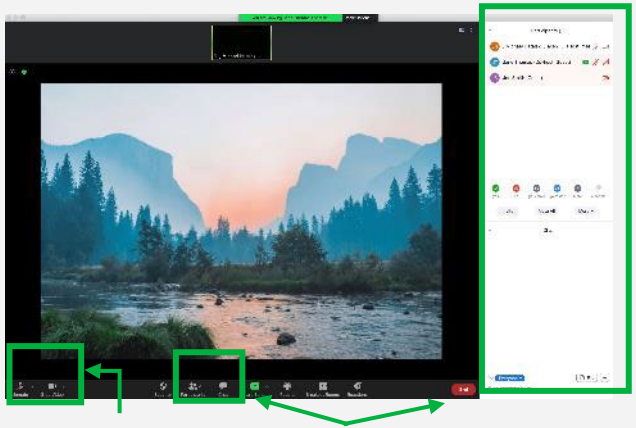
Housekeeping Notes for Faculty

To be announced prior to start of meeting

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

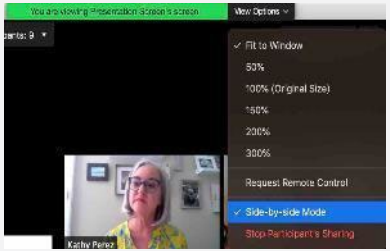
Functionality and Settings

To be announced prior to start of meeting

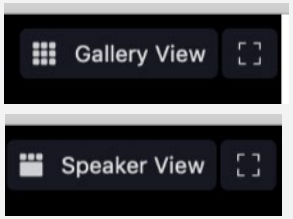


Microphone and Camera
Mute and unmute your camera/microphone by clicking the icons in the lower left-hand corner

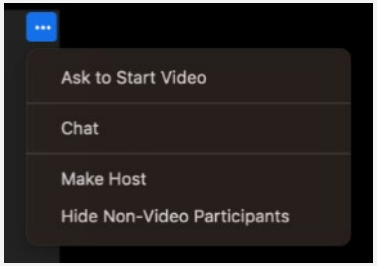
Participant and Chat Window
Reveal or hide the chat and participant window by selecting the corresponding icons in the bottom toolbar



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



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



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

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

Global Multiple Myeloma Academy

Get Ready

When not speaking

When presenting

Use chat

Ask/comment any time

APTITUDE HEALTH®

Global Multiple Myeloma Academy

Global Multiple Myeloma Academy

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

March 25–26, 2026 – Asia-Pacific Region

Pfizer

APTITUDE HEALTH

Global Multiple Myeloma Academy

Welcome and Meeting Overview

Rafael Fonseca, MD

APTITUDE HEALTH®

Co-Chair

Rafael Fonseca, MD
Mayo Clinic Cancer Center, USA

Faculty

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

Hermann Einsele, MD, FRCP
Universitätsklinikum Würzburg, Germany

Andrew Spencer, MBBS, DM, FRACP, FRCPA
Monash University, Australia

Co-Chair

Wee Joo Chng, MB ChB, PhD, FRCP (UK), FRCPath (UK), FAMS
National University of Singapore

James Chim, MBChB, MD, PhD, MRCP, FRCP, FACP, FRCPath, FFSc, FAcadTM, FHKCP, FHKAM
The Chinese University of Hong Kong, China

Juan Du, MD, PhD
Shanghai Jiao Tong University, China

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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 the Asia-Pacific region

Agenda Day 1 – Asia

17.00 – 20.00 (China Standard Time)/3.00 AM – 6.00 AM (Mountain Standard Time)

Time (CST/MST)	Topic	Speaker
17.00 – 17.10 3.00 AM – 3.10 AM (10 min)	**Welcome and Meeting Overview** • Introduction to audience response system (ARS)	Rafael Fonseca, MD; Wee Joo Chng, MB ChB, PhD, FRCP (UK), FRCPath (UK), FAMS
17.10 – 17.40 3.10 AM – 3.40 AM (30 min)	**Overview of Later-Line RRMM Treatment and Management** (20-min presentation; 10-min Q&A)	Rafael Fonseca, MD
17.40 – 18.10 3.40 AM – 4.10 AM (30 min)	**Bispecific Antibodies in RRMM** (20-min presentation; 10-min Q&A)	Andrew Spencer, MBBS, DM, FRACP, FRCPA
18.10 – 18.25 4.10 AM – 4.25 AM (15 min)	**Break**	
18.25 – 18.55 4.25 AM – 4.55 AM (30 min)	**Immunotherapy Sequencing in RRMM: Current and Future Landscape** (20-min presentation; 10-min discussion)	Hermann Einsele, MD, FRCP
18.55 – 19.40 4.55 AM – 5.40 AM (45 min)	**Panel Discussion and Audience Q&A** • Regional challenges of multiple myeloma diagnosis and treatment	All faculty
19.40 – 20.00 5.40 AM – 6.00 AM (20 min)	**Session Close** • ARS questions	Rafael Fonseca, MD

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Introduction to the Audience Response System

Rafael Fonseca, MD

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Functionality and Settings: Q&A

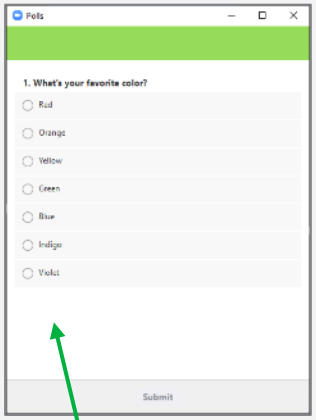
After each presentation, there will be 5 minutes for Q&A

Questions can be asked in two ways

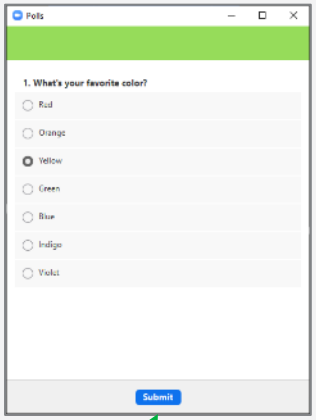
- **Q&A box** – type your question in the box
- **Raise Hand** – click to raise hand; the chair will invite you to comment, and you will be unmuted

Functionality and Settings: Polling Questions

Desktop View



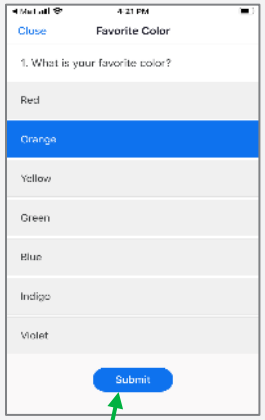
Choose Your Answer
Click on the answer (or answers if multiple choice)



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. China
2. Japan
3. Australia
4. Malaysia
5. India
6. South Korea
7. Vietnam
8. Singapore
9. Other Asia-Pacific region/country
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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Overview of Later-Line RRMM Treatment and Management

Rafael Fonseca, MD

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Rafael Fonseca, M.D.
Chief Innovation Officer
Mayo Clinic in Arizona
GMMA Asia
Overview of Later-Line RRMM Treatment and Management

Phoenix, Arizona

Rochester, Minnesota

Jacksonville, Florida

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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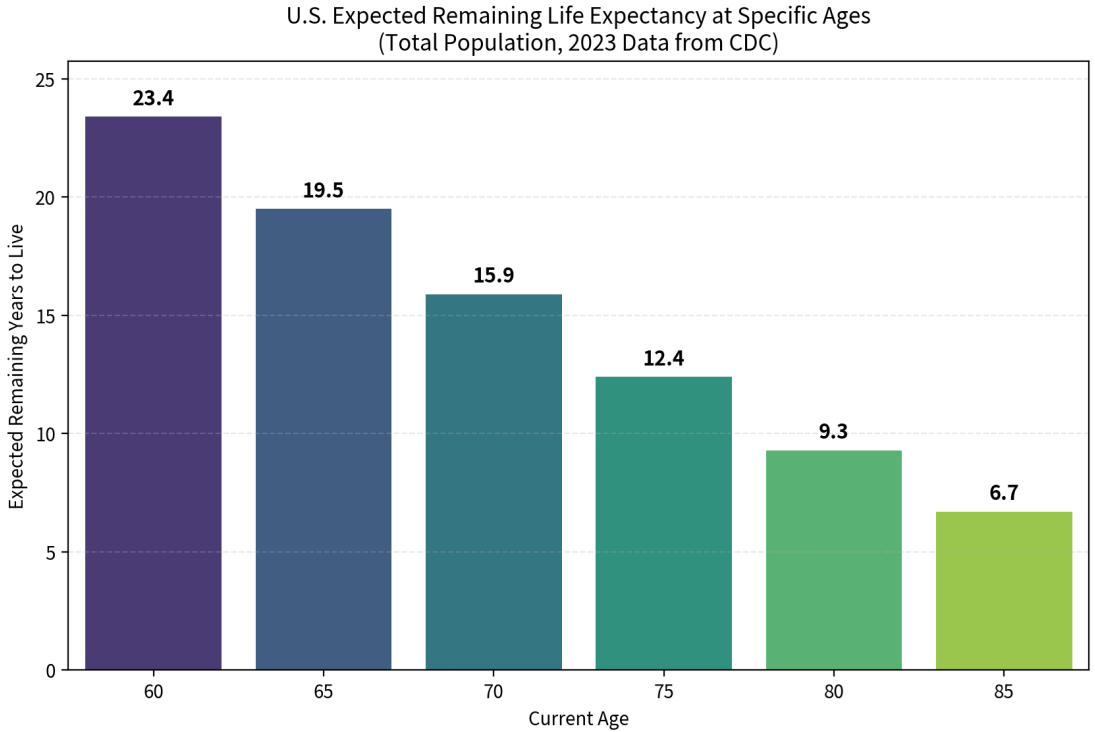
Life years ahead



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, unpublished

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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) 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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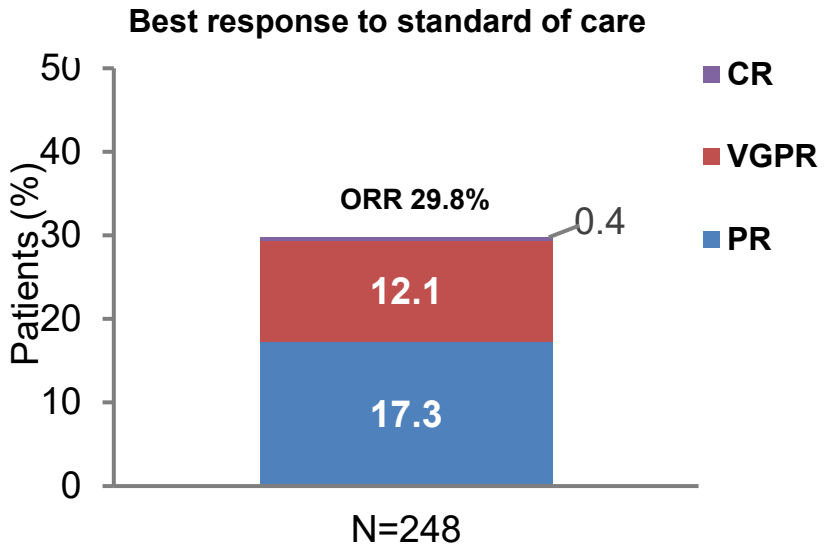
LocoMMotion: Heavily pre-treated patients

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 pre-treated patients

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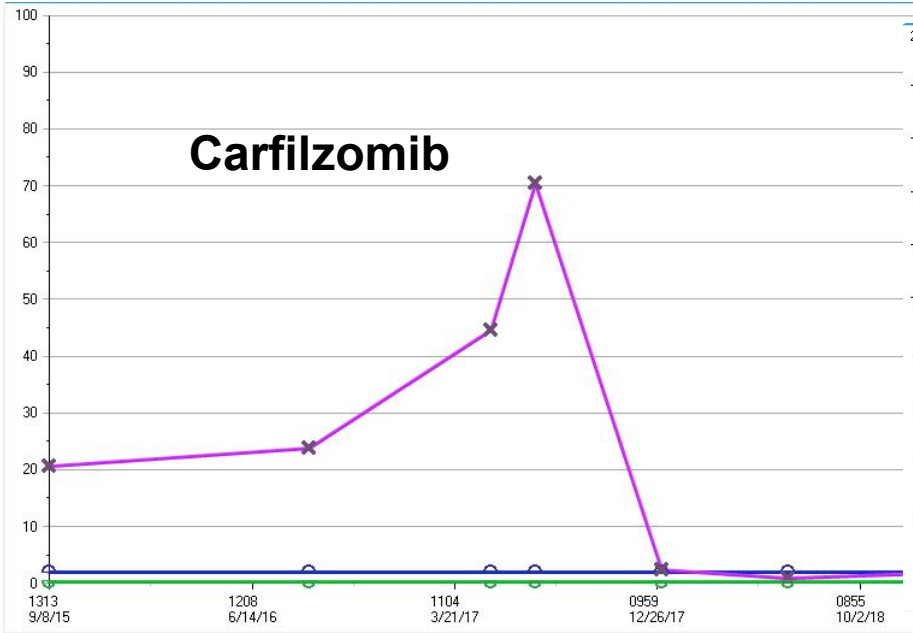
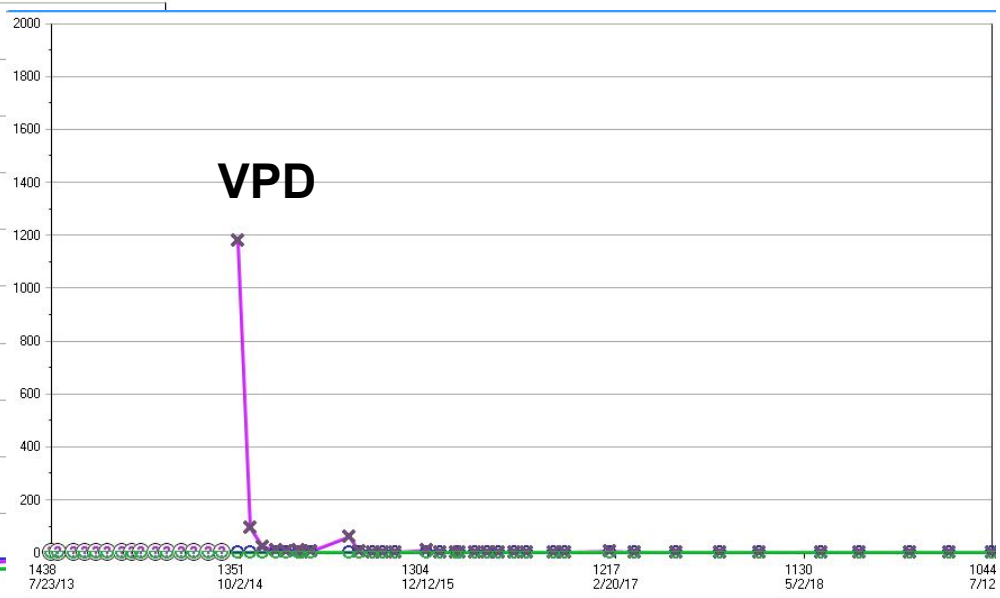
Mateos, MV et al Leukemia. 2022 May;36(5):1371-1376

Everyone is an N of 1





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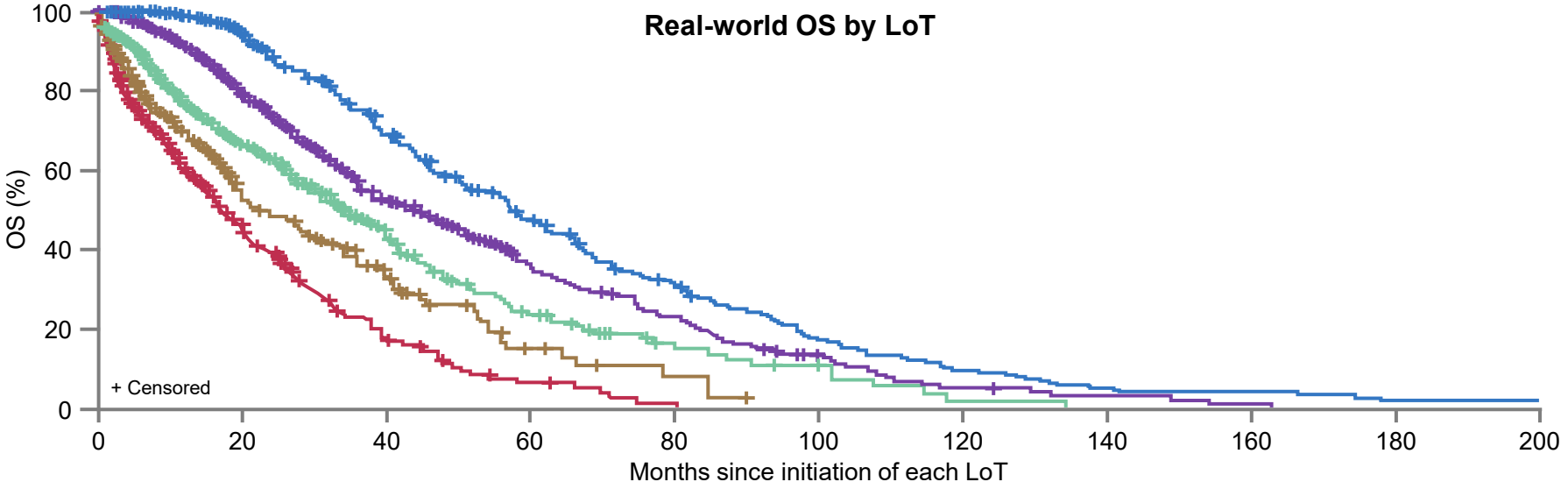
Real-world OS is worse with each LoT



LoT	1L	2L	3L	4L	5L+
Events, n/N	228/514	228/514	228/514	137/260	175/270
Median OS, mos (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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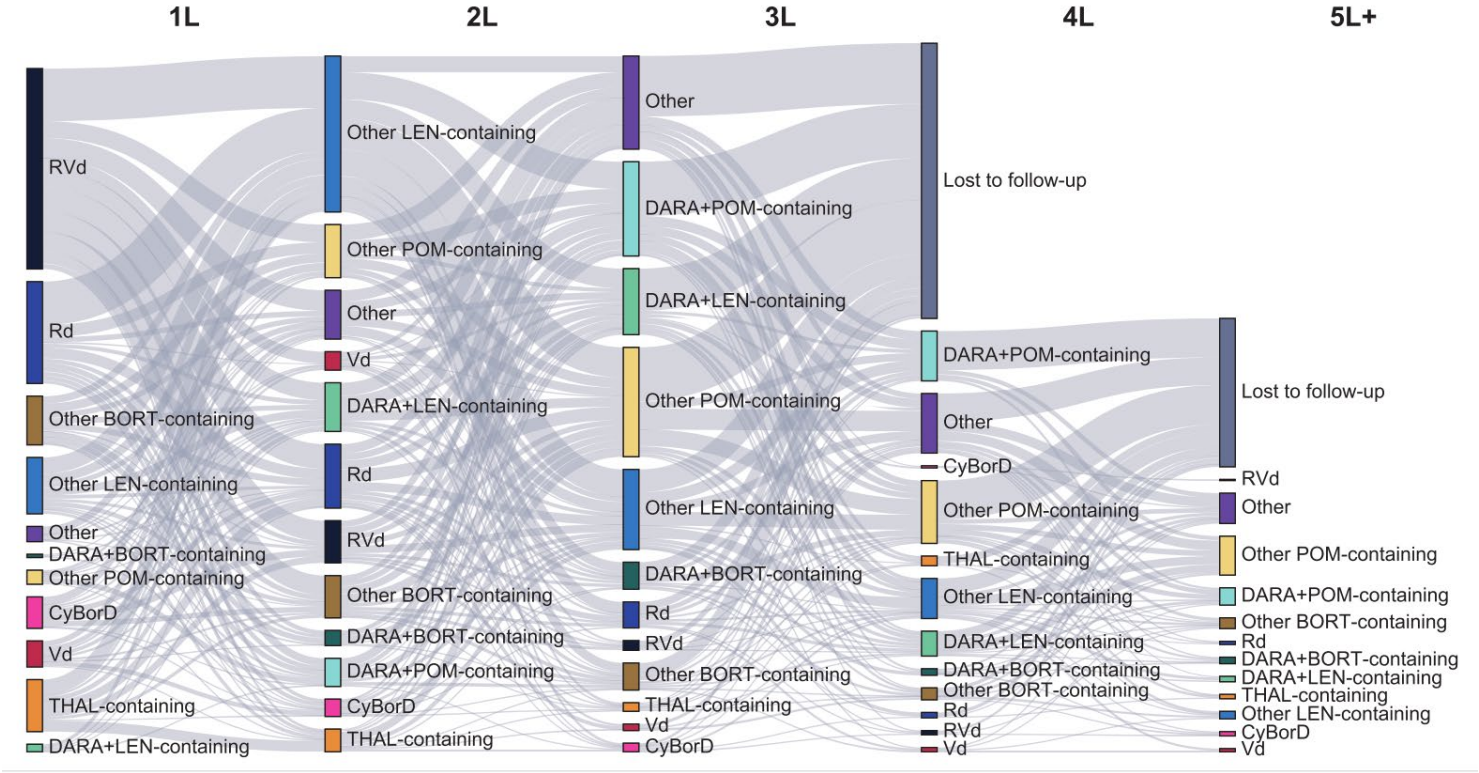
Real-world treatment patterns in MM reported in the US

Summary of treatment regimens reported by LoT



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Key Numbers to Remember

- VD - 9
- RD - 17

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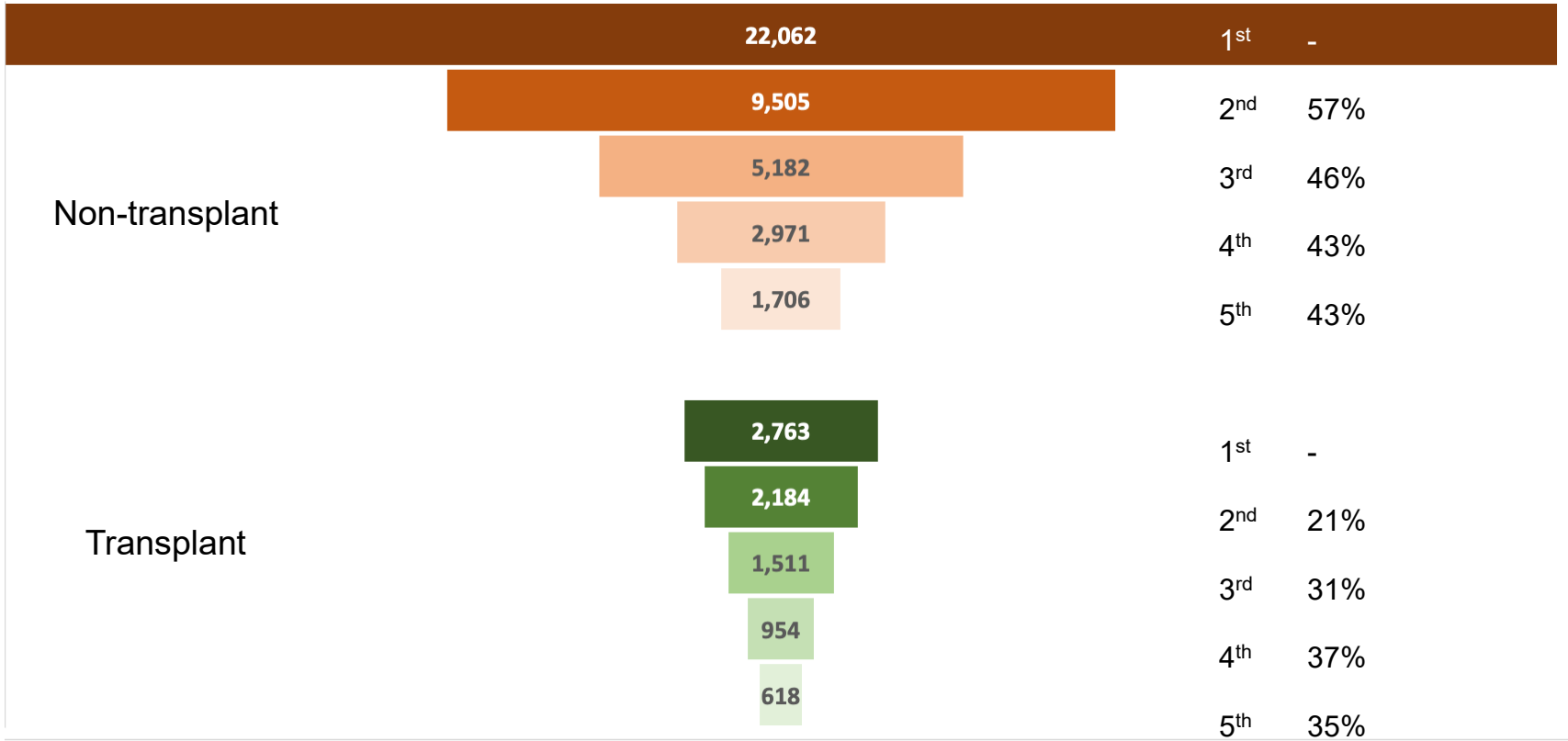
Attrition with subsequent treatment



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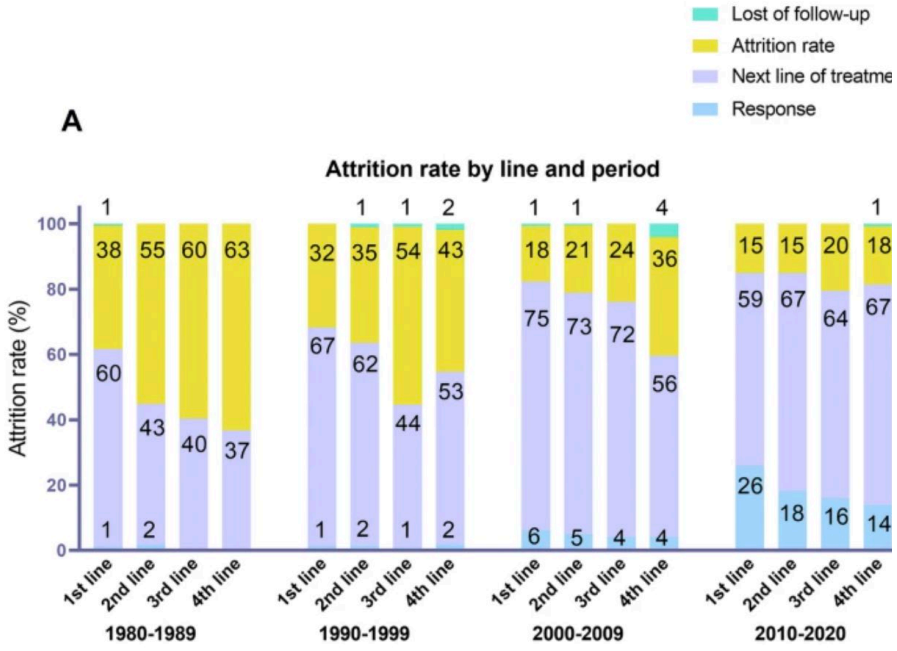
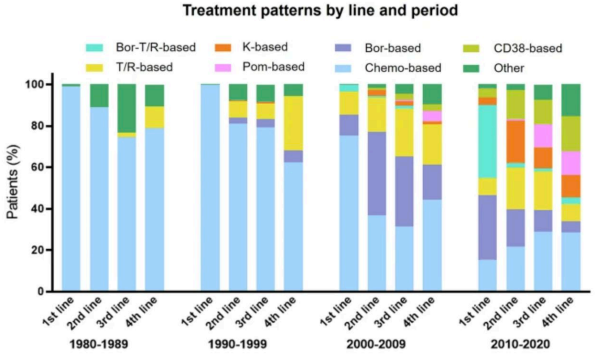
Fonseca et al BMC 20: 1087 (2020)

Attrition – Date of Treatment and Age

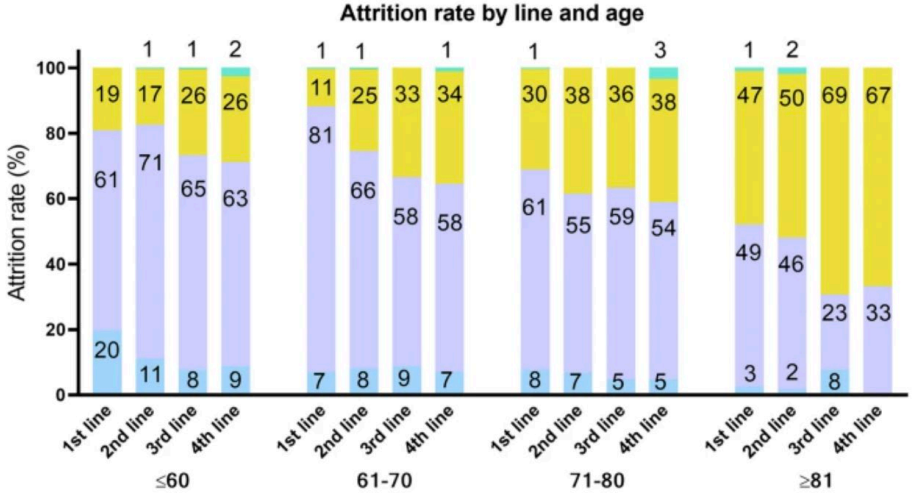
Less attrition with more modern therapies but still a problem in the elderly

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





B



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Rodriguez-Lobato, L et al Blood Can J 15:103 (2025)

ASPIRE—Len/Dex ± Carfilzomib

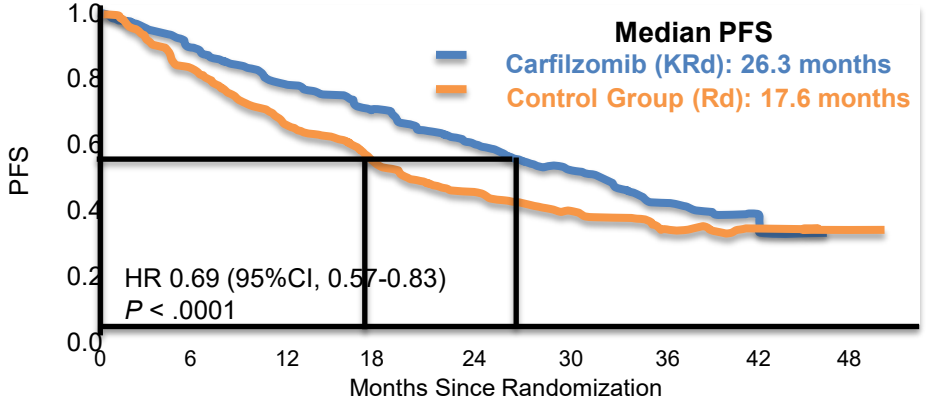
- **Carfilzomib 20mg/m² (27mg/m²)**
  - Cycle 1-12: d 1, 2, 8, 9, 15, 16
  - Cycles 13-18: d 1, 2, 15
- **Lenalidomide 25mg** d1-21
- **Dexamethasone 40mg** d1, 8, 15, 22

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

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

Primary End-Point: PFS

Secondary End-Points: OS, ORR, Duration of response, HRQoL, safety



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

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

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CASTOR Study

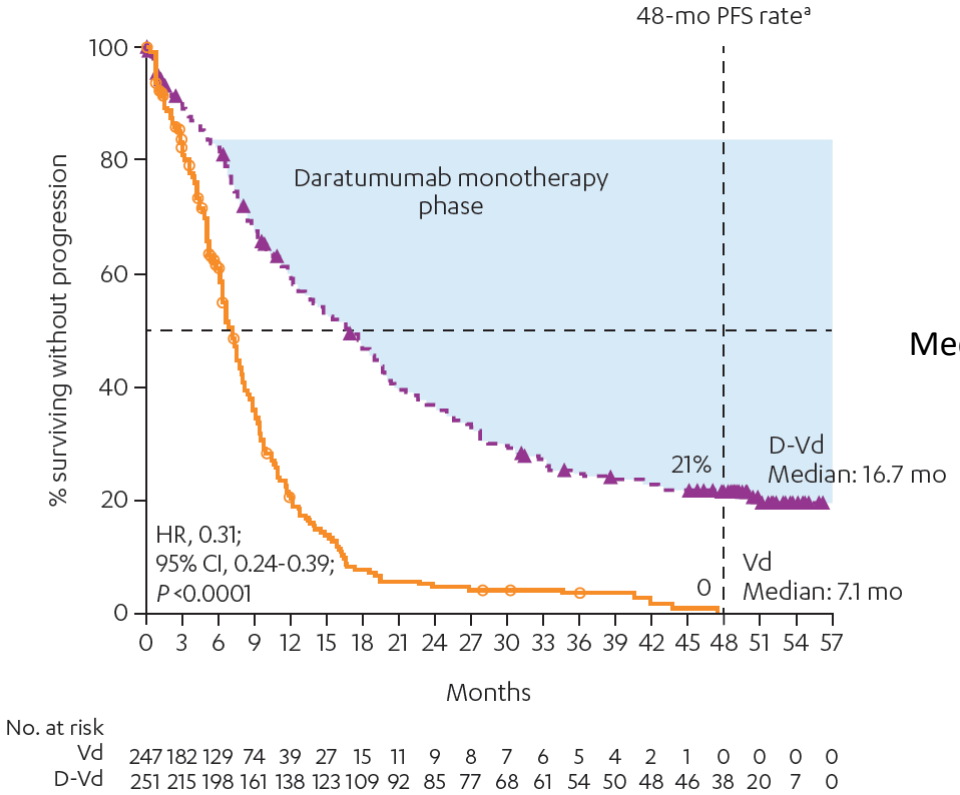
The NEW ENGLAND JOURNAL of MEDICINE

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*

Updated PFS in the ITT Population



Median follow-up: 50.2 months

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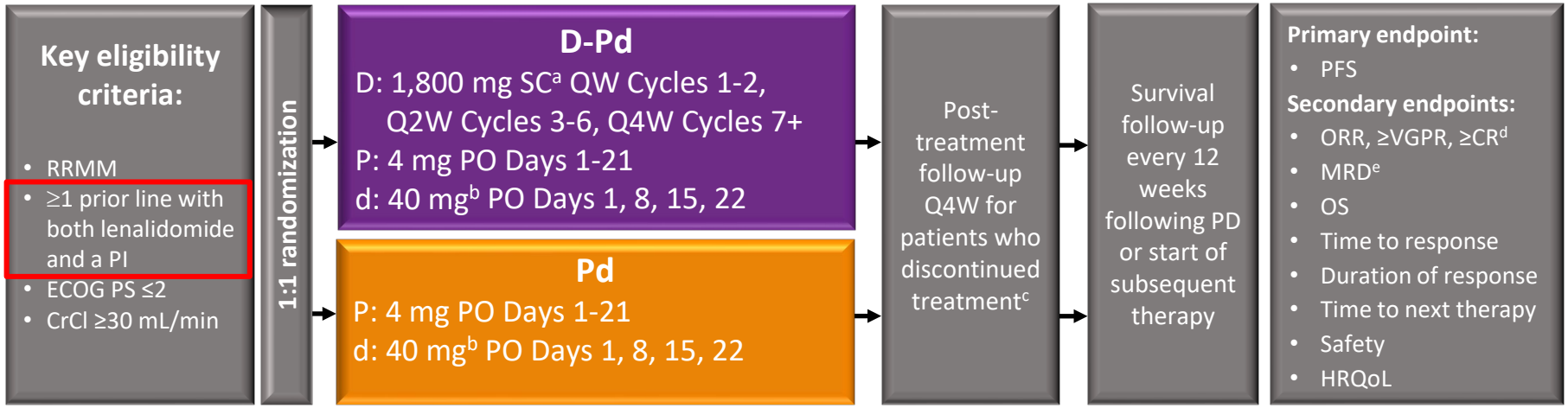
Palumbo et al , et al. N Engl J Med 2016

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)

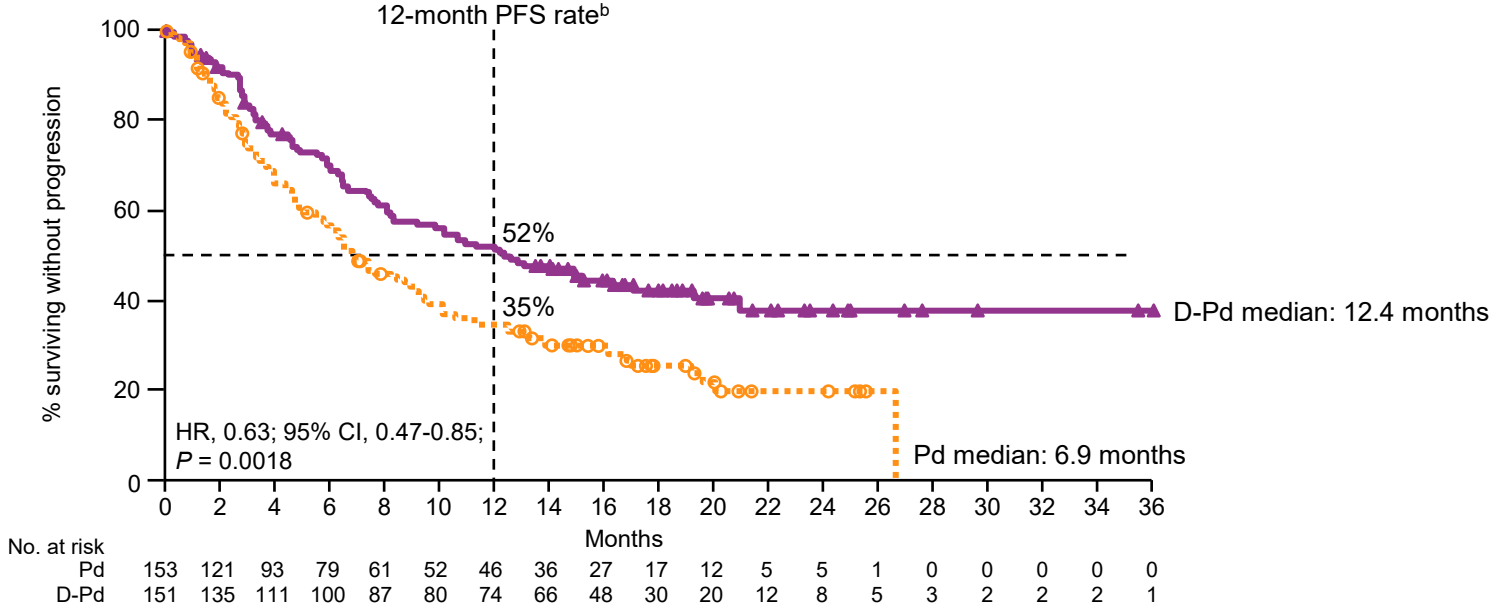
Cycle duration: 28 days
Treatment until PD or unacceptable toxicity

@rfonsi1, fonseca.rafael@mayo.edu

Dimopoulos et al ASH 2020

APOLLO Dara-Pd

Median follow up 17 mos



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

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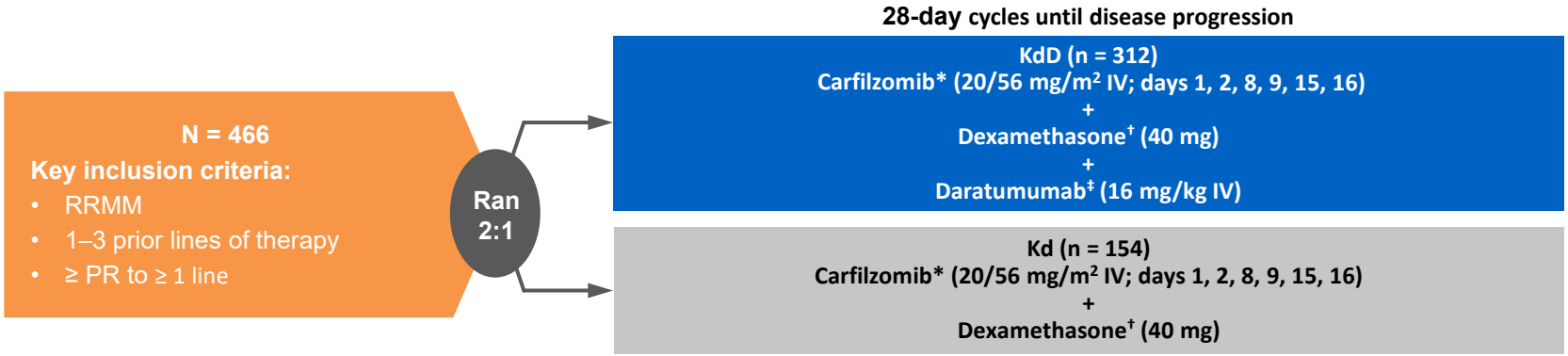
Dimopoulos et al ASH 2020

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 cut-off 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.

CI, confidence interval; 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 M, et al. *Lancet*. 2020;396:186-97. 2. Dimopoulos M, et al. Presented at 62nd ASH Annual Meeting and Exposition; Dec 5–8, 2020; Virtual. Abstract 2325.

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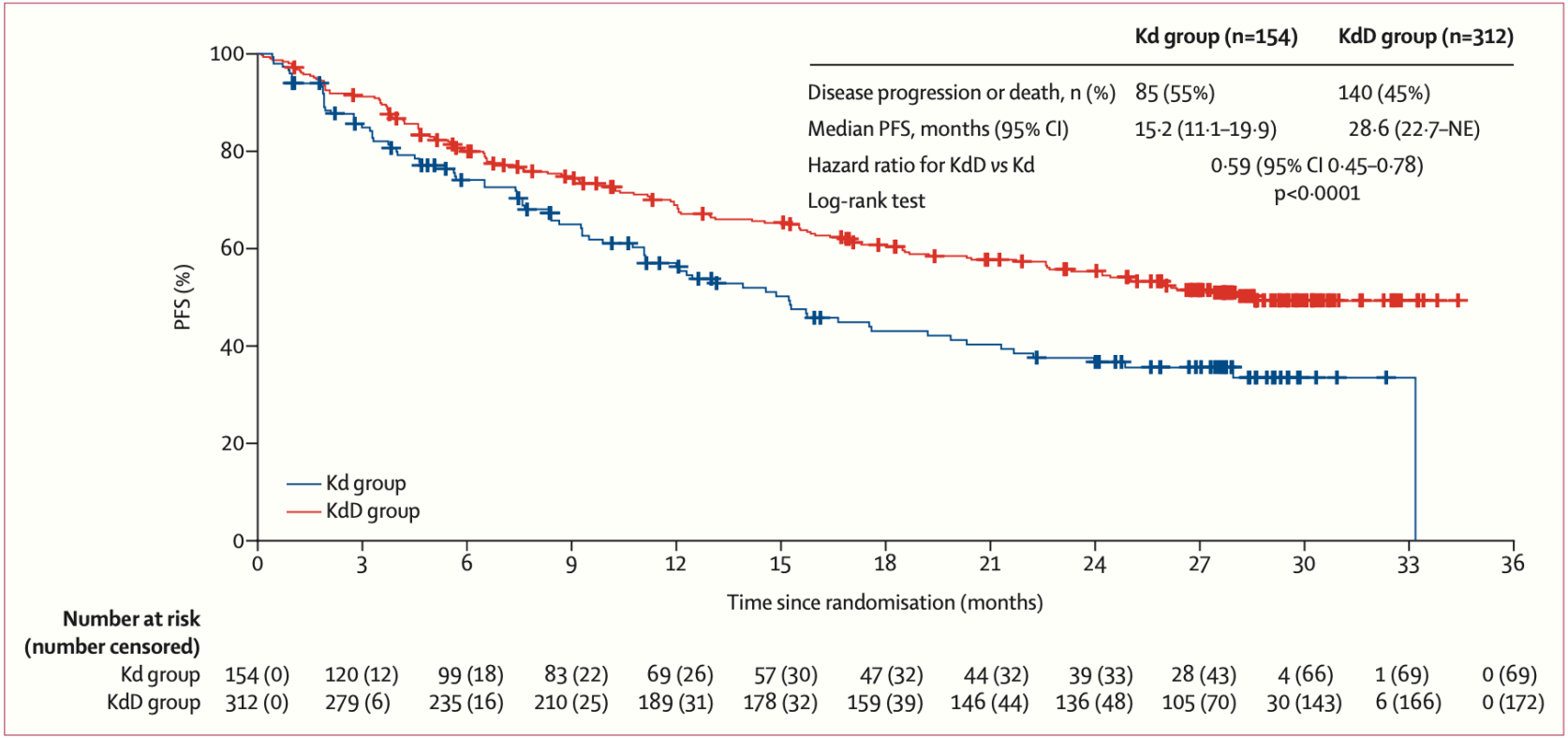
Lancet Oncology. 23(1):65-76, 2022 01

CANDOR (KdD vs Kd in RRMM)



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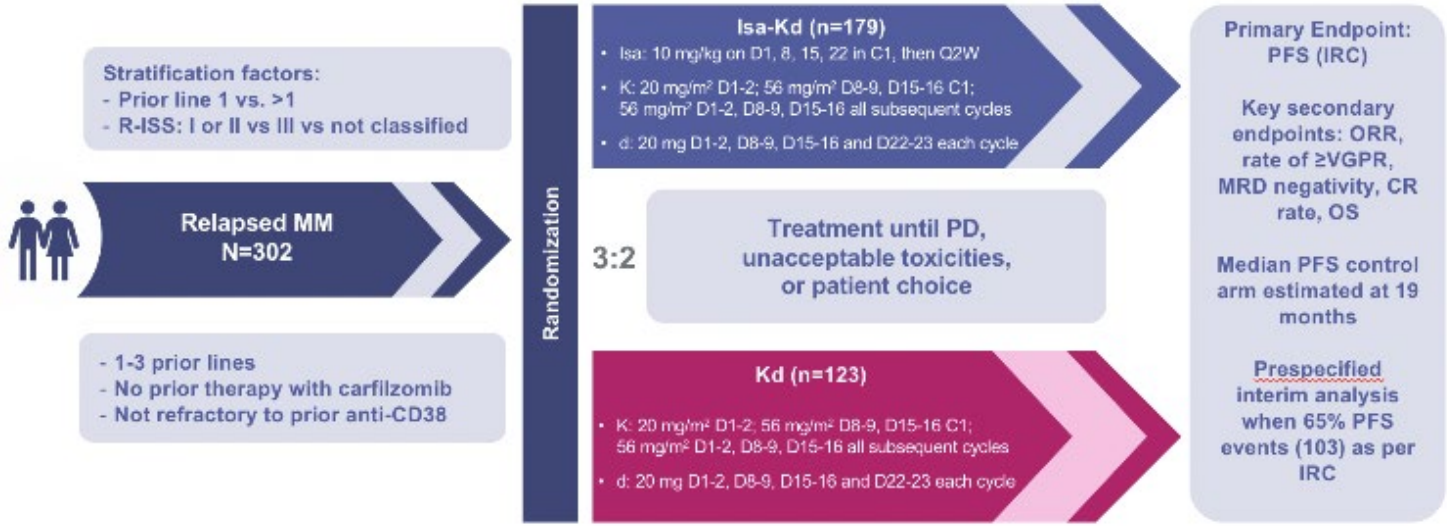
Lancet Oncology. 23(1):65-76, 2022 01

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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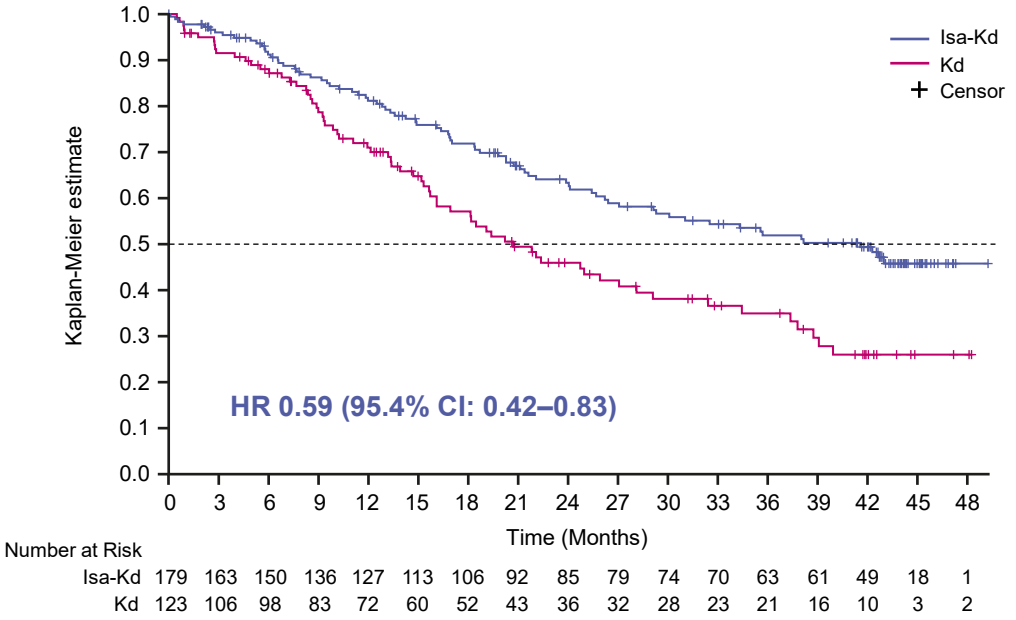
Moreau et al Lancet 2021 https://doi.org/10.1016/S0140-6736(21)00592-41

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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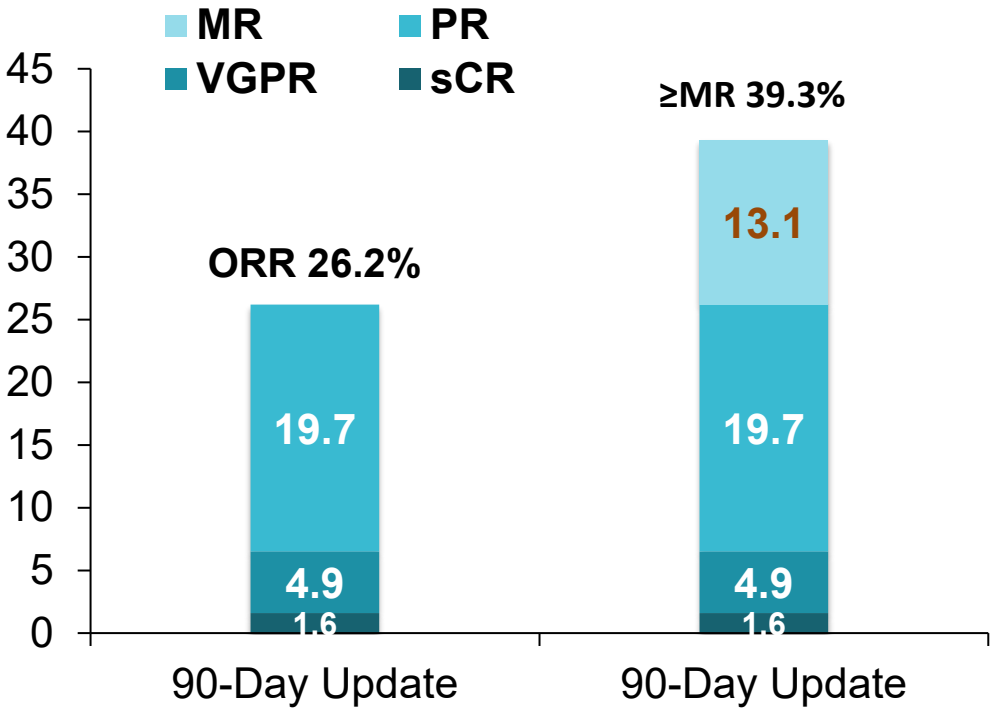
STORM Selinexor Efficacy



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

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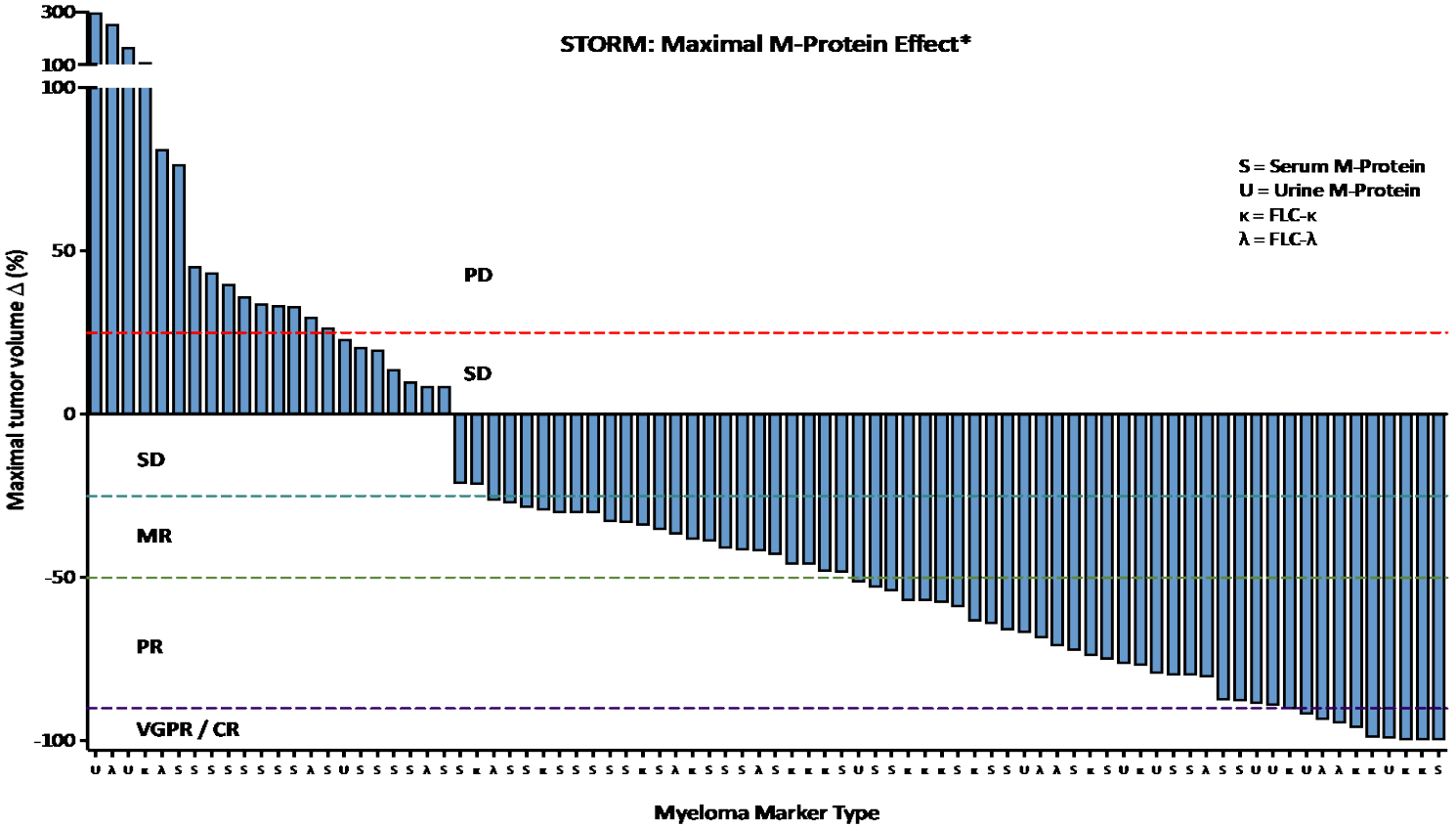
Karyopharm slides

STORM Trial



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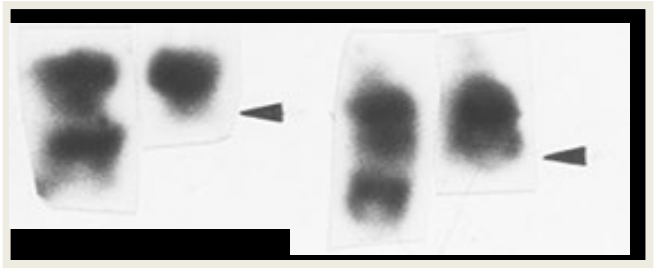
Karyopharm slides

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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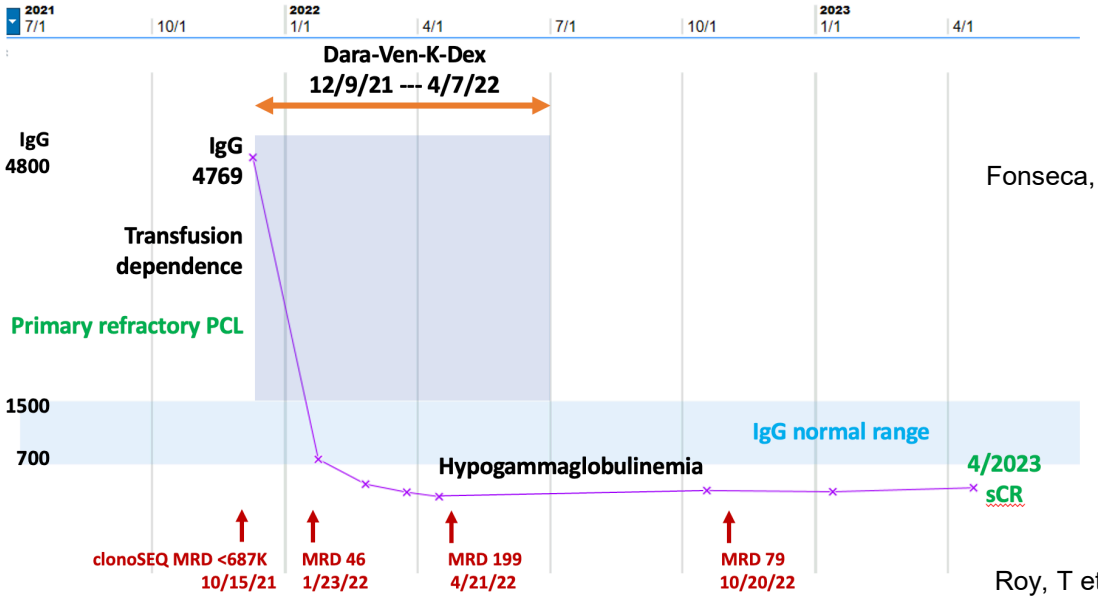
Primary Plasma Cell Leukemia

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

Roy, T et al Leuk Lymphoma 63(3):7592022
Gonsalves et al Case Reports Eur J Haematol 2018
Tiedemann et al Leukemia. 2008 May;22(5):1044-52

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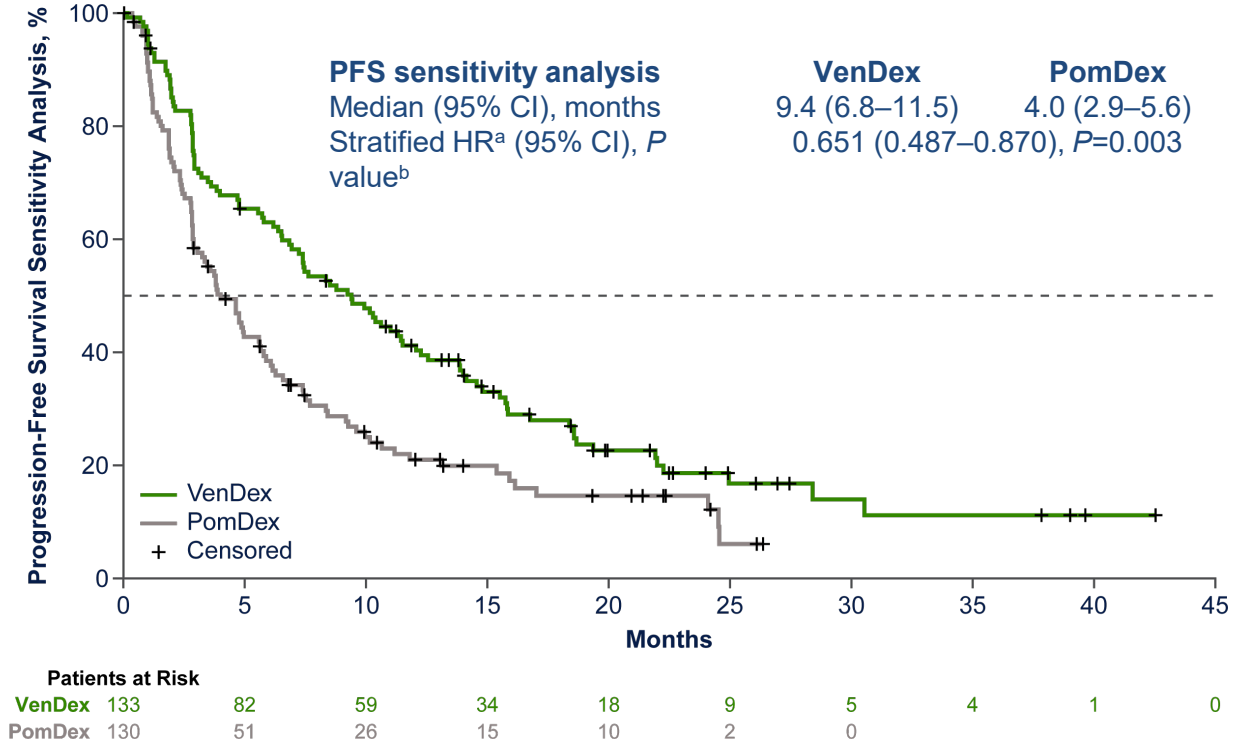
CANOVA Post hoc sensitivity analysis (HR 0.651)

- 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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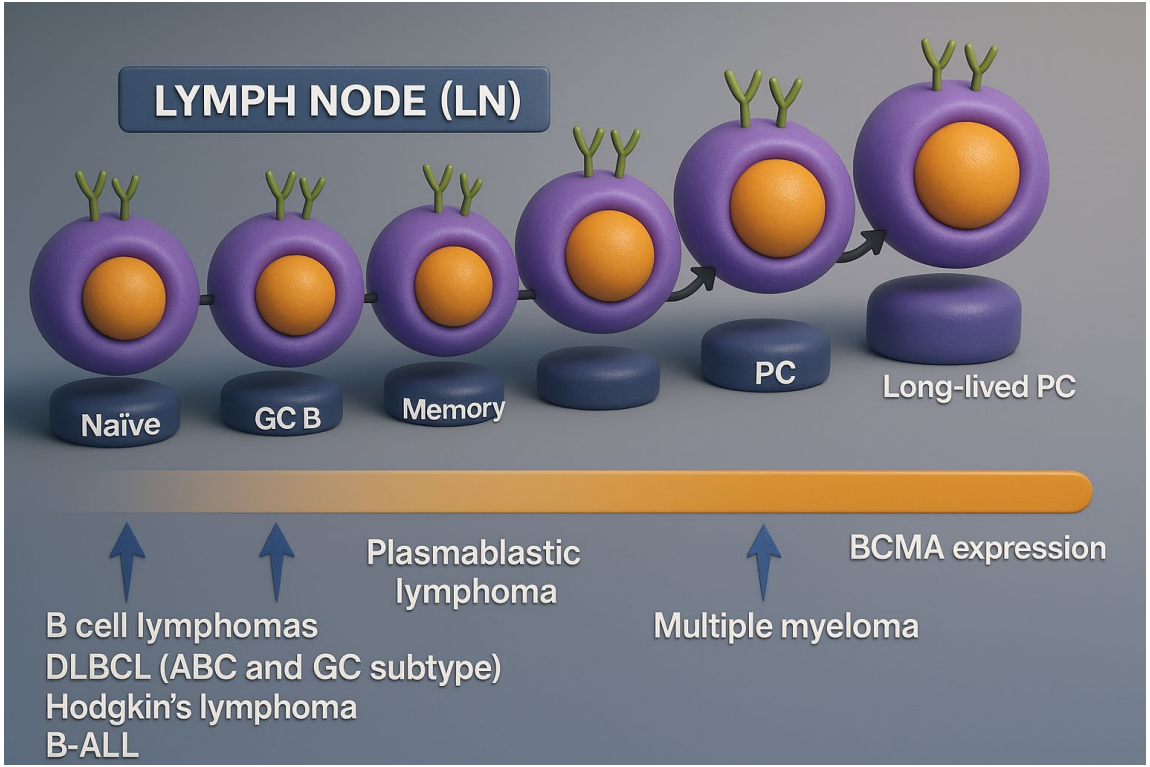
Targets for bispecific antibodies in MM: BCMA



1. Frerichs K et al. Clin Cancer Res. 2020;26(9):2203–2215;
2. Verkleij CPM, et al. Blood Adv. 2021;5(8):2196–2215.
3. Dogan et al Blood C J 2020

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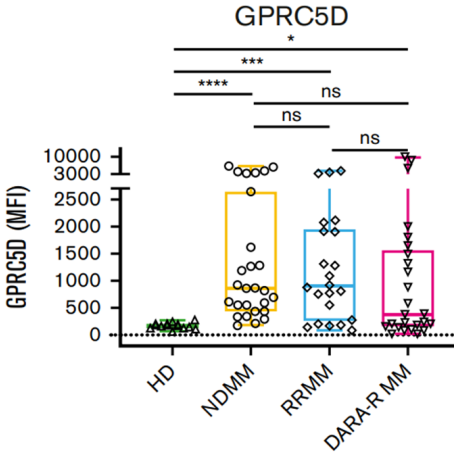
GPRC5D: Talquetamab and forimtamig[1–3]



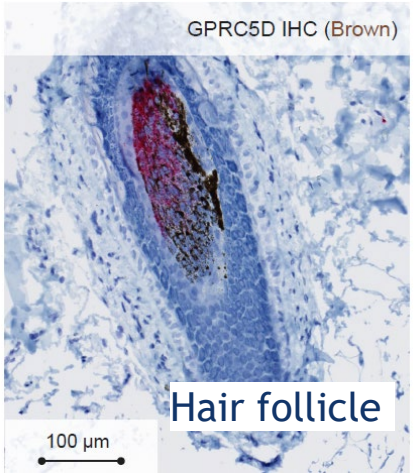
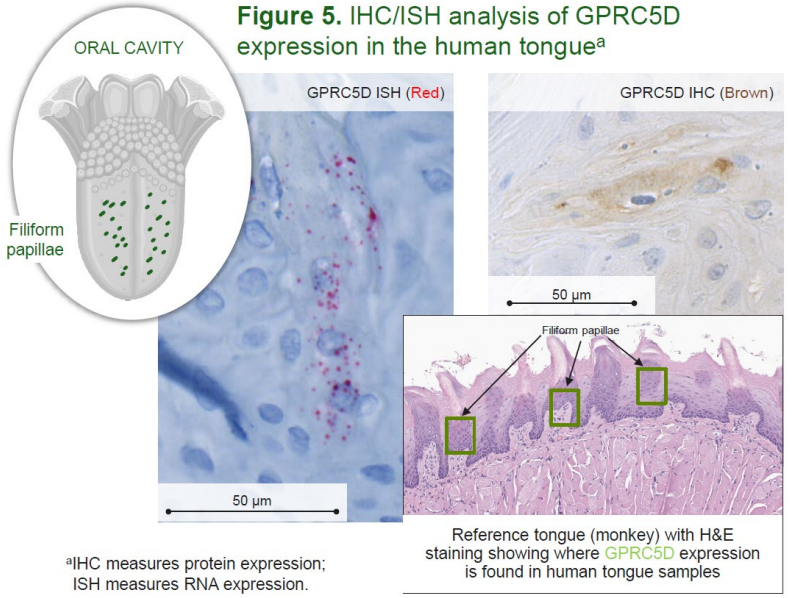


Figure 5. IHC/ISH analysis of GPRC5D expression in the human tongue[a]



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

Reference tongue (monkey) with H&E staining showing where GPRC5D expression is found in human tongue samples

@rfonsi1, fonseca.rafael@mayo.edu

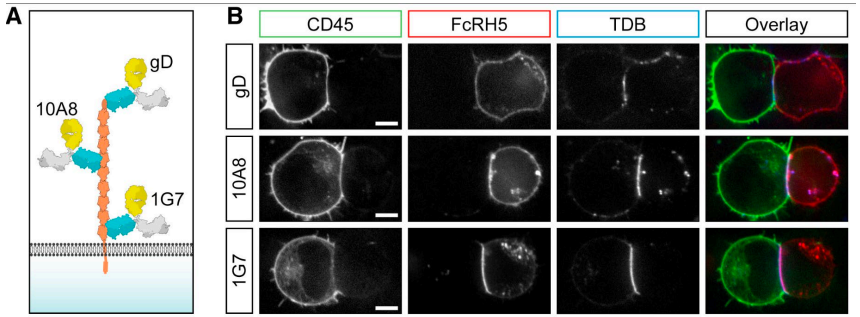
1. Chari A, et al. ASH 2022
2. Verkleij CPM, et al. Blood Adv. 2021;5:2196–2215
1. 3. Goldsmith R, et al. IMW 2021 (Poster).

Cevostamab: FcRH5 x CD3 Bispecific

Backgorund

- 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 x CD3 bispecific antibody

Synapse - binding



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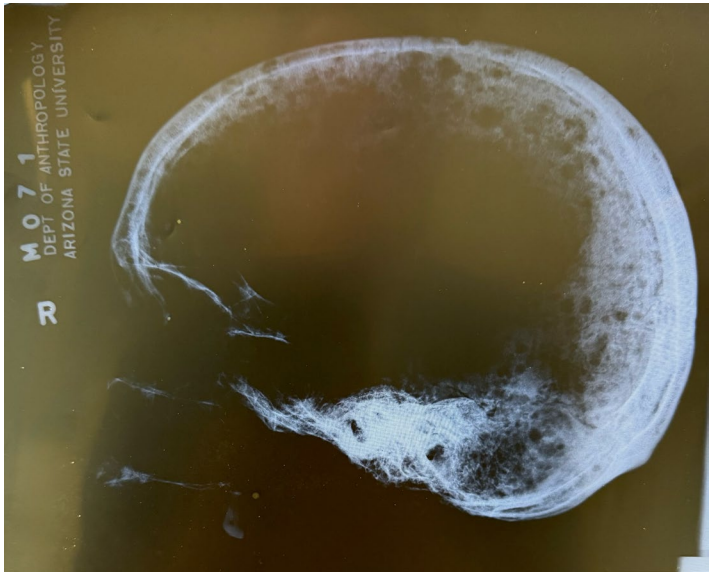
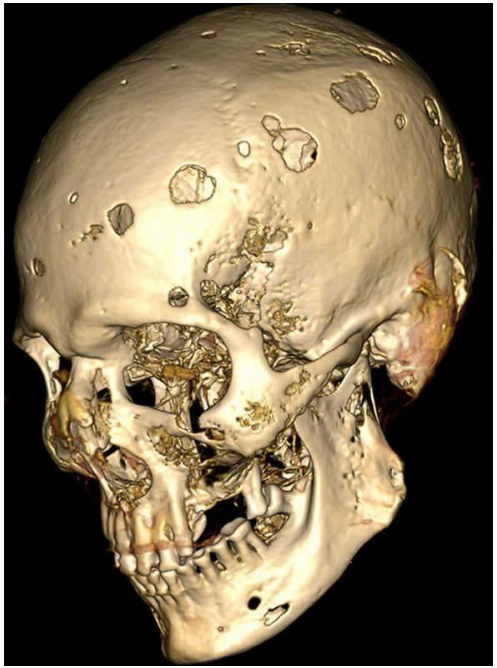
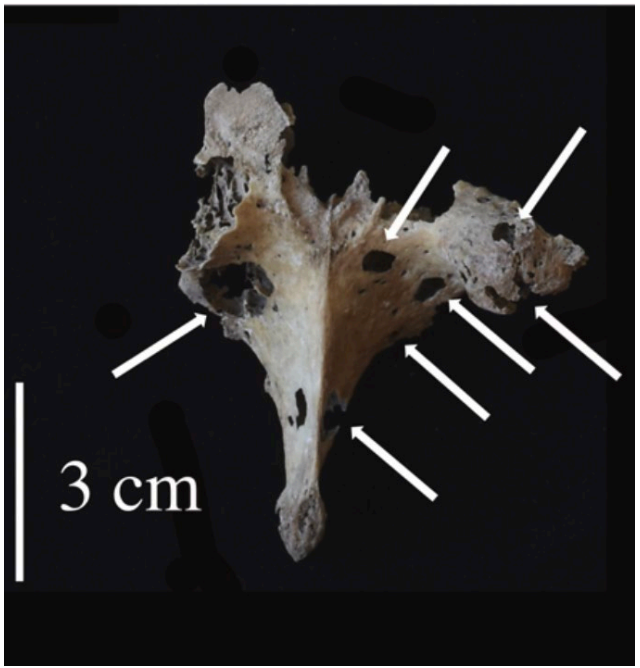
Li et al Cancer Cell 2017

Earliest Myeloma Cases







Nubian Egyptian Mummy 700 BC.

Egyptian Mummy 700 BC.

Bronze age China 1750-1400 BC

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Revista Argentina de Radiologia 2014;78:171-80
Dittmar et al Int J of Paleopathology 31, Dec 2020, 64-70

Global Multiple Myeloma Academy

Discussion

APTITUDE HEALTH®

Global Multiple Myeloma Academy

Bispecific Antibodies in RRMM

Andrew Spencer, MBBS, DM, FRACP, FRCPA

APTITUDE HEALTH®

Bispecific Antibodies in RRMM

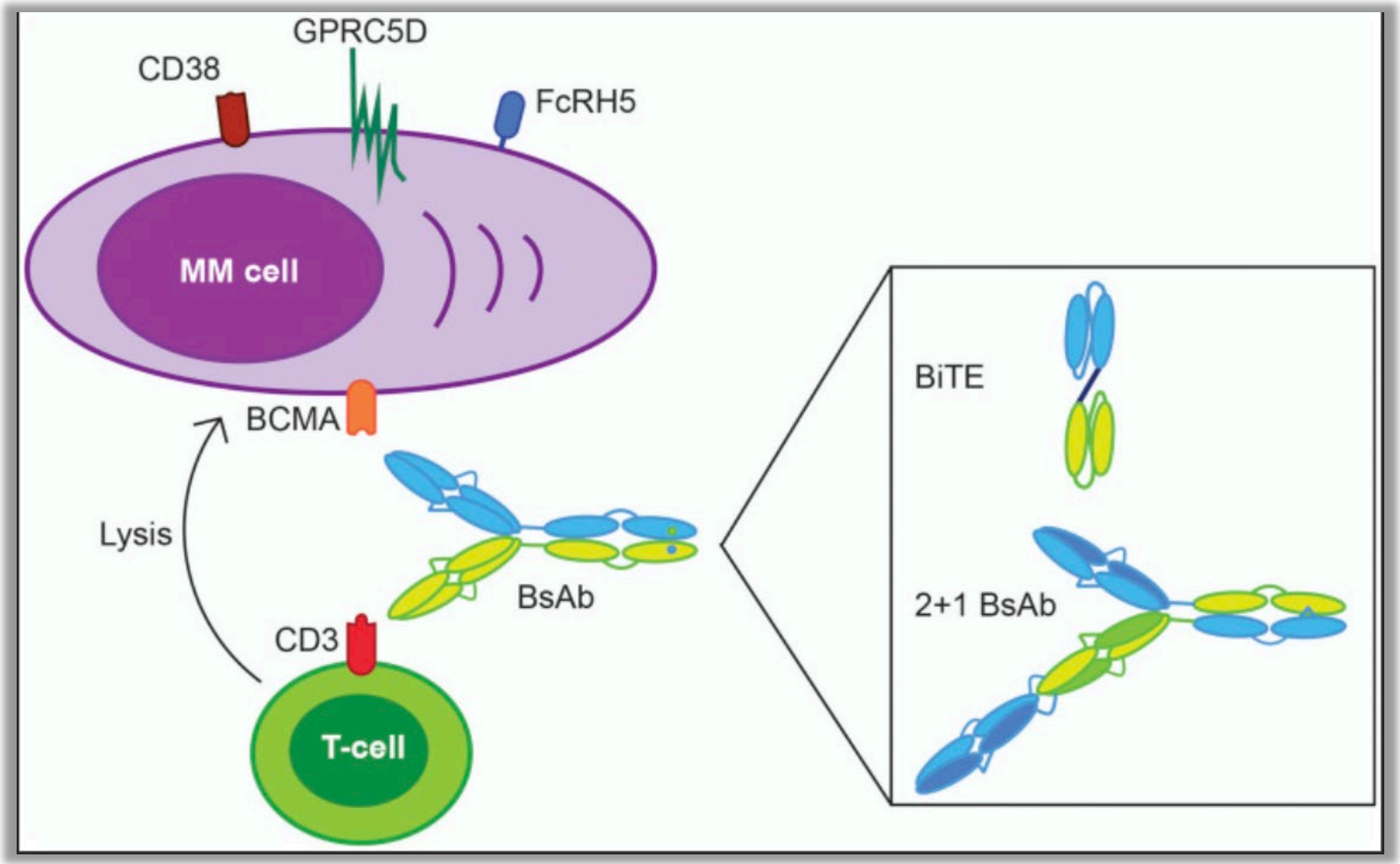
Professor Andrew Spencer

Alfred Health-Monash University

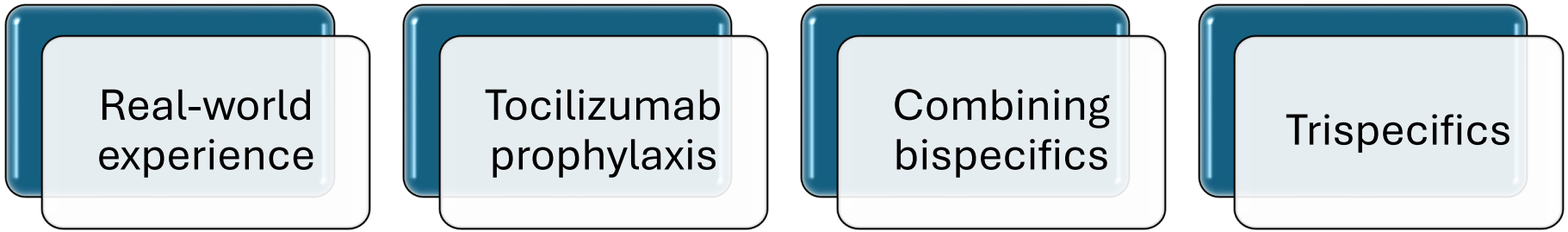
Melbourne

Disclosures

Company Name	Research Support	Employee	Consultant	Stockholder	Speakers Bureau	Advisory Board	Other
Janssen	X		X		X	X	
BMS	X				X	X	
Pfizer					X	X	
HaemaLogiX	X		X	X		X	
Antengene	X					X	
Celltrion			X				
IAS Bio			X				
Arrotex					X		
GSK			X		X	X	


GPRC5D
CD38
FcRH5
MM cell
BCMA
Lysis
BsAb
CD3
T-cell
BiTE
2+1 BsAb

Synopsis


Real-world experience
Tocilizumab prophylaxis
Combining bispecifics
Trispecifics

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 AUGUST 11, 2022 VOL. 387 NO. 6

Teclistamab in Relapsed or Refractory Multiple Myeloma

P. Moreau, A.L. Garfall, N.W.C.J. van de Donk, H. Nahi, J.F. San-Miguel, A. Oriol, A.K. Nooka, T. Martin, L. Rosinol, A. Chari, L. Karlin, L. Benboubker, M.-V. Mateos, N. Bahlis, R. Popat, B. Besemer, J. Martínez-López, S. Sidana, M. Delforge, L. Pei, D. Trancucci, R. Verona, S. Girgis, S.X.W. Lin, Y. Olyslager, M. Jaffe, C. Uhlar, T. Stephenson, R. Van Rampelbergh, A. Banerjee, J.D. Goldberg, R. Kobos, A. Krishnan, and S.Z. Usmani

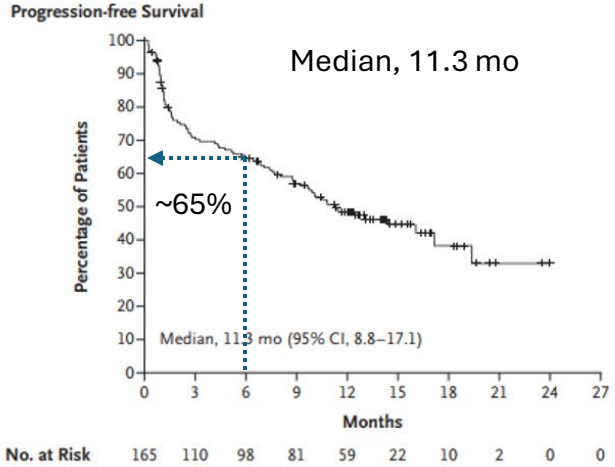
MajesTEC-1

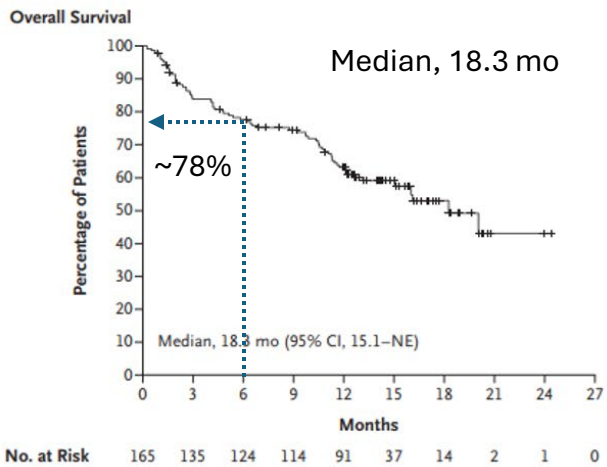
Inclusion Criteria	Exclusion Criteria
Age ≥18 Documented MM	Prior treatment with any therapy that is targeted to BCMA or any other CD3-redirecting drug
R/R MM 2+ prior lines: must include PI, IMID, CD38 mAb	Stem cell transplant (prior to C1D1) • AlloSCT ≤6 mo • ASCT ≤12 wk
ECOG: 0–1 Hb* ≥80 Plts* ≥75 <50% PCs BMAT or ≥50 Neuts* ≥1.0 CrCl ≥40 mL/min/1.73 m^2	CNS disease PCL, WM, POEMS, amyloid

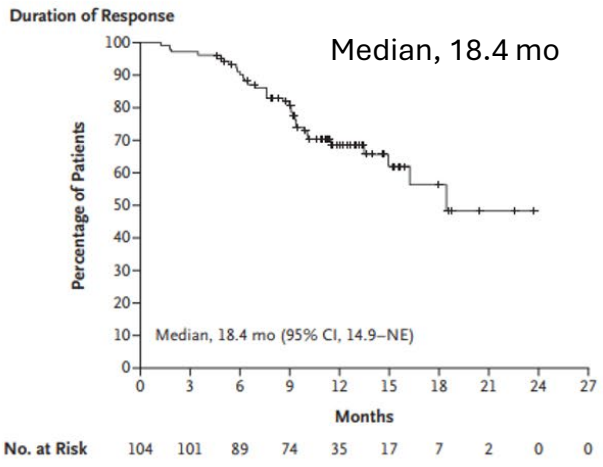
*No PRBC/Plt transfusion or G-CSF in previous 7 days.

MajesTEC-1: PFS, OS, and duration of response

Median FU = 14.1 mo (0.3–24.4)







Blood Cancer Journal

www.nature.com/bcj

ARTICLE OPEN

Check for updates

Real-world evaluation of teclistamab for the treatment of relapsed/refractory multiple myeloma (RRMM): an International Myeloma Working Group Study

Carlyn Rose Tan[1✉], Sireesha Asoori[2], Chiung-Yu Huang[2], Larissa Brunaldi[3], Rakesh Popat[4], Efstathios Kastritis[5], Joaquin Martinez-Lopez[6], Radhika Bansal[3], Andre De Menezes Silva Corraes[3], Saurabh Chhabra[7], Ricardo Parrondo[8], Sikander Ailawadhi[8], Despina Fotiou[5], Meletios A. Dimopoulos[5], Kwee Yong[4], Catriona Mactier[4], Chris Lau[4], Magdalena Corona[6], Adolfo Jesús Sáez Marin[6], Hira Mian[9], Brian GM. Durie[10], Saad Z. Usmani[1], Thomas G. Martin[2✉] and Yi Lin[3]

Blood Cancer Journal www.nature.com/bcj

ARTICLE OPEN

Check for updates

Real-world evaluation of teclistamab for the treatment of relapsed/refractory multiple myeloma (RRMM): an International Myeloma Working Group Study

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TEC – FDA/EMA approved in 2022

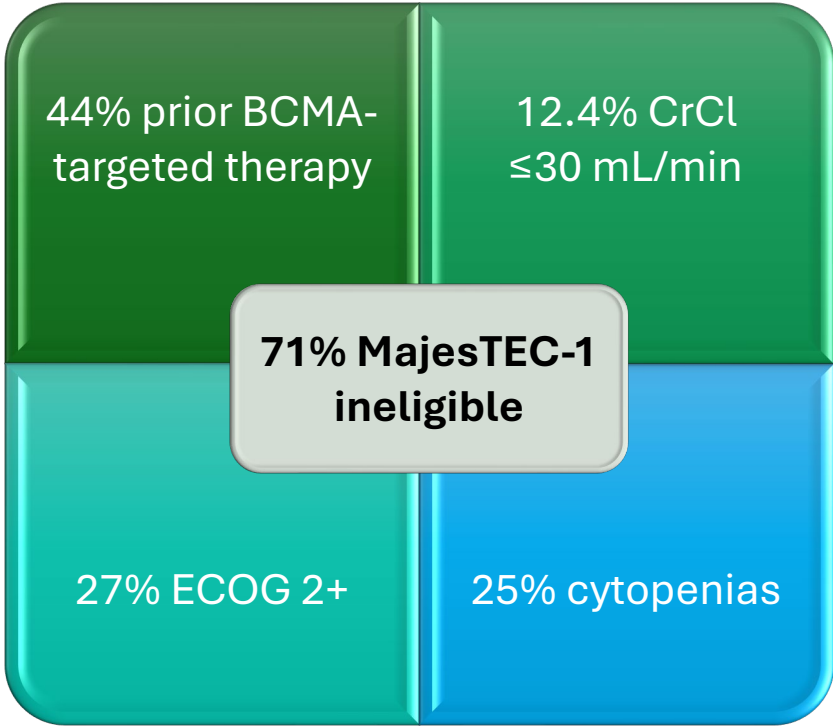
FDA – 4+ prior lines, TCE	EMA – TCE + PD

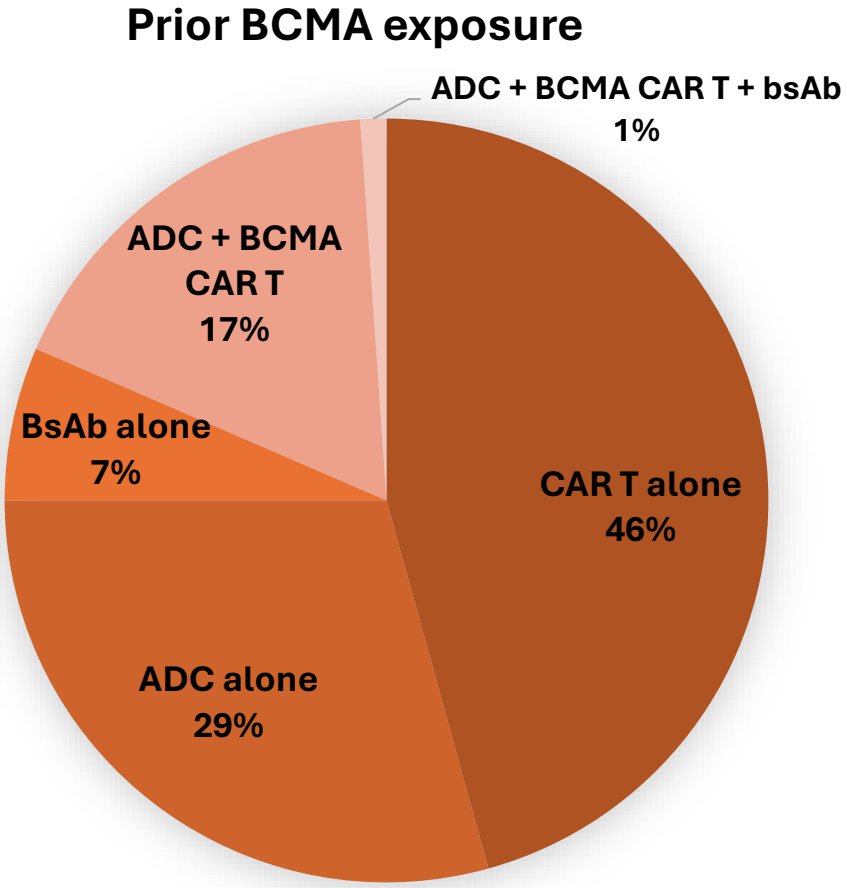
Retrospective study at 9 international centers

USA, UK, Greece, Spain, and Canada	MAY 2022 to OCT 2023

Administration according FDA/EMA approval and institutional standards

TEC-RW (N = 210)


44% prior BCMA-targeted therapy
12.4% CrCl ≤30 mL/min
71% MajesTEC-1 ineligible
27% ECOG 2+
25% cytopenias


Prior BCMA exposure
ADC + BCMA CAR T + bsAb 1%
ADC + BCMA CAR T 17%
BsAb alone 7%
CAR T alone 46%
ADC alone 29%

Demographics

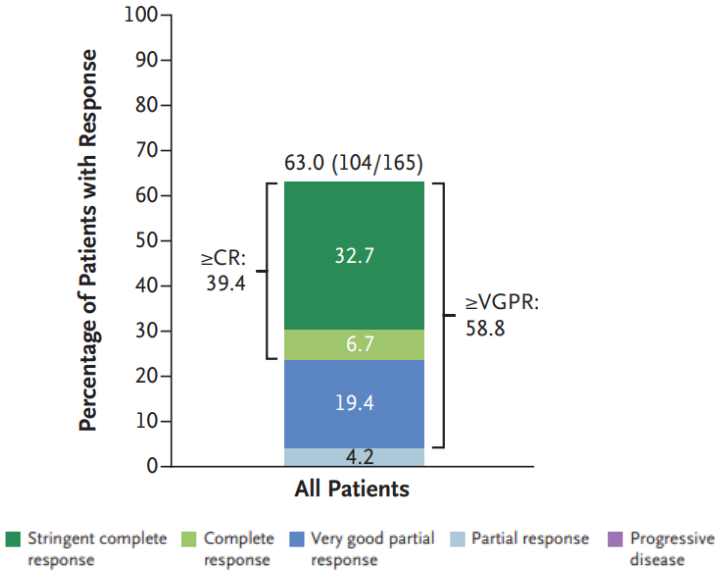
	Phase I/II MajesTEC-1 (N = 165) (%)	TEC-RW (N = 210) (%)
Median age, yr (range)	64 (33–84)	67 (33–91)
≥75	24 (14.5)	49 (23.3)
Gender, n (%) Male	96 (58)	117 (55.7)
ECOG, n (%) 0	55(33.3)	21 (16.2)
1	109 (66)	74 (56.9)
≥2	1 (0.7)	35 (26.9)
ISS III	20/162 (12.3)	38/124 (30.6)
High-risk CG	38/148 (25.7)*	82/164 (50)†

	Phase I/II MajesTEC-1 (N = 165)	TEC-RW (N = 210)
Median LOT, n (range)	5 (2–14)	6 (1–20)
Previous therapy Triple-class, n (%)	165 (100)	N/A
Penta-drug, n (%)	116 (70.3)	N/A
ASCT, n (%)	135 (81.8)	N/A
Refractory status – n (%)		
Triple-class	128 (77.6)	138/167 (82.6)
Penta-drug	50 (30.3)	71/161 (44.1)
Prior BCMA	0	92/210 (43.8)
EMD	26 (17)	37/126 (29.4)

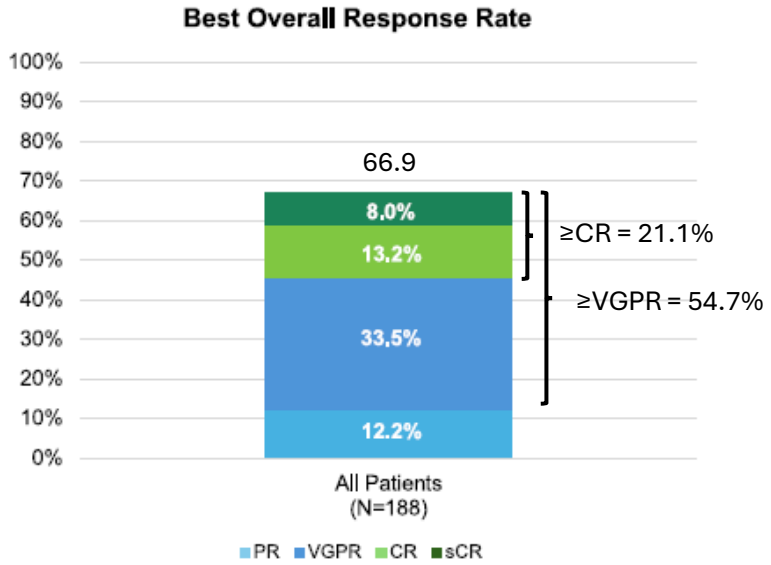
*Defined as del(17p), t(4;14), t(14;16);
†Defined as 1q+, t(4;14), t(14;16), t(14;20), and del(17p).

Response rates

MajesTEC-1 FU = 14.1 mo (0.3–24.4)

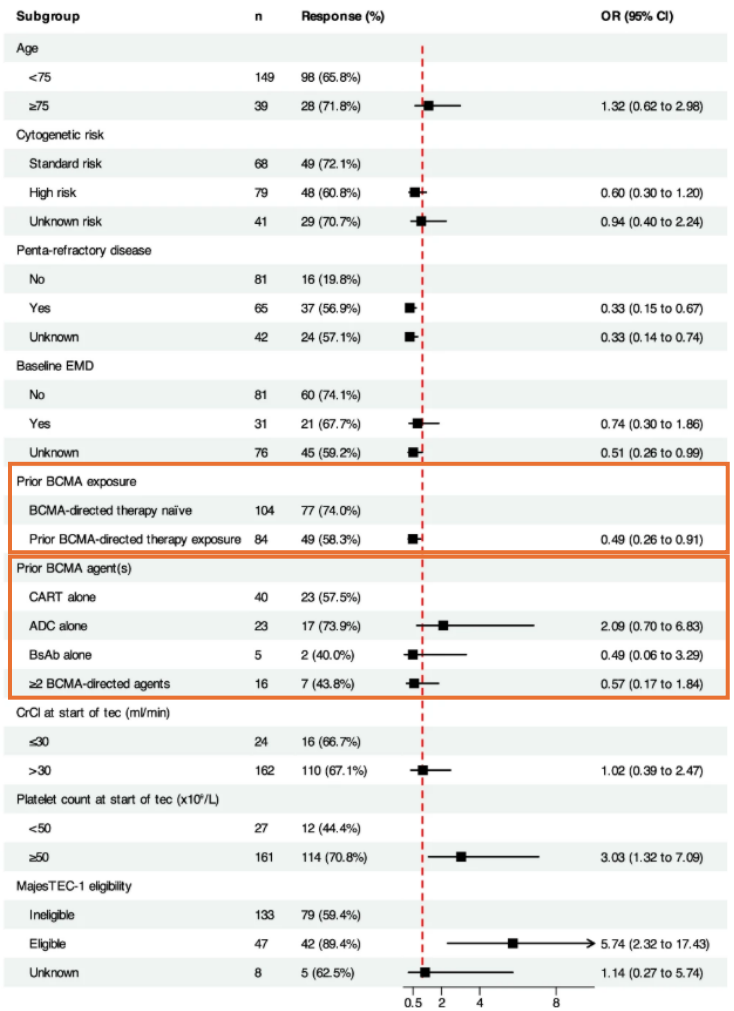


TEC-RW median FU = 5.3 mo



	MajesTEC-1	TEC-RW
ORR	63%	66.9%
Median time to first response	1.2 mo	1.1 mo

Prior BCMA exposure
Naive vs exposed
ORR 74.0% vs 58.3%



Subgroup	n	Response (%)	OR (95% CI)
Age			
<75	149	98 (65.8%)	
≥75	39	28 (71.8%)	1.32 (0.62 to 2.98)
Cytogenetic risk			
Standard risk	68	49 (72.1%)	
High risk	79	48 (60.8%)	0.60 (0.30 to 1.20)
Unknown risk	41	29 (70.7%)	0.94 (0.40 to 2.24)
Penta-refractory disease			
No	81	16 (19.8%)	
Yes	65	37 (56.9%)	0.33 (0.15 to 0.67)
Unknown	42	24 (57.1%)	0.33 (0.14 to 0.74)
Baseline EMD			
No	81	60 (74.1%)	
Yes	31	21 (67.7%)	0.74 (0.30 to 1.86)
Unknown	76	45 (59.2%)	0.51 (0.26 to 0.99)
Prior BCMA exposure			
BCMA-directed therapy naïve	104	77 (74.0%)	
Prior BCMA-directed therapy exposure	84	49 (58.3%)	0.49 (0.26 to 0.91)
Prior BCMA agent(s)			
CART alone	40	23 (57.5%)	
ADC alone	23	17 (73.9%)	2.09 (0.70 to 6.83)
BsAb alone	5	2 (40.0%)	0.49 (0.06 to 3.29)
≥2 BCMA-directed agents	16	7 (43.8%)	0.57 (0.17 to 1.84)
CrCl at start of tec (ml/min)			
≤30	24	16 (66.7%)	
>30	162	110 (67.1%)	1.02 (0.39 to 2.47)
Platelet count at start of tec ($x10^9$/L)			
<50	27	12 (44.4%)	
≥50	161	114 (70.8%)	3.03 (1.32 to 7.09)
MajesTEC-1 eligibility			
Ineligible	133	79 (59.4%)	
Eligible	47	42 (89.4%)	5.74 (2.32 to 17.43)
Unknown	8	5 (62.5%)	1.14 (0.27 to 5.74)

0.5 2 4 8

Factors associated with inferior ORR:
ECOG PS 3
Plt <50
Prior BCMA therapy
Penta-drug refractoriness

Factors associated with superior ORR

MajesTEC-1 eligible vs ineligible
ADC > CAR T > BsAb

PFS, OS, and DOR of real-world patients treated with teclistamab

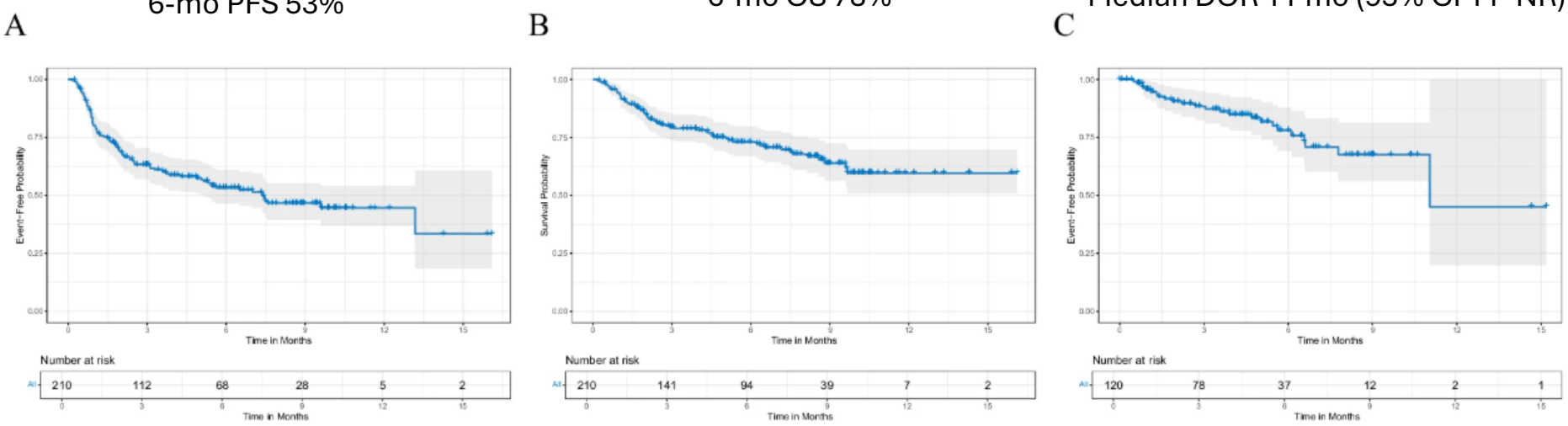
Median FU = 5.3 (0.2–16.3) mo

From: Real-world evaluation of teclistamab for the treatment of relapsed/refractory multiple myeloma (RRMM): an International Myeloma Working Group Study

6-mo PFS 53%

6-mo OS 73%

Median DOR 11 mo (95% CI 11–NR)

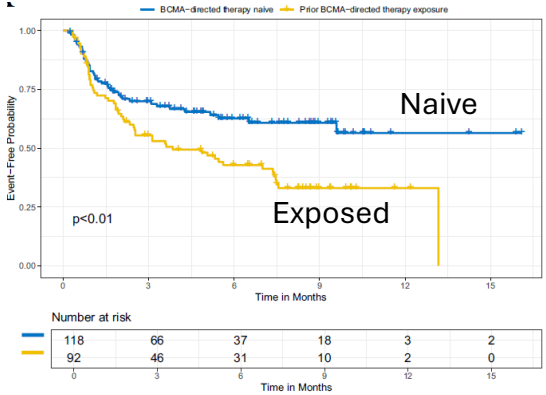


A Progression-free survival (PFS). **B** Overall survival (OS). **C** Duration of response (DoR).

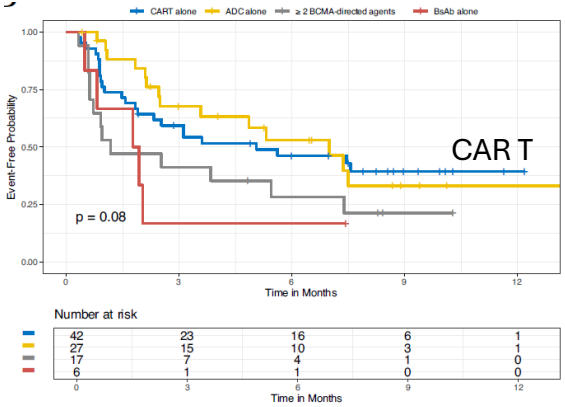
Tan CR, et al. *Blood Cancer J.* 2025;15:53.

PFS by subgroups

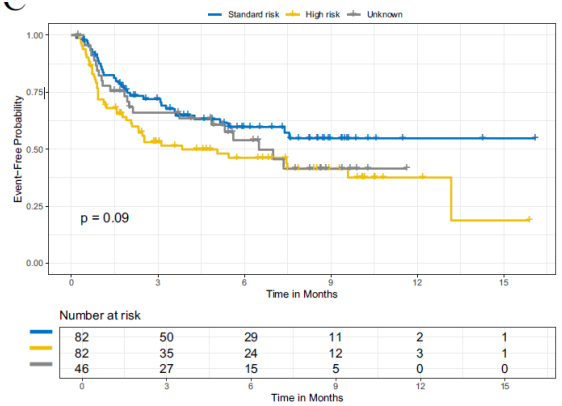
BCMA exposure



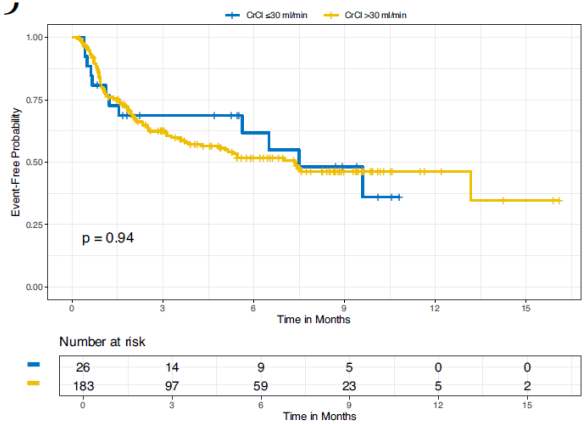
BCMA agent



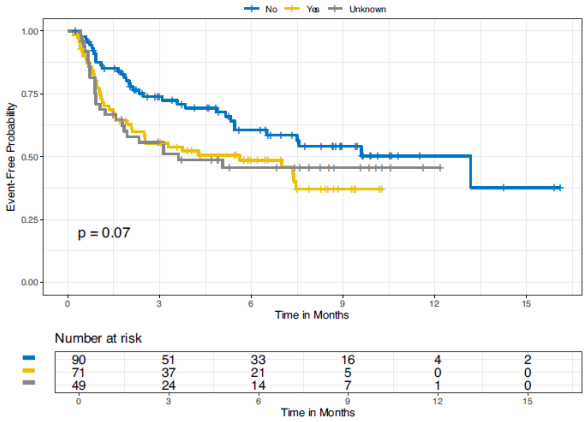
Cytogenetics



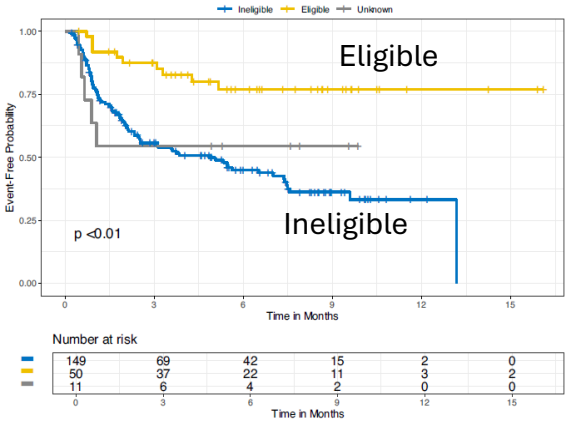
CrCl



Penta-drug refractoriness

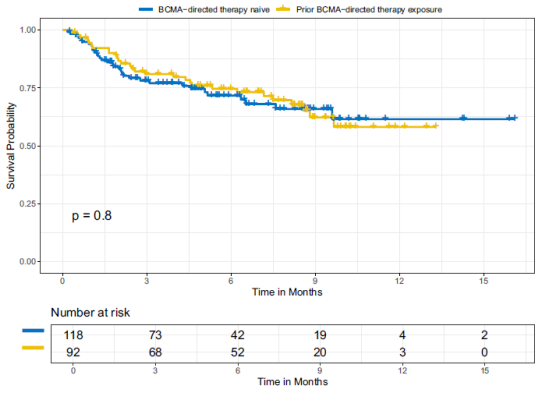


MajesTEC-1 eligibility

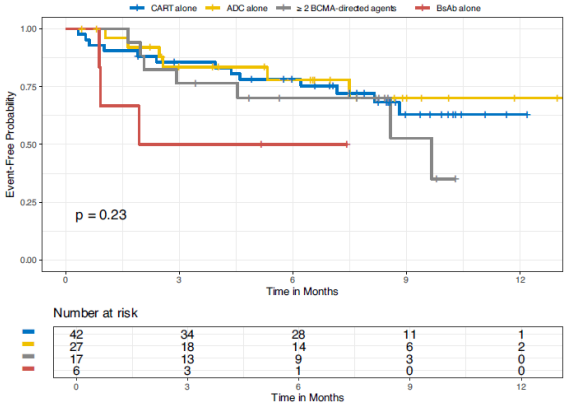


OS by subgroups

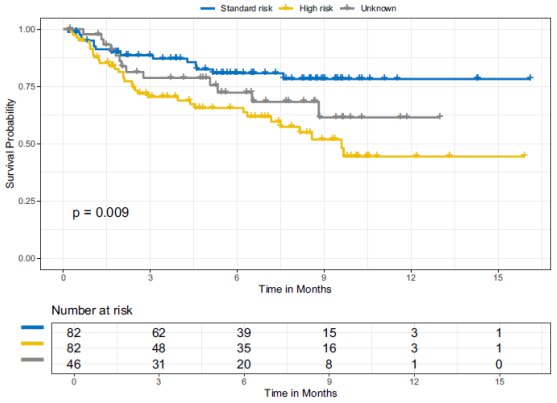
BCMA exposure



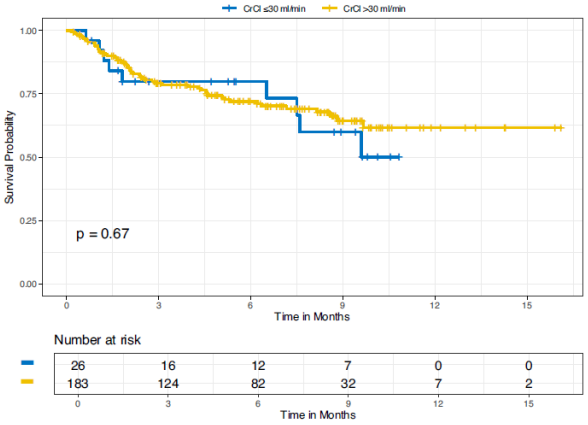
BCMA agent



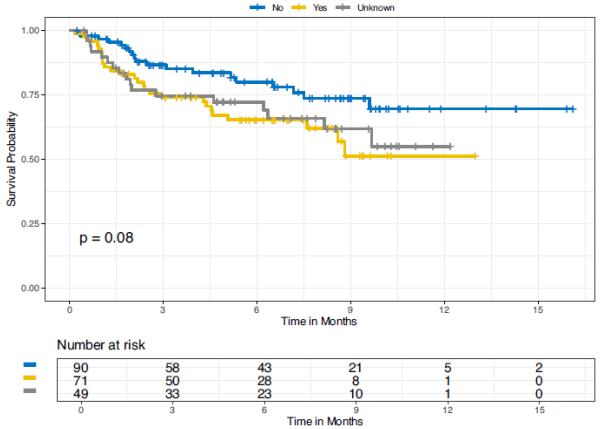
Cytogenetics



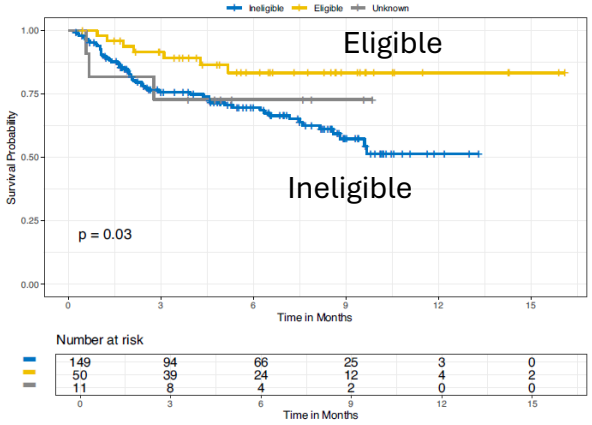
CrCl



Penta-drug refractoriness



MajesTEC-1 eligibility



Mohan et al

N = 110 USA

86% TCR

76% PDR

35% prior BCMA

ORR 62%

≥VGPR 51%

At median FU 3.5 mo

6-mo PFS 52%

Dima et al

N = 106 USA

92% TCR

64% PDR

53% prior BCMA

83% ineligible for MajesTEC-1

ORR 66%

≥VGPR 46%

At median FU 3.8 mo

6-mo PFS ~50%

6-mo OS 70%

Riedhammer et al

N = 123 Germany

93% TCR

60% PDR

37% prior BCMA

39% ineligible for MajesTEC-1

ORR 59.3%

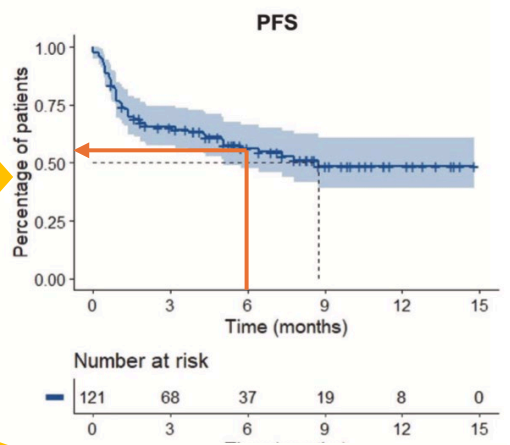
≥VGPR 48%

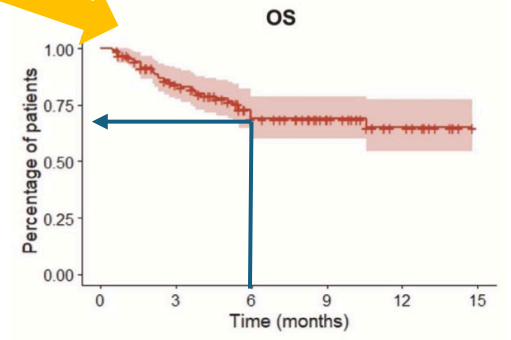
At median FU 5.5 mo

6-mo PFS ~55%

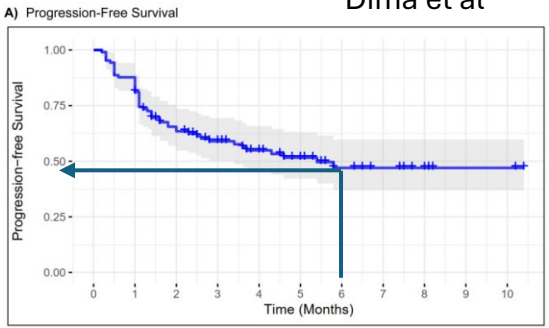
6-mo OS ~70%

Other TEC-RW studies





Dima et al



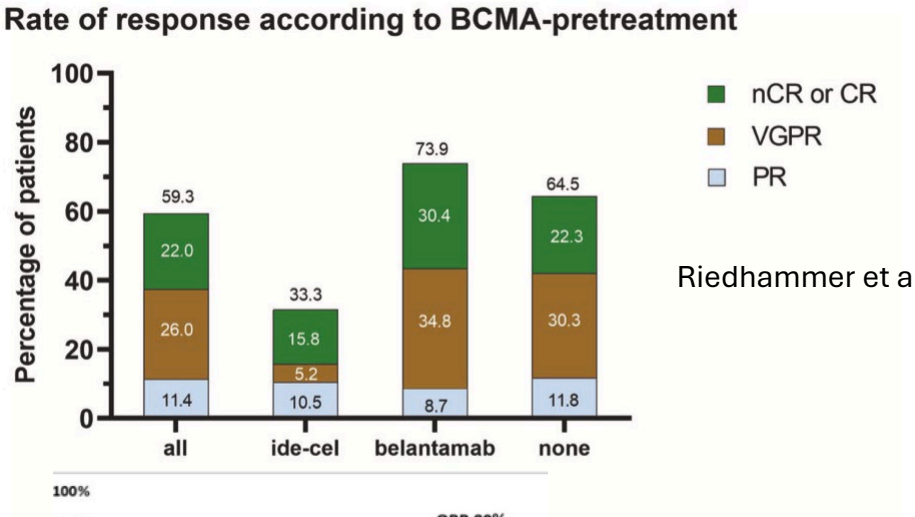
	MajesTEC-1	Tan et al
ORR	63%	**66.9%**
6-mo PFS	~65%	**53%**
6-mo OS	~78%	**73%**

Impact of prior BCMA drug exposure

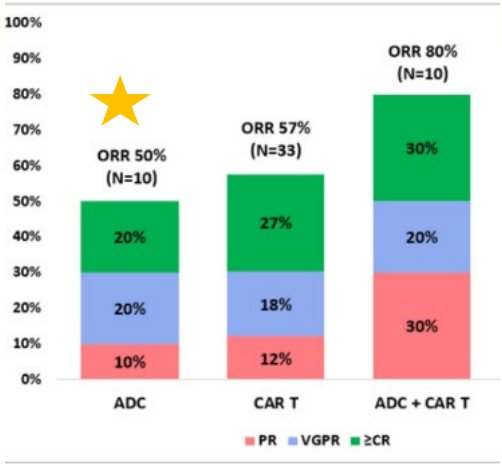
	6-mo PFS	6-mo OS
BCMA exposed	43%	75%
CAR T alone	46%	78%
ADC alone	53%	78%
BsAb alone	17%	50%
BCMA naive	63%	72%
HRCA	46%	66%
SRCA	60%	81%
Unknown	54%	72%

Tan et al	ADC	CAR T	≥BCMA*
ORR	73.9%	57.5%	43.8%

*ADC + BCMA CAR T /ADC + BCMA CAR T + BsAb.



Riedhammer et al



Dima et al

TEC in the real world: Conclusions

- Comparable ORR
  - Even in more heavily pretreated, MajesTEC-1–ineligible patients
- Inferior ORR: ECOG PS 3, Plt <50, prior BCMA therapy, penta-drug refractoriness
- Short median FU (5 mo): 6 mo PFS rate ~50% vs 65% in MajesTEC-1
  - Depth of response may improve with longer duration of treatment
  - Comparable 6-mo OS rates ~70%
- Prior BCMA targeting
  - Belantamab seems to have the least negative impact on ORR/6-mo PFS and OS rates
  - ADC >> CART >> bispecifics
    - May be due to T-cell exhaustion/fitness

nature medicine

Article

https://doi.org/10.1038/s41591-023-02528-9

Elranatamab in relapsed or refractory multiple myeloma: phase 2 MagnetisMM-3 trial results

Received: 18 June 2023

Accepted: 1 August 2023

Published online: 15 August 2023

Check for updates

Alexander M. Lesokhin[1] ✉, Michael H. Tomasson[2], Bertrand Arnulf[3], Nizar J. Bahlis[4], H. Miles Prince[5], Ruben Niesvizky[6], Paula Rodríguez-Otero[7], Joaquin Martinez-Lopez[8], Guenther Koehne[9], Cyrille Touzeau[10], Yogesh Jethava[11], Hang Quach[12], Julien Depaus[13], Hisayuki Yokoyama[14], Afshin Eli Gabayan[15], Don A. Stevens[16], Ajay K. Nooka[17], Salomon Manier[18], Noopur Raje[19], Shinsuke Iida[20], Marc-Steffen Raab[21], Emma Searle[22], Eric Leip[23], Sharon T. Sullivan[23], Umberto Conte[24], Mohamed Elmeliegy[25], Akos Czibere[24], Andrea Viqueira[26] & Mohamad Mohty[27]

Eligibility criteria

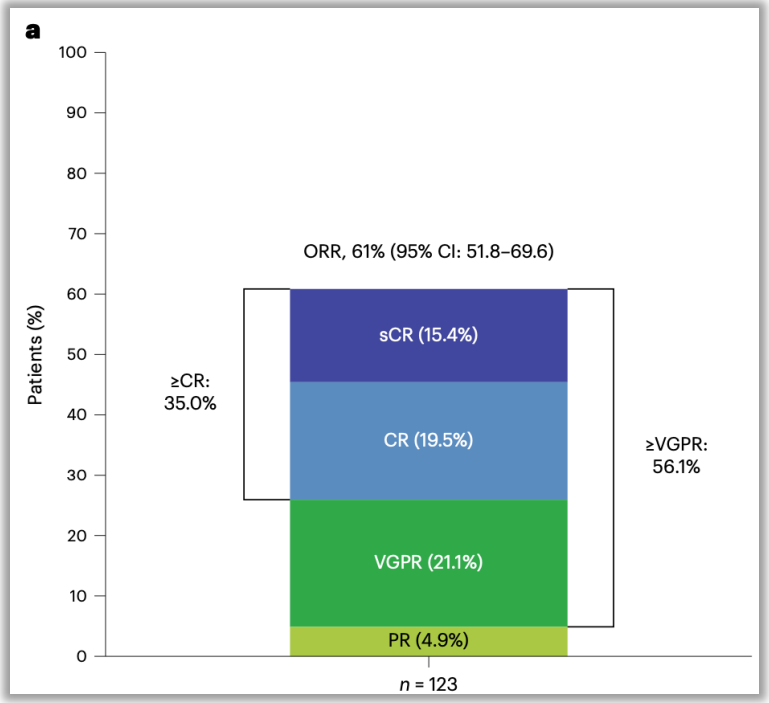
- Triple class refractory and refractory to last LOT
- No prior BCMA-directed therapy (cohort A)
- ECOG 0–2
- Plts ≥25, ANC ≥1.0, Hb ≥80
- CrCL ≥30 mL/min, adequate hepatic function, LVEF ≥40% MUGA/TTE
- Usual exclusions

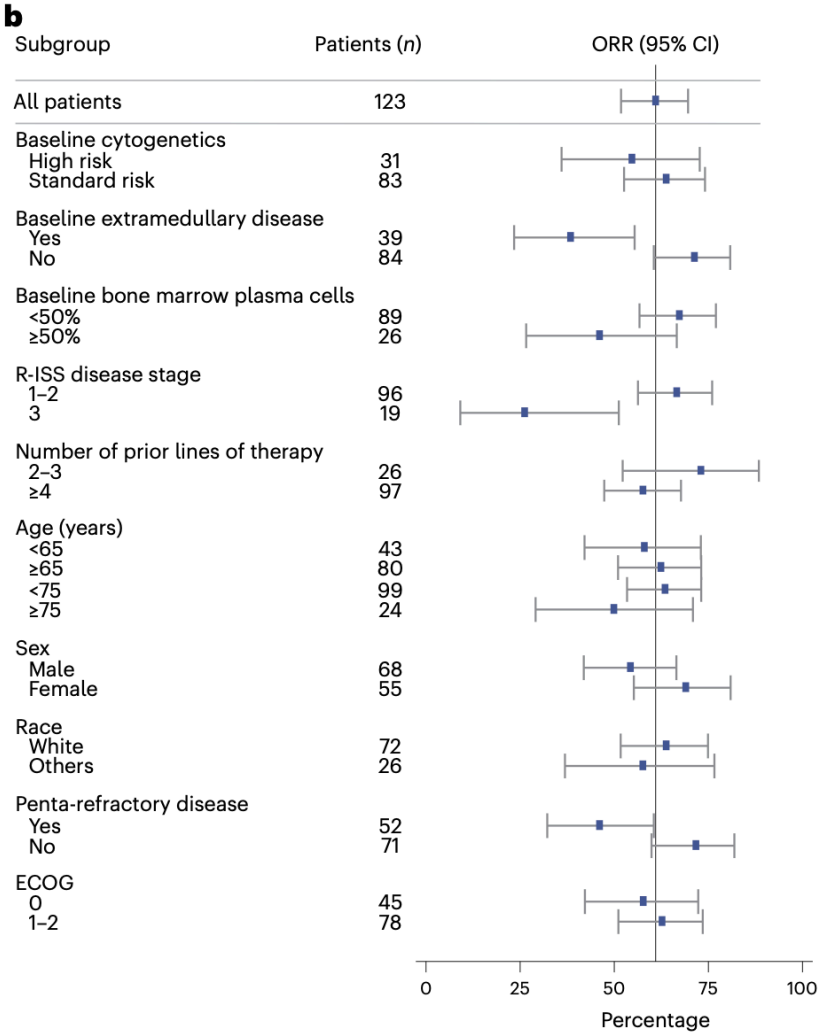
MagnetisMM-3: Demographics

Characteristic	N = 123
Median age (range), yr	68.0 (36–89)
Male, n (%)	68 (55.3)
ECOG 2, n (%)	7 (5.7)
R-ISS 3, n (%)	19 (15.4)
Cytogenetic risk, n (%) High*	 31 (25.2)
Median prior LOT	5 (2–22)
Exposure status, n (%) Triple-class Penta-drug	 123 (100) 87 (70.7)
Refractory status, n (%) Triple-class Penta-drug	 119 (96.7) 52 (42.3)
EMD, n (%)	39 (31.7)

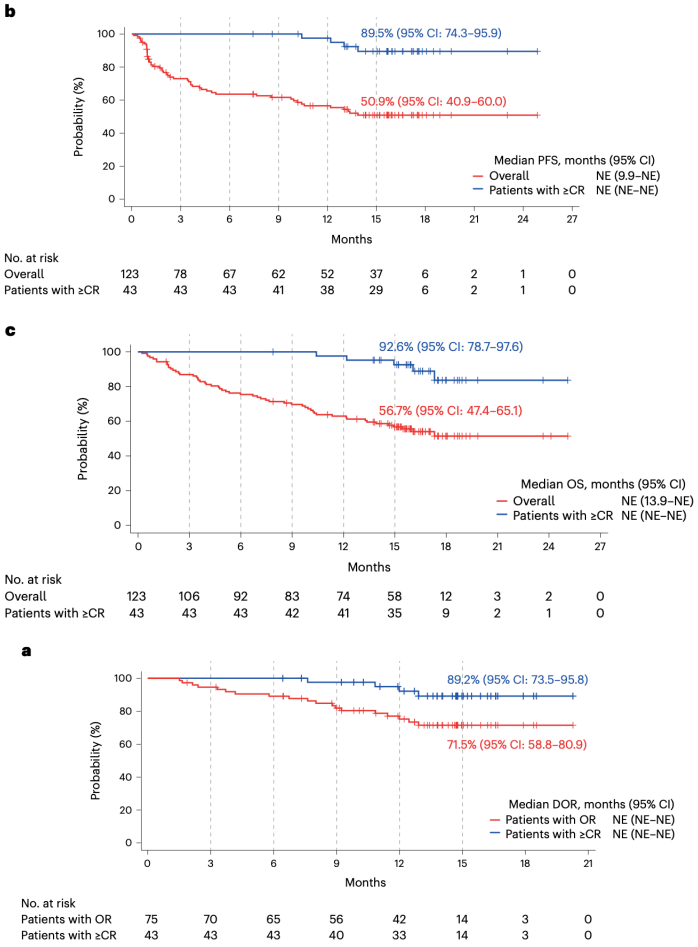
*t(4;14), t(14;16), del(17p).

MagnetisMM-3





Median FU 14.7 mo



Median FU 28.4 mo

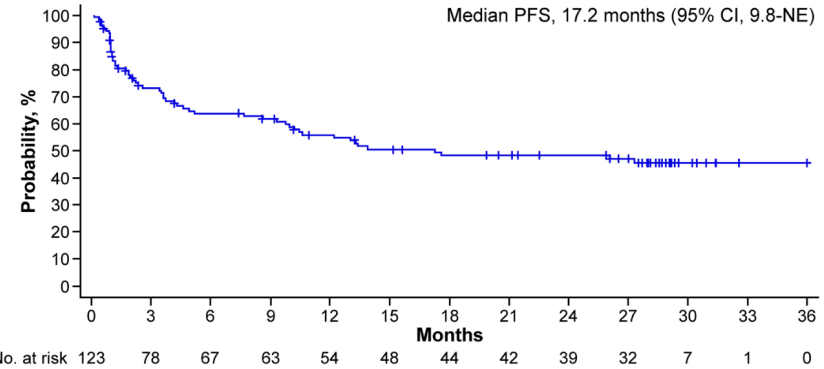


FIGURE 1 Kaplan–Meier analysis of progression-free survival. Progression-free survival in B-cell maturation antigen–naive patients with relapsed or refractory multiple myeloma in the MagnetisMM-3 study. Tick marks indicate censored data.

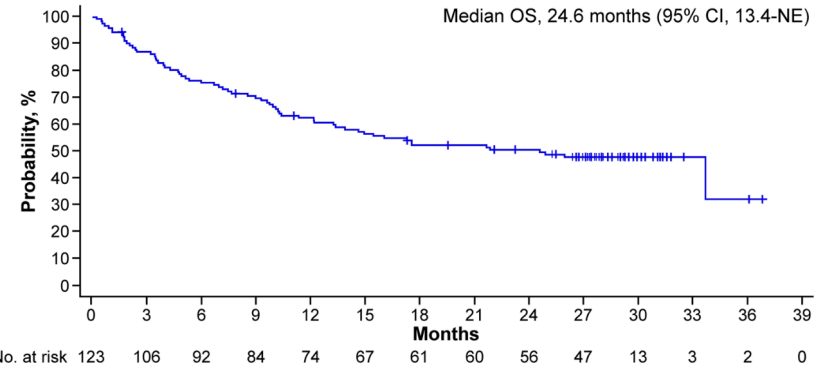
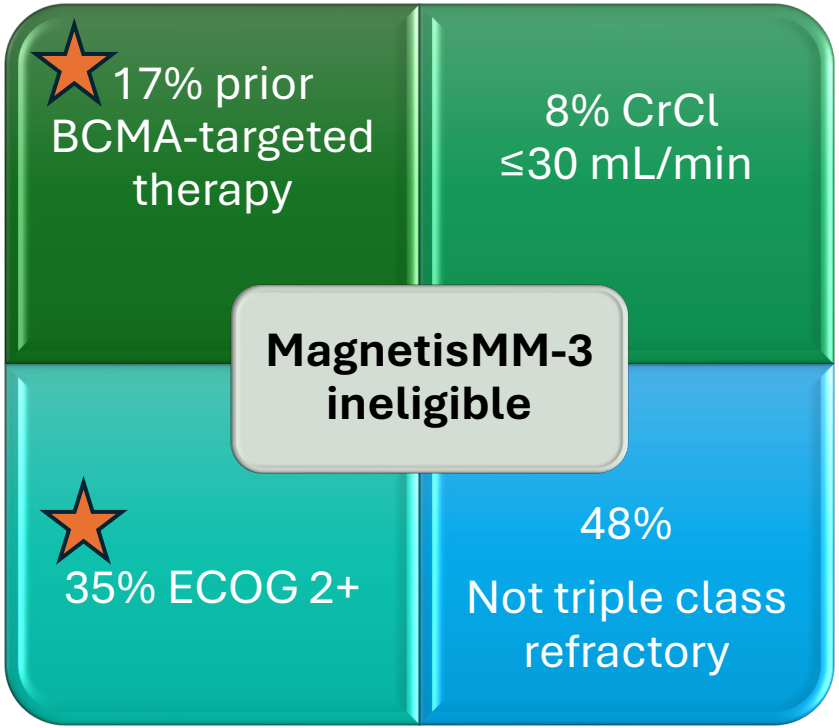


FIGURE 2 Kaplan–Meier analysis of overall survival. Overall survival in B-cell maturation antigen–naive patients with relapsed or refractory multiple myeloma in the MagnetisMM-3 study. Tick marks indicate censored data.

Elranatamab monotherapy in the RW setting in RRMM: Results of the French compassionate use program on behalf of the IFM



- N = 101; 22 centers; 2022–2023

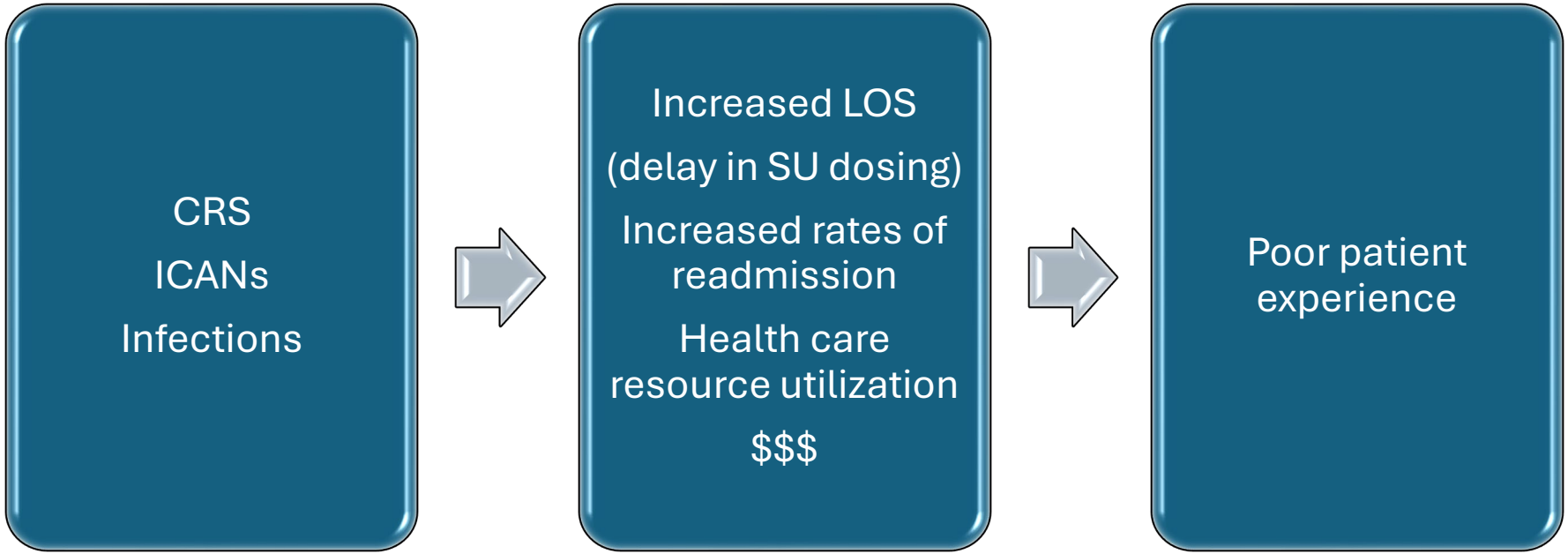
- Median age 68 (39–87)
- Median 5 prior LOT (1–17)
- TCE 96%
- Penta-drug exposed 76%

- **ORR 52%**
- ≥VGPR 36%

- 12-mo OS rate 42%
- 12-mo PFS rate 48%
- Median DOR 11 mo

Blood Cancer J. 2024;14:219. Correspondence.

CAR T and bispecific antibodies



blood advances

American Society of Hematology
2021 L Street NW, Suite 900,
Washington, DC 20036
Phone: 202-776-0544 | Fax 202-776-0545
bloodadvances@hematology.org

Tocilizumab Prophylaxis for Patients with Multiple Myeloma Treated with Bispecific Antibodies

Kowalski A, et al. *Blood Adv.* 2025:4979-4986.

Sylvester CCC, Miami USA

https://doi.org/10.1182/bloodadvances.2025016911

Demographics

N = 119

RW patients

Tec 45

Elra 40

Livo 10

Tal 23

Tec + Tal 1

Median age 67 (35–87)

≥75, 24.6%

ECOG 0–1, 70.6%

2, 23.5%

3–4, 5.9%

26.8% HR (del17p, t[4;4], t[14;16])

Median prior LOT 4.5

89.1% TCE

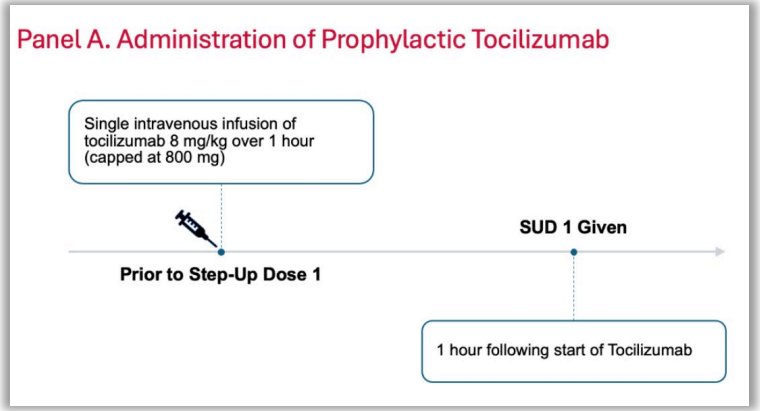
53.8% penta-drug exposed

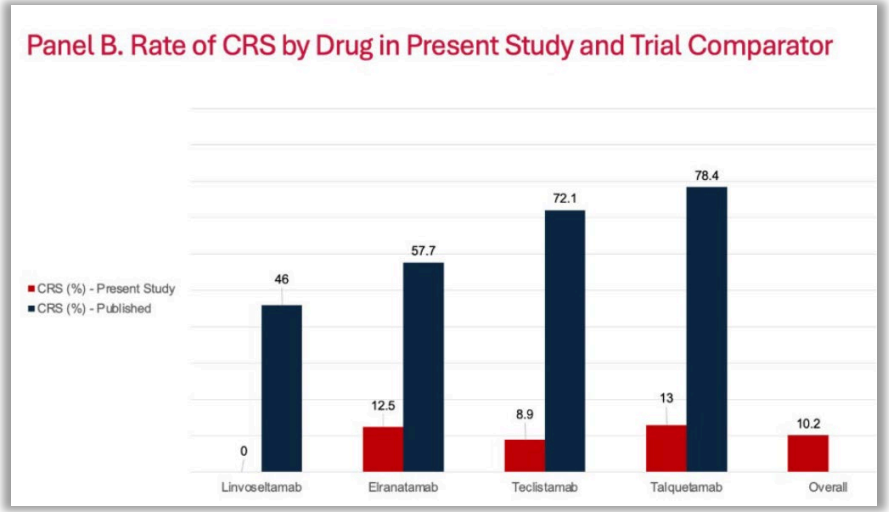
24.8% ≥60% BM PC burden

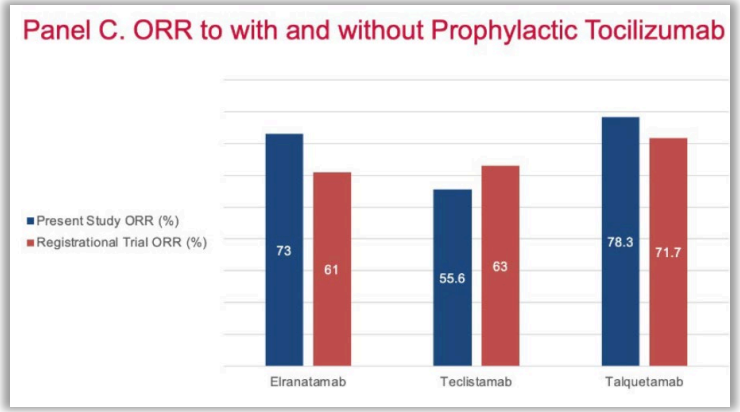
76% did not meet trial eligibility

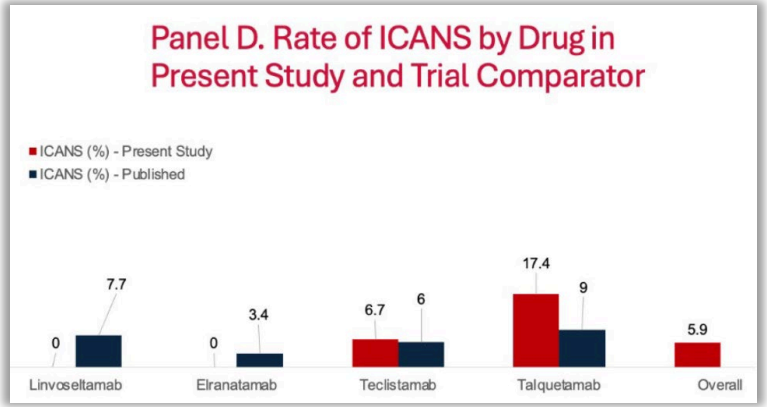
(renal dysfunction, age, prior therapy, hematologic parameters, ECOG)

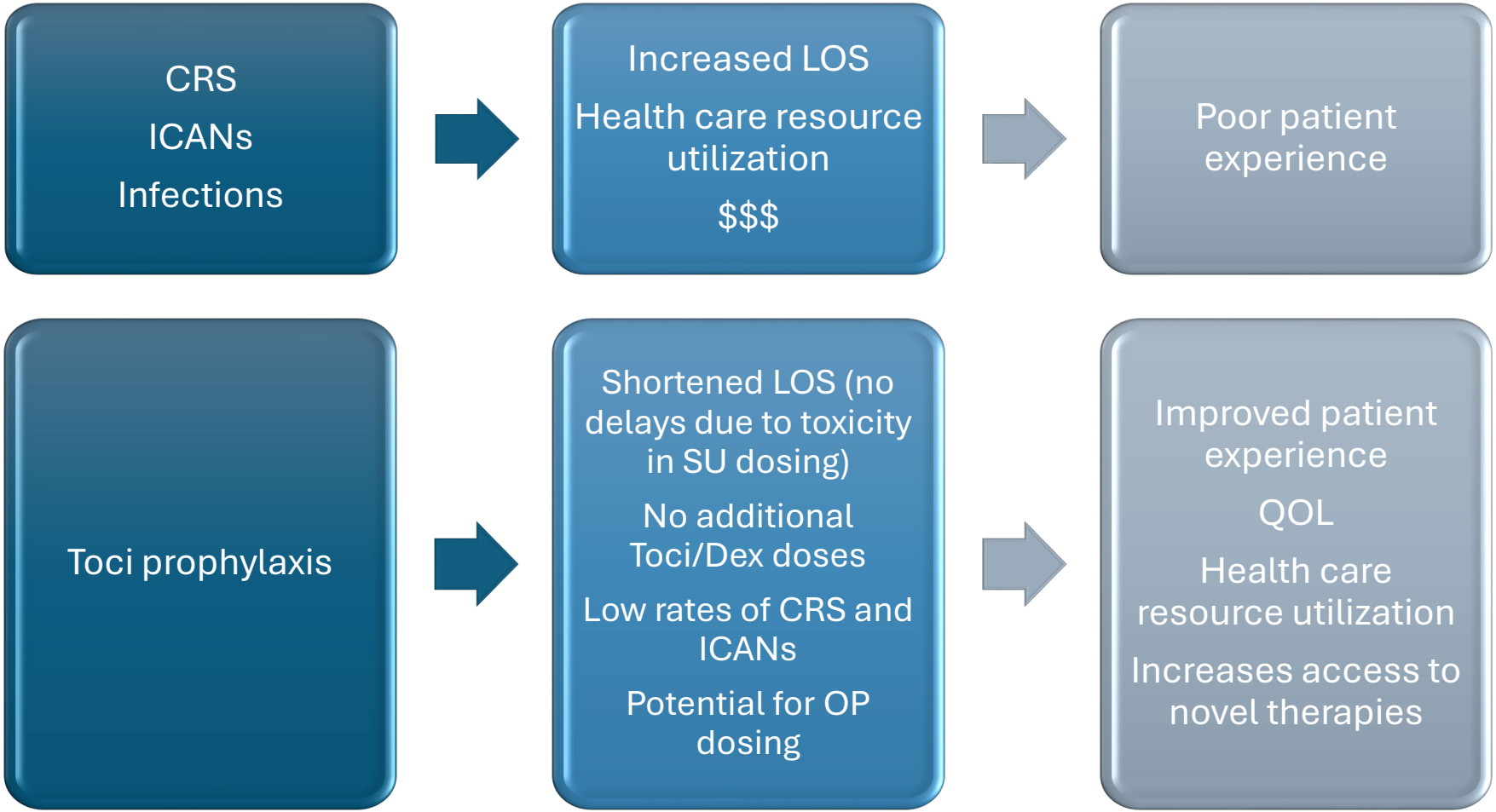
Toci prophylaxis










CRS
ICANs
Infections
Increased LOS
Health care resource utilization
$$$
Poor patient experience
Toci prophylaxis
Shortened LOS (no delays due to toxicity in SU dosing)
No additional Toci/Dex doses
Low rates of CRS and ICANs
Potential for OP dosing
Improved patient experience
QOL
Health care resource utilization
Increases access to novel therapies

HEMATOLOGIC MALIGNANCIES—PLASMA CELL DYSCRASIA

Check for updates

e19504

Publication Only

2025 ASCO meeting abstract

Tocilizumab prophylaxis for outpatient administration of teclistamab in relapsed/refractory multiple myeloma.

Gaspard Jadot, Richard LeBlanc, Imran Ahmad, Karim Benkirane, Nancy Dorneval, Jean Roy, Olivier Veilleux, Rayan Kaedbey, Jean-Sebastien Claveau; Hôpital Maisonneuve-Rosemont, Montreal, QC, Canada; Segal Cancer Centre, Jewish General Hospital, McGill University, Montréal, QC, Canada; Hôpital Maisonneuve-Rosemont, Montréal, QC, Canada

- N = 20 TCE MM; 70% were not eligible for MajesTEC-1
- CRS occurred in 2 pts (10%), grade 1
- 1 pt requires 1 dose Toci, the other pt 1 dose dex
- No hospitalization
- No ICANs reported
- ORR 68%

Baseline demographics.

Characteristics	Cohort (N=20)
Median age in years (range)	72 (31-91)
Male sex (%)	8 (40)
Caucasians (%)	14 (70)
>1 Extramedullary site of disease (%)	10 (50)
High-risk cytogenetic profile - number/total number (%)	9/16 (56)
International Staging System 3 number/total number (%)	6/17(35)
Median time since diagnosis in years (range)	7.0 (1.5-20.9)
Median number of previous lines of therapy (range)	4 (2-8)

Elranatamab patient familiarization program – Alfred Experience

TCR; 3+ lines

N = 24*

- CRS
  - Grade 1 – 38%
  - Grade 2 – 17%
- Fatigue → schedule dependent
- Neutropenia → G-CSF
- CMV reactivation – 29%
- Acral desquamating rash – 13%
- Tocilizumab pre-Rx n = 3. No CRS
- **ORR – 88%†**

Commence ELRA QW
Bactrim M/W/F
Valaciclovir
CMV monitoring Q2–4W
IVIG/scIG

↓

Serologic CR – continue QW for further 4 wk

↓

Repeat PET if done at baseline

↓

Reduce ELRA to Q4W

*Five prior auto-allo; †Pomalidomide 2 mg od n = 3.

ELRANATAMAB FOR MULTIPLE MYELOMA

AlfredHealth

Target audience

Healthcare professionals working within the Clinical Haematology Unit, Alfred Health.

Purpose

This guideline is intended to provide a consistent approach to use of medications at Alfred Health.

Summary

Elranatamab is a humanised B-cell maturation antigen (BCMA)-CD3 bispecific antibody for relapsed/refractory multiple myeloma patients who have received at least 3 lines of treatment (including an immunomodulatory agent, proteasome inhibitor, and an anti-CD38 antibody) and have demonstrated disease progression on the last therapy.

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Talquetamab plus Teclistamab in Relapsed or Refractory Multiple Myeloma

Y.C. Cohen, H. Magen, M. Gatt, M. Sebag, K. Kim, C.-K. Min, E.M. Ocio, S.-S. Yoon, M.P. Chu, P. Rodríguez-Otero, I. Avivi, N.A. Quijano Cardé, A. Kumar, M. Krevvata, M.R. Peterson, L. Di Scala, E. Scott, B. Hilder, J. Vanak, A. Banerjee, A. Oriol, D. Morillo, and M.-V. Mateos, for the RedirecTT-1 Investigators and Study Group*

N Engl J Med 2025;392:138-49.
DOI: 10.1056/NEJMoa2406536

BONE DEPENDENT

Paramedullary disease[1,2]
Plasmacytomas growing contiguously with bone and extending into soft tissue after cortical disruption

BONE INDEPENDENT

True EMD[1,2]
Soft tissue/organ-associated plasmacytomas noncontiguous with bony structures

Inferior outcomes vs patients with paramedullary plasmacytomas and patients with MM without EMD[3-13]

RedirecTT-1 SCHEMA

Key eligibility criteria

EMD defined as:
≥1 nonradiated bone-independent soft tissue plasmacytoma ≥2 cm in greatest dimension confirmed by central review of PET-CT scans[a,b]

- MM per IMWG criteria
- Triple-class exposed[c] RRMM
- Prior CAR-T (≤20% patients) and BsAb therapy permitted
  - BsAbs could not target GPRC5D or BCMA
- Nonsecretory/oligosecretory disease permitted

Step up doses[d] administered 2–4 days apart

- Tal 0.4 mg/kg Tec 1.5 mg/kg
- Tal 0.06 mg/kg Tec 0.3 mg/kg
- Tal 0.01 mg/kg Tec 0.06 mg/kg

Tal 0.8 mg/kg Q2W SC + Tec 3.0 mg/kg Q2W SC[d] until disease progression

Primary endpoint

- ORR[e] (EMD response assessed by central radiology review of whole-body PET-CT scans)

Secondary endpoints

- ≥VGPR, ≥CR, and sCR rate[e]
- Time to response,[e] DOR,[e] PFS, and OS
- Safety
- PK, immunogenicity

Option to reduce dosing frequency for both agents to monthly dosing after:

- ≥VGPR and minimum 4 cycles of therapy, *or*
- 6 cycles, per investigator discretion

1. Ho M, et al. *Curr Oncol* 2025;32:182. 2. Bladé J, et al. *Blood Cancer J* 2022;12:45. 3. Rosiñol L, et al. *Br J Haematol* 2021;194:496-507. 4. Pour L, et al. *Haematologica* 2014;99:360-4. 5. Mangiacavalli S, et al. *Ann Hematol* 2017;96:73–80. 6. Rasche L, et al. *Ann Hematol* 2012;91:1031-7. 7. Richard S, et al. *Blood* 2022;140(Suppl 1):4301-2; 8. Pan D, et al. *Blood* 2023;142(Suppl 1):1006. 9. Dima D, et al. *Blood Cancer J* 2024;14:90. 10. Zanwar S, et al. *J Hematol Oncol* 2024;17:42. 11. Usmani SZ, et al. *Haematologica* 2012;97:1761-7. 12. Beksac M, et al. *Haematologica* 2020;105:201-8. 13. Moreau P, et al. *Clin Lymphoma Myeloma Leuk* 2025:S2152-2650(25)00106-5. mOS, median overall survival; mPFS, median progression-free survival; ORR, overall response rate; RRMM, relapsed/refractory multiple myeloma.

Presented by S Kumar at the European Hematology Association (EHA) 2025 Hybrid Congress; June 12–15, 2025; Milan, Italy

Kumar et al. EHA 2025.

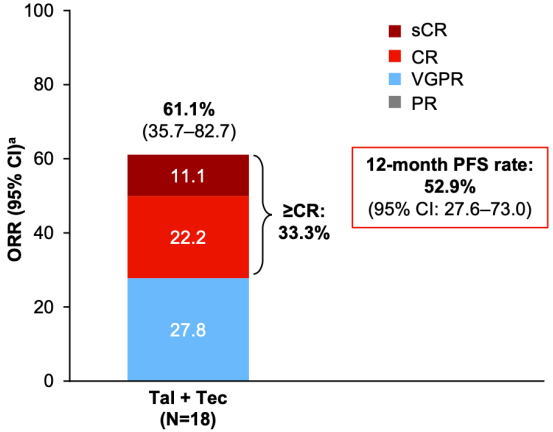
RedirecTT-1 Phase 2 Tal + Tec: Most Patients With True EMD Were Triple-Class Refractory

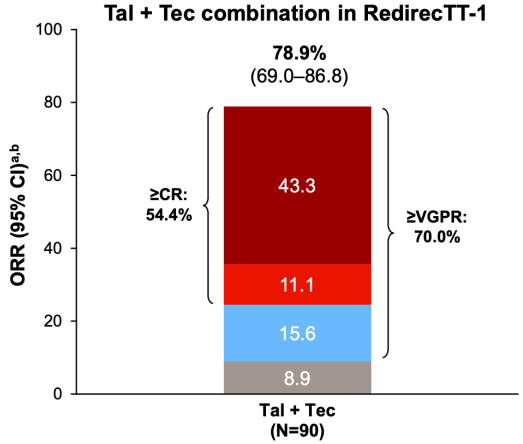
Characteristic	Tal + Tec (N=90)
Median age, years (range)	64.5 (42–84)
Male, n (%)	57 (63.3)
Race, n (%)	
White	64 (71.1)
Black/African American	8 (8.9)
Asian	13 (14.4)
Not reported	5 (5.6)
True extramedullary plasmacytomas ≥1,[a] n (%)	90 (100)[b]
Number of extramedullary plasmacytomas,[a] median (range)	2 (1–7)
Number of extramedullary plasmacytomas,[a] n (%)	
1	38 (42.2)
2–3	29 (32.2)
≥4	23 (25.6)
High-risk cytogenetics,[c] n (%)	14 (21.5)
Measurable disease,[d] n (%)	
Nonsecretory	4 (4.4)
Oligosecretory	31 (34.4)

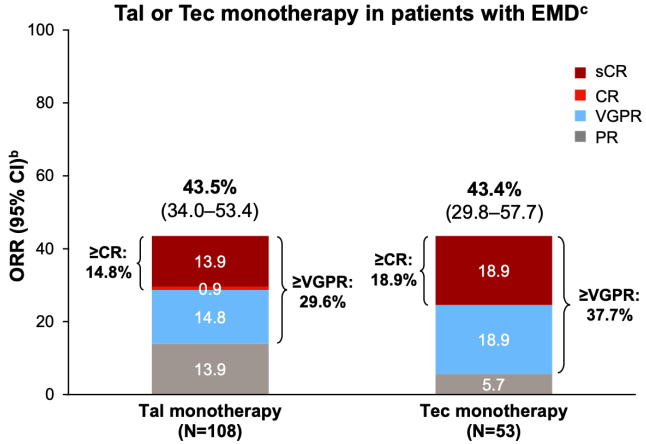
Characteristic	Tal + Tec (N=90)
ECOG performance status, n (%)	
0	32 (35.6)
1	50 (55.6)
2	8 (8.9)
Years since diagnosis, median (range)[e]	4.7 (0.7–21.4)
Median prior LOT, n (range)	4.0 (1–10)
Exposure status, n (%)	
Belantamab mafodotin	11 (12.2)
Anti-BCMA CAR-T therapy	18 (20.0)
BsAb therapy[f]	8 (8.9)
Triple-class	90 (100)
Penta-drug	51 (56.7)
Refractory status, n (%)	
PI	86 (95.6)
IMiD	84 (93.3)
Anti-CD38 monoclonal antibody	85 (94.4)
Triple-class	76 (84.4)
Penta-drug	32 (35.6)
To last LOT	75 (83.3)

Kumar et al. EHA 2025.

RedirecTT-1 phase 1 results showed promising activity of the Tal + Tec RP2R in patients with true EMD[8,9]

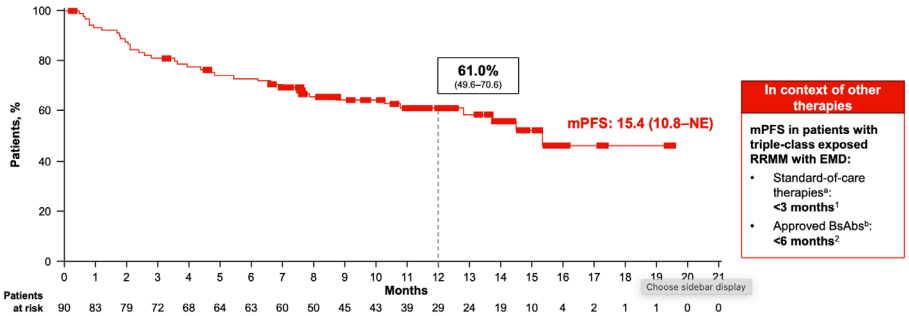




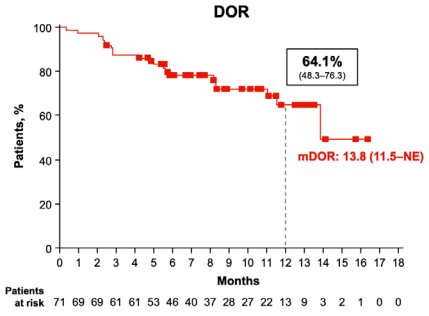


RP2: Tal 0.8 mg/kg and Tec 3.0 mg/kg

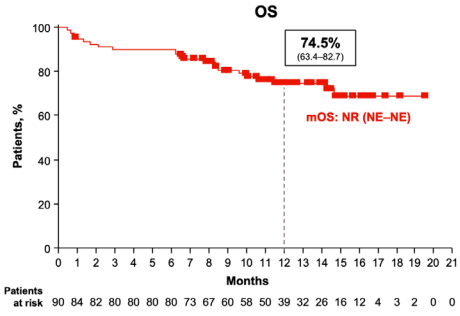
Higher ORR and deeper responses in patients with EMD with Tal + Tec combination vs Tal or Tec monotherapy



Estimated PFS rate at 1 year was 61%



Estimated 12-month freedom from progression rate was 64%



Estimated 12-month OS rate was 75%

Kumar et al. EHA 2025.

RedirecTT-1 Phase 2 Tal + Tec: CRS and ICANS Mostly Low Grade

CRS	Tal + Tec (N=90)
Patients with CRS,[a] n (%)	70 (77.8)
Grade 1	53 (58.9)
Grade 2	17 (18.9)
Grade 3	0 (0)
Occurrence of CRS,[b] n (%)	
Step-up dose 1	40 (44.4)
Step-up dose 2	51 (56.7)
Step-up dose 3	24 (26.7)
Cycle 1	5 (5.6)
Cycle 2 onwards	1 (1.1)
Days to onset,[c] median (range)	2 (1–29)
Duration, days, median (range)	2 (1–8)

ICANS	Tal + Tec (N=90)
Patients with ICANS,[a] n (%)	11 (12.2)
Grade 1	5 (5.6)
Grade 2	4 (4.4)
Grade 3	1 (1.1)
Grade 4	1 (1.1)
Occurrence of ICANS,[b] n (%)	
Step-up dose 1	2 (2.2)
Step-up dose 2	4 (4.4)
Step-up dose 3	7 (7.8)
Cycle 1	2 (2.2)
Cycle 2 onwards	0
Days to onset,[c] median (range)	3 (1–7)
Duration, days, median (range)	2 (1–7)

- CRS[d] was managed with tocilizumab (56.7%), acetaminophen (56.7%), corticosteroids (18.9%), and IV fluids (17.8%)
- ICANS[d] was managed with corticosteroids (10.0%), levetiracetam (4.4%), anakinra (2.2%), and tocilizumab (1.1%)

CRS and ICANS consistent with Tal and Tec monotherapy

Kumar et al. EHA 2025.

Combining bispecifics

- Provides an avenue to treat biologically high-risk disease
  - Circumvent tumor escape mechanisms, eg, heterogenous antigen expression/down regulation

- RedirecTT-1
  - True EMD
  - Triple class exposed, median 4 prior LOT
  - ORR 78.9% at RP2D
  - 12-mo PFS rate 61%; 12-mo OS 74.5%
  - Low-grade CRS ICANS
  - **Infections an issue** – infectious prophylaxis and aggressive management critical

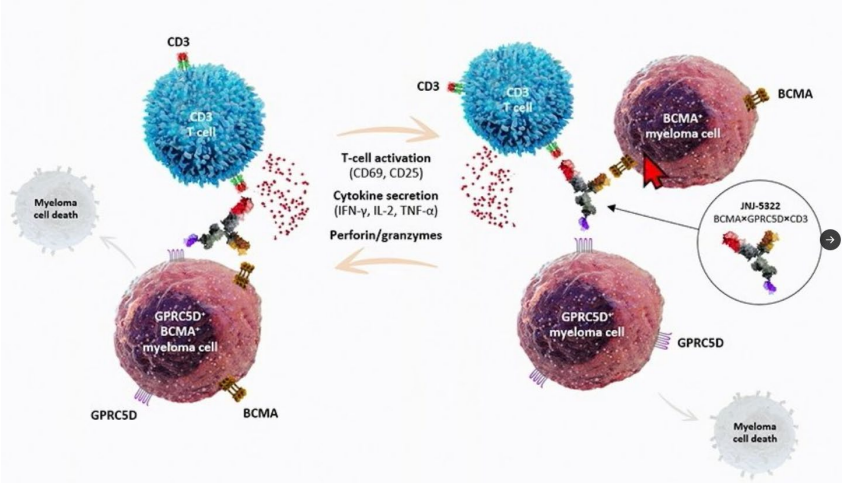
ASCO AMERICAN SOCIETY OF CLINICAL ONCOLOGY

Abstract #: 7505

Oral Abstract Session

First-in-human study of JNJ-79635322 (JNJ-5322), a novel, next-generation trispecific antibody (TsAb), in patients (pts) with relapsed/ refractory multiple myeloma (RRMM): Initial phase 1 results.

Authors: Niels W. van de Donk, Gala Vega, Aurore Perrot, Sébastien Anguille, Albert Oriol, Monique Minnema, Martin F. Kaiser, Hans C. Lee, Alfred Garfall, Jeffrey V. Matous, Larysa J. Sanchez, Azra Borogovac, Lionel Karlin, Saad Z. Usmani, Joseph Weidman, Sangmin Lee, Maria-Victoria Mateos, Paula Rodríguez-Otero, Cyrille Touzeau, Rakesh Popat



- Dose escalation/expansion study
- Triple class exposed; median 4 LOT
- 31% HRCA; 23% prior BCMA/GPC5D therapy
- N = 126, 36/126 at RP2D
- Median FU 8.2 mo
- **75% infections (grade 3/4 28%)**
- ORR 86%, 75% ≥VGPR at RP2D and 73% overall (N = 124)
- ORR 100% at RP2D in BCMA/GPRC5D-naive pts
- Median time to response 1.2 mo

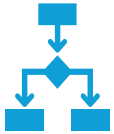
SU 1
5 mg SC

RP2D
100 mg Q4W
SC

Conclusions

Real-world outcomes with TEC and Elra demonstrate comparable ORR to MajesTEC-1, but longer follow-up is needed to assess PFS and OS

Toci prophylaxis reduces CRS rates significantly and may allow us to shift bispecifics safely to the OP



Combining bispecifics may be the way to go for biologically challenging disease eg, EMD/FHR

Trispecifics are coming

Thank you!

Global Multiple Myeloma Academy

Discussion

APTITUDE HEALTH®

Global Multiple Myeloma Academy

Break

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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

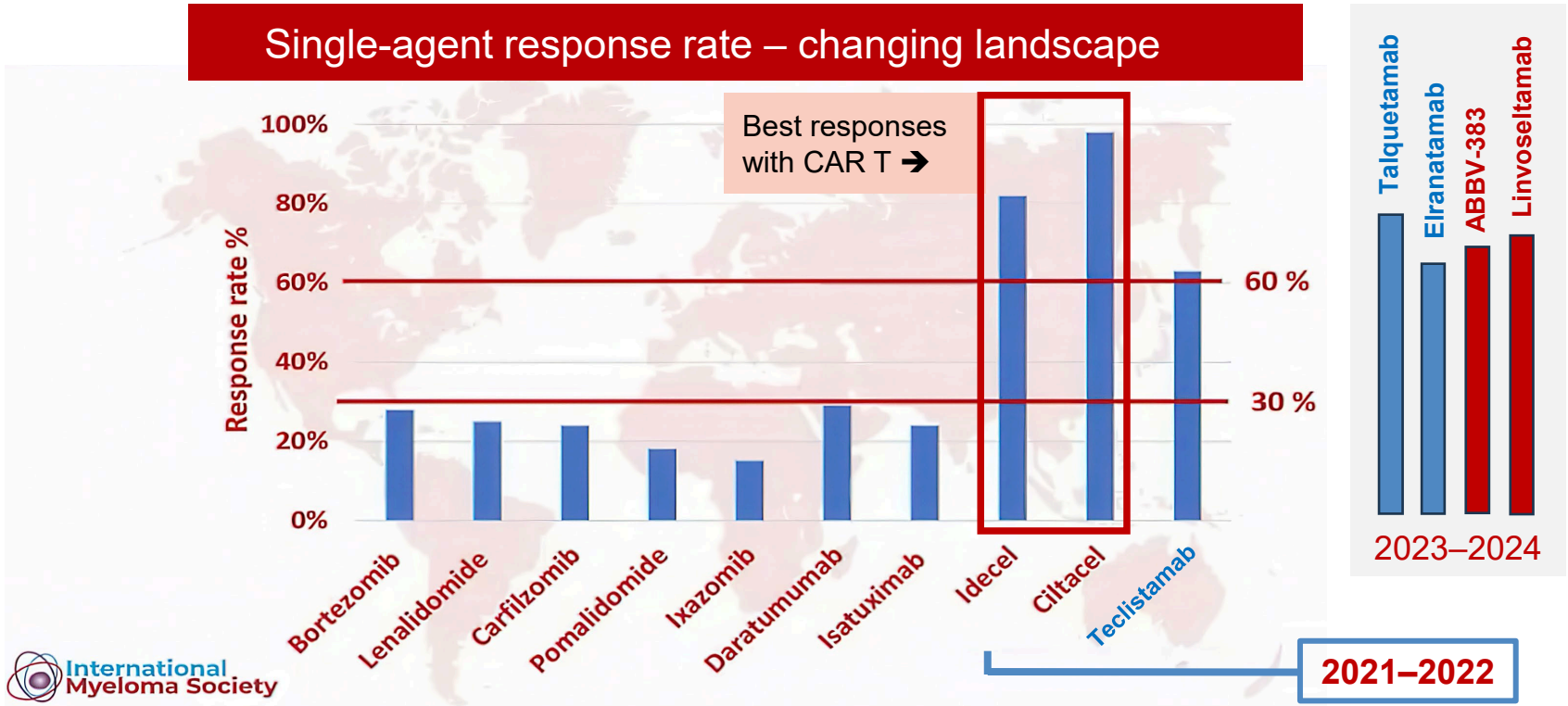
Immunotherapy Sequencing in RRMM: Current and Future Landscape

(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

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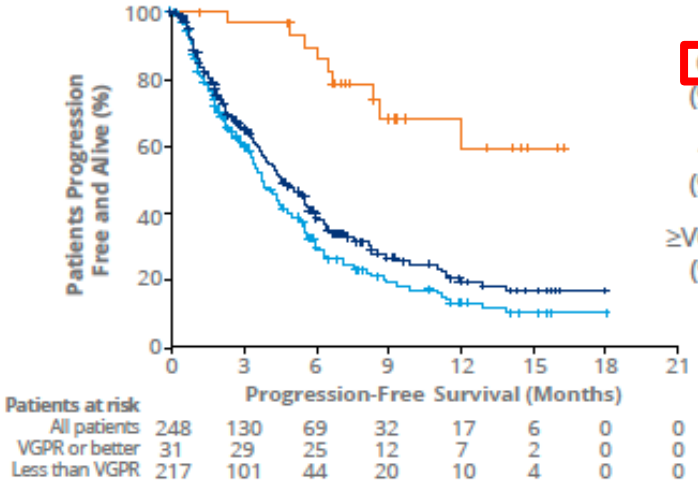
PFS

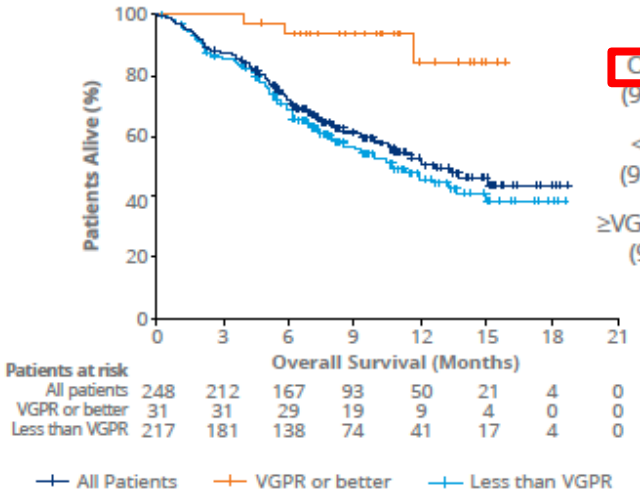


Median PFS
Overall: 4.6 mo
(95% CI: 3.9–5.6)

<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

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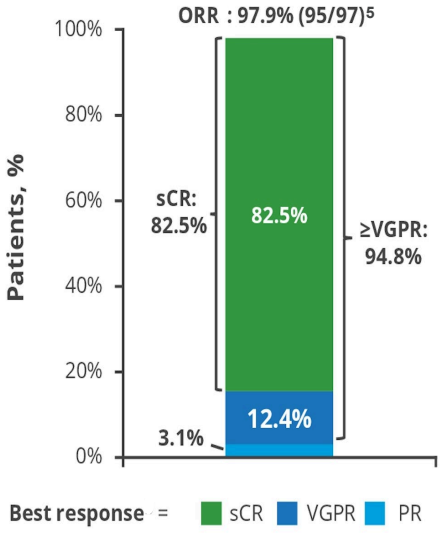
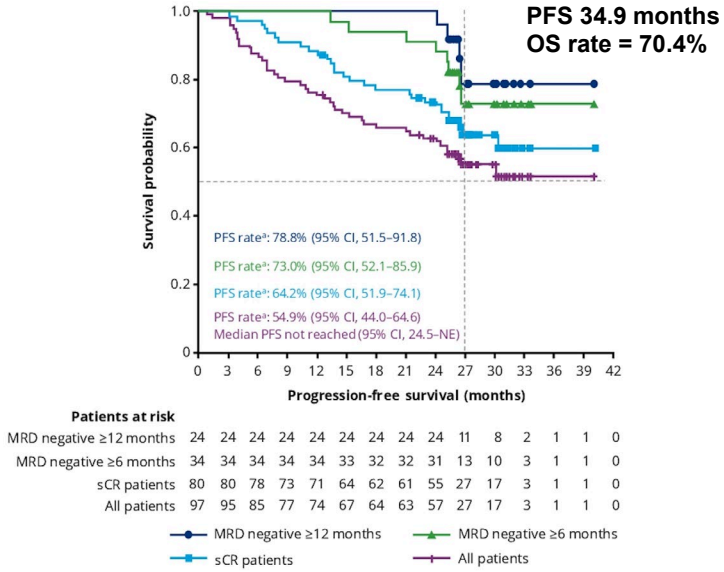
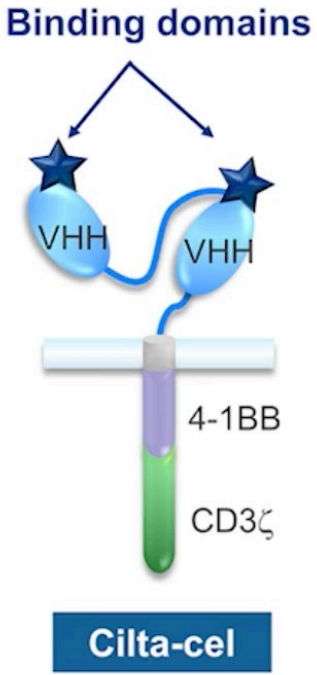
- **Second-generation CAR T cell, 2 anti-BCMA camelid VHH single domains, 4-1BB costimulatory domain**

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



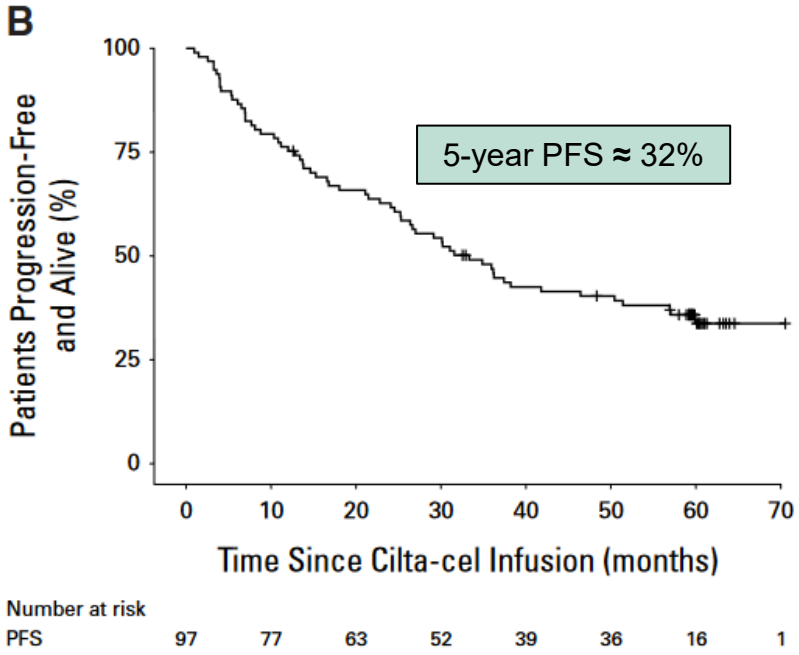


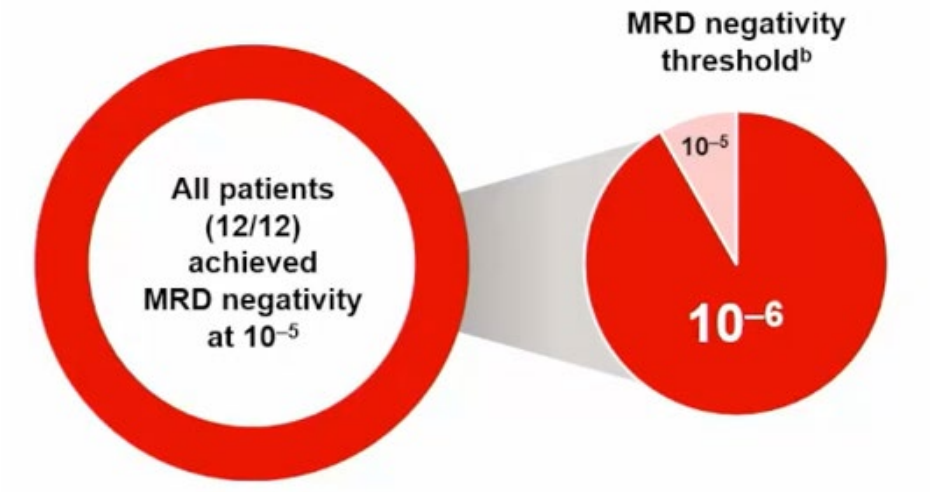


Berdeja J, et al. *Lancet* 2021;398:314-324; Martin T, et al. *J Clin Oncol.* 2022; Usmani S, et al. ASCO 2022. Abstract 8028.

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

Uniklinikum Würzburg





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)

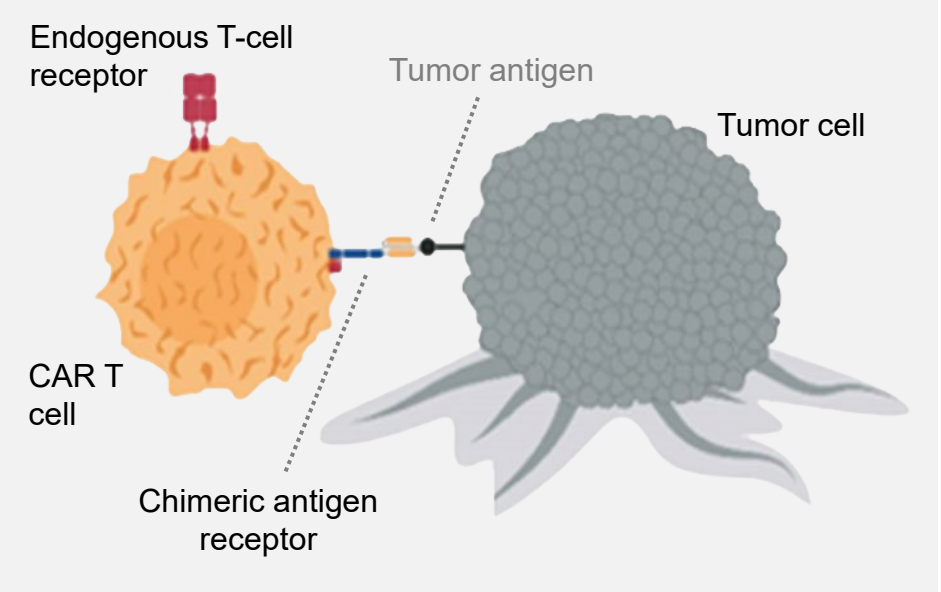
Patients with high-risk cytogenetics and extramedullary plasmacytomas were equally likely to be progression-free. Of note, the percentage of patients with high tumor burden was numerically lower among patients who were progression-free

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!

Uniklinikum Würzburg

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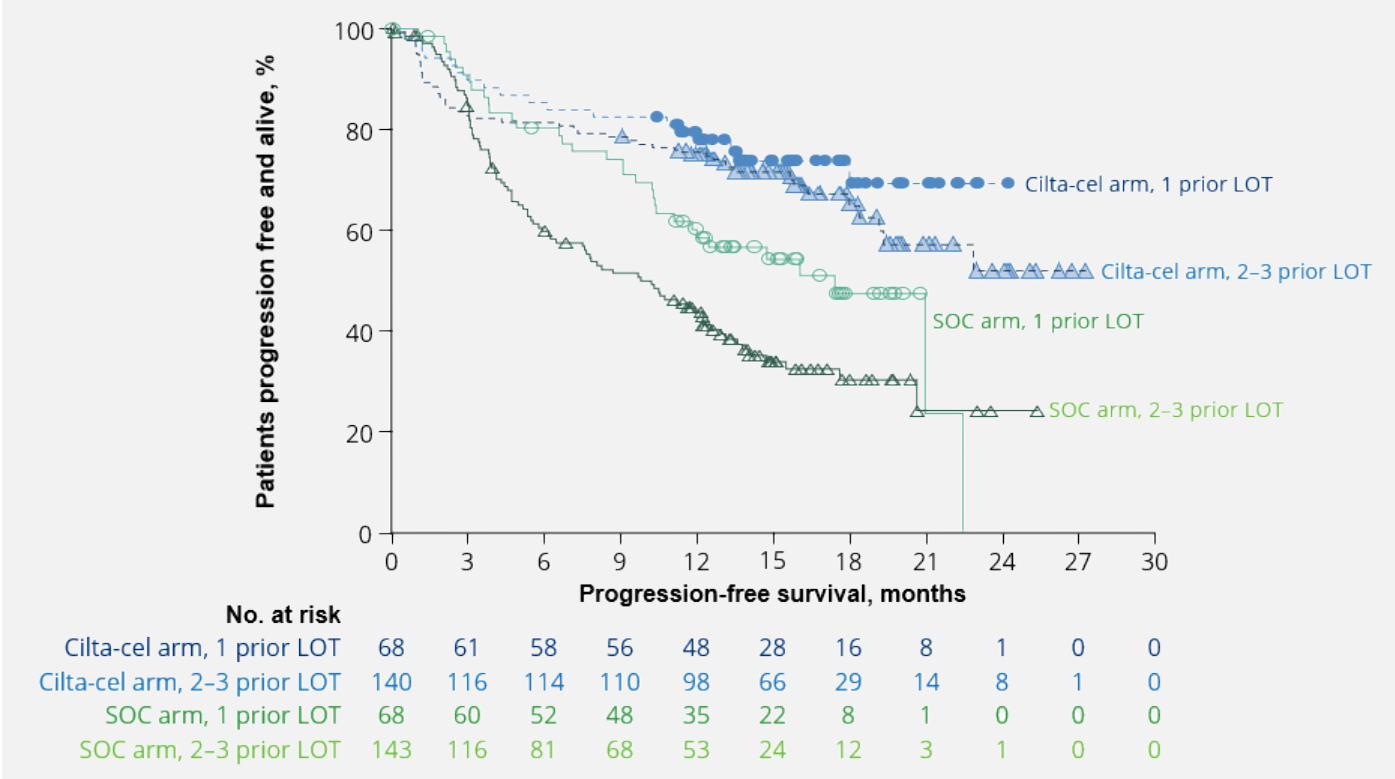
Progression-free survival by treatment and number of prior lines in the ITT set



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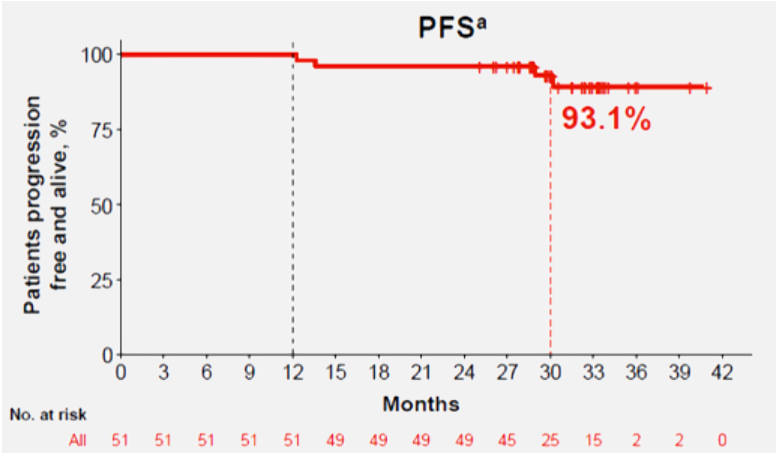
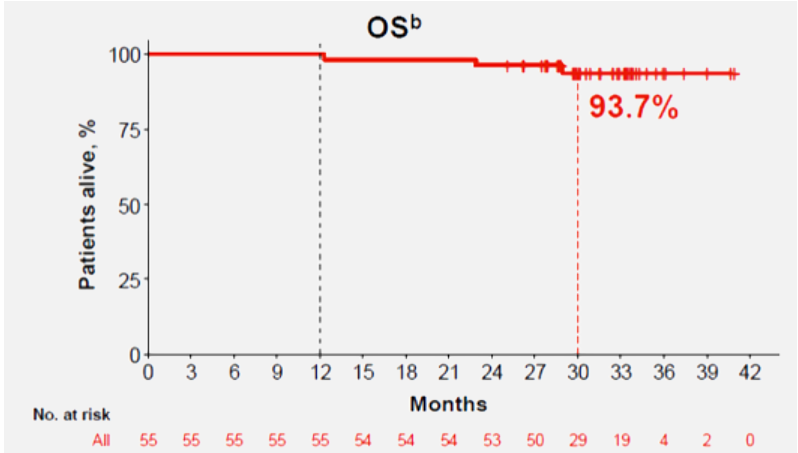
- 86% (51/59) of patients with standard-risk cytogenetics were progression free and alive ≥1 year
  - PFS and OS rates were **~93% at 30 months** for these patients with early sustained responses





- 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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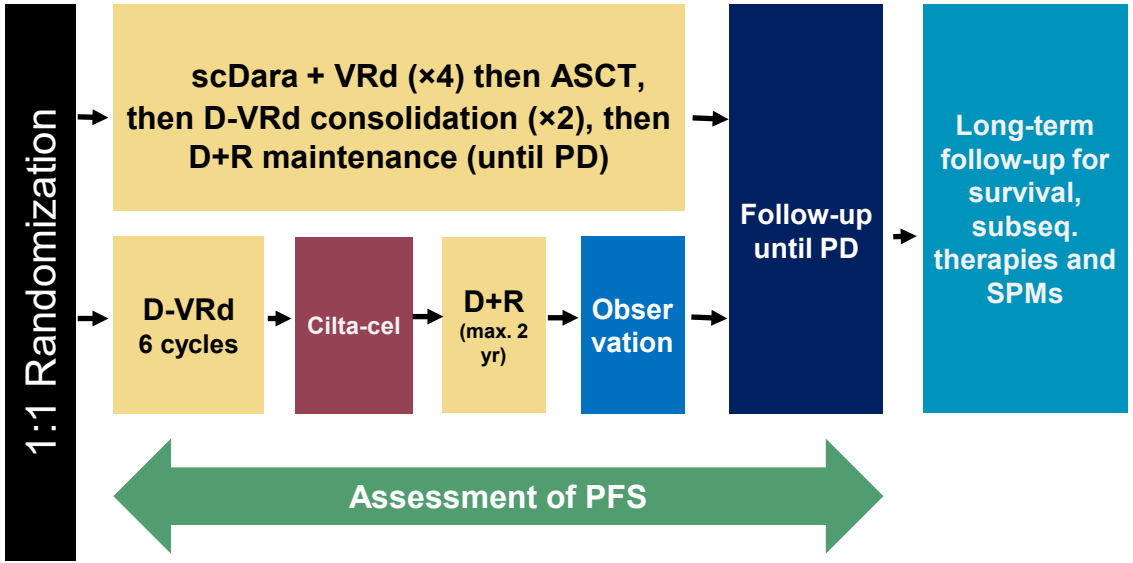
CARTITUDE-6

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

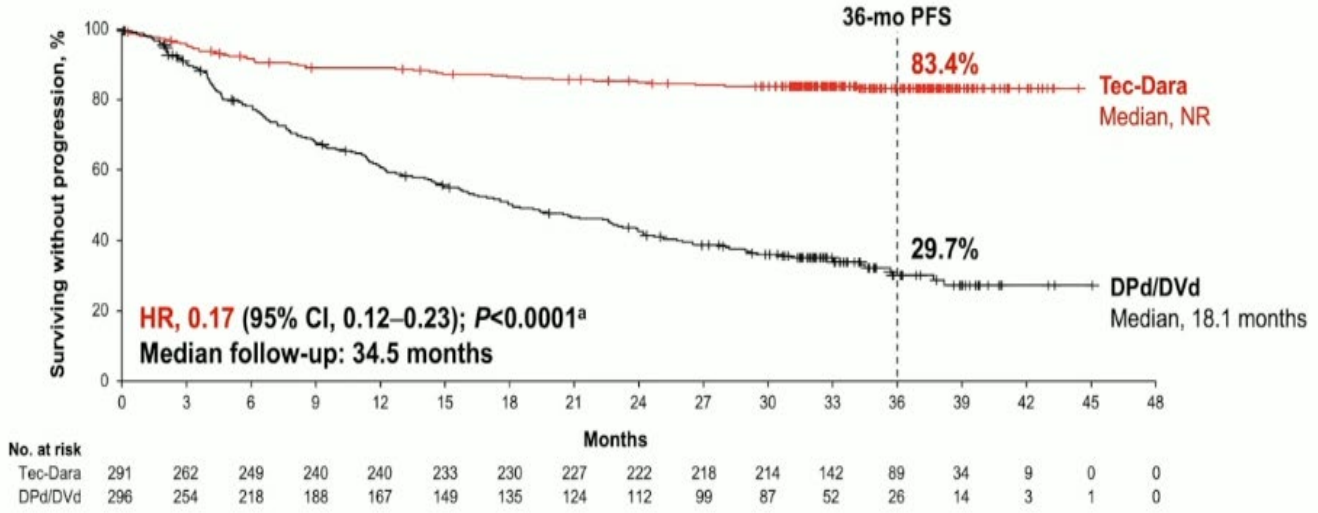
1. Moreau et al NEJM 2022.; 2. Van de Donk et al ASCO 2023, 3. Bahlis et al Nat Med 2023; 4. Lesokhin et al Nat Med 2023; 5. Lee et al J ASCO 2023 ; 6 Wong et al ASH 2022 ; 7. Barr ASH2023, abstract # 2011; 8. D'Souza A J Clin Oncol 2022

Bahlis N, et al. ASH 2023.

Significant Improvement in the Efficacy of TCE: Combination Therapy

Uniklinikum Würzburg

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

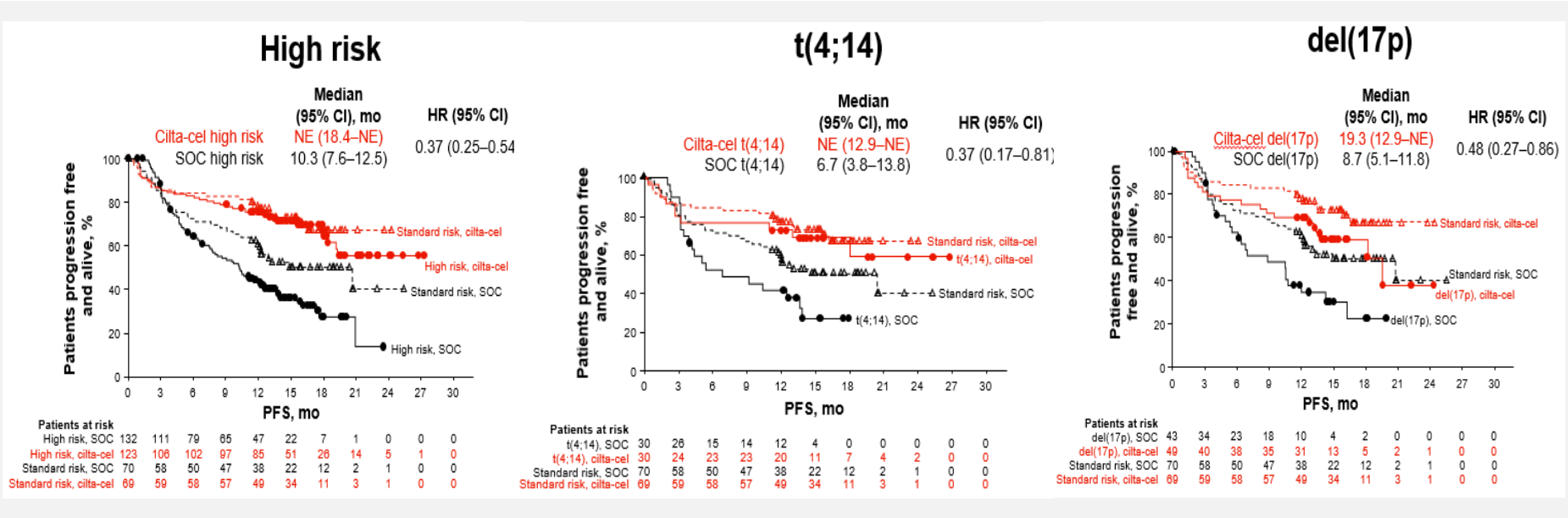
- Allow sufficient washout time for **lymphocytes count recovery and adequate CD4/CD8 ratio prior to apheresis**; may vary between patients (role for IMiDs, CELMoDs, stem cell boost?) → **Optimal CAR T product**

- 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?

Uniklinikum Würzburg

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



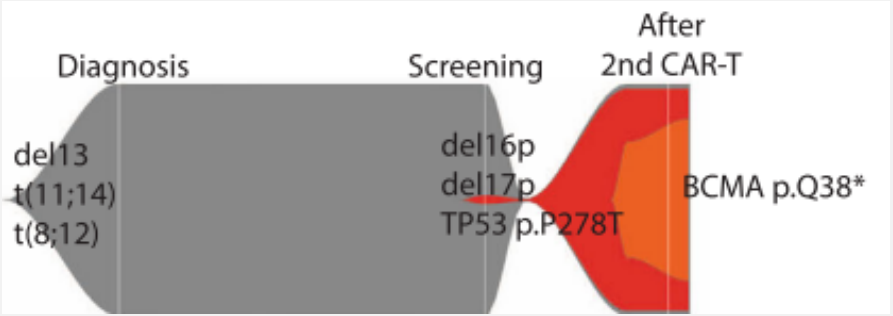
Presented by H Einsele at the Annual Meeting of the German, Austrian and Swiss Associations of Hematology and Medical Oncology (DGHO); October 11–14, 2024; Basel, Switzerland

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

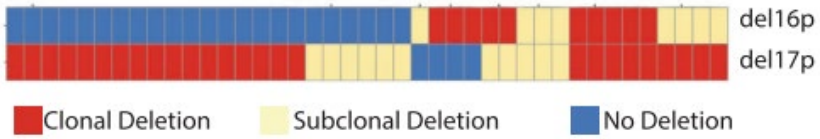
Uniklinikum Würzburg

Tumor-intrinsic changes

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



Patients with NDMM



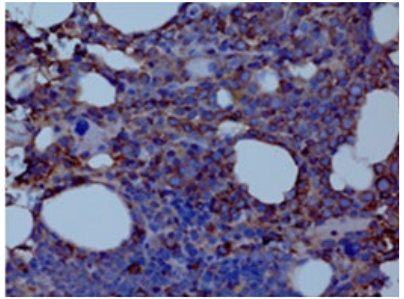
Co-occurrence of HR cytogenetics (del17p, del1p), and del16p (encoding BCMA)

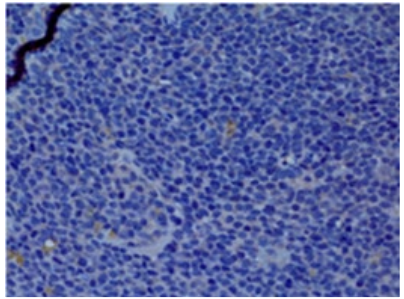
Samur MK, et al. *Nat Commun.* 2021;12:868.

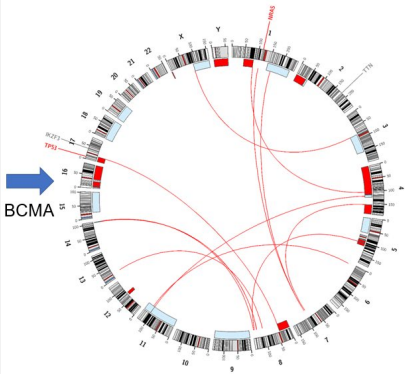
Single Epitope-Targeting Immunotherapies, Especially in RRMM
BCMA Antigen Escape Due to Genetic Instability

Uniklinikum Würzburg

BCMA CAR T cells



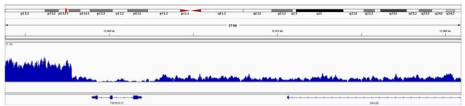




Whole-genome sequencing

4%–6% irreversible BCMA loss

Biallelic deletion TFRSF17



BCMA-targeting TCE

BCMA antigen escape = 15/29 (51%)

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

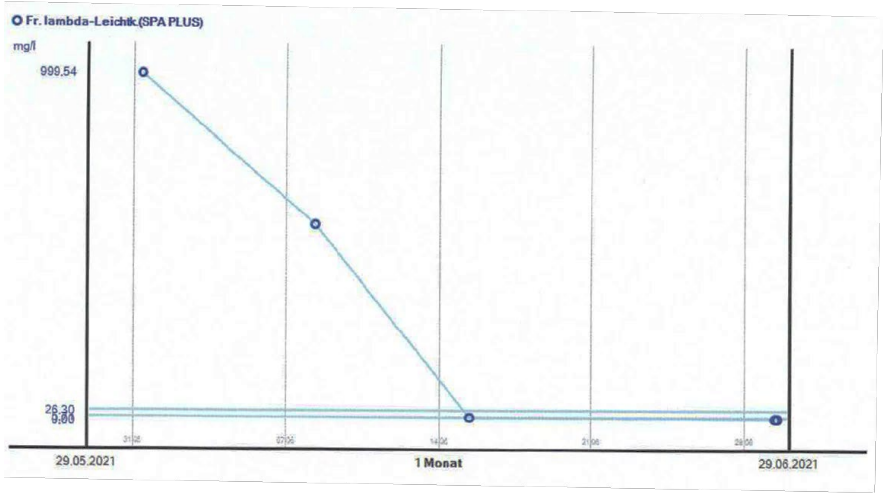
Lee H, et al. ASH 2024.

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

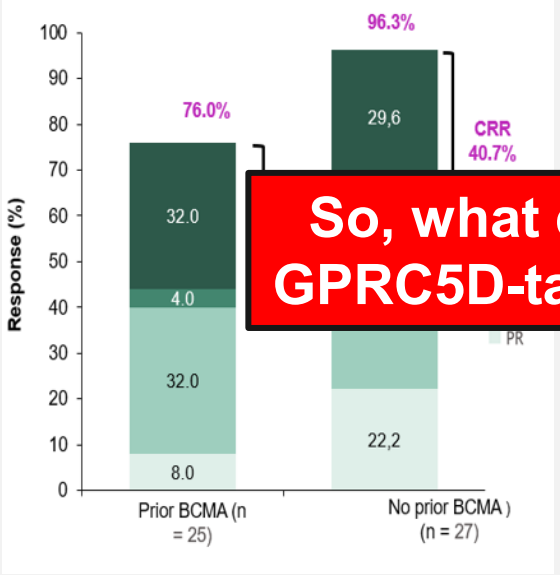
After 15 mo PD!

Personal treatment experience.

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

Uniklinikum Würzburg

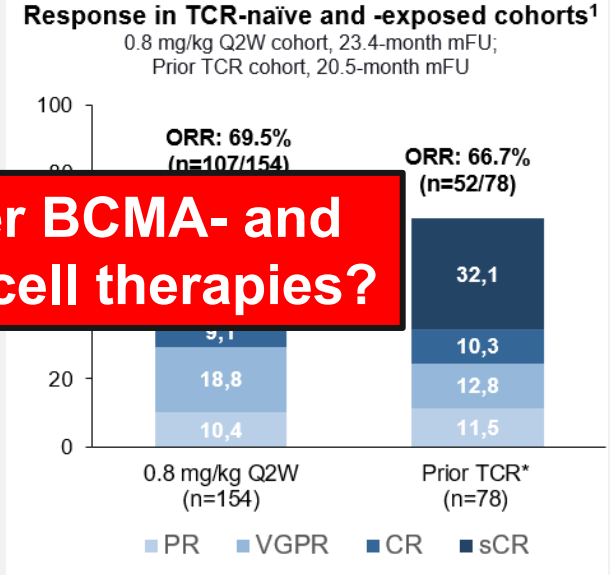
Arlo-Cel for RRMM (no/prior BCMA)



Bal S, et al. ASH 2024.

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

Talquetamab for RRMM (no/prior BCMA)

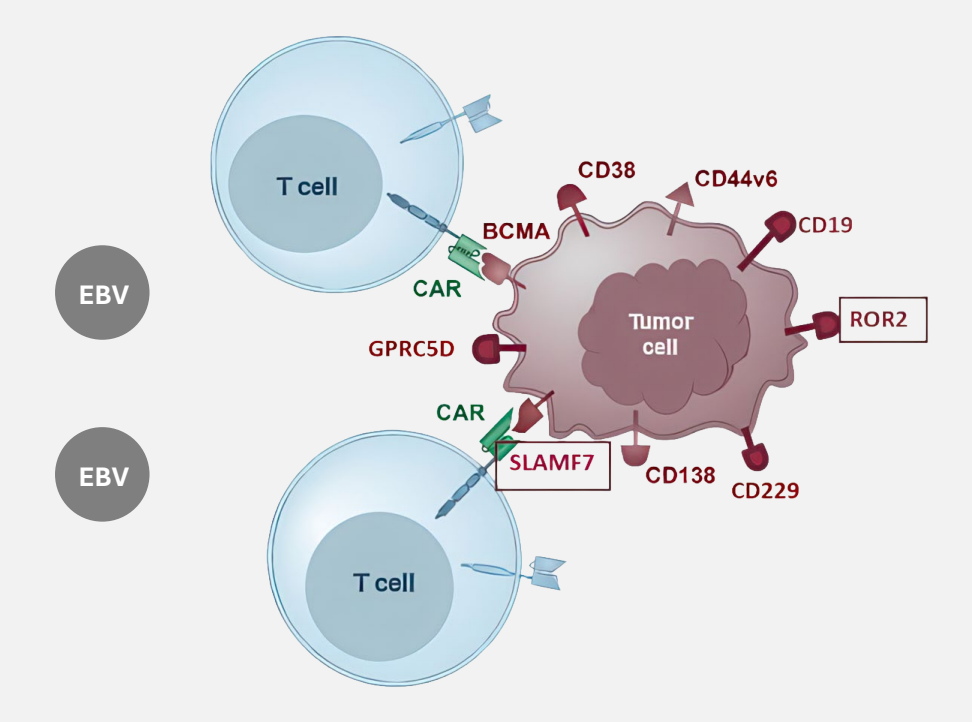


Chari A, et al. *Lancet Haematol.* 2025.

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

Uniklinikum Würzburg

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.

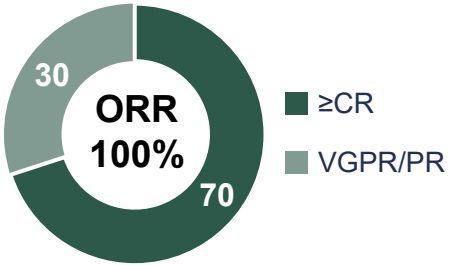
Munshi NC, et al. *N Engl J Med.* 2021.

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

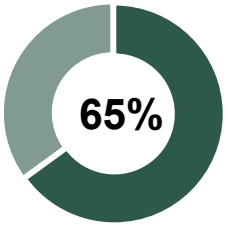
Uniklinikum Würzburg

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

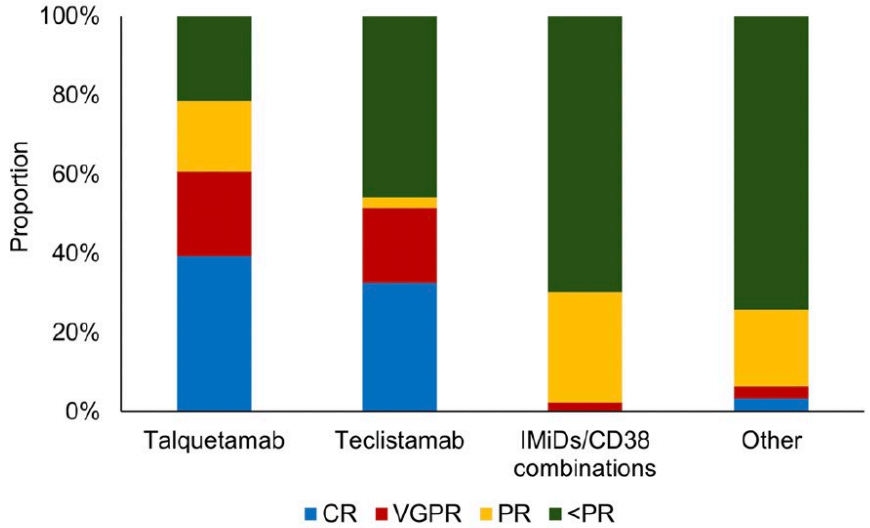
The Majority of Patients Have Relapse After CAR T/TCE Therapy How to Treat These Patients?

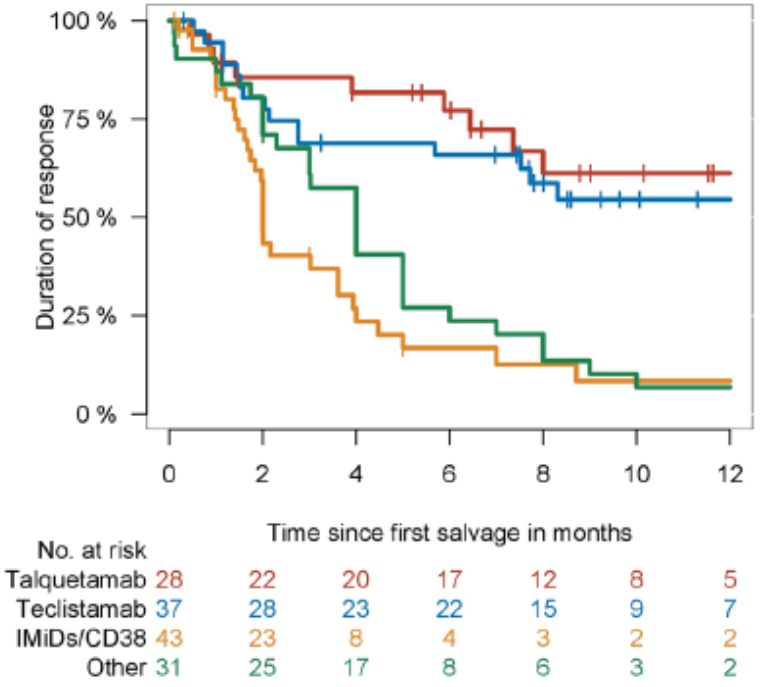
Uniklinikum Würzburg

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

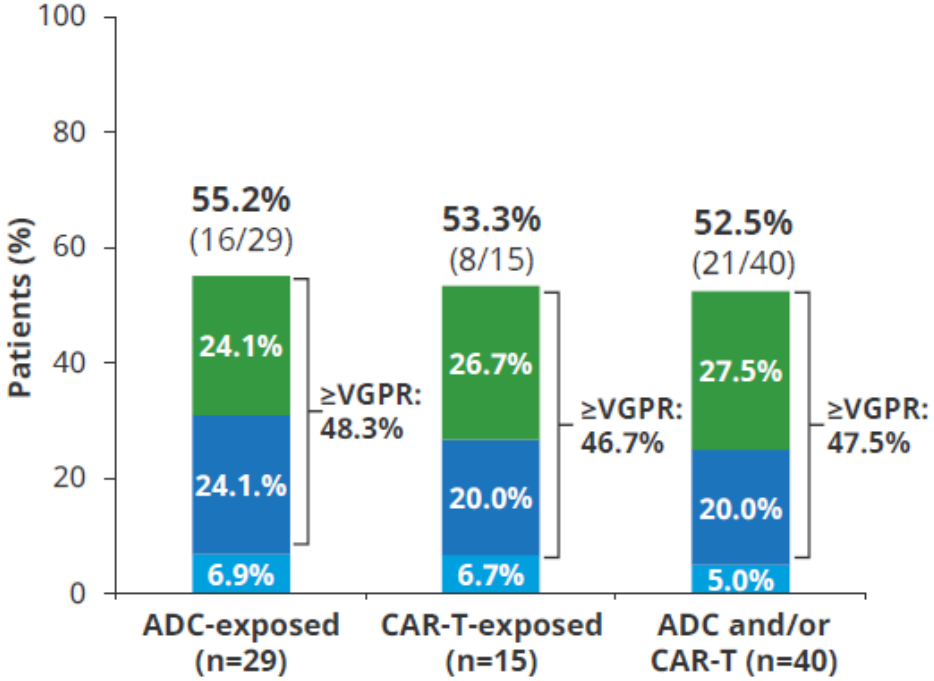
Uniklinikum Würzburg

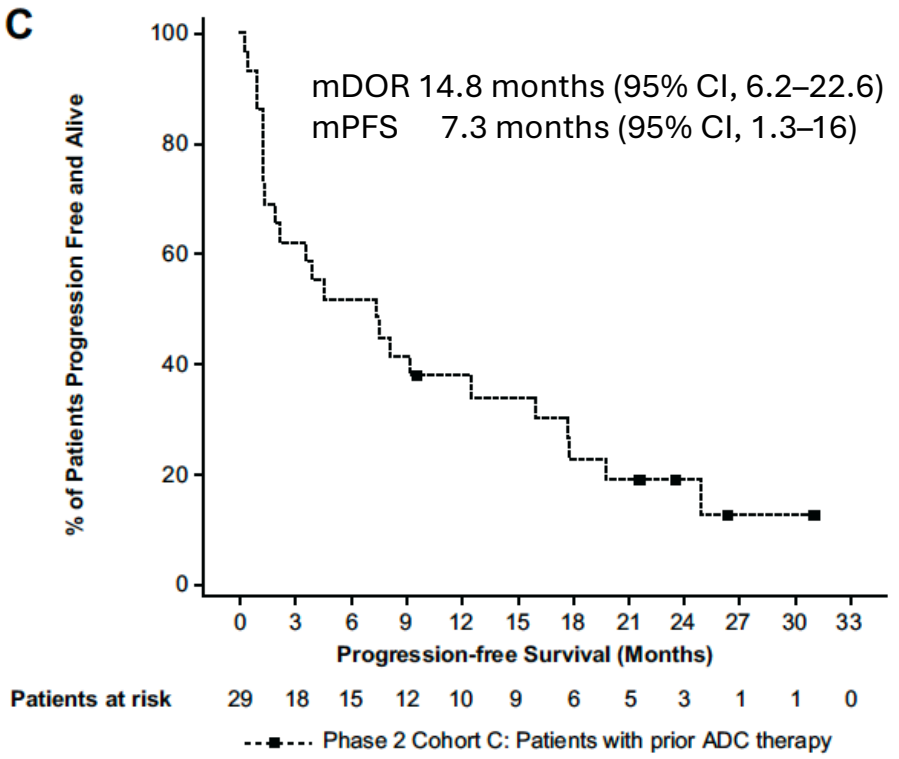




Merz M, et al. *Blood Cancer J.* 2024;14:214.

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

Uniklinikum Würzburg

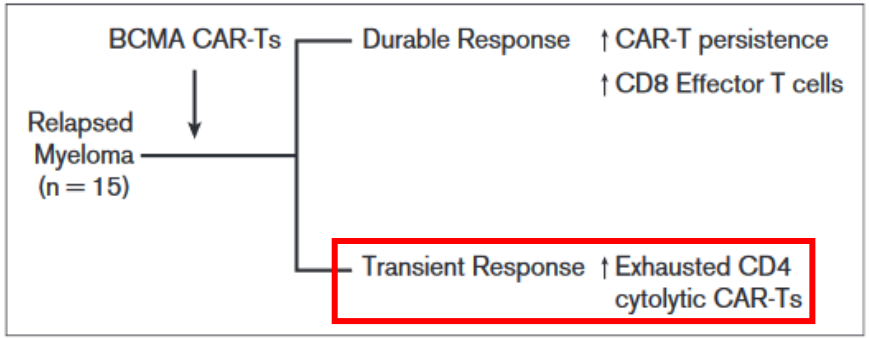
61 yo, IgA lambda (SMM, ED 2005), FISH: t(4;14)

	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

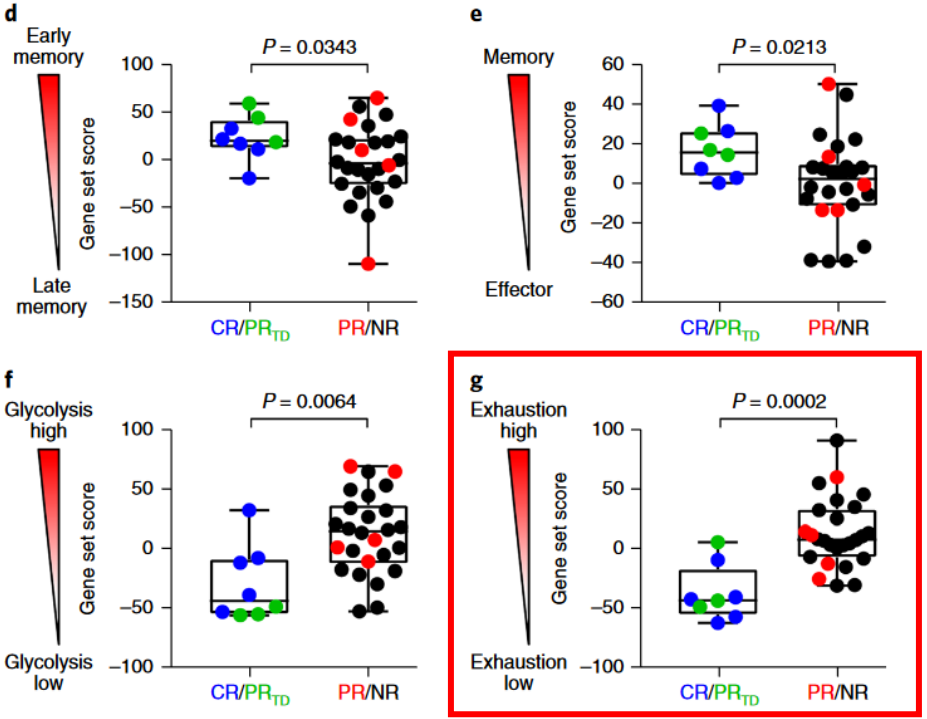
Transcriptional profiles of CAR T cells associated with clinical response

Uniklinikum Würzburg



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

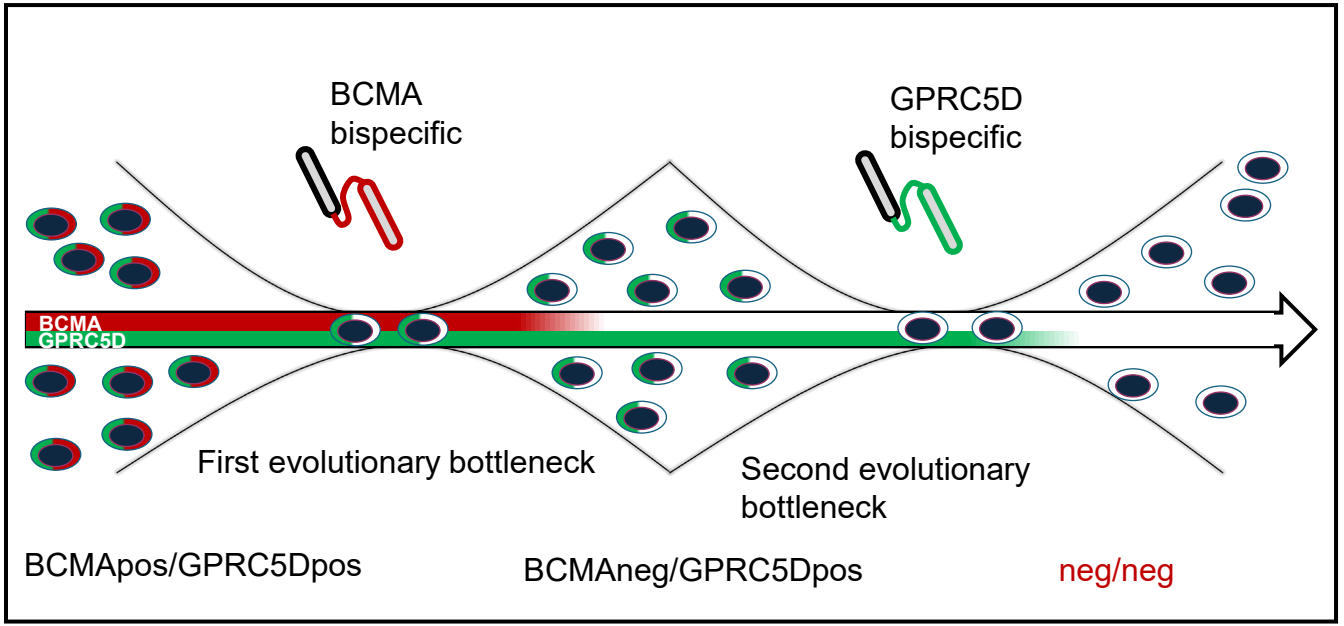
Dhodapkar MV, et al. *Blood Adv.* 2024.



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

Uniklinikum Würzburg

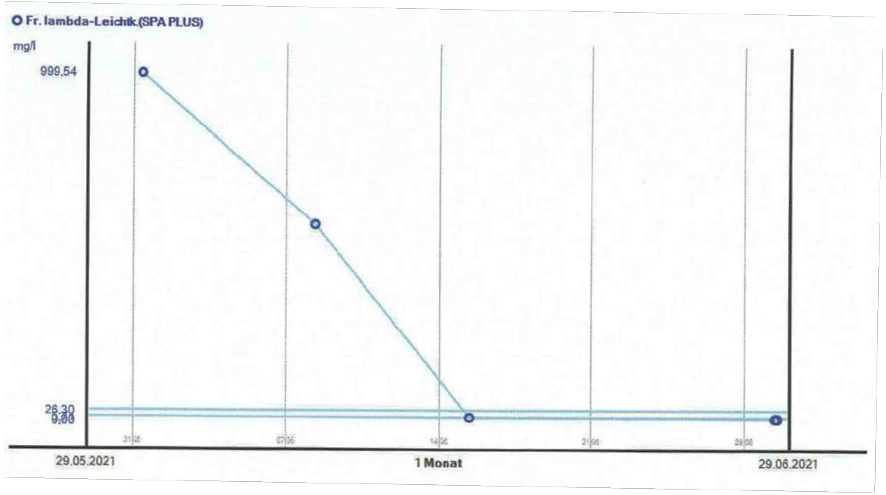
- **Confirm retained target expression** (FCM and/or NGS)
- **Ensure adequate absolute CD3 T-cell count** (CD8 Tem)
- Sequential treatment with anti-BCMA CAR T → TCE or TCE → TCE can yield durable responses if adequate T-cell count (Tem)
- Switching targeted antigen with talquetamab if TNFRSF17 mutational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

Patient Case 1 (cont.)

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

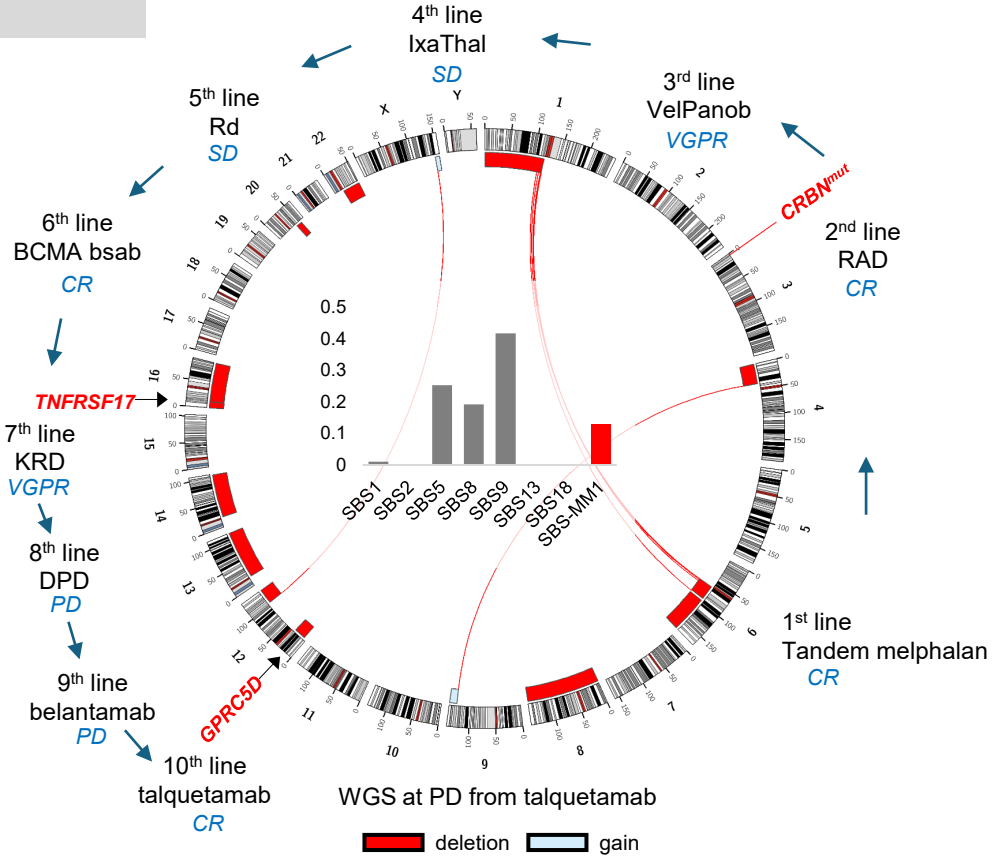
(documented irreversible BCMA loss)

12/20	VTD-PACE 3× → PD

After 15 mo PD!

Personal treatment experience.

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)

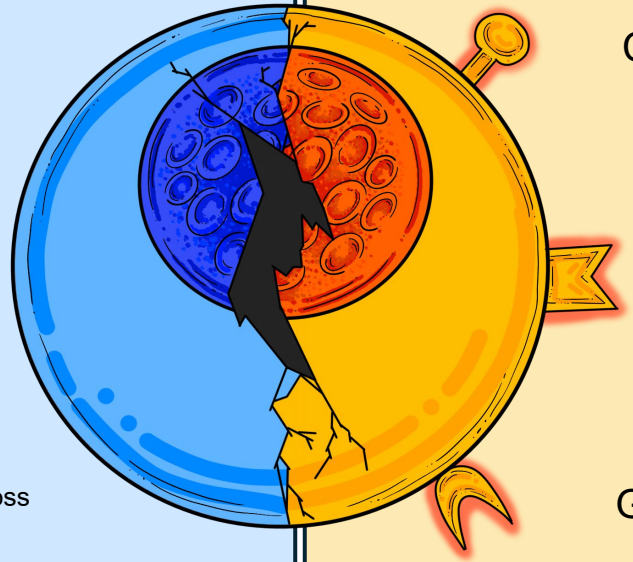
~~BTZ~~ ~~CFZ~~ ~~Len/Thal~~ ~~Pom~~ ~~CD38~~ ~~BCMA TCE/CAR T~~ ~~GPRC5D TCE~~

43% Loss of ≥1 key Ag

$CD38^{loss}$ 12%

$BCMA^{loss}$ 42%

$GPRC5D^{loss}$ 35%



57% wildtype Ag

$CD38^{WT}$

$GPRC5D^{WT}$

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

Uniklinikum Würzburg

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!

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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

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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 – Asia

17.00 – 20.00 (China Standard Time)/3.00 AM – 6.00 AM (Mountain Standard Time)

Time (CST/MST)	Topic	Speaker
17.00 – 17.10 3.00 AM – 3.10 AM (10 min)	**Welcome and Meeting Overview**	Rafael Fonseca, MD; Wee Joo Chng, MB ChB, PhD, FRCP (UK), FRCPath (UK), FAMS
17.10 – 17.30 3.10 AM – 3.30 AM (20 min)	**Overview of RRMM Treatment: Early Lines of Therapy**	Wee Joo Chng, MB ChB, PhD, FRCP (UK), FRCPath (UK), FAMS
17.30 – 17.55 3.30 AM – 3.55 AM (25 min)	**CAR T-Cell Therapy in RRMM: Impact of Earlier Use and Real-World Data**	Juan Du, MD, PhD
17.55 – 18.20 3.55 AM – 4.20 AM (25 min)	**Treatment Options for Non–CAR T-Cell Candidates** • Optimal use of treatment choices in RRMM (15-min presentation; 10-min discussion)	James Chim, MBChB, MD, PhD, MRCP, FRCP, FACP, FRCPath, FFSc, FAcadTM, FHKCP, FHKAM
18.20 – 18.30 4.20 AM – 4.30 AM (10 min)	**Break**	
18.30 – 19.25 4.30 AM – 5.25 AM (55 min)	**Patient Case Discussion: RRMM**	Regional case presentation All faculty
19.25 – 19.55 5.25 AM – 5.55 AM (30 min)	**Future Directions in Early Lines of Therapy for RRMM**	María-Victoria Mateos, MD, PhD
19.55 – 20.00 5.55 AM – 6.00 AM (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!

Pfizer

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