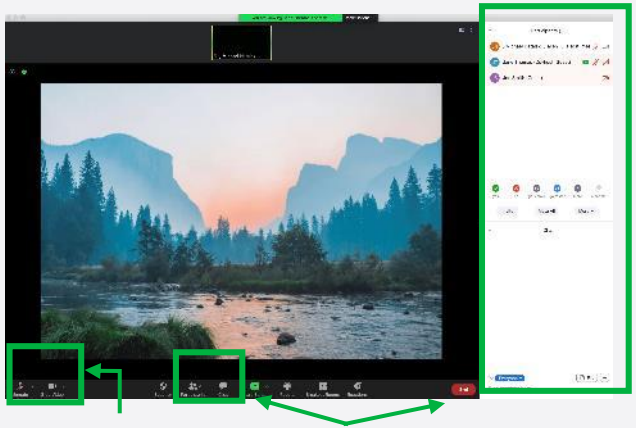
Housekeeping Notes for Faculty

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

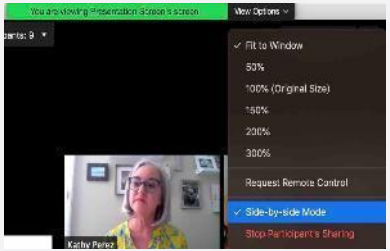
Functionality and Settings

To be announced prior to start of meeting

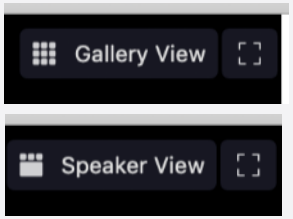


Microphone and Camera
Mute and unmute your camera/microphone by clicking the icons in the lower left-hand corner

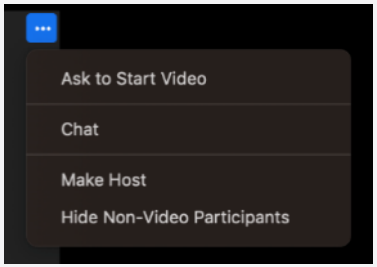
Participant and Chat Window
Reveal or hide the chat and participant window by selecting the corresponding icons in the bottom toolbar



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



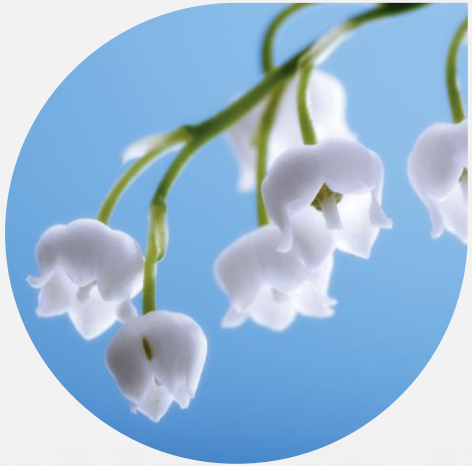
Gallery and Speaker View
In the upper right-hand corner, select "Gallery View" (Note: If button says "Speaker View," you are already seeing "Gallery View")



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

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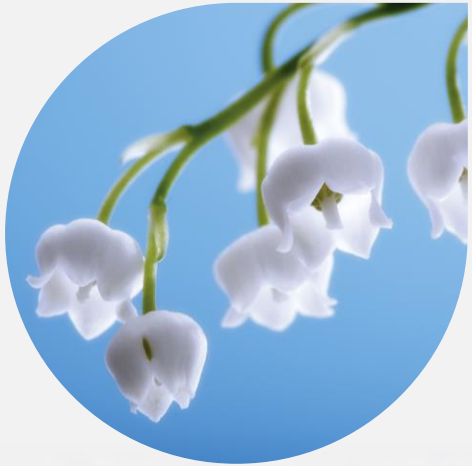

Global Multiple Myeloma Academy

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

April 29–30, 2026 – European Region

Pfizer

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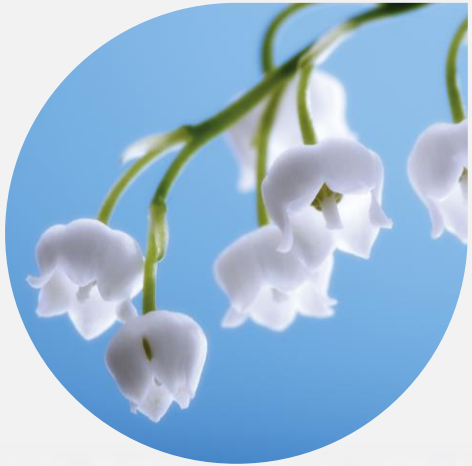
Global Multiple Myeloma Academy



Welcome and Meeting Overview

Philippe Moreau, 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 RRMM 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 1 – 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** • Introduction to audience response system (ARS)	Rafael Fonseca, MD, Philippe Moreau, MD
17.10 – 17.40 30 min	**Bispecific Antibodies in RRMM** (20-min presentation; 10-min Q&A)	Katja Weisel, MD
17.40 – 18.10 30 min	**Overview of Later-Line RRMM Treatment and Management** (20-min presentation; 10-min Q&A)	Rafael Fonseca, MD
18.10 – 18.25 15 min	**Break**	
18.25 – 18.55 30 min	**Immunotherapy Sequencing in RRMM: Current and Future Landscape** (20-min presentation; 10-min Q&A)	Hermann Einsele, MD
18.55 – 19.40 45 min	**Panel Discussion and Audience Q&A** Regional challenges in treating patients with RRMM	All faculty
19.40 – 20.00 20 min	**Session Close** • ARS questions	Rafael Fonseca, MD

Global Multiple Myeloma Academy

Introduction to the Audience Response System

Philippe Moreau, MD

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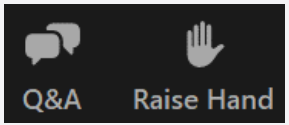
Functionality and Settings: Q&A

After each presentation, there will be 5 minutes for Q&A

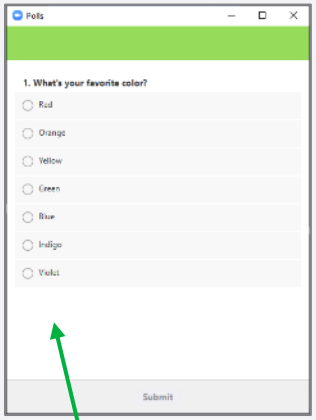
Questions can be asked in two ways

- **Q&A box** – type your question in the box
- **Raise Hand** – click to raise hand; the chair will invite you to comment, and you will be unmuted

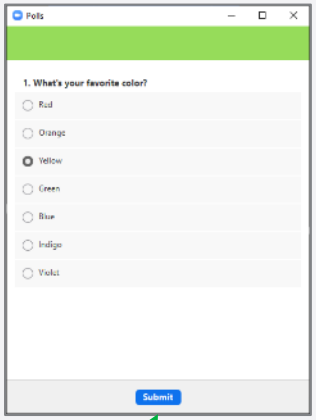


Functionality and Settings: Polling Questions

Desktop View



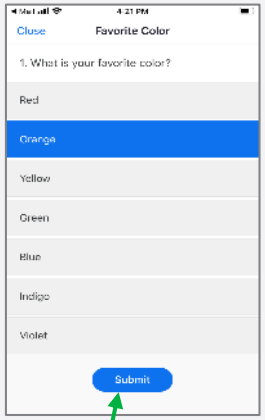
Choose Your Answer
Click on the answer (or answers if multiple choice)



Select Submit
After choosing your answer, select “Submit” to finalize

Mobile View

Choose Your Answer
Click on the answer (or answers if multiple choice)



Select Submit
After choosing your answer, select “Submit” to finalize

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. Other

Question 2

In the last 12 months, how many patients with relapsed/refractory multiple myeloma have you treated?

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

Question 3

Which of the following is not a BCMA-directed bispecific antibody?

1. Elranatamab
2. Linvoseltamab
3. Talquetamab
4. Teclistamab

Question 4

What is true about the MagnetisMM-3 clinical trial?

1. Elranatamab was administered subcutaneously, with step-up dosing
2. Evaluated IV BCMA-targeted antibody in combination with daratumumab
3. Primarily assessed overall survival with CAR T-cell therapy
4. Randomized study comparing elranatamab with standard chemotherapy in 1L MM

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Bispecific Antibodies in RRMM

Katja Weisel, MD

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Bispecific Antibodies in RRMM

Katja Weisel, MD
University Cancer Center Hamburg

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Universitätsklinikum Hamburg-Eppendorf

Disclosures

1. Employment or Leadership Position: none
2. Advisory Role or Expert Testimony: Abbvie, Adaptive, Amgen, Bristol Myers Squibb, Celgene, CellCentric, Janssen, GSK, Karyopharm, Novartis, Oncopeptides, Pfizer, Roche Pharma, Takeda, Sanofi
3. Stock Ownership: none
4. Patent, Copyright, Licensing: none
5. Honoraria: Abbvie, Adaptive, Amgen, Bristol Myers Squibb, Celgene, Janssen, GSK, Karyopharm, Novartis, Oncopeptides, Pfizer, Roche Pharma, Takeda, Sanofi
6. Financing of Scientific Research: Amgen, Celgene, Janssen, Sanofi; GSK, Abbvie
7. Other Financial Relationships: none
8. Other Conflicts of Interest: none

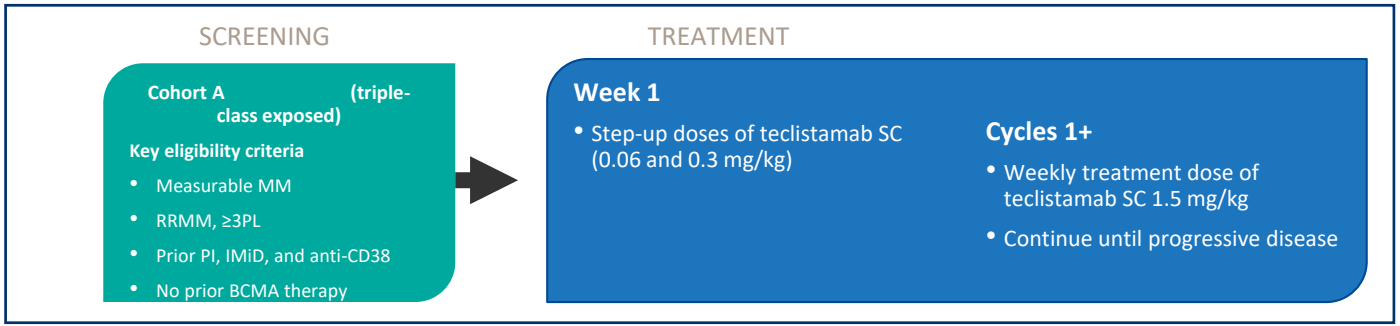
BCMA-directed TCE in Treatment of RRMM

	Teclistamab[1-3]	Elranatamab[4-6]	Linvoseltamab[7-8]
Monotherapy Study Data Summary Source	**MajesTEC-1** Phase 1/2	**MagnetisMM-3** Phase 2	**LINKER-MM1** Phase 1/2
Prior Therapy	Prior PI, IMiD, CD38 No prior BCMA	Prior PI, IMiD, CD38 No prior BCMA	Prior PI, IMiD, CD38 Post-CAR T ≥PR
Monotherapy Efficacy	**ORR 63%** **mDOR 18.4 mo** **mPFS 11.4 mo** **mOS 22.2 mo** **(mF/up 30.4 mo)**	**ORR 61%** **24-mo DOR 67%** **mPFS 17.2 mo** **mOS 24.6 mo** **(mF/up 28.4 mo)**	**ORR 71%** **12- mo DOR 81%** **12-mo PFS 70%** **mOS NR** **(mF/up 14.3 mo)**

BCMA=B-cell Maturation Antigen. CAR T=Chimeric Antigen Receptor. GR=Grade. iMiD=Immunomodulatory Drugs. mDOR=Median Duration of Response. mF/up=Median Follow Up. Mo=Months. mOS=Median Overall Survival. mPFS=Median Progression-Free Survival. NE=Not Evaluable. NR=Not Reached. ORR=Overall Response Rate. PI=Proteasome Inhibitors. PR=Partial Response. Q2W=Every 2 Weeks. RRMM=Relapsed/Refractory Multiple Myeloma.

1. Teclistamab-cqyv. EMA SmPC. Janssen-Cilag International NV, Belgium: 2022. Updated 2024. 2. Teclistamab-cqyv. FDA Label. Janssen Biotech, Inc. Horsham, PA 19044: 2022. Updated 2024.
3. Garfall AL, et al. Poster #7540. ASCO Annual Meeting; May 31-June 4, 2024; Chicago, IL. 4. Elranatamab-bcmm. EMA SmPC. Pfizer Europe MA EEIG, Belgium: 2023. Updated 2024.
5. Elrantamab-bcmm. FDA Package Insert. Initial U.S. Approval: 2023. (Updated Aug 2023). 6. Tomasson MH, et al. HemaSphere. 2024 Jul 24;8(7):e136.
7. Linvoseltamab injection, for intravenous use. EMA SmPC. Regeneron Ireland Designated Activity Company (DAC). Dublin, Ireland . May 2025.

Teclistamab in RRMM – MajesTEC 1-Trial



Characteristic	Safety Analysis N=165
Age (years), median (range)	64.0 (33–84)
Age ≥75 years, n (%)	24 (14.5)
Extramedullary plasmacytomas ≥1[c], n (%)	28 (17.0)
Prior lines of therapy, median (range)	5.0 (2–14)
Refractory status, n (%)	
Triple-class refractory[f]	128 (77.6)
Penta-drug refractory[g]	50 (30.3)

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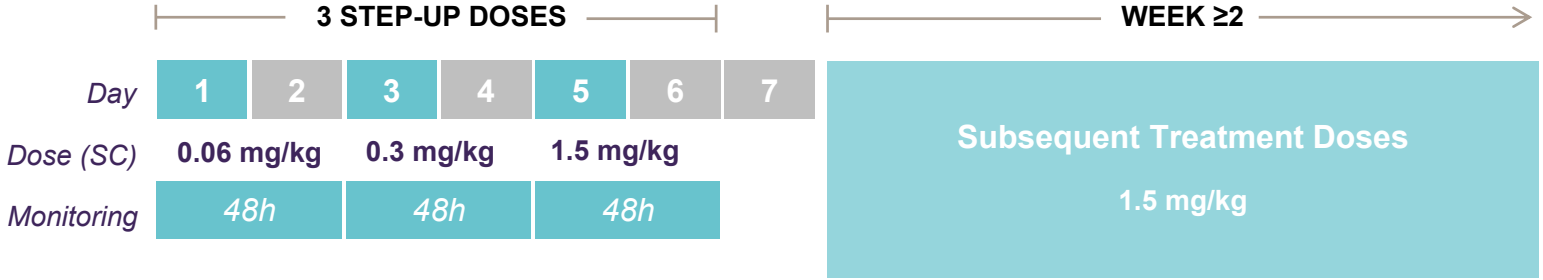
Moreau P et al., N Engl J Med. 2022 Aug 11;387(6):495-505

Dosing Schedule and CRS: Teclistamab

Dosing Schedule[1]



CRS incidence by dose (N=165)[2,*]

Step-up dose 1	Step-up dose 2	First full treatment dose
43.6%	35.2%	24.2%

Subsequent full treatment doses

~10%

of CRS events occurred in subsequent doses following the first treatment dose[†]

Overall incidence of CRS: 72.1%

*Median follow-up: 14.1 months.
†All-grade CRS rate with Cycle 1 Day 8: 4.8%; Cycle 1 Day 15: 2.4%; Cycle 1 Day 22: 1.2%; and ≥Cycle 2: 3.6%.
CRS, cytokine release syndrome; h, hour; SC, subcutaneous.
1. TECVAYLI® (teclistamab) Summary of Product Characteristics. Beerse, Belgium: Janssen-Cilag International; 2024. 2. Martin TG, et al. *Cancer.* 2023;129(13):2035–2046.
Dosing schema based on information from TECVAYLI® (teclistamab) Summary of Product Characteristics. Beerse, Belgium: Janssen-Cilag International; 2024.

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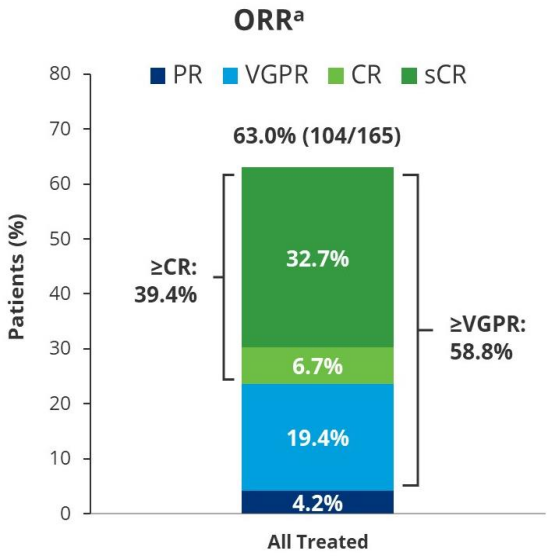
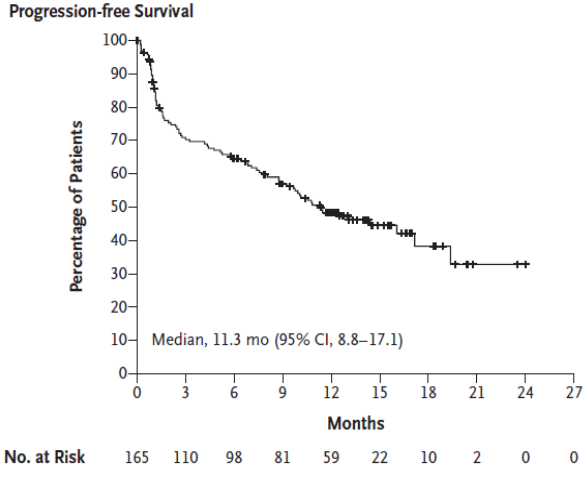
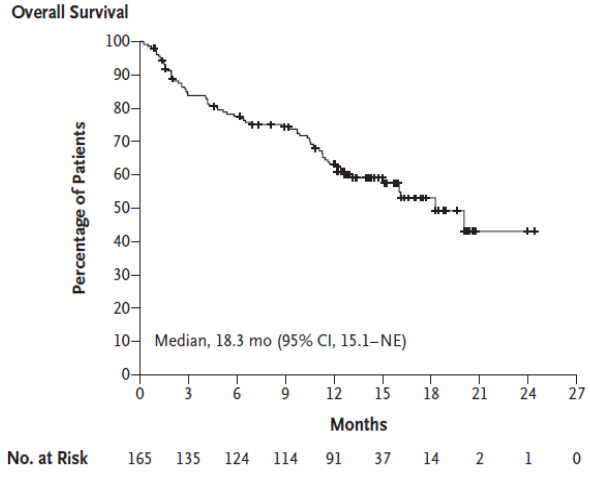
Teclistamab in RRMM – MajesTEC 1-Trial







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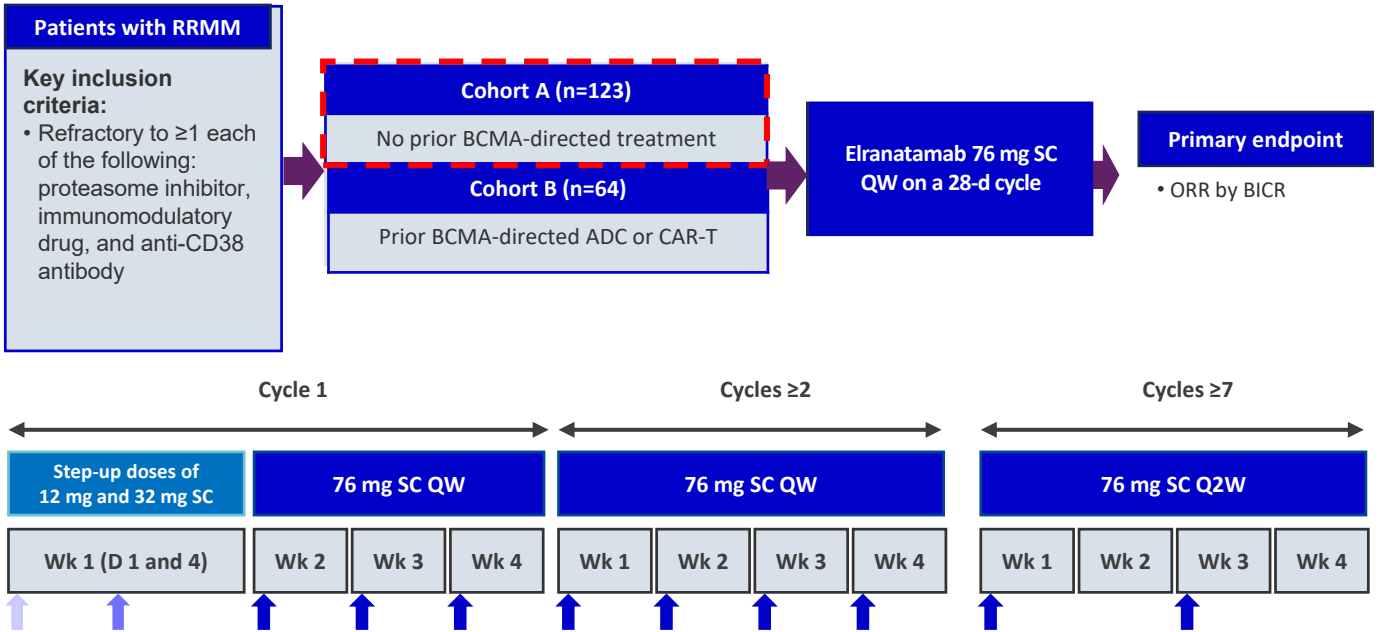
Moreau P et al., N Engl J Med. 2022 Aug 11;387(6):495-505

Elranatamab in RRMM – MagnetisMM-3 Trial

MagnetisMM-3 is an open-label, multicenter, non-randomized, phase 2 study



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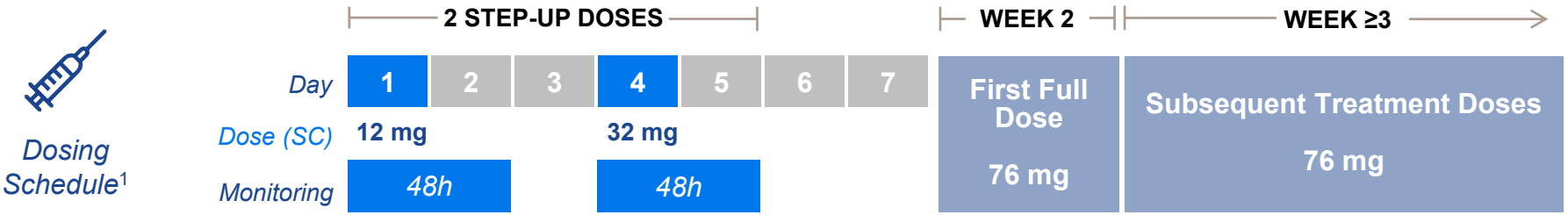
Bahlis NJ et al., Nat Med. 2023 Oct; 29(10):2570-2576

Dosing Schedule and CRS: Elranatamab



CRS incidence by dose (n=119)[2,*]

Step-up dose 1	Step-up dose 2	First full treatment dose	Subsequent full treatment doses
44.5%	**20.2%**	**5.9%**	**0.8%**

Overall incidence of CRS: 56.3%

*Patients receiving the two step-up dose regimen. Median follow-up: 14.7 months.
CRS, cytokine release syndrome; h, hour; SC, subcutaneous.
1. ELREXFIO® (elranatamab) Summary of Product Characteristics. Bruxelles, Belgium: Pfizer Europe; 2025. 2. Lesokhin AM, et al. *Nat Med*. 2023;29(9):2259–2267.
Dosing schema based on information from ELREXFIO® (elranatamab) Summary of Product Characteristics. Bruxelles, Belgium: Pfizer Europe; 2025.

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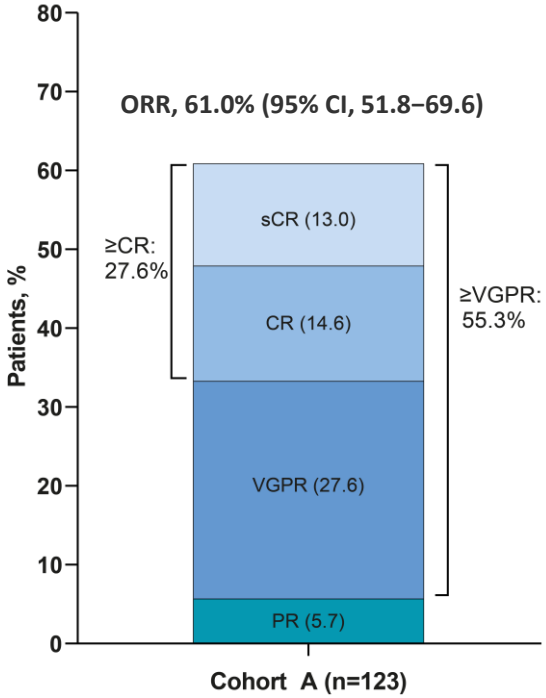
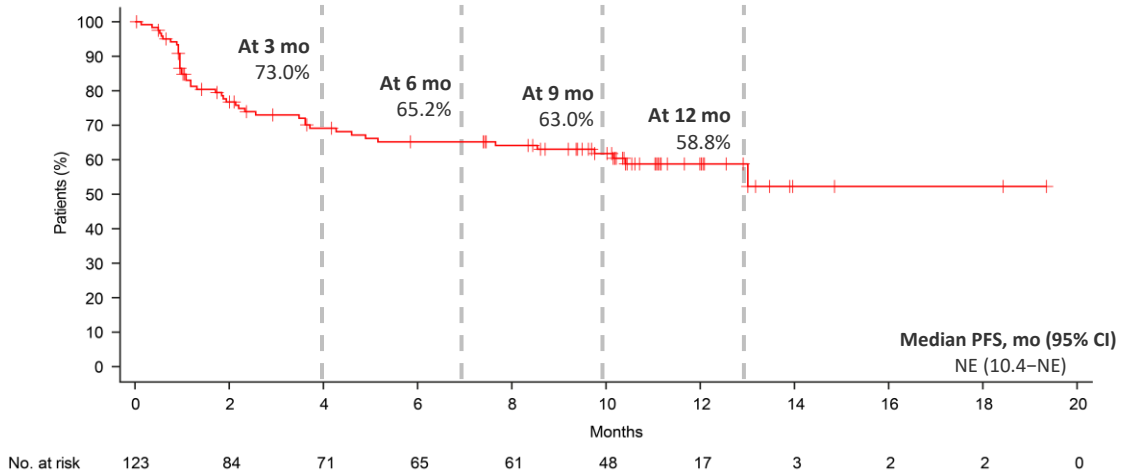
Elranatamab in RRMM – MagnetisMM-3 Trial





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Bahlis NJ et al., Nat Med. 2023 Oct; 29(10):2570-2576

LINKER-MM1 Study: Phase-2 Design

Key eligibility criteria for Phase 2

- Active MM by IMWG
- Progression on or after at least 3 lines of therapy including an IMiD, a PI, and an anti-CD38 Ab, or triple-refractory disease (refractory to at least 1 IMiD + 1 PI +1 anti-CD38 Ab)

Key Phase 2 objectives

- Primary: To assess the antitumor activity as measured by ORR as determined by a blinded IRC (IMWG criteria)
- Secondary: ORR by investigator assessment, DOR, PFS, MRD status, and OS

Linvoseltamab IV dosing schedule for Phase 2 expansion cohorts

	W1	W2	W3–14	W16–23	W24+
	Step-up doses		Cycle 1–3	Cycles 4–5	Cycle 6 onwards
50 mg cohort	5 mg	25 mg	50 mg QW*	50 mg Q2W	50 mg Q2W
200 mg cohort	5 mg	25 mg	200 mg QW	200 mg Q2W	≥VGPR → 200 mg Q4W <VGPR → 200 mg Q2W

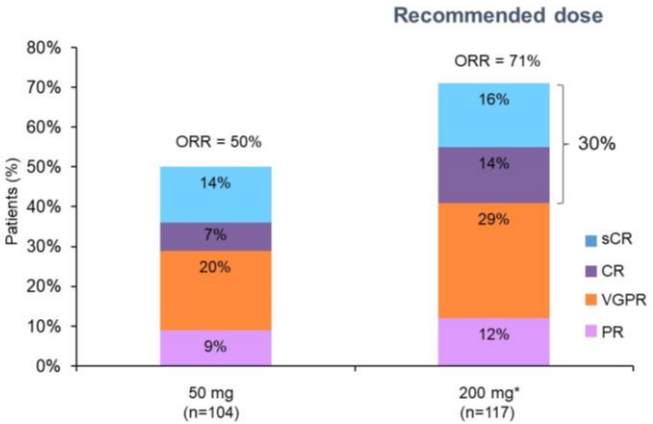
Day 1 Day 8

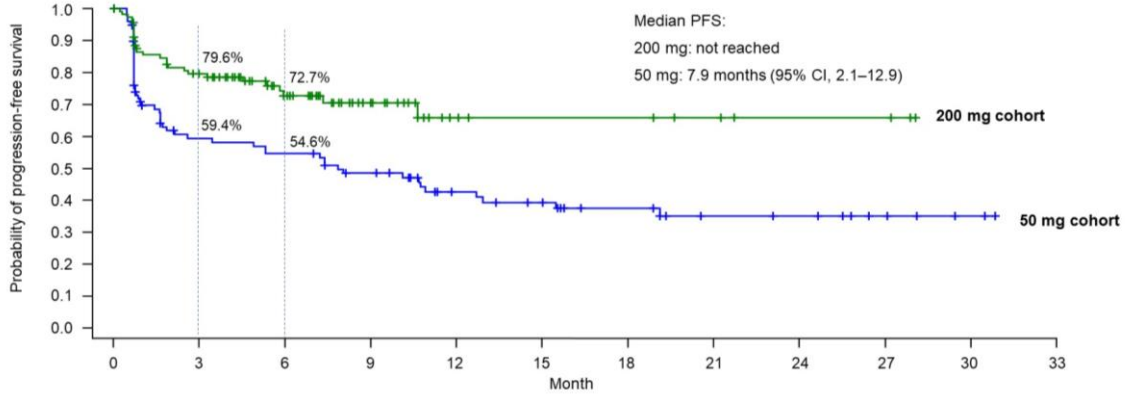
24 h Hospitalization

*Patients in the 50 mg cohort who progress within 4-12 weeks of treatment were allowed to escalate to 200 mg dosing.

Ab, antibody; CD, cluster of differentiation; DOR, duration of response; IMiD, immunomodulatory drug; IMWG, International Myeloma Working Group; IRC, independent review committee; IV, intravenous; MM, multiple myeloma; MRD, minimal residual disease; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; PI, proteasome inhibitor; QW, once every week; Q2W, once every 2 weeks; Q4W, once every 4 weeks; VGPR, very good partial response; W, week.

Linvoseltamab in RRMM – LINKER-MM-1 Trial





Data cut-off: 28 Feb 2023. Median duration of follow-up for 50 mg was 7.7 months (range 0.3–31.3), and for 200 mg was 5.6 months (range 0.2–28.2).
*PFS as measured using the IMWG criteria (Kumar, 2016)
CI, confidence interval; PFS, progression-free survival.

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Dosing Schedule and CRS: Linvoseltamab

Dosing Schedule

3 STEP-UP DOSES — **WEEK ≥4**

	Day	1	2	3	4	5	6	7	1	2	3	4	5	6	7	1	2	3	4	5	6	7
Dose (IV)		**5 mg**							**25 mg**							**200 mg**						
Infusion + Monitoring		*4+24h*							*4+24h**													

**Patients who have experienced CRS, IRR or a neurologic adverse reaction, or any Grade ≥2 AE with the first step-up treatment.*

Subsequent Treatment Doses

200 mg

CRS incidence by dose (N=117)

Step-up dose 1	Step-up dose 2	First full treatment dose	Second full treatment dose
38%	**17%**	**10%**	**3.6%**

Overall incidence of CRS: 46%

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AE, adverse event; CRS, cytokine release syndrome; h, hour; IRR, infusion-related reaction; IV, intravenously.

LYNOZYFIC™ (linvoseltamab) Summary of Product Characteristics. Dublin, Ireland: Regeneron Ireland Designated Activity Company; 2025.
Dosing schema based on information from LYNOZYFIC™ (linvoseltamab) Summary of Product Characteristics. Dublin, Ireland: Regeneron Ireland Designated Activity Company; 2025.

Safety Profiles: BCMA-directed TCE

Key Adverse Events of Special Interest

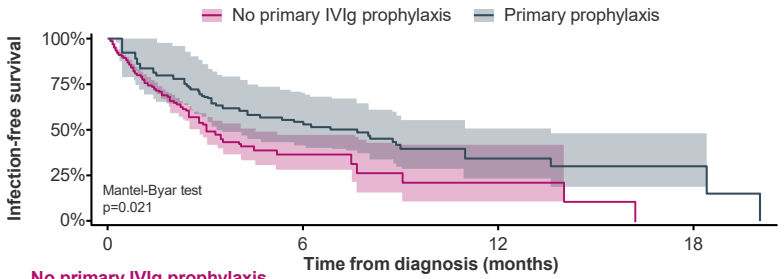
Agent Trial	Teclistamab[1,2] MajesTEC-1	Elranatamab[3,4] MagnetisMM-3	Linvoseltamab LINKER-MM1[5]
Safety set, N	BCMA-naïve n=165	BCMA-naïve n=123	n=117
CRS, %			
All grade	**72.1**	**57.7**	**46.2**
Grade 3 / 4	**0.6**	**0**	**NR**
ICANS, %			
All grade	**3**	**4.9**	**7.7**
Grade 3 / 4	**0**	**0**	**2.6**
Grade 3 / 4 cytopenias, %			
Neutropenia	**65.5**	**49.6**	**NR**
Anaemia	**37.6**	**37.4**	**NR**
Thrombocytopenia	**23.0**	**23.6**	**NR**
Infections, %			
All grade	**78.8**	**70.7**	**75.2**
Grade 3 / 4	**55.2**	**41.5**	**36.8**

1. Garfall AL, et al. Abstract 7540. Poster presentation at: 2024 ASCO Annual Meeting, Chicago, IL, USA. 2. Sidana S, et al. Abstract P879. Poster presentation at: EHA 2023 Hybrid Congress, Frankfurt, Germany.
Table adapted from Garfall AL, et al. Abstract 7540. Poster presentation at: 2024 ASCO Annual Meeting, Chicago, IL, USA and includes data from Sidana S, et al. Abstract P879. Poster presentation at: EHA 2023 Hybrid Congress, Frankfurt, Germany.
3. Prince HM, et al. Abstract 4738. Poster presentation at: 2024 ASH Annual Meeting and Exposition, San Diego, CA, USA. 4. Tomasson MH, et al. *HemaSphere*. 2024;8(7):e136.
Table created with data from Prince HM, et al. Abstract 4738. Poster presentation at: 2024 ASH Annual Meeting and Exposition, San Diego, CA, USA, and Tomasson MH, et al. *HemaSphere*. 2024;8(7):e136.
5. Shah MR, et al. Abstract 3369. Poster presentation at: 2024 ASH Annual Meeting and Exposition, San Diego, CA, USA.
Table created with data from Shah MR, et al. Abstract 3369. Poster presentation at: 2024 ASH Annual Meeting and Exposition, San Diego, CA, USA.

Supplemental Administration of IVIg During BCMA-directed BsAbs Treatment Is Associated With Improved Clinical Outcomes

N=225 patients with RRMM receiving teclistamab or investigational BCMA-directed BsAb

Infection-free survival for all-grade infection*

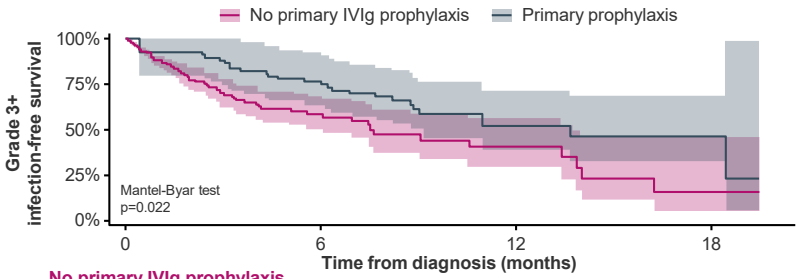


No primary IVIg prophylaxis				
At Risk	221	12	2	0
Events	0	89	92	94
Primary prophylaxis				
At Risk	13	41	10	2
Events	0	25	36	37

Median infection-free survival, months (95% CI)

Primary prophylaxis	7.7 (3.3–14)
No primary IVIg prophylaxis	3 (2.6–4.5)

Infection-free survival for Grade ≥3 infection*



No primary IVIg prophylaxis				
At Risk	223	33	9	2
Events	0	60	67	71
Primary prophylaxis				
At Risk	13	48	13	2
Events	0	12	23	24

Median infection-free survival, months (95% CI)

Primary prophylaxis	14 (8.8–NR)
No primary IVIg prophylaxis	7.5 (6.1–14)

Median **infection-free survival** for all-grade infections and for Grade ≥3 infections **was longer** in patients **with** **vs** **without** primary IVIg prophylaxis

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*Based on a retrospective study between November 2017 and December 2023. Primary prophylaxis was defined as IVIg after the start of BsAb but before any documented infection.
BCMA, B-cell maturation antigen; BsAb, bispecific antibody; CI, confidence interval; IVIg, intravenous immunoglobulin; RRMM, relapsed and/or refractory multiple myeloma.
Mohan M, et al. *Blood Cancer J.* 2025;15(1):74.
Figures reproduced from Mohan M, et al. *Blood Cancer J.* 2025;15(1):74.

Phase 1/2 MonumenTAL Study of Talquetamab in Patients With RRMM: Extended Follow-Up

Key Eligibility Criteria

- Phase 1: Intolerant to or progressed on established therapies; ECOG PS 0-1
- Phase 2: ≥3 prior LOT (≥1 PI, ≥1 IMiD, ≥1 anti-CD38 mAb); ECOG PS 0-2

TCR Naive: 0.4 mg/kg SUBQ qw[a] (n=143)

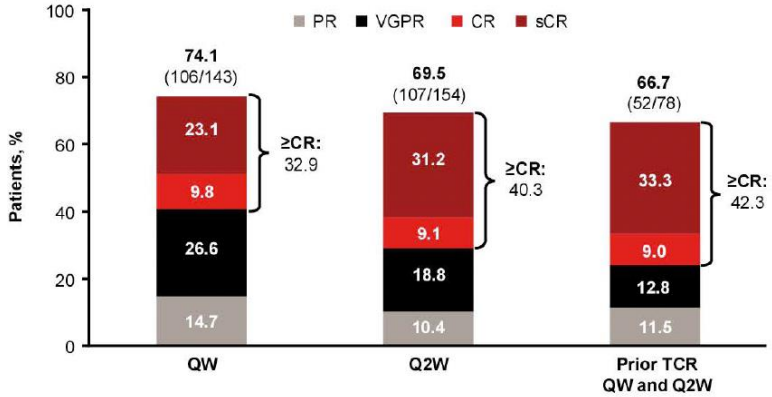
TCR Naive: 0.8 mg/kg SUBQ q2w[a] (n=154)

Prior TCR: 0.4 mg/kg SUBQ qw or 0.8 mg/kg SUBQ q2w[a] (n=78; 70 qw; 8 q2w)

Extended median follow-up: 30-38 months

Primary endpoint: ORR (IRC via IMWG criteria)
Secondary endpoints: DOR, PFS, OS, MRD-neg rate (BM aspirate via NGS), safety

ORR

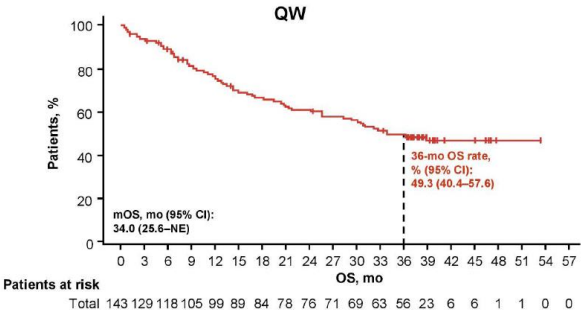


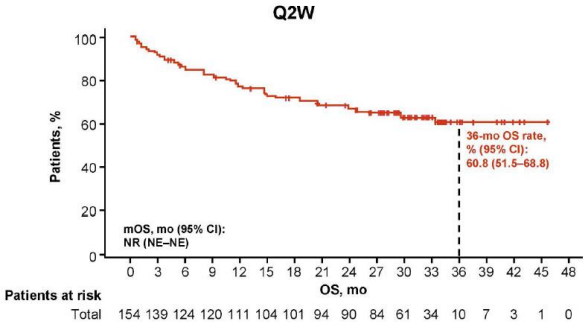
Efficacy Outcomes	qw (n=143)	q2w (n=154)	Prior TCR: qw/q2w (n=78)
Median FU, months	38.2	31.2	30.3
Median DOR, months (95% CI)	9.5 (6.7-13.4)	17.5 (12.5-25.1)	19.2 (8.1-24.7)
Median PFS, months (95% CI)	7.5 (5.7-9.4)	11.2 (7.7-14.6)	7.7 (4.1-14.5)
MRD neg. (10^{-5}) (95% CI)[a]	64.3 (51.9-75.4)	65.2 (52.8-76.3)	57.1 (37.2-75.5)

Rasche L, et al. ASCO 2025. Abstract 7528.

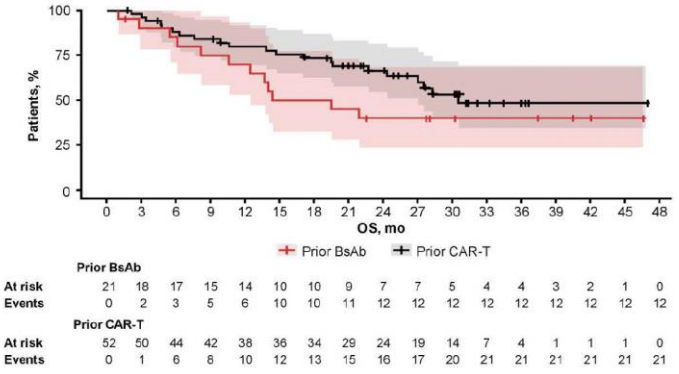
Phase 1/2 MonumenTAL Study of Talquetamab in Patients With RRMM: Extended Follow-Up

Median OS by Cohort: qw, q2w, and qw/q2w (Prior TCR)





OS in Prior TCR Cohort by Prior BsAb and CAR-T Exposure[a]



[a] 5 patients who received both prior BsAb and CAR-T were excluded from this analysis.

Rasche L, et al. ASCO 2025. Abstract 7528.

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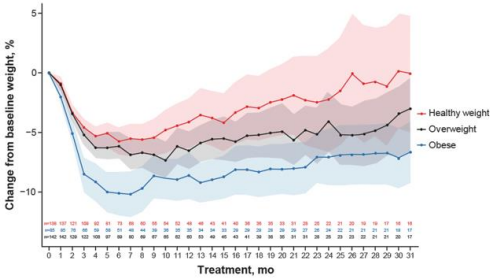
Phase 1/2 MonumenTAL Study of Talquetamab in Patients With RRMM: Extended Follow-Up

	AEs (≥30% in Any Cohort), n (%)	qw (n=143)		q2w (n=154)		Prior TCR (n=78)	
		Any Grade	Grade 3/4	Any Grade	Grade 3/4	Any Grade	Grade 3/4
Hematologic	Anemia	65 (45.5)	46 (32.2)	67 (43.5)	39 (25.3)	38 (48.7)	22 (28.2)
	Neutropenia	50 (35.0)	44 (30.8)	44 (28.6)	33 (21.4)	40 (51.3)	37 (47.4)
	Thrombocytopenia	39 (27.3)	29 (20.3)	46 (29.9)	28 (18.2)	30 (38.5)	22 (28.2)
Nonhematologic	CRS	113 (79.0)	3 (2.1)	116 (75.3)	1 (0.6)	57 (73.1)	1 (1.3)
	Dysgeusia	103 (72.0)	N/A	111 (72.1)	N/A	59 (75.6)	N/A
	Infections	87 (60.8)	33 (23.1)	109 (70.8)	33 (21.4)	61 (78.2)	20 (25.6)
	Skin related	85 (59.4)	0	113 (73.4)	1 (0.6)	53 (67.9)	0
	Nail related	80 (55.9)	0	84 (54.5)	0	47 (60.3)	0
	Weight decreased	59 (41.3)	3 (2.1)	64 (41.6)	9 (5.8)	29 (37.2)	1 (1.3)
	Rash related	57 (39.9)	2 (1.4)	48 (31.2)	8 (5.2)	25 (32.1)	2 (2.6)
	Pyrexia	57 (39.9)	4 (2.8)	44 (28.6)	2 (1.3)	27 (34.6)	0
	Dry mouth	38 (26.6)	0	60 (39.0)	0	34 (43.6)	0
	Fatigue	36 (25.2)	5 (3.5)	44 (28.6)	1 (0.6)	25 (32.1)	1 (1.3)

Change in Weight From Baseline



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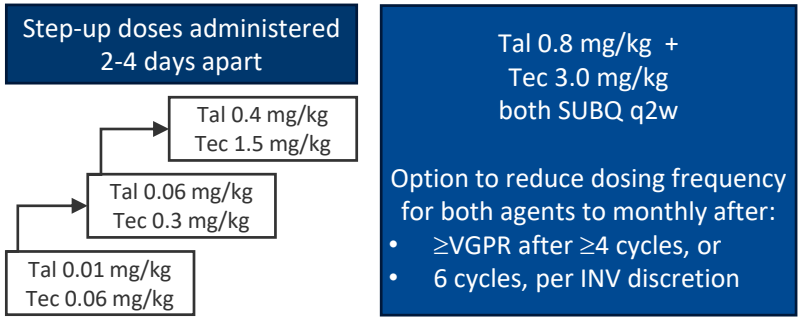
Rasche L, et al. ASCO 2025. Abstract 7528.

Phase 2 RedirecTT-1 Study of Talquetamab + Teclistamab in Patients With RRMM and EMD: Study Design and Patients

Key Eligibility Criteria

- Triple-class exposed RRMM, prior CAR-T (≤20%) and BsAb therapy permitted (BsAbs could not target GPRC5D or BCMA)
- EMD (≥1 nonradial bone-independent soft tissue plasmacytoma ≥2 cm in greatest dimension confirmed by central review of PET-CT scans)



Patient Characteristics		Tal + Tec (N=90)
Median age (range), years		64.5 (42-84)
True EMDs ≥1, n (%)		90 (100)
Median EMD (range)		2 (1-7)
High-risk cytogenetics, n (%)		14 (21.5)
Measurable disease, n (%)	Nonsecretory	4 (4.4)
	Oligosecretory	31 (34.4)
Median years since diagnosis (range)		4.7 (0.7-21.4)
Median prior LOT(range), n		4.0 (1-10)
Exposure status, n (%)	Belamaf	11 (12.2)
	Anti-BCMA CAR-T	18 (20.0)
	BsAb therapy	8 (8.9)
Refractory status, n (%)	Triple-class	76 (84.4)
	Penta-drug	32 (35.6)
	To last LOT	75 (83.3)

Primary endpoint: ORR
Secondary endpoints: ≥VGPR, ≥CR, and sCR rate; TTR, DOR, PFS, and OS; safety; PK, immunogenicity

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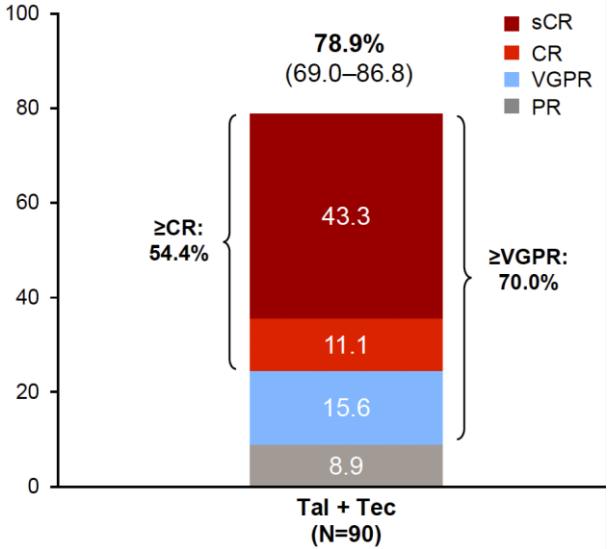
Kumar S, et al. EHA 2025. Abstract LB4001.

Phase 2 RedirecTT-1 Study of Tal + Tec in Patients With RRMM and EMD: Response

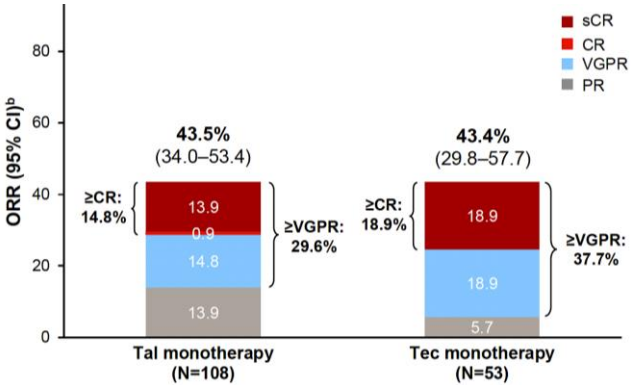
ORR[a] (95% CI)



Response Parameter		Tal + Tec (N=90)
Median follow-up (range), months		12.6 (0.5-19.5)
Median time to first response (range), months		2.6 (1.0-5.8)
Median time to best response (range), months		4.7 (1.0-11.9)
ORR by prior therapy, % (n/N) [95% CI]	Anti-BCMA CAR-T	83.3 (15/18) [58.6-96.4]
	Anti-FcRH5 BsAb	75.0 (6/8) [34.9-96.8]
	Belamaf	90.9 (10/11) [58.7-99.8]

- 66.2% of responders remain on therapy at data cutoff, with median follow-up of 13.4 months
- Of 71 responders, 55 (77.5%) switched to monthly dosing
  - Majority of patients switched to monthly dosing after cycles 4-6
  - Most responses (92.7%) deepened or were maintained after switching

ORR[a] (95% CI) With Tal or Tec Monotherapy in Patients With EMD

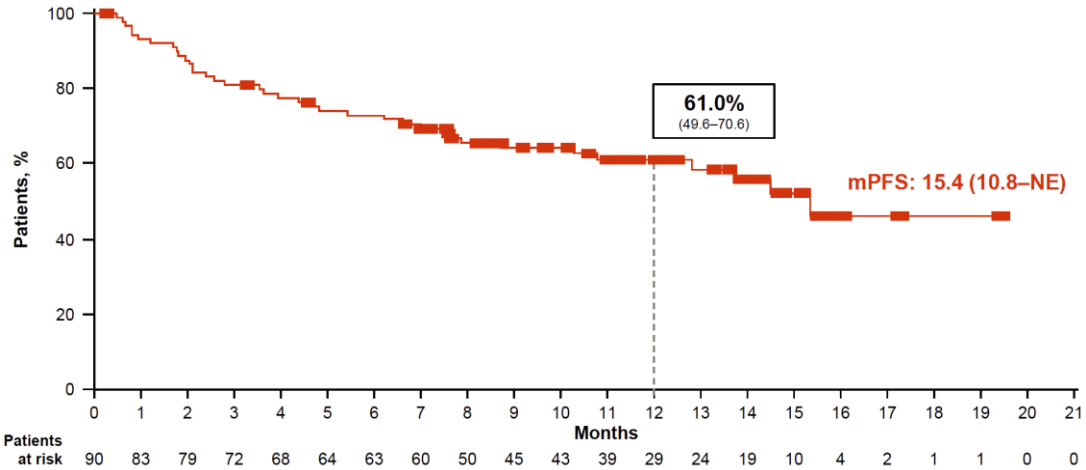


[a] Per IRC by IMWG.

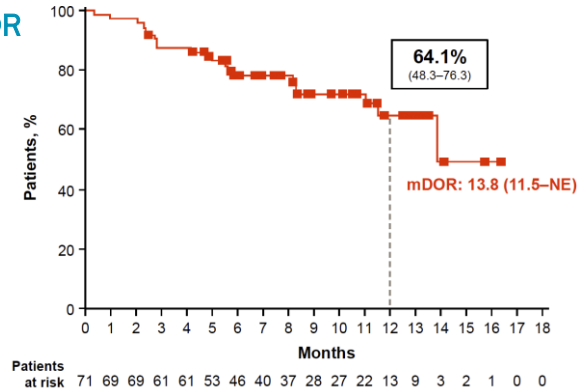
Kumar S, et al. EHA 2025. Abstract LB4001.

Phase 2 RedirecTT-1 Study of Tal + Tec in Patients With RRMM and EMD: PFS, DOR, and OS

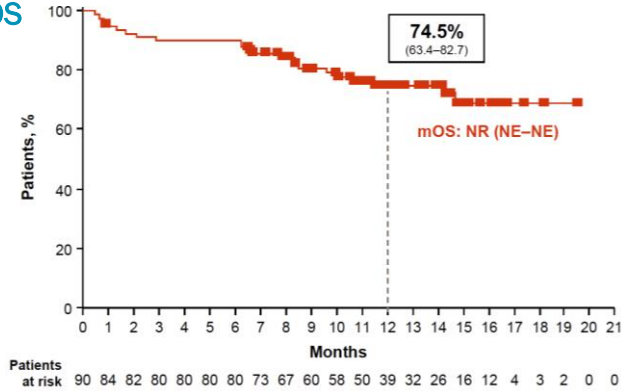
PFS



DOR



OS



Kumar S, et al. EHA 2025. Abstract LB4001.

Teclistamab-Daratumumab in RRMM – MajesTEC-3 Trial

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

- **Tec-Dara**
- **DPd/DVd per investigator's choice[b]**

Primary endpoint

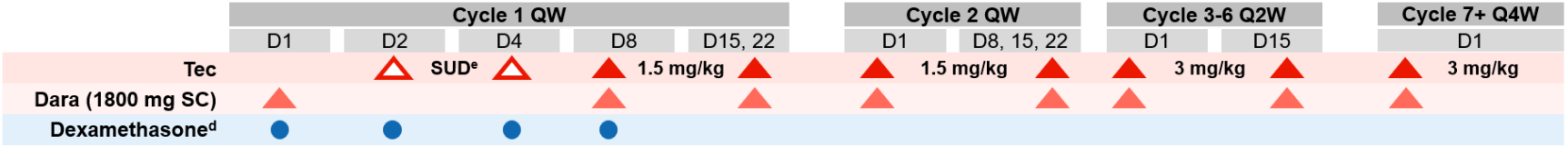
- PFS per IRC

Key secondary endpoints

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

Other secondary endpoints

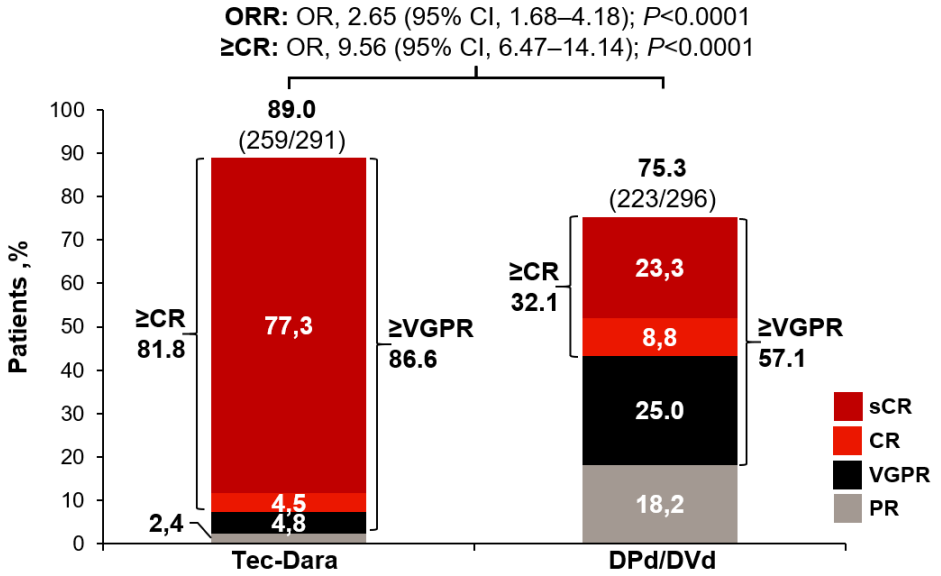
- Safety
- PK and immunogenicity



Tec-Dara was dosed using an established Dara SC schedule; steroid free after Cycle 1 Day 8

Teclistamab-Daratumumab in RRMM – MajesTEC-3 Trial

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)
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)



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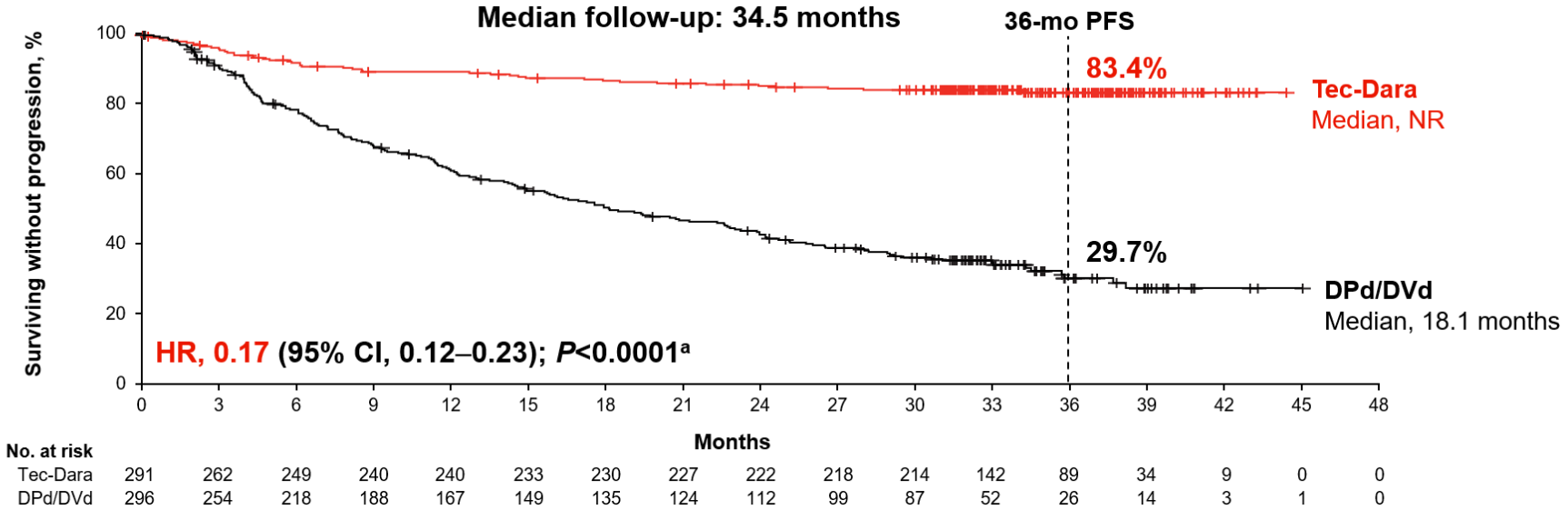
Teclistamab-Daratumumab in RRMM – MajesTEC-3 Trial



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Teclistamab-Daratumumab in RRMM – MajesTEC-3 Trial

OS curves crossed around 10 months

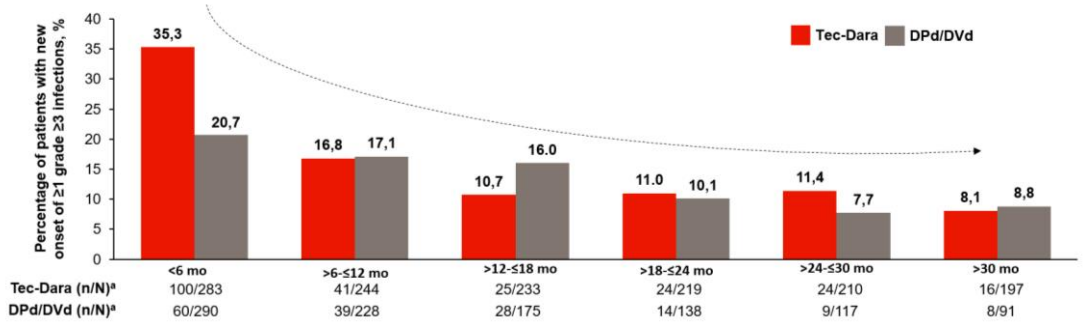
- 29 deaths in each group prior to cross
  - In Tec-Dara, primarily driven by early infectious deaths (n=12)
    - All 12 deaths occurred <6 months
    - 9 patients did not receive any IgRT
  - Remaining 17 Tec-Dara patients died due to AEs (n=6), PD (n=5), or "Other" (n=6)[a]

Authors' Conclusions

- Highest PFS treatment effect to date (HR, 0.17), with plateauing curve after ~6 months suggesting potential for functional cure; PFS benefit was maintained across patient subgroups
- Superior OS (HR, 0.46)
- Though grade ≥3 infections declined over time, patients should receive supportive care with infection prophylaxis, monitoring, and established IgRT supplementation protocols

Safety, n (%)	Tec-Dara (n=283)		DPd/DVd (n=290)	
	Any grade	Grade 3/4	Any grade	Grade 3/4
Hematologic				
Neutropenia	222 (78.4)	214 (75.6)	240 (82.8)	288 (78.6)
Thrombocytopenia	103 (36.4)	55 (19.4)	126 (43.4)	68 (23.4)
Nonhematologic				
CRS	170 (60.1)	0	-	-
Diarrhea	147 (51.9)	10 (3.5)	89 (30.7)	7 (2.4)
Any infection	273 (96.5)	153 (54.1)	244 (84.1)	126 (43.4)

- New-onset grade ≥3 infections decreased after 6 months of treatment



Conclusions - Bispecific Antibodies in RRMM

- Bispecific Antibodies are widely approved for treatment of triple-class exposed RRMM after 3 prior lines
- Approvals were based on single-arm phase I/II trials
- BCMA directed TCE are a therapeutic alternative in case CAR-T cell treatment is not available or not feasible
- Infections are the most relevant non-hematological toxicity, IVIG substitution is urgently recommended
- GPRC5D directed TCE is a therapeutic alternative, potential side effects affecting HRQoL have to be considered
- Combination treatment of Teclistamab and Talquetamab shows unprecedented results in treatment of EMD
- In early relapses, combination of Teclistamab and Daratumumab is strongly superior to SOC conventional triplet therapy, comparisons to other BCMA directed treatments are missing

UKE
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Global Multiple Myeloma Academy

Discussion

APTITUDE HEALTH®

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Overview of Later-Line RRMM Treatment and Management

Rafael Fonseca, MD

APTITUDE HEALTH®

MAYO CLINIC

Rafael Fonseca, MD
Chief Innovation Officer
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GMMA EU
Overview of Later-Line Relapsed/Refractory Multiple Myeloma (RRMM) Treatment and Management

Phoenix, Arizona

Rochester, Minnesota

Jacksonville, Florida

MAYO CLINIC

Disclosures

- **Consulting:** AbbVie, Adaptive Biotechnologies, Amgen, Apple, BMS/Celgene, Fortiva, GSK, Janssen, Karyopharm, Pfizer, RA Capital, Regeneron, Sanofi
- **Scientific Advisory Board:** Caris Life Sciences, NexCure, Ryght AI
- **Board of Directors**: Antengene
- **Patent for FISH in MM:** ~$2000/year
- **Believe in stem cell transplant**

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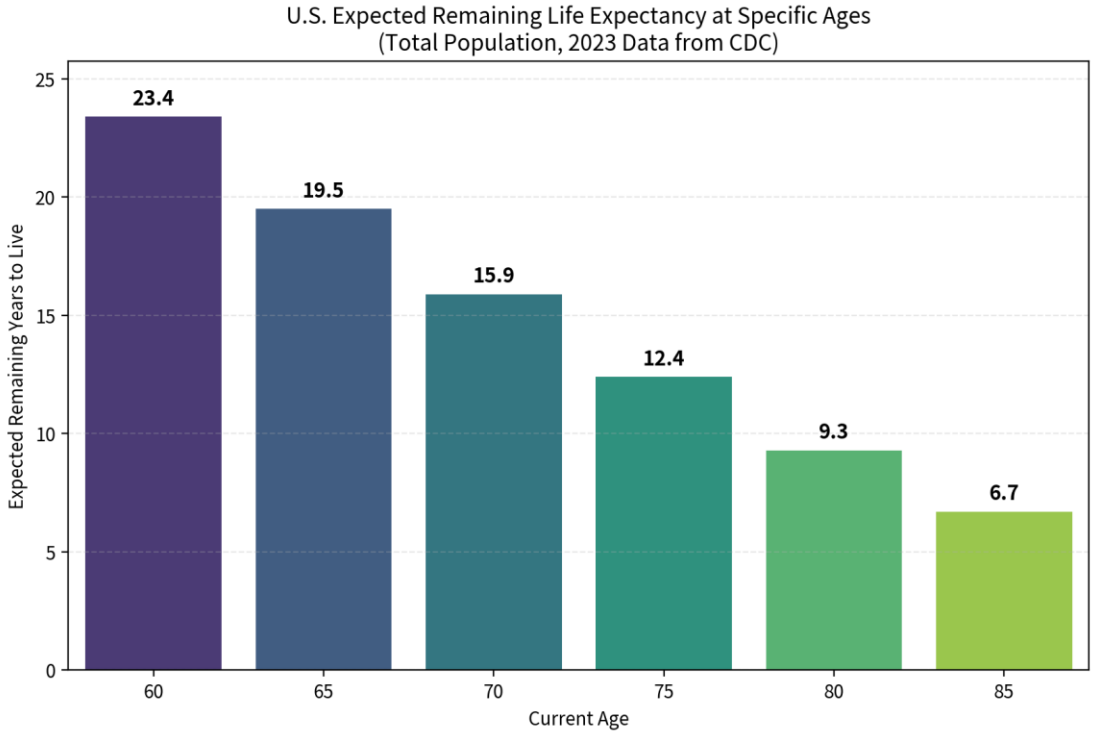
Life Years Ahead



Key data points (remaining years)

- Age 60 → **23.4 years**
- Age 65 → **19.5 years**
- Age 70 → **15.9 years**
- Age 75 → **12.4 years**
- Age 80 → **9.3 years**
- Age 85 → **6.7 years**

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Fonseca R. Unpublished.

FDA Approvals for Multiple Myeloma Since 2006

- 40 approvals for 20 drugs
- 13 through accelerated approval pathway (3 withdrawn, 1 re-entered)
- Most approvals for: daratumumab (11), lenalidomide (9), and bortezomib (8)

	Year	Type	Clinical trial	Antibody 1	Antibody 2	CART	Molecule	Molecule 2	Supportive
1	2026	R	MajesTEC-3	Dara	Tec				
2	2026	R	CEPHEUS	Dara			Bor	Len	
3	2025	R	AQUILA	Dara					
4	2025	R	DREAMM-8	Bela			Bor		
5	2025	A	LINKER	Linvo					
6	2024	R	IMROZ	Isa			Len	Len	
7	2024	R	PERSEUS	Dara			Bor	Len	
8	2024	R	CARTITUDE-4			Ciltacel			
9	2024	R	KARMMA-3			Idecel			
10	2023	A	MAGNETISMM	Elra					
11	2023	A	MONUMENTAL-1	Tal					
12	2022	A	MAJESTEC-1	Tec					
13	2022	A	CARTITUDE-1			Ciltacel			
14	2021	R	CANDOR	Dara			Car		
15	2021	R	APOLLO	Dara			Pom		
16	2021	R	IKEMMA	Isa			Car		
17	2021	A	KARMMA-1			Idecel			
18	2021	A	Horizon				Melflufen		
19	2020	R	BOSTON				Seli	Bor	
20	2020	R	ENDEAVOR				Car		

	Year	Type	Clinical trial	Antibody 1	Antibody 2	CART	Molecule	Molecule 2	Supportive
21	2020	A	BEL	Bela					
22	2020	R	COLUMBA	Dara					
23	2020	R	ICARIA	Isa			Pom		
24	2019	R	CASSIOPEA	Dara			Bor	Thal	
25	2019	A	STORM				Seli		
26	2019	R	MAIA	Dara			Len	Len	
27	2016	R	POLLUX/CASTOR	Dara			Len	Len	
28	2015	R	ELOQUENT	Elo			Len	Len	
29	2015	R	TOURMALINE-MM1				Ixa		
30	2015	A	MMY2002 (SIRIUS)	Dara					
31	2015	R	ASPIRE				Car	Len	
32	2015	R	PANORAMA				Pano	Bor	
33	2013	A	CC-4047-MM-002				Pom		
34	2012	A	003-A1				Car		
35	2010	R	482 study						Denosumab
36	2008	R	Mozobil						Plerixafor
37	2008	R	VISTA				Bor	Mel	
38	2007	R	DOXIL-MMY-3001				Doxo	Bor	
39	2006	R	MM 009-010				Len	Len	
40	2006	A	E1A00				Thal		

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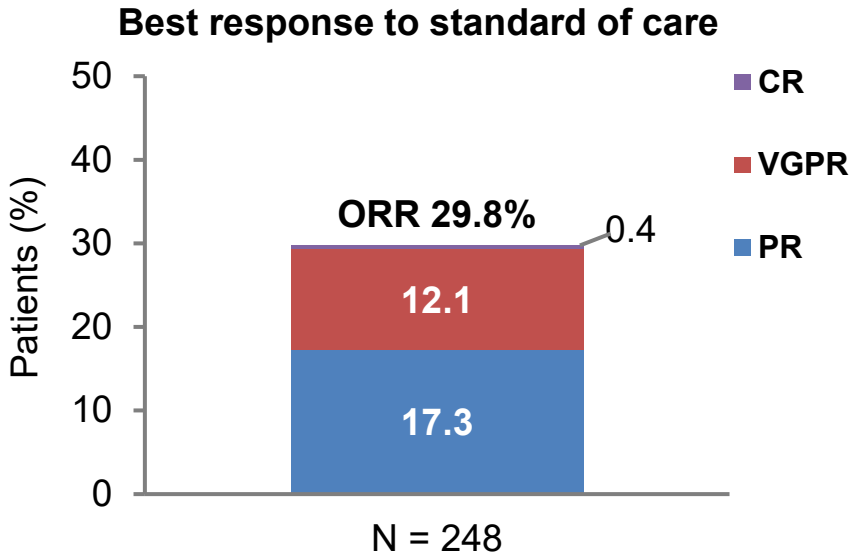
Fonseca, R. Personal opinion.

LocoMMotion: Heavily Pretreated Patients

Patient characteristics	N = 248
Median age, yr	68
Median prior LOT, n (range)	4 (2–13)
Triple-class exposed, n (%)	248 (100)

92 unique standard-of-care regimens

Carfilzomib (25.4%), pomalidomide (29.8%), and daratumumab (9.3%) are the most common agents for each treatment class



Survival Outcomes	N = 248
Median PFS, months (95% CI)	4.6 (3.9–5.6)
12-month PFS rates, % (95% CI)	19.9 (13.6–27.0)
Median OS, months (95% CI)	12.4 (10.28–NE)
12-month OS rates, % (95% CI)	51.8 (44.1–58.8)

TEAE, n (%)	N = 248
Any grade	207 (83.5)
Grade ≥3	139 (56)
TEAE leading to death	19 (7.7)

No clear standard of care and poor outcomes in heavily pretreated patients

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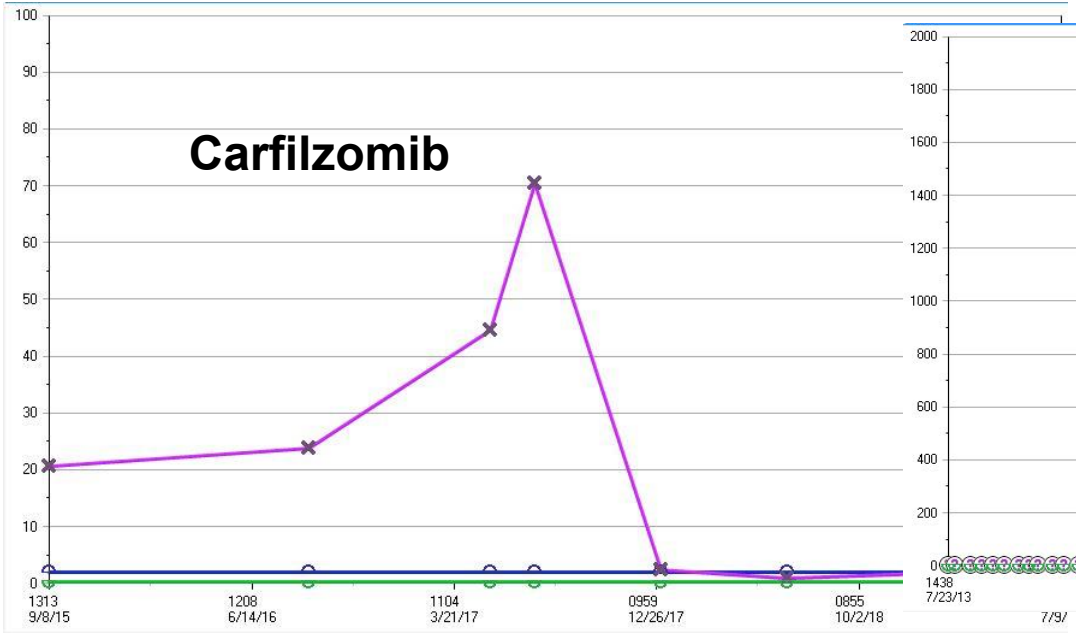
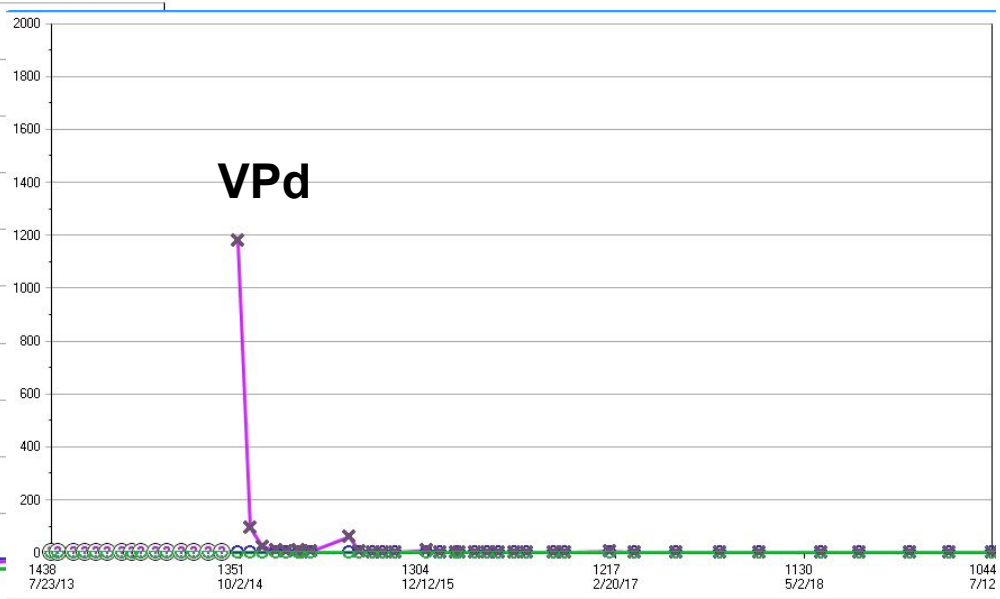
Mateos MV, et al. *Leukemia*. 2022;36:1371-1376.

Everyone Is an N of 1

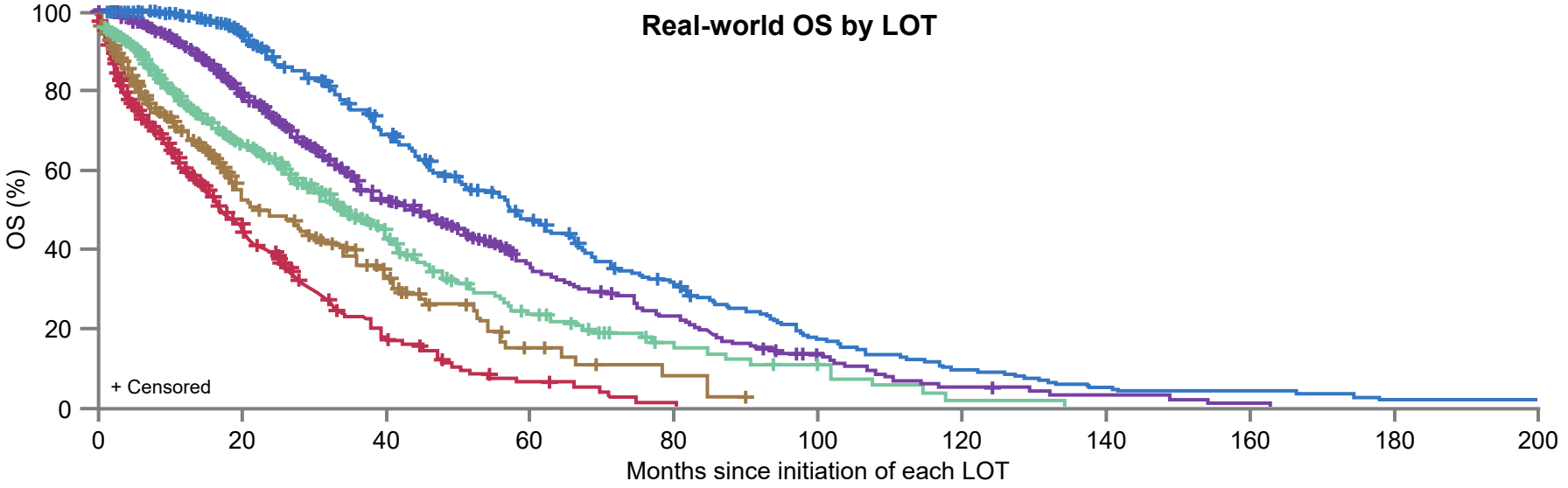




@rfonsi1, fonseca.rafael@mayo.edu

Fonseca R. Unpublished information.

Real-World OS Is Worse With Each LOT



LOT	1L	2L	3L	4L	5L+
Events, n/N	228/514	228/514	228/514	137/260	175/270
Median OS, mo (95% CI)	58.4 (51.4–63.4)	44.1 (36.8–51.4)	34.8 (30.2–40.5)	23.4 (19.1–31.4)	18.3 (14.6–21.8)
HR (95% CI)	Reference	1.43 (1.19–1.73)	2.2 (1.81–2.66)	3.2 (2.56–4.00)	4.74 (3.84–5.85)

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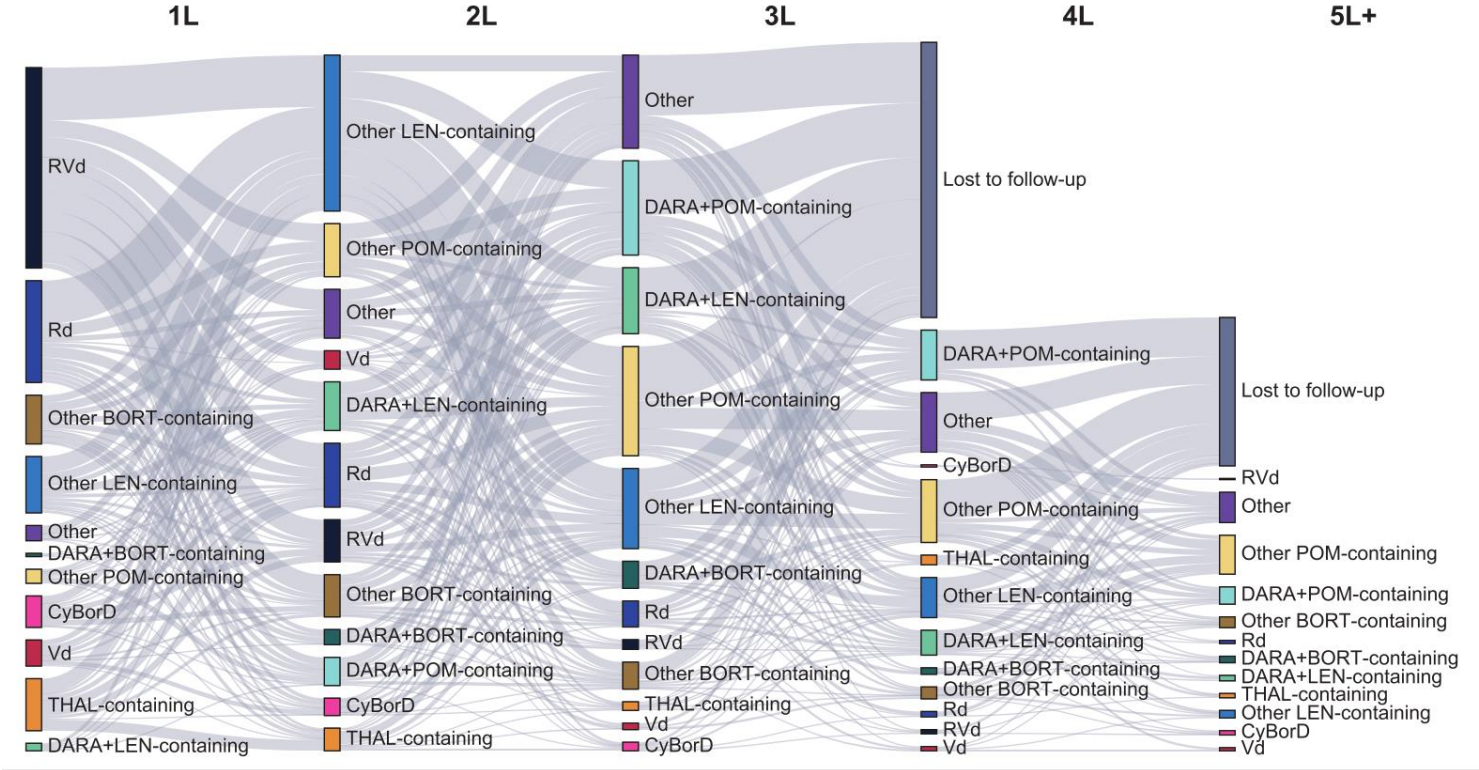
Real-World Treatment Patterns in MM Reported in the US

Summary of treatment regimens reported by LOT



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Key Numbers to Remember

- **Vd: 9**
- **Rd: 17**

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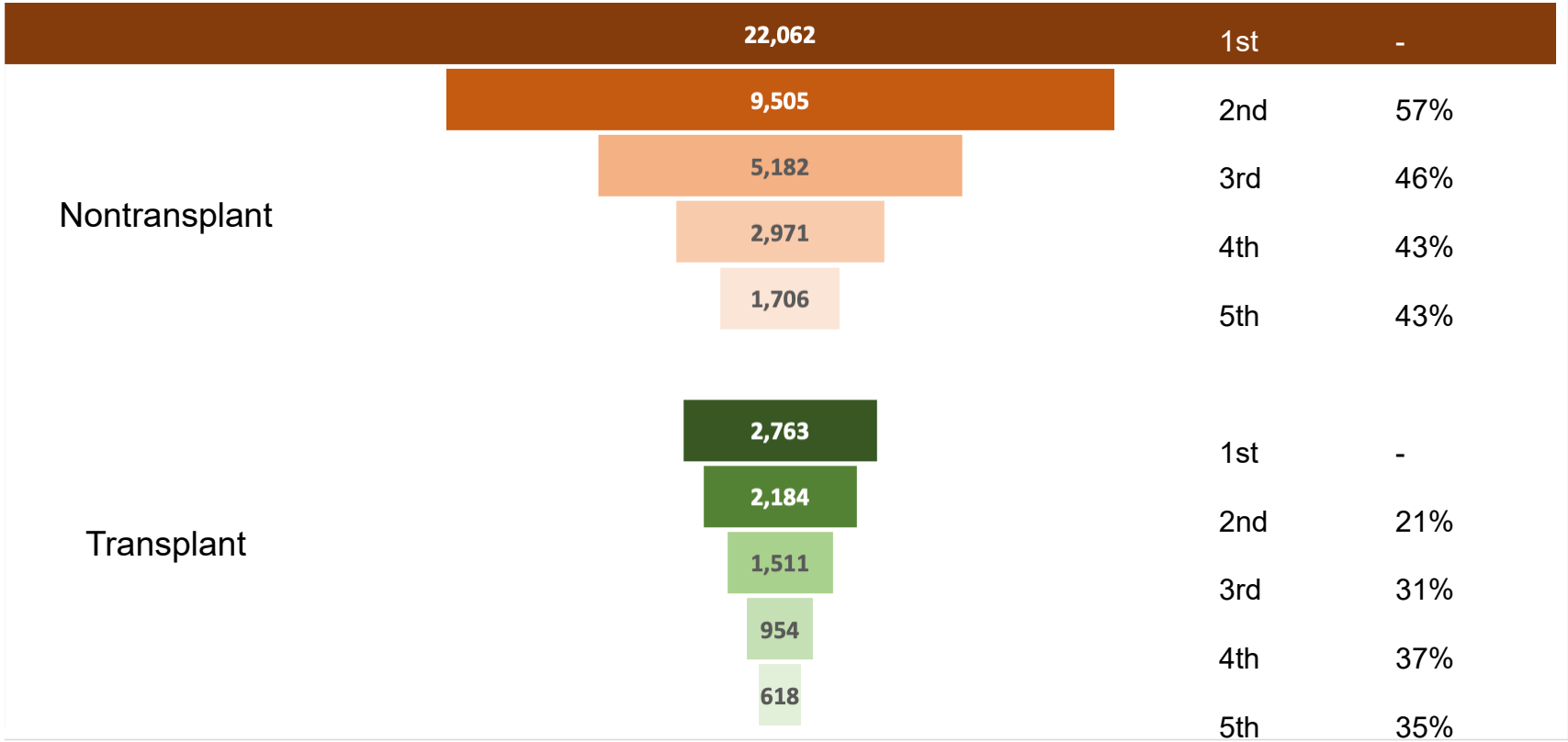
Fonseca R. Unpublished information.

Attrition With Subsequent Treatment



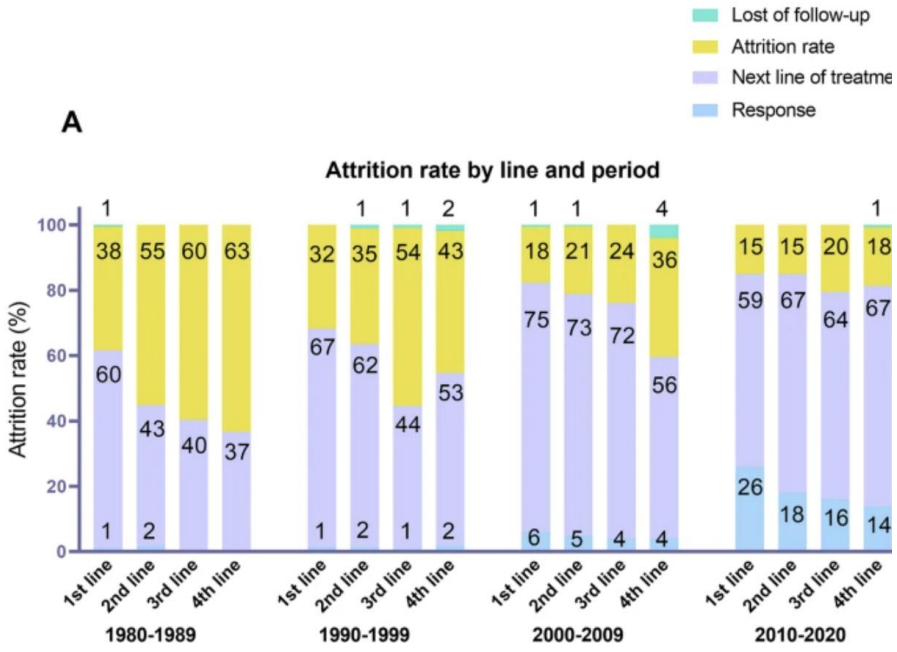
@rfonsi1, fonseca.rafael@mayo.edu

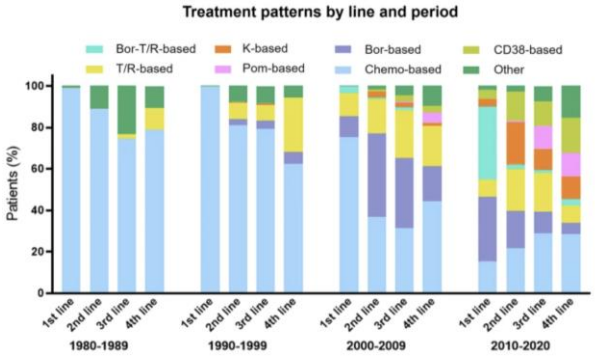
Fonseca R, et al. *BMC Cancer*. 2020;20:1087.

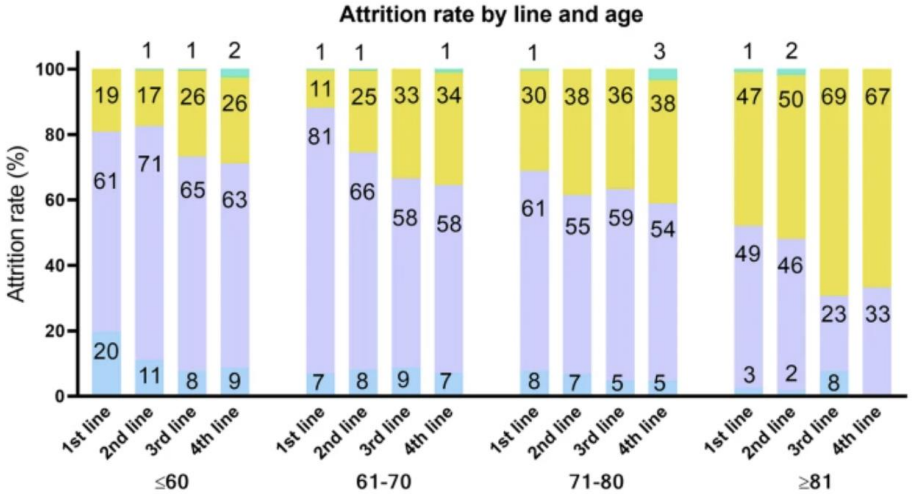
Attrition – Date of Treatment and Age

Less attrition with more modern therapies but still a problem in the elderly

Fig. 2: Attrition rate across successive lines of therapy.







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Rodríguez-Lobato L, et al. *Blood Cancer J*. 2025;15:103.

ASPIRE – Len-Dex ± Carfilzomib

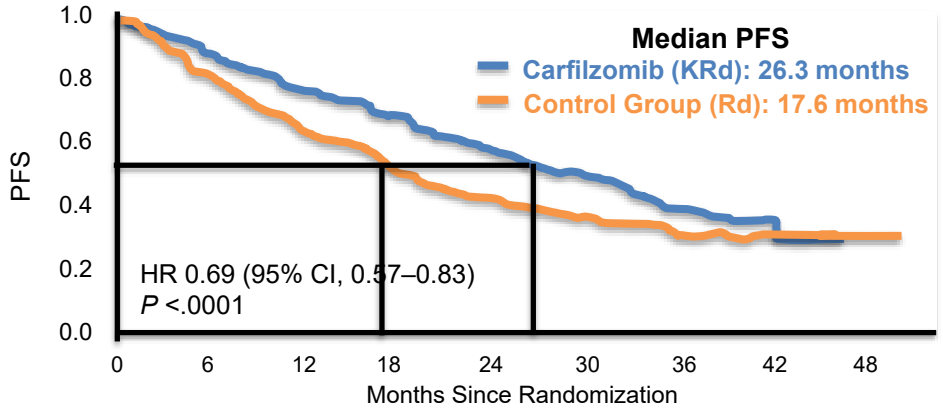
- **Carfilzomib 20 mg/m² (27 mg/m²)**
  - Cycle 1–12: d 1, 2, 8, 9, 15, 16
  - Cycles 13–18: d 1, 2, 15
- **Lenalidomide 25 mg** d1–21
- **Dexamethasone 40 mg** d1, 8, 15, 22

- **Lenalidomide** 25 mg d1–21
- **Dexamethasone** d1, 8, 15, 22

After cycle 18, Len-Dex was continued until POD or toxicity

Primary Endpoint: PFS

Secondary Endpoints: OS, ORR, Duration of response, HRQOL, safety



Risk Group by FISH	KRd (n = 396)		Rd (n = 396)		HR	*P* Value
	n	Median PFS, mo	n	Median PFS, mo		
High	48	23.1	52	13.9	0.70	.083
Standard	147	29.6	170	19.5	*0.66*	.004

@rfonsi1, fonseca.rafael@mayo.edu

Stewart AK, et al. *N Engl J Med*. 2015;372:142-152.

MAYO CLINIC

CASTOR Study

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Daratumumab, Bortezomib, and Dexamethasone for Multiple Myeloma

Antonio Palumbo, M.D., Asher Chanan-Khan, M.D., Katja Weisel, M.D., Ajay K. Nooka, M.D., Tamas Masszi, M.D., Meral Beksac, M.D., Ivan Spicka, M.D., Vania Hungria, M.D., Markus Munder, M.D., Maria V. Mateos, M.D., Tomer M. Mark, M.D., Ming Qi, M.D., Jordan Schecter, M.D., Himal Amin, B.S., Xiang Qin, M.S., William Deraedt, Ph.D., Tahamtan Ahmadi, M.D., Andrew Spencer, M.D., and Pieter Sonneveld, M.D., for the CASTOR Investigators*

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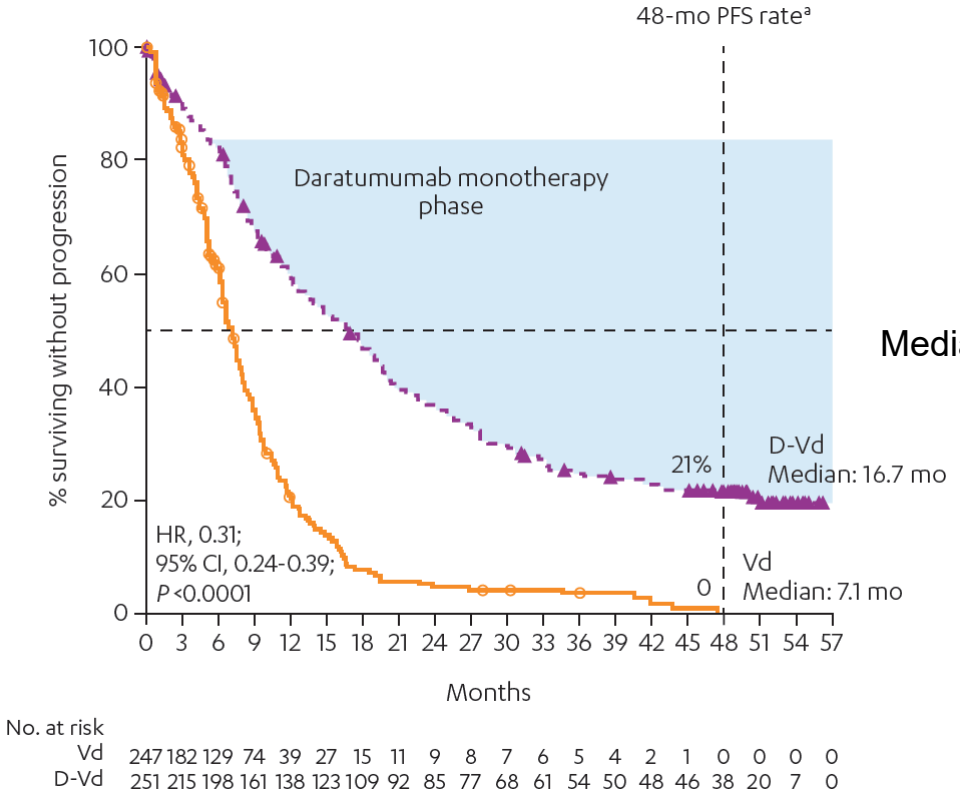
Palumbo A, et al. *N Engl J Med*. 2016;375:754-766.

Updated PFS in the ITT Population



Median follow-up: 50.2 months

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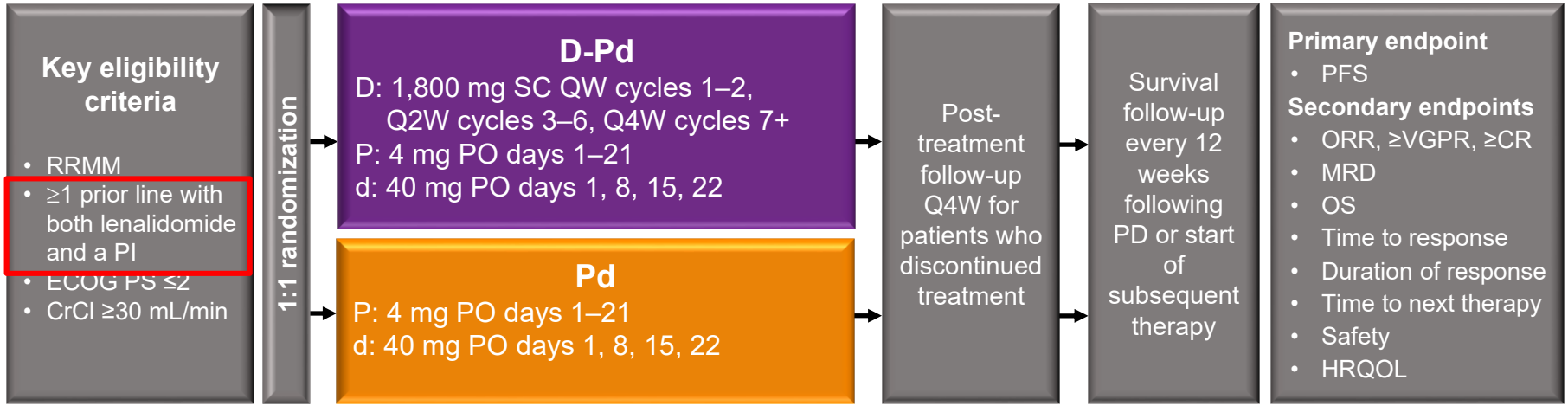
Palumbo A, et al. *N Engl J Med*. 2016;375:754-766.

APOLLO – Dara-Pd



Stratification factors
- Number of lines of prior therapy (1 vs 2–3 vs ≥4)
- ISS disease stage (I vs II vs III)

Cycle duration: 28 days
Treatment until PD or unacceptable toxicity

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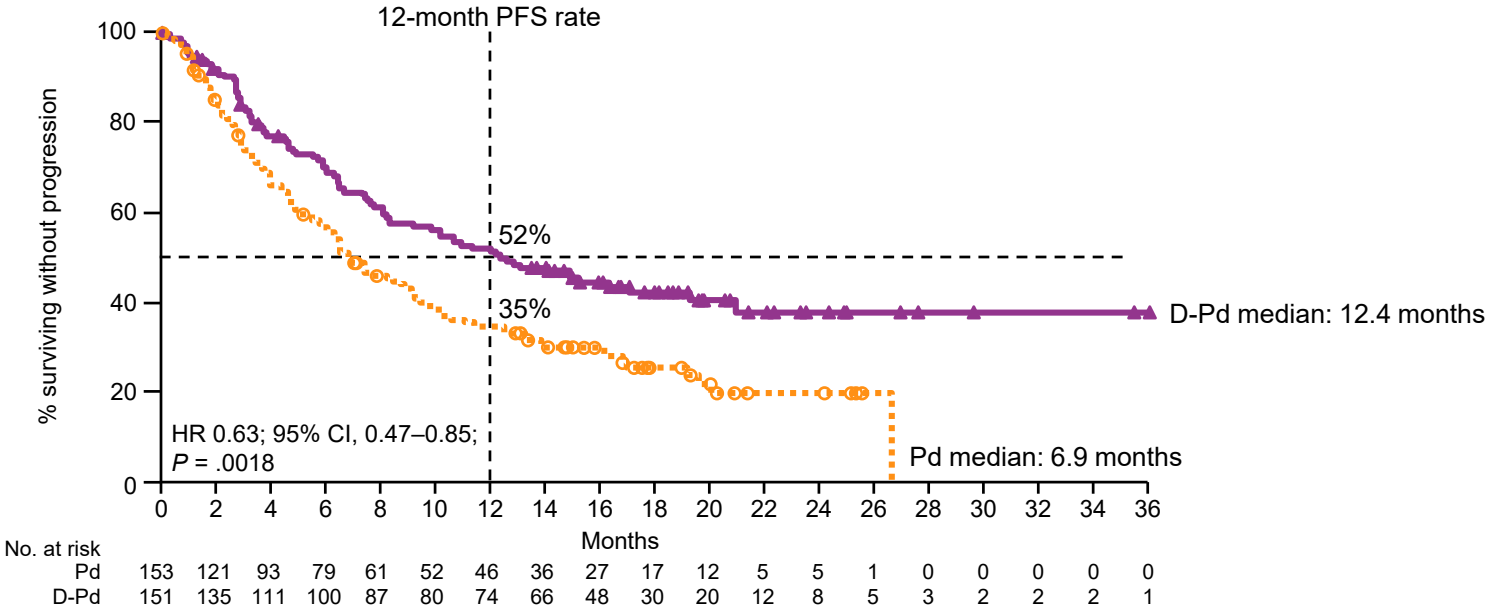
Dimopoulos MA, et al. ASH 2020. Abstract 412.

APOLLO – Dara-Pd

Median follow-up: 17 mo



- Median PFS among patients whose disease is refractory to lenalidomide was 9.9 mo for D-Pd and 6.5 mo for Pd

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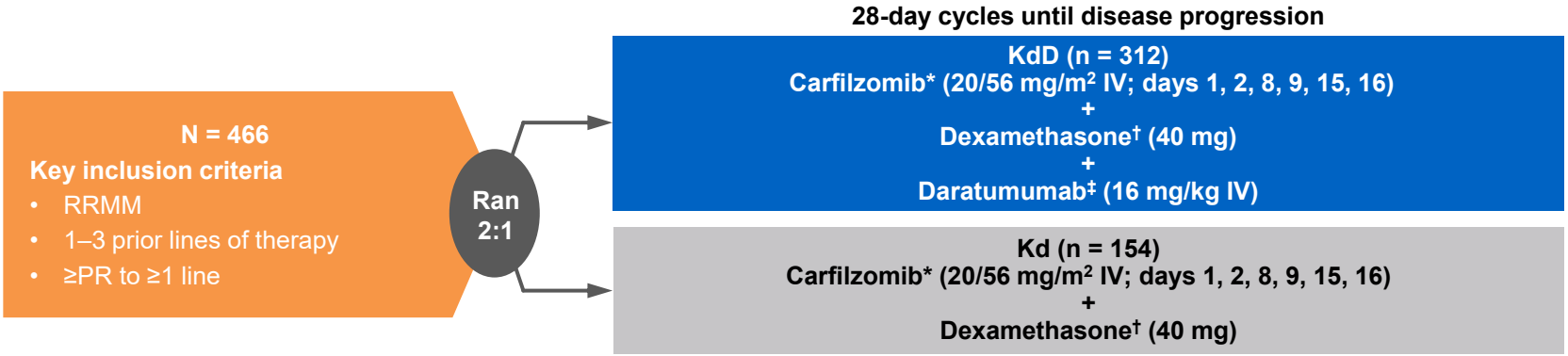
Dimopoulos MA, et al. ASH 2020. Abstract 412.

CANDOR (KdD vs Kd in RRMM)

- The CANDOR study previously demonstrated that KdD improved progression-free survival (PFS) vs Kd (HR 0.63, 95% CI, 0.46–0.85) in patients with RRMM[1]
- This abstract reports updated efficacy and safety outcomes from CANDOR up to the data cutoff of ~36 months after enrollment of the first patient[2]



Primary endpoint: PFS§

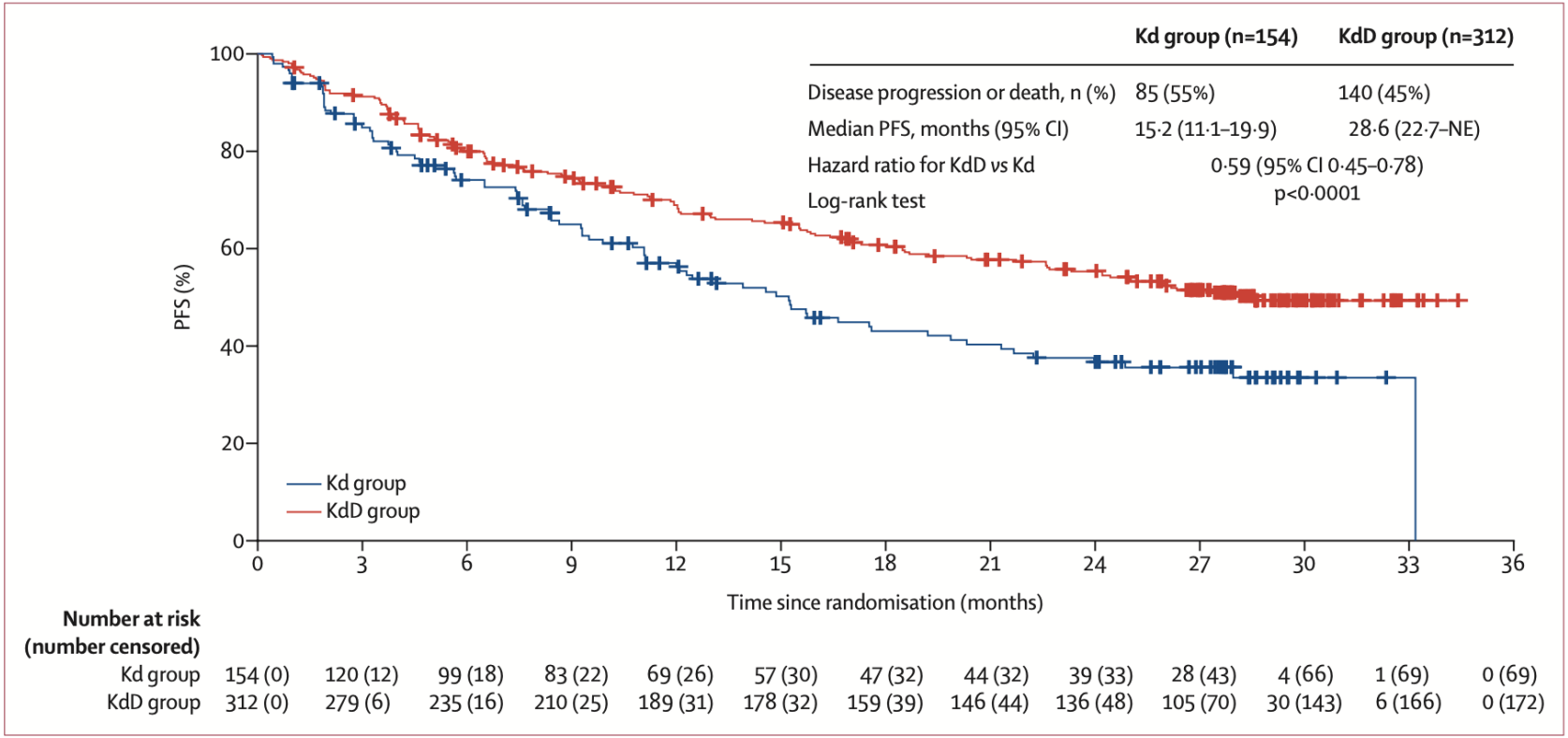
Select secondary endpoints: ORR, MRD-negative CR at 12 months, OS, safety

*Carfilzomib dose was 20 mg/m² on days 1 and 2 of cycle 1; †PO or IV weekly; 20 mg for patients >75 years; ‡8 mg/kg on days 1 and 2 of cycle 1, 16 mg/kg weekly thereafter for cycles 1–2, Q2W for cycles 3–6, and Q4W thereafter; §Disease progression was determined locally by investigators in an unblinded manner and centrally by the sponsor using a validated computer algorithm (ORCA) in a blinded manner.
CR, complete response; HR, hazard ratio; IV, intravenous; Kd, carfilzomib, dexamethasone; KdD, carfilzomib, dexamethasone, daratumumab; MRD, minimal residual disease; ORCA, Onyx Response Computer Algorithm; ORR, overall response rate; OS, overall survival; PFS, progression-free survival; PO, per oral; PR, partial response; Q2W, once every 2 weeks; Q4W, once every 4 weeks; Ran, randomized; RRMM, relapsed or refractory multiple myeloma.
1. Dimopoulos MA, et al. *Lancet*. 2020;396:186-197; 2. Dimopoulos MA, et al. ASH 2020. Abstract 2325.

@rfonsi1, fonseca.rafael@mayo.edu

Usmani SZ, et al. *Lancet Oncol*. 2022;23:65-76.

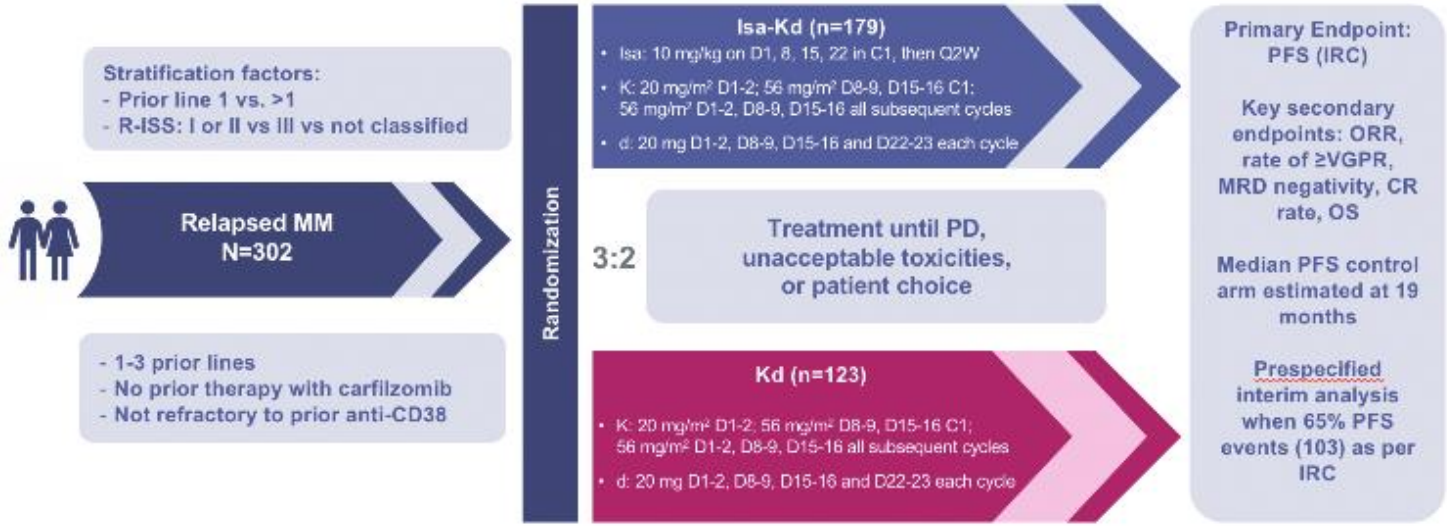
CANDOR (KdD vs Kd in RRMM)



@rfonsi1, fonseca.rafael@mayo.edu

Usmani SZ, et al. *Lancet Oncol*. 2022;23:65-76.

IKEMA



Sample size calculation: ~300 patients and 159 PFS events to detect 41% risk reduction in hazard rate for PFS with 90% power and one-sided 0.025 significance level

Patients refractory to, n (%)		
IMiD	78 (43.6)	58 (47.2)
Lenalidomide	57 (31.8)	42 (34.1)
PI	56 (31.3)	44 (35.8)

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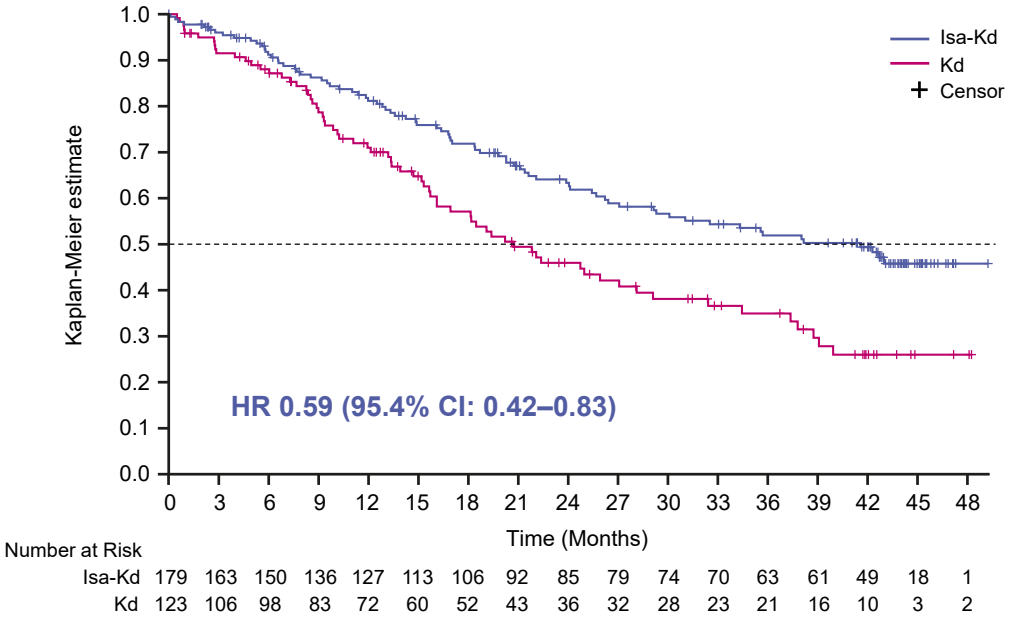
Moreau P, et al. *Lancet*. 2021;397:2361-2371.

Updated PFS – IRC Assessment by FDA Censoring Rules



Isa-Kd
mPFS: 41.7 months
(95% CI: 27.1–NC)

Kd
mPFS: 20.8 months
(95% CI: 16.2–28.2)

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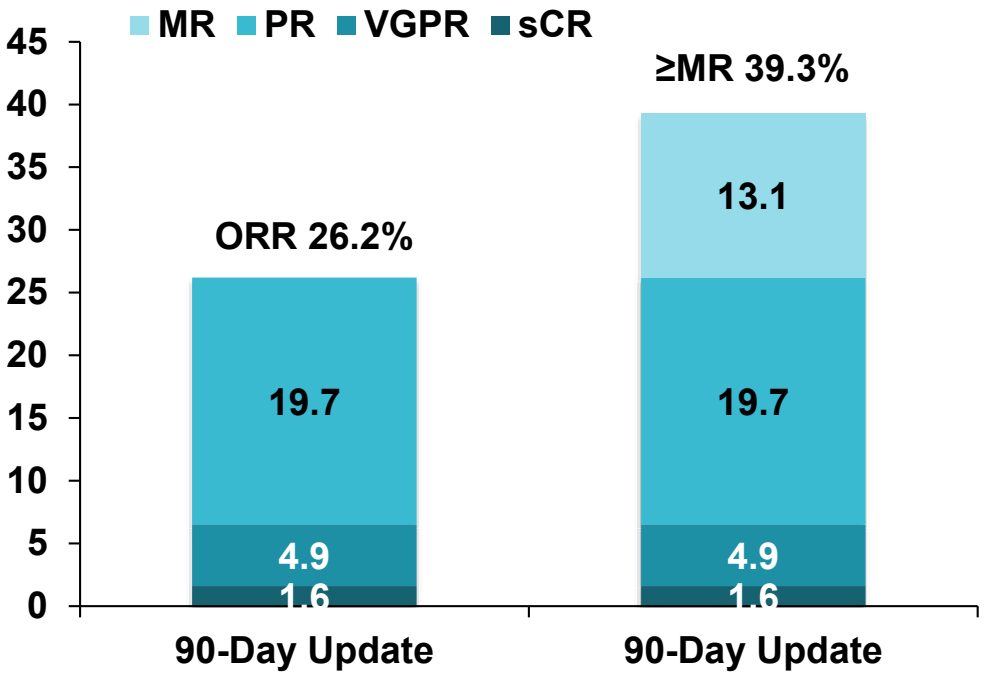
STORM Selinexor Efficacy



- Median of 7 prior treatment regimens, **ORR of 26.2%**, including **2 stringent CRs**
  - **sCRs MRD negative** at 10^{-6} and 10^{-4}
- 2 patients with prior progression after CAR T demonstrated a PR
- Median time to response was 1 month (range 1–14 weeks)
- Median duration of response was 4.4 months
- 96% refractory to carfilzomib, pomalidomide, and daratumumab

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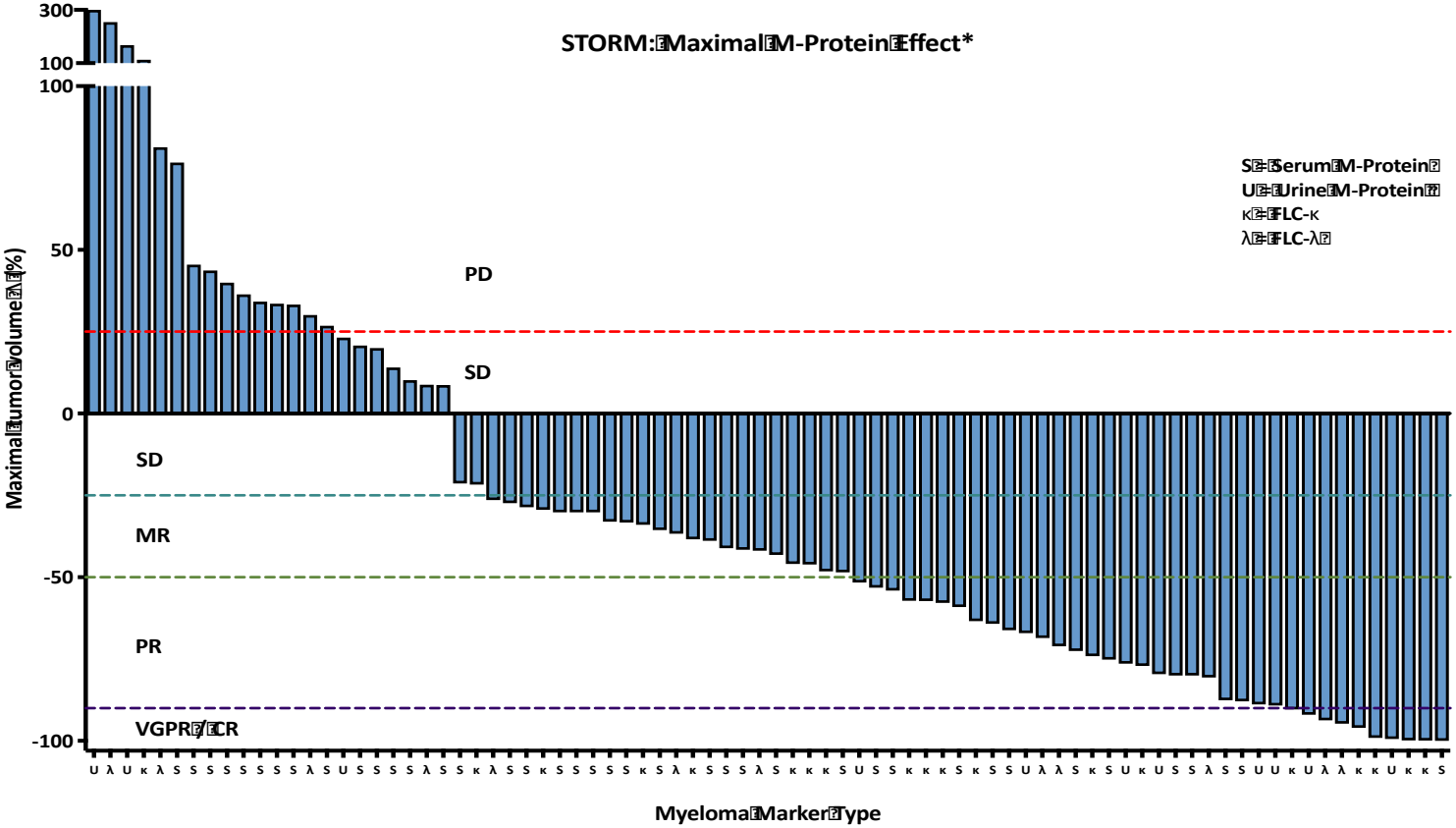
Karyopharm slides.

STORM Trial



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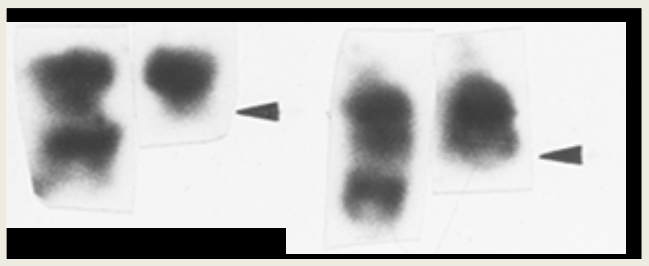
Karyopharm slides.

Translocation t(11;14)(q13;q32)



- Only translocation clearly visible on karyotypes
- Present in 15% of cases

British Journal of Haematology, 1998, **101**, 296–301

Multiple myeloma and the translocation t(11;14)(q13;q32): a report on 13 cases

RAFAEL FONSECA,[1] THOMAS E. WITZIG,[1] MORIE A. GERTZ,[1] ROBERT A. KYLE,[1] JAMES D. HOYER,[2] SYED M. JALAL[2] AND PHILIP R. GREIPP[1] [1]*Division of Hematology and Internal Medicine, and* [2]*Department of Laboratory Medicine and Pathology, Mayo Clinic and Mayo Foundation, Rochester, Minnesota, U.S.A.*

Received 3 November 1997; accepted for publication 13 February 1998

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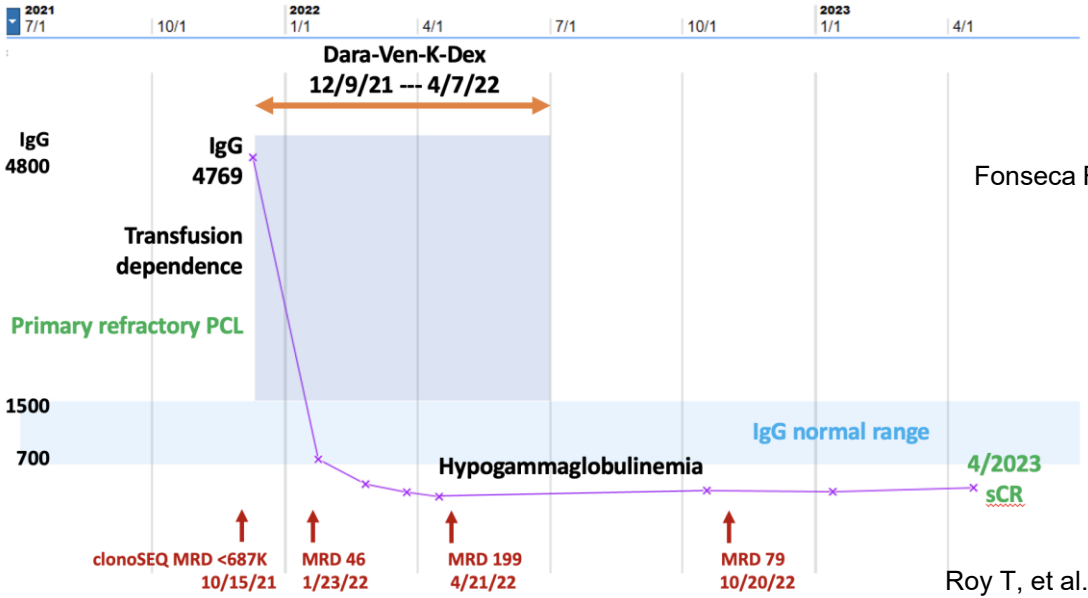
Fonseca R, et al. *Br J Haematol*. 1998:101;296-301.

Primary Plasma Cell Leukemia

Abnormality	Tested (n)[a]	Prevalence (%)			OS: pPCL (median)			OS: sPCL (median)		
		pPCL	sPCL	P-value[b]	Negative	Positive	P-value[c]	Negative	Positive	P-value[c]
t(11;14) by FISH or by informative karyotype[e]	30	71	23	0.03[a]	11.2	11.4	0.76	1.33	0.53	0.18



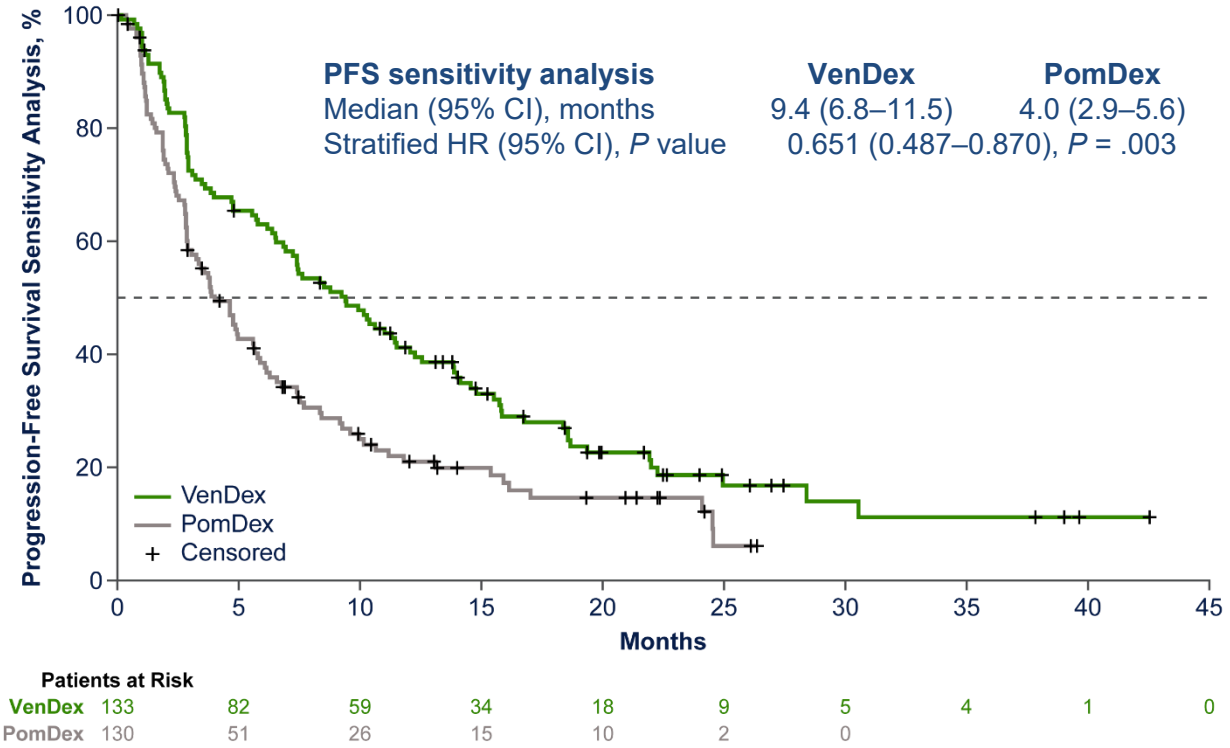
Fonseca R. Unpublished observation.

@rfonsi1, fonseca.rafael@mayo.edu

Roy T, et al. *Leuk Lymphoma*. 2022;63:759-761;
Gonsalves WI, et al. *Eur J Haematol*. 2018;100:215-217;
Tiedemann RE, et al. *Leukemia*. 2008;22:1044-1052.

CANOVA Post Hoc Sensitivity Analysis (HR 0.651)

- Patients who were initiated on subsequent anti-MM therapy without meeting the definition of PD per IMWG (eg, patients with clinical relapse) were censored in the primary PFS analysis
- The post hoc PFS sensitivity analysis accounted for the start of a new anti-MM therapy as an event, whereas the primary PFS analysis did not



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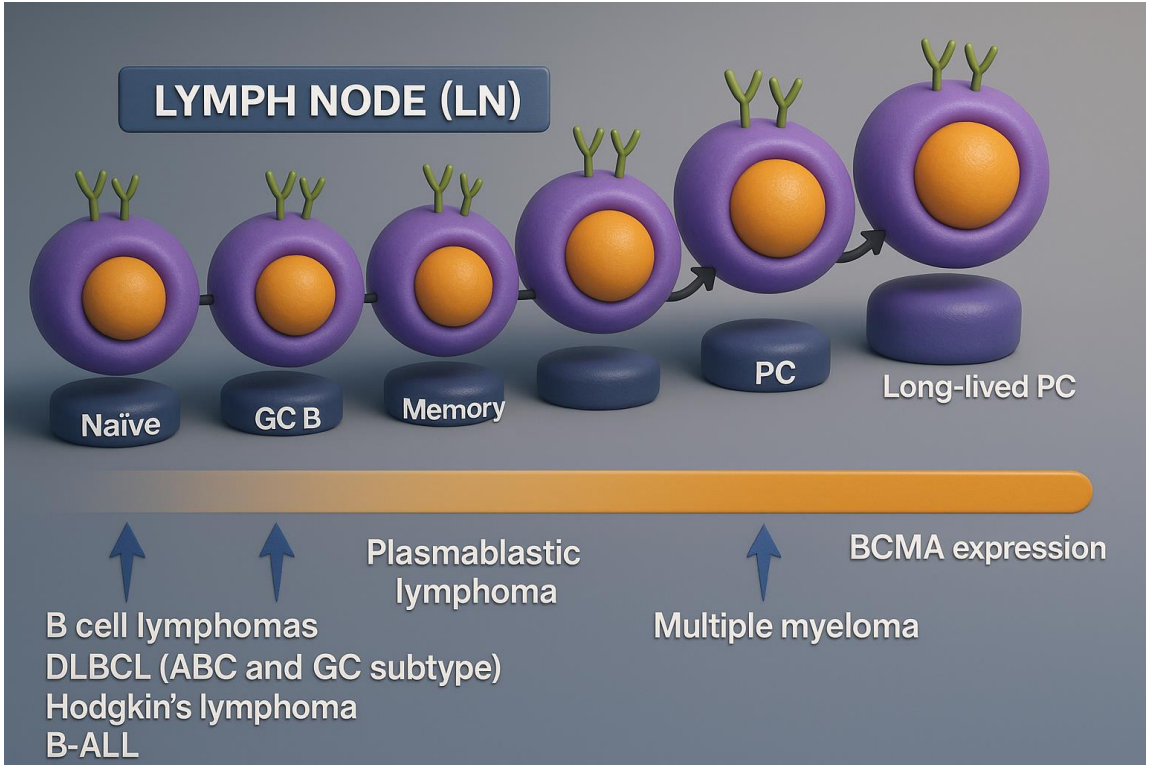
Mateos MV, et al. IMS 2023. Abstract OA-52.

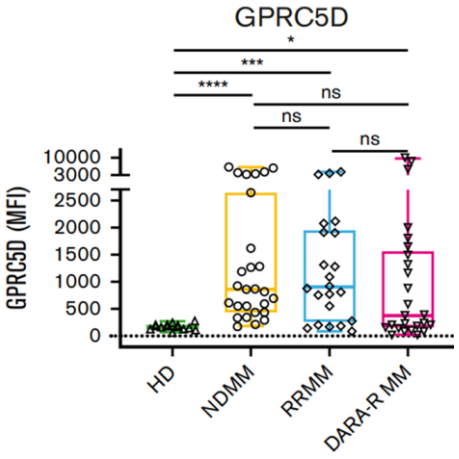
Targets for Bispecific Antibodies in MM: BCMA[1-3]



@rfonsi1, fonseca.rafael@mayo.edu

1. Frerichs K, et al. *Clin Cancer Res*. 2020;26:2203-2215; 2. Verkleij CPM, et al. *Blood Adv*. 2021;5:2196-2215; 3. Dogan A, et al. *Blood Cancer J*. 2020;10:73.

GPRC5D: Talquetamab and Forimtamig[1-3]



Expression in nonhematopoietic tissues is limited to hair follicles and filiform papillae of the tongue (nail bed in mice)

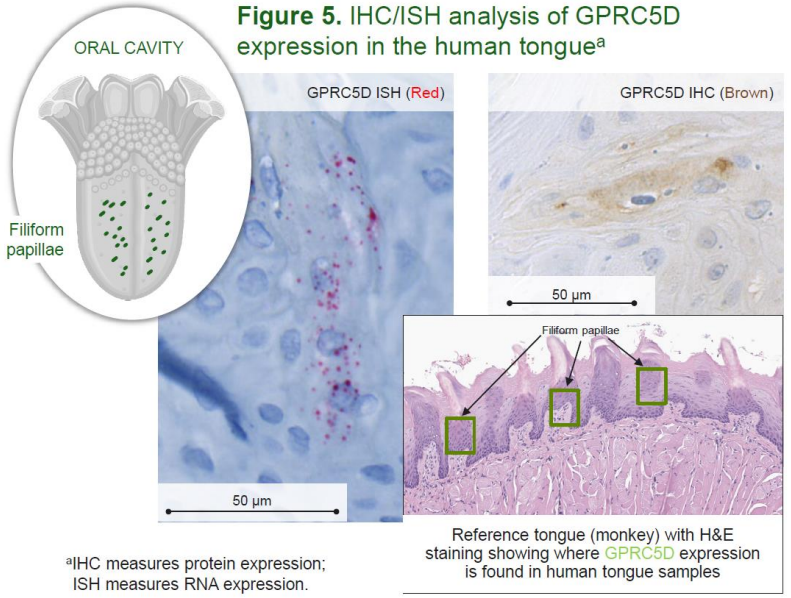


Figure 5. IHC/ISH analysis of GPRC5D expression in the human tongue[a]

[a]IHC measures protein expression; ISH measures RNA expression.

@rfonsi1, fonseca.rafael@mayo.edu

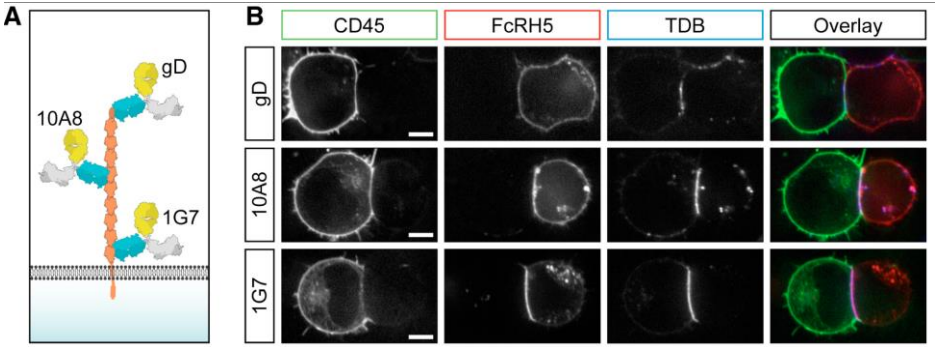
1. Chari A, et al. ASH 2022. Abstract 157; 2. Verkleij CPM, et al. *Blood Adv*. 2021;5:2196-2215; 3. Goldsmith R, et al. IMW 2021. Poster P-095.

Cevostamab: FcRH5 × CD3 Bispecific

Background

- Fc receptor-homolog 5 (FcRH5)
  - Expressed on myeloma cells with near 100% prevalence
  - Also expressed on normal B cells but higher in myeloma and plasma cells
  - Gene located on chromosome 1
- Cevostamab BFCR4350A
  - Humanized IgG-based FcRH5 × CD3 bispecific antibody

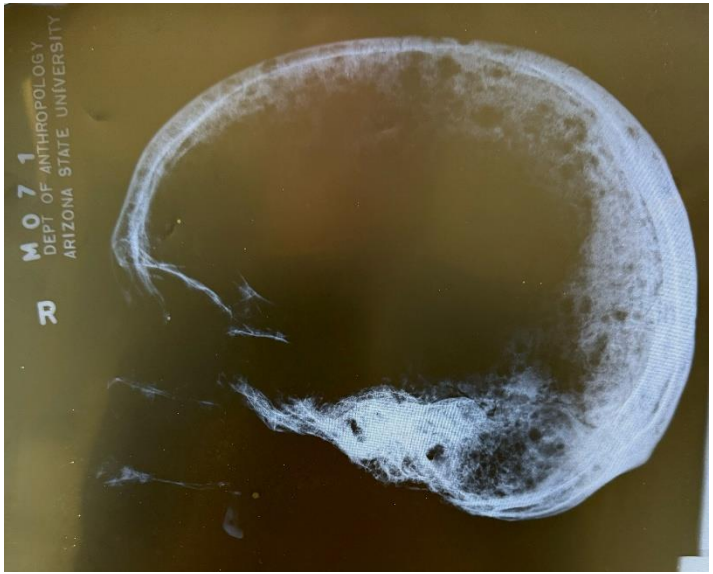
Synapse-binding



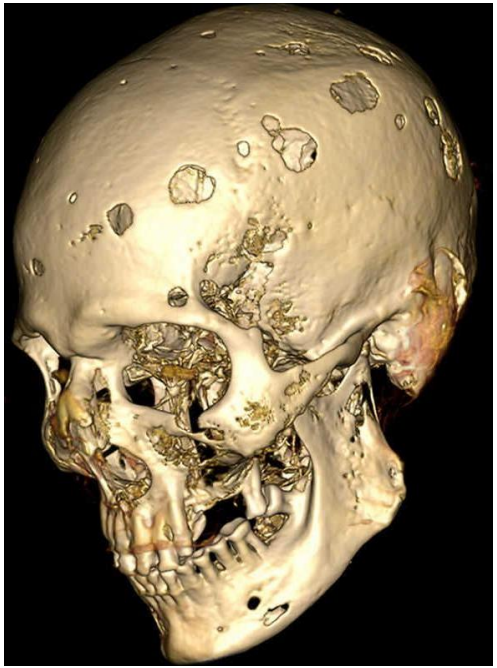
@rfonsi1, fonseca.rafael@mayo.edu

Li J, et al. *Cancer Cell*. 2017;31:383-395.

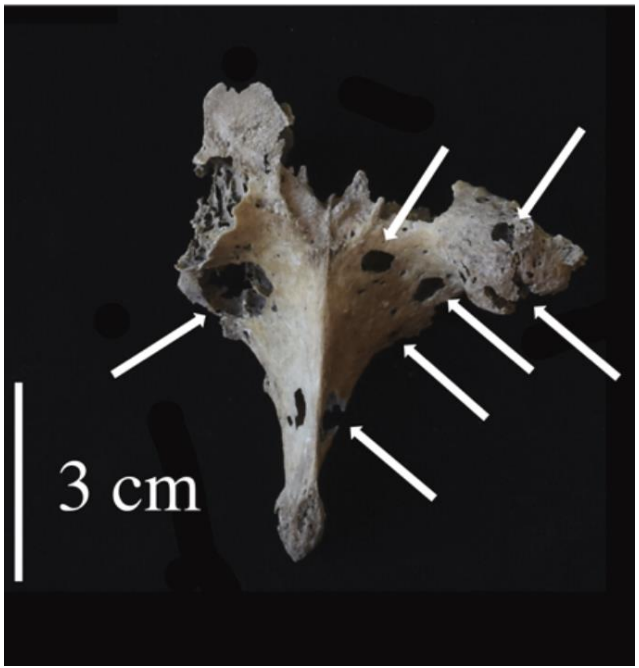
Earliest Myeloma Cases



Nubian Egyptian Mummy: 700 BC



Egyptian Mummy: 700 BC



Bronze Age China: 1750–1400 BC

@rfonsi1, fonseca.rafael@mayo.edu

Lesyk S, Abramzon F. *Revista Argentina de Radiologia*. 2014;78:171-180;
Dittmar J, et al. *Int J of Paleopathol*. 2020;31:64-70.

Global Multiple Myeloma Academy

Discussion

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Global Multiple Myeloma Academy

Break

APTITUDE HEALTH®

Global Multiple Myeloma Academy

Immunotherapy Sequencing in RRMM: Current and Future Landscape

Hermann Einsele, MD, FRCP

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Global Multiple Myeloma Academy
Emerging and Practical Concepts in
Relapsed/Refractory Multiple Myeloma
March 25–26, 2026 – Asia-Pacific Region

Uniklinikum Würzburg

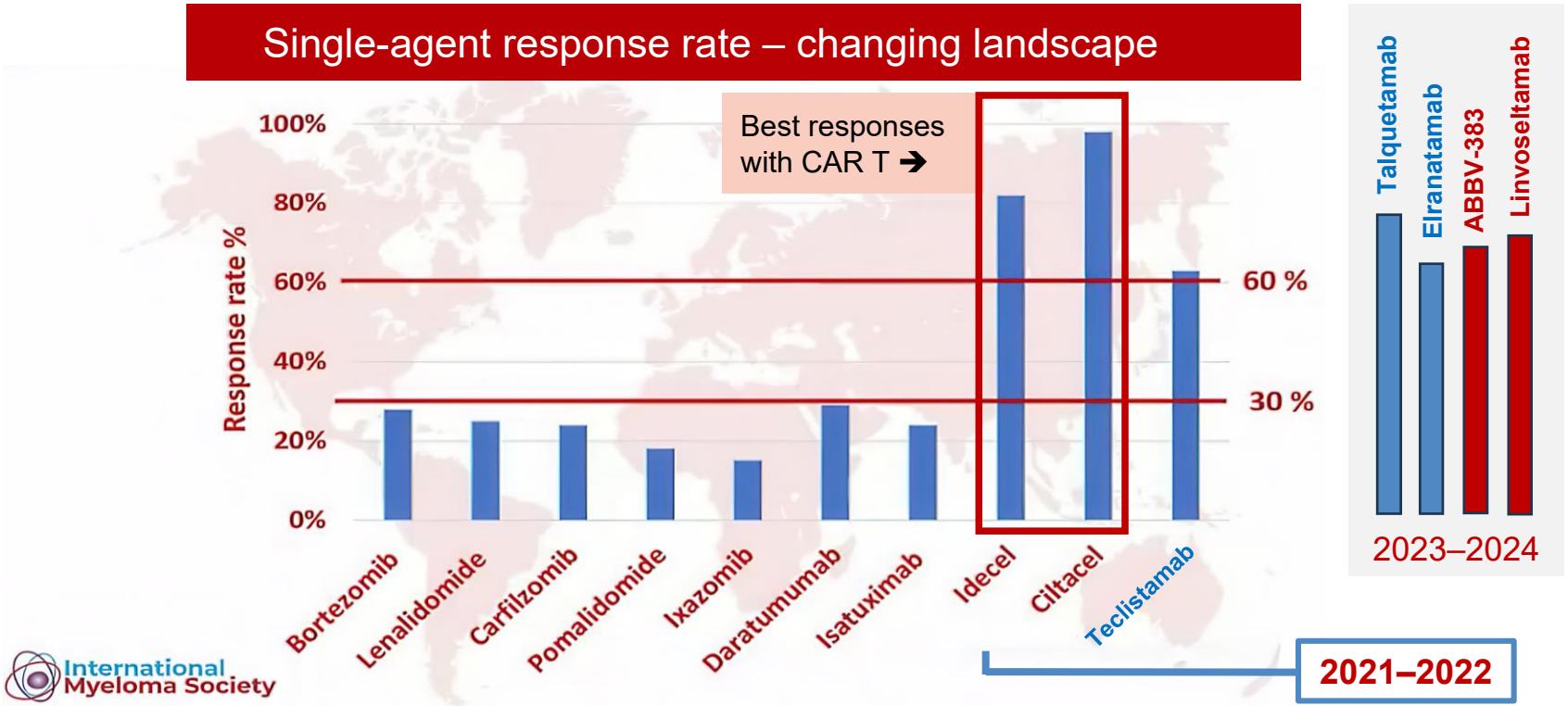
Immunotherapy Sequencing in RRMM: Current and Future Landscape

(20-min presentation; 10-min discussion)

Prof Dr Hermann Einsele
Department of Internal Medicine II
University Hospital Würzburg

Always Use the Most Effective Therapy First!

Uniklinikum Würzburg



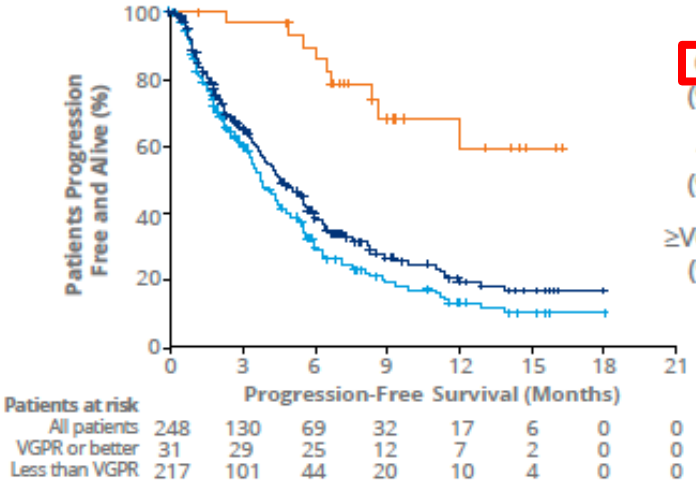
Right patient, right treatment, right time

Munshi N, et al. COMy 2023.

Unmet Medical Need in 2020: Triple Class Exposed/Refractory MM: LocoMMotion Study

Uniklinikum Würzburg

PFS

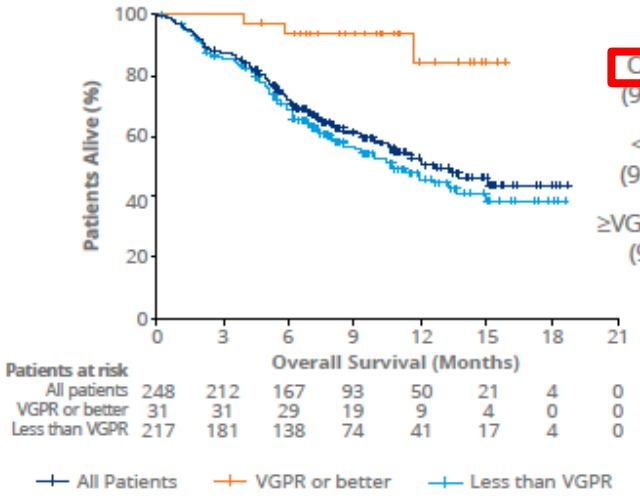


Median PFS
Overall: 4.6 mo
(95% CI: 3.9–5.6)

<VGPR: 3.9 mo
(95% CI: 3.4–4.6)

≥VGPR: not reached
(95% CI: 8.5–NE)

OS



Median OS
Overall: 12.4 mo
(95% CI: 10.3–NE)

<VGPR:10.9 mo
(95% CI: 8.4–14.2)

≥VGPR: not estimable
(95% CI: NE–NE)

- Median age: 68 years
- Median prior lines: 4 (2–13)
- Triple-class refractory: 73.8%
- ORR: 29.8%
- mDOR: 7.4 months

Mateos MV, et al. *Leukemia.* 2022.

BCMA CAR T-Cell Therapy in Late Line Treatment: Efficacy and Safety – Idecabtagene Vicleucel (ide-cel; bb2121): KarMMa Study

Uniklinikum Würzburg

- Open-label, single-arm study: N = 140
- ≥3 prior therapies (including an IMiD, a PI, and an anti-CD38 antibody); median: 6 lines of prior therapy
- 94% of patients refractory to anti-CD38 antibody; 84% triple-refractory, EMD: 39%
- Median follow-up: 11.3 months

Approved by FDA/EMA 2021

Efficacy

	Ide-Cel Treated Population			
	150 × 10^6 CAR+ T cells (N = 4)	**300 × 10^6 CAR+ T cells (N = 70)**	**450 × 10^6 CAR+ T cells (N = 54)**	**150–450 × 10^6 CAR+ T cells (N = 128)**
ORR, n (%)	2 (50.0)	48 (68.6)	44 (81.5)	94 (73.4)
CR/sCR, n (%)	1 (25.0)	20 (28.6)	19 (35.2)	40 (31.3)
Median DOR, months	---	9.9	11.3	10.6
Median PFS, months	---	5.8	11.3	8.6

- Grade ≥3 CRS: 5.5%
- Grade ≥3 investigator identified neurotoxicity events: 3.1%

In the subgroup of patients demonstrating a CR: DOR 21.9 months

17% of patients with a BOR of sCR or CR were still in remission after 64 months

Munshi N, et al. *N Engl J Med.* 2021.

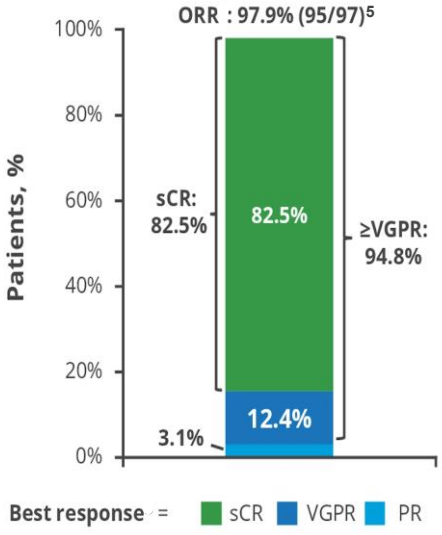
BCMA CAR T-Cell Therapy in Late Line Treatment: Efficacy and Safety – Ciltacabtagene Autoleucel (Cilta-Cel): CARTITUDE-1 Trial

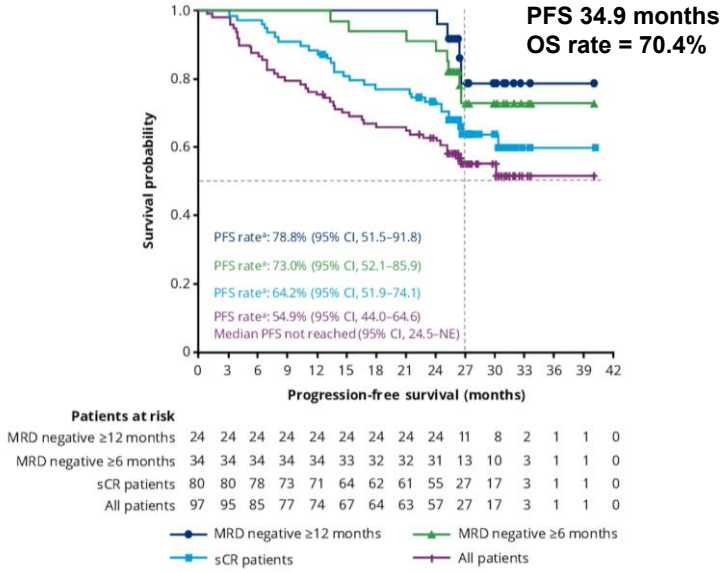
Uniklinikum Würzburg

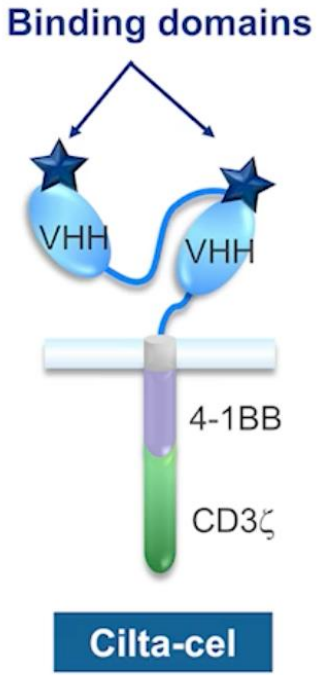
- **Second-generation CAR T cell, 2 anti-BCMA camelid VHH single domains, 4-1BB costimulatory domain**

FDA approved in 2022
EMA approved in 2022

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







Berdeja J, et al. *Lancet* 2021;398:314-324; Martin T, et al. *J Clin Oncol.* 2022; Usmani S, et al. ASCO 2022. Abstract 8028.

Long-Term (≥5 year) Remission and Survival After Treatment With Cilta-Cel in CARTITUDE-1 – Patients With RRMM

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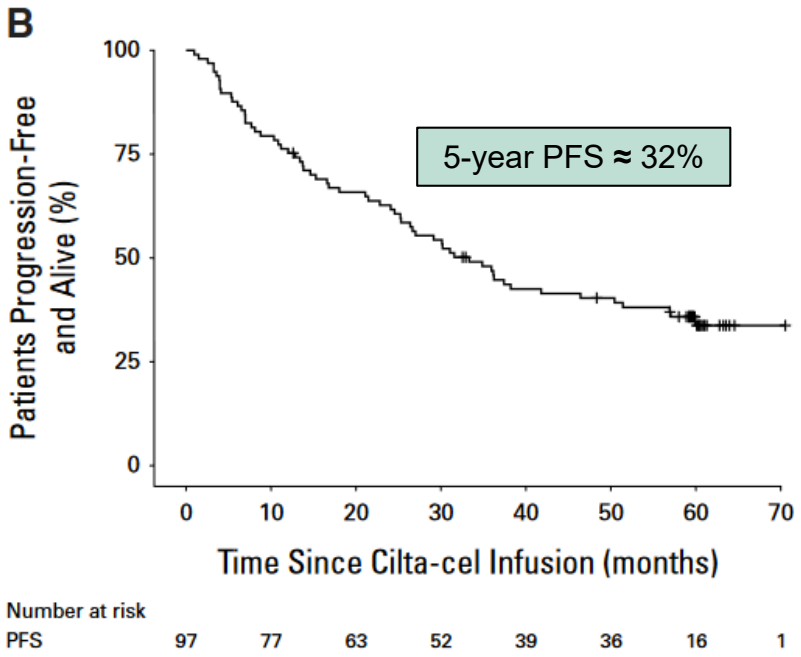

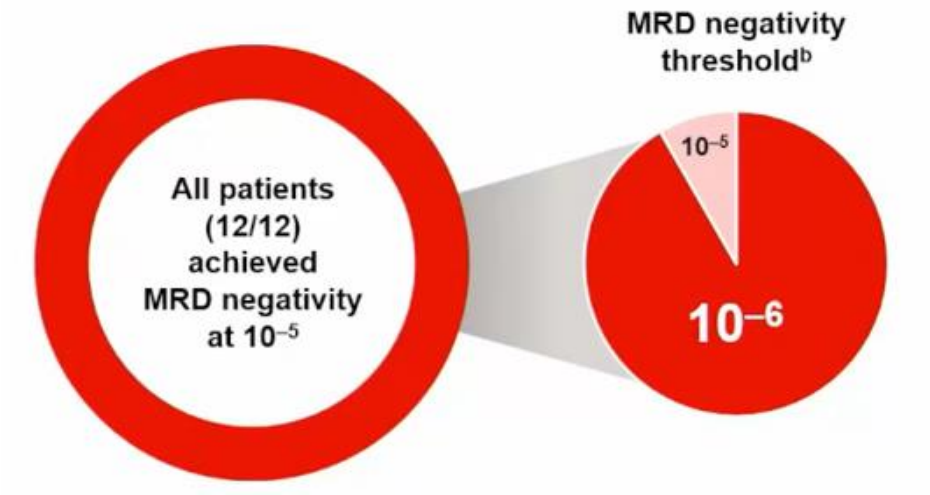

All patients (12/12) were MRD-negative and imaging negative at year 5 or later following cilta-cell infusion

→ Fulfills the definition of a functional cure!!
→ Use CAR T cells first in CAR T-eligible patients!

Jagannath S, et al. *J Clin Oncol.* 2025;43:2766-2771.

CARTITUDE-1 Long-Term Remission: Baseline Demographics and Disease Characteristics Were Generally Comparable Between Patients With or Without PD Within 5 Years (Post Hoc Analyses)

	≥5 years progression-free (n=32)	PD within 5 years (n=46)
Age, years, median (range)	60.0 (43–78)	61.5 (47–77)
High-risk cytogenetics,[a] n/N (%)	**7/30 (23.3)[b]**	**12/45 (26.7)**
Extramedullary plasmacytomas, n (%)	**4 (12.5)[c]**	**6 (13.0)**
Time to progression on last prior LOT, months, median (range)	3.98 (0.7–48.6)[d]	3.89 (0.7–21.5)[e]
Prior LOT, median (range)	6.5 (3–14)	5.0 (3–18)
Triple-class[f] refractory, n (%)	29 (90.6)	39 (84.8)
Penta-drug[g] refractory, n (%)	15 (46.9)	15 (32.6)
Bone marrow plasma cells, %, median (range)	**5.0 (0.8–80.0)**	**24.0 (0.0–95.0)**
Soluble BCMA, µg/L, median (range)	**36.0 (3.7–864.6)**	**58.5 (3.8–1342.9)**
High baseline tumor burden,[h] n (%)	2 (6.3)	8 (17.4)

Patients with high-risk cytogenetics and extramedullary plasmacytomas were equally likely to be progression-free. Of note, the percentage of patients with high tumor burden was numerically lower among patients who were progression-free

Presented by PM Voorhees at the American Society of Clinical Oncology (ASCO) Annual Meeting; May 30–June 3, 2025; Chicago, IL, USA & Virtual

How to Improve Efficacy of CAR T Cells? Earlier Application!

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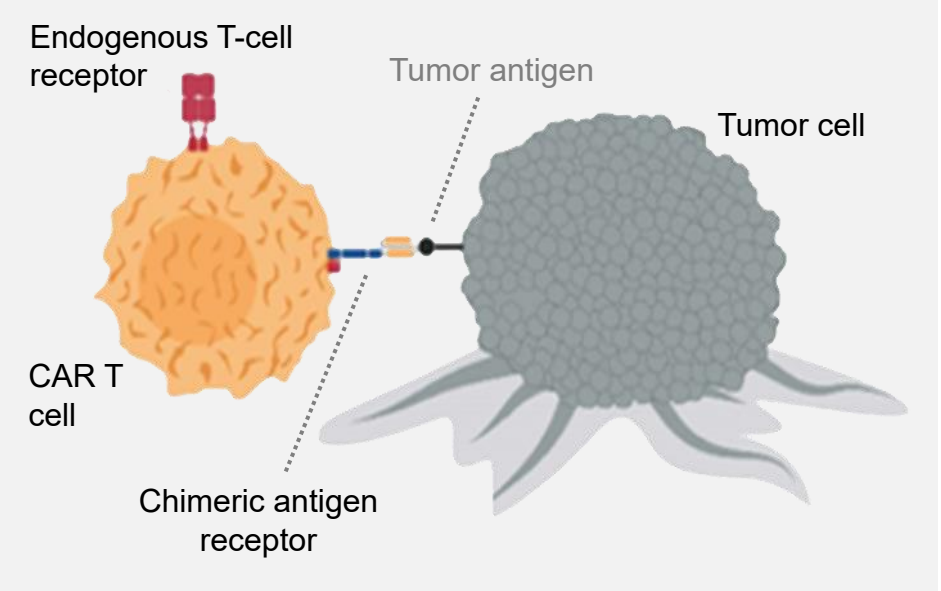
- Fitter T cells
  - Improved persistence of CAR T cells
  - Improved myeloma cell killing
- Increased immunogenicity of tumor cells
  - No selection of resistant clones
  - Lower tumor burden
  - Lower proliferative potential of tumor cells
- Better tolerability
  - High attrition rate with each treatment line
  - Lower hematotoxicity
  - Lower risk of secondary malignancies



CARTITUDE-4: PFS by Prior Line of Therapy

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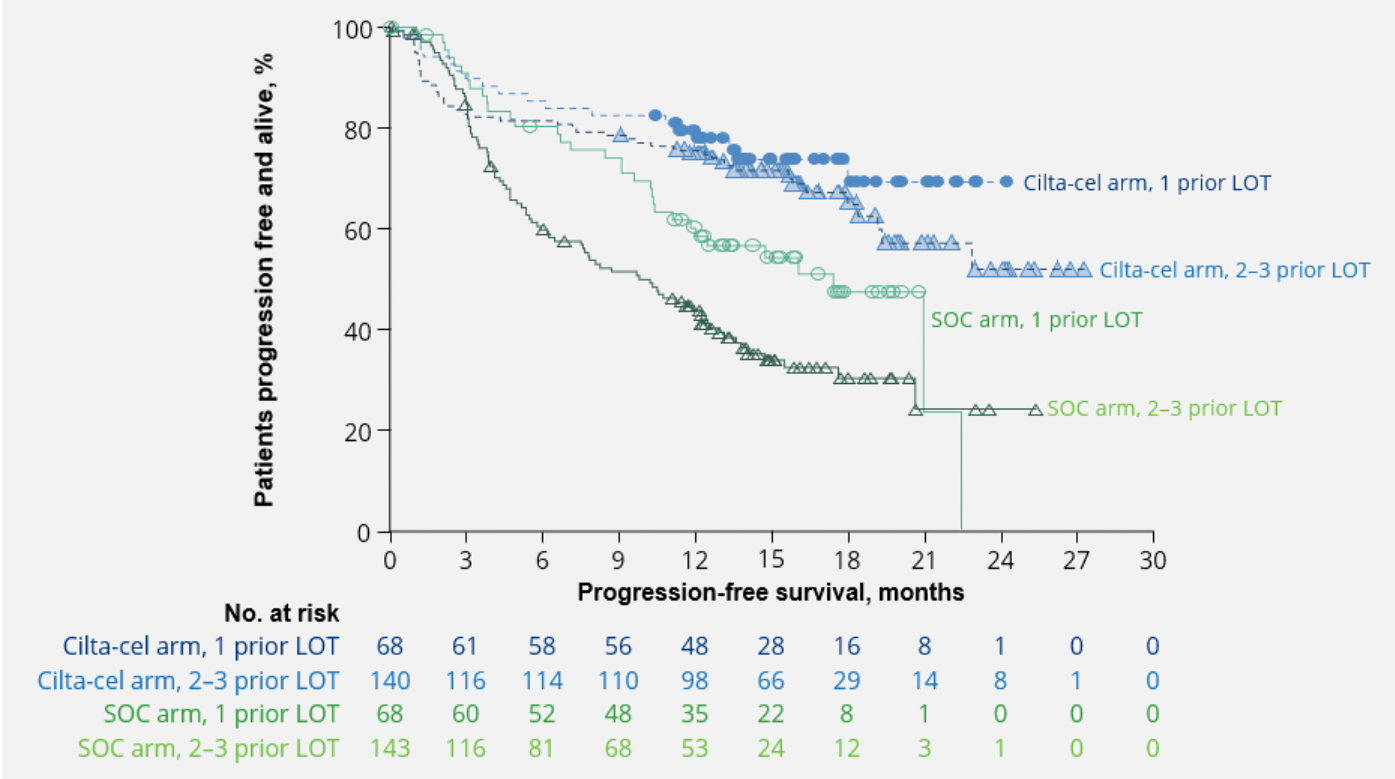
Progression-free survival by treatment and number of prior lines in the ITT set



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

Cilta-cel, ciltacabtagene autoleucel; ITT, intent-to-treat; LOT, line of therapy; PFS, progression-free survival; SOC, standard of care.

San Miguel J, et al. *N Engl J Med.* 2023.

Standard-Risk Patients With Sustained MRD Negativity for 1 Year: 30-Month PFS >93%!

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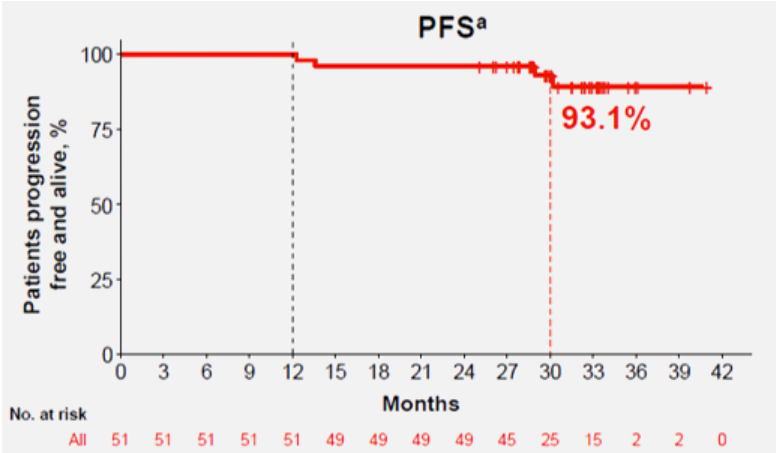
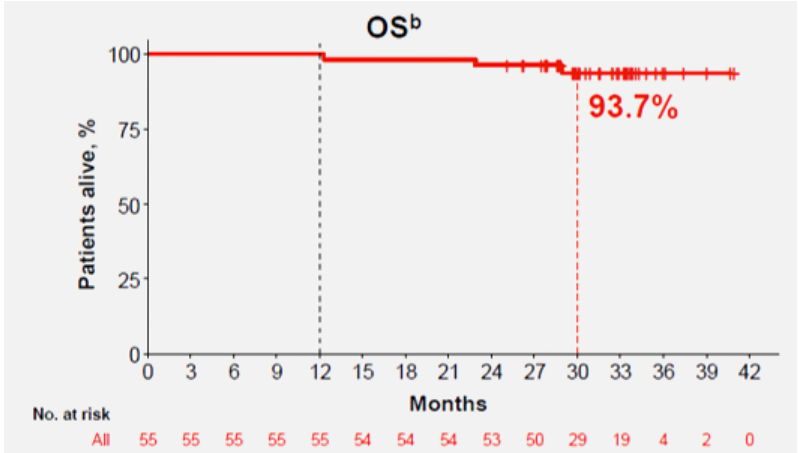
- 86% (51/59) of patients with standard-risk cytogenetics were progression free and alive ≥1 year
  - PFS and OS rates were **~93% at 30 months** for these patients with early sustained responses





- MRD-negative CR rate at 1 year was **81%** (26/32; MRD-evaluable population at 1 year)
  - **All 26** patients remained progression free at 30 months

Treating standard-risk RRMM early with cilta-cel delivered high rates of durable remissions

→ Can we cure the majority of standard-risk patients after 1–3 prior LOT?

[a]Includes 51 patients who were alive and progression free at 12 months; [b]Includes 55 patients alive at 12 months.

Costa L, et al. ASH 2025.

Will Frontline Therapy With CAR T Cells Allow to Cure All Standard-Risk Patients With MM?!

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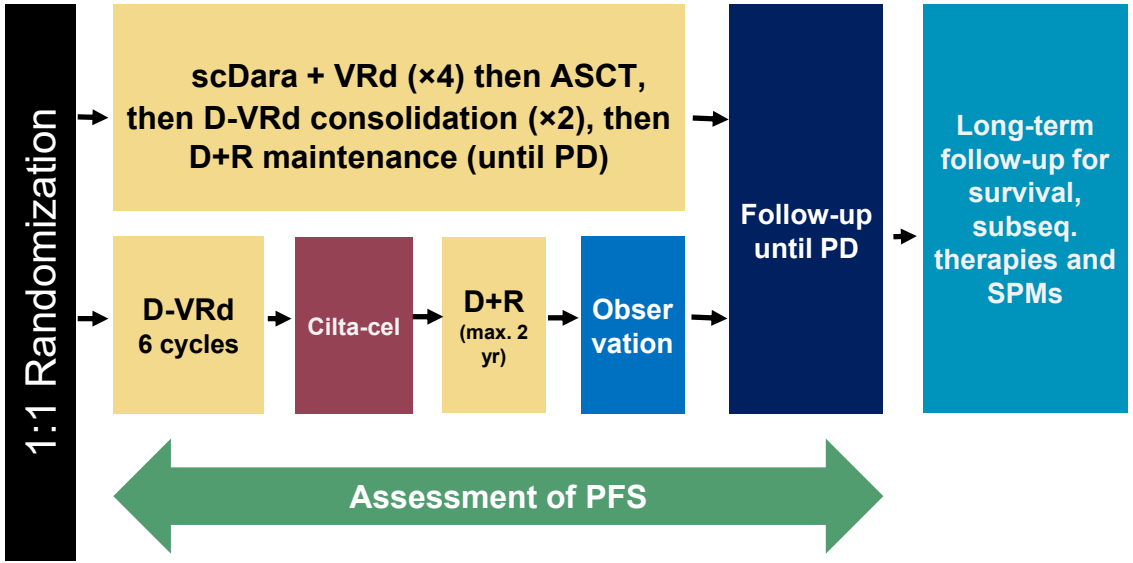
CARTITUDE-6

Key eligibility criteria:

- Newly diagnosed patients
  - Age ≤70
  - Eligible for initial ASCT
- **Sample size: ~750**



Currently, CAR T cells in early lines provide the highest likelihood of cure and a long TFI!

Prior Anti-BCMA TCE/ADC → Reduced Efficacy of Anti-BCMA CAR T-Cell Therapy!

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	CAR T	n	ORR/CR, %	PFS, mo	DOR, mo
Cohen A, et al 2023[1]	Cilta-cel	Full cohort, n = 20	60.3/30	9.1	11.5
		Prior ADC, n = 13	61.5/37.8	9.5	11.5
		Prior TCE, n = 7	57.1/14.3	5.3	8.2
Hansen D, et al 2023[2]	Ide-cel	Any BCMA TT[a] → CAR T, n = 33	73/33	3.2	---
		No BCMA TT → CAR T, n = 126	87/44	9.0	---
Ferreri C, et al 2023[3]	Ide-cel	Any BCMA TT[b] → CAR T, n = 50	74	3.2	7.4
		No BCMA TT → CAR T, n = 153	88	9.0	9.6
		Median time from last BCMA TT in R vs NR: 1695.5 vs 84 days *P* = .017			
Sidana S, et al 2025[4]	Ide-cel	No BCMA TT → CAR T, n = 702	---	9.7[d]	---
		BCMA TT[c] ≥6 mo → CAR T, n = 34	---	4.9[d]	---
		BCMA TT[c] <6 mo → CAR T, n = 69	---	5.9[d]	---
Sidana S, et al 2025[5]	Cilta-cel	No BCMA TT → CAR T, n = 203	92/75	9.7[d]	NR
		Any BCMA TT[f] → CAR T, n = 33	70/42	13.6	NR
		BCMA TT[f] ≥6 mo → CAR T, n = 13	94/56	16.8[e]	12 mo: 81%
		BCMA TT[f] <6 mo → CAR T, n = 16	54/31	6.2[e]	12 mo: 69%

[a]Prior bispecific n = 4; [b]Prior bispecific n = 7; [c]Prior bispecific n = 3; [d]*P* <.001; [e]*P* = .29; [f]Prior bispecific n = 8/33.

1. Cohen A, et al. *Blood*. 2023;141:219-230; 2. Hansen D, et al. *J Clin Oncol*. 2023;41:2087-2097; 3. Ferreri C, et al. *Blood Cancer J*. 2023, 13:117; 4. Sidana S, et al. *Blood*. 2025. Online ahead of print; 5. Sidana S, et al. *Blood*. 2025;145:85-97.

BCMA targeting bispecific antibodies in RRMM

	Teclistamab[1,2]	Elranatamab[3]	Elranatamab[4]	Linvoseltamab[5]	Alnuctamab[6,7]	ABBV-383[8]
Patients (n)	165	55	123	117	73	124
Dosing schedule	weekly /q2w SC	weekly / q2w SC	weekly/q2w IV	weekly/ q2 or 4 w IV	weekly/ q2-4w IV/SC	q3 weeks IV
med Prior LOT	5	6	5	5	4	5
ISS III / ↑↑PC (%)	12.3 / 11.2	20 / --	15.4 /21.1	18.8 /22.2	16 / --	31 / --
HR / EMD (%)	25.7 / 17	29.1/ 30.9	25.2 / 31.7	35.9/ 13.7	26 / 21	18 / --
TCR (%)	77.6	90.9*	100	73.5	63	82
ORR / ≧ CR (%) @ RP2D	63 / 45.5 1500 µg/kg SC	64 / 38.2 76 mg SC	61 / 35 76 mg SC	71 / 30 200 mg IV	69/ 43 30 mg SC	57 17 40-60 mg IV
mDOR	21.6 mos	17.1 mos	71.5% @ 15 mos	--	--	72.2 % @ 12 mos†
mPFS	11.3 mos ≦ 3 LOT 18.1 mos	11.8 mos	50.9% @ 15 mos	72.7% @ 6 mos	53% @ 12 mos	10.4 mos 57.9% @ 12 mos†
mOS	21.9 mos	21.2 mos	56.7% @ 15 mos	--	--	--
CRS (%)	72.1 (0.6 G3)	87.3 (0 G3)	56.3 (0 G3)	45.3 (0.9 G3)	56 (0 G3)	57 (2 G3)
Infections (%)	80 (55.2 G3-4)	74.5 (27.3 G3-4)	69.9 (39.8 G3-4)	59.8 (36.8 G3-4)	62 (16 G3-4)	41 (5 G3-4)

LOT = lines of therapy, HR = high risk cytogenetics, EMD = extramedullary disease, ↑↑PC = > 50-60% bone marrow plasma cells, TCR = triple class refractory, ORR = overall response rate, DOR = duration of response, PFS = progression free survival, OS = overall survival, SC = subcutaneous, IV = intravenous, mos = months, * = 23.6% prior anti-BCMA, -- = not reported, †mPFS at ≥ 40 mg dose level

1. Moreau et al NEJM 2022.; 2. Van de Donk et al ASCO 2023, 3. Bahlis et al Nat Med 2023; 4. Lesokhin et al Nat Med 2023; 5. Lee et al J ASCO 2023 ; 6 Wong et al ASH 2022 ; 7. Barr ASH2023, abstract # 2011; 8. D'Souza A J Clin Oncol 2022

Bahlis N, et al. ASH 2023.

Significant Improvement in the Efficacy of TCE: Combination Therapy

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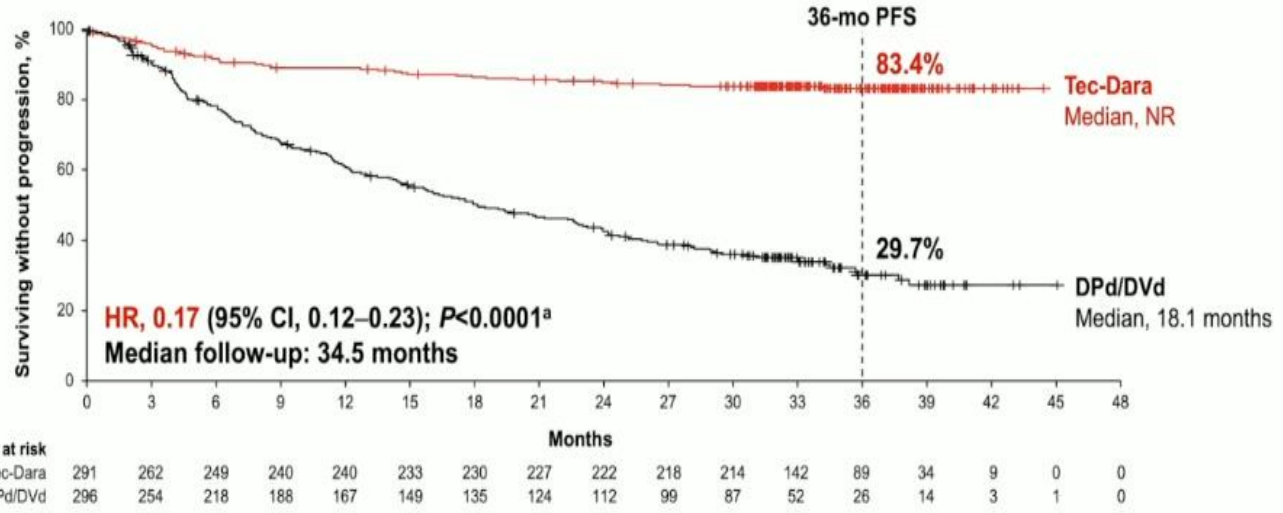
MajesTEC-3: PFS (Primary Endpoint)



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.
Reproduced with permission © The *New England Journal of Medicine* (2025).

8

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 M, et al. ASH 2025. Abstract LBA-6.

Anti-BCMA TCE → Anti-BCMA CAR T Recommendations

Uniklinikum Würzburg

- Allow sufficient washout time for **lymphocytes count recovery and adequate CD4/CD8 ratio prior to apheresis**; may vary between patients (role for IMiDs, CELMoDs, stem cell boost?) → **Optimal CAR T product**

- Bridging with TCE prior to CAR T infusion does not negatively impact outcomes (Fandrei D, et al. *Blood Cancer Discov.* 2024; Dhakal B, et al. *Blood.* 2025)

Does CAR T-Cell Therapy Overcome the Negative Impact of High-Risk Cytogenetic Abnormalities?

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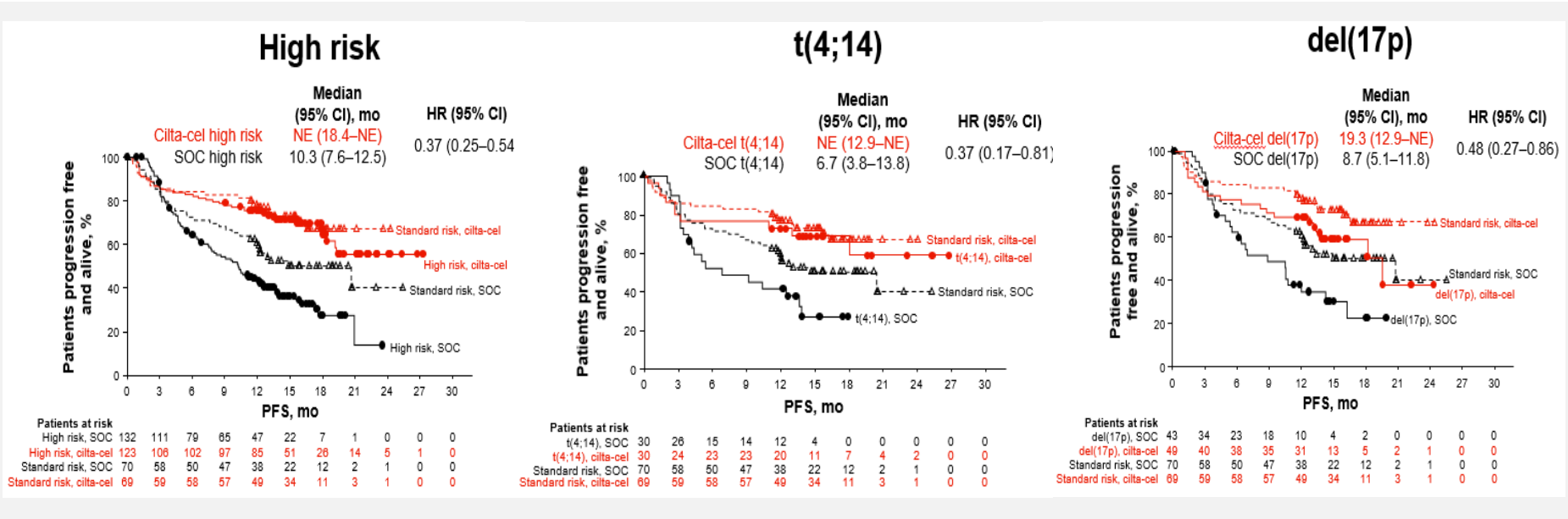
Cilta-cel lessens the impact of high-risk cytogenetics on PFS and improved PFS vs SOC



Presented by H Einsele at the Annual Meeting of the German, Austrian and Swiss Associations of Hematology and Medical Oncology (DGHO); October 11–14, 2024; Basel, Switzerland

High-Risk Cytogenetics Associated With an Increased Risk of Target Antigen Loss

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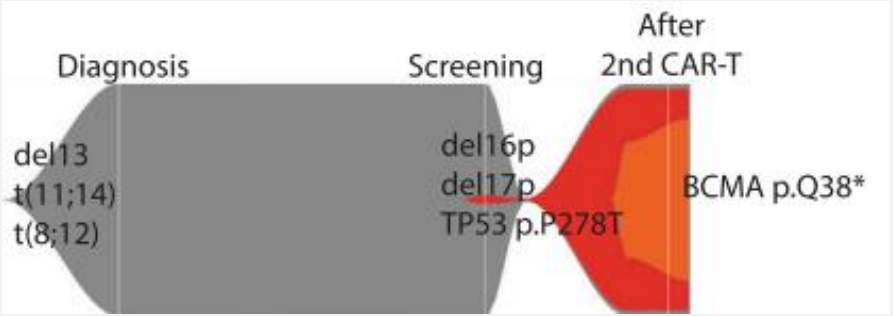
Tumor-intrinsic changes

Clonal evolution of MM cells from diagnosis to relapse after second CAR T-cell infusion



Patients with NDMM

Co-occurrence of HR cytogenetics (del17p, del1p), and del16p (encoding BCMA)

Samur MK, et al. *Nat Commun.* 2021;12:868.

Single Epitope-Targeting Immunotherapies, Especially in RRMM
BCMA Antigen Escape Due to Genetic Instability

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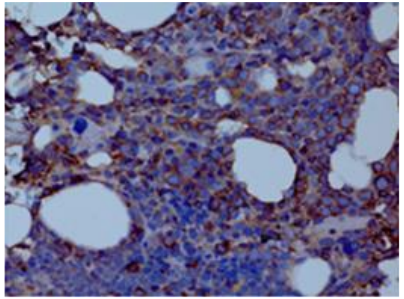
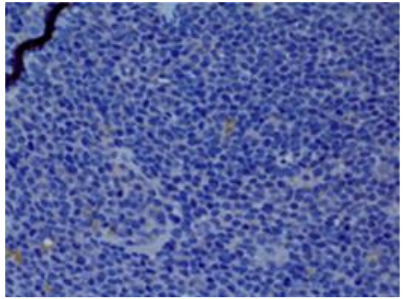
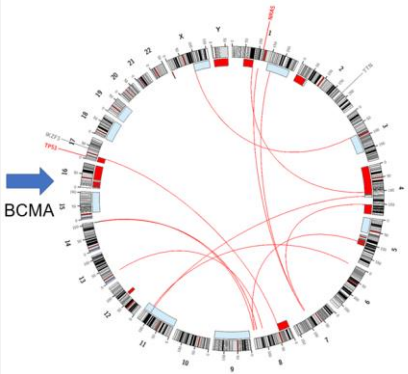
BCMA CAR T cells



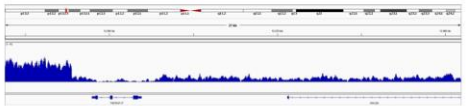




Whole-genome sequencing

4%–6% irreversible BCMA loss

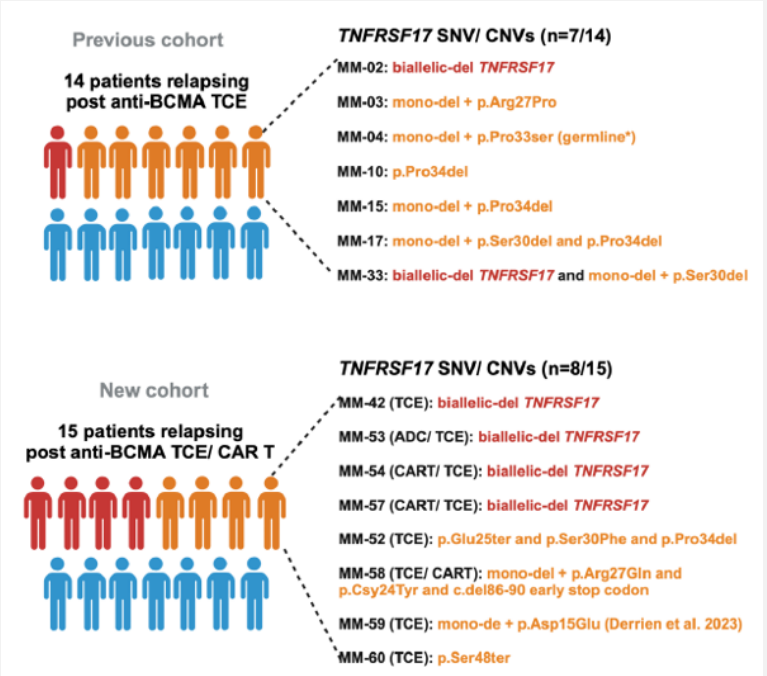
Biallelic deletion TFRSF17



Da Vià MC, et al. *Nat Med.* 2021; Samur MK, et al. *Nat Med.* 2021; Lee H, et al. *Nat Med.* 2023.

BCMA-targeting TCE

BCMA antigen escape = 15/29 (51%)



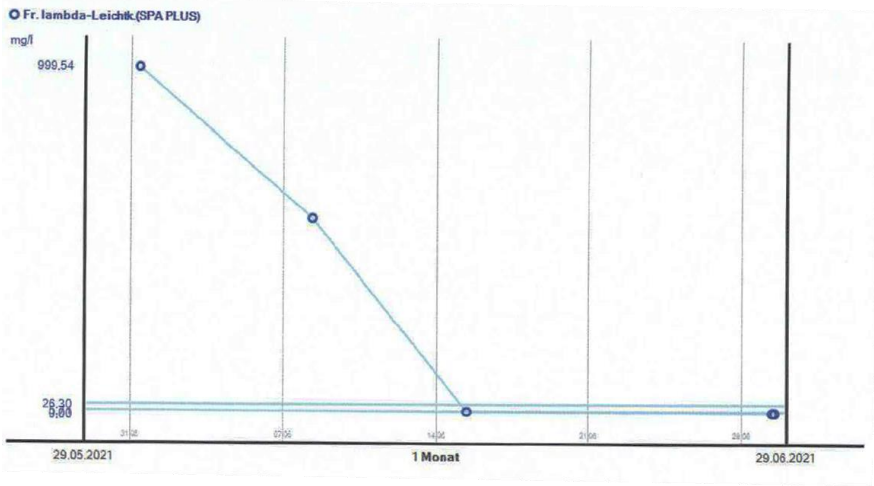
Lee H, et al. ASH 2024.

Patient Case 1

Uniklinikum Würzburg

57 yo, LC-MM, ISS-IIIB, acute renal failure, hypercalcemia (short-term dialysis), multiple osteolysis

GPRC5D-directed T-cell therapy



Treatment:

02/2011	3× PAD
05/u. 08/2011	Tandem-Mel → CR
04/14	PD → RD 6 cycles
12/15 – 12/16	RD → 16 cycles
	Panobinostat-Bortezomib-Dex → PD
05 – 11/17	6× Ixa-Thal-Dex → PD
11 – 12/12	1× Rd → PD
01/18	BCMA-directed T-cell therapy
09/19	PD → KRd
07/20	PD → Dara-Vel-Dex → PD
12/20	Belantamab → PD

(documented irreversible BCMA loss)

12/20	VTD-PACE 3× → PD

After 15 mo PD!

Personal treatment experience.

GPRC5D-Targeting T-Cell–Engaging Therapies After BCMA T-Cell Therapy

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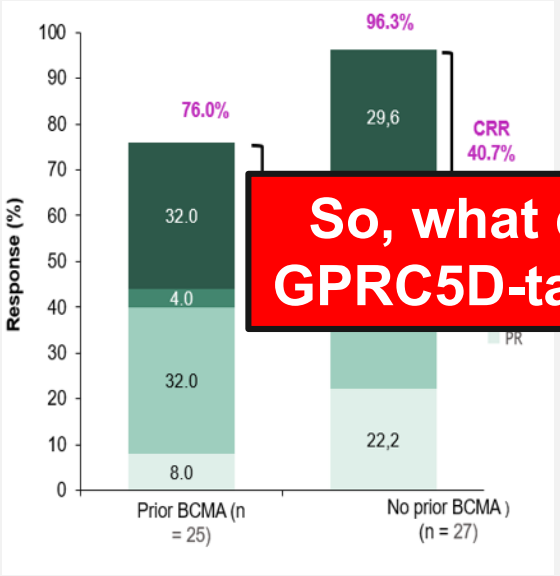
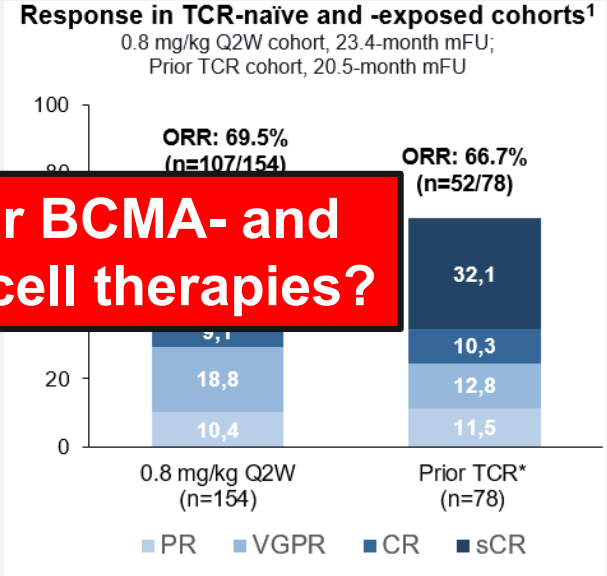
Arlo-Cel for RRMM (no/prior BCMA)



Bal S, et al. ASH 2024.

Talquetamab for RRMM (no/prior BCMA)



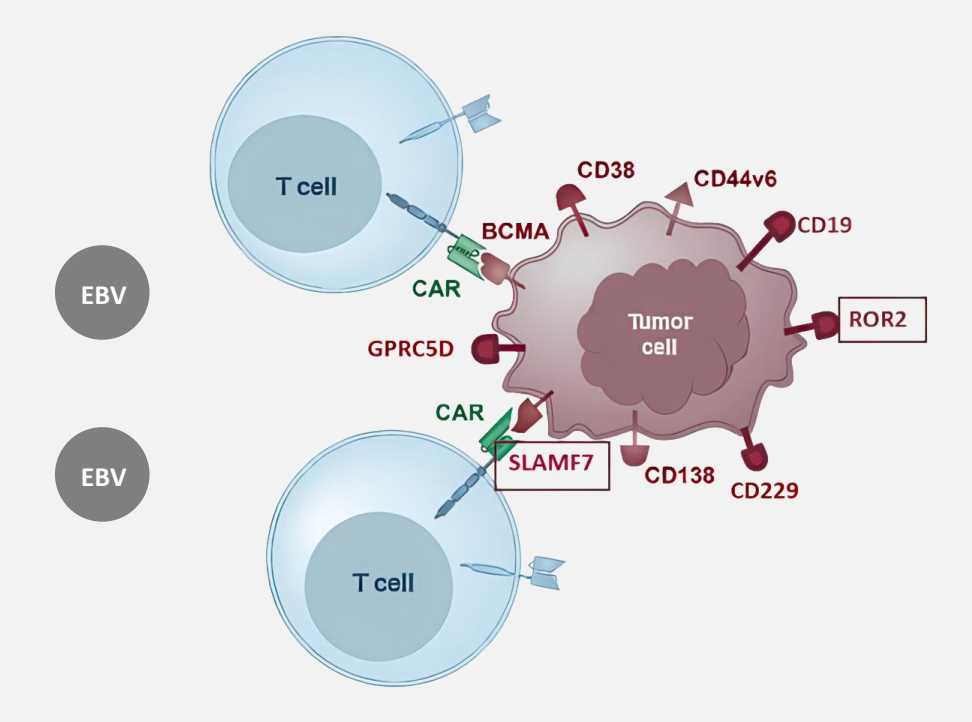
Chari A, et al. *Lancet Haematol.* 2025.

So, what comes after BCMA- and GPRC5D-targeting T-cell therapies?

But: GPRC5D-targeting T-cell–engaging therapy is also associated with target antigen loss.
13/17 cases relapsing during talquetamab therapy and 8/10 patients relapsing after Arlo-cel showed GPRC5D antigen escape

Lee et al. ASH 2024;
Htut et al. ASH 2024.

CAR T-Cell Therapy in Multiple Myeloma: Beyond BCMA and GPRC5D



Danhof S, et al. Safety and Feasibility of SLAMF7 CAR T Cells in Multiple Myeloma

Weber J, et al. ROR2-CART Elicit Potent Antitumor Reactivity in MM and ccRCC

Anti-BCMA TCE → Anti-BCMA CAR T Recommendations

Uniklinikum Würzburg

- Allow sufficient washout time for **lymphocytes count recovery and adequate CD4/CD8 ratio prior to apheresis**; may vary between patients (role for IMiDs, CELMoDs, stem cell boost?) → **Optimal CAR T product**
- **Confirm retained target expression** (FCM and/or NGS)
- Bridging with TCE prior to CAR T infusion does not negatively impact outcomes (Fandrei D, et al. *Blood Cancer Discov.* 2024; Dhakal B, et al. *Blood.* 2025)

The Majority of Patients Have Relapse After CAR T/TCE Therapy How to Treat These Patients?

Uniklinikum Würzburg

1. Use a therapy again that was no longer effective before the CAR T-cell therapy
2. HD therapy with stem cell transplantation (auto/allo)
3. Second CAR T-cell therapy
4. Other immunotherapies, eg, bispecific antibodies

The Majority of Patients Have Relapse After CAR T/TCE Therapy How to Treat These Patients?

Uniklinikum Würzburg

1. **Use a therapy again that was no longer effective before the CAR T-cell therapy**
2. HD therapy with stem cell transplantation (auto/allo)
3. Second CAR T-cell therapy
4. Other immunotherapies, eg, bispecific antibodies

Salvage Therapy After BCMA-Directed CAR T Therapy: Therapies Used Prior to CAR T Cells/Targeted Therapies

Uniklinikum Würzburg

Characteristics and response rates of first and subsequent salvage treatments

Treatment group	First line of salvage treatment				All lines of salvage treatment			
	N	% used	N ≥ PR *ORR*	N ≥ VGPR %	N	% used	N ≥ PR *ORR*	N ≥ VGPR %
Doublet/triplet/ quadruplet combination of approved agents	23	29.1%	7 out of 22 31.8%	2 out of 22 9.1%	56	23.6%	15 out of 53 28.3%	4 out of 53 7.5%
Selinexor-based therapy	5	6.3%	2 out of 5 40.0%	2 out of 5 40.0%	15	6.3%	3 out of 14 21.4%	3 out of 14 21.4%
Venetoclax-based therapy	3	3.8%	2 out of 3 66.7%	1 out of 3 33.3%	14	5.9%	5 out of 14 35.7%	2 out of 14 14.3%
Other combinations (including MAPKi, checkpoint inhibitor or other trial)	11	13.9%	1 out of 11 9.1%	0 out of 11 0.0%	31	13.1%	12 out of 31 38.7%	1 out of 31 3.2%
All treatment groups	79	100.0%	33 out of 76 43.4%	16 out of 76 21.1%	237	100.0%	101 out of 224 45.1%	48 out of 224 21.4%
	Total N = 79		Total N = 76		Total N = 237		Total N = 224	

Van Oekelen O, et al. *Blood*. 2023.

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

The Majority of Patients Have Relapse After CAR T/TCE Therapy How to Treat These Patients?

Uniklinikum Würzburg

1. Use a therapy again that was no longer effective before the CAR T-cell therapy
2. **HD therapy with stem cell transplantation (auto/allo)**
3. **Second CAR T-cell therapy**
4. Other immunotherapies, eg, bispecific antibodies

Salvage Therapy After BCMA-Directed CAR T Therapy: AutoSCT/AlloSCT/Bispecific Antibodies

Uniklinikum Würzburg

Characteristics and response rates of first and subsequent salvage treatments

Treatment group	First line of salvage treatment				All lines of salvage treatment			
	N	% used	N ≥ PR *ORR*	N ≥ VGPR %	N	% used	N ≥ PR *ORR*	N ≥ VGPR %
Allo-SCT	0	0.0%	0/0 N/A	0/0 N/A	7	3.0%	4/4 100.0%	2/4 50.0%
Auto-SCT	3	3.8%	1/3 33.3%	1/3 33.3%	14	5.9%	10/14 71.4%	7/14< 50.0%
BCMA ADC	1	1.3%	0/1 0.0%	0/1 0.0%	9	3.8%	2/8 25.0%	2/8 25.0%
Bispecific trial	11	13.9%	7/10 70.0%	5/10 50.0%	32	13.5%	17/29 58.6%	12/29 41.4%
BCMA-directed bispecific trial	2	2.5%	1 out of 2 50.0%	0 out of 2 0.0%	9	3.8%	4 out of 9 44.4%	3 out of 9 33.3%
Non-BCMA–directed bispecific trial	9	11.4%	6 out of 8 75.0%	5 out of 8 62.5%	23	9.7%	13 out of 20 65.0%	9 out of 20 45.0%
CAR T trial	2	2.5%	2 out of 2 100.0%	1 out of 2 50.0%	6	2.5%	5 out of 6 83.3%	3 out of 6 50.0%
Chemotherapy with or without stem cell support	20	25.3%	11 out of 19 57.9%	4 out of 19 21.1%	53	22.4%	29 out of 51 56.9%	12 out of 51 23.5%

Van Oekelen O, et al. *Blood*. 2023.

Repeating the CAR T-Cell Therapy With the Same CAR T-Cell product

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Tumor response and progression-free survival in all enrolled and retreated patients

	Total Enrolled (N=140)	Total Retreated (N=28)
Best overall response—no. (%)	94 (67)	6 (21)
Stringent complete response	41 (29)	0
Complete response	1 (1)	0
Very good partial response	25 (18)	1 (4)
Partial response	27 (19)	5 (18)
Stable disease	22 (16)	5 (18)
Progressive disease	8 (6)	15 (54)
Not evaluable*	14 (10)	2 (7)
Median progression-free survival (95% CI)—mo	9.5 (6.9–12.5)	1.0 (1.0–2.1)

Antidrug antibody status: Response after retreatment

Retreatment response	ADA-Positive (N=16)	ADA-Negative (N=12)
	number of patients (percent)	
Yes	0	6 (50)
No	16 (100)	6 (50)

ADA denotes antidrug antibody.

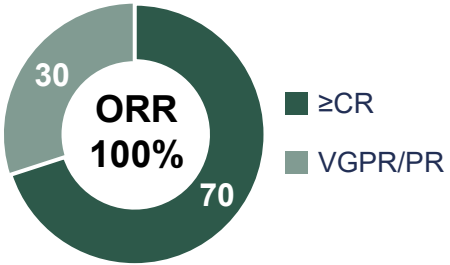
Munshi NC, et al. *N Engl J Med.* 2021.

Repeated BCMA CAR T-Cell Therapy in Refractory MM (after relapse following ide-cel+ treatment with cilta-cel)

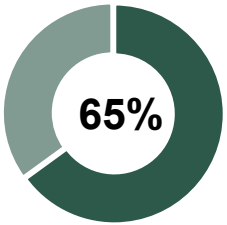
Uniklinikum Würzburg

Efficacy and safety (median follow-up 8.8 months)

- **Median interval between CAR T-cell therapies**: 1.9 years
- **Bridging therapy included:** belantamab mafodotin (n = 1) and talquetamab (n = 3)



6-month PFS rate



- No new safety signals or grade ≥3 CRS/ICANS
- Trochlear palsy was observed in 1 patient; there was no other NT

Patients with **<12 months PFS after ide-cel** had significantly poorer outcomes (*P* = .0024) following **retreatment with cilta-cel**

This study provides the largest real-world analysis supporting the feasibility and efficacy of sequential BCMA-directed CAR T therapy (ide-cel → cilta-cel). The findings may help inform clinical decisions in the management of post-CAR T-cell therapy relapse in RRMM

Richardson T, et al. EHA 2025. Abstract PF758.

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

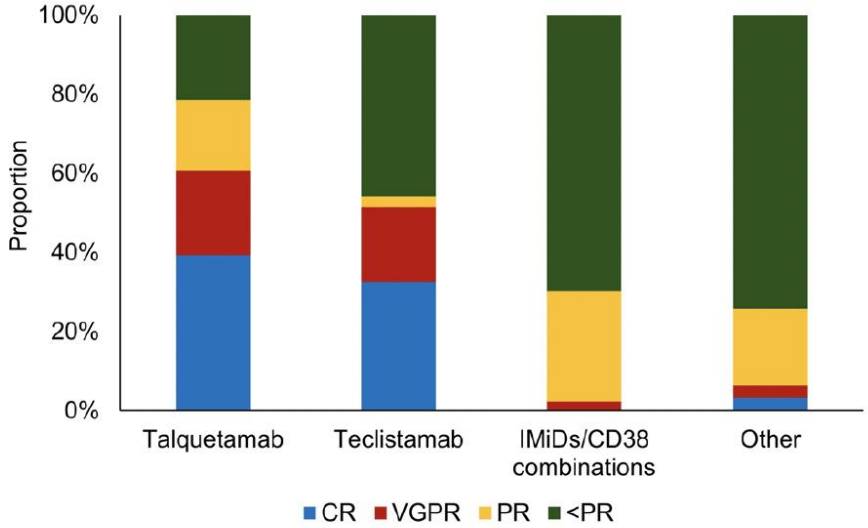
The Majority of Patients Have Relapse After CAR T/TCE Therapy How to Treat These Patients?

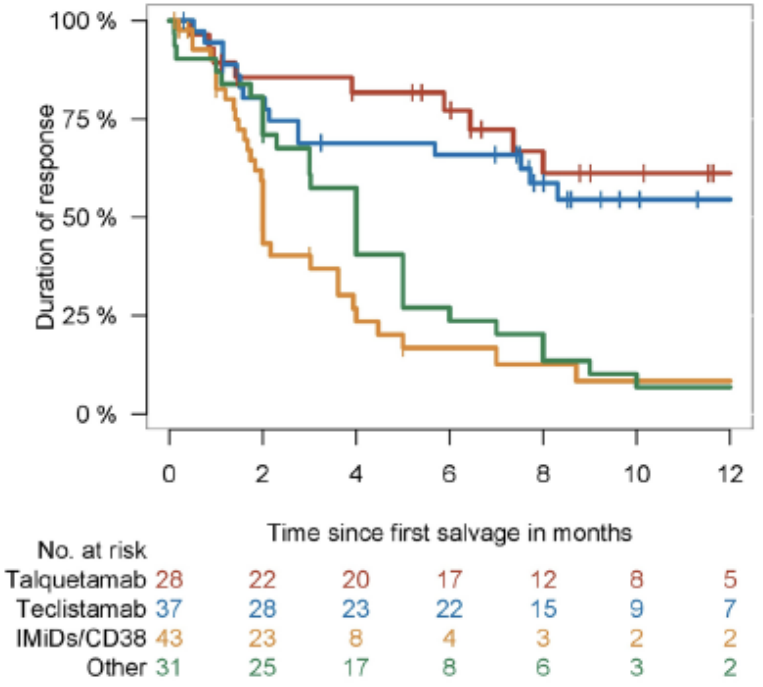
Uniklinikum Würzburg

1. Use a therapy again that was no longer effective before the CAR T-cell therapy
2. HD therapy with stem cell transplantation (auto/allo)
3. Second CAR T-cell therapy
4. **Other immunotherapies, eg, bispecific antibodies**

Bispecific Antibodies Targeting BCMA or GPRC5D Are Highly Effective in Relapsed Myeloma After CAR T-Cell Therapy

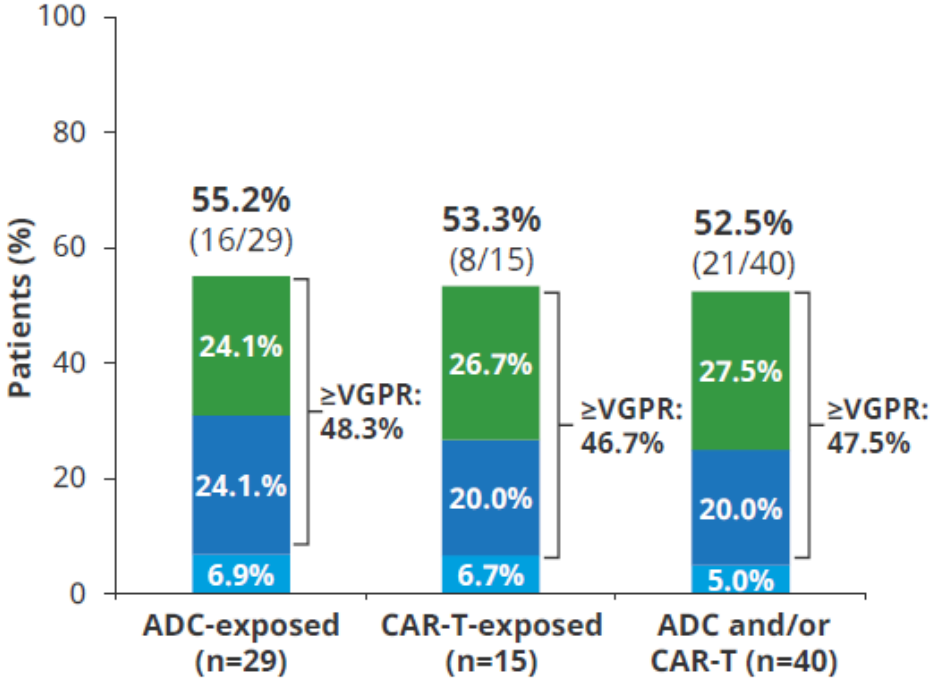
Uniklinikum Würzburg

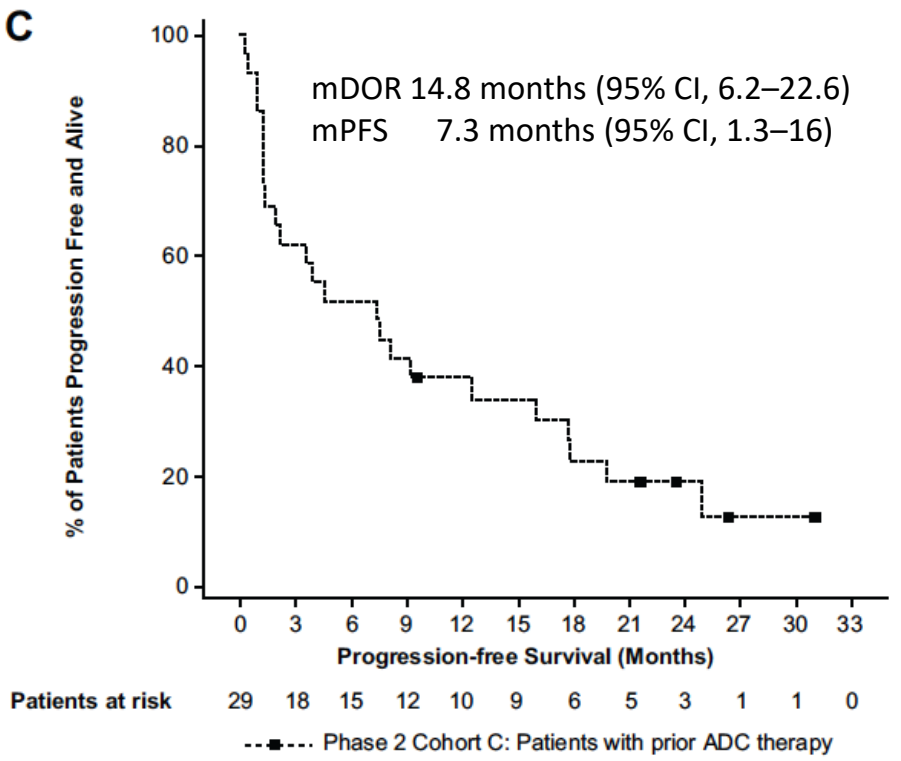




Merz M, et al. *Blood Cancer J.* 2024;14:214.

Teclistamab in Patients With RRMM After BCMA-Targeting Therapies





Touzeau C, et al. *Blood*. 2024.

Do Patients Who Do Not Have Response to CAR T Cells Benefit From Bispecific Antibodies?
Patient Case 4

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61 yo, IgA lambda (SMM, ED 2005), FISH: t(4;14)

	VCd for 3 cycles
09/2016	CAD + SC collection
11/16	Mel 200 + ASCT, serological CR
04/17	Lenalidomide-ixazomib maintenance therapy (study) → PD
08/17	KRd
06/19	Dara-Pd
04/22	CAR T-cell infusion (ide-cel) **→ SD**
	2 cycles of KRd → SD
	Teclistamab → MRD-negative CR
08/2022	**Teclistamab for 4 weeks**, ongoing MRD-negative, imaging-negative CR
12/2025	**→ MRD-negative CR**

Impact of T-Cell Exhaustion on T-Cell–Engaging Therapies

Transcriptional profiles of CAR T cells associated with clinical response

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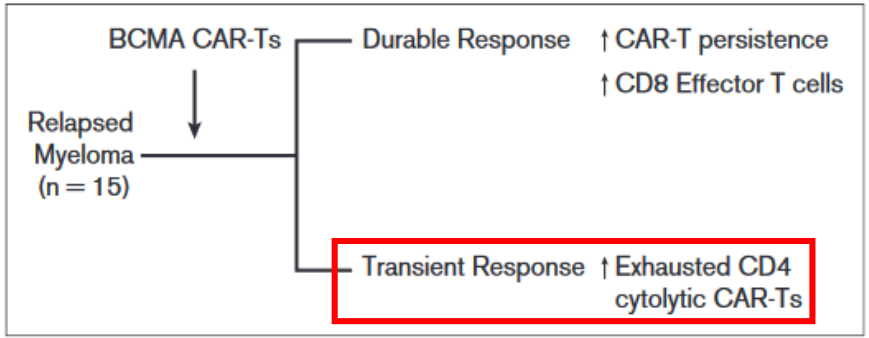
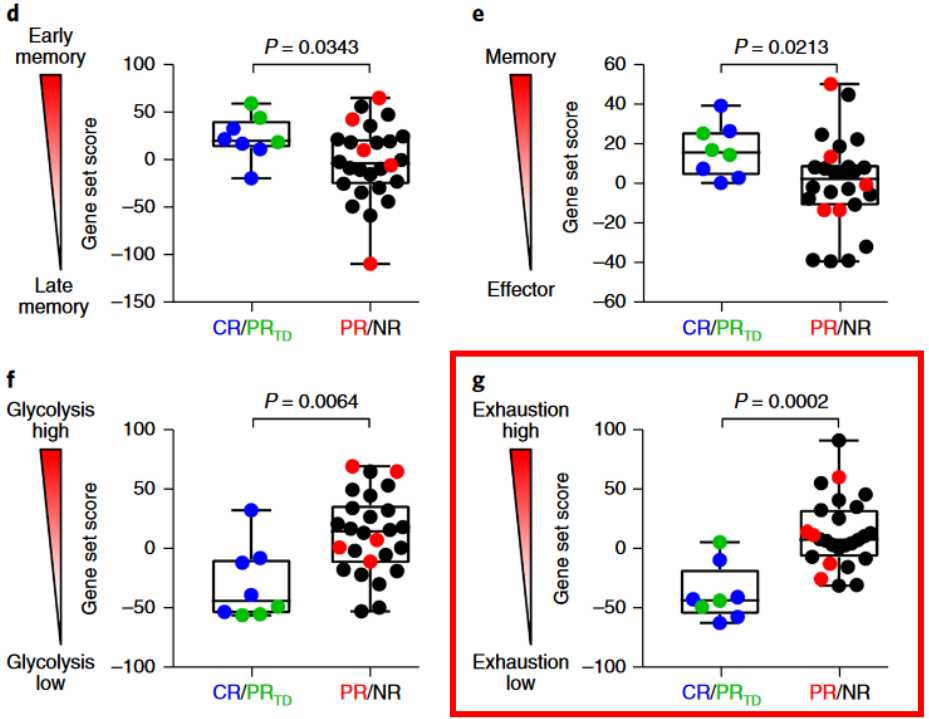


Correlates of outcome after BCMA CAR-T therapy in MM in the study by Ledergor et al.

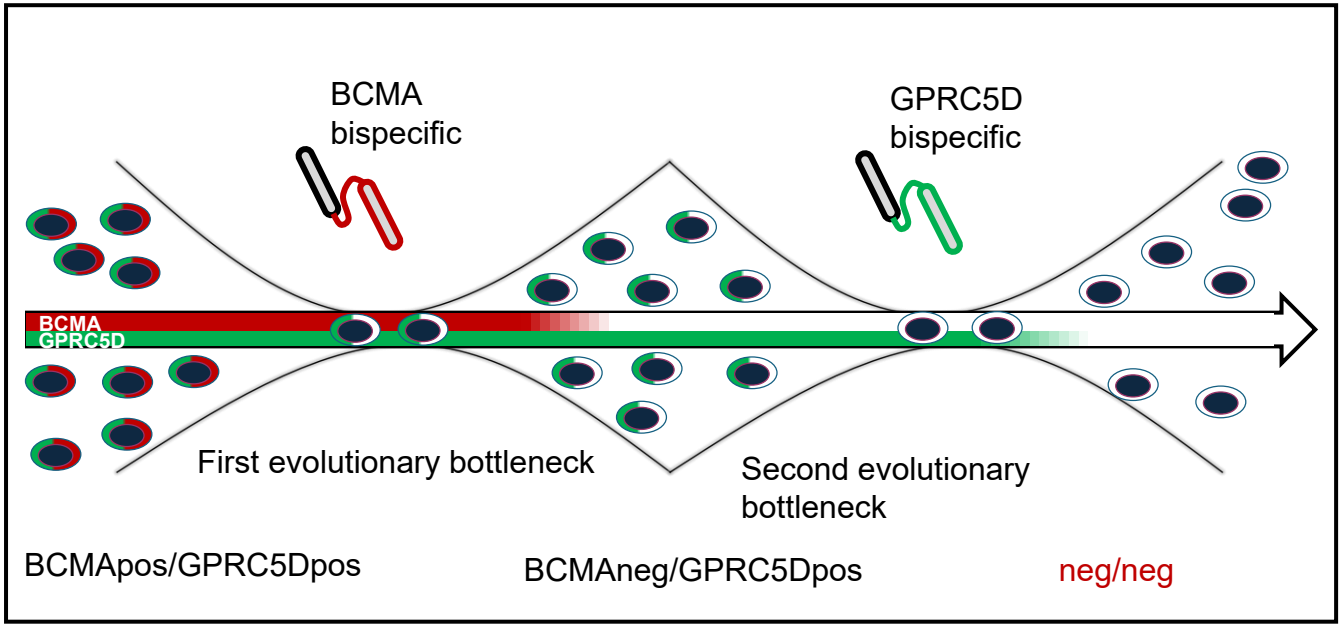
Dhodapkar MV, et al. *Blood Adv.* 2024.



T-cell exhaustion is associated with a lower response rate/quality

Fraietta JA, et al. *Nat Med.* 2018.

Sequential Immunotherapy



Anti-BCMA CAR T or ADC → Anti-BCMA or Anti-GPRC5D TCE

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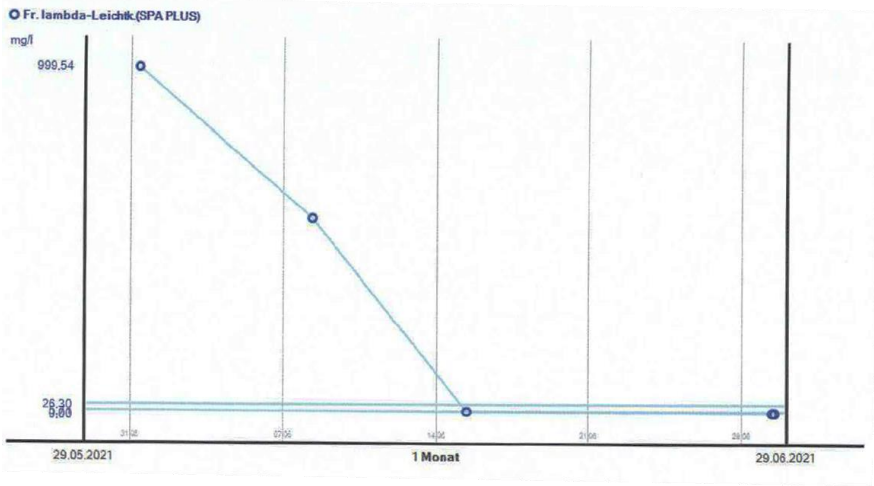
- **Confirm retained target expression** (FCM and/or NGS)
- **Ensure adequate absolute CD3 T-cell count** (CD8 Tem)
- Sequential treatment with anti-BCMA CAR T → TCE or TCE → TCE can yield durable responses if adequate T-cell count (Tem)
- Switching targeted antigen with talquetamab if TNFRSF17 mutational status is unknown

Patient Case 1 (cont.)

57 yo, LC-MM, ISS-IIIB, acute renal failure, hypercalcemia (short-term dialysis), multiple osteolysis

GPRC5D-directed T-cell therapy



Treatment:

02/2011	3× PAD
05/u. 08/2011	Tandem-Mel → CR
04/14	PD → RD 6 cycles
12/15 – 12/16	RD → 16 cycles
	Panobinostat-Bortezomib-Dex → PD
05 – 11/17	6× Ixa-Thal-Dex → PD
11 – 12/12	1× Rd → PD
01/18	BCMA-directed T-cell therapy
09/19	PD → KRd
07/20	PD → Dara-Vel-Dex → PD
12/20	Belantamab → PD

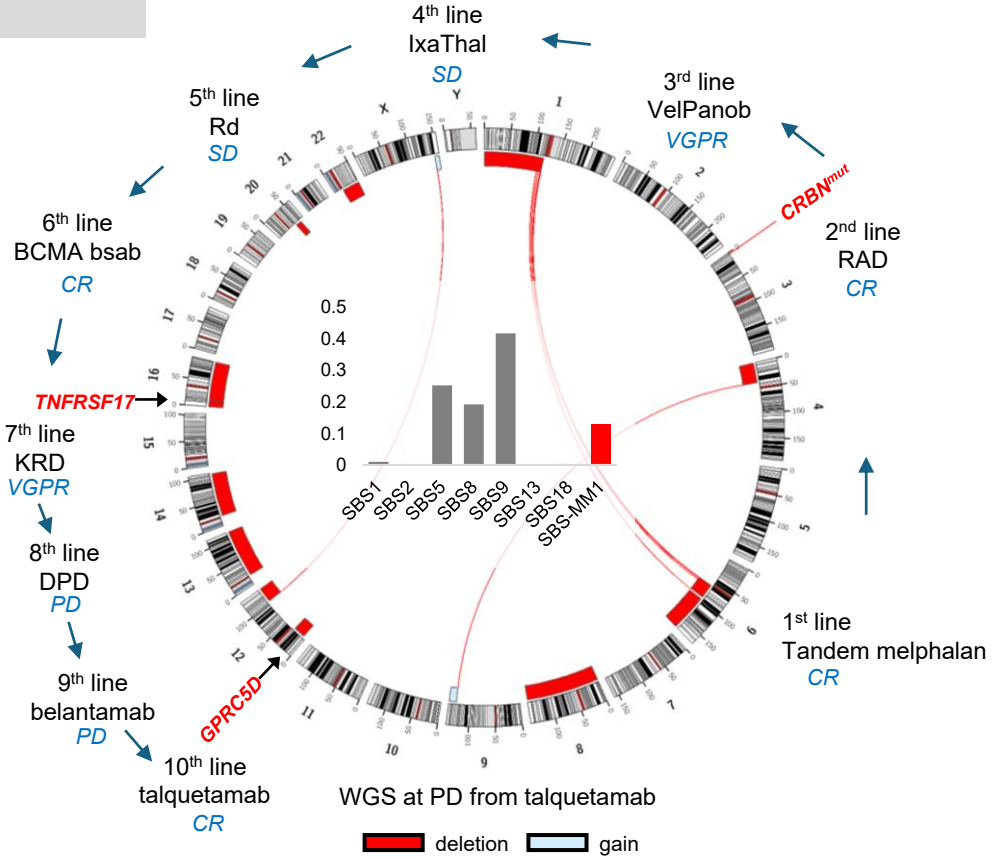
(documented irreversible BCMA loss)

12/20	VTD-PACE 3× → PD

After 15 mo PD!

Personal treatment experience.

WGS in a patient with RRMM after 10 lines of therapy



Resistance to BCMA

Resistance to IMID

Resistance to GPRC5D

Riedhammer et al. *Leukemia.* 2026. In press.

Hepta-refractory RRMM (N = 17)

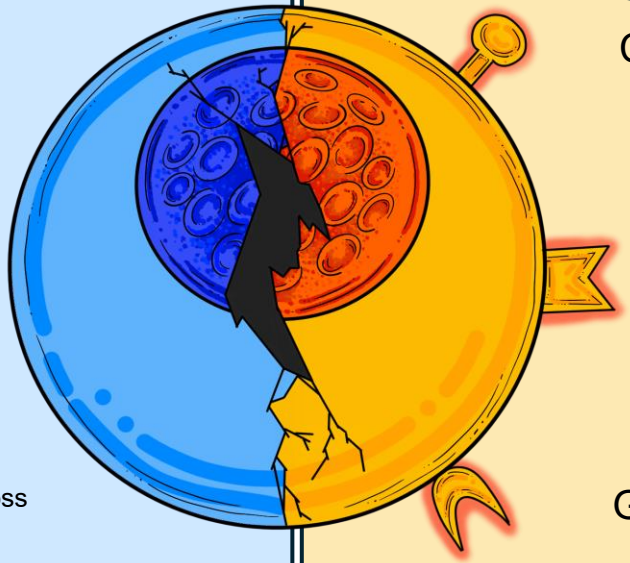
~~BTZ~~ ~~CFZ~~ ~~Len/Thal~~ ~~Pom~~ ~~CD38~~ ~~BCMA TCE/CAR T~~ ~~GPRC5D TCE~~

43% Loss of ≥1 key Ag

$CD38^{loss}$ 12%

$BCMA^{loss}$ 42%

$GPRC5D^{loss}$ 35%



57% wildtype Ag

$CD38^{WT}$

B

$GPRC5D^{WT}$

Roughly 50% of patients experienced relapse due to an unknown mechanism, such as epigenetic adaptation or effector T-cell dysfunction.

○ Retreatment not possible

✓ Retreatment possible

The Majority of Patients Have Relapse After CAR T TCE Therapy for RRMM – How to Treat These Patients

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1. **Use a therapy again that was no longer effective before the CAR T-cell therapy**
   → Suboptimal responses

2. **Use novel agents/combinations:** Selinexor, CELMoDs: interesting option

3. **HD therapy with stem cell transplantation (auto/allo)**
   → Effective option if stem cells are available, few cases of alloSCT

4. **Second CAR T-cell therapy**
   → Only with another construct and/or targeting a different target antigen

5. **Other immunotherapy, eg, T-cell–engaging antibodies**
   → Very effective option, but screening for target antigen loss
   → If TCE after TCE → no T-cell–engaging therapy for at least 6 months

Many thanks for your kind attention!

Uniklinikum Würzburg

Global Multiple Myeloma Academy

Discussion

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Panel Discussion: Regional Challenges of Multiple Myeloma Diagnosis and Treatment

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Session Close – Audience Response Questions

Rafael Fonseca, MD

APTITUDE HEALTH®

Question 5

[REPEATED] Which of the following is not a BCMA-directed bispecific antibody?

1. Elranatamab
2. Linvoseltamab
3. Talquetamab
4. Teclistamab

Question 6

[REPEATED] What is true about the MagnetisMM-3 clinical trial?

1. Elranatamab was administered subcutaneously, with step-up dosing
2. Evaluated IV BCMA-targeted antibody in combination with daratumumab
3. Primarily assessed overall survival with CAR T-cell therapy
4. Randomized study comparing elranatamab with standard chemotherapy in 1L MM

Agenda Day 2 – Europe

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

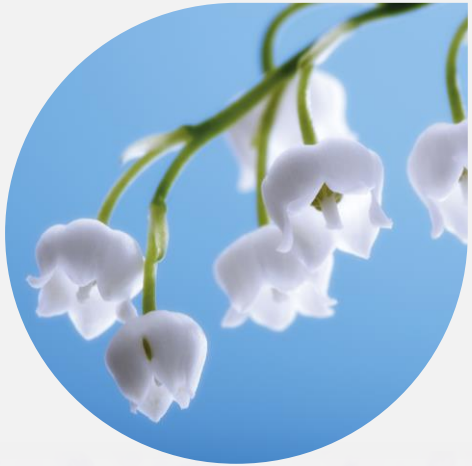
Time (CEST)	Topic	Speaker
17.00 – 17.10 10 min	**Welcome and Meeting Overview**	Rafael Fonseca, MD Philippe Moreau, MD
17.10 – 17.30 20 min	**Overview of RRMM Treatment: Early Lines of Therapy**	Philippe Moreau, MD
17.30 – 17.55 25 min	**CAR T-Cell Therapy in RRMM: Impact of Earlier Use and Real-World 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

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

See you tomorrow!

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