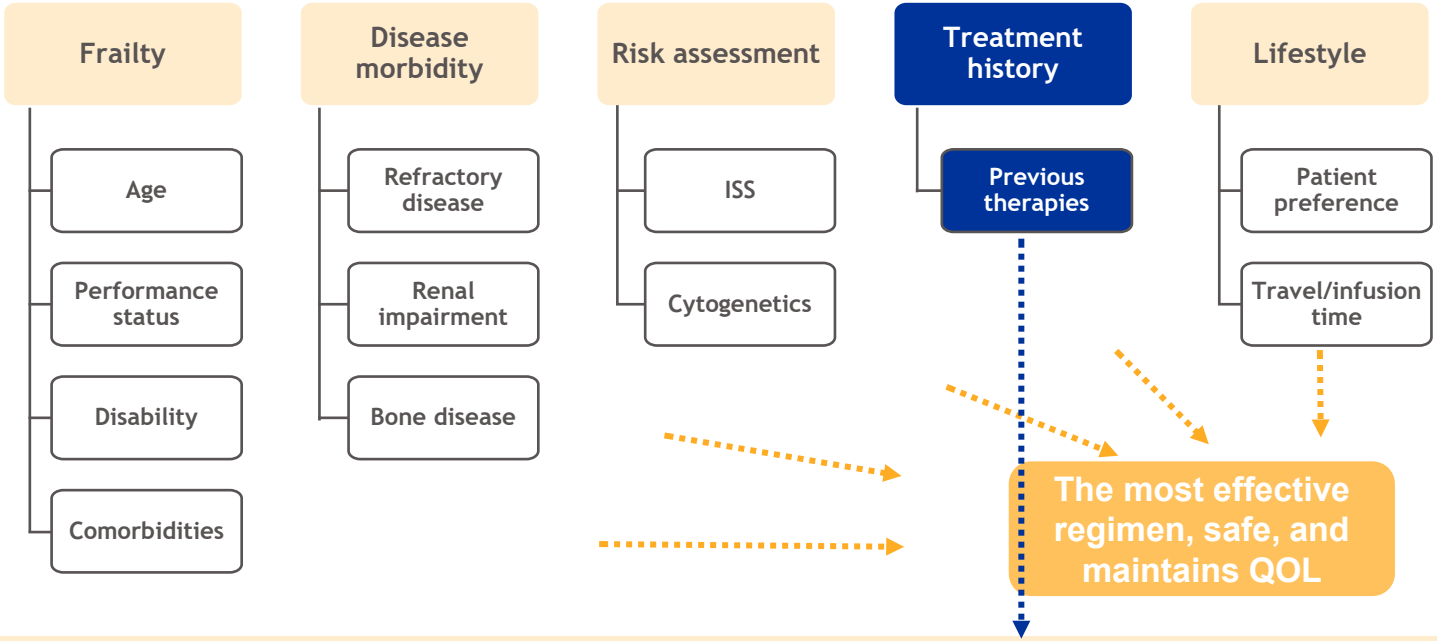
What Are the Key Administration Considerations for Anti-BCMA Therapies?

Aspect	ADC (belantamab)	CAR T (cilta-cel)	BCMA BsAb
Indication	RRMM after ≥1 prior LOT (PI + IMiD exposed)	RRMM after ≥1 prior LOT (PI + IMiD; often lenalidomide-refractory)	RRMM after ≥1 prior LOT (PI + IMiD)
Efficacy	Improved outcomes vs DVd/PVd	Marked efficacy benefit vs standard of care	Clinically meaningful efficacy benefit vs standard of care with the best HR so far reported
Key safety	Ocular toxicity, thrombocytopenia, infections	CRS, ICANS, serious infections, delayed neurotoxicity	Infections requiring prophylaxis and IVIG
Eligibility	Few formal contraindications	Required normal function of vital organs	Few formal contraindications
Treatment burden	Regular ophthalmologic assessments	Lymphodepletion and close post-infusion monitoring	Clinical monitoring focused on infectious risk
Administration	Intravenous, short infusion time	Single infusion at certified centers	Subcutaneous; monthly admin in the f/u for most of them

What Is Relevant for Treatment Decision-Making?

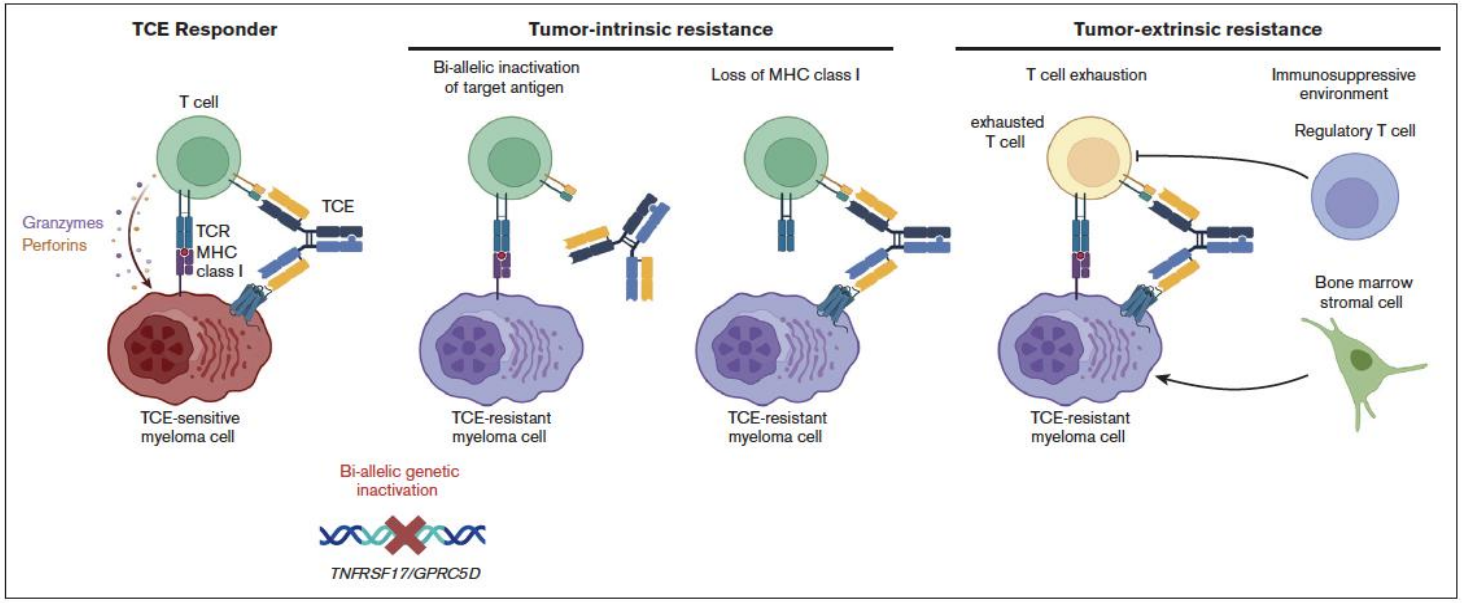


Disease and Patient-Based Factors Influencing Treatment Decision-Making in the Relapse Setting



Many patients might be equally eligible for CAR T-cell therapy, antibody-drug conjugates, or bispecific antibodies. In these situations, patient preference—based on toxicity concerns, family and personal circumstances, and the patient's geographic location—will play an important role in treatment selection.

Mechanisms of Resistance and Clinical Implications for BCMA-TT Are Crucial in Terms of Sequencing



After the use of BCMA-targeted therapy at first relapse, would it be possible to sequence BCMA-TT in subsequent relapses?

MHC, major histocompatibility complex; TCE, trichloroethylene; TCR, talquetamab crossover regimen.

Figure adapted from Letouzé E, et al. *Blood Adv*. 2024;8:2952-2959.

Mechanisms of Resistance and Clinical Implications

Table 1. Clinical impact of resistance mechanisms

	Alteration	Disease stage	Frequency	Detection technique*	Clinical impact	R
BCMA	16p loss (*TNFRSF17*)	Pretreatment screening	3%-4% of TCE-naive MM	WGS	May facilitate biallelic target inactivation by second hit	
	TNFRSF17 mutation	Pretreatment screening	1.1% (somatic) and 0.7% (germ line) of TCE-naive MM	WGS	May facilitate biallelic target inactivation by second hit	
	Abundance of exhausted T-cell clones	Pretreatment screening	TBD	scRNA/VDJ-seq	Predicts response failure to BCMA-targeting TCE	
BCMA	*TNFRSF17* homozygous deletion	At relapse	1/14 relapses after BCMA-targeting TCE	WGS	Precludes response to other BCMA-targeting therapy	
	TNFRSF17 p.Arg27Pro	At relapse	1/14 relapses after BCMA-targeting TCE	WGS	Confers resistance to teclistamab and elranatanab	
	TNFRSF17 p.Pro34del	At relapse	3/14 relapses after BCMA-targeting TCE	WGS	Confers resistance to teclistamab and elranatanab	
	TNFRSF17 p.Ser30del	At relapse	2/14 relapses after BCMA-targeting TCE	WGS	Confers resistance to teclistamab	

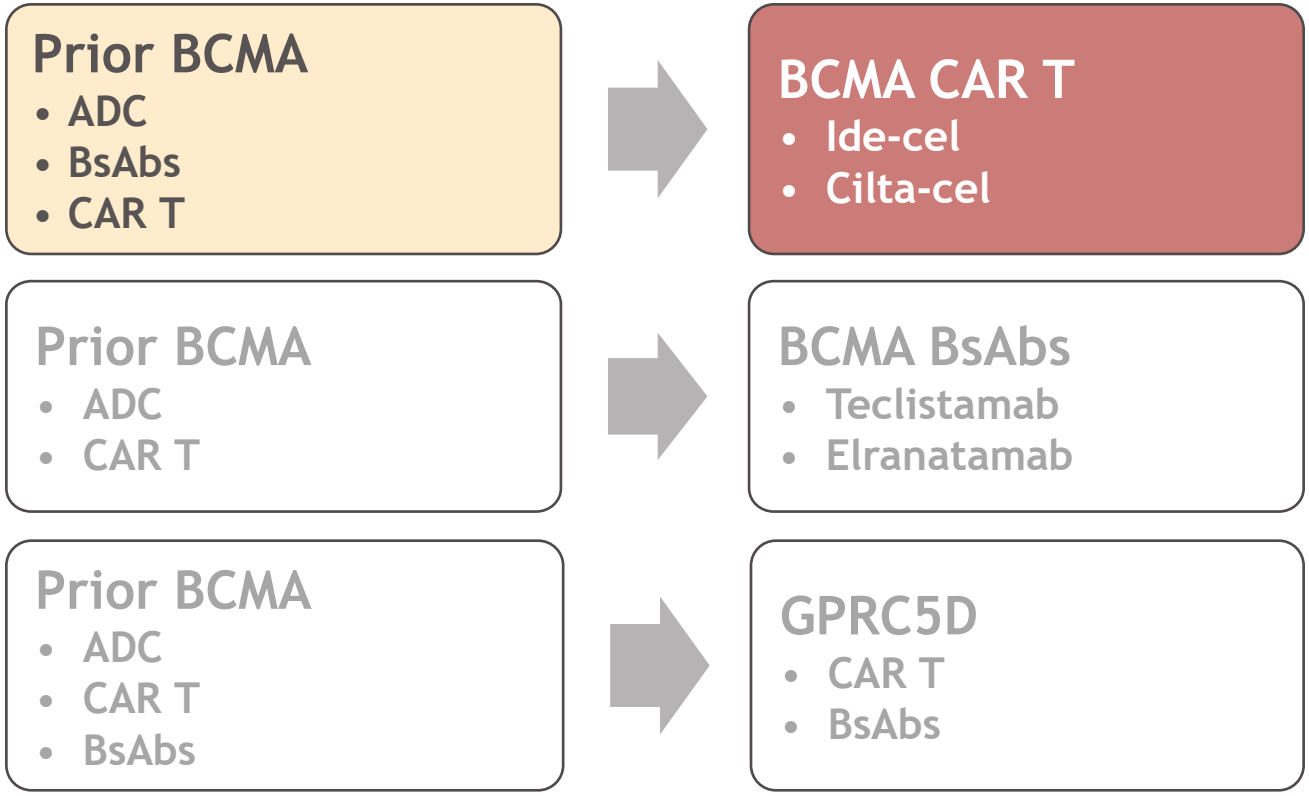
BCMA antigen escape via biallelic TNFRSF17 loss has been observed at relapse after BCMA-directed therapies in up to 14%-15% of the patients

T-cell exhaustion is another mechanism of resistance, applicable mainly to continuous treatment with bispecific antibodies

ATAC-seq, Assay for Transposase-Accessible Chromatin using sequencing; BCMA, B cell maturation antigen; MM, multiple myeloma; RNA-seq, RNA sequencing; TBD, to be determined; TCE, Trichloroethylene; WGS, whole-genome sequencing.

Letouzé E, et al. *Blood Adv*. 2024;8:2952-2959; Lee H, et al. *Nat Med*. 2023;29:2295-2306.

Would It Be Possible to Sequence Both Approaches?

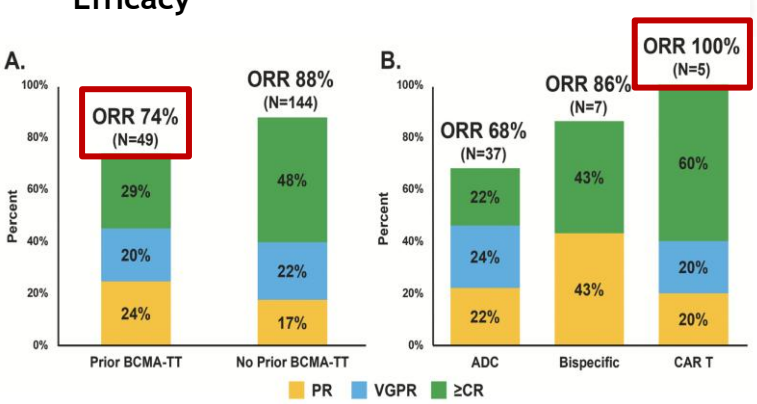


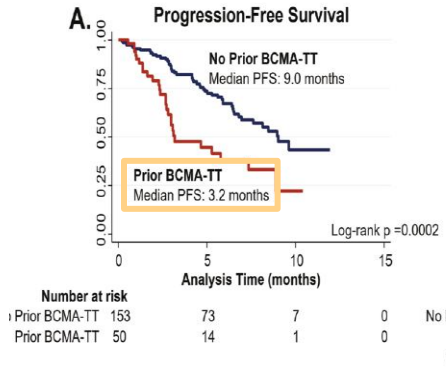
Ide-Cel for RRMM: Real-World Experience in Patients Previously Exposed to BCMA-Targeted Therapy

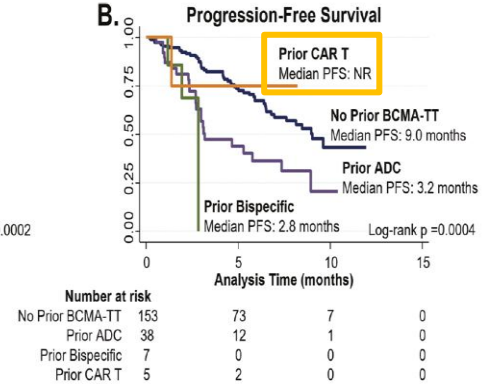
50 patients treated with Ide-cel after prior BCMA-TT (ADC 76%/BsAbs 14%/CAR T 10%); timing of prior BCMA TT: 40% <6 months

153 patients treated with Ide-cel and no prior BCMA-TT. Median follow-up duration of 4.5 months and 6 months, respectively

Efficacy







Ide-cel administered to patients previously exposed to BCMA-targeted therapy

The achievement of ≥PR after the BCMA-targeted therapy was predicted to reach CR

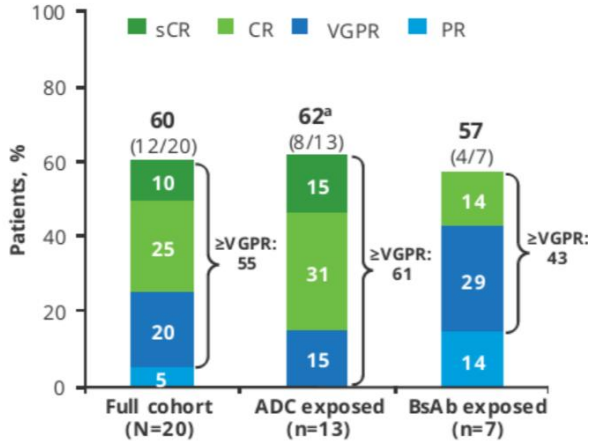
Shorter PFS in prior BCMA-TT than that observed in BCMA-naive patients

The shorter duration of prior BCMA-TT (<6 months) and the longer interval between BCMA-TT and Ide-cel predicted response

Ferreri C, et al. *Blood Cancer J.* 2023;13:117

Cilta-Cel for RRMM: CARTITUDE-2 Cohort C Patients Previously Exposed to BCMA-Targeted Therapy (n = 20)

FIGURE 2: Overall response rate



[a]Percentages may not sum appropriately due to rounding.
PR, partial response; sCR, stringent complete response.

ADC: 1 out of 4 patients who received anti-BCMA ADC as immediate pretreatment responded to Cilta-cel (vs 7 out of 9 patients who received intermediate treatments).[1,2]

BsAb: 2 out of 2 patients who received BsAb anti-BCMA as an immediate pretreatment against BCMA responded to Cilta-cel (vs 2 out of 5 patients who received intermediate treatments).[1,2]

TABLE: Median DOR, PFS, and OS

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)
OS	16.0 (8.3–NE)	21.0 (9.4–NE)	13.2 (0.6–NE)

NE, not estimable.

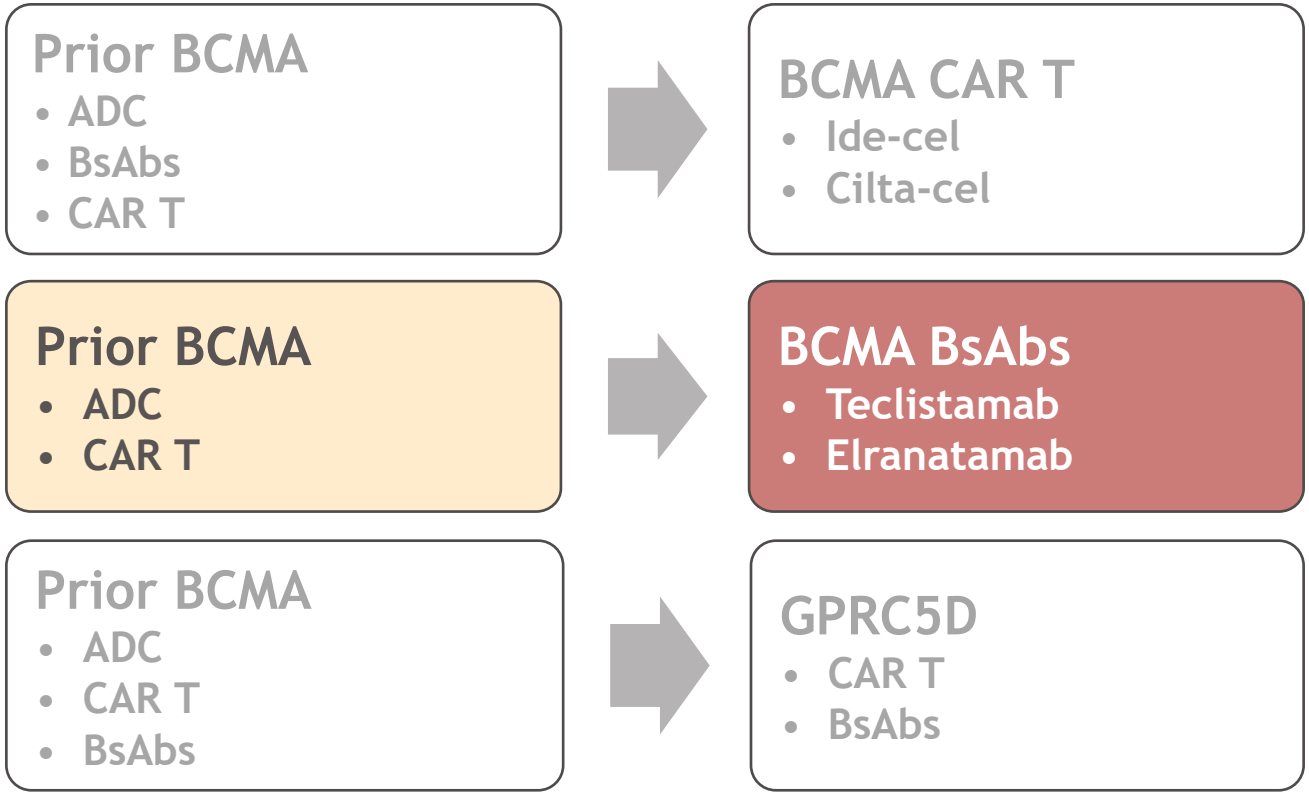
Cilta-cel induced favorable responses in highly pretreated patients with MM with prior exposure to anti-BCMAs[1,2]

The efficacy of Cilta-cel in patients enrolled in CARTITUDE-1 appears to be higher than in this cohort of patients, but the sample size is very small[1,2]

ADC, antibody-drug conjugate; BCMA, B-cell maturation antigen; Cilta-cel, ciltacabtagene autoleucel; MM, multiple myeloma.

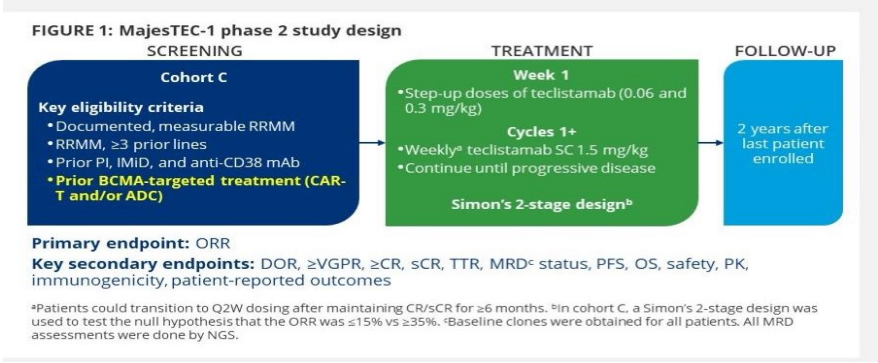
1. Cohen AD, et al. *Blood*. 2023;141:219-230; 2. Cohen AD, et al. IMS 2023. Abstract P-240.

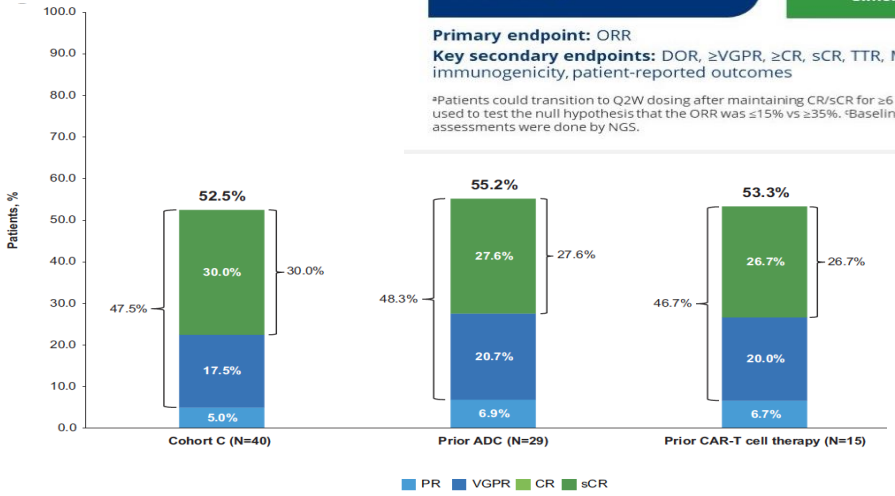
Would It Be Possible to Sequence Both Approaches?



Teclistamab: BCMA Plus CD3 Bispecific mAb – Update of MajesTEC-1 in Patients Previously Exposed to BCMA-Targeted Therapy

40 patients previously exposed to BCMA-TT/Median of 6 PL/72.5% ADC/37.5% CAR T





	Cohort C	Prior CAR T	Prior ADC
Median PFS, months	4.5	4.4	7.6
Median OS, months	15.5	14.9	16

Touzeau C, et al. *Blood*. 2024;144:2375-2388.

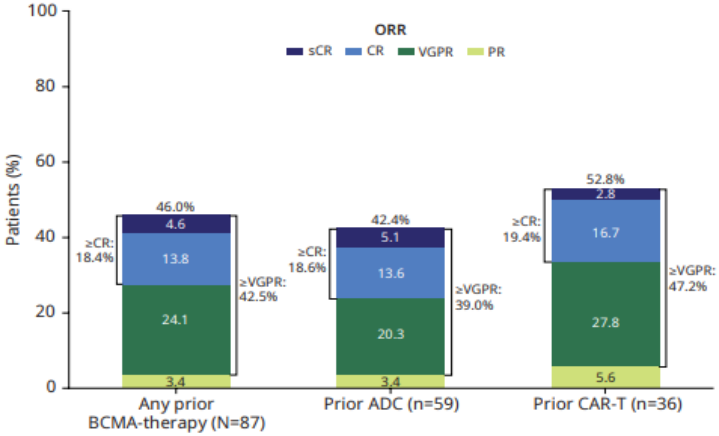
Elranatamab: Outcomes in RRMM With Prior BCMA-Directed Therapy

87 patients previously exposed to BCMA-TT from pooled analysis of MagnetisMM trials (at least 3 PL)

Median of 7 PL/68% ADC/41% CAR T/9% CAR + ADC

Median follow-up of 11.3 months (range, 0.3–32.3)

Primary endpoint: ORR



PFS

Median Survival, months (95% CI)	Prior BCMA (n = 87)	Prior ADC (n = 59)	Prior CAR T (n = 36)
PFS	5.5 (2.2–10.0)	3.9 (1.9–6.6)	10.0 (1.9–NE)
OS	12.1 (7.5–NE)	12.1 (6.4–NE)	12.1 (6.5–NE)

Manier S, et al. *HemaSphere*. 2023;7(suppl):e26808c7.

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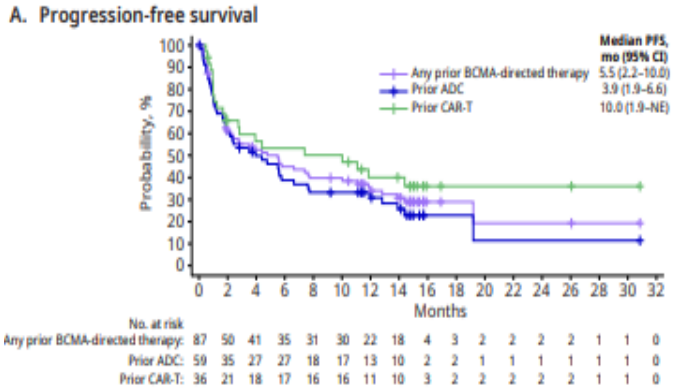
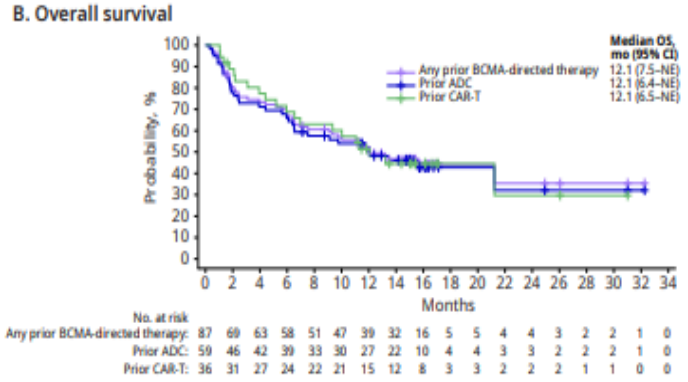
PFS



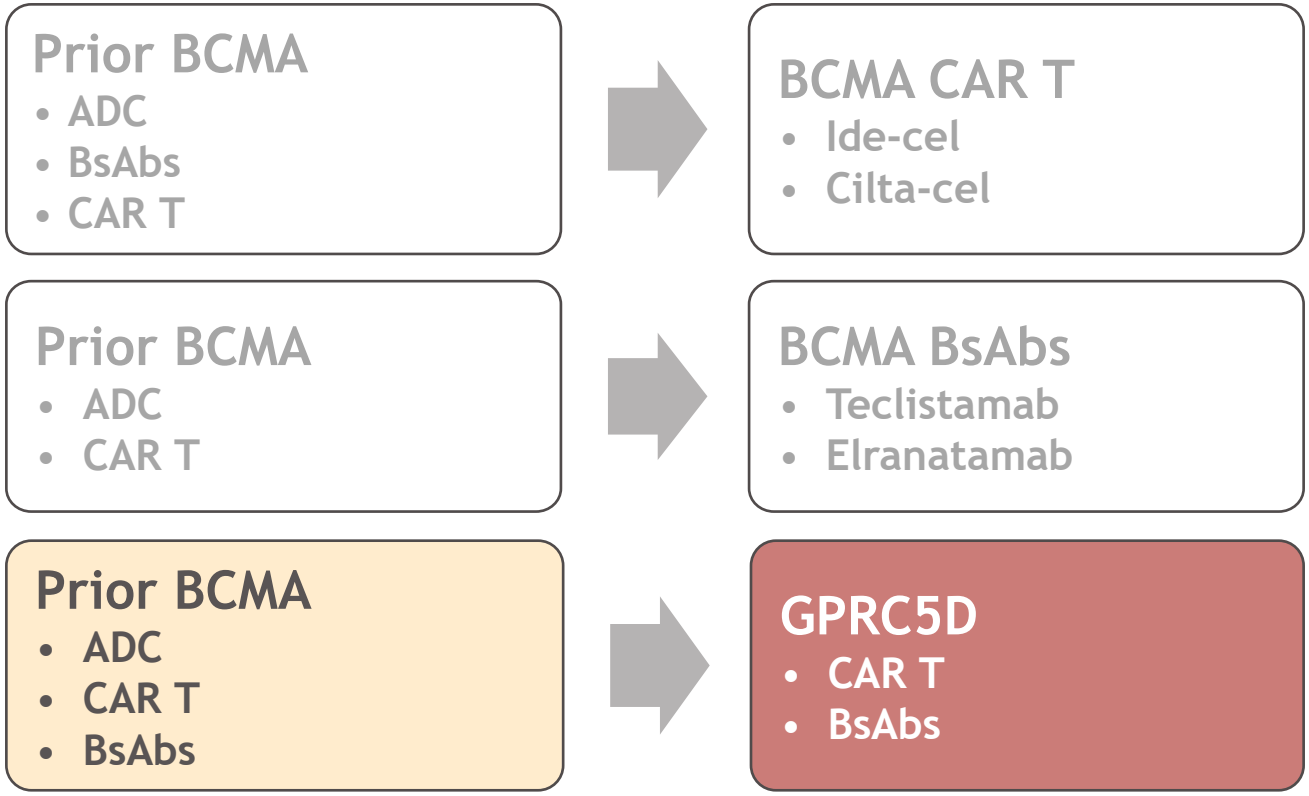
OS



Median PFS and median OS were 5.5 (95% CI, 2.2–10.0) months and 12.1 (7.5–NE) months, respectively

Manier S, et al. *HemaSphere*. 2023;7(suppl):e26808c7.

Would It Be Possible to Sequence Both Approaches?

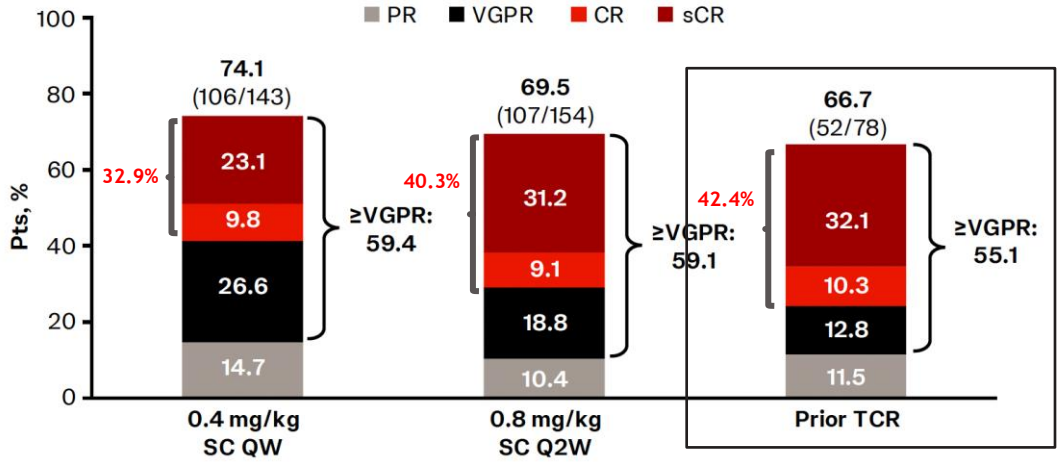


MonumenTAL-1 First-in-Human Phase I Trial: Talquetamab (GPRC5D/CD3 duo Ab) for RRMM – Efficacy With Longer FU

Cohort 0.4 mg/kg SC QW → PL: 5/TCE 100%/TCR 74%/Penta-ref: 29%/EMD 23%/HR CTG 31%/Prior ADC BCMA 15%

Cohort 0.8 mg/kg Q2W→ PL: 5/ TCE 100%/TCR 69%/Penta-ref: 23%/EMD 25%/HR CTG 29%/Prior ADC BCMA **11%**

Prior TCR (n = 78) → PL: 6/TCE 100%/TCR 84%/Penta-ref: 41%/EMD 31%/HR CTG 41%/**Prior ADC BCMA 12%/Prior BCMA BsAbs 31%/Prior BCMA CAR T 67%**



prior BCMA CAR T therapy
- ORR → 71% (n = 40/56)
- mPFS 12 months

prior BCMA bispecific mAbs
- ORR → **58%** (n = 15/26)
- mPFS 4.1 months

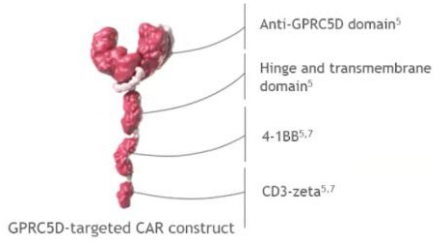
ORR 67% in the prior TCR cohort at the approved Tal doses
mPFS when previously treated with BCMA CAR T 12 months as compared with 4 months when treated with prior BCMA BsAbs

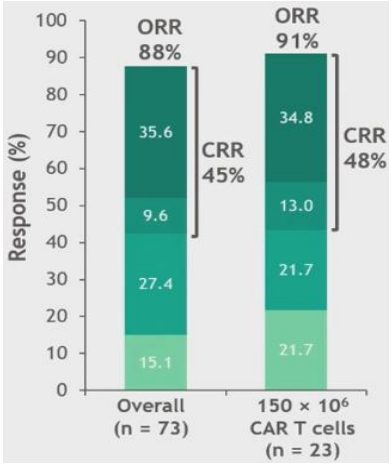
BMS-986393 (CC-95266), a GPRC5D CAR T for RRMM: Updated Results From a Phase I Study

84 patients with RRMM with ≥3 PL including PI, IMiD, and anti-CD38 antibody, and progression within <12 months of last regimen

Median 5PL; 74% were TCR. 44% EMD, 40% HRCA. 26 patients had received 150 × 10^6 CAR Ts

Prior BCMA allowed → 39 patients (46%) prior exposed to BCMA-TT and 30 BCMA CAR T





ORR in subgroups of interest (all dose levels)

Disease characteristic, % (n/N)	Present	Absent
Prior BCMA treatment	78% 25/32	95% 39/41
Extramedullary disease	84% 26/31	91% 38/42
High-risk cytogenetics[b]	83% 24/29	91% 40/44
Triple-class refractory	88% 50/57	88% 14/16

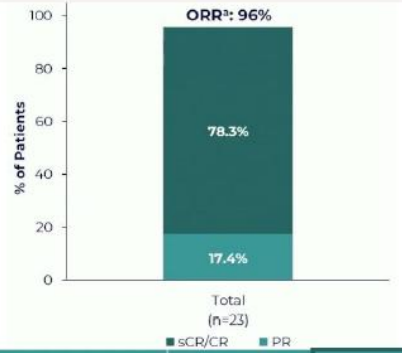
Promising efficacy and safety data even in patients previously exposed to BCMA-TT

DURGA-1: AZD0120 – BCMA-CD19 Dual CAR T in Patients With TCE RRMM

Key inclusion: ≥3PL, triple-class-exposed.
Median age: 63 y (44-78); Triple-class refractory 69%; 27% received BT
6 patients had prior BCMA-therapy: 5 prior CAR (median time since last CAR T 2.6 years) and 1 prior BsAbs (Teclistamab), median time of 0.6 years
N=32 enrolled, n=26 LD chemo, n=26 infused [n=12 at DL1 (1x10e5 cells/kg) and n=14 at DL2 (3x10e5cells/kg)]

ORR (n=23)

N=17 MRD evaluable > MRDneg in 94% (NGS)



	Total (n=23)	BCMA CAR T Exposed (n=5)
ORR	96%	100%
sCR/CR	78%	80%
Follow-up, median (range), months	3.9 (0.9–19.7)	3.9 (3.0–4.0)

Overall Safety

n=26

CRS	DL1 (n=12)	DL2 (n=14)	Total (n=26)
CRS, overall	**9 (75%)**	**7 (50%)**	**16 (62%)**
Grade 1	9 (75%)	6 (43%)	15 (58%)
Grade 2	0	1 (7%)	1 (4%)
Grade 3+	0	0	0
Onset time, median (range), days	9 (2–11)	9 (8–10)	9 (2–11)*
Duration, median (range), days	1 (1–4)	2 (1-2)	1.5 (1–4)
CRS management			
Tocilizumab	7 (58%)	5 (36%)	12 (46%)
Dexamethasone	1 (8%)	2 (14%)	3 (12%)
Anakinra	0	1 (7%)	1 (4%)

- No grade 3+ CRS reported
- *CRS onset on day 8–11 for 15 of 16 patients

ICANS	DL1 (n=12)	DL2 (n=14)
ICANS, overall	**0**	**1 (7%)**
Grade 1	0	1 (7%)
Grade 2	0	0
Grade 3+	0	0
Onset time, days	NA	10
Duration, day	NA	1

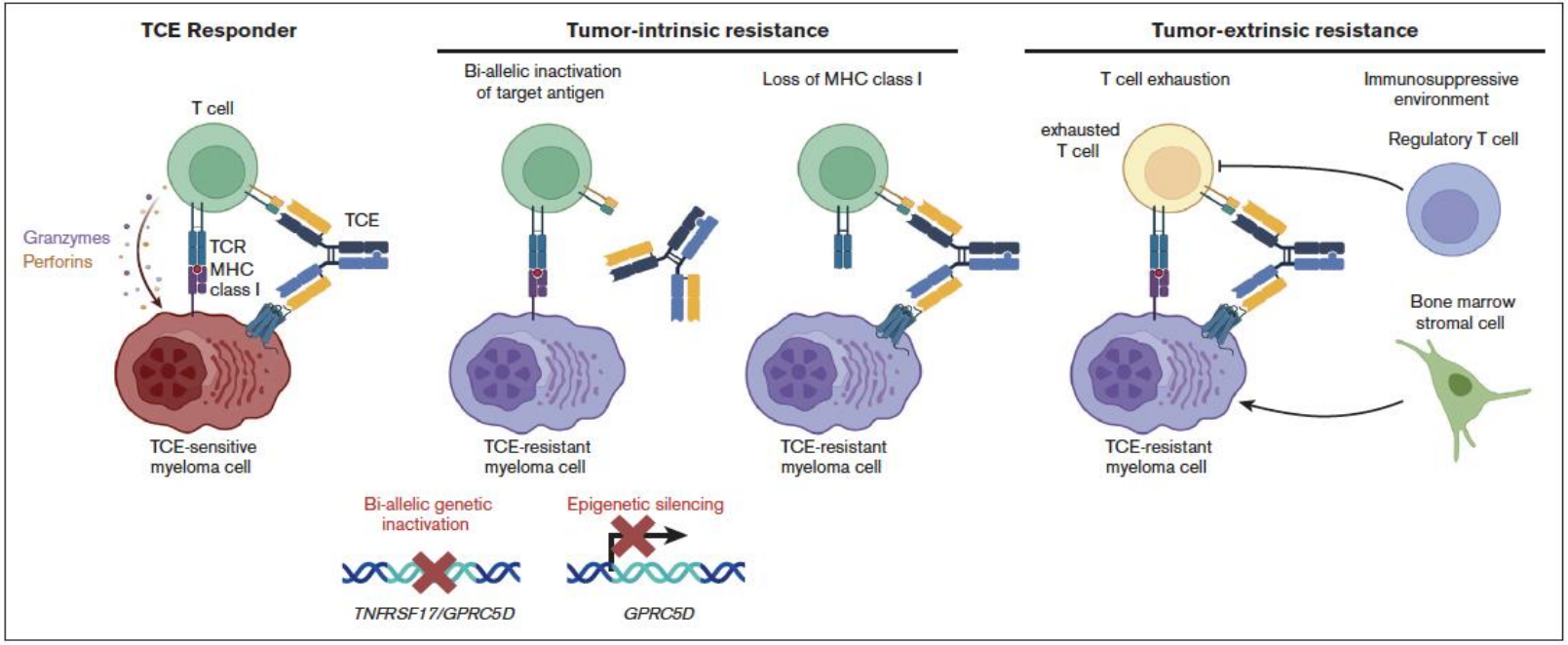
- **No delayed neurotoxicities, including no Parkinsonism, no cranial nerve palsies, and no Guillain-Barré syndrome reported**
- **No IEC-associated colitis reported**
- **Only one grade 1 ICANS event**
- **One patient with IEC-HS (DL1, grade 2); resolved within 7 days**

- **Neutropenia** grade 3–4, overall 81%, 83% at DL1 and 79% at DL2
- **Infections** 8% grade 3–4 overall, and 8% at DL1 and 7% at DL2
- **No DLTs**
- **Similar toxicity profiles between DL1 and DL2**

BCMA, b-cell maturation antigen; BT, bridging therapy; CAR, chimeric antigen receptor; CR, complete response; CRS, cytokine release syndrome; DLT, dose-limiting toxicity; EMD, extramedullary disease; FUP, follow-up; ICANS, immune effector cell–associated neurotoxicity syndrome; IEC-HS, immune effector cell-associated hemophagocytic syndrome; MRD, minimal residual disease; ORR, overall response rate; PL, three prior lines; PR, partial response; RRMM, relapsed/refractory multiple myeloma; sCR, stringent complete response; SPL, single prior line.

1. Richard S, et al. Oral presentation at ASH 2025. Presentation no. 704.

Mechanisms of Resistance and Clinical Implications for BCMA-TT



MHC, major histocompatibility complex; TCE, trichloroethylene; TCR, talquetamab crossover regimen.

Figure adapted from Letouzé E, et al. *Blood Adv*. 2024;8:2952-2959.

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	TNFRSF17 mutation	Pretreatment screening	1.1% (somatic) and 0.7% (germ line) of TCE-naive MM	WGS	May facilitate biallelic target inactivation by second hit	
GPRC5D	12p loss (*GPRC5D*)	Pretreatment screening	13%-15% of TCE-naive MM	WGS	May facilitate biallelic target inactivation by second hit	
	GPRC5D mutation	Pretreatment screening	4% TCE-naive MM	WGS	May facilitate biallelic target inactivation by second hit	
	Low GPRC5D expression	Pretreatment screening	TBD	RNA-seq	Associated with reduced talquetamab efficacy in vitro. May facilitate epigenetic inactivation of the target	
	Abundance of exhausted T-cell clones	Pretreatment screening	TBD	scRNA/VDJ-seq	Predicts response failure to BCMA-targeting TCE	
BCMA	*TNFRSF17* homozygous deletion	At relapse	1/14 relapses after BCMA-targeting TCE	WGS	Precludes response to other BCMA-targeting therapy	
	TNFRSF17 p.Arg27Pro	At relapse	1/14 relapses after BCMA-targeting TCE	WGS	Confers resistance to teclistamab and elranatanab	
	TNFRSF17 p.Pro34del	At relapse	3/14 relapses after BCMA-targeting TCE	WGS	Confers resistance to teclistamab and elranatanab	
	TNFRSF17 p.Ser30del	At relapse	2/14 relapses after BCMA-targeting TCE	WGS	Confers resistance to teclistamab	
GPRC5D	Bi-allelic genetic GPRC5D inactivation	At relapse	5/7 post-talquetamab relapses	WGS	Likely precludes response to other GPRC5D-targeting therapy	
	Epigenetic GPRC5D inactivation	At relapse	2/3 post-talquetamab relapses	scMultiome (RNA-seq + ATAC-seq)	Likely precludes response to other GPRC5D-targeting therapy	

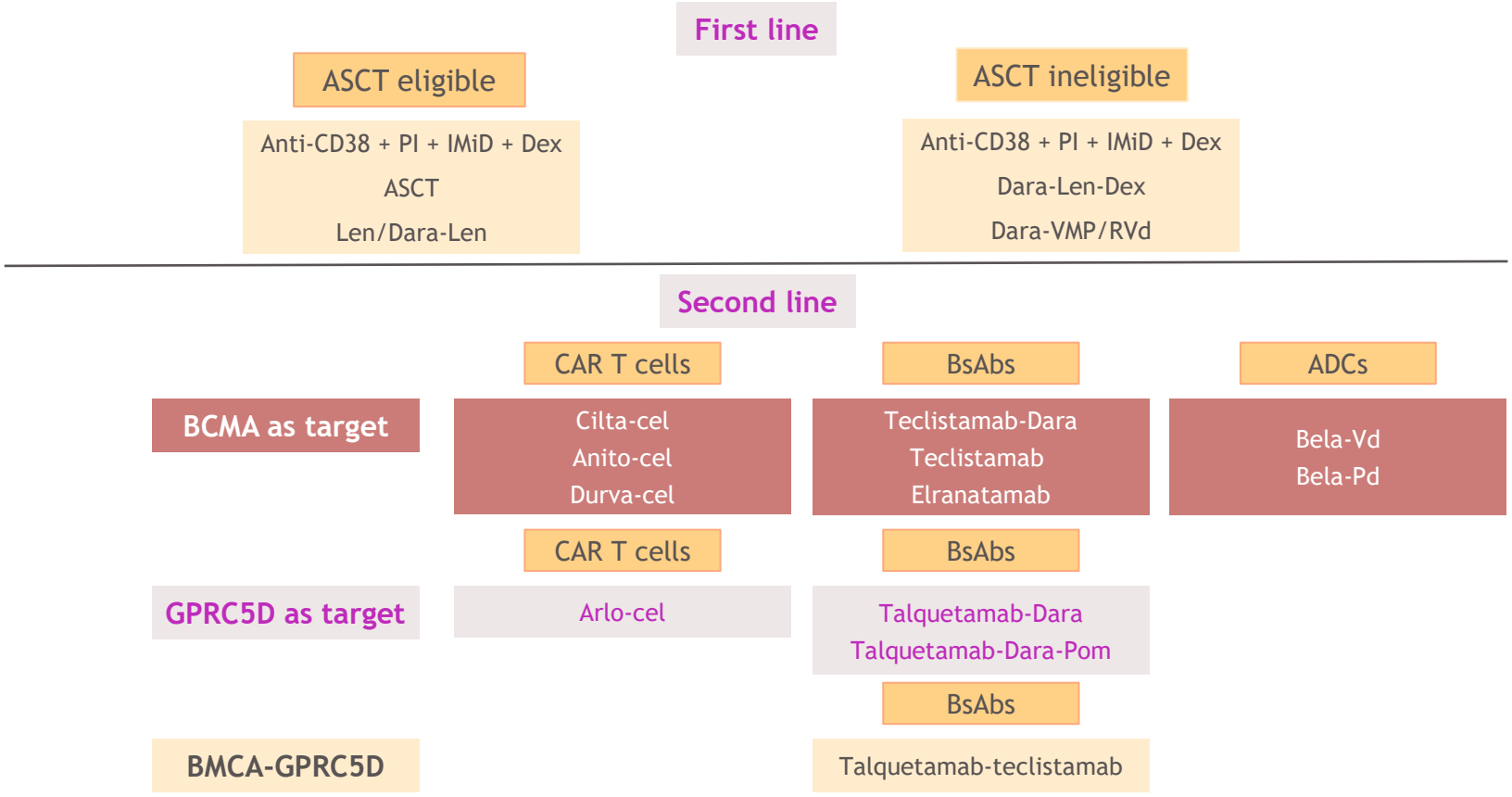
GPRC5D antigen escape via mutations has been observed at relapse after GPRC5D-directed therapies in up to 50% of the patients

T-cell exhaustion is another mechanism of resistance applicable mainly to continuous treatment with bispecific antibodies

ATAC-seq, Assay for Transposase-Accessible Chromatin using sequencing; BCMA, B cell maturation antigen; MM, multiple myeloma; RNA-seq, RNA sequencing; TBD, to be determined; TCE, Trichloroethylene; WGS, whole-genome sequencing.

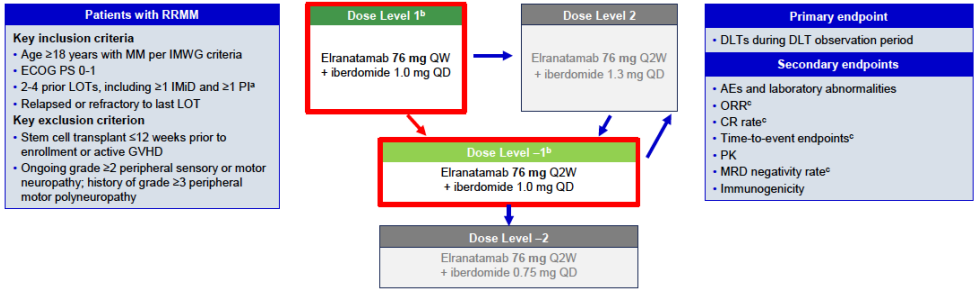
Letouzé E, et al. *Blood Adv*. 2024;8:2952-2959; Lee H, et al. *Nat Med*. 2023;29:2295-2306.

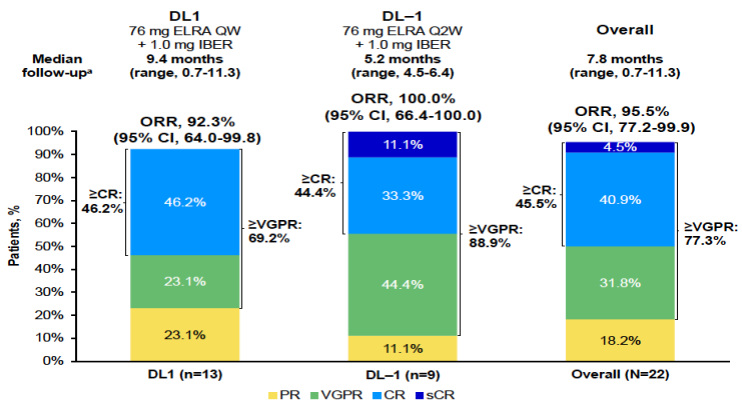
Treatment Landscape in Multiple Myeloma in Early Relapse in the Future



Mateos MV, personal communication; Dimopoulos MA, et al. *Ann Oncol*. 2021;32:309-322.

Other Combinations Are Ongoing but in the Early Phase of Clinical Trials: MagnetisMM-30





Responses are expected to deepen with further follow-up

- 22 patients with RRMM after a median number of 2.5 PL
- 50% triple-class refractory
- 100% triple-class exposed

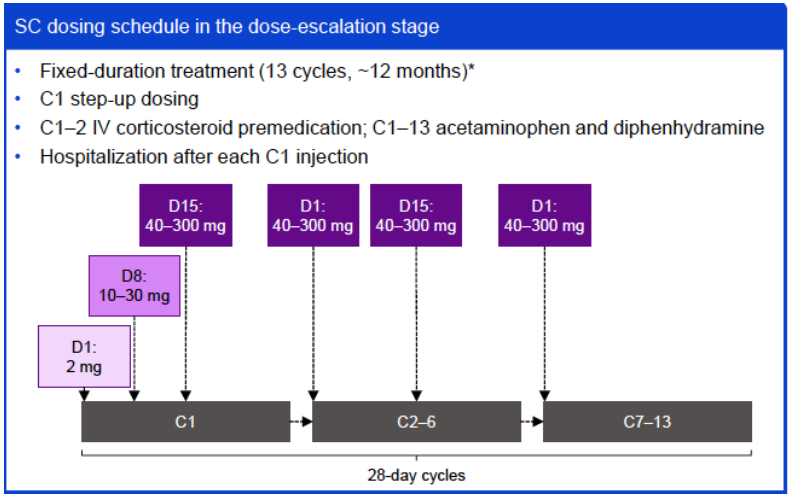
	N=22	
TEAE, n (%)[a]	**Any grade**	**Grade 3/4**
Any	22 (100.0)	19 (86.4)
Hematologic		
Neutropenia	17 (77.3)	16 (72.7)
Anemia	7 (31.8)	3 (13.6)
Lymphopenia	4 (18.2)	4 (18.2)
Nonhematologic		
CRS	15 (68.2)	0
Fatigue	14 (63.6)	0
Diarrhea	11 (50.0)	0
Headache	10 (45.5)	0
Cough	10 (45.5)	0
Nausea	9 (40.9)	1 (4.5)
Injection site reaction	9 (40.9)	0
Decreased appetite	8 (36.4)	1 (4.5)

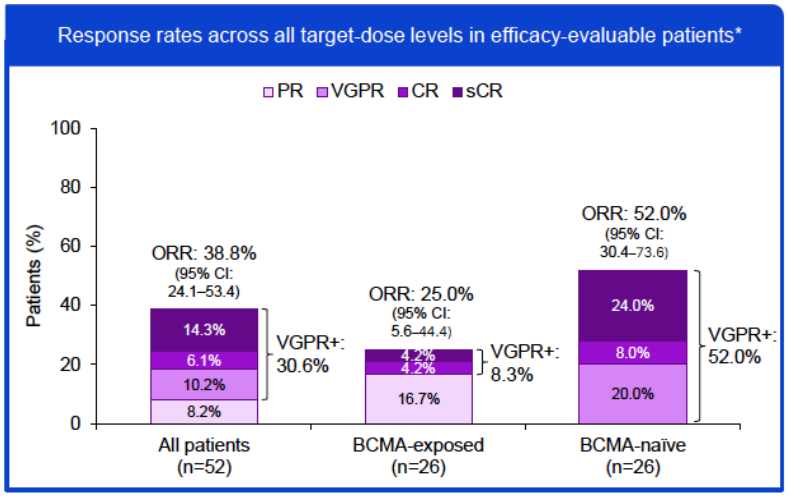
Infections occurring in >5% of patients	**N=22**	
TEAE, n (%)[a]	**Any grade**	**Grade 3**
Infections[b]	9 (40.9)	2 (9.1)
Upper respiratory tract infection	6 (27.3)	0
Candida infection	3 (13.6)	0
Urinary tract infection	2 (9.1)	0

IVIG prophylaxis was administered approximately every 4 weeks to maintain IgG levels above 400 mg/dL

Cevostamab, Subcutaneous FcRH5 Bispecific mAb: Results of the Phase Ib CAMMA Study

- 58 patients with RRMM were included in the trial. Median number of PL: 5 (64% triple-class refractory and 48% prior anti-BCMA therapy, including CAR T, ADC, and bispecific monoclonal antibodies)





- Median DOR was 12 months, NR in BCMA-naive, and 8.3 months in BCMA-exposed patients
- CRS in 69% (G3 in 1 patient); infections in 45% (G3–5 in 15%); IVIG administration in 41% of patients

Cevostamab Plus Pomalidomide-Dex in Patients With RRMM

Adults with RRMM with ≥1 prior LoT including an IMiD and a PI; not refractory to pomalidomide; ECOG PS 0/1
(N = 64)

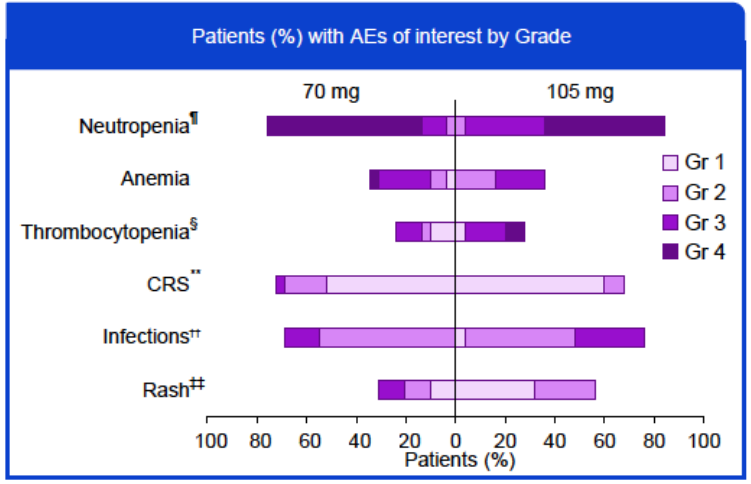
Cevostamab* 70 mg IV Q2W in cycles 1-6 of 28-day cycles then Q4W (D1) in cycles 7+
+ Pomalidomide 2 mg PO on D1-21 from cycle 1+
+ Dexamethasone 20 mg IV/PO on D1, 8, 15, 22 from cycle 1+
(n = 29 BCMA naive)

Cevostamab* 105 mg IV Q2W in cycles 1-6 of 28-day cycles then Q4W in cycles 7+
+ Pomalidomide 2 mg PO on D1-21 from cycle 1+
+ Dexamethasone 20 mg IV/PO on D1, 8, 15, 22 from cycle 1+
(n = 25 BCMA naive)

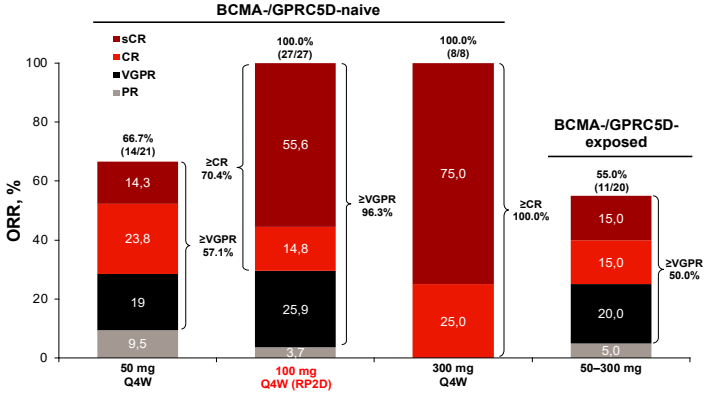
*Prephase dosing of cevostamab: double-step up dosing (0.3/3.3 mg) in a 14-day prephase or triple step-up (0.3/1.2/3.6 mg) in a 21-day prephase. Patients hospitalized after prephase cevostamab infusions for ≥48 hr.

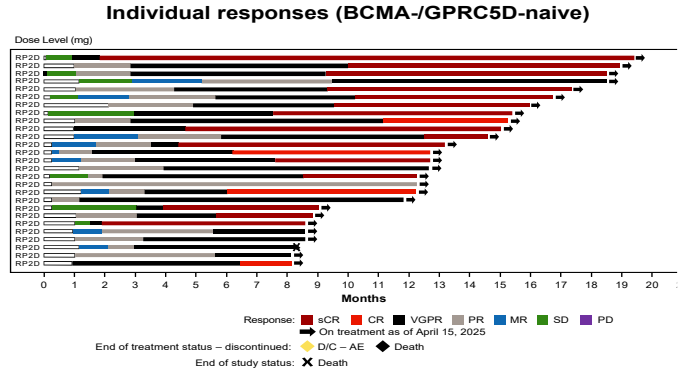
Parameter, %	Cevo 70 mg/ Pom/Dex (n = 29)	Cevo 105 mg/ Pom/Dex (n = 25)
ORR, % (95% CI)	86.2 (71.9–100)	88.0 (73.3–100)
sCR, %	34.5	44.0
CR, %	10.3	16.0
VGPR, %	27.6	16.0
PR, %	13.8	12.0
≥ CR, %	44.8	60.0
≥ VGPR, %	72.4	76.0
Responders with ongoing response at DCO, n/N (%)	20/25 (80.0)	18/22 (81.8)
6-mo DoR, % (95% CI)	96.0 (88.3–100)	90.9 (78.9–100)
MRD− CR in MRD-evaluable CR+ patients, n/N (%)		
• MRD− CR at 10^{-5}	10/11 (90.9)	11/12 (91.7)
• MRD− CR at 10^{-6}	8/11 (72.7)	10/12 (83.3)
MRD− CR at 10^{-5} in all patients, n/N (%)	10/29 (34.5)	11/25 (44.0)

- 29 patients included in this cohort, after a median of 2L of therapy; 72.4% TCE and 31% TCR
- 25 patients included in this cohort, after a median of 2L of therapy; 56% TCE and 24% TCR

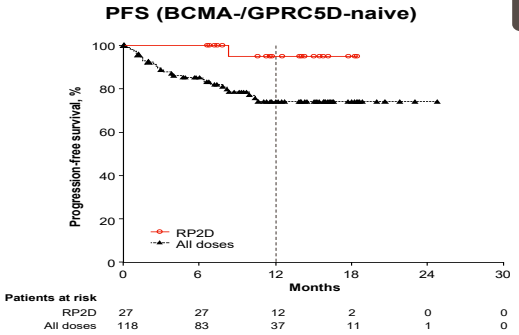


First-in-Human Study of JNJ-79635322 (JNJ-5322): Ramantamig, a BCMA-GPRC5D-CD3 mAb and Novel Next-Generation Trispecific Antibody, in Patients With RRMM – Initial Phase I Results





Only one discontinuation to date at the RP2D



12-month PFS 95.0% at the RP2D (74.1% across all doses) PFS data support the RP2D

AE, adverse event; BCMA, B cell maturation antigen; CR, complete response; D/C, discontinued; ORR, overall response rate; MR, minimal response; PD, progressive disease; PFS, progression free survival; Q4W, every 4 weeks; RP2D, recommended phase II dose; RRMM, relapsed/refractory multiple myeloma; SD, stable disease; vGPR, very good partial response.

Figures adapted from Popat R, et al. EHA 2025. Abstract S100.

TRIgnite-1 ISB 2001 (BCMA × CD38 × CD3): First TREAT TM Trispecific Antibody for RRMM

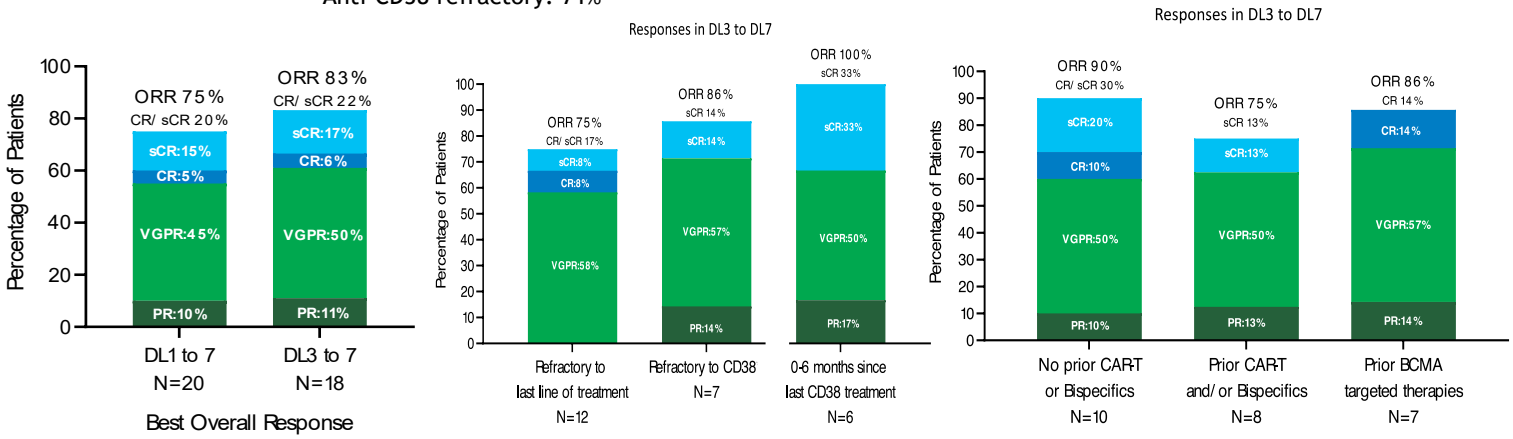
Dose escalation/expansion study in dose escalation. ISB 2001 is administered SC QW in 28-day cycles, starting with 2 step-up doses on days 1 and 4, followed by the full target dose from day 8 onward

Population (n = 40)

Median number of 6 PL. 100% TCE and 25% TCR

Prior BCMA therapy: 46%; Prior BCMA CAR T: 10%; Prior BCMA BsAbs: 20%; Prior BCMA ADC: 25%

Anti-CD38 refractory: 71%



Safety profile: G3–4 neutropenia in 30%, and G3–4 infections in 15%; CRS in 75%, but G1–2; median time to onset was 3 days and duration of 2 days

Trial is ongoing to define the RP2D

TREAT ™, Trispecific Engagement by Antibodies based on the TCR; BEAT®, Bispecific Engagement by Antibodies based on the TCR.

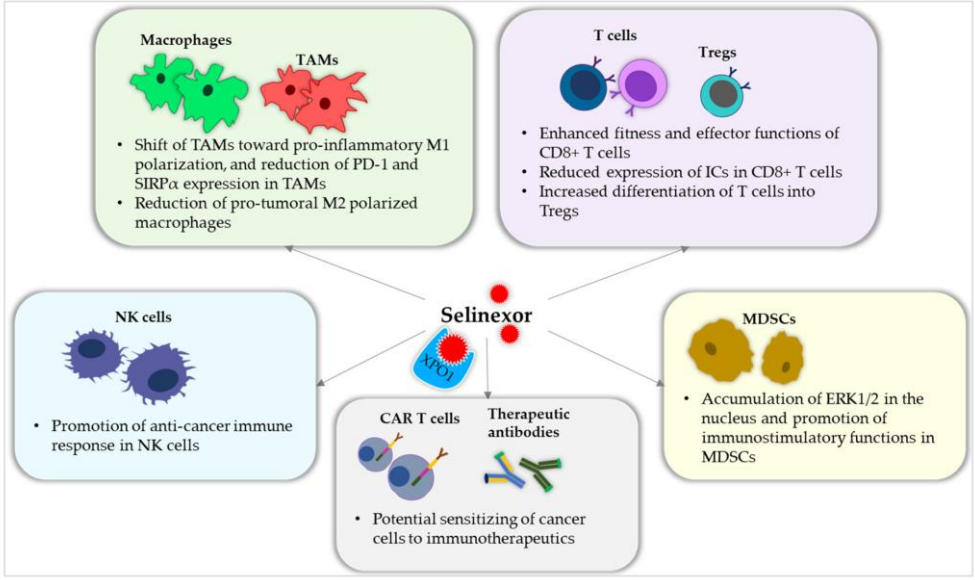
Carretero-Iglesia L, et al. *Nat Cancer*. 2024;5:1494-1514; Quach H, et al. ASH 2024. Abstract P898.

And Beyond the T-Cell Redirecting Therapies . . .

- We have to implement the use of therapies to enhance the immune system to facilitate adequate sequencing

Selinexor Influences Multiple Immune Cells Pathways

Schematic illustration of selinexor's influence on immune cells and immunotherapy



Selinexor is suggested to **impact macrophages** and **tumor-associated macrophages** (TAMs), **myeloid-derived suppressor cells** (MDSCs), **natural killer** (NK) **cells**, and T cells in the **tumor microenvironment**

Selinexor potentially **sensitizes cancer cells** to **CAR T cells** and therapeutic **antibodies**[a]

[a]Selinexor SmPC does not specify guidance on its use in sequence with CAR T cells.
CAR-T, chimeric antigen receptor T cell; ERK1/2, extracellular-signal regulated kinases 1/2; IC, immune checkpoint; MDSC, myeloid-derived suppressor cell; NK, natural killer; PD-1, programmed death 1; SIRPα, signal regulatory protein alpha; TAM, tumor-associated macrophage; Treg, regulatory T cell.

UPREGULATION OF BCMA EXPRESSION BY SELINEXOR

Christina Verbruggen[1], Umair Munawar[1], Seungbin Han[1], Julia Mersi[1], Emma Besant[1], Shilpa Kurian[1], Silvia Nerreter[1], Nina Rein[1], Johanna Lehmann[1], Max Koeppel[1], Hermann Einsele[1], Johannes Waldschmidt[1], Martin Kortüm[1]

1. University Hospital Wuerzburg, Department of Internal Medicine II, Wuerzburg, Germany

Abstract # 6102

INTRODUCTION

- Selinexor is a selective inhibitor of nuclear export that targets XPO1
- XPO1 exports tumor suppressor proteins and oncogenic factors from nucleus to cytoplasm.
- Selinexor + bortezomib + dexamethasone (SVd) is FDA-approved (BOSTON trial) for ≥1 prior-line multiple myeloma.
- Prior work reports Selinexor increases BCMA expression (Wang et al., 2023), but solely based on flow cytometry, no functional assays.
- Flow cytometry is limited in sensitivity and cannot quantify receptor density on a single-cell level.

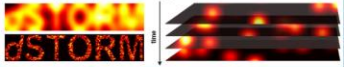
AIM

Provide first insights into BCMA receptor density changes after Selinexor treatment using *d*STORM.

METHOD

Treatment of MM cell models (OPM-2, AMO1) with Selinexor for 1, 2 and 5 days at 10 nM and 50 nM concentration followed by:

- Gene expression analysis via qPCR
- Receptor expression analysis via *d*STORM



RESULTS

1. BCMA GENE EXPRESSION INCREASED BY SELINEXOR TREATMENT

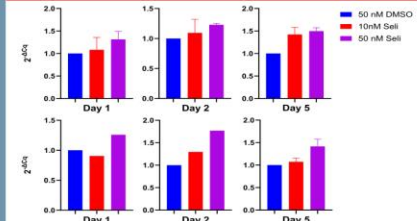


Figure 1. qPCR quantification of BCMA gene expression in OPM-2 (top) and AMO1 (bottom) cells treated with 50 nM DMSO (blue), 10 nM Selinexor (red) or 50 nM Selinexor (magenta) for 1, 2 and 5 days. OPM-2 cells showed a 1.2- and 1.5-fold increase and AMO1 cells revealed a 1.8- and 1.5-fold increase in BCMA gene expression on days 2 and day 5, respectively.

2. SELINEXOR CONCENTRATIONS DO NOT IMPACT CELL VIABILITY

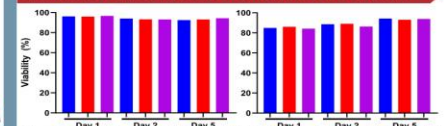


Figure 2. Cell viability of OPM-2 (left) and AMO1 (right) cells when treated with 50 nM DMSO (blue), 10 nM Seli (red) or 50 nM Seli (magenta). Viability of OPM-2 cells remained above 90% and AMO1 cell viability even improved from 84% to 93% by day 5

3. BCMA RECEPTOR EXPRESSION INCREASED BY SELINEXOR TREATMENT

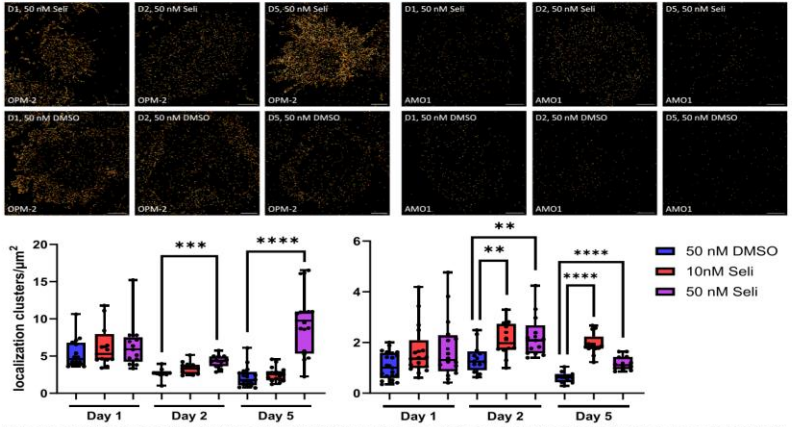


Figure 3. Top: *d*STORM images of OPM-2 (first three columns) and AMO1 (last three columns) after respectively 1, 2 and 5 days of treatment. Top panels show 50 nM Selinexor treated cells, bottom panel 50 nM DMSO. Scale bars, 3 µm. Each yellow dot corresponds to one BCMA receptor, an increase in signal can be seen in the Selinexor treated samples compared to DMSO treated cells. Bottom: Corresponding quantifications of BCMA receptor density from *d*STORM measurements plotted in a box plot. Here, each dot respresents the BCMA expression in one cell and the line in the middle corresponds to the median receptor density. Significant increases in BCMA receptor density corresponding to a 1.6- and 4.2-fold increase in OPM-2 cells and 1.9- and 1.6-fold increase in AMO1 cells on day 2 and 5, respectively.

CONCLUSIONS

Selinexor may enhance target antigen availability on the cell surface, potentially improving the efficacy of BCMA-directed immunotherapies.

- BCMA gene and receptor expression are significantly increased in AMO1 and OPM-2 cell lines by Selinexor in a time- and dose- dependent fashion
- Cell viability is not impacted by the chosen Selinexor concentrations

OUTLOOK

- Verify BCMA upregulation by Selinexor in patient samples
- Correlate receptor expression with therapeutic efficacy (BiSpecs, BCMA CAR-T cells, ADCs)
- Study impact of Selinexor on T cell fitness
- Study Selinexor modulation of other immunotherapy targets (CD38, FcRH5, GPRC5D)

CONTACT INFORMATION

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Summary

- Treatment is rapidly evolving
- The first line of therapy seems to be now well established with PIs, IMiDs, and anti-CD38 mAbs
- BCMA-targeted therapies are options at early relapse: today with Cilta-cel and Belamaf-based combinations, and BCMA BsAbs are coming
- CELMoDs will be also be available soon, with 2 combinations based on Iber-Dara-Dex and mezigdomide-carfilzomib-Dex
- The availability of all these options may allow for a more individualized therapy based on the disease and patient-based characteristics
- T-cell redirecting therapies against other targets are coming and will facilitate the sequencing
- Sequencing is also a challenge, and we should generate information from the real-world experiences

Global Multiple Myeloma Academy

Discussion

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Session Close – Audience Response Questions

Rafael Fonseca, MD

APTITUDE HEALTH®

Question 10

[REPEATED]: True or False: BCMA is the most common antigen targeted by currently approved CAR T-cell therapies in multiple myeloma.

1. True
2. False

Question 11

[REPEATED]: What is the primary mechanism of action for CELMoDs?

1. Direct inhibition of the proteasome
2. Modulating cereblon E3 UL, leading to degradation of signaling proteins
3. Blockade of BCMA signaling
4. Activation of immune checkpoint pathways

Thank You!

- Please complete the **evaluation survey** that will be sent to you via chat
- The meeting recording and slides presented today will be shared on the www.globalmmacademy.com website

THANK YOU!

Global Multiple Myeloma Academy

Global Multiple Myeloma Academy: Emerging and Practical Concepts in RRMM

Thank you!

Pfizer

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