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

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

Question 1

In which country do you currently practice?

1. China
2. Japan
3. Australia
4. New Zealand
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 have you treated using CAR T-cell therapy?

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

Question 3

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

1. True
2. False

Question 4

What is the primary mechanism of action for CELMoDs?

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

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Overview of RRMM Treatment: Early Lines of Therapy

Wee Joo Chng, MB ChB, PhD, FRCP, FRCPath, FAMS

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National University Cancer Institute Singapore

Overview of RRMM: Early Lines of Therapy

Professor Chng Wee Joo

Yong Loo Lin Professor in Medical Oncology

Vice President (Biomedical Science Research)

Office of Deputy President (Research and Technology)

National University of Singapore (NUS)

Senior Consultant

National University Cancer Institute, Singapore

National University Health System

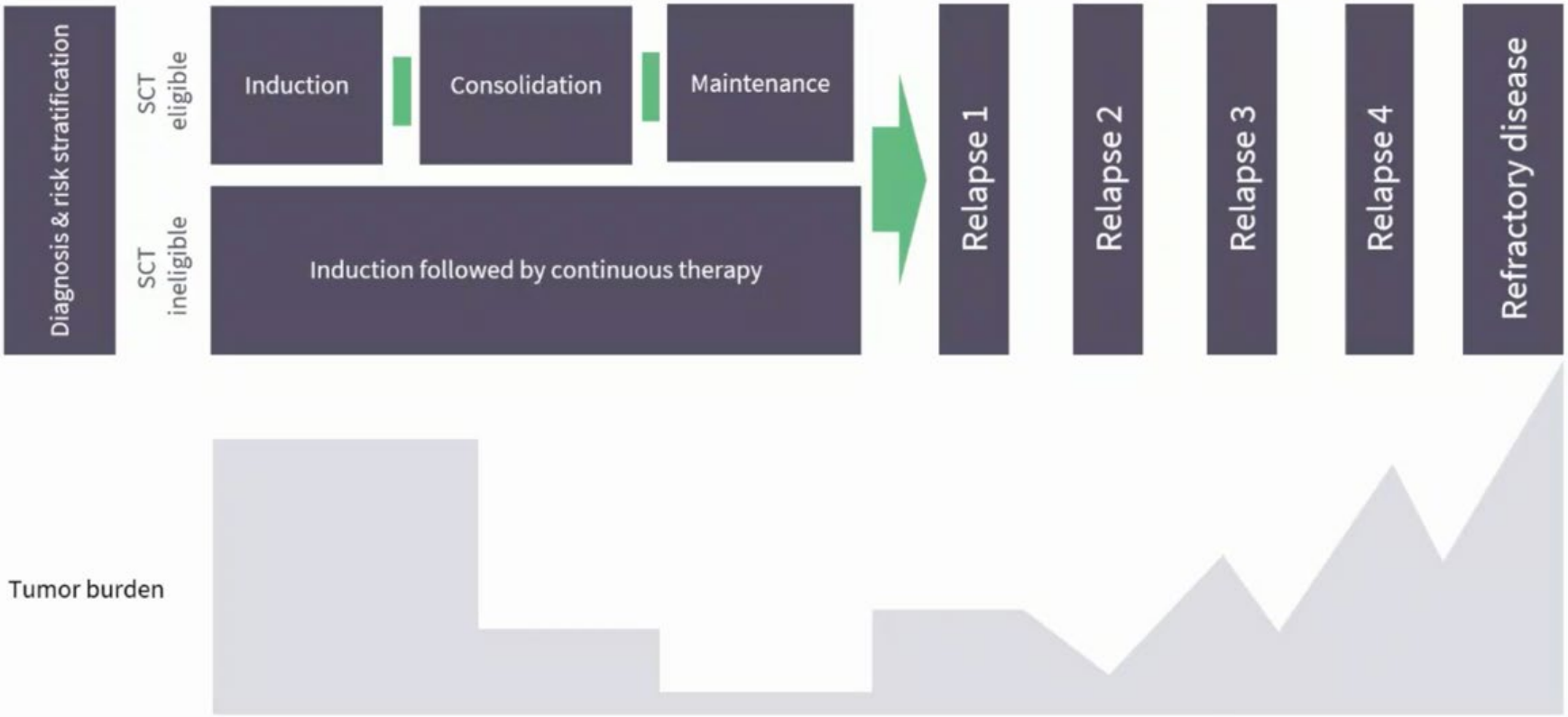
Disclaimer

Any views or opinions expressed herein are solely those of the author/speaker and do not necessarily represent those of any company.

Disclosures

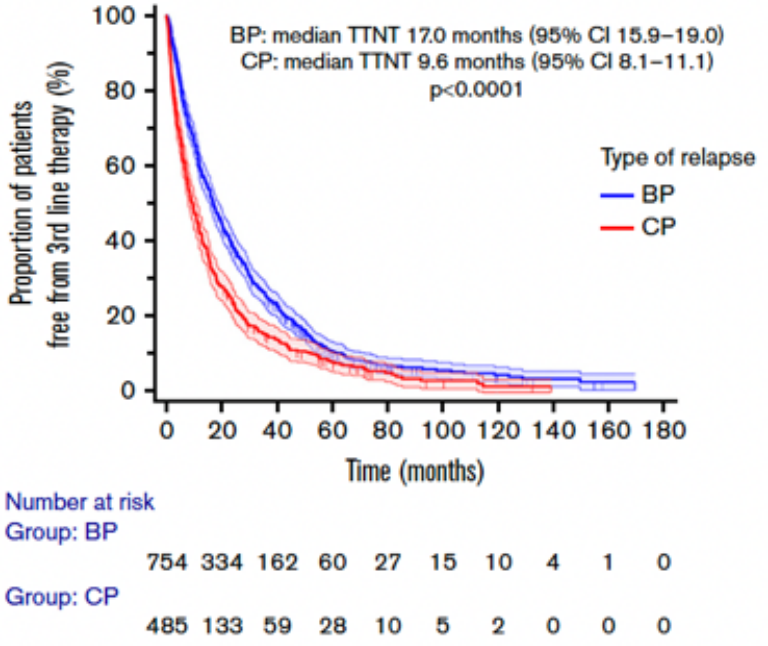
Name of Company	Advisory Board	Honoraria	Research Funds
Amgen	x	x	
Janssen	x	x	x
Celgene/BMS	x	x	x
Sanofi	x	x	
Takeda	x	x	
GSK	x	x	
Antengene	x	x	
Novartis		x	
Aslan			x

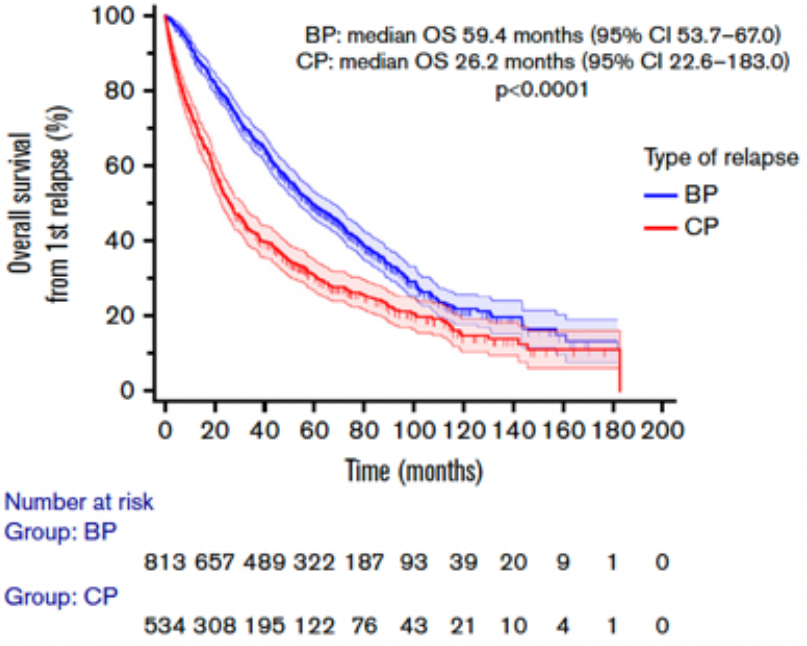
Myeloma treatment paradigm



SCT, stem cell transplant.
Shaji Kumar. Personal communication; Jun 9, 2023

When to treat relapse disease: Biochemical relapse or clinical relapse





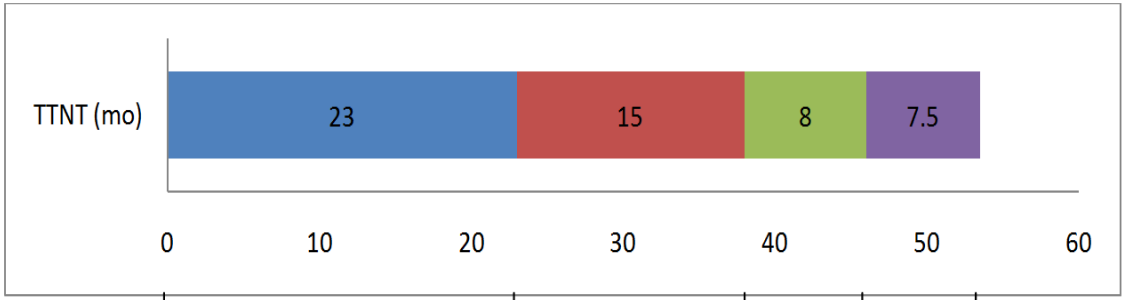
Goldman-Mazur S, et al. *Blood Adv*. 2023.

Optimal choice for relapsed MM? Challenging equation

- **Patient characteristics**: age, comorbidities, PS, renal impairment, frailty
- **Disease characteristics**: aggressive vs biochemical, cytogenetics, extra-medullary disease
- **Frontline therapy**: classes of agents, duration of first response, progression on therapy
- **Drug access**, approval of combinations, reimbursement, cost
- **Patient's choice**

Moreau et al. *Blood Cancer J.* 2019;20;9:38.

Concept 1: Best response and impact in first 1–2 lines



Proportion of patients receiving each line of therapy

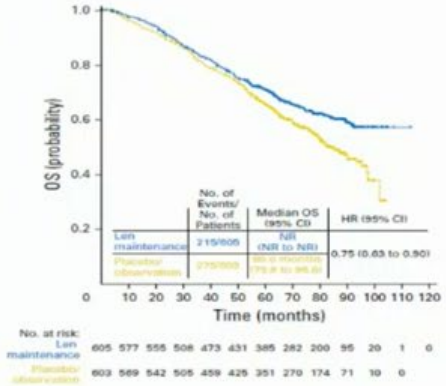
- 1L 100%
- 2L 73.8%
- 3L 45.3%
- 4L 21.0%
- 5L 11.5%

Soekojo et al. Manuscript in preparation.

Line 2 refractory/not refractory to lenalidomide

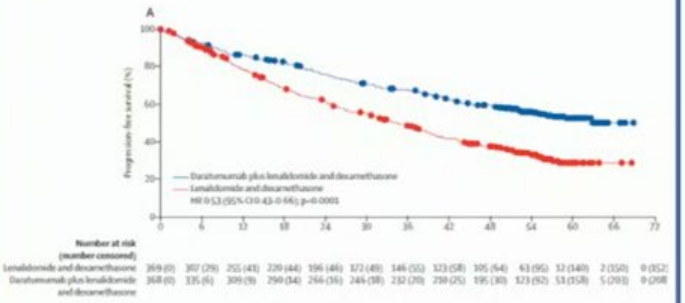
Len given until disease progression in both TE and TNE NDMM patients

Post ASCT maintenance



Mc Carthy et al. J Clin Oncol 2017

DRd



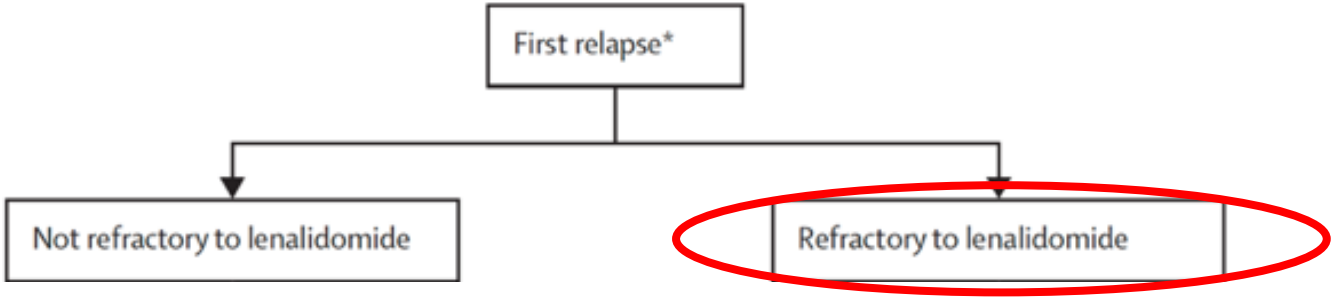
Facon et al. Lancet Oncol 2021

VRd

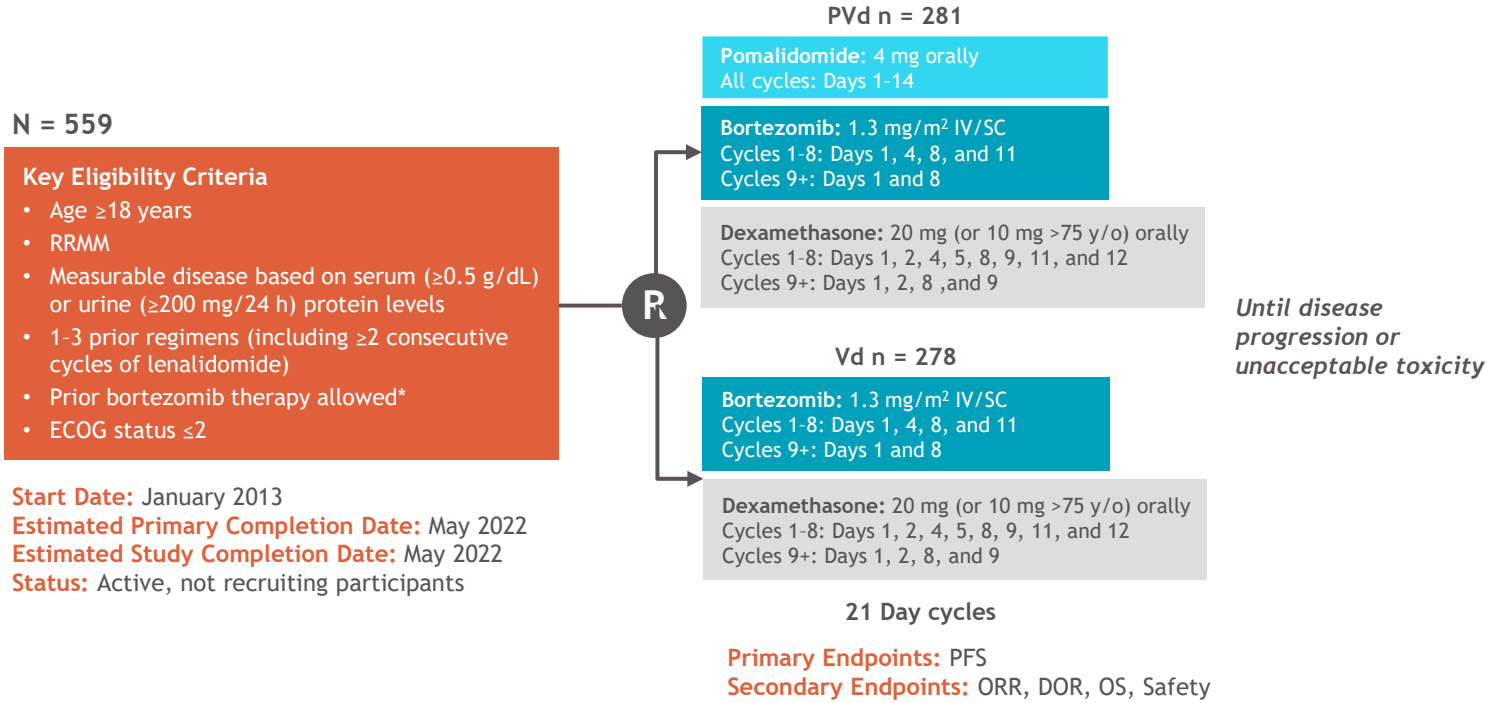
Durie B et al. ASH 2022

-> The majority of patients are becoming len refractory at first relapse

Treatment decision at first relapse

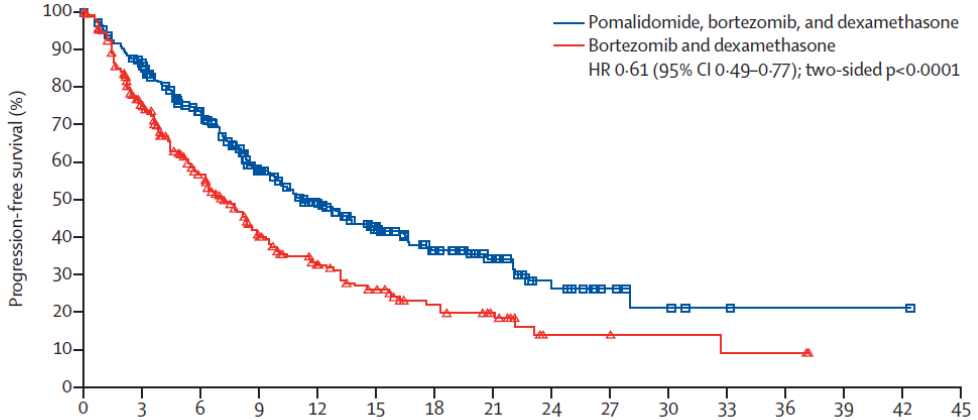


Pomalidomide clinical program: OPTIMISMM – phase III study of PVd vs Vd in RRMM



*Patients with progressive disease during treatment or within 60 days of last dose of bortezomib-containing regimen (dosing schedule 1.3 mg/m^2 twice weekly) were excluded.
DOR, duration of response; h, hours; ORR, overall response rate; OS, overall survival; PFS, progression-free survival; PVd, pomalidomide, bortezomib, and dexamethasone; RRMM, relapsed/refractory multiple myeloma; Vd, bortezomib and dexamethasone; y/o, years old.
Clinicaltrials.gov. NCT01734928; Richardson PG, et al. *Lancet Oncol*. 2019;20:781-794.

Pomalidomide clinical program: OPTIMISMM efficacy results – PFS[1]



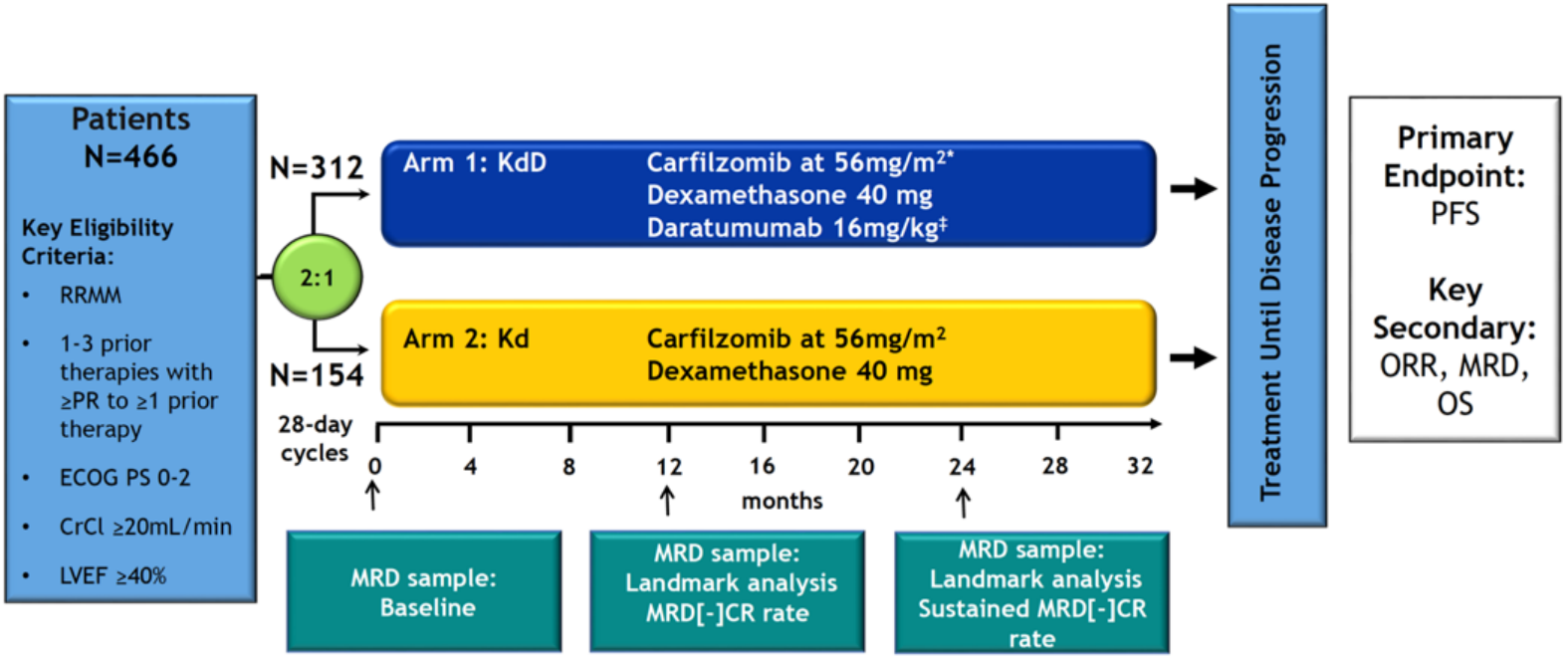
Number at risk (number censored)																
Pomalidomide, bortezomib, and dexamethasone	281	233	182	128	94	67	47	28	13	7	4	2	1	1	1	0
	(0)	(11)	(28)	(46)	(62)	(76)	(88)	(105)	(115)	(121)	(123)	(125)	(126)	(126)	(126)	(127)
Bortezomib and dexamethasone	278	176	112	66	42	30	20	14	4	4	3	2	2	0	0	0
	(0)	(39)	(63)	(79)	(92)	(96)	(102)	(106)	(113)	(113)	(114)	(114)	(114)	(116)	(116)	(116)

- Median follow-up time was 15.9 months (IQR 9.9–21.7)
- Patients treated with PVd had a significantly better PFS than those treated with Vd (median of 11.2 vs 7.1 months respectively, *P* <.0001)

HR, hazard ratio; IQR, interquartile range; PFS, progression-free survival, PVd, pomalidomide, bortezomib, and dexamethasone; Vd, bortezomib and dexamethasone.

1. Richardson PG et al. *Lancet Oncol*. 2019;20:781-794.

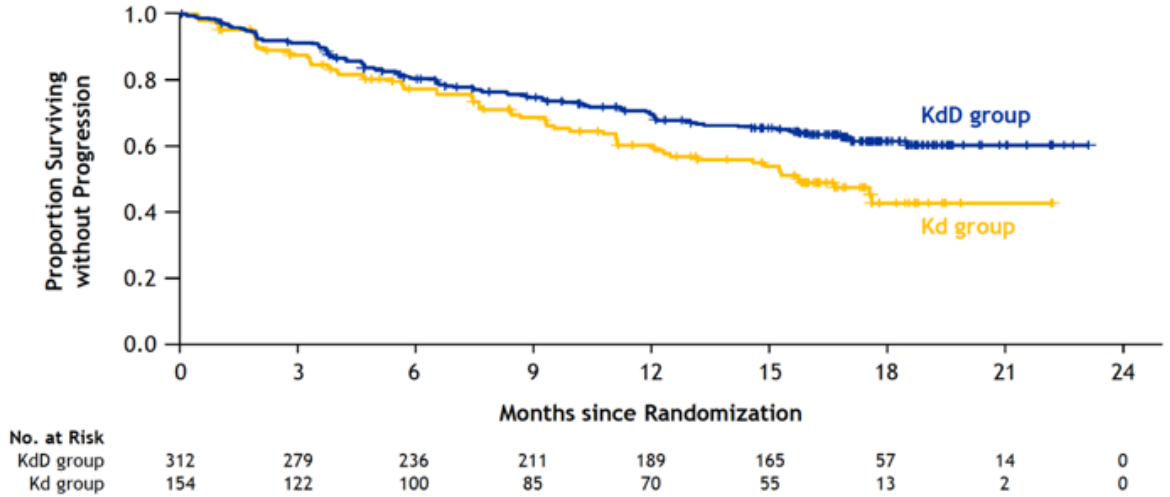
CANDOR study design



*Carfilzomib 20 mg/m² administered on days 1 and 2 of cycle 1 only
‡The first dose of daratumumab is split over two days (8 mg/kg each).
CrCl, creatinine clearance; ECOG PS, Eastern Cooperative Oncology Group Performance Status; LVEF, left ventricular ejection fraction; PD, progressive disease; RRMM, relapsed or refractory multiple myeloma

Dimopoulos et al. *Lancet*. 2020.

Primary endpoint met: KdD significantly prolonged PFS compared with Kd



	KdD (n=312)	Kd (n=154)
Median follow-up time, months	16.9	16.3
Progression/Death, n (%)	110 (35%)	68 (44%)
Median PFS, months	NE	15.8
HR (KdD/Kd) (95% CI)	0.63 (0.46-0.85)	
p-value (1-sided)	0.0014	

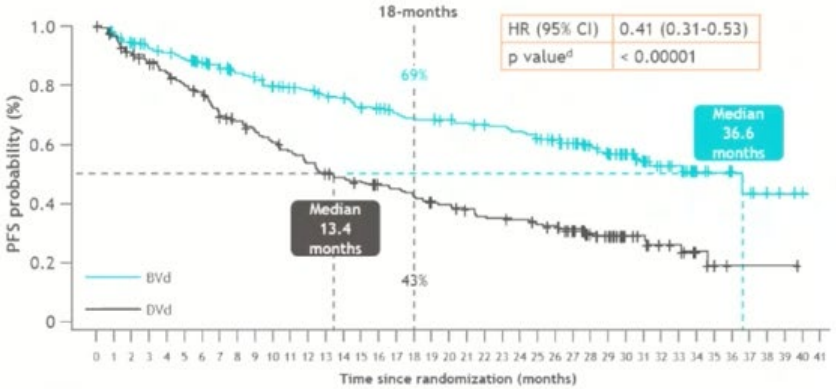
Dimopoulos et al. *Lancet*. 2020.

Phase 3 trials investigating bela-maf combinations in RRMM

EHA 2024 late breaking oral session
Sunday 16 June at 10:00-10:15

DREAMM 7 - BVd vs DVd

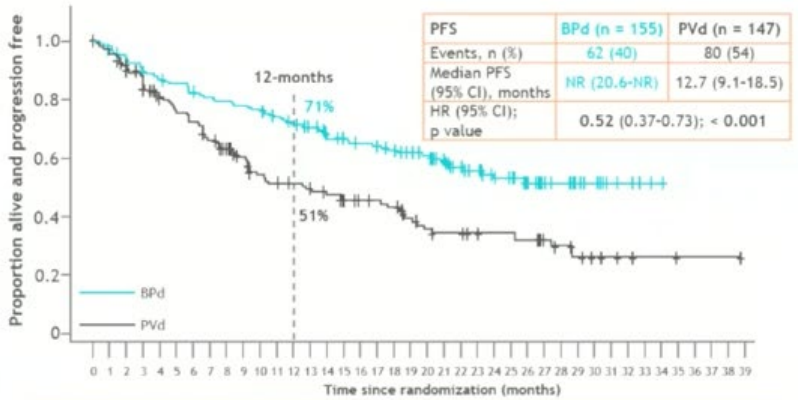
494 patients after a median of 1PL
Len exp/ref: 52%/34% len



- ORR: 83% vs 71%; CR rate: 34% vs 17%
- MRD-ve rate: 39% vs 17%, early benefit in OS as well as DoR
- G3-4 thrombocytopenia: 55 vs 35%
- G3-4 infections: 31 vs 20% (pneumonias: 12 vs 4%)
- All grade ocular toxicity for BVd: 80% and 34% G3-4 (blurred vision: 66 and 22%)
- BVd arm:
  - Dose reductions: 75%; dose interruptions/delay: 94%
  - 9% of patients required to discontinue belamaf

DREAMM 8 - BPd vs PVd

302 patients with ≥ 1PL (median: 1)
Len exp/ref: 100/78%; anti-CD38 exp/ref: 25/22%

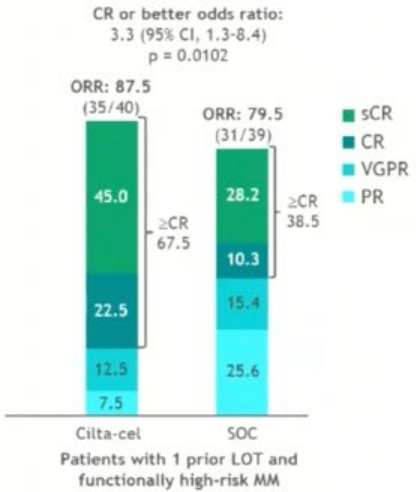


- ORR: 77% vs 72%; ≥CR rate: 40% vs 16%
- MRDng and ≥CR rate: 24% vs 5%, improved DoR, positive trend for OS (not significant, assessment ongoing)
- G3-4 thrombocytopenia: 38% vs 29%; G3-4 infections: 49% vs 26%
- All grade ocular toxicity for BPd: 89% and 43% G3-4 (blurred vision: 79 and 17%)
- BVd arm:
  - Dose reductions: 59%; dose interruptions/delay: 83%
  - 9% of patients required to discontinue belamaf

The mentioned agent/combinations are under investigation and have not been approved by any regulatory authority.

Bela-maf, belantamab mafodotin; BVd, bendamustine + BORT + DEX; DOR, duration of response; DVd, DARA + BORT + DEX; OR, overall survival; PBd, panobinostat + BORT + DEX; PVd, POM + BORT + DEX; PFS2, time from randomization to second disease progression or death. Mateos MV, et al. J Clin Oncol 2024;42(36 Suppl). Abstract 439572; Trudel MV, et al. J Clin Oncol 2024;42(17 Suppl). Abstract LBA105.

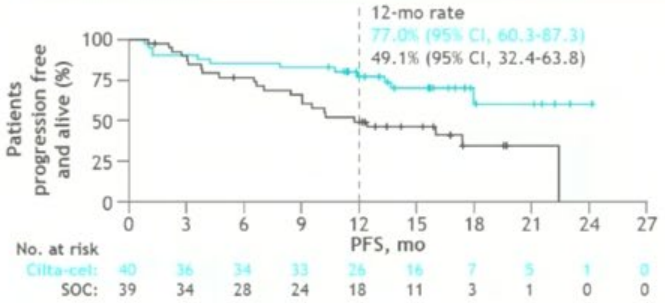
CARTITUDE 4 trial: Early relapses after 1st line of therapy (subgroup analysis)
Cilta-cel vs SoC after initial therapy



65% vs 10.3% of patients achieved MRD-ve
3-5% pt were anti CD38 exposed

Early relapse defined as PD less than 18m after ASCT or from initiation of frontline therapy for MM patients not eligible for ASCT
40 and 39 pts in cilta-cel or SoC, respectively, were functional HR: 2 or more HRCA in near 30% and 10-12% had EMD
Median follow up is 28 months

	Patients with 1 prior LOT and functionally high-risk MM	
	Cilta-cel (n = 40)	SOC (n = 39)
Median PFS (95% CI), mo	NR (18.00-NE)	11.79 (8.44-NE)
HR (95% CI); p value	0.27 (0.12-0.60); 0.0006	



	Patients with 1 prior LOT Cilta-cel (n = 68)		Patients with 1 prior LOT and functionally HR MM Cilta-cel (n = 40)	
	All	Grade ≥3	All	Grade ≥3
AEs of special interest, n (%)				
CRS	44 (64.7)	1 (1.5)	25 (62.5)	0
ICANS	2 (2.9)	0	2 (5.0)	0
CNP	6 (8.8)	2 (2.9)	3 (7.5)	0
MNTs	1 (1.5)	0	0	0
Peripheral neuropathy	2 (2.9)	0	2 (5.0)	0

A single cilta-cel infusion substantially improved PFS and depth of response vs SOC regardless of functionally high-risk MM status in lenalidomide-refractory patients with MM after 1 prior LOT, supporting its potential use in patients who relapse early after initial therapy

Cilta-cel is approved for adult patients with RRMM after ≥ 1 prior LOT, including a PI and Len and are and are refractory to lenalidomide.

AE, adverse event; CI, confidence interval; CRS, cytokine release syndrome; EMA, European Medicines Agency; FDA, Food and Drug Administration; HR, hazard ratio; HRCA, high-risk cytogenetic abnormality; ICANS, immune effector cell-associated neurotoxicity syndrome; NR, not reached; ORR, objective response rate; PD, progressive disease; PFS, progression-free survival; PR, partial response; sCR stringent complete response; SOC, standard of care; VGPR, very good partial response.

Costa L, et al. J Clin Oncol 2024;42(16 Suppl). Abstract 7504.

MajesTEC-3: Phase 3 Study Design

Key inclusion criteria

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

Key exclusion criteria

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

1:1 randomization N=587

22 Oct 2021 to 29 Sept 2023[b]

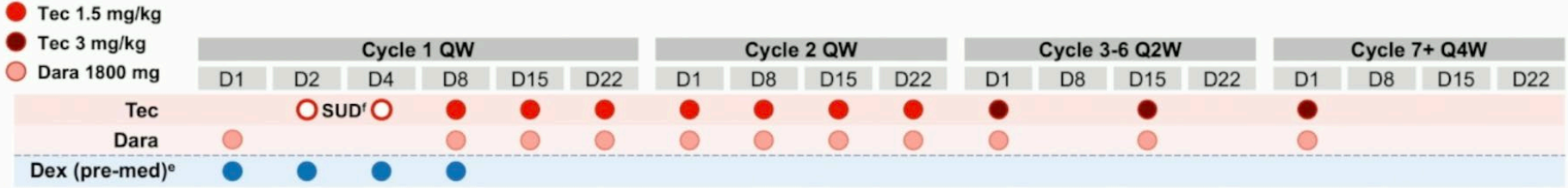
Tec-Dara
N=291
SC dosing following Dara schedule

DPd/DVd
N=296 (91% DPd) by investigator's choice[c]

Primary endpoint
- PFS per IRC

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

Other secondary endpoints
- Safety
- PK and immunogenicity



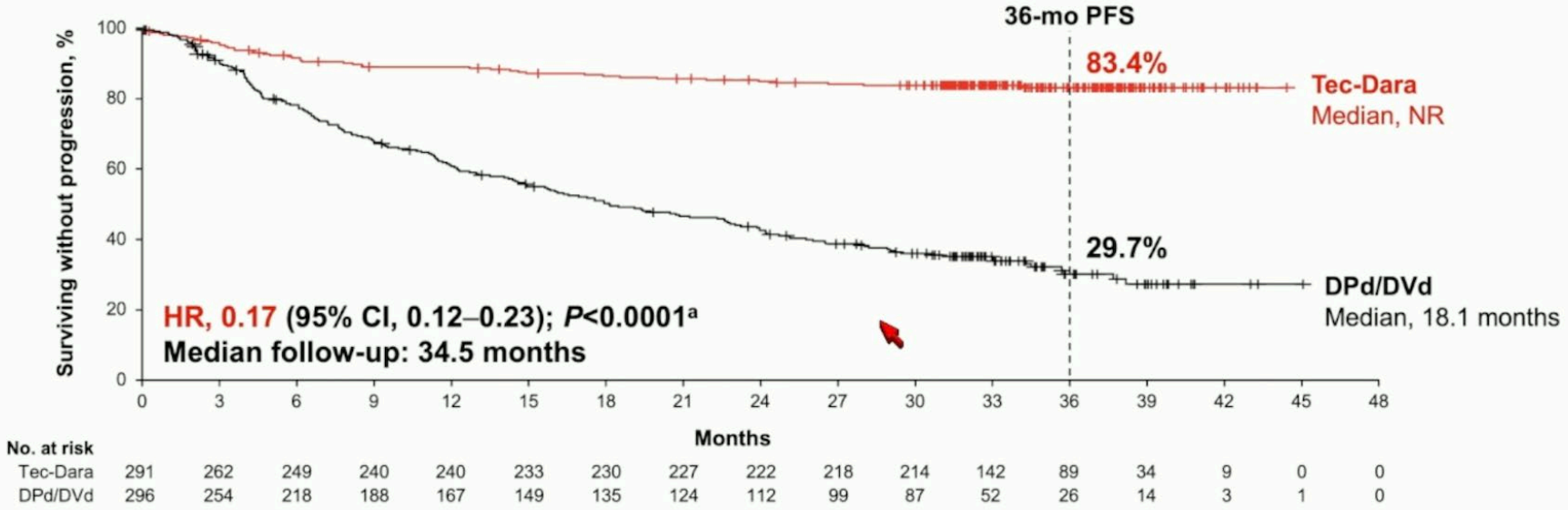
SC dosing aligned with Dara schedule, with monthly dosing after 6 cycles; steroid sparing after Cycle 1 Day 8

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

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

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

MajesTEC-3: PFS (Primary Endpoint)



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

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

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

Lenalidomide refractoriness in early lines

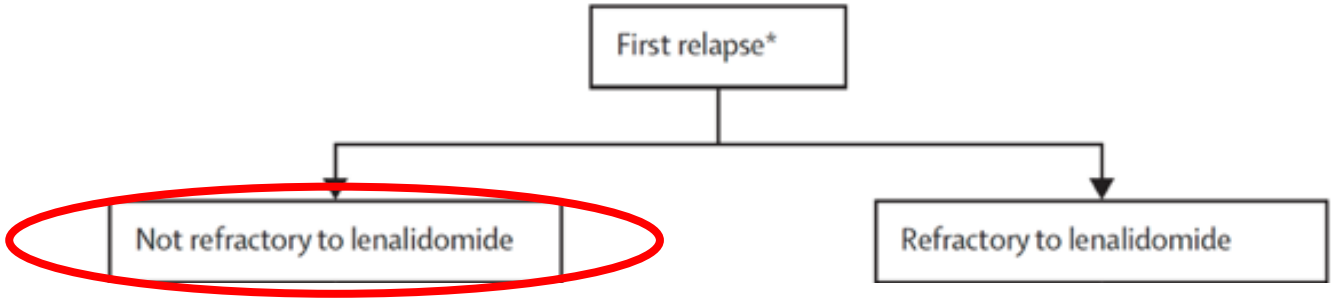
	OPTIMISMM		CANDOR		DREAMM-7		DREAMM-8		MajesTEC-3		CARTITUDE-4	
	PVd	Vd	DaraKd	Kd	BelaVd	DVd	BelaPd	PVd	Tec-Tal	DaraPd/DVd	Cilta-cel	DaraPd/PVd
Len refractory to any prior line, n	120	118	99	55	82	84	125	111	247	253	208	211
Median PFS, months	9.5	5.6	28.1	11.1	36.6	13.4	NR	12.7	NC	NC	NR	11.8
36-month PFS, %	NC	NC	NC	NC	NC	NC	NC	NC	83.4	29.7	NC	NC
Len refractory 1 prior line, n	64	65	19	6	NC	NC	NC	NC	108	114	68	68
Median PFS, months	17.8	9.5	25.0	9.3	NC	NC	NC	NC	NC	NC	NC	NC

Data shown are from independent randomized clinical studies in the relapsed multiple myeloma setting. Eligibility, treatment duration/exposure and other important study design features may differ across the studies, therefore cross-study comparison must be interpreted with caution. Bela, belantamab mafodotin; d, dexamethasone; Dara, daratumumab; Elo, elotuzumab; K, carfilzomib; Len, lenalidomide; NC, not calculated; P, pomalidomide; PFS, progression-free survival; UK, unknown; V, bortezomib.

Dimopoulos MA, et al. *Leukemia*. 2021;35:1722-1731; Dimopoulos MA, et al. *Lancet*. 2020;396(10245):186-197; Usmani SZ, et al. *Lancet Oncol*. 2022;23(1):65-76; Hungria V, et al. *Lancet Oncol*. 2025;26(8):1067-1080; Dimopoulos MA, et al. *Lancet Haematol*. 2025;12(11):e876-e886; Mateos M-V, et al. *Blood*. 2025;146(suppl 2):LBA6. Presented at ASH 2025; Einsele H, et al. ASCO Post. Jan 2026; San-Miguel J, et al. *N Engl J Med*. 2023;389:335-347.

*Please note these data are presented side by side for information, but cannot be formally compared due to differences in study design.

Treatment decision at first relapse



Lenalidomide-based studies

	POLLUX DRd vs Rd	ASPIRE KRd vs Rd[1]	ELOQUENT-2 ERd vs Rd[2,3]	TOURMALINE-MM1 IRd vs Rd[4]
PFS HR (95% CI)	0.37 (0.27-0.52)	0.69 (0.57-0.83)	0.73 (0.60-0.89)	0.74 (0.59-0.94)
ORR	93%	87%	79%	78%
≥VGPR	76%	70%	33%	48%
≥CR	43%	32%	4%	14%
Duration of response, mo	NE	28.6	20.7	20.5
OS HR (95% CI)	0.64 (0.40-1.01)	0.79 (0.63-0.99)	0.77 (0.61-0.97)	NE

1. Stewart AK, et al. *N Engl J Med*. 2015;372(2):142-152.
2. Lonial S, et al. *N Engl J Med*. 2015;373(7):621-631.
3. Dimopoulos MA, et al. *Blood*. 2015;126(23):Abstract 28.
4. Moreau P, et al. *N Engl J Med*. 2016;374(17):1621-1634.

POLLUX 4-year follow-up
Kaufman et al. ASH 2019. Abstract 1866.

*Please note these data are presented side by side for information, but cannot be formally compared due to differences in study design.

KRd Asia real-word data

Superior outcomes and high-risk features with carfilzomib, lenalidomide, and dexamethasone combination therapy for patients with RRMM

59% patients did not meet the eligibility criteria for the ASPIRE trial

ORR was 90%, with a **VGPR or higher response of 69%**

Median follow-up 34.8 months, **PFS 23.4 months**, OS 69.5 months

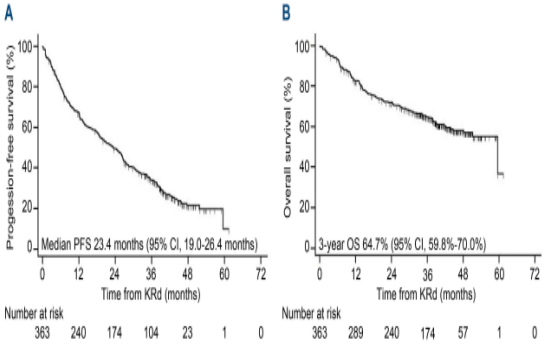
Table 1. Baseline patient demographic, disease, and treatment data

Study design Patient number, n	Current Retrospective 364	ASPIRE Phase III 396
Age, median years (range)	63 (28-85)	66 (38-91)
≥65 years, n (%)	149 (41)	192 (53)
≥75 years, n (%)	26 (7)	
Extramedullary plasmacytoma	88 (24)	N/A (at any time)
Paraskeletal	55 (15)	
Soft tissue	32 (9)	
Not specified	1 (0.3)	
Number of prior regimens, median (range)	1 (1-4)	
1 prior regimen, n (%)	311 (85)	224 (62)
2 prior regimens, n (%)	41 (11)	136 (38)
3 prior regimens, n (%)	10 (3)	
4 prior regimens, n (%)	2 (1)	
Prior therapies, n (%)		
Bortezomib	326 (90)	248 (69)
Thalidomide	239 (66)	157 (44)
Lenalidomide	1 (0.3)	44 (12)
Autologous SCT	201 (55)	212 (59)
Allogeneic SCT	4 (1)	
Refractory to bortezomib	120 (33)	4 (1)
Refractory to thalidomide	92 (25)	
Time from diagnosis to KRd treatment, median, months (range)	25.0 (1.1-183.8)	44.2 (3-281)

Abbreviations: n, number; ECOG PS, Eastern Cooperative Group Performance Status; ISS,

Table 2. Comparison of the effectiveness and efficacy of KRd treatment from current and phase II ASPIRE study

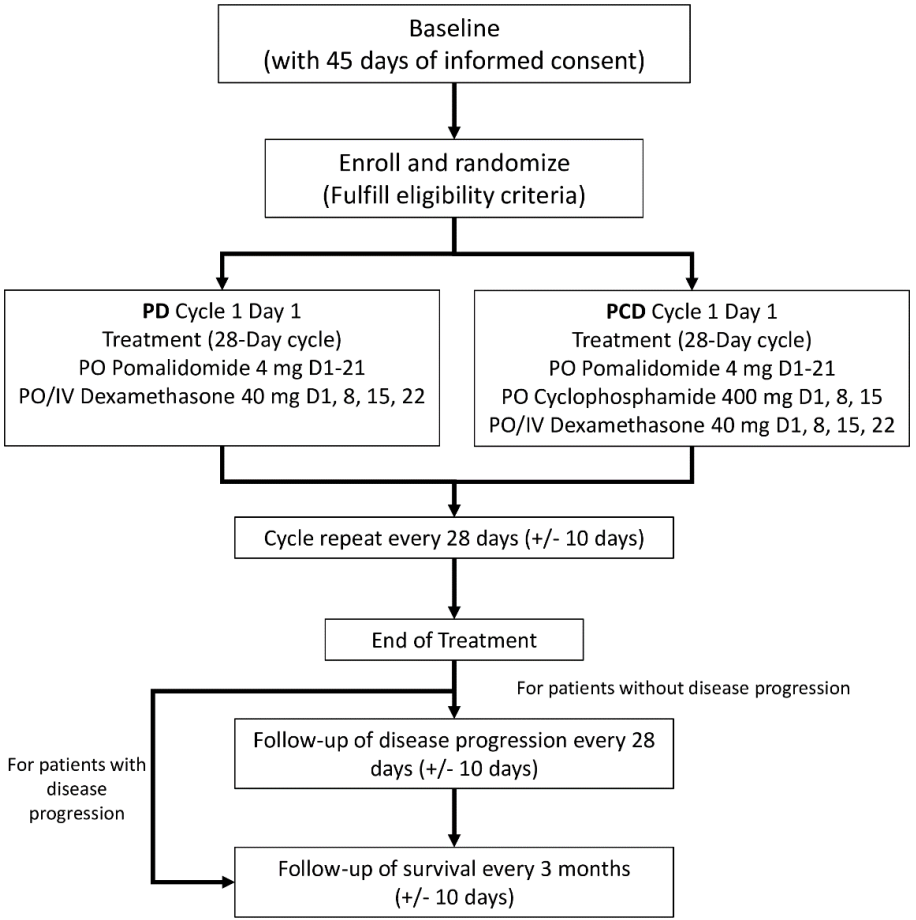
Patient number, n	Current 364	ASPIRE phase III 396
Response evaluable patients, n (%)	354 (97)	
Flow MRD-negative	22 (6)	
sCR	23 (6)	9 (2)
CR	113 (31)	42 (12)
VGPR	88 (24)	131 (36)
PR	71 (20)	240 (67)
MR	3 (1)	N/A
SD	15 (4)	40 (11)
PD	19 (5)	
Not evaluable	10 (3)	
Overall response rate*, ≥PR, N (%) (n=354)	317 (90)	282 (78)
Treatment cycles, median (range)	13 (1-55)	17 (1-34)
Time to response, mo, median (range)	1.9 (0.1-39.6)	1.1
Time to best response, mo, median (range)	3.9 (0.3-39.6)	N/A



Lee JH, et al. *Haematologica*. 2024;109:3681-3692.

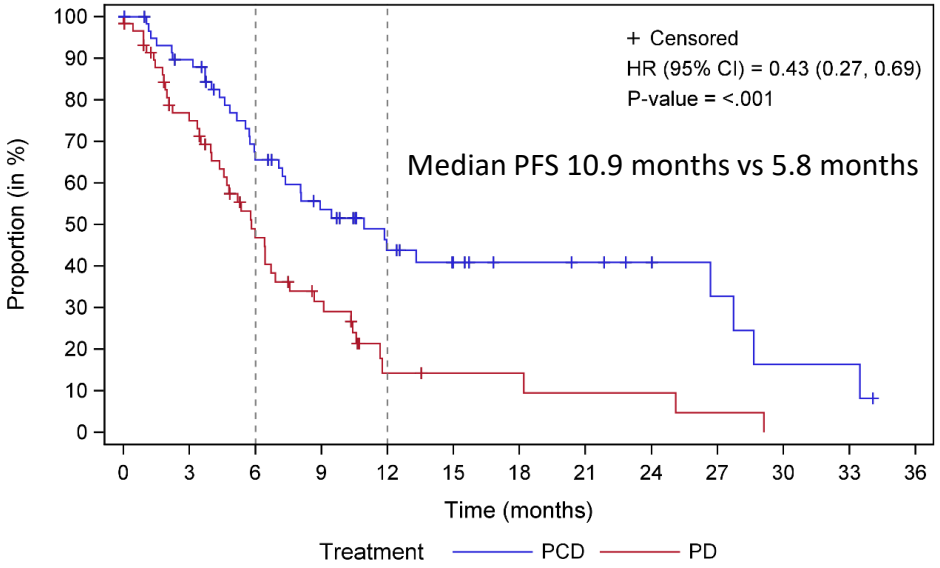
AMN003 – PCD vs PD

- Patients randomized in a 1:1 ratio to receive PCD or PD
- Dosing schedule for PCD
  - 4-weekly: pom 4 mg day 1–21, dexamethasone 40 mg once a week, cyclophosphamide 400 mg weekly for 3 weeks
- Dosing schedule for PD
  - 4-weekly: pom 4 mg day 1–21, dexamethasone 40 mg once a week



Kim JS, et al. *Blood Cancer J.* 2025;15:155.

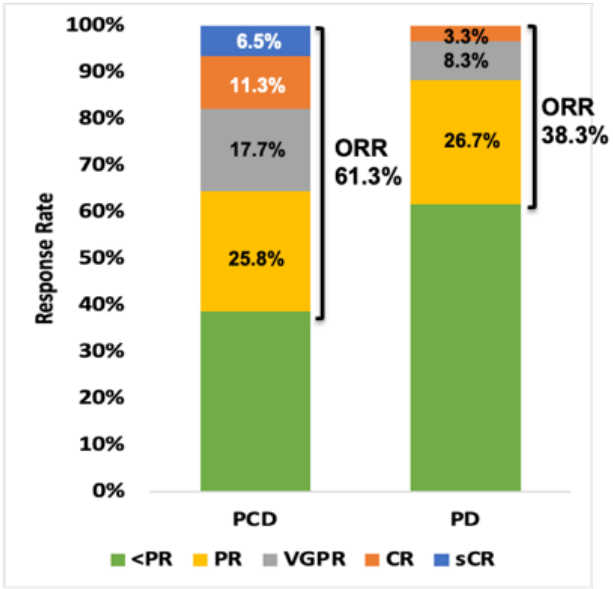
AMN003 – PCD vs PD



No. of patients at risk:

PD	60	40	22	13	4	3	3	2	2	1	0	
PCD	62	51	35	26	17	12	9	8	6	4	2	2	0

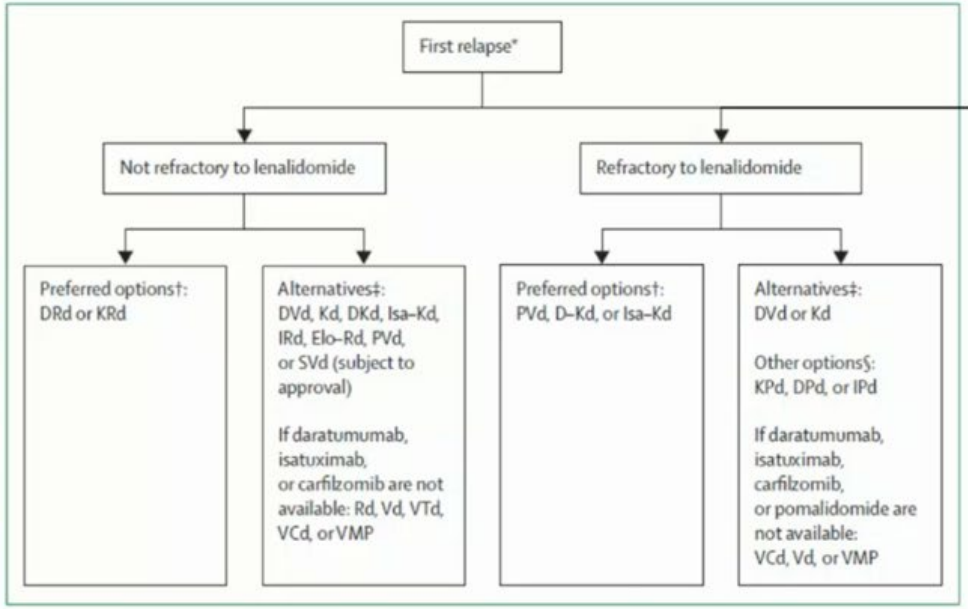
Kaplan-Meier plot – PFS
Efficacy Evaluable Population



Kim JS, et al. *Blood Cancer J.* 2025;15:155.

Triple-refractory disease

In the future, most patients will present with len- and anti-CD38 refractory disease at first relapse (post-MAIA or post-PERSEUS)



Refractory to len and anti CD38 !

PVd
Kd
KCd
PCD
DT-PACE
BelaVD
BelaPD
Cilta-cel
Tec-Dara?

Moreau et al. *Lancet Oncol*. 2021.

Treatment choices

- Switch class and use best treatment for optimal effect
- Status of lenalidomide and daratumumab refractoriness will be an important determinant
- Chemo (DT-PACE) may be considered for relapse with predominant extramedullary disease and young
- Allogeneic transplant for young HR disease
- Data suggest that earlier use of BCMA-targeted therapy may improve outcomes in RRMM – drug access and affordability becomes an important issue

Thank you.

Professor Chng Wee Joo

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Global Multiple Myeloma Academy

Discussion

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

Juan Du, MD, PhD

APTITUDE HEALTH®

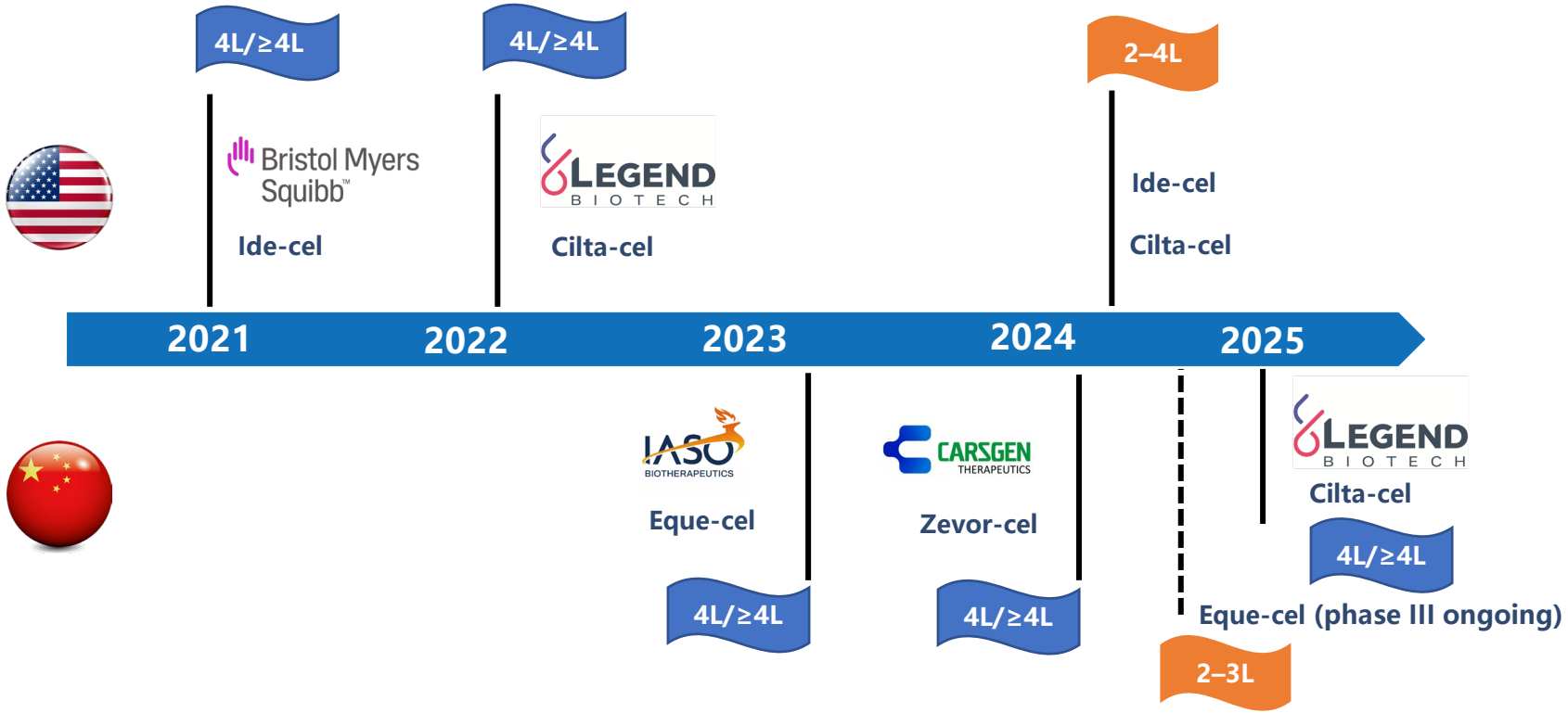
CAR T Therapy in RRMM: Impact of Earlier Use and Real-World Data

Juan Du, MD, PhD

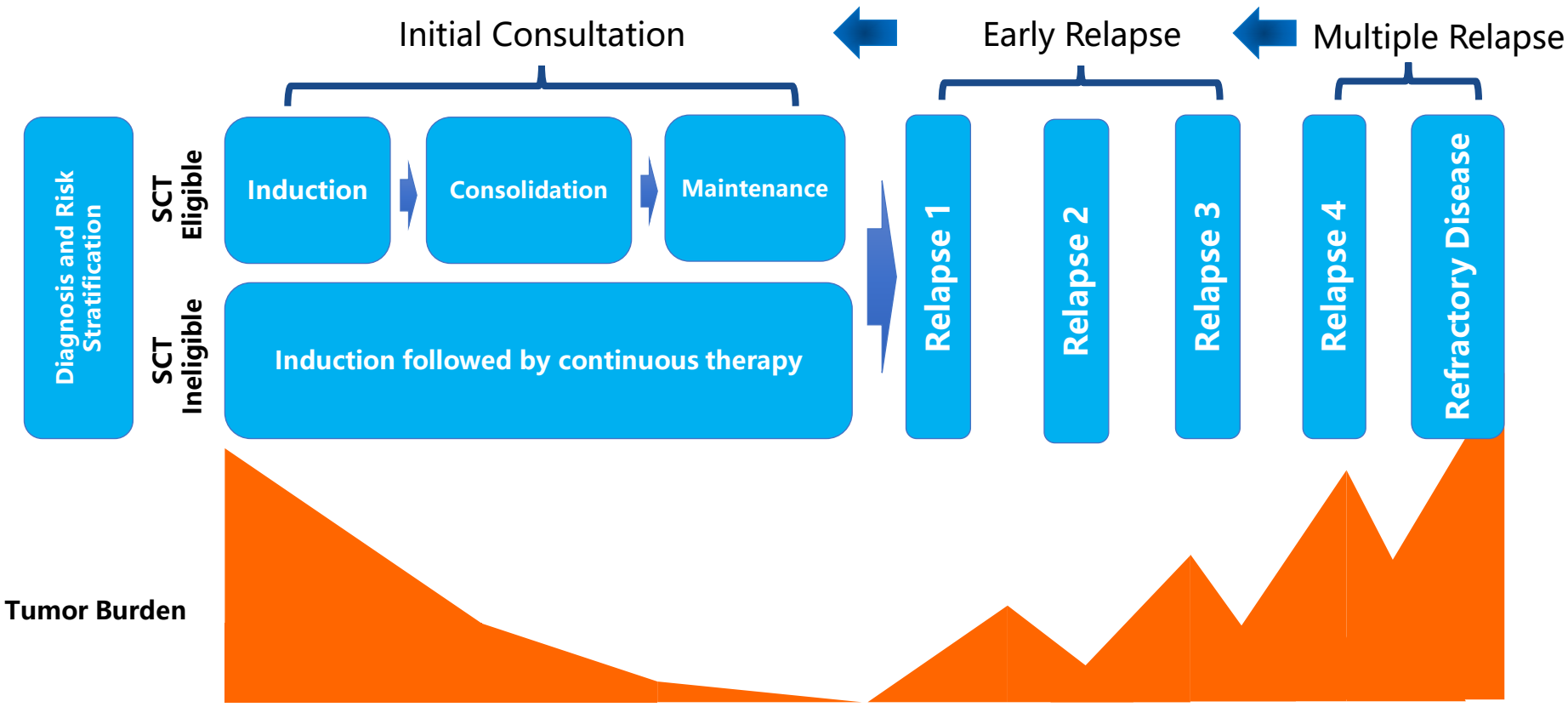
Hematology Department, Renji Hospital

Shanghai Jiao Tong University School of Medicine, China

The Development Milestones of CAR T-Cell Therapy



Management Strategies for Multiple Myeloma



Courtesy of Prof Shaji Kumar.

BCMA-Targeted CAR T ≥3 Lines

CAR T products and studies	Ide-Cel			Cilta-Cel			Eque-Cel	Zevor-Cel
	Phase II study	Phase III study	REW study	Phase Ib/II study in US	Phase III study	REW study	Phase II study in China	Phase Ib/II study	Phase II study
Clinical trial	KarMMa	KarMMa-3	-	CARTITUDE-1	CARTITUDE-4	-	NCT03758417	FUMANBA-1	LUMMICAR
Number	128	254	821	97	208	236	48	103	102
Median prior lines	6	3	7	6	2	NA	4	4	4
Median follow-up	15.4	18.6	11.6	27.7	15.9	13	18	13.8	20.3
ORR, %	73	71	73	97.9	84.6	89	89.6	96	92.2
CR, %	33	39	25	82.5	73.1	70	77.1	74.3	71.6
MRD negativity, %	26	20	-	91.8	60.6	39	97.5	95	95.7 (≥VGPR)
AEs, % (grade ≥3, %)	100 (99)	99 (≥93)	NA	100 (94)	100 (96.6)	NA	100 (100)	99 (94.2)	100 (100)
CRS, % (grade ≥3, %)	84 (5)	88 (5)	80 (3)	95 (4)	76.1 (1.1)	75 (5)	97.9 (35.4)	93.2 (1)	90.2 (6.9)
ICANS, % (grade ≥3, %)	18 (3)	15 (3)	28 (5)	17 (2)	4.5 (0)	14 (4)	2.1 (0)	1.9 (0)	2.0 (0)
SPM, %	NA	6	4	7	4.3	8.5	NA	NA	NA
Median PFS, months	8.8	13.3	8.8	NR	NR	NR	NR	NA	NA
Median OS, months	19.4	41.9	>12	NR	NR	NR	NR	NA	NA

Song Z, Fu Q, Du J. *Hematol Oncol.* 2026.

US Real-World CAR T Experience in Myeloma

	KarMMa-1[1] N=128	Ide-cel RWE[2] N=211	Ide-cel CIBMTR[3] N=821
Ineligibility conditions for registration studies		**75% ineligible** 28% organ dysfunction 7% PCL, POEMS, amyloid, non-secretory MM 8% history of CNS pathology 6% prior alloSCT	77% clinically significant comorbidity 18% prior BCMA therapy
CRS rate	84% total 5% grade ≥3	82% total 3% grade ≥3	80% total 3% grade ≥3
ICANS rate	18% total 3% grade ≥3	8% total 6% grade ≥3	28% total 5% grade ≥3
ORR **CR/sCR** **Median PFS, months**	73% 33% 8.8	84% 42% 8.5	73% 25% 9.0

The data presented are provided for ease of viewing information from multiple trials. Direct comparison between trials is not intended and should not be inferred. Ide-cel and cilta-cel are approved for patients with RRMM after ≥4 (FDA) or ≥3 (EMA) prior therapies including an IMiD agent, a PI, and an anti-CD38 mAb and who have demonstrated disease progression on the last therapy (EMA).

alloSCT, allogeneic stem cell transplant; cilta-cel, ciltacabtagene autoleucel; CR, complete response; CRS, cytokine release syndrome; EMA. European Medicines Agency; FDA. Food and Drug Administration; ICANS, immune effector cell-associated neurotoxicity syndrome; ide-cel, idecabtagene vicleucel; IMiD, immunomodulatory imide drug; mAb, monoclonal antibody; MM, multiple myeloma; ORR, objective response rate; PI, proteasome inhibitor; PLC, plasma cell leukemia; POEMS, polyneuropathy, organomegaly, endocrinopathy, monoclonal gammopathy, skin abnormalities; RRMM, relapsed/refractory MM; RWE, real-world evidence; sCR, stringent CR.

1. Munshi N, et al. *N Engl J Med.* 2021; 2. Hansen DK, et al. *J Clin Oncol.* 2023;41:2087-2097; 3. Sidana S, et al. ASH 2023.

Courtesy of Prof Lin Yi.

US Real-World CAR T Experience in Myeloma

	CARTITUDE-1[1,2,3] N=97	Cilta-cel RWE[4,*] N=164
Ineligibility conditions for registration studies		**57% ineligible** 12% organ dysfunction 26% PCL, POEMS, amyloid, non-secretory MM 6% history of CNS pathology
CRS rate	95% total 5% grade ≥3	80% total 5% grade ≥3
ICANS rate	17% total 2% grade ≥3 12% late neurotoxicity; 5% neuro cognitive movement disorder	18% total 6% grade ≥3 12% late neurotoxicity; 2% neurocognitive movement disorder
ORR	98%	84%*
CR/sCR	83%	53%*
Median PFS, months	34.9	NR

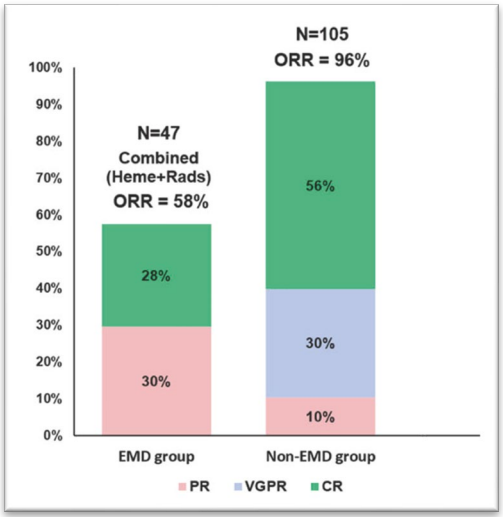
*Median follow-up 5.8 months. Clinical response will continue to deepen over time. Longer follow-up is needed to identify best clinical response and PFS.

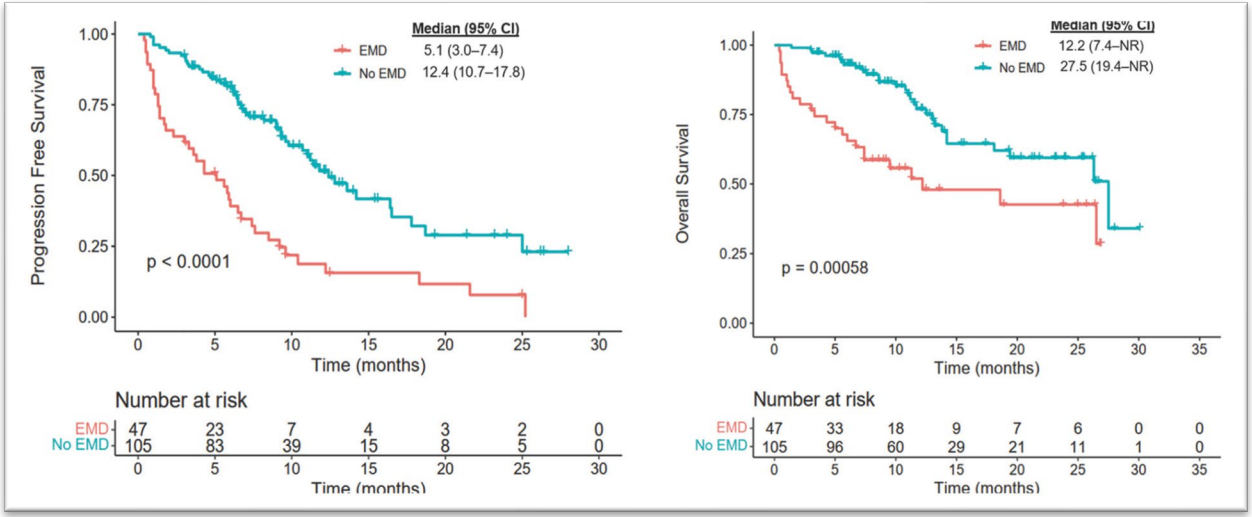
1. Berdejas J, et al. *Lancet.* 2021; 2. Martin T, et al. *J Clin Oncol.* 2023; 3. Lin Y, et al. ASCO 2023; 4. Hansen DK, et al. *J Clin Oncol.* 2023;41(suppl 16): 8012.

Courtesy of Prof Lin Yi.

CAR T Therapy in Extramedullary Disease

This study retrospectively analyzed 152 patients with RRMM who received SOC CAR T-cell infusion at 3 US institutions, comparing the outcomes between patients with and without extraosseous EMD.



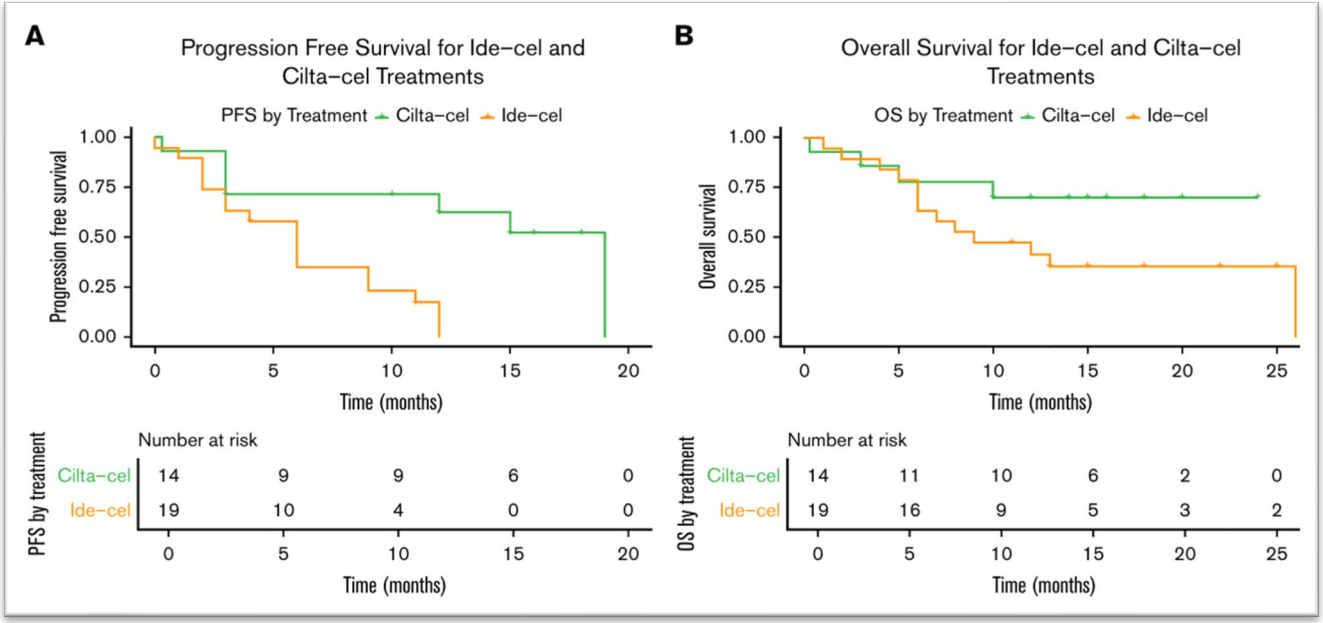


CAR T yielded meaningful clinical outcomes in real-world RRMM patients with extraosseous EMD, though responses and survival outcomes were suboptimal compared with patients without EMD – **ORR (58% vs 96%), mPFS (5.1 vs 12.4 months), mOS (12.2 vs 27.5 months).**

Dima D, et al. *Blood Cancer J.* 2024;14:90.

CAR T Therapy in Plasma Cell Leukemia

A multicenter retrospective analysis was conducted on 34 patients with plasma cell leukemia treated with standard of care BCMA-directed CAR T products (ide-cel or cilta-cel).



- Cilta-cel was associated with longer PFS (19.0 vs 6.0 months) and OS (>23 vs 9.0 months) compared with ide-cel, with similar toxicity profiles consistent with those observed in MM
- CAR T is safe, feasible, and associated with improved outcomes when compared with historic standards

Galarza Fortuna GM, et al. *Blood Adv*. 2025;9:6009-6018.

Eque-Cel: Real-World CAR T Experience in Myeloma

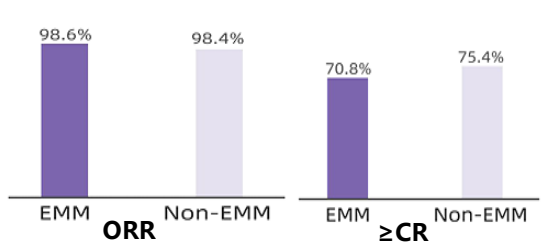
A total of 150 patients with RRMM were enrolled from 48 clinical centers between June 2023 and August 31, 2024

Characteristics (N=150)		
Features		% (n/total N)
Median age, years		60 (35–78)
High-risk cytogenetics		**71.3% (107/150)**
PCL		**12.7% (19/150)**
EMM		**52.7% (79/150)**
CNS involved		**10% (15/150)**
Triple exposed		78.6% (118/150)
Penta exposed		40.7% (61/150)
Prior CD38		82% (123/150)
ASCT		53.3% (80/150)
CAR-HEMATOTOX	**Low**	12
	High	70

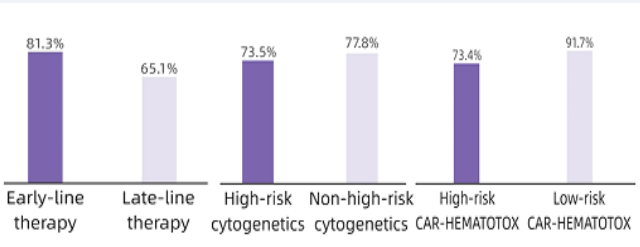
Response

- **ORR 98.5%, 73% ≥CR**
- MRD evaluated 90 patients, 97.8% MRD negatively
- CR rate was 81.3% in early-line treatment, compared with 65.1% in late-line treatment

ORR/CR



CR



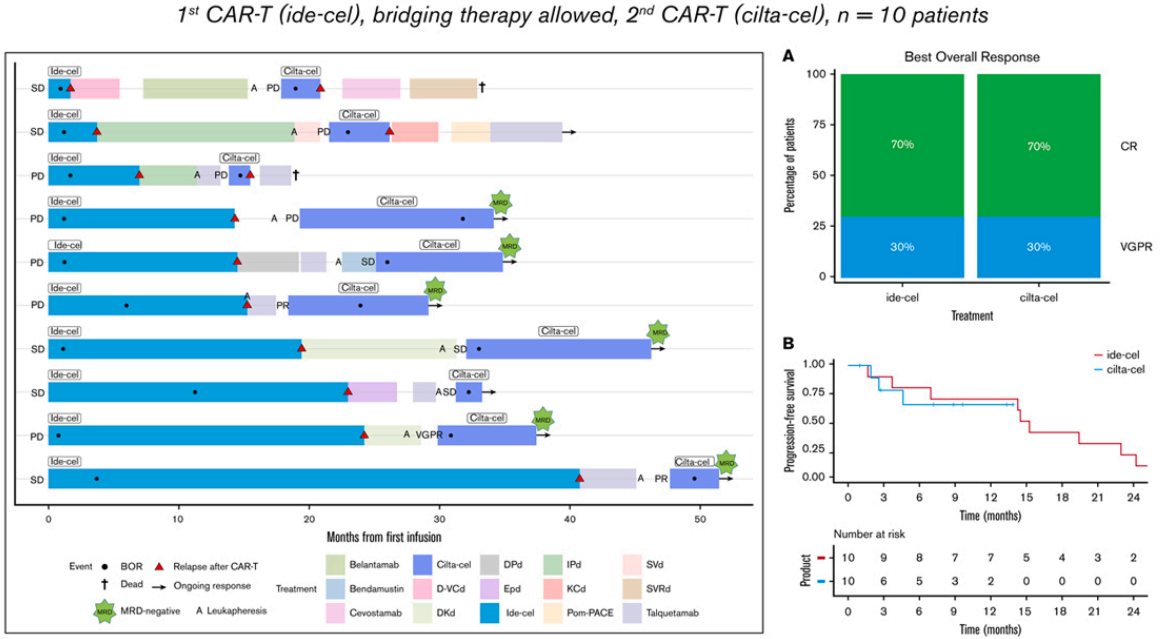
AEs

AE	ALL	Grade 1	Grade 2	Grade ≥3
CRS, n (%)	**136 (90.7%)**	**71 (47.3%)**	**58 (38.7%)**	**7 (4.7%)**
ICANs, n (%)	**16 (10.7%)**	**5 (3.3%)**	**5 (3.3%)**	**7 (4%)**

Lu J, et al. IMS 2025. Abstract PA-065.

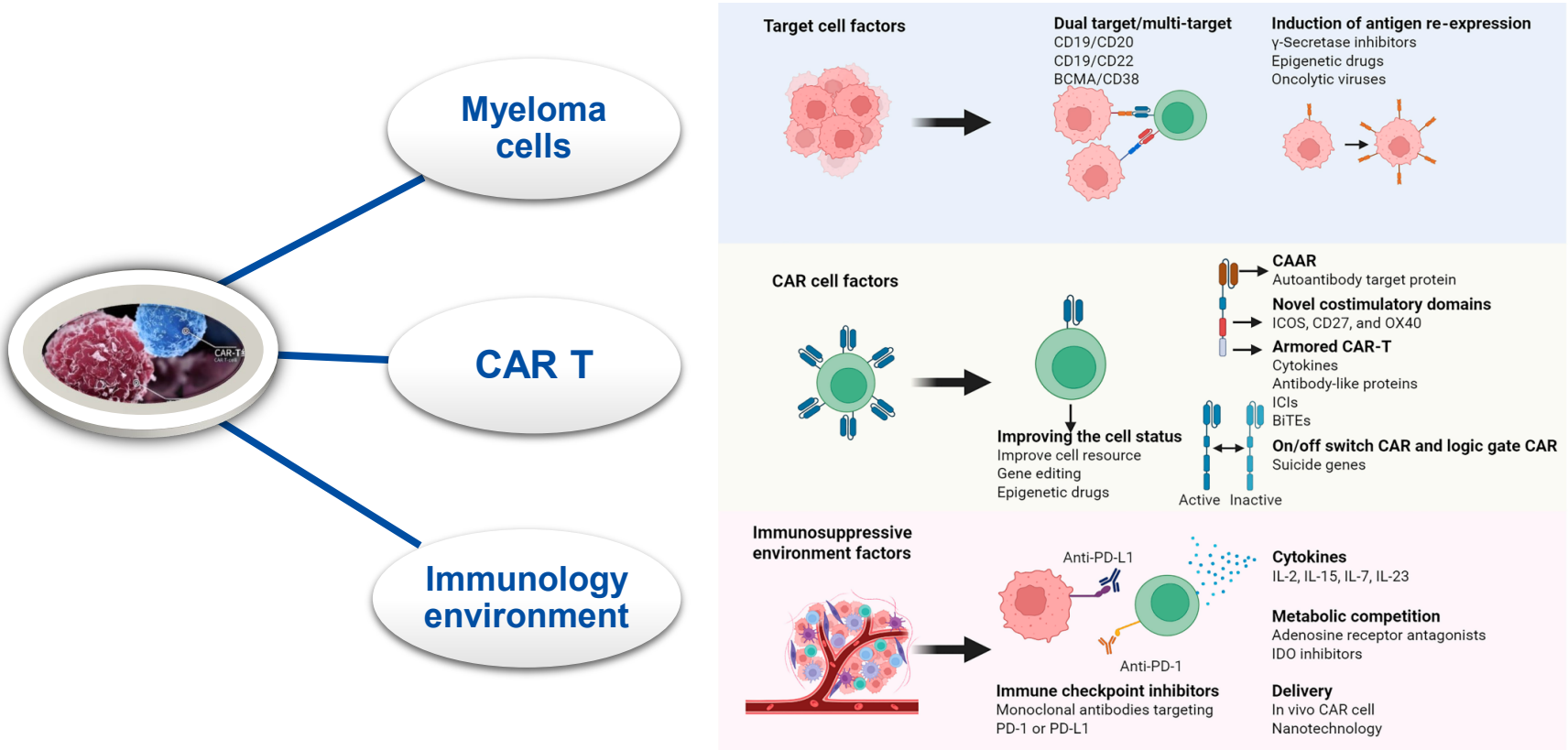
Sequential BCMA CAR T-Cell Therapy in RRMM in a Real-World Setting

- N=10 patients with RRMM
- A median of 7 prior lines of therapy
- High-risk cytogenetics: 70%; EMD: 40%
- The median interval between the first and second CAR T-cell treatment was 1.9 years
- ORR 100% with >CR 70%
- The median PFS was 14.9 months, which is comparable to previously published data on PFS in this setting



Richardson T, et al. *Blood Adv.* 2025.

CAR T Therapy: Resistance, Recurrence, and Management Strategies



Wang Y, et al. *Research (Wash D C)*. 2026;9:1068. Published 2026 Jan 5.

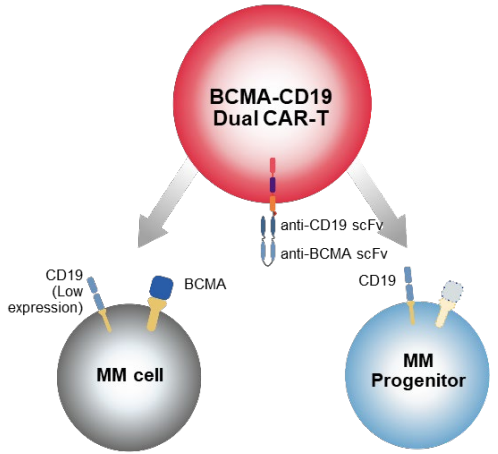
GC012F/AZD0120 (BCMA/CD19) in RRMM-IIT Study

Multicenter, open label, single-arm IIT study (N=29), FPI October 2019, LPI January 2022

BCMA
Universally expressed on malignant plasma cells and a well-established target

\+

CD19
Expressed on majority MM cells and progenitor cells[1-3]



Next-generation manufacturing
based on FAST CAR platform

Faster availability to patients

- Manufactured in <3 days

Enhanced T-cell fitness

- Younger, fitter, naive T cells

- GC012F/AZD0120 is an autologous CAR T therapy that targets both BCMA and CD19
- GC012F/AZD0120 has demonstrated deep and durable responses with a manageable safety profile in RRMM patients[4]

1. Boucher K, et al. *Clin Cancer Res*. 2012;18:6155-6168; 2. Garfall AL, et al. *JCI Insight.* 2018;3:e120505; 3. Jiang H, et al. ASH 2020; Abstract 178; 4. Du J, et al. EHA 2023. Poster presentation P869.

Du J, et al. ASH 2025. Abstract 258; Qiang W, et al. *JAMA Oncol.* 2024;10:1259-1263.

AZD0120 in ≥4L RRMM Studies

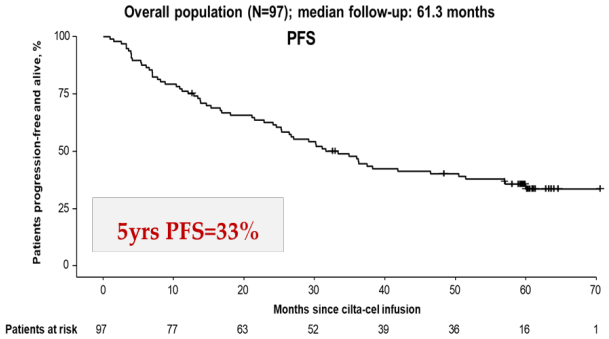
	RRMM-IIT (China, 2019)	DURGA-1 (US, 2024)	DURGA-3 (China, 2025)
Dose	1.0 or 3.0 × 10^5/kg	1.0 or 3.0 × 10^5/kg	1.5 or 3.0 × 10^5/kg
Source	2024 ASH, ASCO, EHA	2025 ASH	Inner source
Total number	N=29	N=26	N=11
Median age, years, (range)	57 (27–76)	63 (44–78)	65 (60–70)
R-ISS Stage II–III	-	-	7 (78%)
High-risk genetic features	26 (90%)	9 (35%)	6 (55%)
Extramedullary diseases	8 (28%)	4%	7 (53%)
Prior lines of therapy (range)	5 (2–9)	4 (3–7)	5 (3–10)
CRS (grade ≥3)	86% (7%)	63% (0%)	88.9% (11.1%)†
Neurotoxicity (grade ≥3)	0% (0%)	3.8% (0%)*	11.1% (0%)
Median follow-up	30.7 months (n=29)	3.9 months (n=23)	8.8 months (n=8 on RP2D‡)
ORR	93.1%	96%	100%
≥CR	82.8%	78%§	87.5%

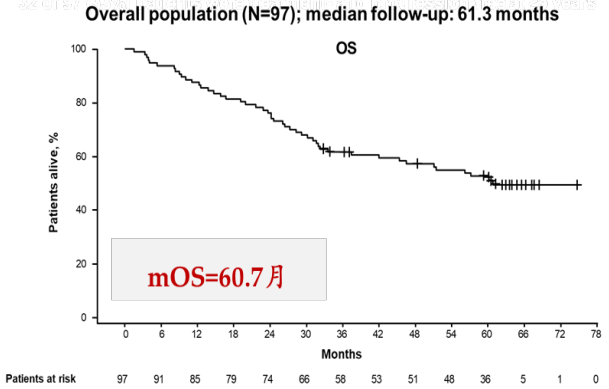
*One patient for grade 1 confusional state in DL1. One patient for grade 1 peripheral sensory neuropathy in DL2; †n=9 for safety evaluation; ‡Date were not 100% clean; §Low CRR due to short follow-up.

CARTITUDE-1 Long-Term Follow-Up

≥4L

Median 6 prior lines, 5-year PFS rate was 33% (without maintenance therapy)



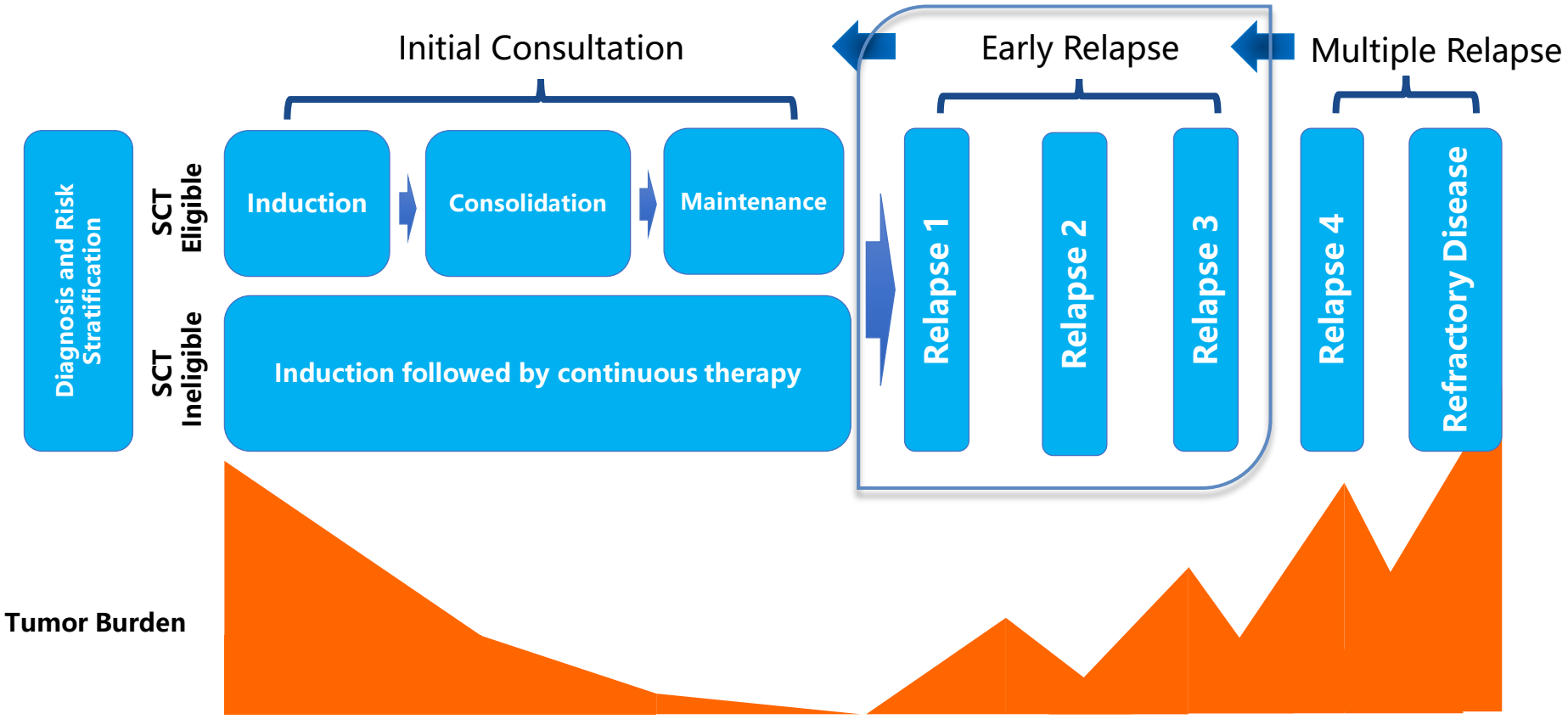


97 patients with MM (≥3 prior lines or dual-refractory to PI and IMiD, with prior anti-CD38 exposure)

	≥5-Year PFS (n=32)	<5-Year PFS (n=46)
High-risk Cytogenetics, n/N (%)	7/30 (23.3)	12/45 (26.7)
Extramedullary plasmacytomas, n (%)	4 (12.5)	6 (13.0)
Bone marrow plasma cells, % (range)	5.0 (0.8–80.0)	**24.0 (0.0–95.0)**
Soluble BCMA, ug/L (range)	36.0 (3.7–864.6)	**58.5 (3.8–1342.9)**

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

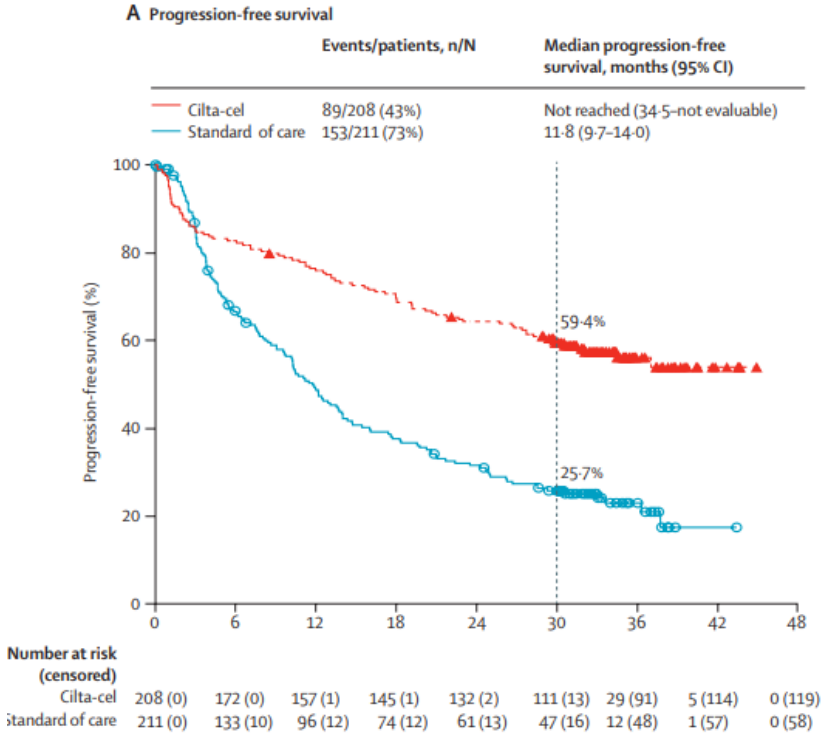
Management Strategies for Multiple Myeloma

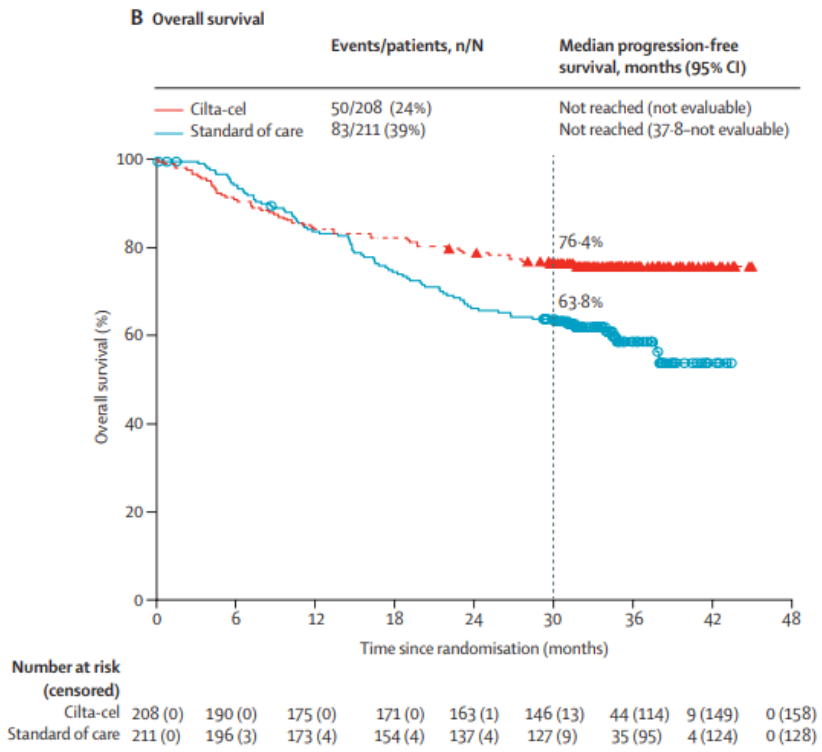


Courtesy of Prof Shaji Kumar.

CARTITUDE-4: An Updated Analysis (33.6 months)

2–4L



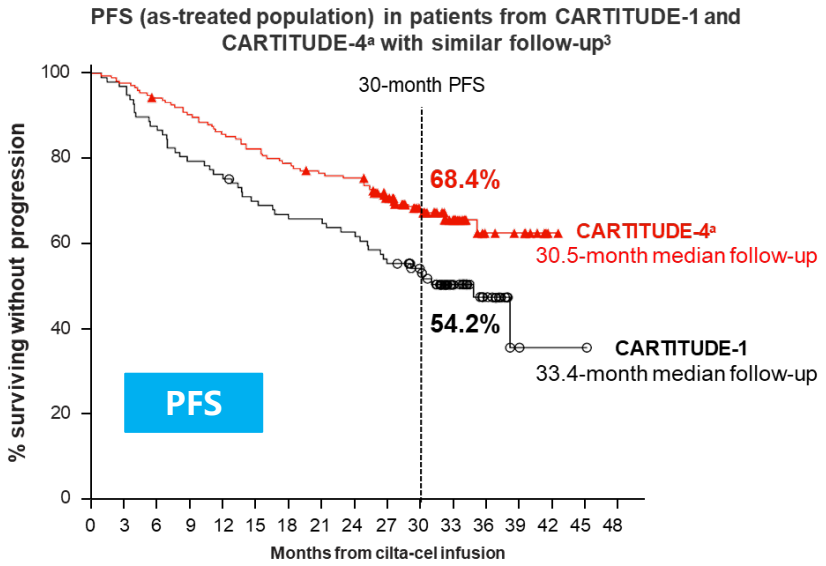


San-Miguel J, et al. *N Engl J Med.* 2023;389:335-347; Mateos MV, et al. IMS 2024. Oral presentation OA-65; Einsele H, et al. *Lancet Oncol.* 2026;27:254-268.

CARTITUDE-1/4: Earlier-Line CAR T Therapy Benefits More Patients

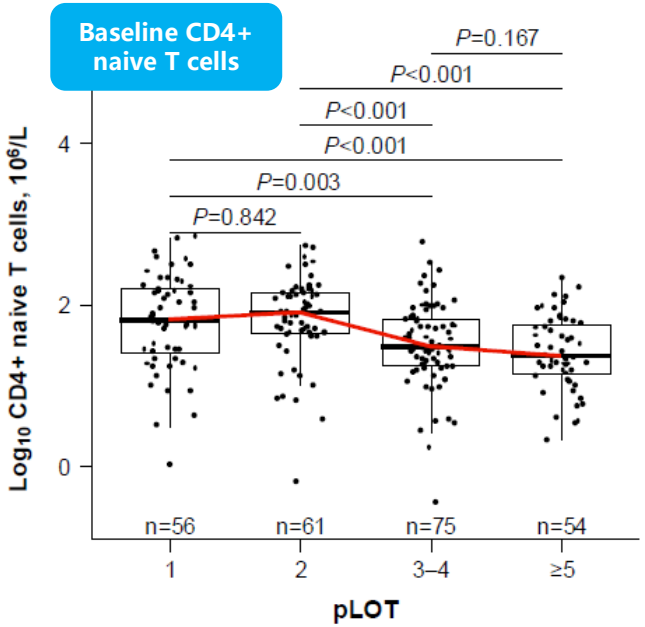
2–4L

Earlier use of cilta-cel may further extend long-term remission



In a pooled analysis of patients from CARTITUDE-1 and CARTITUDE-4, time 0 was reset from cilta-cel infusion, and the median follow-up was 30.5 months.

Preserved peripheral immune function at earlier lines may prolong PFS



Baseline CD4⁺ naive T cells ≥35.7 cells/μL

1. Mateos MV, et al. IMS 2024. Abstract 1437; 2. Parekh S, et al. *Blood*. 2025;146(suppl 1):92.

KarMMa-3: With Longer Follow-Up (30.6 months), Significantly Longer Median PFS Was Maintained With Ide-Cel vs SRs

Key Inclusion criteria

- Refractory to the last regimen
- Patients in a 2 versus 1 ratio received either ide-cel or one of five standard regimens with triple-class-exposed.

Ide-cel (n=254)

Optional Bridging Therapy (≤ 1cycel) → Day 1: Ide-celinfusion → Day 1-112: collect safety, efficacy, PK/PD data every 28 days → Follow-up

(DPd, DVd, IRd, Kd, EPd) SOC (n=132) → Follow-up

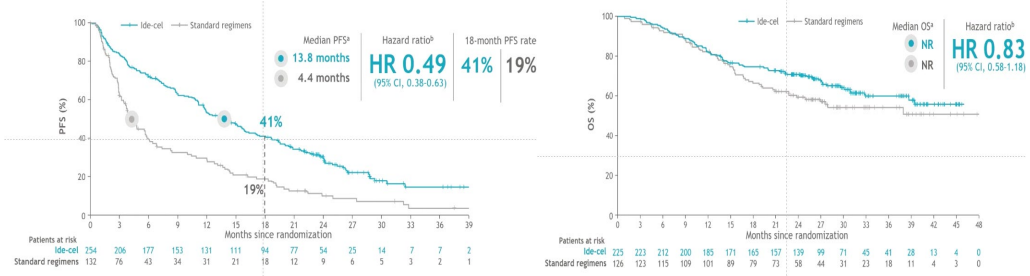
Ide-cel crossover therapy allowed after confirmed PD

This is the main different design compare to the CARTITIUDE 4

Primary endpoint
PFS by IRC

Key secondary endpoints
ORR, OS
Other endpoints
≥CR, DOR, MRD negative, CR, PFS2, Safety

PFS and OS of ide-cel vs std



- **Ide-cel vs std significantly improved median PFS in ITT patients (13.8 months vs 4.4 months, HR 0.59, *P* <.0001)**
- Ide-cel vs std in patients with RRMM showed improved OS (HR 0.83)

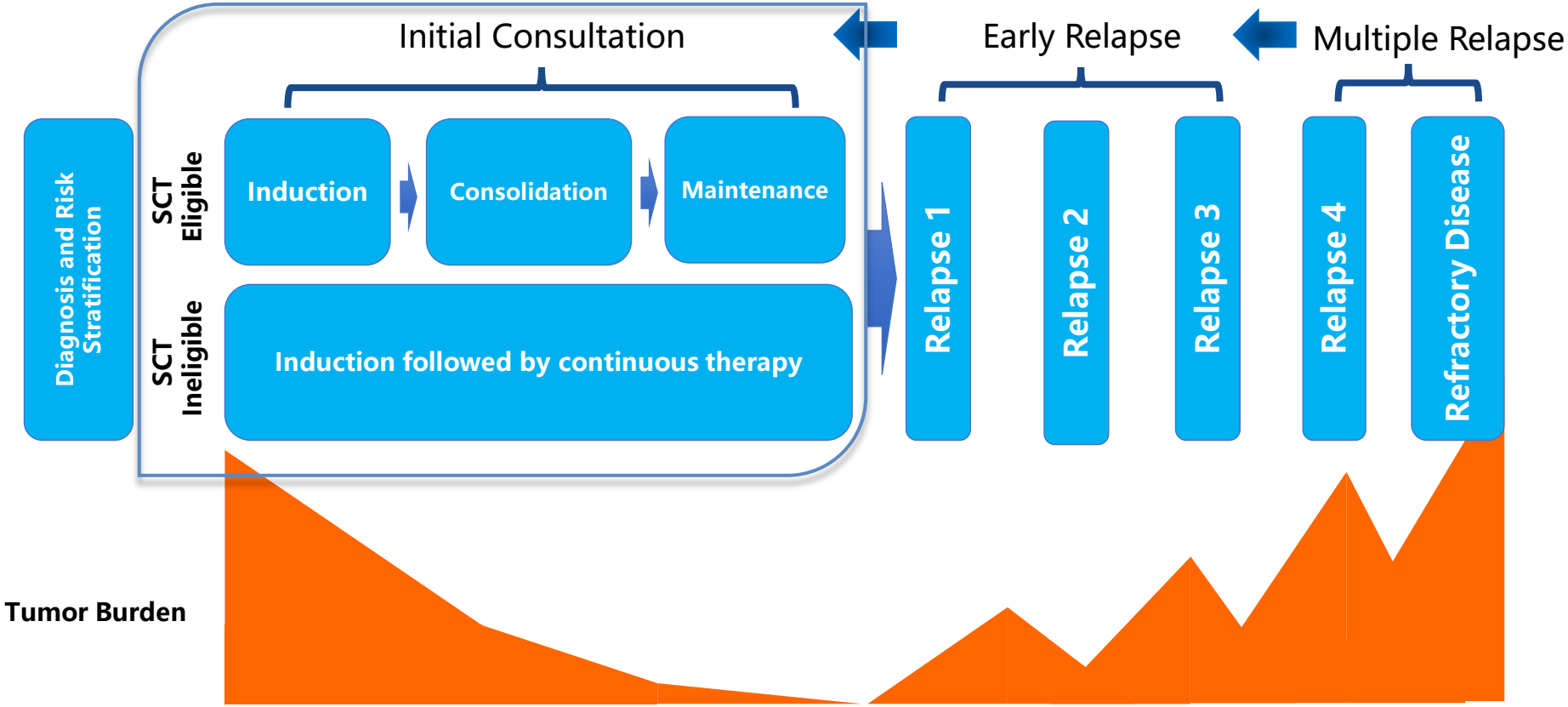
On April 5, 2024, the FDA granted approval to ide-cel for the treatment of triple class-exposed RRMM after 2 or more prior therapies.

Efficacy outcomes of ide-cel vs std

	Ide-Cel (n=254)	Std (n=132)
ORR, % (95% CI)	**71 (66–77)**	**42 (34–51)**
OR (95% CI)	3.36 (2.17–5.22)	
CR rate, % (95% CI)	44 (38–50)	5 (2–9)
mDOR, mo (95% CI)	16.6 (12.1–19.6)	9.7 (5.5–16.1)
DOR rate at 18 mo, % (SE)	46.1 (3.8)	27.6 (6.4)
MRD negativity in patients with ≥CR, n/N (%) (95% CI)	57/163 (35) (28–42)	1/54 (2) (0–5)
mTTNT, mo (range)	20.9 (16.6–24.2)	7.0 (5.3–8.5)
mPFS, mo (95% CI)	13.3 (11.3–15.7)	3.9 (3.0–5.3)
mPFS2, mo (95% CI)	23.5 (18.4–27.9)	16.7 (12.2–20.3)

Rodriguez-Otero P, et al. *N Engl J Med*. 2023;388:1002-1014;
Rodriguez-Otero P, et al. *Blood*. 2024.

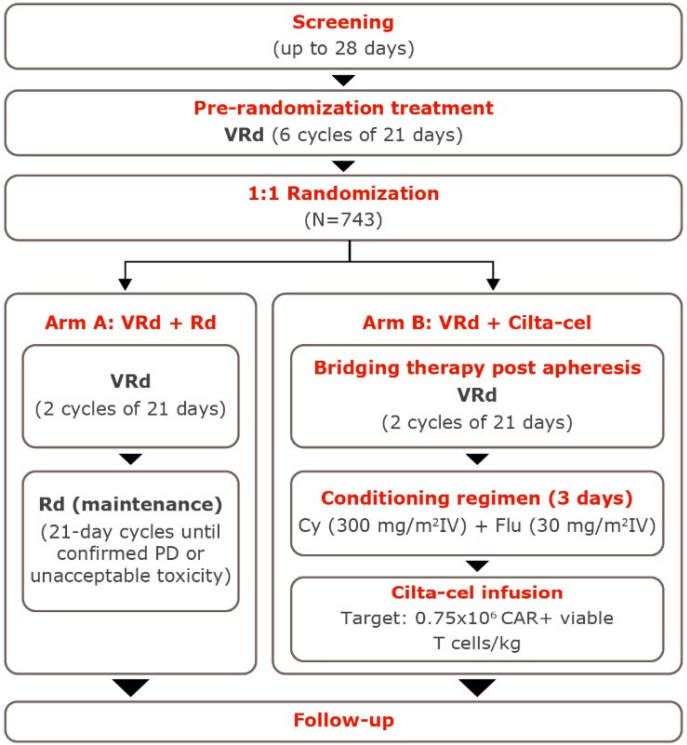
Management Strategies for Multiple Myeloma



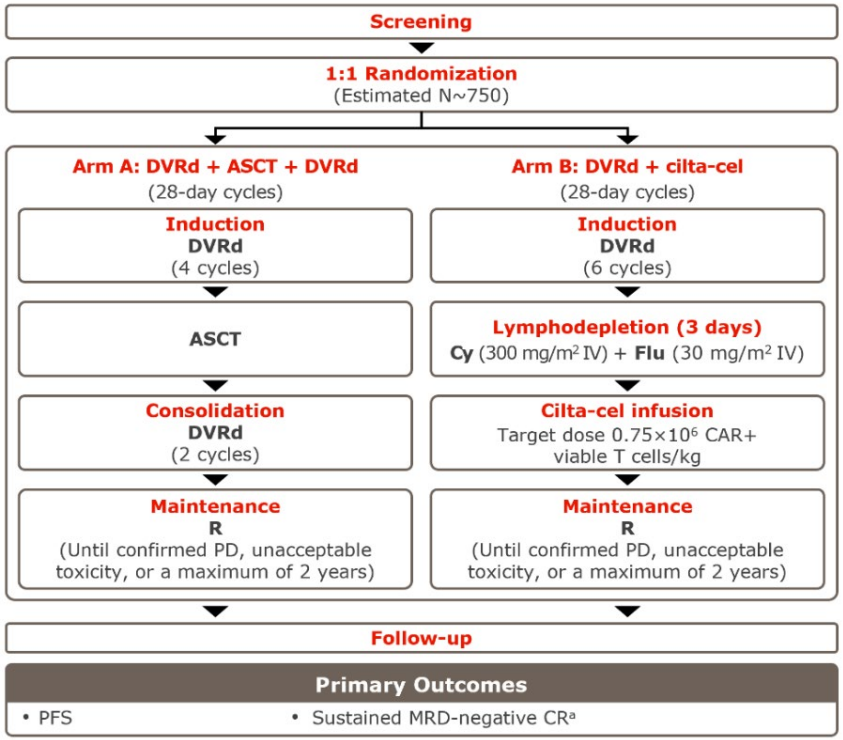
Courtesy of Prof Shaji Kumar.

CAR T in NDMM

CARTITUDE-5 (1L ineligible SCT, N=743)



CARTITUDE-6 (1L eligible SCT, N=750)



AZD0120 (BCMA/CD19) in NDMM-IIT Study

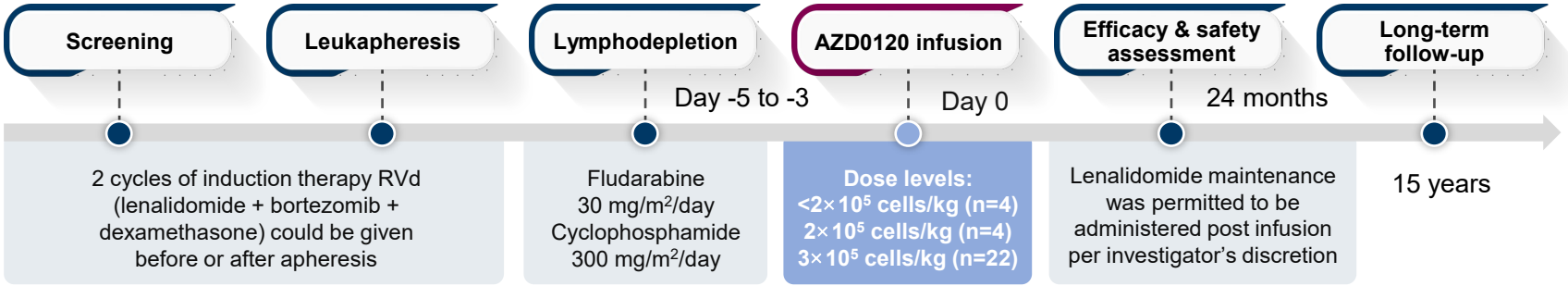
(From 2021) — 2025 Golden Globule Award for Multiple Myeloma

Key eligibility criteria

- Diagnosed with MM per IMWG criteria
- ECOG PS ≤3
- Measurable disease
- **Study 1 (NCT04935580): high-risk (HR)* transplant eligible (TE) NDMM (N=22)**
- **Study 2 (NCT05840107): transplant-ineligible (TI) NDMM (N=8)**

Key endpoints

- **Safety:** incidence and severity of AEs
- **Efficacy:** ORR, per 2016 IMWG criteria
- CRR; MRD negativity rate
- DOR, OS, PFS



*High-risk was defined as meeting at least one of the following: a) R-ISS stage II or III; b) High-risk cytogenetics: del17p, t(4;14), t(14;16), or 1q21 ≥4 copies; c) Extramedullary disease; d) IgD or IgE subtype; e) High-risk definition according to mSMART3.0; f) LDH > the upper limit of normal.
IMWG, International Myeloma Working Group; ECOG PS, Eastern Cooperative Oncology Group performance status; AE, adverse events; ORR, overall response rate; CRR, complete response rate; MRD, minimal residual disease; PFS, progression-free survival; DOR, duration of response; OS, overall survival.

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

AZD0120 in NDMM

Baseline Characteristics		All (N=30)	TE HR NDMM (N=22)	TI NDMM (N=8)
Median age, years (range)		64 (43–78)	59 (43–69)	72 (70–78)
Male, n (%)		19 (63)	14 (64)	5 (63)
Induction therapy (IT), n (%)	2 cycles RVd	29 (97)	21 (95)	8 (100)
Response to induction therapy	ORR, %	93.3	90.9	100
R-ISS stage, n (%)	II / III	25 (83)	20 (91)	5 (63)
Cytogenetics†, n (%)	High risk	14 (48)	11 (52)	3 (37)
Plasmacytomas, n (%)	All	17 (57)	12 (55)	5 (63)
	Soft tissue related	3 (10)	3 (14)	0 (0)
ECOG PS, n (%)	0–1	22 (73)	16 (73)	6 (75)
	≥2	8 (27)	6 (27)	2 (25)
Apheresis, n (%)	Before IT	4 (13)	4 (18)	0 (0)
	After 1 cycle of IT	16 (53)	8 (36)	8 (100)
	After 2 cycles of IT	10 (33)	10 (45)	0 (0)

Median time from diagnosis to infusion was 3 months (range, 2–5 months)

*One patient received 1 cycle of PAD (bortezomib, doxorubicin, and dexamethasone) and 1 cycle of RVd; †The definition of high-risk cytogenetics: del (17p), t (4;14), t (14;16), amp (1q21).
ECOG, Eastern Cooperative Oncology Group performance status; HR, high risk; NDMM, newly diagnosed multiple myeloma; R-ISS, revised international staging system; RVd, lenalidomide + bortezomib + dexamethasone; IT, induction therapy; TE, transplant eligible; TI, transplant ineligible.

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

AZD0120 in NDMM

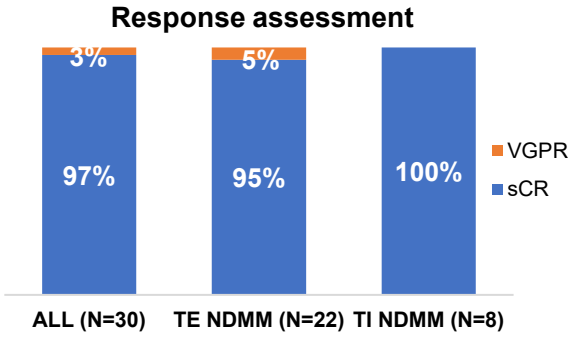
Median study follow-up: 36.5 months

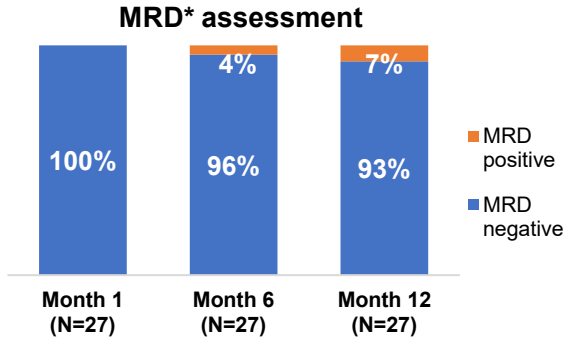
Fast and Deep Responses

ORR: 100%

sCR rate: 97%

MRD-negative: 100% ($<10^{-6}$), all achieved at month 1



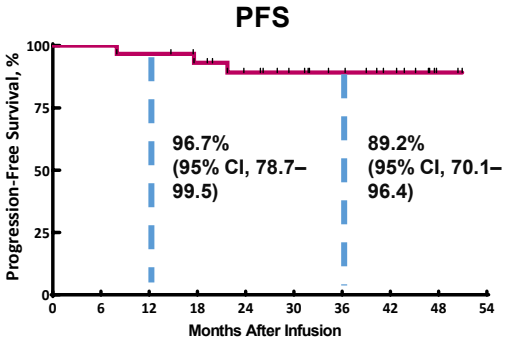


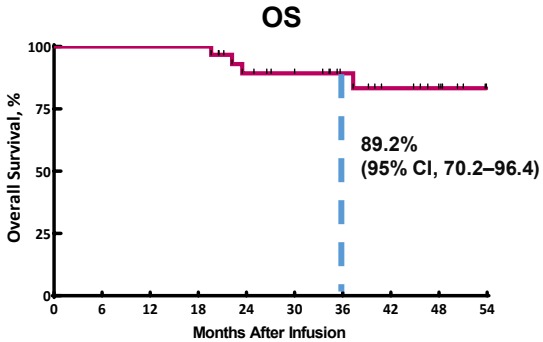
Median PFS and OS not reached

12-month PFS rate: 96.7%

36-month PFS rate: 89.2%

36-month OS rate: 89.2%





*The subjects who did not complete the MRD testing at month 1, 6, and 12 were different.

HR, high risk; MRD, minimal residual disease; NDMM, newly diagnosed multiple myeloma; ORR, overall response rate; OS, overall survival; PD, progressive disease; PFS, progression-free survival; sCR, stringent complete response; TE, transplant eligible; TI, transplant ineligible; VGPR, very good partial response.

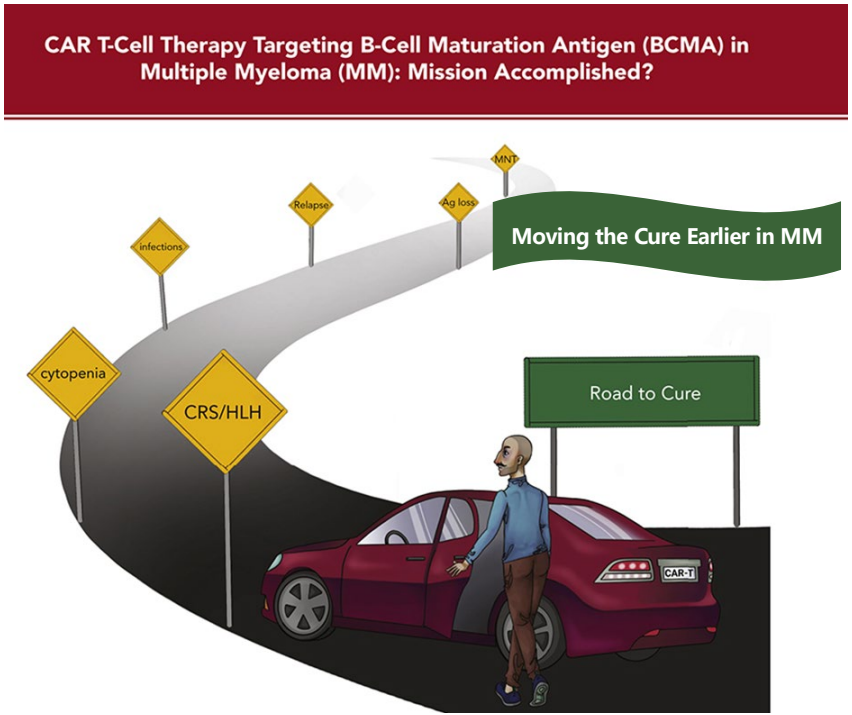
Du J, et al. ASH 2025. Abstract 258.

Challenges and Perspectives

- *Single vs Dual Targeting*
- *BCMA vs GPRC5D: Sequencing?*
- *Rapid Manufacturing Platform, Off-the-Shelf?*
  - *Universal CAR T*
  - *In vivo CAR T*
- *Moving Earlier: NDMM?*
- *Biomarkers?*
- *Combination Strategies: With SOC? ASCT?*

The 3 Rs principle

- *Right time*
- *Right target*
- *Right patient*



Global Multiple Myeloma Academy

Discussion

APTITUDE HEALTH®

Global Multiple Myeloma Academy

Treatment Options for Non–CAR T-Cell Candidates

James Chim, MBChB, MD, PhD, MRCP, FRCP, FACP, FRCPath, FFSc, FAcadTM, FHKCP, FHKAM

APTITUDE HEALTH®

Management of RRMM Non-CAR-T candidate & An Asian Perspective

James CS Chim

MBChB, MD, PhD, FRCP(London), FRCP(Edinburgh), FRCP(Glasgow), FACP, FRCPath(UK), FHKAM, FHKCP

Honorary Consultant, Hong Kong Sanatorium Hospital

Honorary Clinical Professor, Department of Medicine, University of Hong Kong

Honorary Clinical Professor, Department of Medicine & Therapeutics, Chinese University of Hong Kong

&

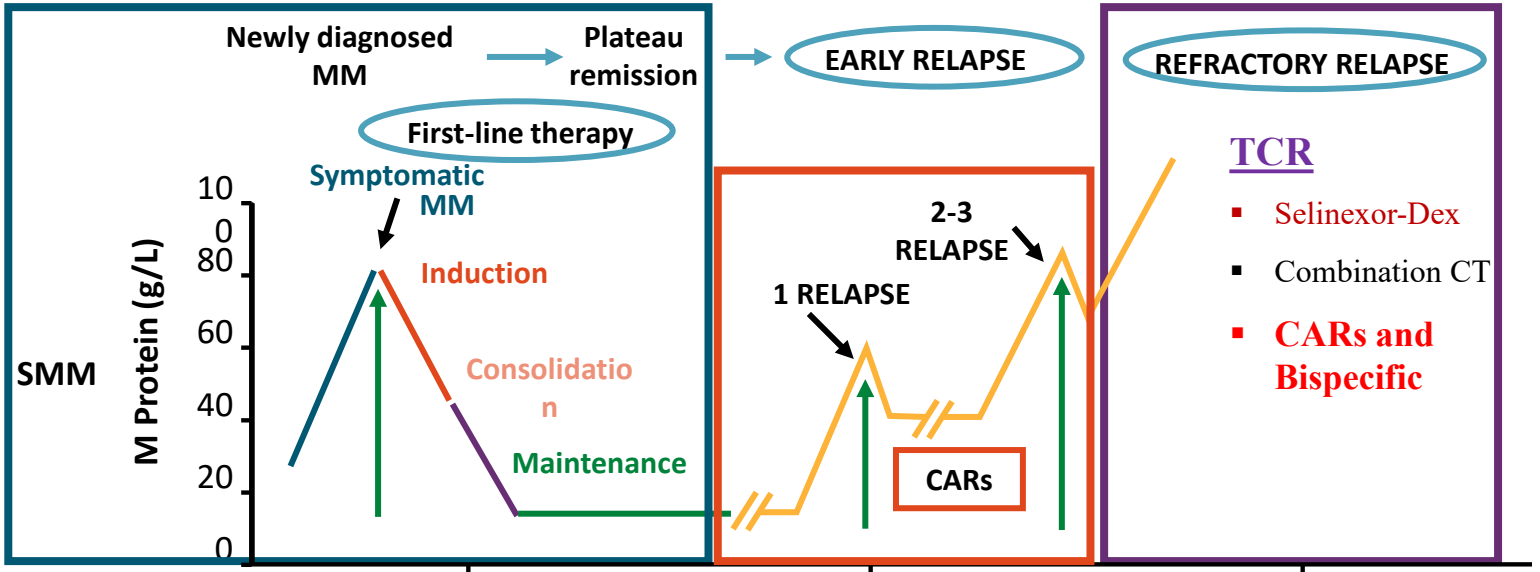
Member, International Myeloma Working Group (IMWG)

Executive Council Member, Asian Myeloma Network (AMN)

Founding member, International Academy of Clinical Hematology (IACH)

Founder & Chairman, Hong Kong Society of Myeloma (HKSOM)

RRMM



Frontline
Triplets: VRd/KRd
Quads: CD38 + VRd/KRd

Early Relapse (1-3 PLOT)
- Triplets (PI-, IMiD-, CD38-)
- Bela-Vd, Bela-Pd
- Cilta-cel

Late Relapse
Recycle agents, Survival <12 mos

Trials: **Bispecifics/CAR T-cell therapies** **Bispecifics/ trispecifics**

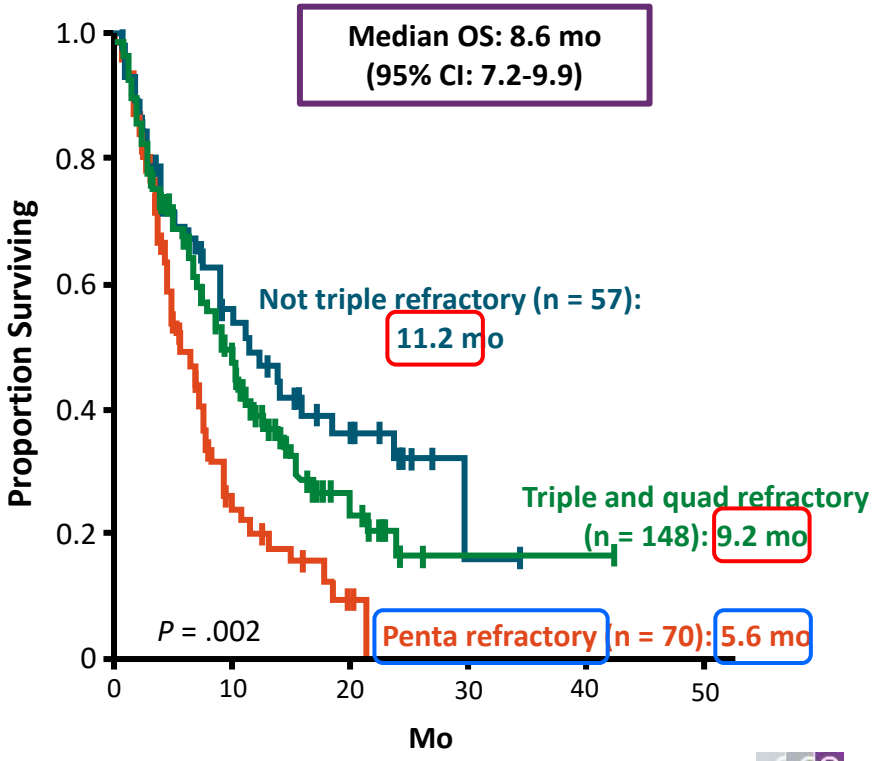
Courtesy of Thomas Martin, MD.

Slide credit: clinicaloptions.com

R/R MM in the Modern Era: *CD38–Refractory* Disease in MAMMOTH

- Retrospective study of patients with MM refractory to CD38 antibodies from 14 academic institutions (N = 275)
  - Triple refractory: CD38 antibody + 1 PI + 1 IMiD
  - Quad refractory: CD38 antibody + 1 PI + 2 IMiDs *or* 2 PIs and 1 IMID
  - Penta refractory: CD38 antibody + 2 PIs + 2 IMiDs
- 54% triple or quad refractory, 25% penta refractory
- Median prior lines of therapy: 4 (range: 1-16)

Refractory, %	N = 275
Bortezomib	68.4
Carfilzomib	47.3
Lenalidomide	76.7
Pomalidomide	65.1

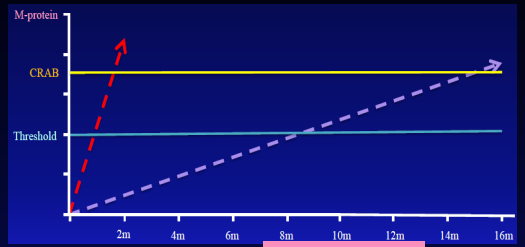


Gandhi. Leukemia. 2019;33:2266.

Slide credit: clinicaloptions.com

Factors impacting salvage treatment

- ***Disease:***
  - *Early* (1-3PLOT) vs Late (>3LOT)
  - Indolent vs aggressive/extramedullary myeloma
  - In "asymptomatic" biochemical relapse :
    - To treat OR not to treat
- ***Patient:*** frailty, organ function (renal, BM), co-morbid illness
- ***Prior treatment:***
  - resistant disease (PI, IMiD, CD38; double- or triple-class resis
  - residual toxicities (peripheral neuropathy, marrow failure)
- ***Goal of salvage*** (QOL in frail elderly vs CR in the young fit)
- ***Access & Cost***
- ***What are the evidences?***
  - Scientific rationale
  - Clinical trial-based



When to treat?

How to treat?

What to use?

Chim et al, Leukemia, 2018

How to choose in the armamentarium?

Mechanism-Based

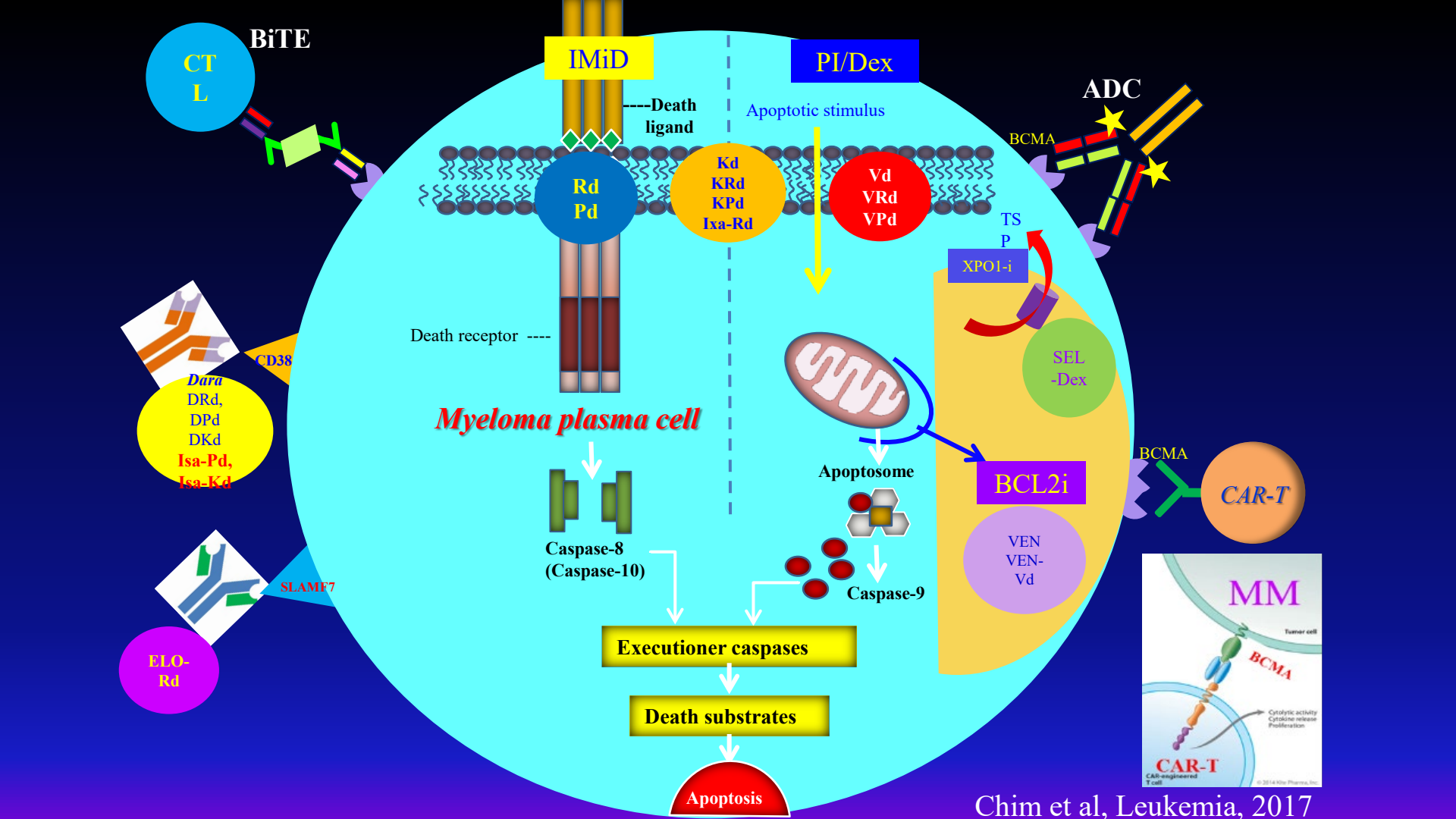
Scientific Rationale

- PI: 2G
- IMiD : 2G 3G
- mAb : CD38;
- Immuno : ADC, BiSP, CAR-T
- Apoptosis: BCL2 inhibitor
- Exportin-1 inhibitor
- RAS/RAF/MEK/ERK

Ultimately, the most important factor is what's the previous regimen, & what is the patient refractory to?

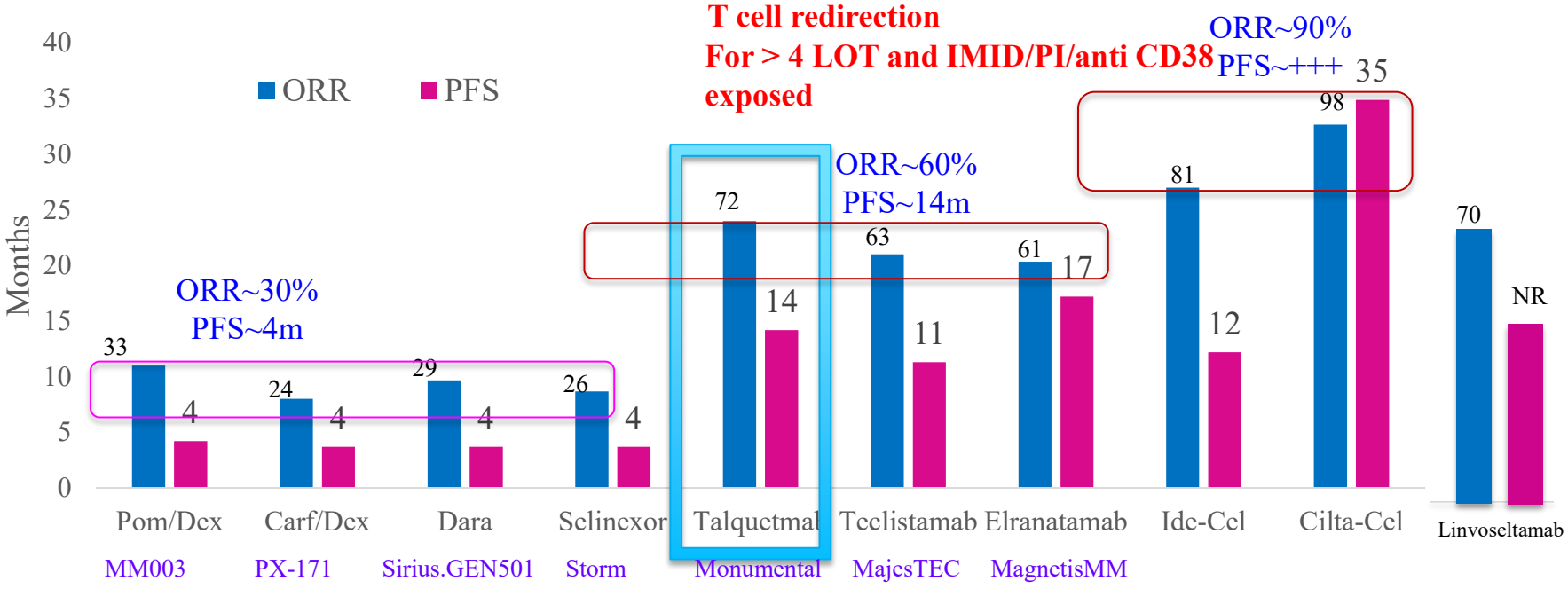
Evidence-Based

- Studies : Phase 3 vs Phase 2; RCT: 3 drugs vs 2 drugs
- PI CARFIZOMIB:
  - Aspire: KRD vs RD
  - Endeavor: Kd Vs Vd
- CD38 Ab DARA / ISA:
  - Dara:
    - ICARIA: Isa-Pd vs Pd
- BCMA:
  - (A) ADC: Belantamab:
    - DREAMM7: Bel-Vd vs Vd
    - DREAMM8: Bel-Pd vs Pd
  - (B) BiSP:
    - MajecTEC-1: TECLISTAMAB
    - MagnetisMM: Elranatamab
  - (C) CAR-T:
    - KARMMA (P2): Ide-cel
    - CARTITUDE 1 (P2): Cilta-cel



Chim et al, Leukemia, 2017

Overall Response Rate (ORR) and Progression Free Survival (PFS) of Recently Approved Therapies in RRMM



Richardson P et al Blood 2014;123(12):1826-32
Siegel DS et al. Blood 2012;120(14): 2817–2825
Lonial S et al. Lancet 2016;387:1551-1560
Chari A et al. N Eng J Med 2019;381:727-738

Touzeau et al EHA 2023
Nooka A et al ASCO 2022;abstract 8007 (oral presentation)
Lesohkin et al Nat Med 2023
Anderson L et al. ASCO 2021;abstract 8016 (poster presentation)
Usmani S et al ASCO 2022;abstract 8028 (poster presentation)

Lentsch et al; EHA 2024

[a]This is not a head-to-head comparison and cross-trial comparisons should not be interfered from these data Data represent two populations, PFS includes all patients, DOR includes responding patients only

Carfilzomib and dexamethasone versus bortezomib and dexame
multiple
open-lab

Meletios A Dimopou
Hartmut Goldschmi
Vesselina Goranova-
Andrew Spencer, Rol

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

The NEW ENGLAND JOURNAL of MEDICINE

Carfilzomib, I
for Re

A. Keith Stewart, M.B., Ch
Tamás Masszi, M.D
Roman Hájek, M.D., Ph
Georgi G. Mihaylov, M
Péter Rajnics, M.D., F
Andrzej J. Jakubo
Heinz Ludwig, M.D.
Jiri Minarik, M.D., Ph.D.,
Dina Ben-Yehuda,
Margaret E. Tonc
Philippe Moreau, M.D.,

ORIGINAL ARTICLE

Castor : Dara-Vd vs Vd

Da
and Dexa

Antonio Palum
Ajay K. No
Ivan Spicka
Maria V. M
Jordan S
William Deraed
and Piet

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 OCTOBER

Pollux : Dara-

Daratumumab, Lenalidomic
for Multiple

M.A. Dimopoulos, A. Oriol, H. Nahi, J. San-Miguel, N.J
M. Komarnicki, K. Suzuki, T. Plesner, S.-S. Yoon, D. B
D. Reece, S. Lisby, N.Z. Khokhar, L. O'Rourke,
and P. Moreau, for the POL

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Eloquent 2 : Elo-Rd vs Rd

Elotuzumab Therapy for Relapsed or Refractory Multiple Myeloma

Sagar Lonial, M.D., Meletios Dimopoulos, M.D., Antonio Palumbo, M.D., Darrell White, M.D., Sebastian Grosicki, M.D., Ph.D., Ivan Spicka, M.D., Adam Walter-Croneck, M.D., Philippe Moreau, M.D., Maria-Victoria Mateos, M.D., Ph.D., Hila Magen, M.D., Andrew Belch, M.D., Donna Reece, M.D., Meral Beksac, M.D., Andrew Spencer, M.D.,

ANTI-CD38 TRIPLET REGIMENS
IMPROVED PFS IN PATIENTS WITH MM

DKd

CANDOR[1]
***DKd** vs. Kd after ≥ PR to 1-3 prior lines*

	PFS HR
mPFS 29 v	
HR 0.59	

DKd was associ

DPd

APO
***Dara-Pd** vs. Pd after ≥1 prior line with len and PI*

	PFS HR
mPFS 12 vs. 7 mo	
HR 0.63	
Len-refractory	0.66
2-3 prior LOT	0.66
High risk	0.85

No new safety concerns were identified with the daratumumab combination

Isa-Kd

IKEMA[2]
***Isa-Kd** vs. Kd after 1-3 prior lines,*

	PFS HR
	0.60
	0.48
	0.72

In these RCTs, not only do they establish :
a) Triplet better than doublets
b) Efficacy of these triplet regimens(DKd, Isa-Kd; DPd, Isa-Pd) in RRMM,
c) Utility of these regimens in LEN-ref RRMM

***Isa-Pd** vs. Pd after ≥2 prior lines with len and PI*

	PFS HR
mPFS 12 vs. 6 mo	
HR 0.60	
Len-refractory	0.59
≥3 prior LOT	0.59
High risk	0.66

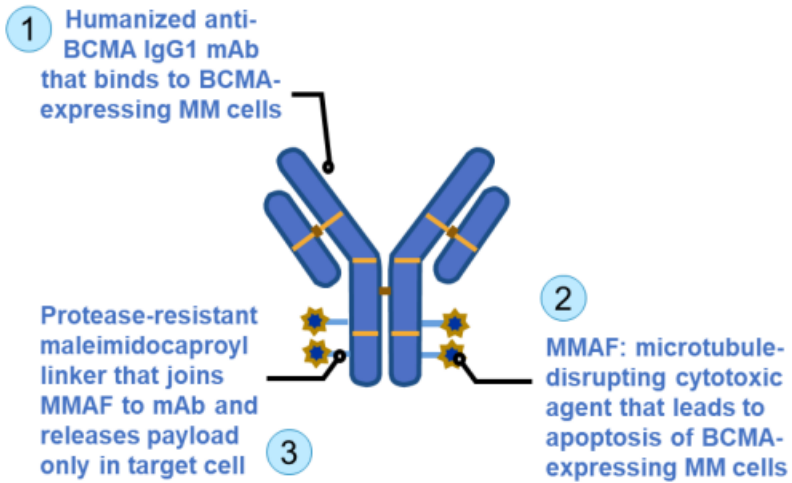
The addition of isatuximab to pomalidomide and dexamethasone was well tolerated

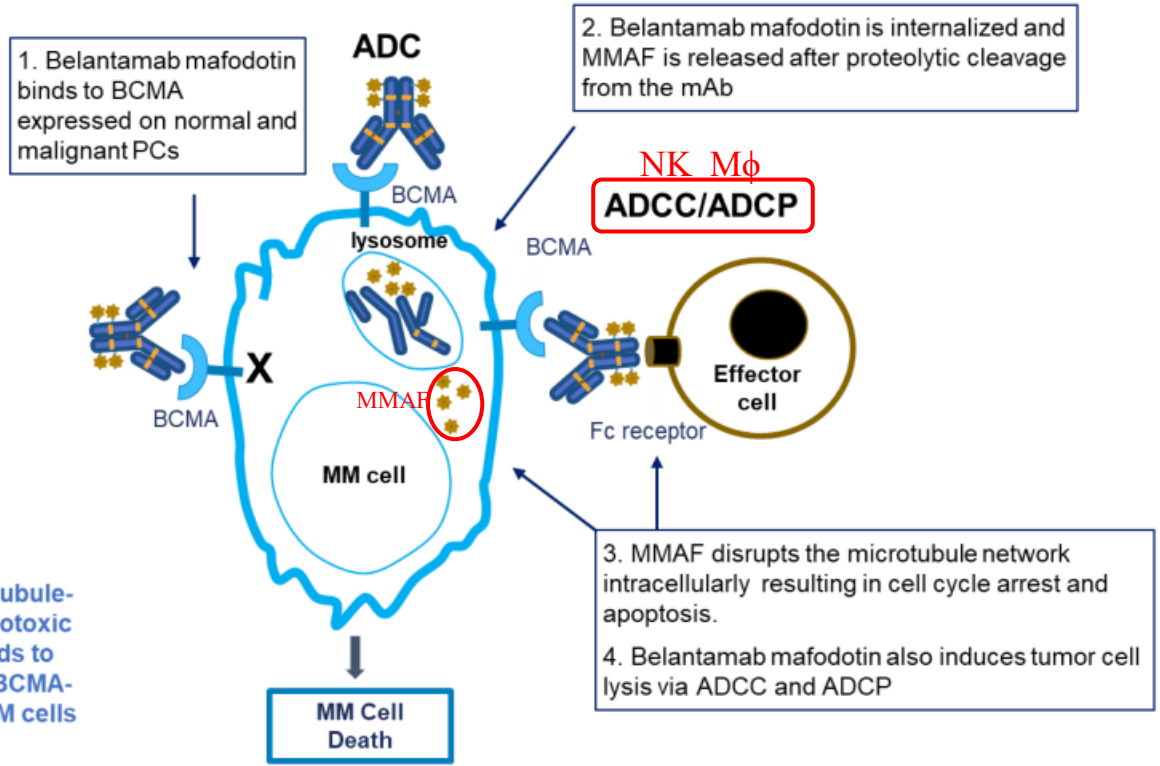
CD38, cluster of differentiation 38; d, dexamethasone; D, daratumumab; HR, hazard ratio; Isa, isatuximab; len, lenalidomide; K, carfilzomib; LOT, line of therapy; MM, multiple myeloma; mo, months; (m)PFS, (median) progression-free survival; P, pomalidomide; PI, proteasome inhibitor; PR, partial response

1. Usmani SZ, et al. Lancet. Oncol. 2022;23:65-76; 2. Moreau P, et al. Lancet. 2021;397:2361-2371; 3. Dimopoulos MA, et al. Lancet Oncol. 2021;22:801-812; 4. Attal M, et al. Lancet. 2019;394:2096-2107

Belantamab Mafodotin MOA

Belantamab mafodotin:
a BCMA-directed antibody and microtubule inhibitor conjugate, comprising 3 components





MMAF = monomethylauristatin F; ADCC = antibody-dependent cellular cytotoxicity; ADCP = antibody-dependent cellular phagocytosis; PC = plasma cell.

Tai YT, et al. *Blood*. 2014;123(20):3128-3138. Farooq AV, et al. *Ophthalmol Ther*. 2020;9(4):889-911.

DREAMM-7 (2nd line) Ph 3 study BeVd vs DVd*Castor* in RRMM (NCT04246047)

Recruitment period
~13-month from FPI (May 7, 2020) to LPI (June 28, 2021)

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

Follow-up period

Eligibility criteria

- ≥1 prior line of MM therapy, and documented PD during or after their most recent therapy
- No prior treatment with anti-BCMA
- **Not refractory or intolerant to *dara*tumumab or *bort*ezomib**

1:1 Randomization

	Cycle 1-8	Cycle 9+
Arm A (BVd)[1]	**Belantamab mafodotin IV 2.5 mg/kg Q3W** + **Bortezomib** 1.3 mg/m² SC on days 1,4,8, and 11 of cycle 1-8 (21-day cycle) + **Dexamethasone** 20 mg[a] on the day of, and day after bortezomib for cycles 1-8	**Belantamab mafodotin monotherapy** IV 2.5 mg/kg Q3W
Arm B (DVd)[1]	**Daratumumab** IV 16 mg/kg cycle 1-3; Q1W and cycle 4-8; Q3W + **Bortezomib** 1.3 mg/m² SC on days 1,4,8, and 11 of cycle 1-8 (21-day cycle) + **Dexamethasone** 20 mg[a] on the day of, and day after bortezomib for cycles 1-8	**Daratumumab monotherapy** IV 16 mg/kg Q4W

End of treatment visit

Follow-up for PFS Q3W (for patients who discontinue due to reasons other than PD)

Disease assessments Q3W

Follow-up for OS Q12W (for patients who discontinue due to PD, or other reasons)

- The comparator arm is a triplet instead of the usual doublet
- DVd is established by CASTOR in RRMM

Stratification:
- Prior lines of treatment (1 vs 2 c ≥4)
- R-ISS (I vs II/III)
- Prior bortezomib (yes vs no)

ease progression

- **Primary endpoint:** PFS
- **Key secondary endpoints:** OS, DOR, MRD
- **Additional secondary endpoints:** CRR, ORR, CBR, TTR, TTP, PFS2, AEs, Ocular findings, QOL

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SGH 200

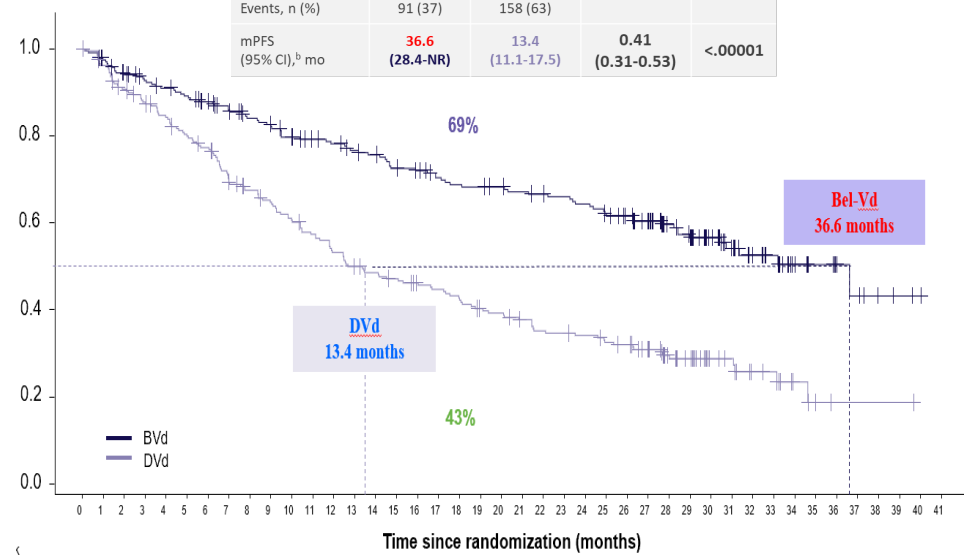
DREAMM 7 : PFS

Bel-Vd vs DVd

Bel-Vd yielded greater PFS benefit in :
a) LEN-R than Len-sensitive, &
b) HR than SR cytogenetics

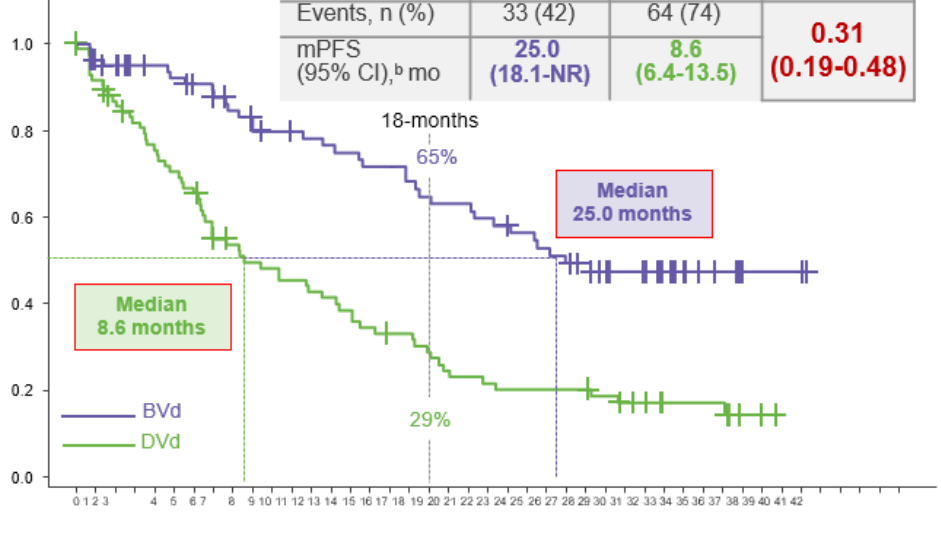
Entire cohort

PFS[a]	BVd (n=243)	DVd (n=251)	HR[c] (95% CI)	*p*-value[d]
Events, n (%)	91 (37)	158 (63)		
mPFS (95% CI),[b] mo	36.6 (28.4-NR)	13.4 (11.1-17.5)	0.41 (0.31-0.53)	<.00001



Lenalidomide refractory

PFS[a]	BVd (N=79)	DVd (N=87)	HR[c] (95% CI)
Events, n (%)	33 (42)	64 (74)	0.31 (0.19-0.48)
mPFS (95% CI),[b] mo	25.0 (18.1-NR)	8.6 (6.4-13.5)	



DREAMM-8 Phase 3 study of Be-Pd vs VPd*Optimismm* in 2L+ RRMM (NCT04484623)[1,2]

Recruitment period
October 2020 to December 2022

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

Eligibility criteria

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

Stratification[b]:
- Prior LOT (1 vs 2 or 3 vs ≥4)
- Prior bortezomib (yes vs no)
- Prior anti-CD38 therapy (yes vs no)

N=302

1:1 randomization

BPd (Q4W)

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

PVd (Q3W)

Bortezomib
1.3 mg/m² SC on Day1,4,8,11 of cycles 1-8 then days 1 & 8 (21-day cycles)
+
Pomalidomide 4 mg PO days 1-14 (21-day cycles)
+
Dexamethasone 20 mg[a] on the day and day after bortezomib

30-day post-treatment visit

Primary endpoint:
PFS (IRC assessed per IMWG)

Key secondary endpoints:
OS, MRD negativity, and DOR

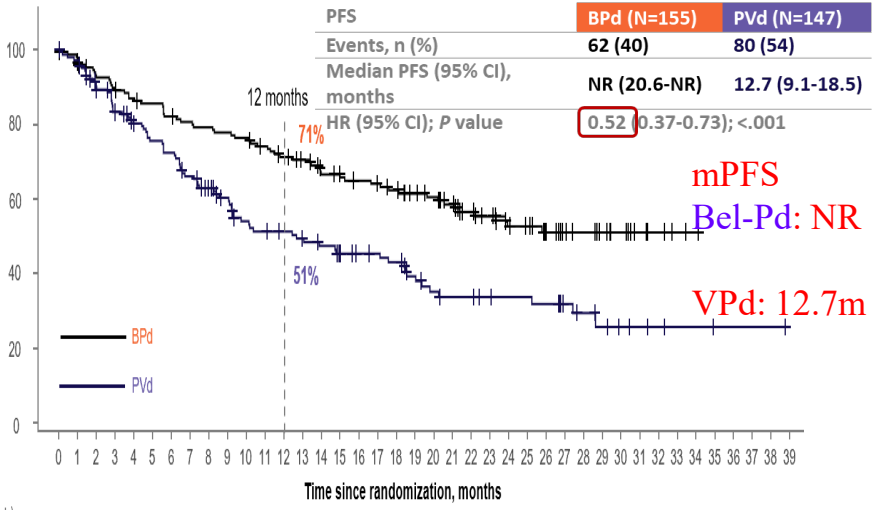
Additional secondary endpoints include:
ORR, safety, AEs, ocular findings, HRQOL, and PROs

VPd is a triplet established by OptimisMM In RRMM

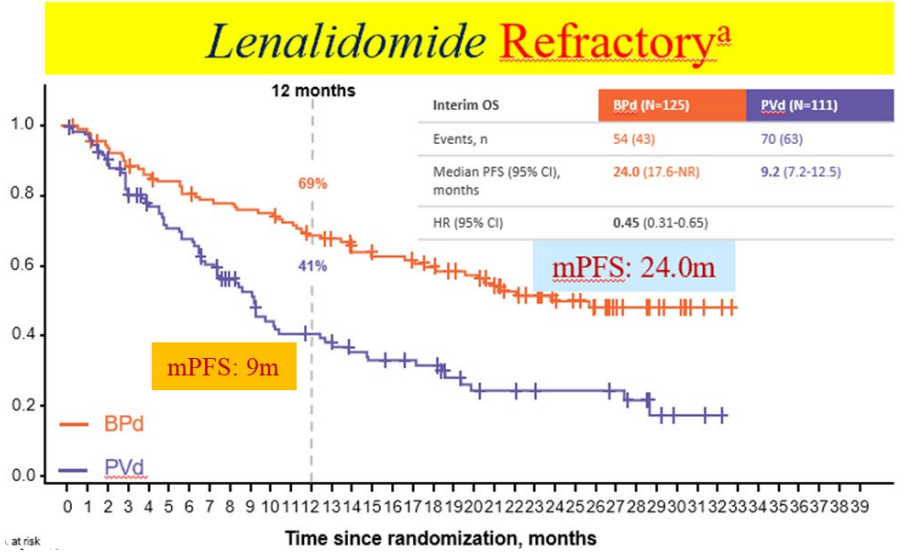
DREAMM 8 : PFS

Bel-Pd vs VPd

Entire cohort

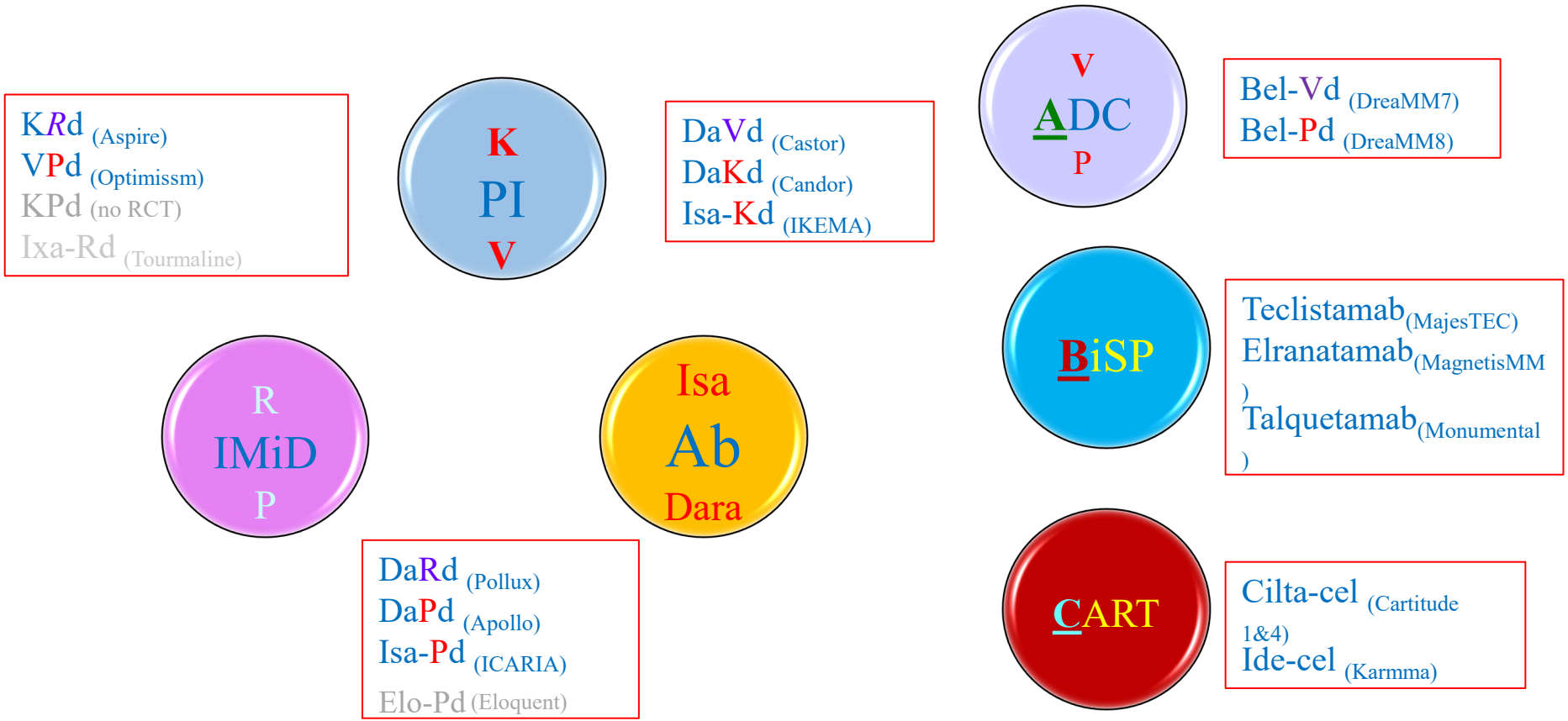


Lenalidomide Refractory[a]



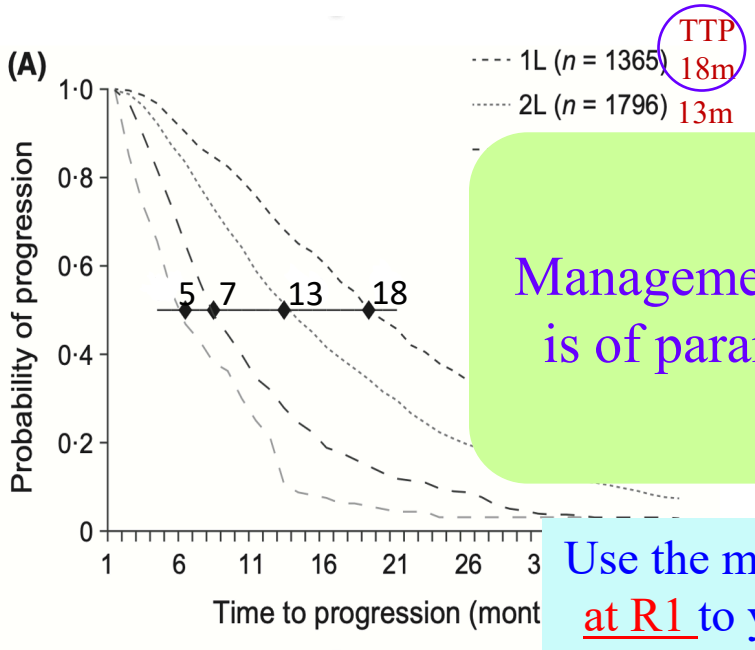
RCT showed 3 drugs > 2 drugs

Possible permutation 3C2 in RRMM



Time to progression by line of therapy

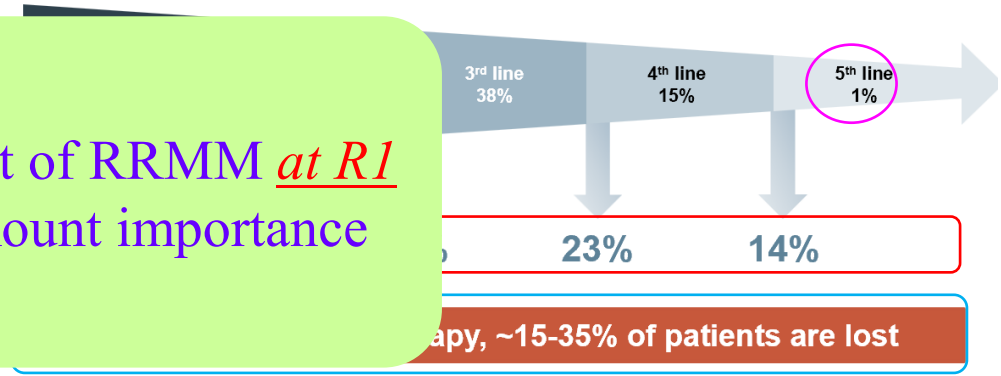
First remission is the longest



TTP
18m
13m

Only few patients with MM reach later lines of therapy

% of patients with multiple myeloma reaching the next line of therapy



Management of RRMM *at R1* is of paramount importance

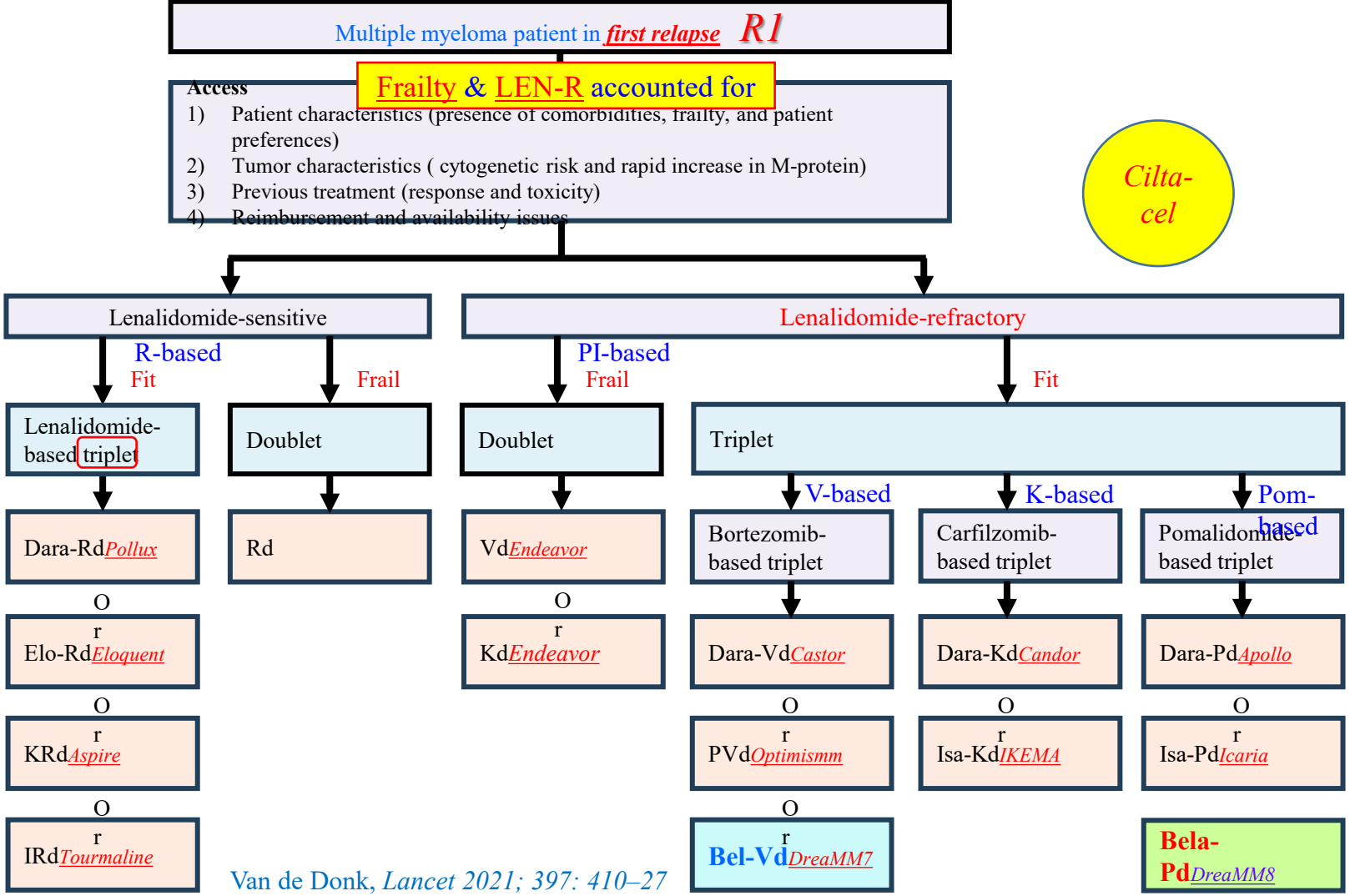
Use the most effective regimen at R1 to yield the longest PFS

This study investigated MM patient characteristics, treatment durations and outcomes, and symptom burden across the treatment pathway in Belgium, France, Germany, Italy, Spain, Switzerland and the UK. In total, 435 physicians retrospectively reviewed 4997 patient charts.

Only patients who had progressed at the time of inclusion in the study were included in this analysis.

1L–5L, first line–fifth line

Yong K, et al. Br J Haematol. 2016;175(2):252-264.


Multiple myeloma patient in first relapse R1
Frailty & LEN-R accounted for
Access
1) Patient characteristics (presence of comorbidities, frailty, and patient preferences)
2) Tumor characteristics (cytogenetic risk and rapid increase in M-protein)
3) Previous treatment (response and toxicity)
4) Reimbursement and availability issues
Cilta-cel
Lenalidomide-sensitive
Lenalidomide-refractory
R-based
Fit
Frail
PI-based
Frail
Fit
Lenalidomide-based triplet
Doublet
Doublet
Triplet
V-based
K-based
Pom-based
Dara-RdPollux
O r
Elo-RdEloquent
O r
KRdAspire
O r
IRdTourmaline
Rd
VdEndeavor
O r
KdEndeavor
Bortezomib-based triplet
Dara-VdCastor
O r
PVdOptimismm
O r
Bel-VdDreaMM7
Carfilzomib-based triplet
Dara-KdCandor
O r
Isa-KdIKEMA
Pomalidomide-based triplet
Dara-PdApollo
O r
Isa-PdIcaria
Bela-PdDreaMM8
Van de Donk, Lancet 2021; 397: 410–27

Salvage Rx in *LEN-ref* subgroup

	PI-based	
Study (of the exp arm)	IKEMA IsaKd	CANDOR Dara-Kd
N (total)	179	312
#PLOT median	1-3 (2)	1-3 (2)
ORR/CR	86.6/39.7%	84/22%
mFU	44m	27.8m
PFS	35.7m	28.6m
LEN-R cohort		
LEN-R (N) (%)	57 (32%)	99 (32%)
ORR/ ≥CR	82.5% 38.6%[1] (at mFU 20m)	79.8% 31%
PFS	NA (HR=0.59 at 44m FU)	28.1m

Salvage Rx in *LEN-ref* subgroup

	PI-based		
Study (of the exp arm)	IKEMA IsaKd	CANDOR Dara-Kd	DreaMM7 Bel-Vd
N (total)	179	312	243
#PLOT median	1-3 (2)	1-3 (2)	1-4+ (1)
ORR/CR	86.6/39.7%	84/22%	83.1/35.8%
mFU	44m	27.8m	39.4m
PFS	35.7m	28.6m	
LEN-R cohort			
LEN-R (N) (%)	57 (32%		79 (33%)
ORR/ ≥CR	82.5%	79.8%	84%
	38.6%[1] (at mFU 20m)	31%	35%
PFS	NA (HR=0.59 at 44m FU)	28.1m	25m

ORR~80%
CR ~33% (1/3)
PFS~20+m

Salvage Rx in *LEN-ref* subgroup

	PI-based			Pomalidomide-based		
Study (of the exp arm)	IKEMA IsaKd	CANDOR Dara-Kd	DreaMM7 Bel-Vd	Optimismm VPd	ICARIA Isa-Pd	APOLLO Dara-Pd
N (total)	179	312	243	281	154	151
#PLOT median	1-3 (2)	1-3 (2)	1-4+ (1)	1-3(1L+) 2	2L+ (3)	1-5(1L+) (2)
ORR/CR	86.6/39.7%	84/22%	83.1/35.8%	82.2/15.7%	63/9.7%	69/27.5%
mFU	44m	27.8m	39.4m	15.9m	35.3m	30.7m
PFS	35.7m	28.6m		11.2m	11.5m	12.4m
LEN-R cohort						
LEN-R (N) (%)	57 (32%)	(32%)	79 (33%)	200 (71%)	(94%)	120 (79%)
ORR/ ≥CR	82.5% 38.6%[1] (at mFU 20m)	79.8% 31%	84% 35%	NA for LEN-R cohort	59% NA	65% 27.5%*
PFS	NA (HR=0.59 at 44m FU)	28.1m	25m	9.5m (suppl)	*11.1m**	*9.9m*

ORR~80%
CR ~33% (1/3)
PFS~20+m

ORR~60%
CR NA / 27%
PFS~10-11m

Salvage Rx in *LEN-ref* subgroup

	PI-based			Pomalidomide-based			
Study (of the exp arm)	IKEMA IsaKd	CANDOR Dara-Kd	DreaMM7 Bel-Vd	Optimismm VPd	ICARIA Isa-Pd	APOLLO Dara-Pd	DreaMM8 Bel-Pd
N (total)	179	312	243	281	154	151	155
#PLOT median	1-3 (2)	1-3 (2)	1-4+ (1)	1-3(1L+) 2	2L+ (3)	1-5(1L+) (2)	1-4+ (1)
ORR/CR	86.6/39.7%	84/22%	83.1/35.8%	82.2/15.7%	63/9.7%	69/27.5%	77/43%
mFU	44m	27.8m	39.4m	15.9m	35.3m	30.7m	35.8m
PFS	35.7r			11.2m		12.4m	
LEN-R cohort							
LEN-R (N) (%)	57 (32%)	99 (32%)	79 (33%)	200 (71%)	144 (94%)	120 (79%)	125 (81%)
ORR/ ≥CR	82.5% 38.6%[1] (at mFU 20m)	79.8% 31%	84% 35%	NA for LEN-R cohort	59% NA	65% 27.5%*	77% 40%
PFS	NA (HR=0.59 at 44m FU)	28.1m	25m	9.5m (suppl)	*11.1m**	*9.9m*	24m

ORR~80%
CR ~33% (1/3)
PFS~20+m

ORR~60%
CR NA / 27%
PFS~10-11m

ORR~80%
CR ~40%
PFS~24m

Salvage Rx in *LEN-ref* subgroup

	PI-based			Pomalidomide-based				CAR-T	BiSP
Study (the exp arm)	IKEMA IsaKd	CANDOR Dara-Kd	DreaMM7 Bel-Vd	Optimismm VPd	ICARIA Isa-Pd	APOLLO Dara-Pd	DreaMM8 Bel-Pd	Ciltacel (CAR-4)	MajesTEC3 TEC-Dara
N (total)	179	312	243	281	154	151	155	208	291
#PLOT median	1-3 (2)	1-3 (2)	1-4+ (1)	1-3(1L+) 2	2L+ (3)	1-5(1L+) (2)	1-4+ (1)	1-3	1-3 (2)
ORR/CR	86.6/39.7%	84/22%	83.1/35.8%	82.2/15.7%	63/9.7%	69/27.5%	77/43%	84.6/76.9%	89/82%
mFU	44m	27.8m	39.4m	15.9m	35.3m	30.7m	35.8m	33.6m	34.5m
PFS	35.7			11.2m		12.4m			NR (3y:83%)
LEN-R cohort									
LEN-R (N) (%)	57 (32%)	99 (32%)	79 (33%)	200 (71%)	144 (94%)	120 (79%)	125 (81%)	208 (100%)	240 (82.5%)
ORR/ ≥CR	82.5% 38.6%[1] (at mFU 20m)	79.8% 31%	84% 35%	NA for LEN-R cohort	59% NA	65% 27.5%*	77% 40%	84.6% 76.9%	89%* 82%*
PFS	NA (HR=0.59 at 44m FU)	28.1m	25m	9.5m (suppl)	*11.1m**	*9.9m*	24m	NR 59.4% at 30m	83.4% at 36m*

ORR~80%
CR ~33% (1/3)
PFS~20+m

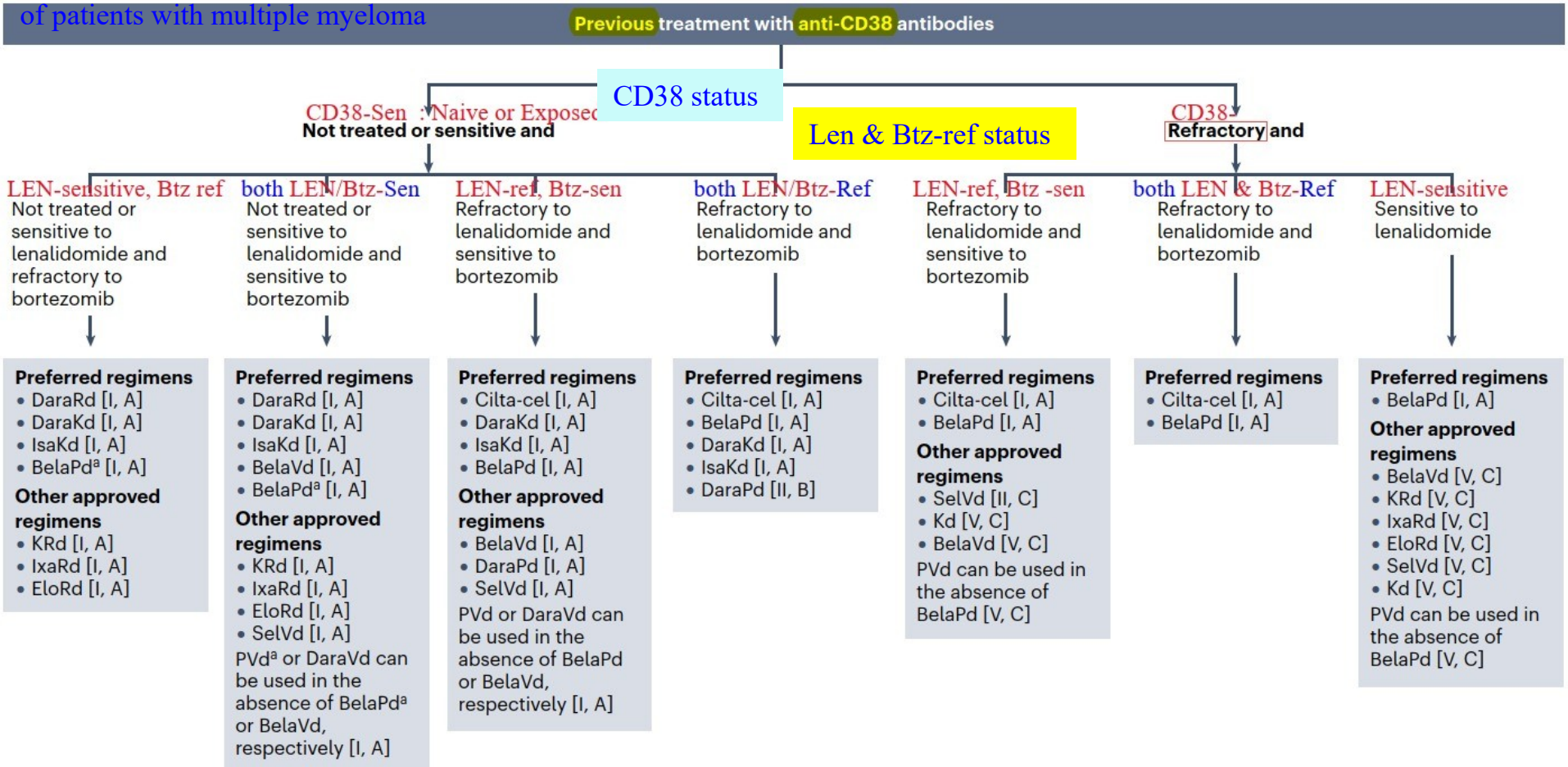
ORR~60%
CR NA / 27%
PFS~10-11m

ORR~80%
CR ~40%
PFS~24m

ORR~85%
CR ~80%
PFS~NR

EHA–EMN Evidence-Based Guidelines
for diagnosis, treatment and follow-up
of patients with multiple myeloma

nature reviews clinical oncology



In first relapse…

CD38 status

Anti-CD38 sensitive

Anti-CD38 refractory

Len & Btz-ref status

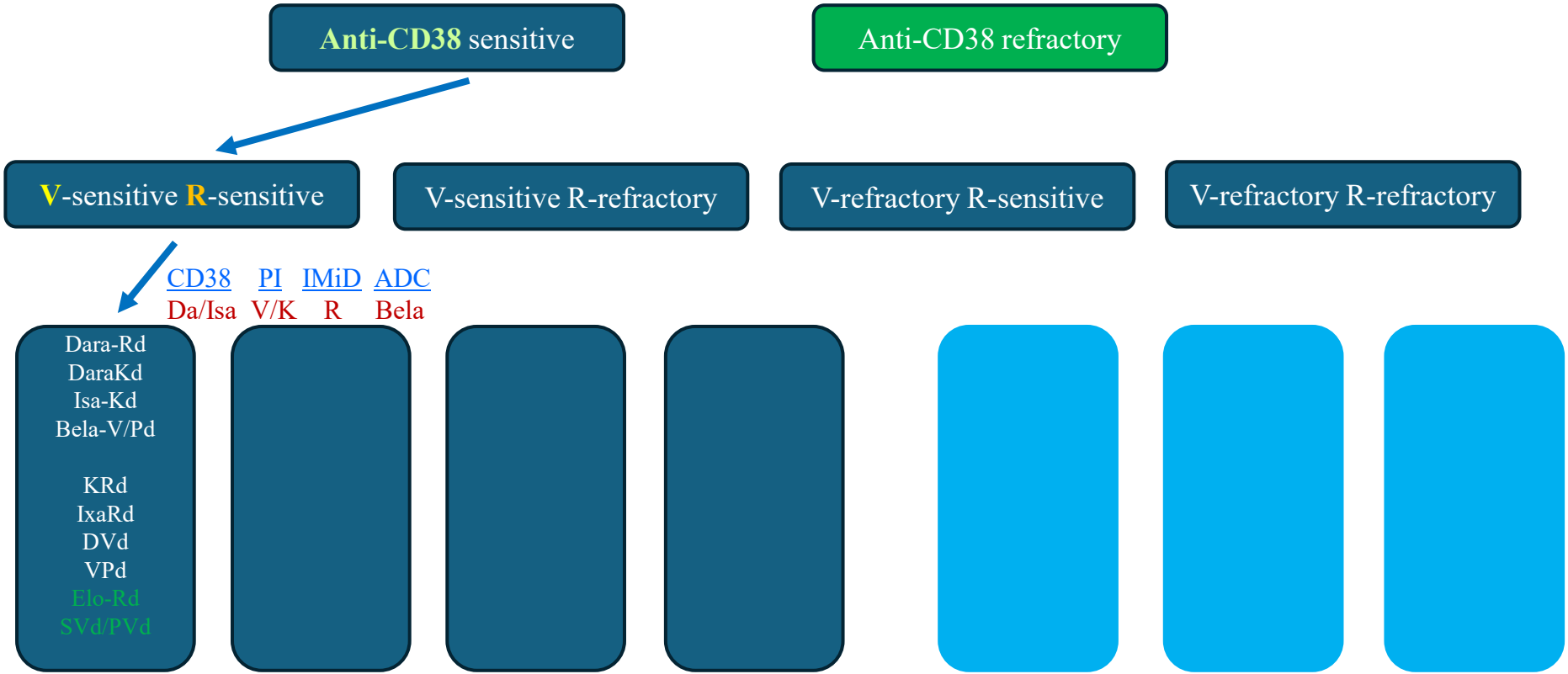
V-sensitive R-sensitive

V-sensitive R-refractory

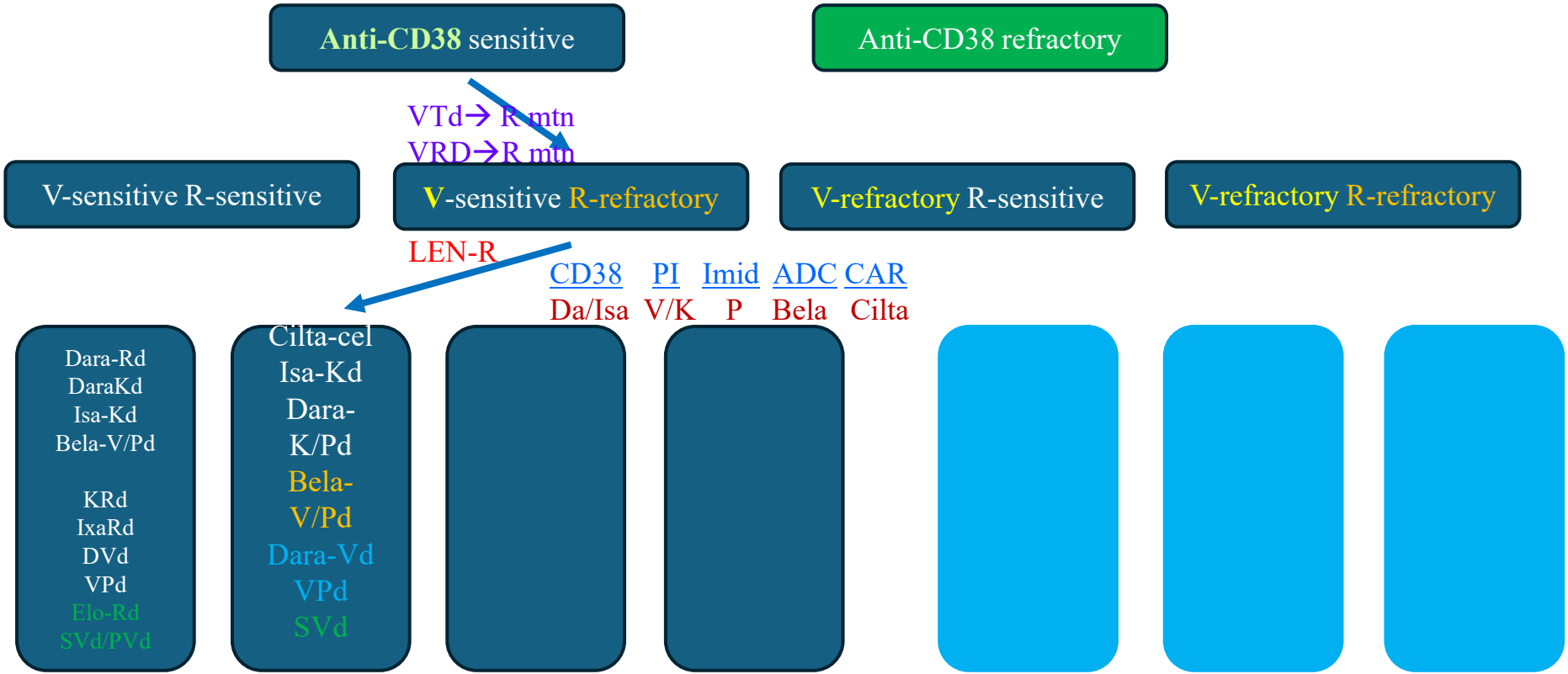
V-refractory R-sensitive

V-refractory R-refractory

In first relapse…



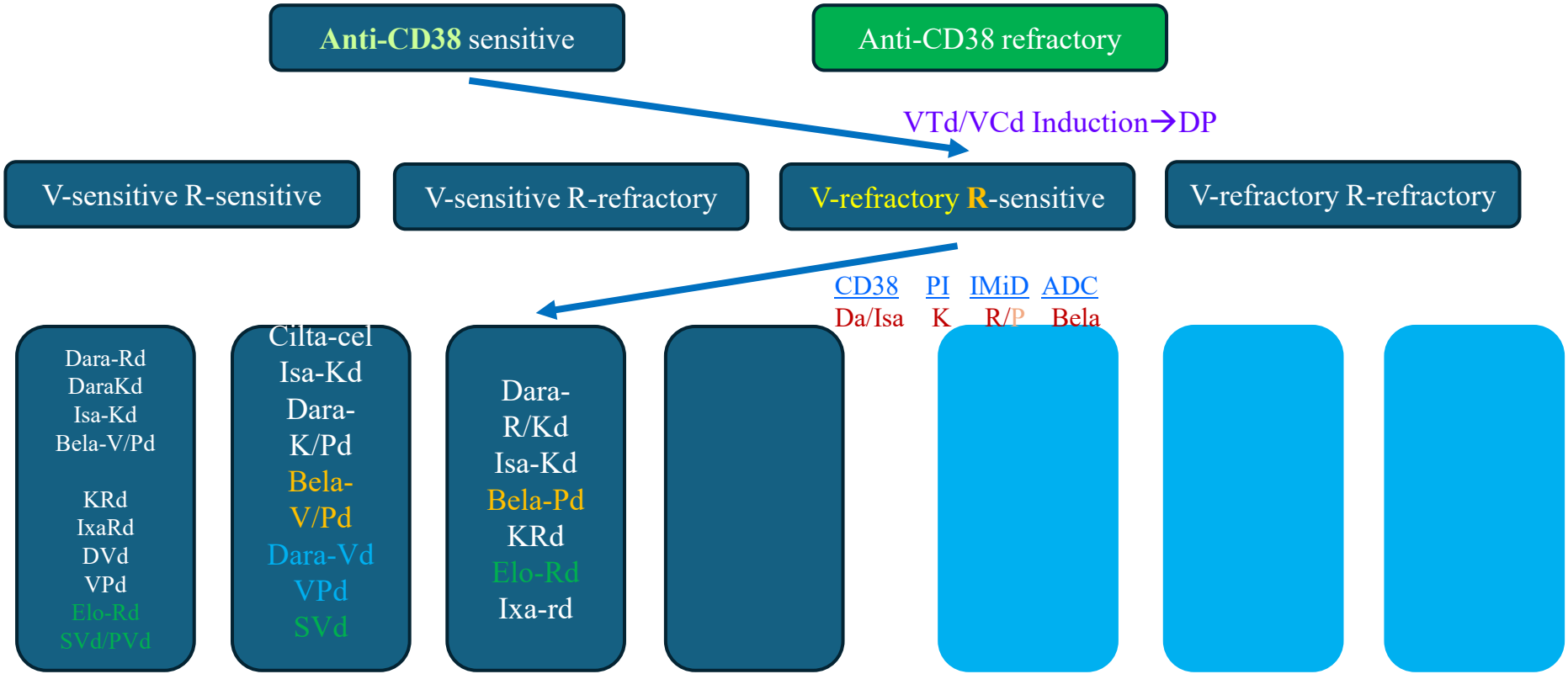
In first relapse…



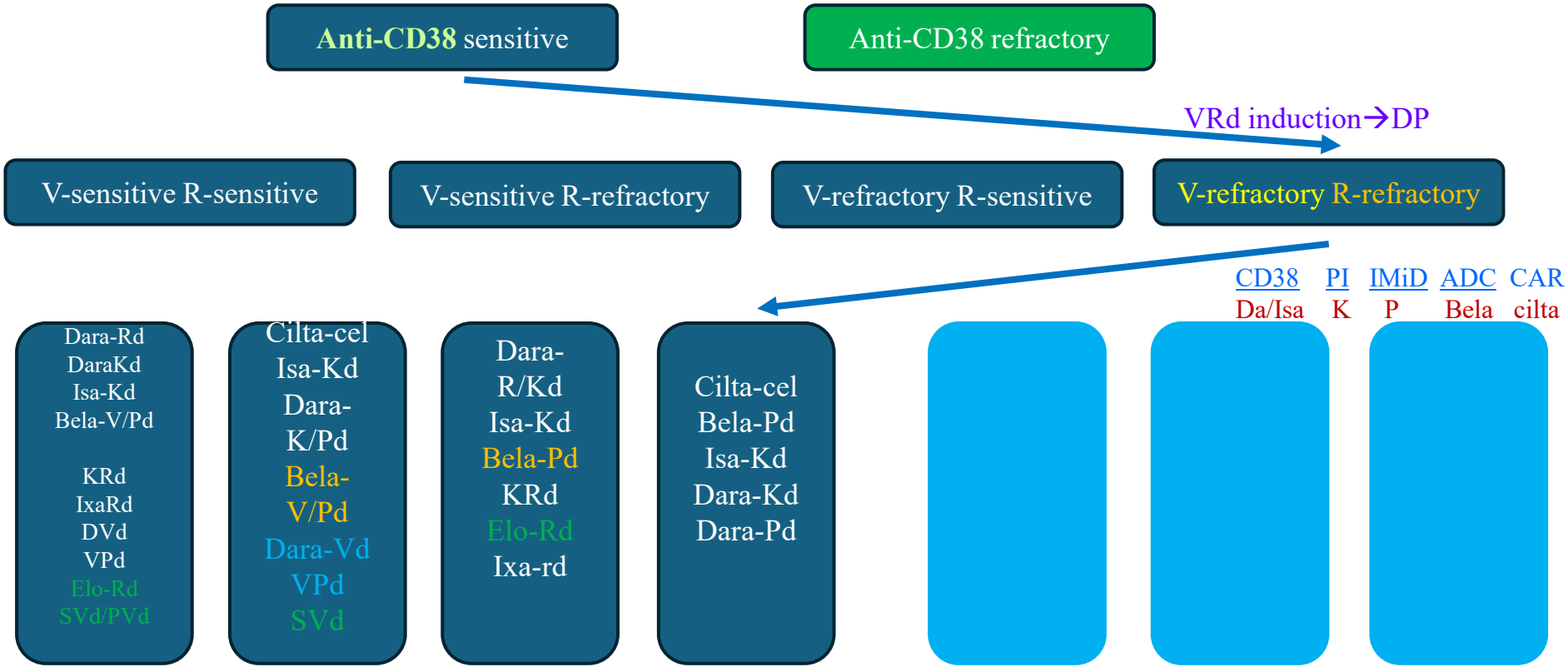
IsaPd 3rd line

***

In first relapse…

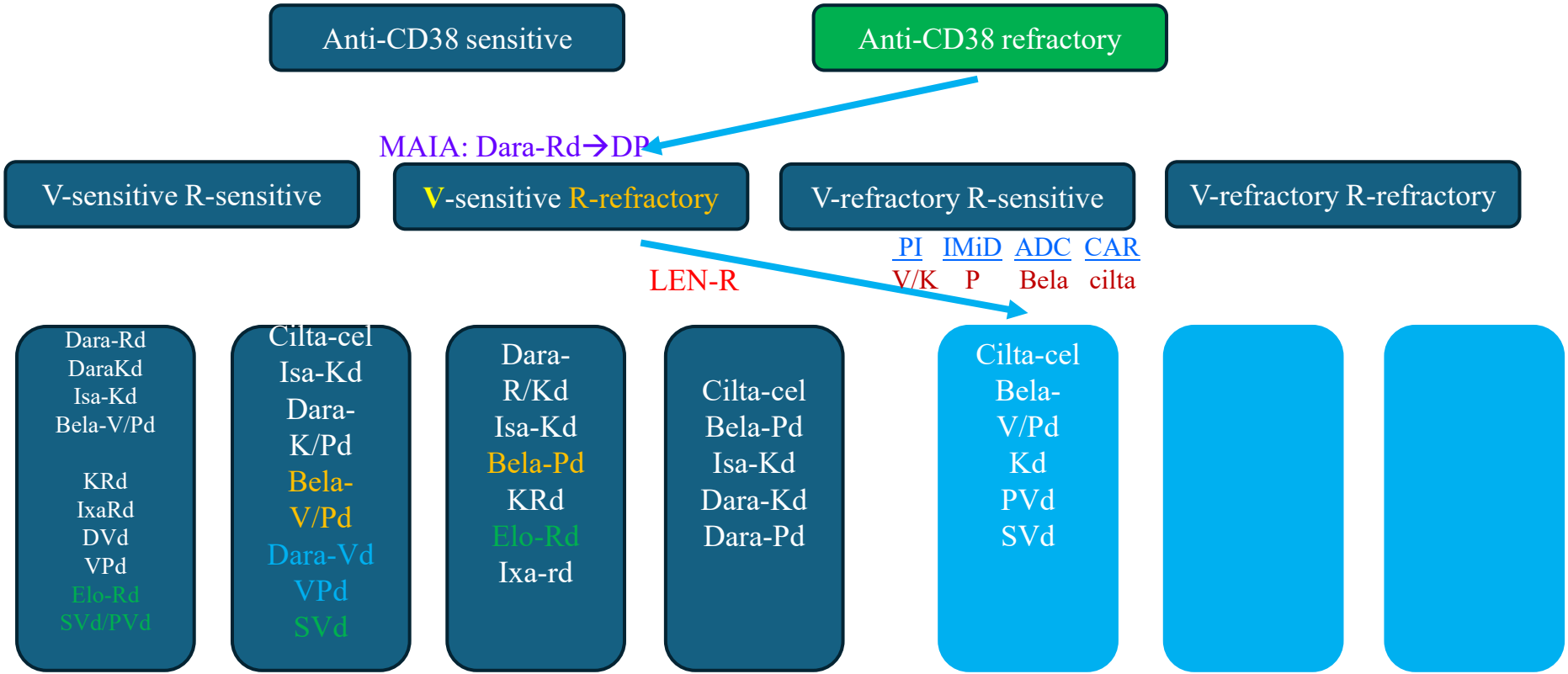


In first relapse…

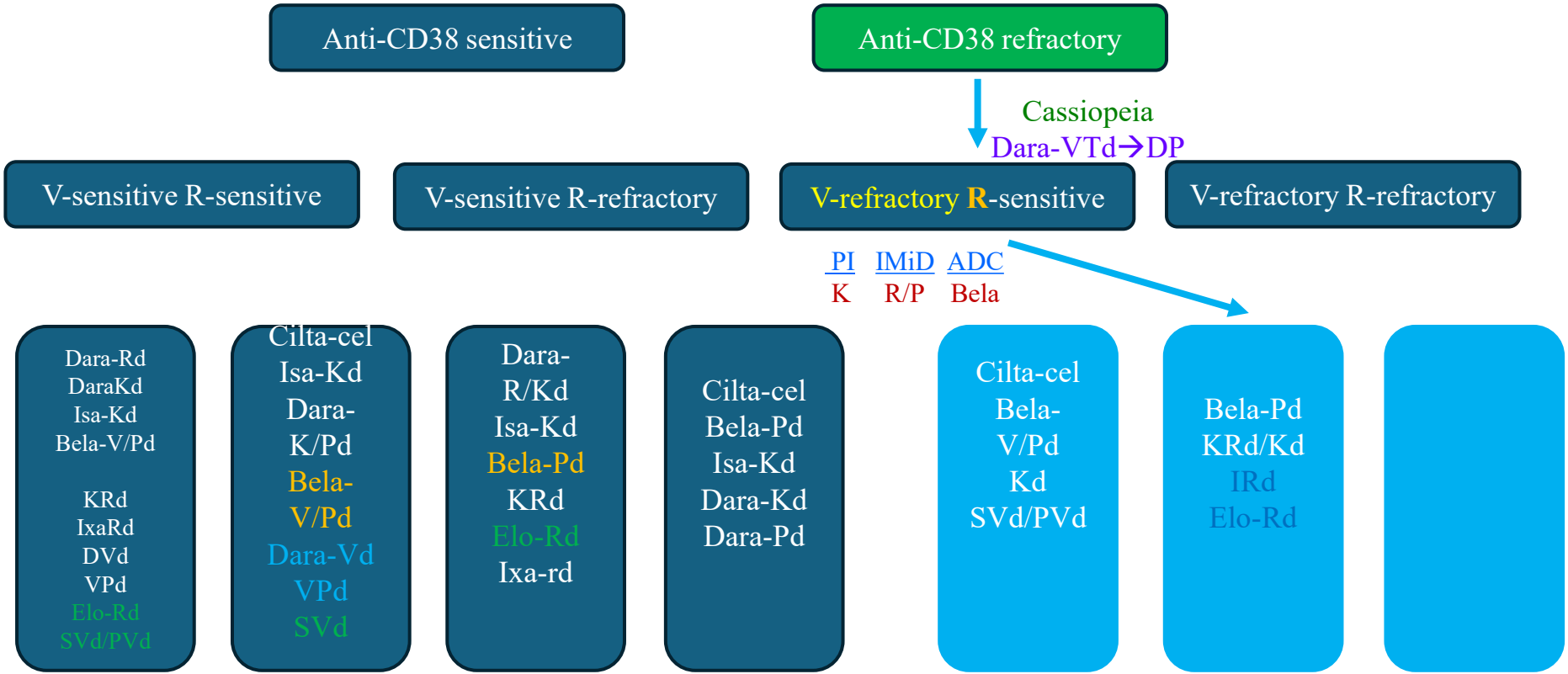


Isa-Pd at later relapse

In first relapse…



In first relapse…



In first relapse…

Anti-CD38 sensitive

Anti-CD38 refractory

DVRd induction→DP
TCR dire outcome
TCRT

V-sensitive R-sensitive

V-sensitive R-refractory

V-refractory R-sensitive

V-refractory R-refractory

Triple Class Ref
(OS~6m Mammoth)
K/Bela-Pd → CAR-T →BiSP

Dara-Rd
DaraKd
Isa-Kd
Bela-V/Pd

KRd
IxaRd
DVd
VPd
Elo-Rd
SVd/PVd

Cilta-cel
Isa-Kd
Dara-K/Pd
Bela-V/Pd
Dara-Vd
VPd
SVd

Dara-R/Kd
Isa-Kd
Bela-Pd
KRd
Elo-Rd
Ixa-rd

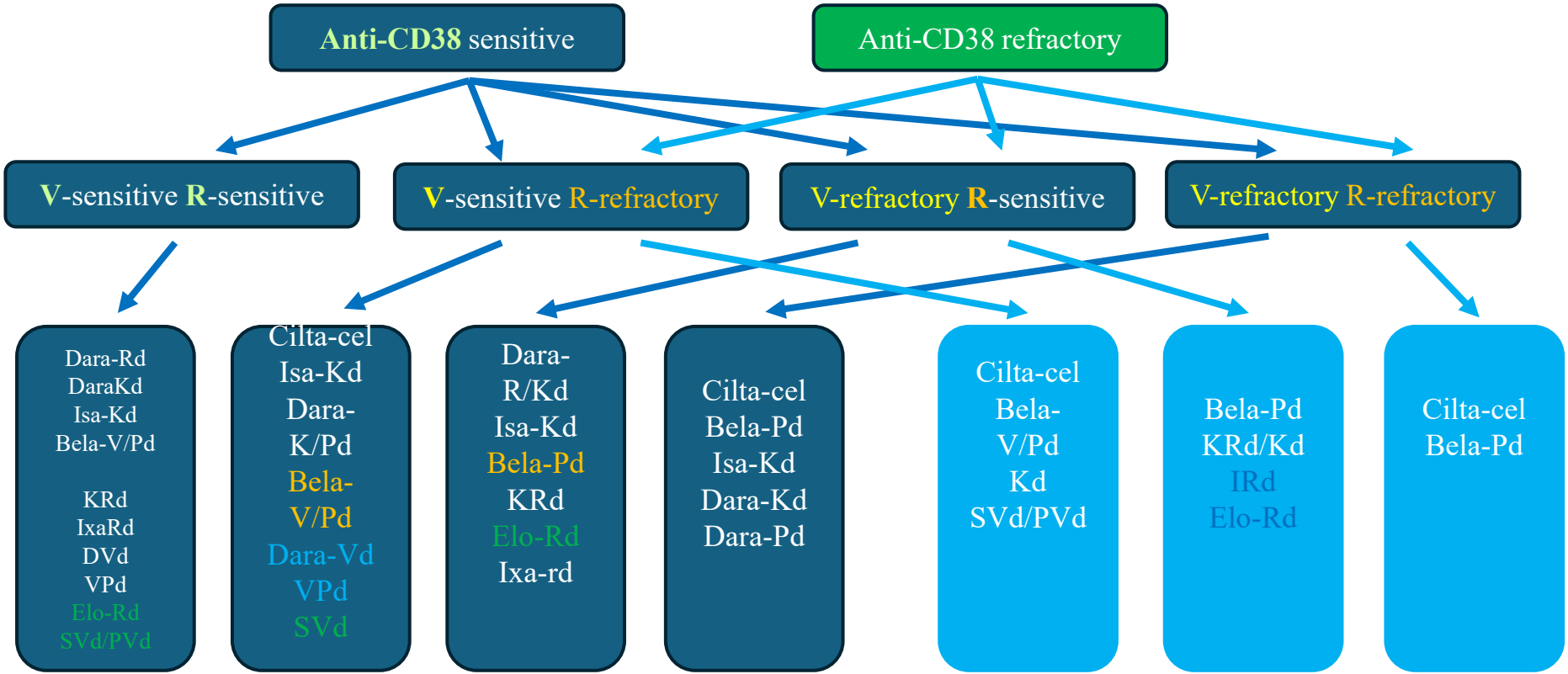
Cilta-cel
Bela-Pd
Isa-Kd
Dara-Kd
Dara-Pd

Cilta-cel
Bela-V/Pd
Kd
SVd/PVd

Bela-Pd
KRd/Kd
IRd
Elo-Rd

Cilta-cel
Bela-Pd

In first relapse…



At Second or Subsequent Relapse
After 1L+ or 2L+

3rd / 4th line according to prior lines of therapy (mainly PI, and treated with / refractory to lenalidomide)

2L+, i.e 3rd or 4th LOT

- Cilta-cel [I, A]
- Ide-cel [I, A]
- BelaPd [I, A]
- DaraPd [I, A]
- IsaPd [I, A]
- EloPd [I, A]
- BelaVd [I, A]

Other regimens to consider if not given before

- DaraKd [I, A]
- IsaKd [I, A]
- DaraVd [I, A]
- Kd [I, A]
- SelVd [I, A]

Patient treated with / or refractory to proteasome inhibitor, immunomodulatory agent and anti-CD38 antibody

TCR (PI-IMiD-CD38)

BCMA-targeted therapy

- CAR T cells (cilta-cel and ide-cel) at third or fourth line [I, A]; or after fourth line [II, B]
- Bispecific antibodies (teclistamab, elranatamab and linvoseltamab) [II, B]
- ADC (BelaPd) [I, A]

GPRC5D-targeted therapy

- Bispecific antibody (talquetamab) [II, B]

Other regimens

- Melflufen [I, B]
- Seld [II, B]

Patient treated with / or refractory to PI, IMiD and CD38 antibody, and CAR T cells or ADC

Relapse after IMT → IMT of alternative target

GPRC5D-targeted therapy

- Bispecific antibody (talquetamab) [II, B]

BCMA-targeted therapy

- Bispecific antibodies (teclistamab, elranatamab and linvoseltamab) [II, B]

Other regimens

- Melflufen [I, B]
- Seld [II, B]

Clinical trials

BiSP

Teclistamab vs Elranatamab

MajesTEC-1: Study Design[1,a]

Key eligibility criteria:
- ≥18 y
- RRMM[2]
- ECOG PS 0 or 1
- Triple-class exposed (PI, IMiD, anti-CD38 mAb)
- No prior BCMA-directed therapy

Phase 1

Dose escalation: IV cohorts; SC cohorts

Dose expansion: RP2D 1.5 mg/kg SC QW

Phase 2

Phase 2 efficacy cohort

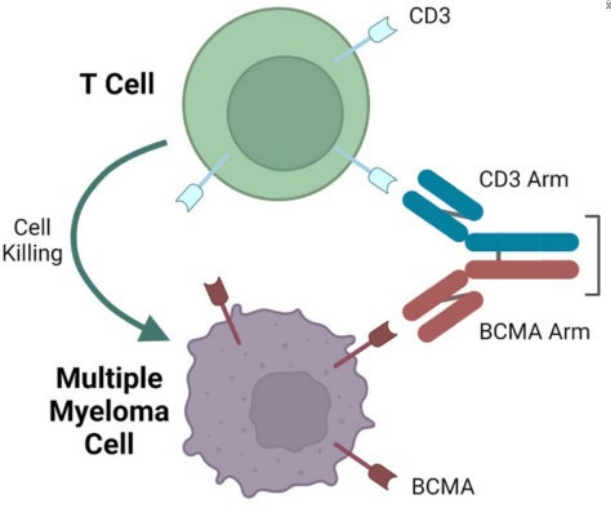
Primary endpoint: ORR

Key secondary endpoints:
- PK/PD
- DOR
- PFS
- OS
- MRD negativity
- AEs
- HRQoL

Step-up dose (SUD) 1: 0.06 mg/kg (4% target dose) → SUD 2: 0.3 mg/kg (20% target dose) → Treatment dose 1: 1.5 mg/kg (100% target dose) → Subsequent treatment doses: 1.5 mg/kg QW

Option to switch to Q2W[a] (Q4W[b]) dosing if:
- ≥PR after ≥4 cycles (phase 1)
- ≥CR for ≥6 months (phase 2)

performance status; HRQoL, health-related quality of life; codynamics; PI, proteasome inhibitor; PK, pharmacokinetics;



MagnetisMM-3 Study

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

Patients with RRMM

Key inclusion criteria:
- Refractory to ≥1 each of the following: proteasome inhibitor, immunomodulatory drug, and anti-CD38 antibody[a]
- ECOG performance status ≤2
- Creatinine clearance ≥30 mL/min
- Platelets ≥25 × 10^9/L
- ANC ≥1.0 × 10^9/L
- Hemoglobin ≥8 g/dL

Cohort A (n=123): No prior BCMA-directed treatment

Cohort B (n=64): Prior BCMA-directed ADC or CAR-T

- Patients will be followed for ~2 y from enrollment

Elranatamab 76 mg SC QW on a 28-d cycle

Primary endpoint
- ORR by BICR[b]

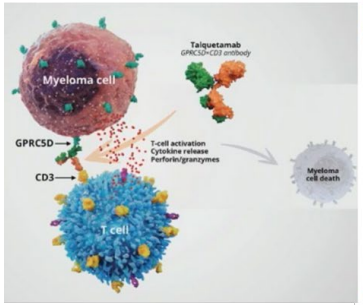
Secondary endpoints
- Duration of response[b,c]
- CR rate[b,c]
- ORR[c]
- ORR by baseline extramedullary disease status[b]
- Duration of CR[b,c]
- Time-to-response[b,c]
- PFS[b,c]
- MRD-negativity rate
- OS
- Safety
- Pharmacokinetics

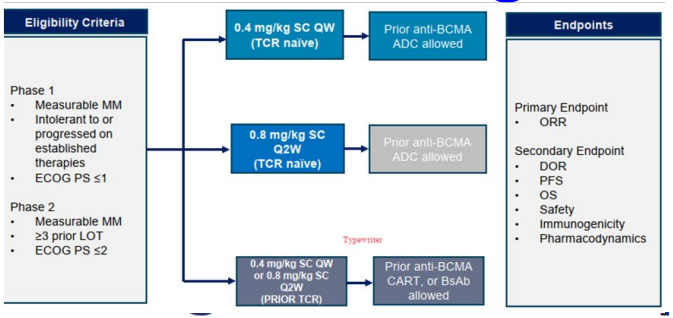
Cycle 1				Cycles ≥2				Cycles ≥7			
Step-up doses of 12 mg and 32 mg SC			76 mg SC QW				76 mg SC QW				76 mg SC Q2W
Wk 1 (D 1 and 4)	Wk 2	Wk 3	Wk 4	Wk 1	Wk 2	Wk 3	Wk 4	Wk 1	Wk 2	Wk 3	Wk 4

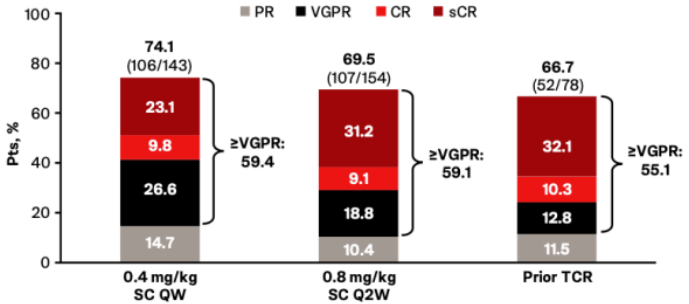
Elranatamab
- SUD1: 16% target dose
- SUD2: 42% target dose
- 100% target dose

For patients receiving ≥6 cycles and achieving partial response or better with responses persisting for ≥2 mo, the dosing interval will be changed to Q2W

Talquetamab MonumenTAL-1 Long-Term FU

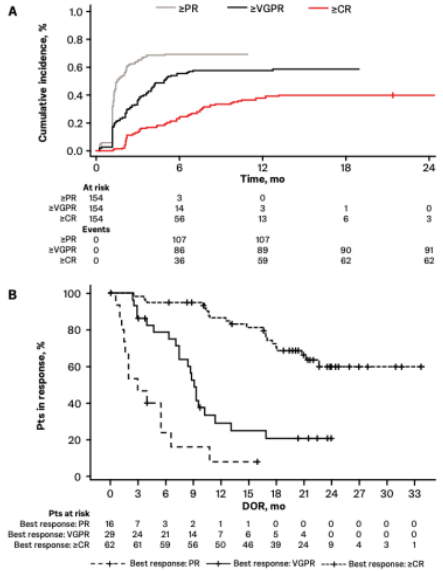






Outcome	0.4 mg/kg SC QW (n=143)	0.8 mg/kg SC Q2W (n=154)	Prior TCR (n=78)
mFU, mo	29.8	23.4	20.5
mDOR (95% CI), mo	9.5 (6.7–13.4)	17.5 (12.5–NE)	N/A
mDOR in pts with ≥CR (95% CI), mo	28.6 (19.4–NE)	NR (21.2–NE)	N/A
mPFS (95% CI), mo	7.5 (5.7–9.4)	11.2 (8.4–14.6)	7.7 (4.1–14.5)
24-mo OS rate (95% CI), %	60.6 (51.7–68.4)	67.1 (58.3–74.4)	57.3 (43.5–68.9)

Figure 3: Time to first confirmed response per IRC (A) and DOR by depth of response (B) in the Q2W cohort



IRC = independent review committee.

Rasche L, et al. Presented at: European Haematology Association Congress; June 13, 2024; Madrid, Spain. Abstract P915.
NIH. Accessed October 25, 2024. https://www.clinicaltrials.gov/study/NCT04634552.

Agent	Teclistamab (SC)	Elranatamab (SC)	Talquetamab biweekly (SC)	Idecabtagene vicleucel (IV)	Ciltacabtagene autoleucel (IV)	Eque-cel (IV)
N	165	123	145	128	97	103
Target	BCMA x CD3	BCMA x CD3	GPRC5D x CD3	BCMA	BCMA	BCMA
EMP	17%		26.9%	39%		13.6%
TCR	77.6%		69%	84%		20.4%
Penta-Ref	30.3%		23.4%	26%		12.6%
ORR	63.0%		73.1%	73.0%	97	96%
≥CR	45.5%		32.4%	33.0%	82	74.3%
mFU	30.4m	14.7m	8.6m	13.3m	33.4m	13.8m
PFS	11 mo	50.9%(15m)	11.9 mo	8.8 mo	34.9 mo	NR
OS	22 mo	56.7%(15m)	NR	24.8 mo	NR	
		Nat Med 2024				
CRS	72.1%		72.4%	84.0%	95.	93%
CRS ≥ G3	0.6%		0.7%	5.0%	4.(	1%
ICANS	3.0%		10.1%	18.0%	21.	2% (G1/2)
ICANS ≥ G3	0.6%	0.0%	1.8%	3.0%	9.0%	0%

EMP~20%
TCR~75%
Penta-R~30%

Heavily pretreated
But Eque-Cel Lower risk
c.f. Ide- & Cilta-cel

ORR~60%
CR~35-40%

ORR~70-97%
CR~30-80%

CRS~60-70%
>G2: <1%
ICANS~5%
>G2: <1%

CRS~90%
>G2: 4-5%
ICANS~20%
>G2: 3-9%

Scenarios of relapse based on regimens used in *Asia*

Len-sensitive first relapse (LS-R1)

VCD/VTD→ T
L-sensitive

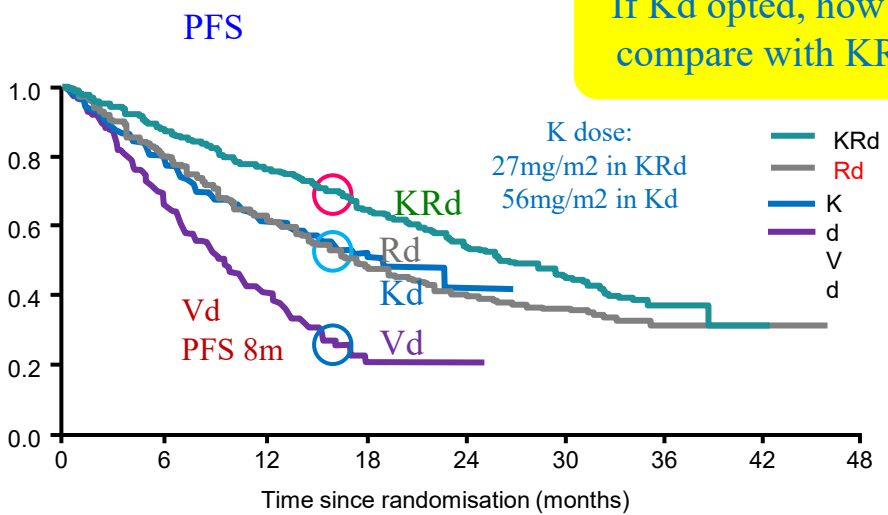
→ Dara-Rd (Pollux) OS*
KRd (Aspire) OS*

Patient is only
V-exposed, hence
remains V-sensitive

→ Vd – yes
But Kd > Vd
(Endeavor)

If Kd opted, how to compare with KRd

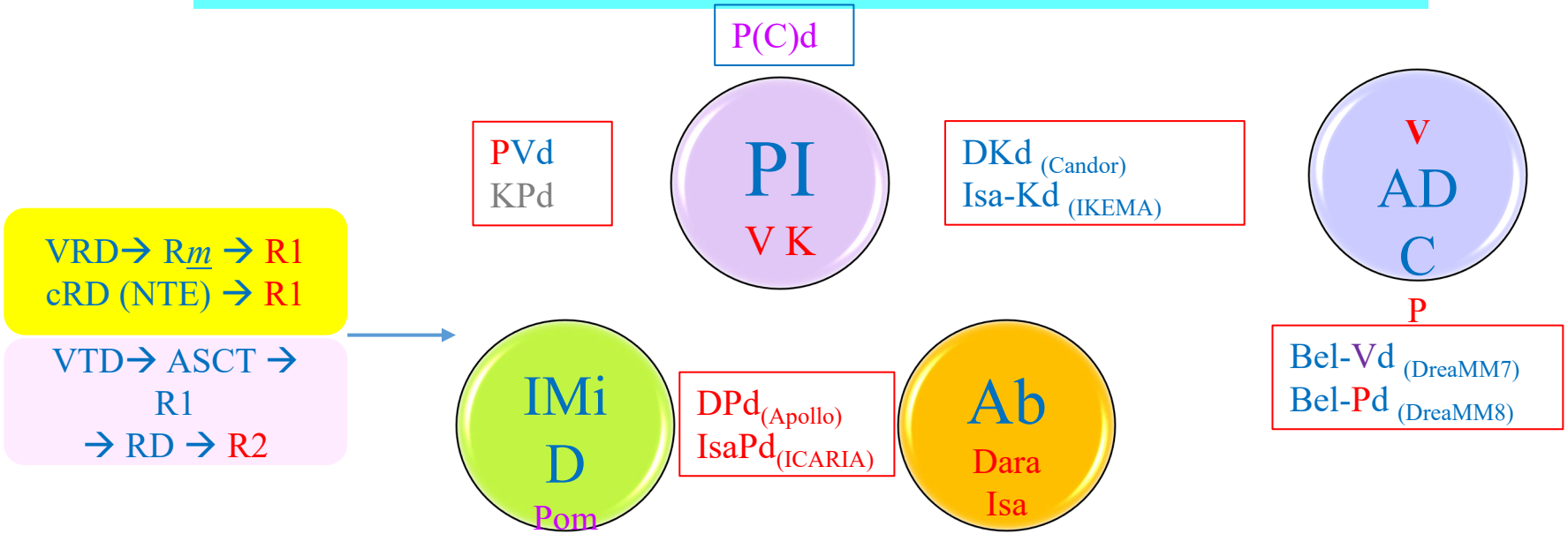
→ Overlay PFS curves of Vd, Kd, Rd & KRd



KRd > Kd
& Even Rd > Vd

Vd had worst PFS of only 8m, even < Rd
NOT considered

Len-resistant relapse (LR-R1 or R2)



Pom-based RCT	PFS
Pd vs PCd	4.4m → 9.5m
Pd vs DPd (Apollo)	6.9m → 12.4m
Pd vs Isa-Pd (ICARIA)	5.9m → 11.5m
VPd vs Bel-Pd (DreaMM8)	9.2m → 24m

K-based combo with either CD38 or Bela yields a good PFS c.f Pom-based combo except Bel-pom

Kd vs DKd (Candor)	11m → 28m / NR
Kd vs Isa-Kd (Ikema)	11m → 23m (HR: 0.59 at 44m mFU)
VPd vs Bela-Vd (DreaMM7)	8.6m → 25m

Key points about RRMM

1. Focus on R1, maximize duration of remission
2. Alternative MOA: switch class
3. Upgrade to next generation agents (V→K; R→P)
4. Triplets supersedes Doublets
5. Continuous therapy needed in RRMM except CAR-T
6. PI-based regimens good for LEN-R RRMM
7. Belantamab-based regimens at R1 markedly prolonged PFS
8. Cilta-cel is approved for LEN-R MM at R1
9. Advanced MM at late line of relapse need immunotherapy of CAR-T & BiSP

Phase 3 MajesTEC

← Resources for Information | Approved Drugs

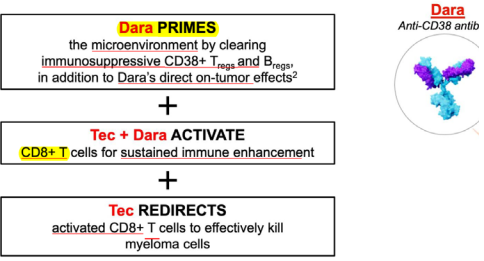
d / DPd in RRMM

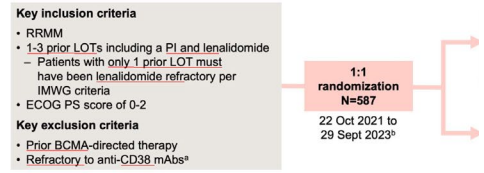
FDA approves teclistamab in combination with daratumumab hyaluronidase-fihj for relapsed or refractory multiple myeloma

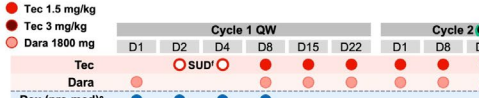
On March 5, 2026, the Food and Drug Adr , Jar dar patients with relapsed or refractory multiple myeloma who have received at least one prior line of therapy including a proteasome inhibitor and an immunomodulatory agent.

Guidelines needs to be re-written!

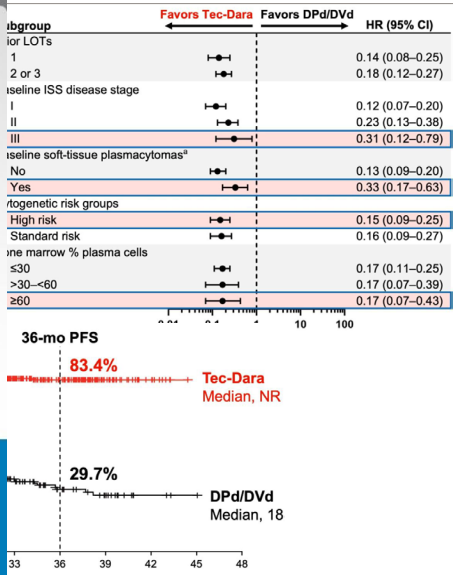
Feedback







Characteristic	Tec-Dara (n=291)
Prior therapy exposure, n (%)	
PI	290 (99.7)
IMiD	291 (100)
Anti-CD38	15 (5.2)
Refractory status, n (%)	
To last prior LOT	250 (85.9)
Any PI	117 (40.2)
Any IMiD	247 (84.9)
Lenalidomide	240 (82.5)
Double (PI and IMiD)	99 (34.0)




Thank You!

Global Multiple Myeloma Academy

Discussion

APTITUDE HEALTH®

Global Multiple Myeloma Academy

Break

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Patient Case Discussion: RRMM

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Global Multiple Myeloma Academy

Patient Case 1: RRMM

James Chim, MBChB, MD, PhD, MRCP, FRCP, FACP, FRCPath, FFSc, FAcadTM, FHKCP, FHKAM

APTITUDE HEALTH®

Patient History

- 50/F
- ISS III IgAk myeloma diagnosed in March 2016
- Hb 9.3g/dL, Ca 3.19mmol/L, Cr > 200umol/L
- IgAK 25g/L
- Serum free kappa 11900, K/L ratio 1043
- BM: 56% plasma cells
- FISH 1q21 gain
- FDG-PET-CT
  - No osteolytic/ hypermetabolic bone lesions
  - Soft tissue mass at the lower pole of right kidney representing renal cell carcinoma

Question 5

How common is it for your patients with MM to have a second primary malignancy?

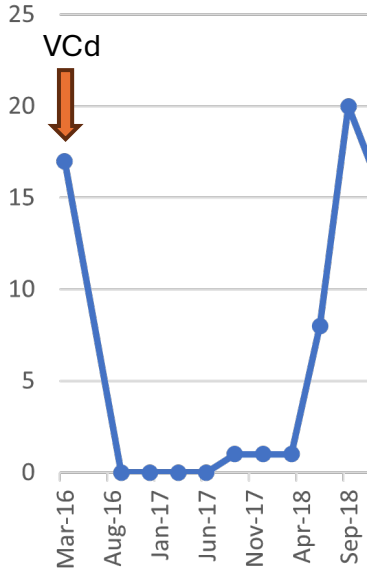
1. Very uncommon (<1%)
2. Uncommon (1%–10%)
3. Common (11%–25%)
4. Very common (>25%)

Patient History

Year of Treatment	Treatment Given	Response
2016	Started VCD induction in March 2016, given 4 cycles total → bortezomib maintenance • Resection of RCC in December 2016 • ASCT not performed due to lack of renal recovery post induction and concomitant RCC • Stem cells cryopreserved	CR

Patient History

- Slow rise in SPE since Sept 2017
- Progressed to SPE 20g/dL in Sept 2018
- PET CT Jan 2019 showed multiple new focal, hypermetabolic lesions in the axial skeleton
- BME Jan 2019 showed 20% abnormal pleomorphic plasma cells



Patient History

Year of Treatment	Treatment Given	Response
2016	VCD + bortezomib MTN (ASCT not intended due to borderline renal function and concomitant renal cell carcinoma)	CR
2019	Dara Rd x 6 cycles since Jan 2019 → continued on lenalidomide maintenance since Nov 2019	CR

Question 6

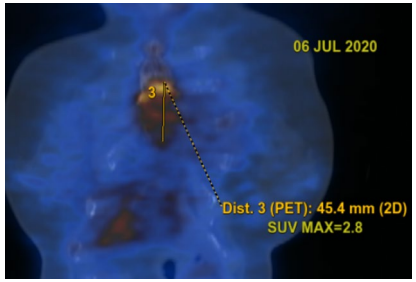
How do you routinely monitor your patients receiving maintenance therapy for RRMM?

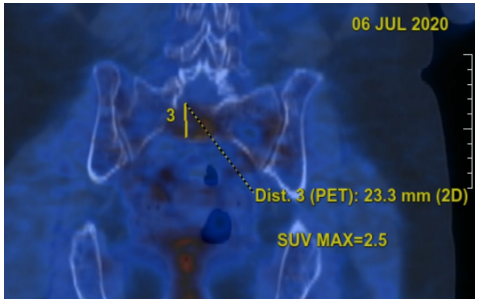
1. Peripheral blood counts
2. Serum creatinine
3. Serum protein electrophoresis (SPE)
4. Urinary protein monitoring/electrophoresis
5. Bone marrow biopsy
6. Other

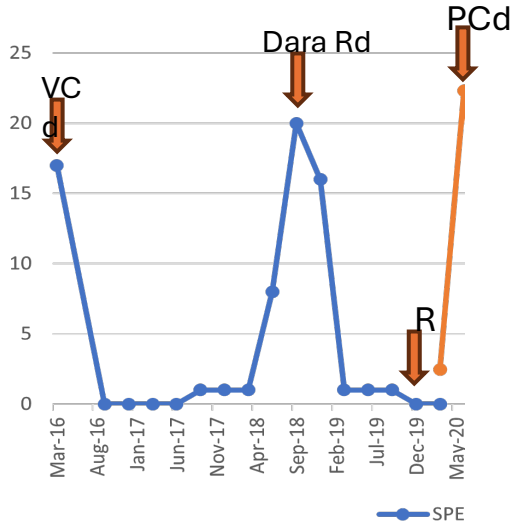
Patient History

- Noted positive kappa light chains in urine electrophoresis in Mar 2020
- SPE and immunofixation negative
- Rising serum free kappa 41→ 98 →193 → 893

  ⇒ Disease relapse with light chain escape
- BM June 2020 showed *no* increase in plasma cells
- PET CT July 2020 showed new lytic sternal and sacral uptake





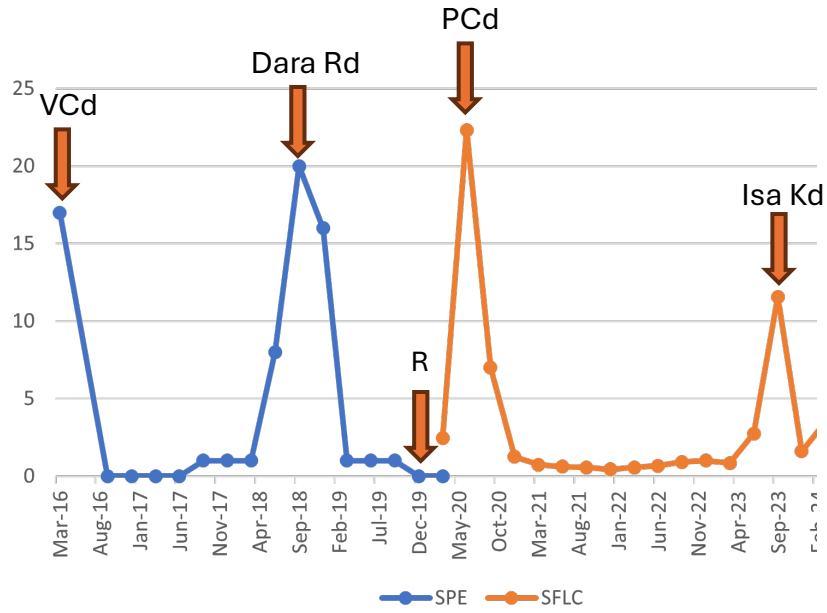


Patient History

Year of Treatment	Treatment Given	Response
2016	VCD + bortezomib MTN (ASCT not intended due to borderline renal function and concomitant renal cell carcinoma)	CR
2019	Dara Rd + Len MTN	CR
2020	PCd (AMN trial)	Triple CR (sero-negativity, PET CT negativity and MRD 10^{-5} negativity by NGS)

Patient History

- Serum FK rose to 100 in Jun 2023
- PET CT Aug 2023 showed new osteolytic lesion in the high right parietal bone
- BM Sept 2023 showed no increase plasma cells
- Switched to *Isa Kd* in Sept 2023 when free kappa level was 460



Question 7

What is typically the limiting factor for lines of therapy administered for MM?

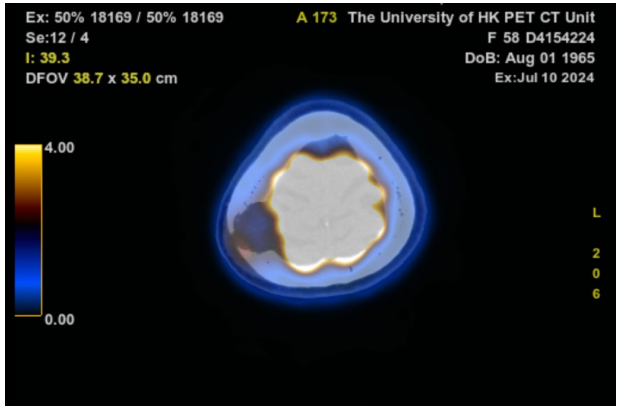
1. Lack of therapies with potential efficacy
2. Cost/coverage
3. Patient ineligible/unable to tolerate available therapies
4. Patient decision

Patient History

Year of Treatment	Treatment Given	Response
2016	VCD + bortezomib MTN (ASCT not intended due to borderline renal function and concomitant renal cell carcinoma)	CR
2019	Dara Rd + Len MTN	CR
2020	PCd (AMN trial)	Triple CR (sero-negativity, PET CT negativity and MRD 10^{-5} negativity by NGS)
2023	Isa Kd started in Sept 2023	PR

Patient History

- Free kappa rose to 150 in Mar 2024
- Developed *soft tissue mass at the right parietal scalp* in May 2024 (no Bx)
- PET CT showed plasmacytoma in the right vertex with destruction to the right parietal bone with intracranial extension



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2023	Isa Kd	PR
2024	SVd + RT to bone associated EMD on the skull	PR

Patient History

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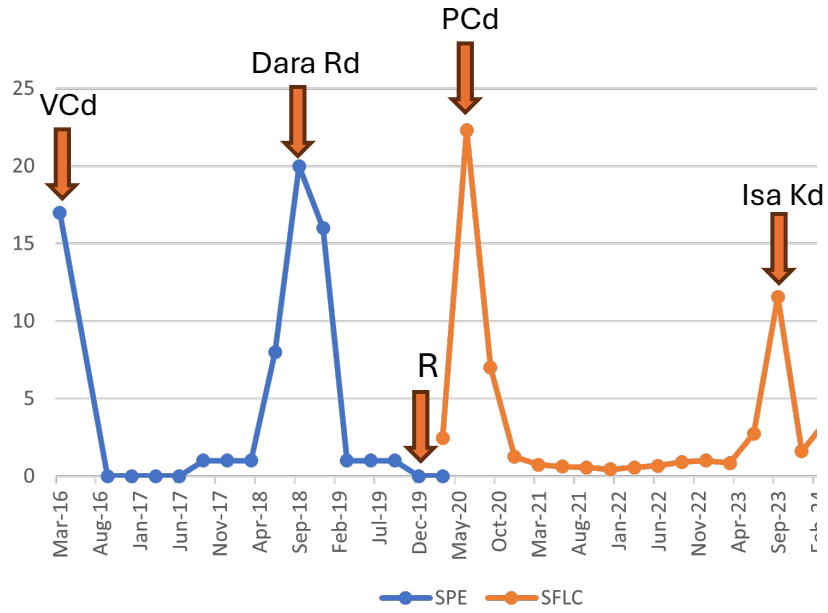

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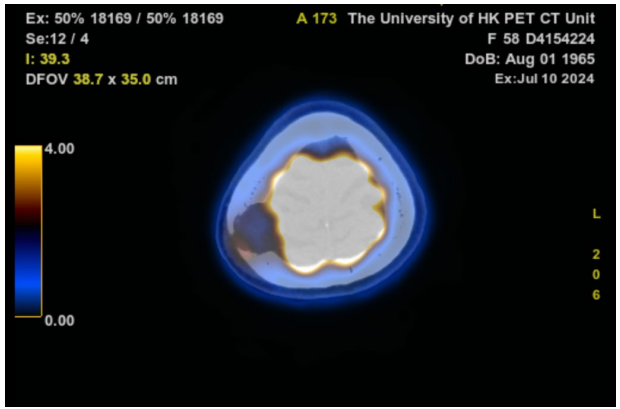

Patient History

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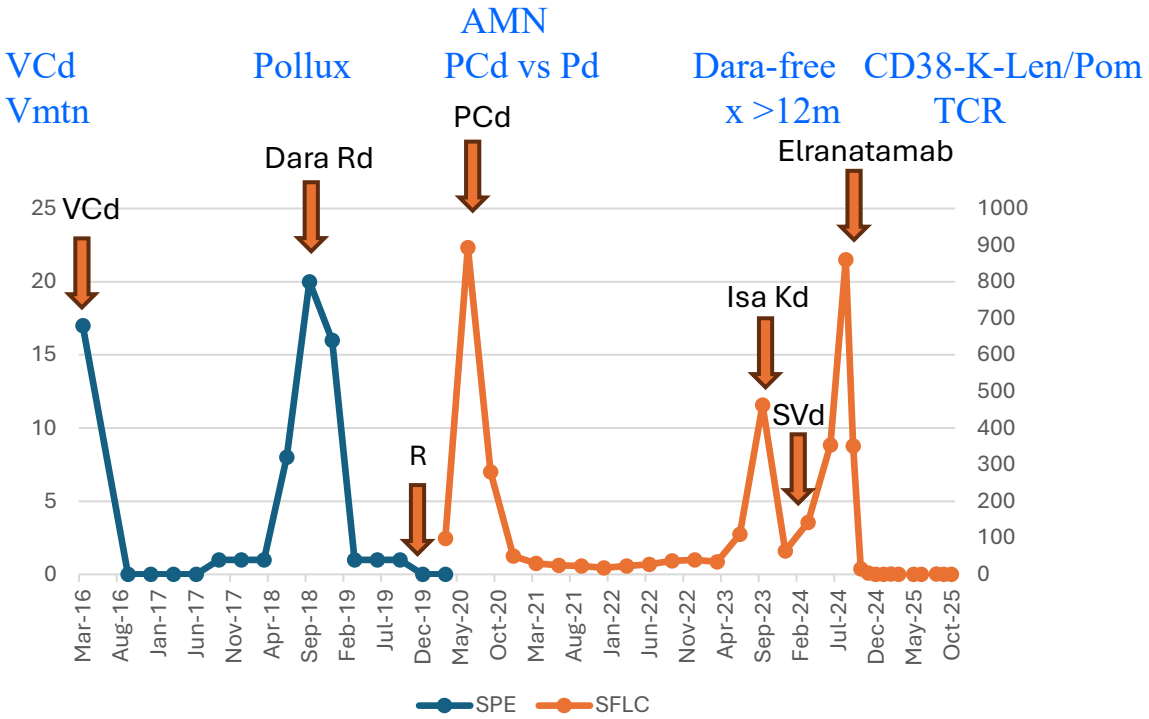
2023	Isa Kd	PR
2024	SVd + RT to bone associated EMD on the skull	PR

The Uphill Battle

- Penta-refractory myeloma with poor survival
- Impaired renal function and thus not a candidate for CAR-T cell trials
- Unable to afford commercial CAR-T cell therapy
- The timely availability of BCMA BiSP changed the later course of her disease

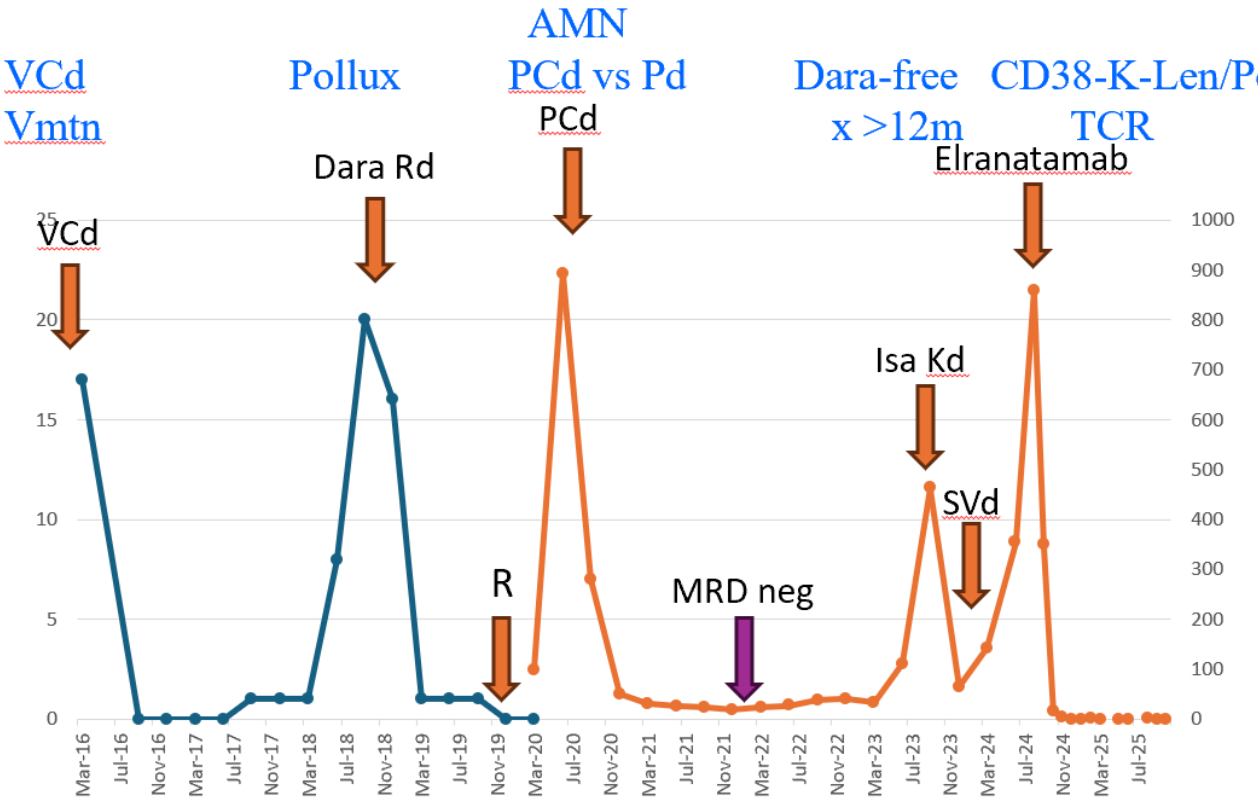


Patient History

- Started elranatamab in Sept 2024
- SFLC 351 → 19 → 3.6 → <0.58
- *SPE negative*
- BME + trephine March 2025: no increase in plasma cells
- Clinical resolution of the plasmacytoma
- PET-CT May 2025: no new lytic lesions, right skull vertex lesion not hypermetabolic
- Decreased elranatamab dosing to q2w in Jan 2025 → q4w in Feb 2025 → q6w in May 2025 → q8w in Dec 2025

Patient's Treatment Journey

Year of Treatment	Treatment Given	Response
2016	VCD + bortezomib MTN (ASCT not intended due to borderline renal function and concomitant renal cell carcinoma)	CR
2019	Dara Rd + Len MTN	CR
2020	PCd (AMN trial)	Triple CR (sero-negativity, PET CT negativity and MRD 10^{-5} negativity by NGS)
2023	Isa Kd	PR
2024	SVd + RT to bone associated EMD on the skull	PR
2024	Elranatamab	CR



	Dx	R1	R2	R3	R4	**CR**
BM	56% PCs	20% PCs	2% PC	1% PCs	ND	No plasmacytosis
AK	**17.3 g/L**	**20.3 g/L**	wq	2 g/L	3.5 g/L	**NMD**
FK	11900	ND	**893 mg/L**	**464 mg/L**	**860 mg/L**	1.04 mg/L
FD	mg/L	lytic lesions	plasmacytom	lytic lesions	plasmacyto	ND

Question 8

How common is it for a patient to be unable to access CAR T because of financial considerations only in RRMM?

1. Very uncommon (<1%)
2. Uncommon (1%–10%)
3. Common (11%–25%)
4. Very common (26%–50%)
5. Usual (51%–75%)
6. Almost always (>75%)

Question 9

Do you have access to a facility that can administer bispecific antibodies for RRMM?

1. Yes, and it is easy to get patients treated with bispecifics
2. Yes, but it is challenging to arrange
3. Yes, but it is often too costly for patients
4. No

Global Multiple Myeloma Academy

Discussion

APTITUDE HEALTH®

Global Multiple Myeloma Academy

Future Directions in Early Lines of Therapy for RRMM

María-Victoria Mateos, MD, PhD

APTITUDE HEALTH®

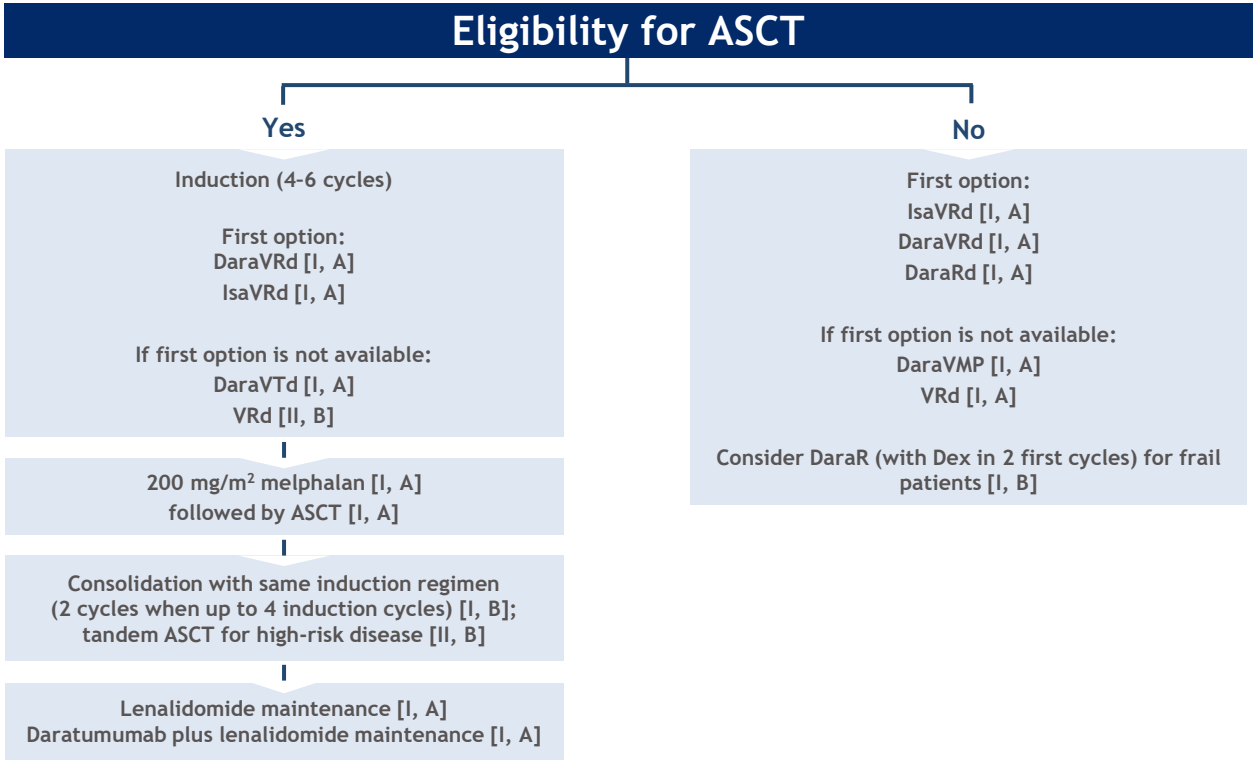
Future Directions in Early Lines of Therapy for Patients With RRMM

María-Victoria Mateos
Salamanca, Spain

Disclosures

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

EHA-EMN 2025 Guidelines

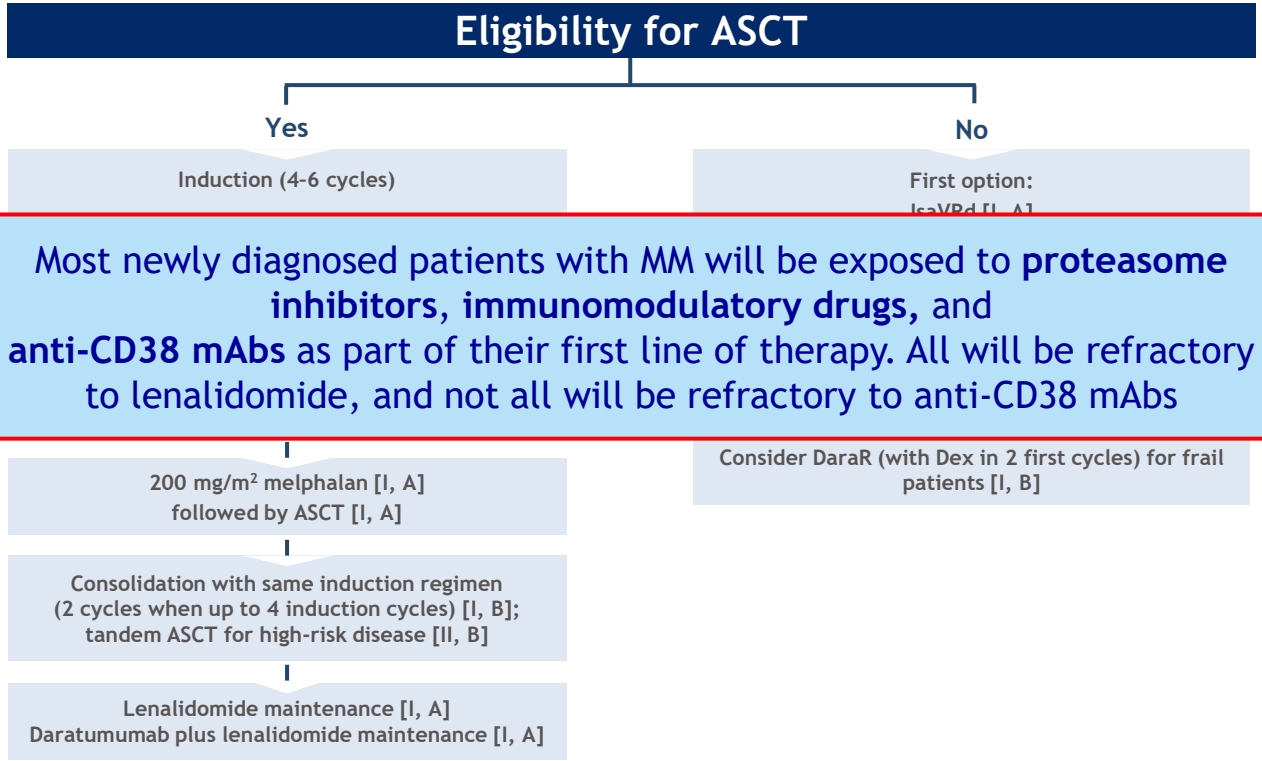


ASCT, autologous stem cell transplantation; Dara, daratumumab; Dex, dexamethasone; EHA, European Hematology Association; EMN, European Myeloma Network; Isa, isatuximab; mAb, monoclonal antibody; MM, multiple myeloma; R, lenalidomide; Rd, lenalidomide-dexamethasone; VMP, bortezomib-melphalan-prednisone;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

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

EHA-EMN 2025 Guidelines

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



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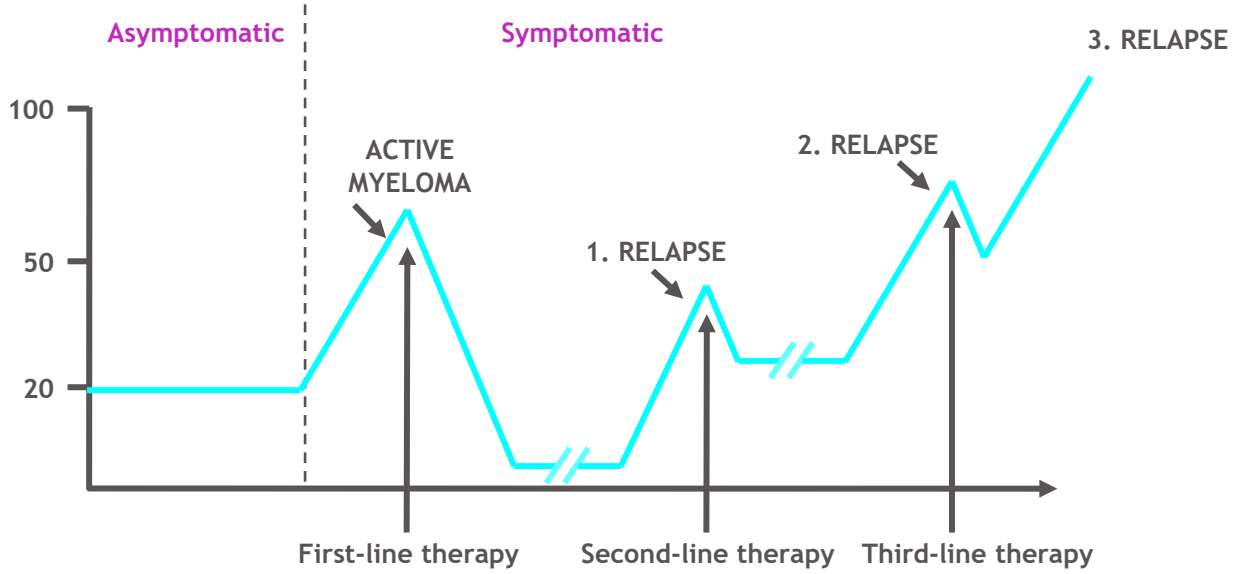
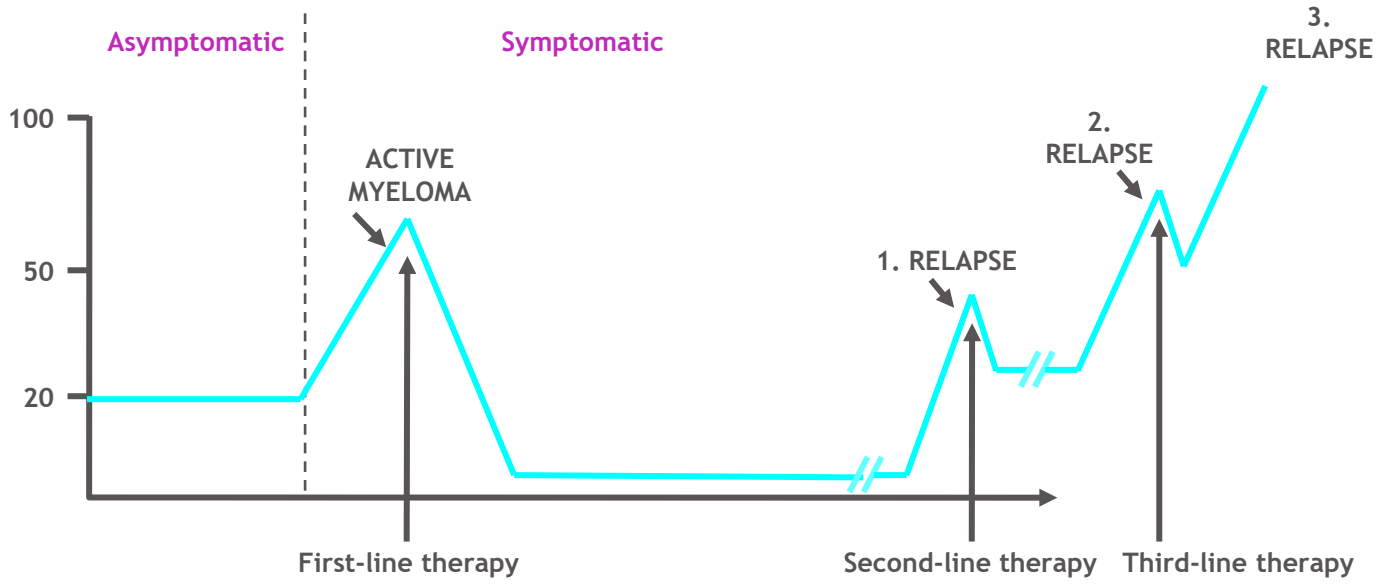
Dimopoulos MA, et al. *Nat Rev Clin Oncol*. 2025;22:680-700. (under minor revision)

Natural History of Multiple Myeloma

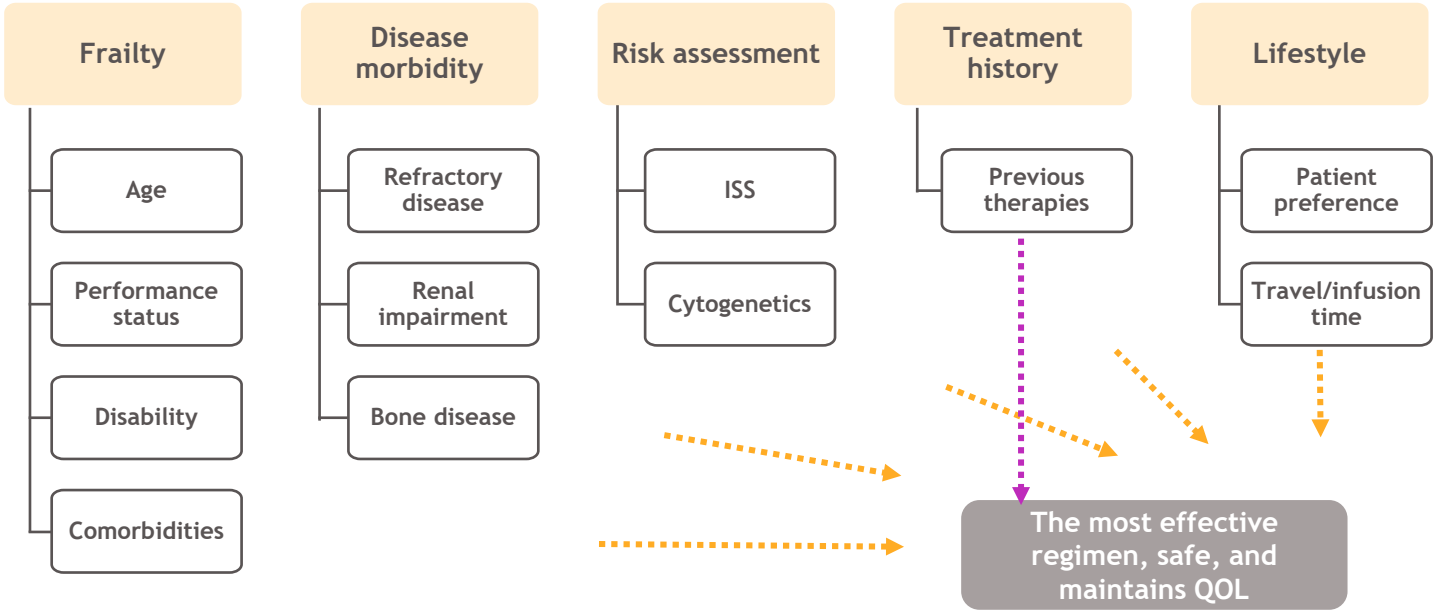


Natural History of Multiple Myeloma



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

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



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

Treatment Landscape in Multiple Myeloma

First line

ASCT eligible

Anti-CD38 + PI + IMiD + Dex

ASCT

Len/Dara-Len

ASCT ineligible

Dara-Len-Dex

Dara-VMP/RVd

Anti-CD38 + PI + IMiD + Dex

Second line

Based on sensitivity/refractoriness to daratumumab and lenalidomide

Anti-CD38 + carfilzomib-Dex

Anti-CD38 + pomalidomide-Dex

Pomalidomide-bortezomib-Dex

Selinexor-bortezomib-Dex

Carfilzomib-Dex

Cilta-cel

New combinations

Teclistamab-Dara/Elra-Dara/Elra monotherapy

Talquetamab-Dara

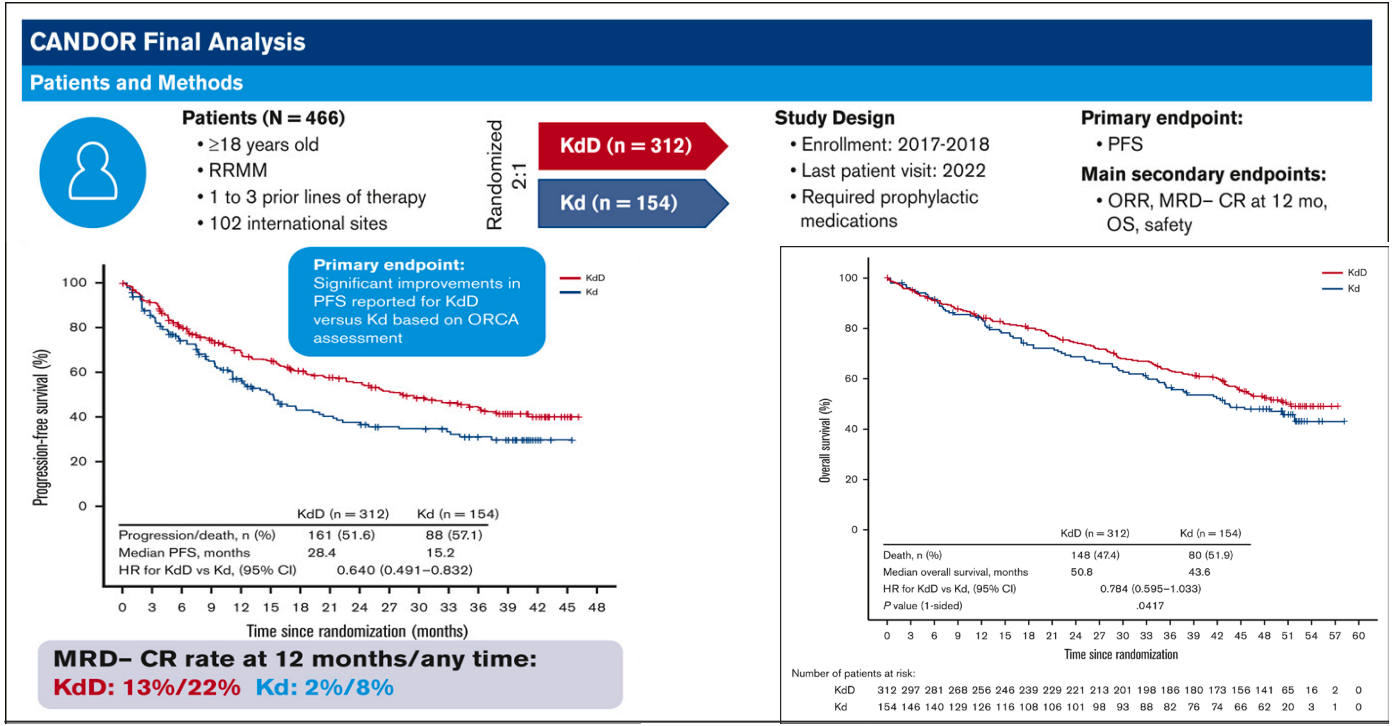
Belantamab-Vd (DREAMM-7)

Belantamab-Pd (DREAMM-8)

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

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

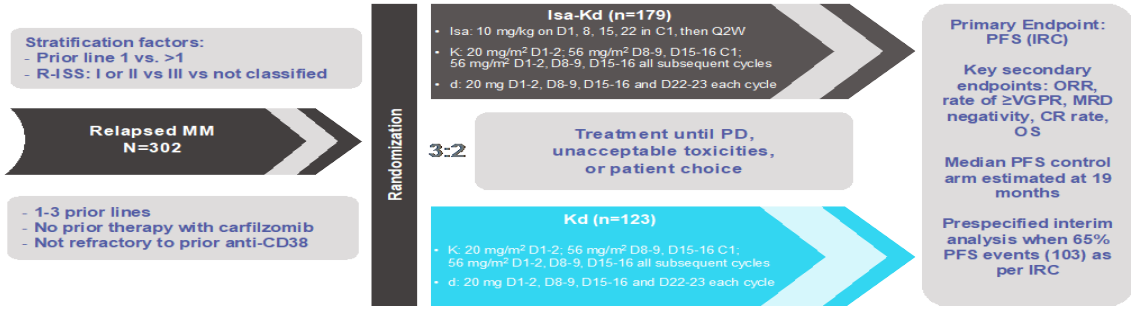
CANDOR: Study Design

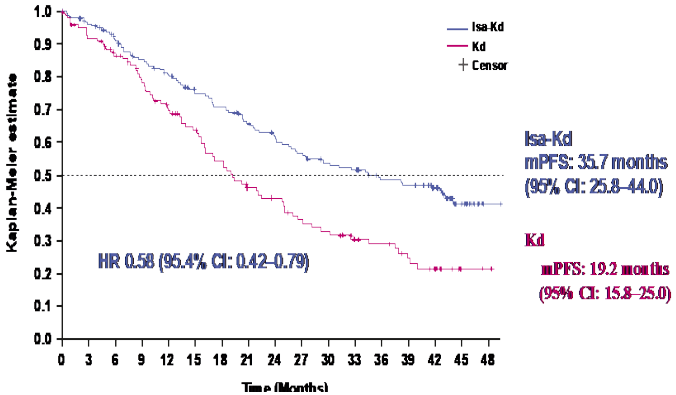


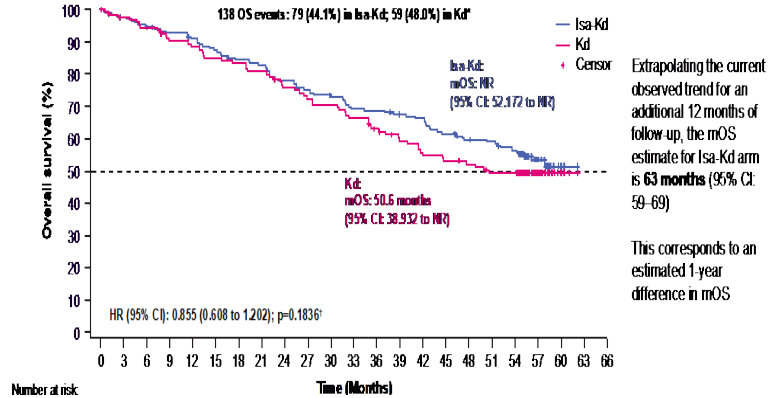
- Hazard ratio for PFS is sustained across all subgroups of patients, including those refractory to lenalidomide (30%) after 1 or more prior lines of therapy
- Safety profile acceptable

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

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







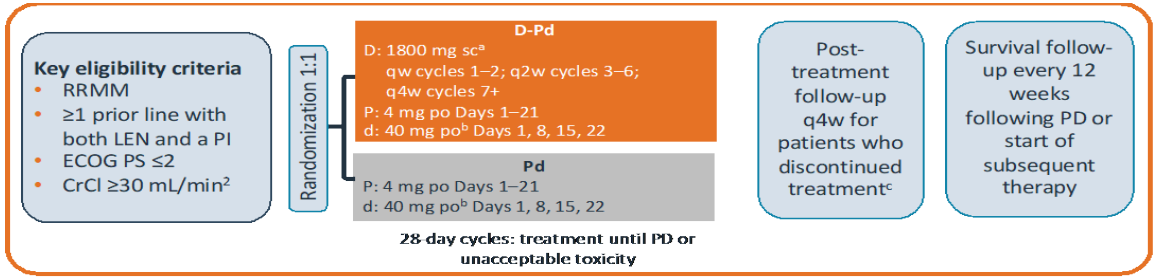
Extrapolating the current observed trend for an additional 12 months of follow-up, the mOS estimate for Isa-Kd arm is **63 months** (95% CI: 59–69)

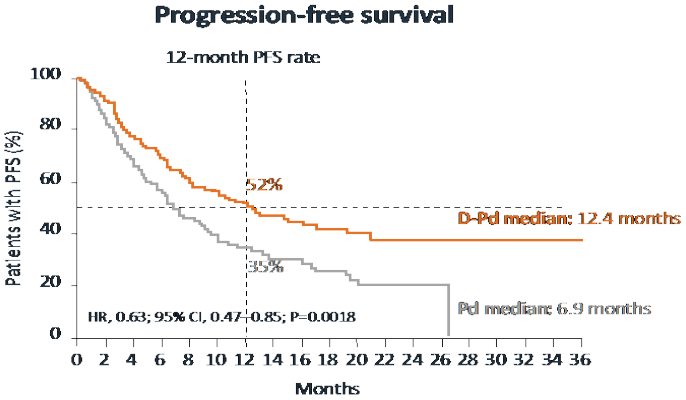
This corresponds to an estimated 1-year difference in mOS

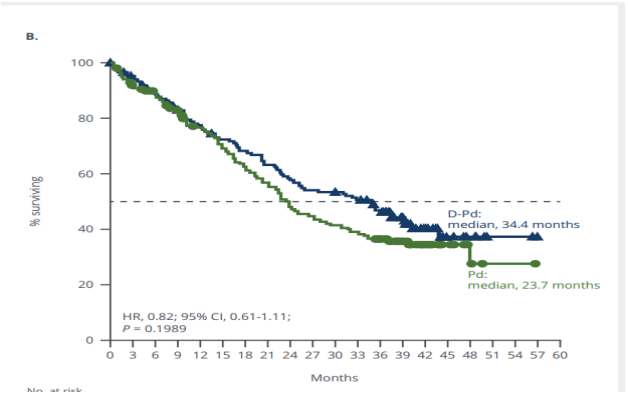
- Hazard ratio for PFS is sustained across all subgroups of patients, including those refractory to lenalidomide (30%) after 1 or more prior lines of therapy
- Safety profile acceptable

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

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







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

Treatment Landscape in Multiple Myeloma

First line

ASCT eligible

Anti-CD38 + PI + IMiD + Dex

ASCT

Len/Dara-Len

ASCT ineligible

Dara-Len-Dex

Dara-VMP/RVd

Anti-CD38 + PI + IMiD + Dex

Second line

Based on sensitivity/refractoriness to daratumumab and lenalidomide

Anti-CD38 + carfilzomib-Dex

Anti-CD38 + pomalidomide-Dex

Pomalidomide-bortezomib-Dex

Selinexor-bortezomib-Dex

Carfilzomib-Dex

Cilta-cel

New combinations

Teclistamab-Dara/Elra-Dara/Elra monotherapy

Talquetamab-Dara

Belantamab-Vd (DREAMM-7)

Belantamab-Pd (DREAMM-8)

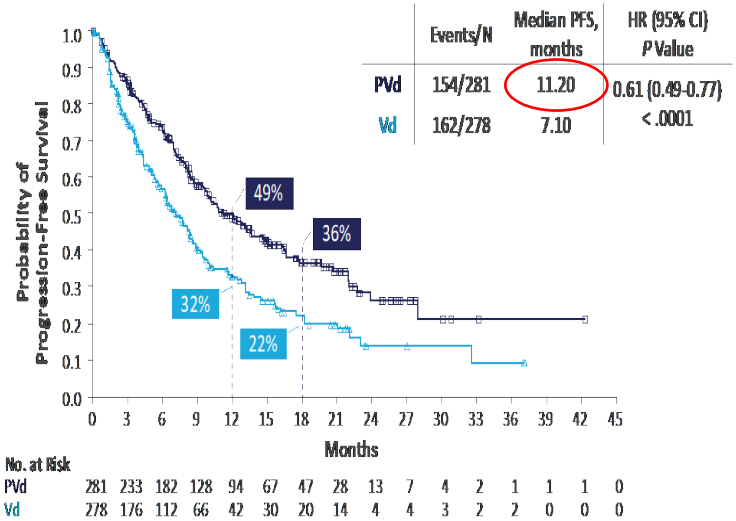
How to select the right combination in the near future???

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

OPTIMISMM: PVd vs Vd in Patients With RRMM

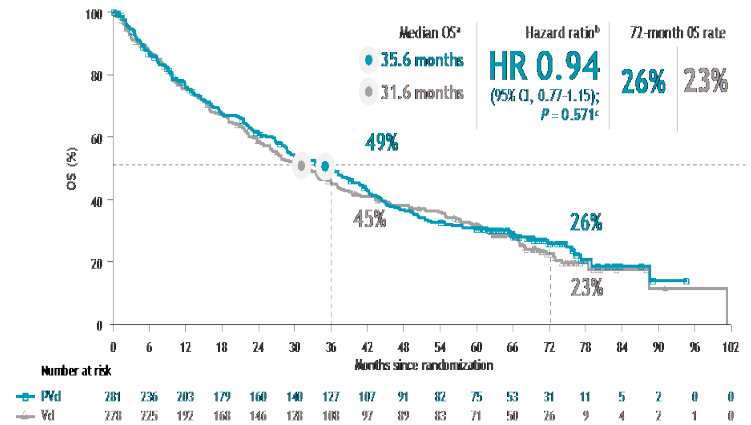
559 patients; median 2 prior lines of therapy; 100% Len exposed; 70% Len refractory; 63% Len refractory as part of the last line of therapy

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



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

OS: ITT population



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

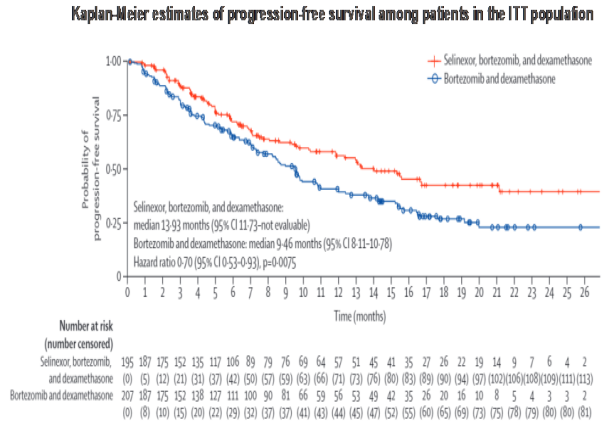
- Median PFS for PVd in patients refractory to Len after the first line of therapy was 17.8 months
- Safety profile acceptable

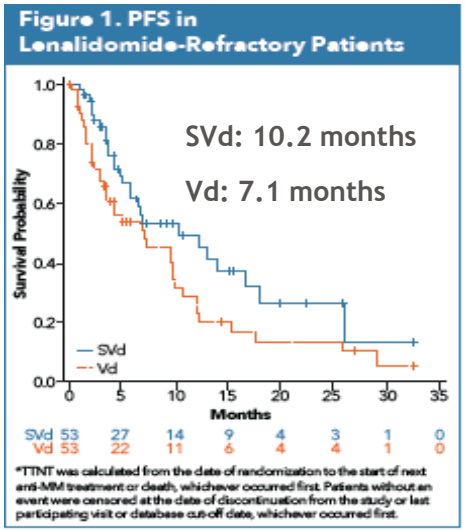
Richardson P, et al. *J Clin Oncol*. 2018;36:2492-2503. Abstract 8001.

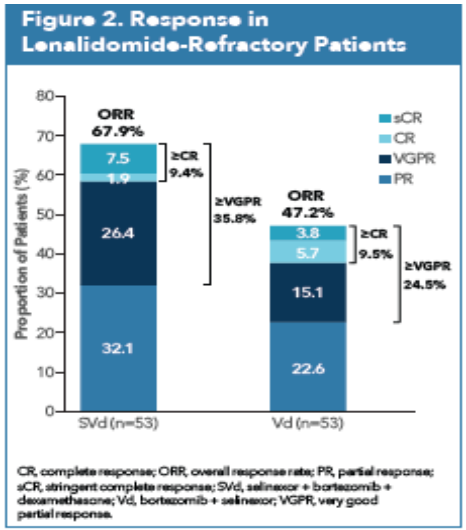
BOSTON: Selinexor Vd vs Vd in Patients With RRMM

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

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







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

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

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

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Talquetamab-Dara

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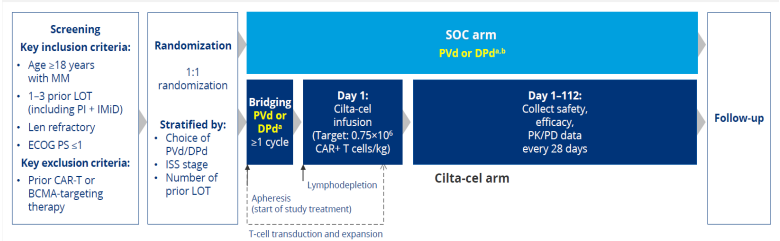
Belantamab-Pd (DREAMM-8)

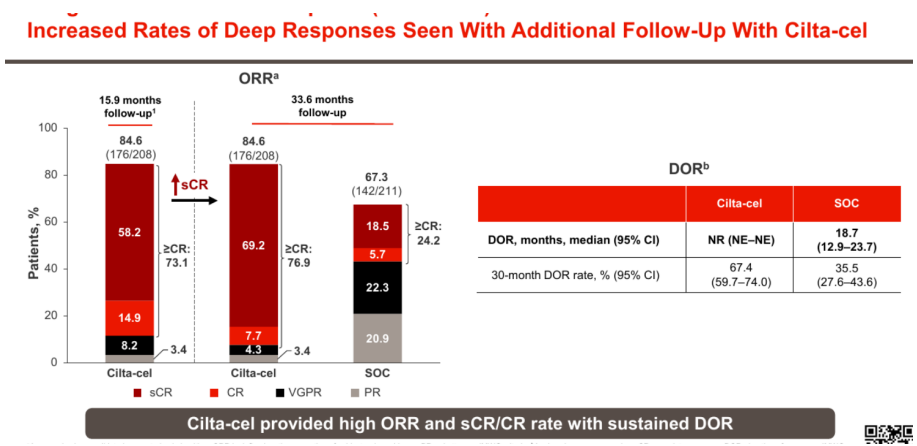
How to select the right combination in the near future???

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

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

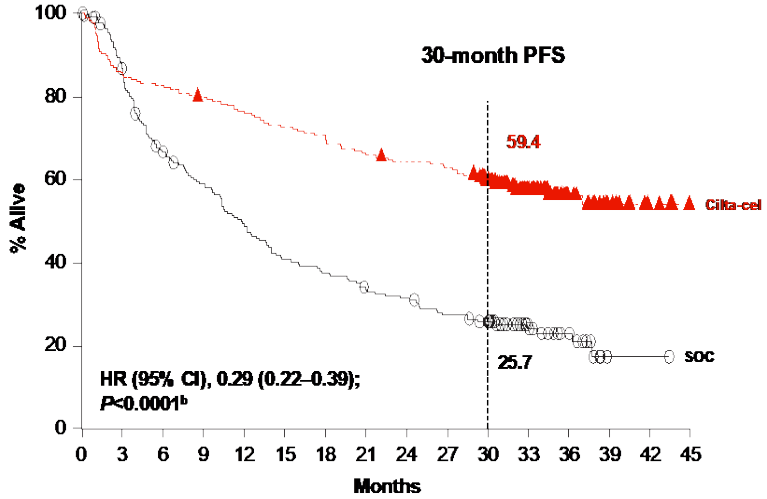


- Median number of PL: 2
- 33% of patients with HRCA and 21% double hit
- 25% TC exposed and 14% TC refractory
- 100% Len refractory

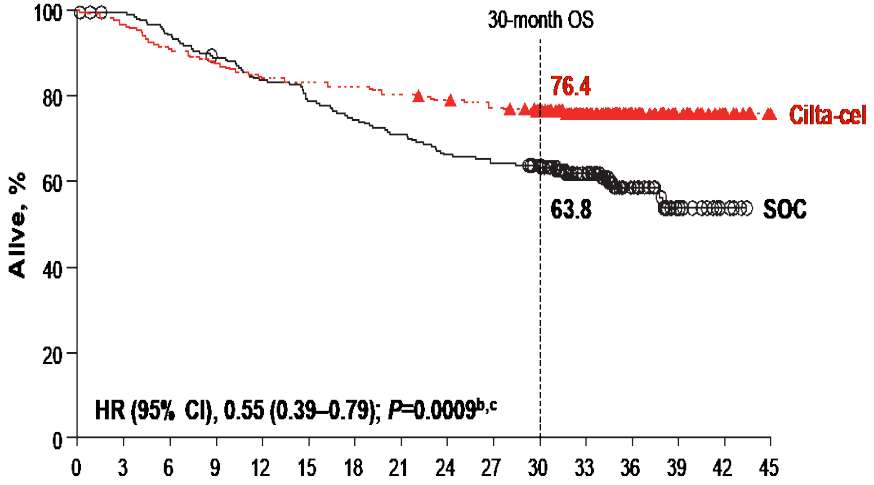


Phase III CARTITUDE-4 Trial: Efficacy

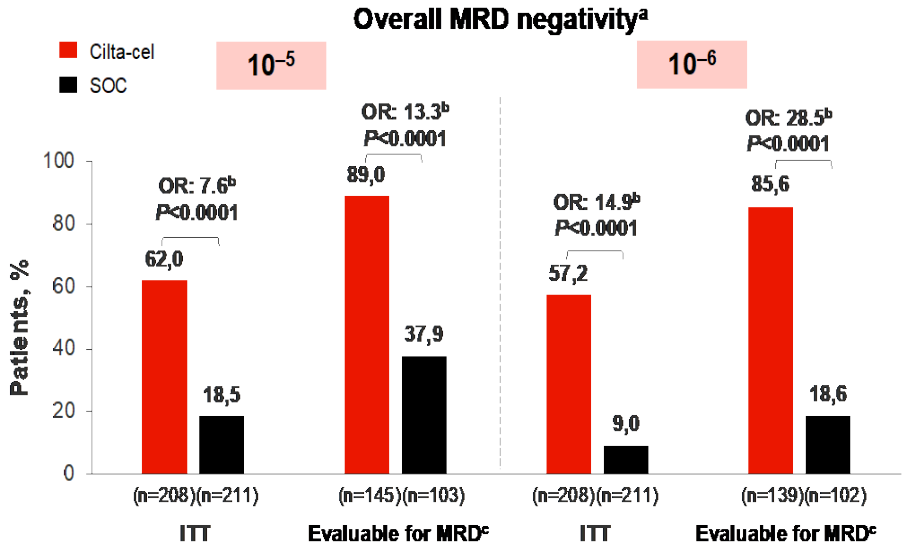
PFS (ITT; 33.6-mo median follow-up)

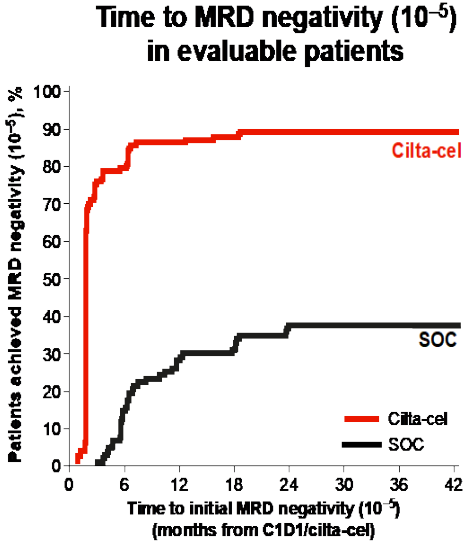


OS (ITT; 33.6-mo median follow-up)



Phase III CARTITUDE-4 Trial: MRD-Negativity Analysis

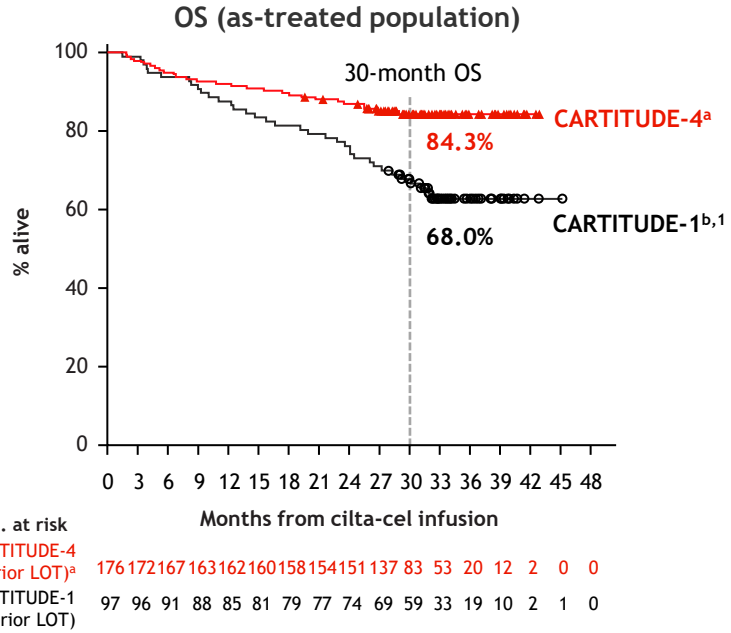


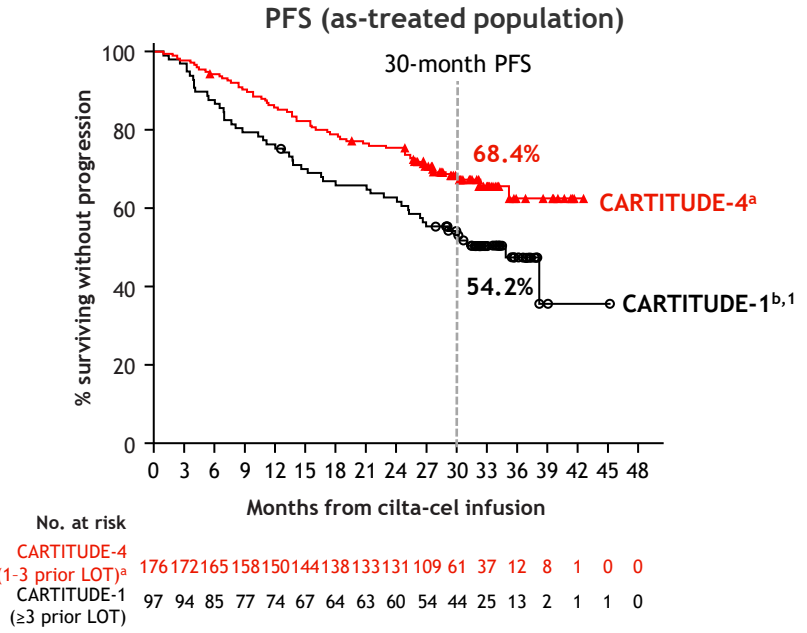


- 69% of evaluable patients achieved MRD negativity (10^{-5}) by day 56 (ITT, 48%), rising to 86% (ITT, 60%) by 6 months post cilta-cel infusion

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

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





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

[a]Re-baselined to begin at time of cilta-cel infusion for patients who received cilta-cel as study treatment, with median follow-up of 30.5 months; [b]33.4-month median follow-up.
Cilta-cel, ciltacabtagene autoleucel; LOT, line of therapy; OS, overall survival; PFS, progression-free survival; SOC, standard of care.
1. Lin Y, et al. ASCO 2023.Abstract 8009.

Treatment Landscape in Multiple Myeloma

First line

ASCT eligible

Anti-CD38 + PI + IMiD + Dex

ASCT

Len/Dara-Len

ASCT ineligible

Dara-Len-Dex

Dara-VMP/RVd

Anti-CD38 + PI + IMiD + Dex

Second line

Based on sensitivity/refractoriness to daratumumab and lenalidomide

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Pomalidomide-bortezomib-Dex

Selinexor-bortezomib-Dex

Carfilzomib-Dex

Cilta-cel

Belantamab-Vd (DREAMM-7)

Belantamab-Pd (DREAMM-8)

New combinations

Teclistamab-Dara/Elra/Tec monotherapy

Talquetamab-Pom or Tec-Tal

Tal-Dara or Tal-Pom-Dara

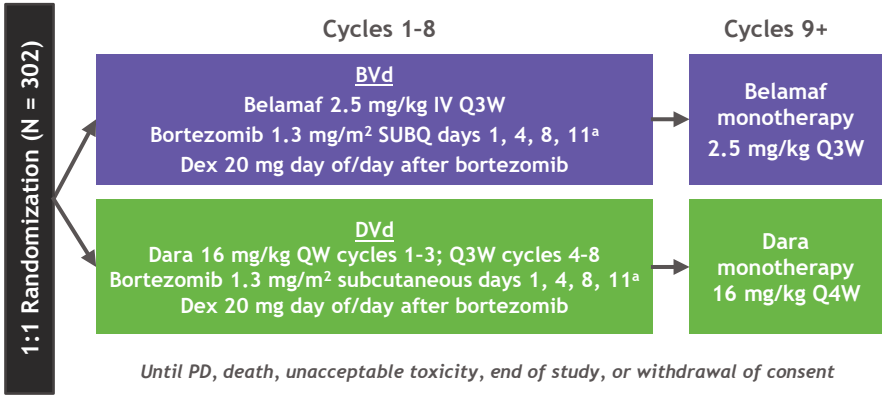
Linvoseltamab

Etentamig

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

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

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



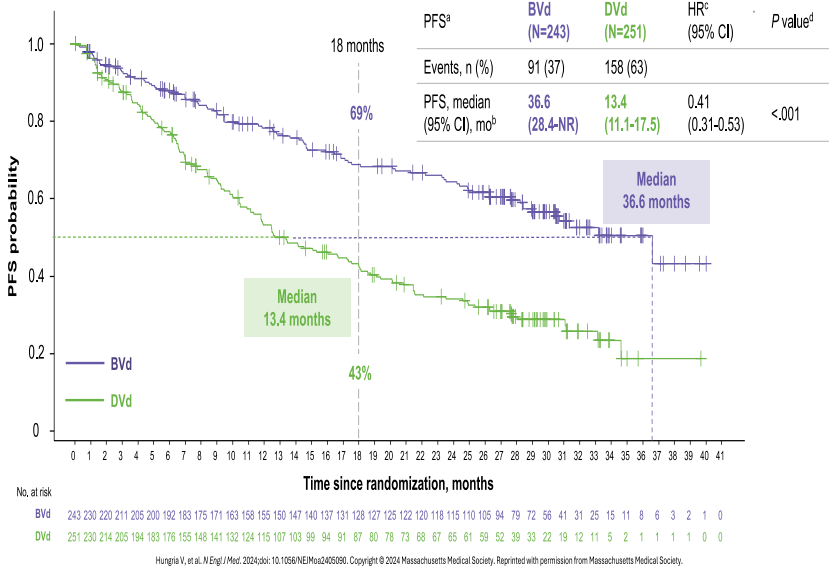
Primary endpoint: PFS (IRC)
Key secondary endpoints: OS, DOR, MRD

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

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

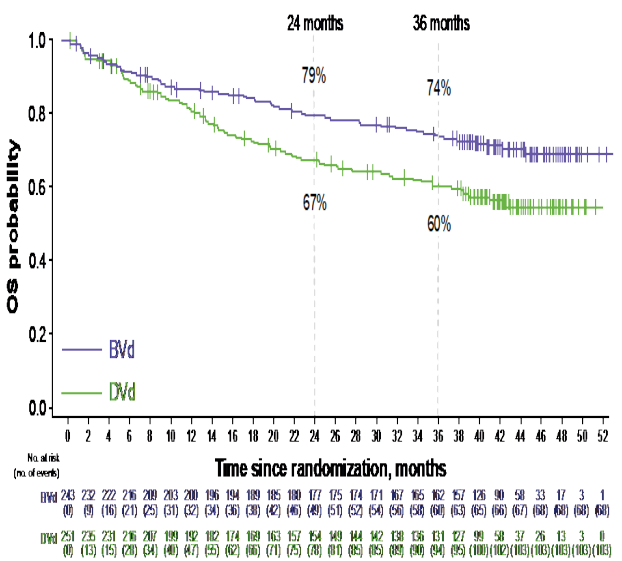
DREAMM-7: Phase III Trial of BVd vs DVd in RRMM – PFS/OS in All Patients

PFS



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

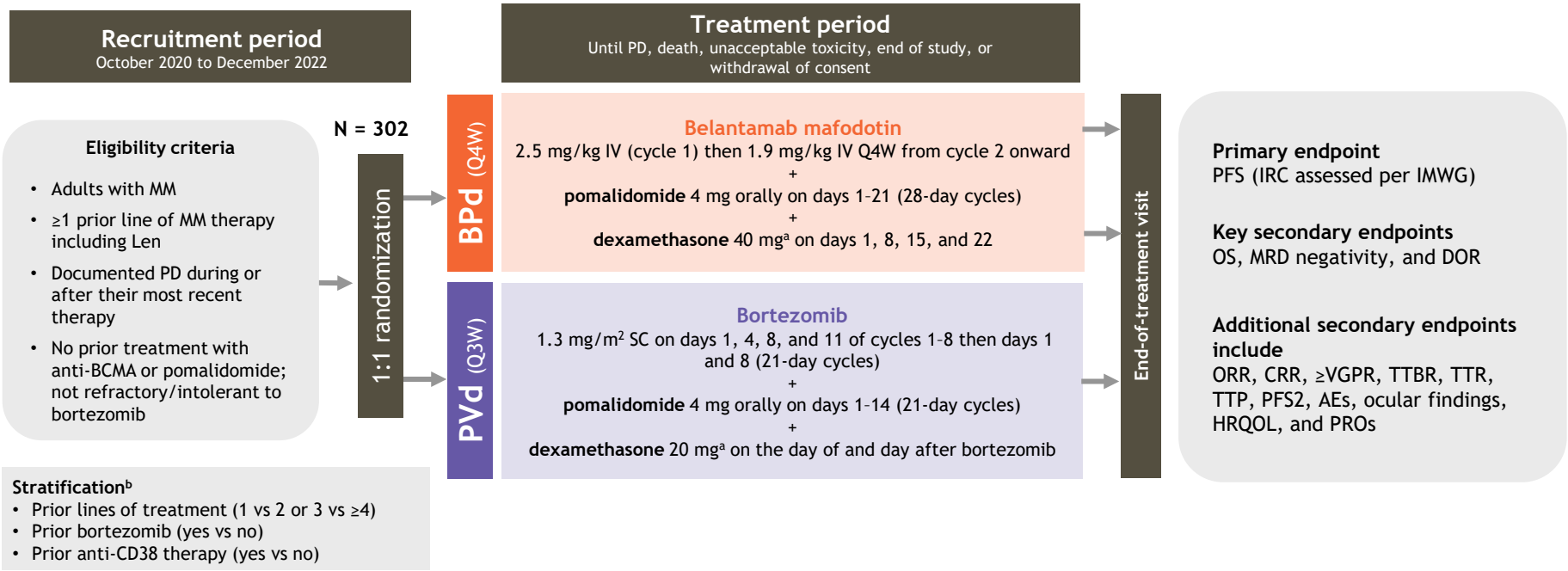
OS



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

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

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



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

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

DREAMM-8: Baseline Disease Characteristics and Clinical Characteristics

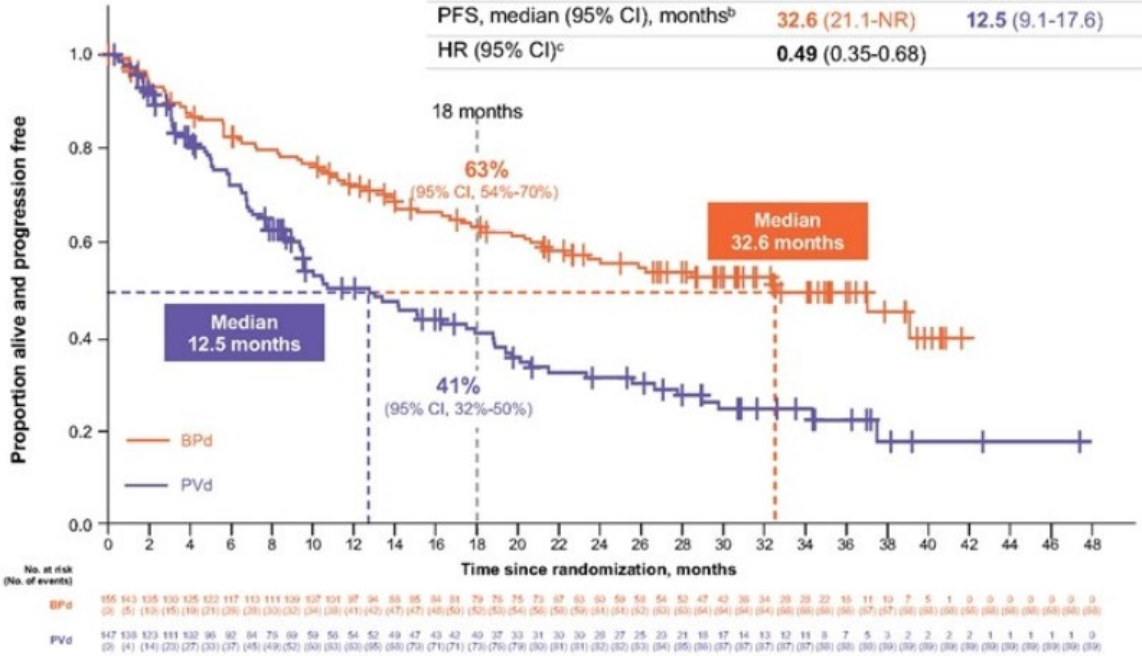
Baseline Characteristics	ITT Population	
	BPd (n = 155)	PVd (n = 147)
Age, median (range), years	67 (40-82)	68 (34-86)
<65, n (%)	64 (41)	53 (36)
65 to <75, n (%)	72 (46)	59 (40)
≥75, n (%)	19 (12)	35 (24)
Male/female, n (%)	99 (64)/56 (36)	82 (56)/65 (44)
White/Black/Asian/Mixed race, n (%)[a]	133 (86)/0/20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

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

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

DREAMM-8: PFS

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

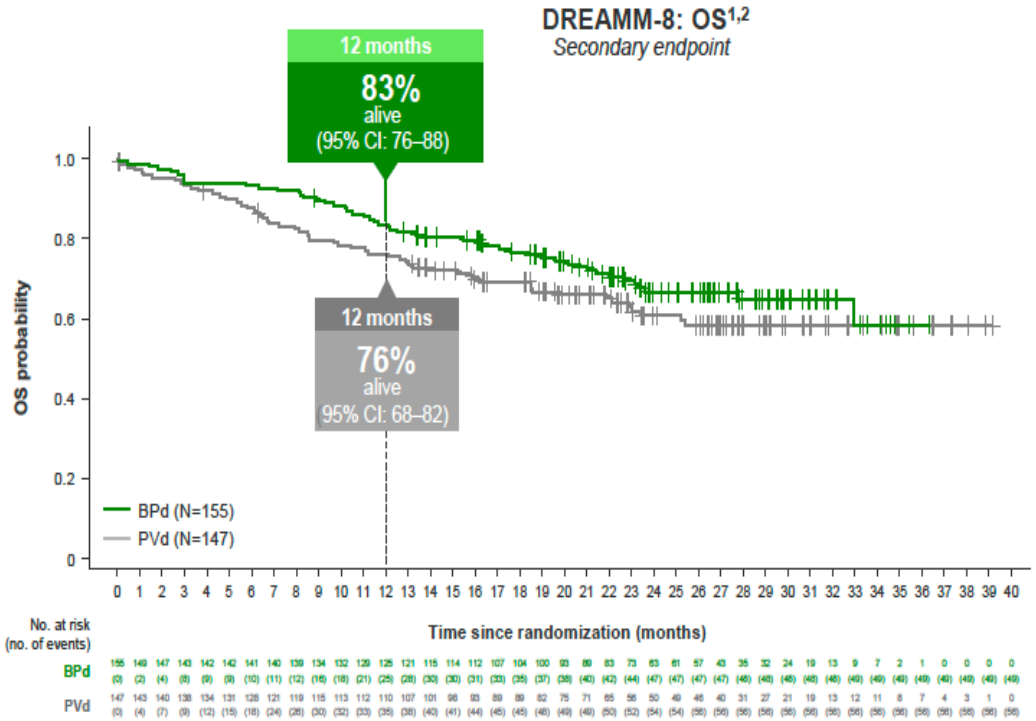


PFS benefit was observed across all prespecified subgroups, including

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

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

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



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

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

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

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ASCT

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Anti-CD38 + carfilzomib-Dex

Anti-CD38 + pomalidomide-Dex

Pomalidomide-bortezomib-Dex

Selinexor-bortezomib-Dex

Carfilzomib-Dex

Cilta-cel

Belantamab-Vd (DREAMM-7)

Belantamab-Pd (DREAMM-8)

Teclistamab-daratumumab

What information do we have about BsAbs in earlier lines?

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

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

Key inclusion criteria

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

Key exclusion criteria

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

1:1 randomization N=587

22 Oct 2021 to 29 Sept 2023[b]

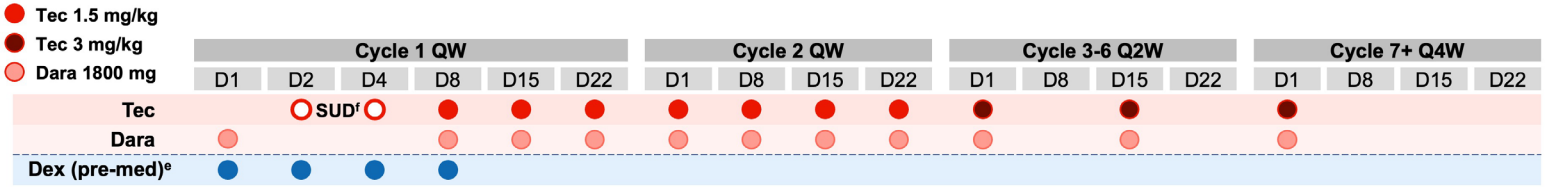
Tec-Dara
N=291
SC dosing following Dara schedule

DPd/DVd
N=296 (91% DPd)
by investigator's choice[c]

Primary endpoint
- PFS per IRC

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

Other secondary endpoints
- Safety
- PK and immunogenicity



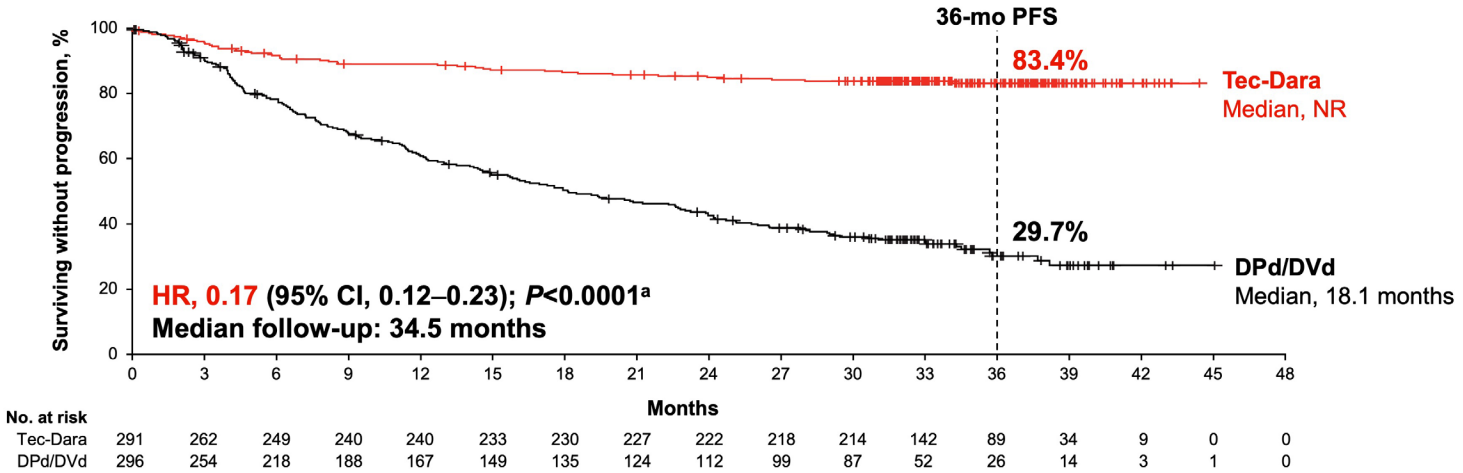
SC dosing aligned with Dara schedule, with monthly dosing after 6 cycles; steroid sparing after Cycle 1 Day 8

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

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

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

MajesTEC-3: PFS (primary endpoint)



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

[a]The *P* value crossed the prespecified stopping boundary for superiority for the first interim analysis (*P*=0.0139).
CI, confidence interval; HR, hazard ratio; NR, not reached.
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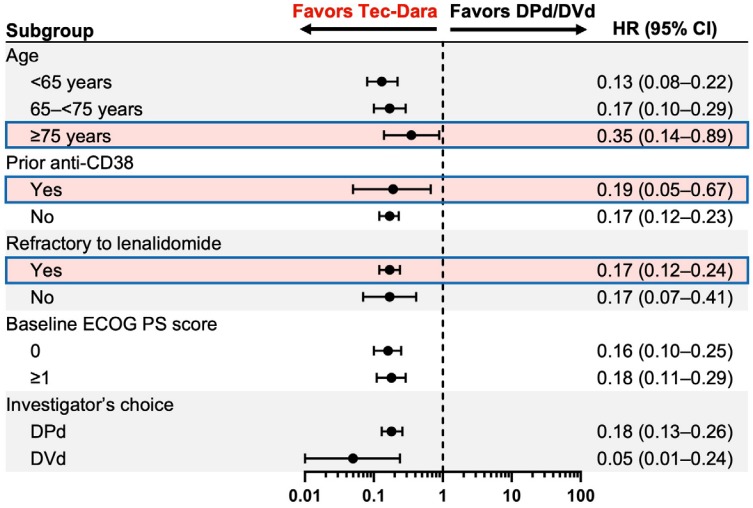
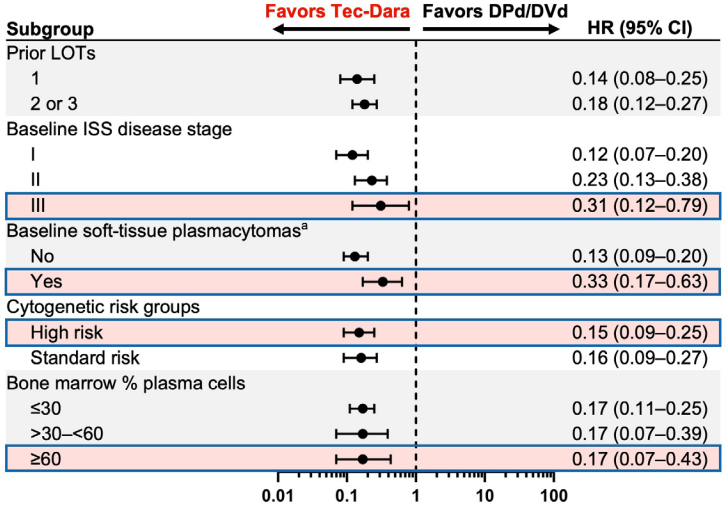
MajesTEC-3: PFS Subgroup Analysis



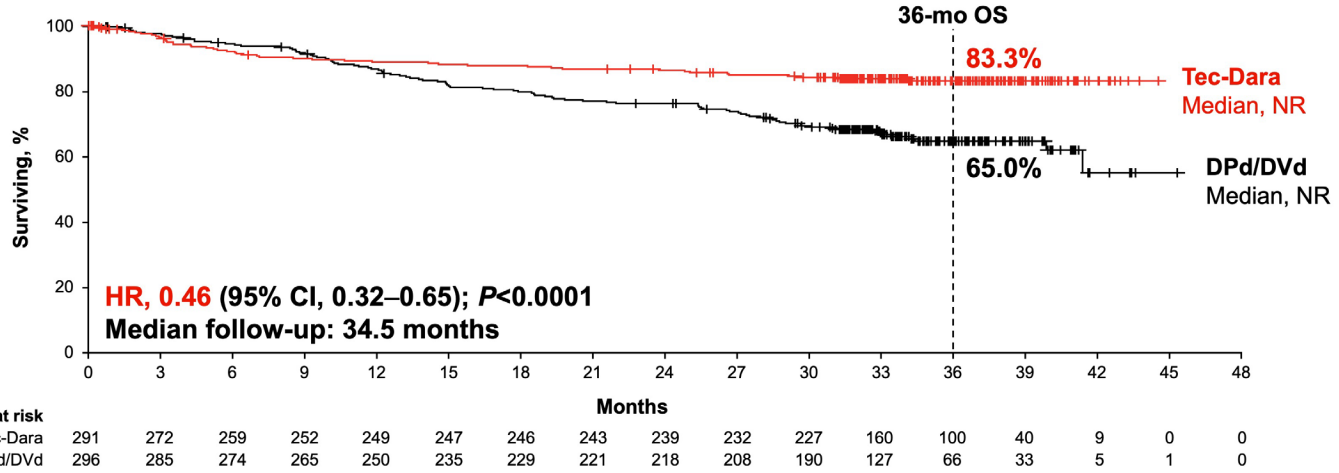


Superior PFS with Tec-Dara was consistent across all subgroups[b]

[a]Baseline soft-tissue plasmacytomas contain both extramedullary and paraskeletal plasmacytomas. [b]Not all clinically meaningful and prespecified subgroups that were assessed are shown; however, PFS was improved versus DPd/DVd across all subgroups.
Adapted with permission © The *New England Journal of Medicine* (2025).

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

MajesTEC-3: OS



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

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

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

MajesTEC-3: Summary of Infections

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

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

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

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

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

MajesTEC-3: Conclusions

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

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

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

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

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

This combination has just been approved by the FDA

Phase III Clinical Trials With BsAbs in Earlier Lines of Therapy

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

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

Information on the trials is from clinicaltrials.gov.

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

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

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

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

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

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

This study will report data soon

Treatment Landscape in Multiple Myeloma

First line

ASCT eligible

Anti-CD38 + PI + IMiD + Dex

ASCT

Len/Dara-Len

ASCT ineligible

Dara-Len-Dex

Dara-VMP/RVd

Anti-CD38 + PI + IMiD + Dex

Second line

Based on sensitivity/refractoriness to daratumumab and lenalidomide

Anti-CD38 + carfilzomib-Dex

Anti-CD38 + pomalidomide-Dex

Pomalidomide-bortezomib-Dex

Selinexor-bortezomib-Dex

Carfilzomib-Dex

Cilta-cel

Belantamab-Vd (DREAMM-7)

Belantamab-Pd (DREAMM-8)

Teclistamab-daratumumab

Teclistamab s/a

Elranatamab s/a

Tal-Dara-Pom and Tal-Dara

Tal-Tec

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

Treatment Landscape in Multiple Myeloma

First line

ASCT eligible

Anti-CD38 + PI + IMiD + Dex

ASCT

Len/Dara-Len

ASCT ineligible

Dara-Len-Dex

Dara-VMP/RVd

Anti-CD38 + PI + IMiD + Dex

Second line

Based on sensitivity/refractoriness to daratumumab and lenalidomide

Anti-CD38 + carfilzomib-Dex

Anti-CD38 + pomalidomide-Dex

Pomalidomide-bortezomib-Dex

Selinexor-bortezomib-Dex

Carfilzomib-Dex

Iberdomide-Dara-Dex

Mezigdomide-Kd

Cilta-cel

Belantamab-Vd (DREAMM-7)

Belantamab-Pd (DREAMM-8)

Teclistamab-daratumumab

Teclistamab s/a

Elranatamab s/a

Tal-Dara-Pom and Tal-Dara

Tal-Tec

What about CELMoDs in early lines of therapy?

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

EXCALIBER-RRMM: Phase III Study

EXCALIBER
1-2 priors
RRMM

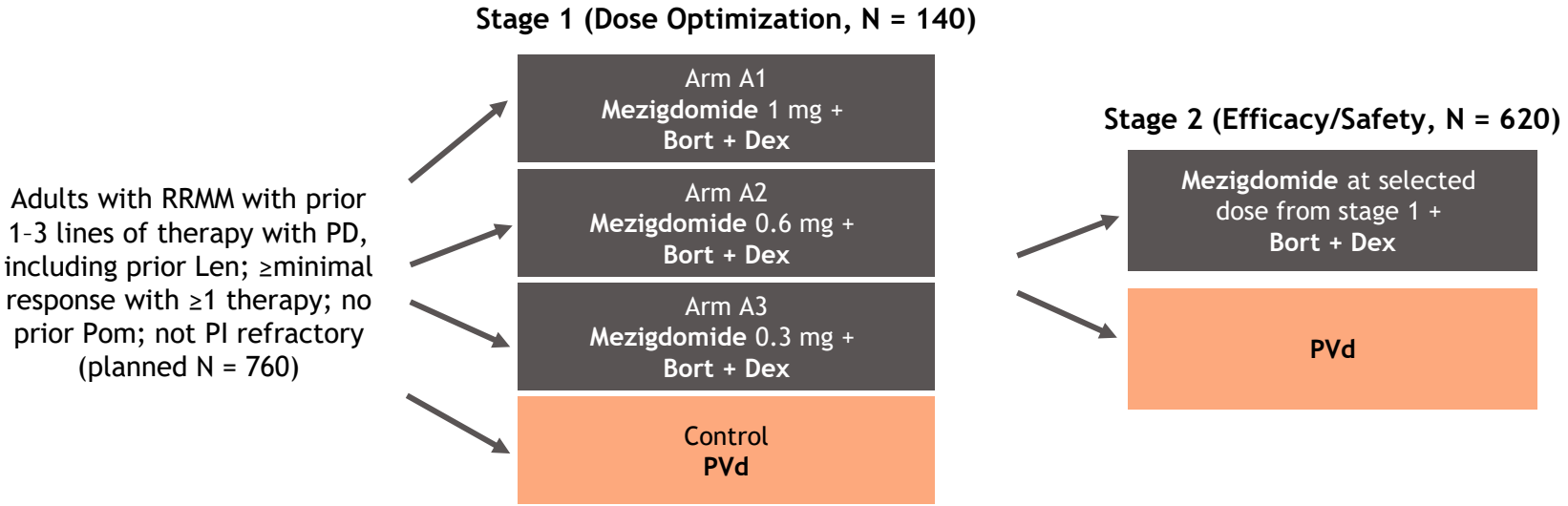
Phase III, 2-stage seamless adaptive inferential design

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

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

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

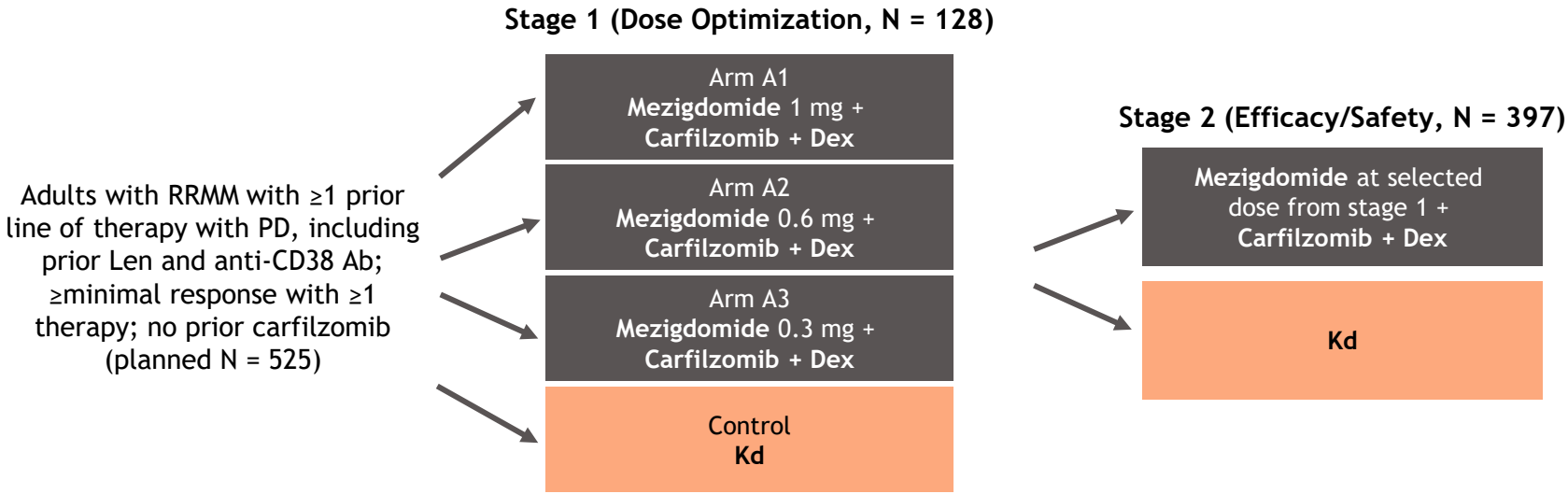
- 2-stage, randomized phase III trial



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

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

- 2-stage, randomized phase III trial



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

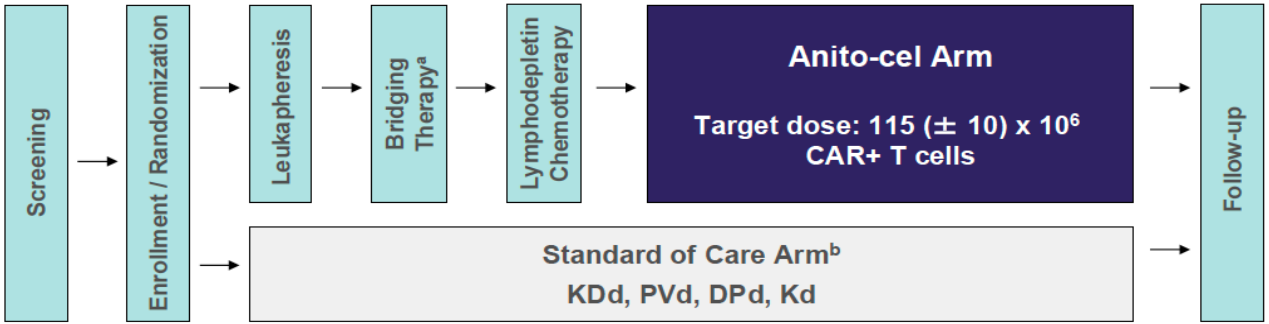
More Innovation in Early Lines of Therapy in the Future?

iMMagine-3: Phase III Clinical Trial

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

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

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



Study Design

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

Study Endpoints

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

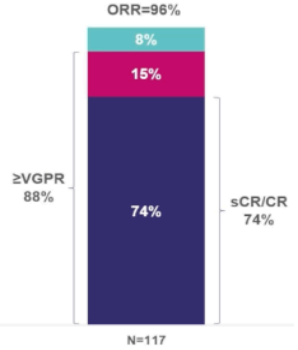
[a] Optional Bridging therapy will be the SOC regimen selected prior to randomization
[b] Cycles will continue until unacceptable toxicity, progression as per IMWG criteria, or patient withdrawal of consent

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

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

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

Overall response rate
Efficacy evaluable (n=117)



PFS and OS
Efficacy evaluable (n=117)

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

Key safety data
Safety evaluable (n=98)

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

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

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

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

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

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

QUINTESSENTIAL-2: Phase III Clinical Trial

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

STUDY SNAPSHOT

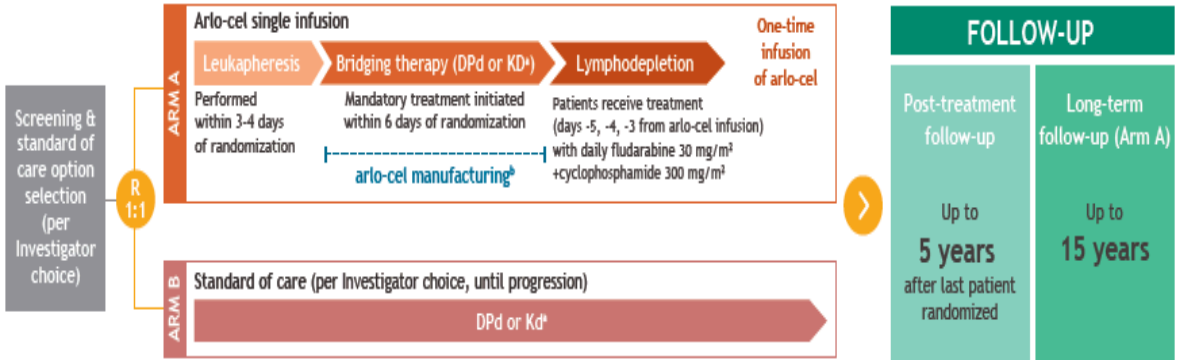
Phase 3
Ongoing trial

RRMM exposed to lenalidomide
N ~ 440 (planned)

Randomized, open label

Multicenter
~125 sites in 31 countries

Figure 1. Study design overview



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

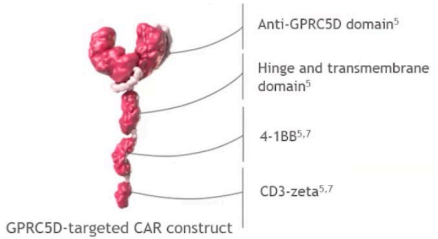
arlo-cel, arlocabtagene autoleucel; DPd, daratumumab, pomalidomide, and dexamethasone; GPRC5D, G protein-coupled receptor class C group 5 member D; Kd, carfilzomib and dexamethasone; R, randomization; RRMM, relapsed and refractory multiple myeloma.

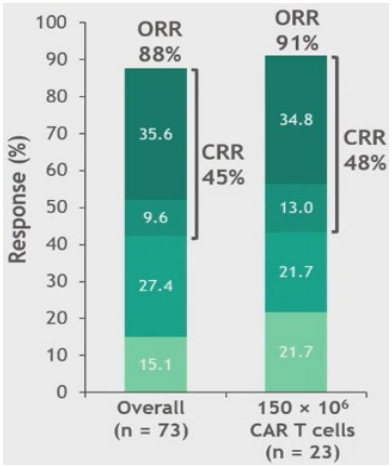
BMS-986393 (CC-95266), a GPRC5D CAR T for RRMM: Updated Results From a Phase I Study

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

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

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



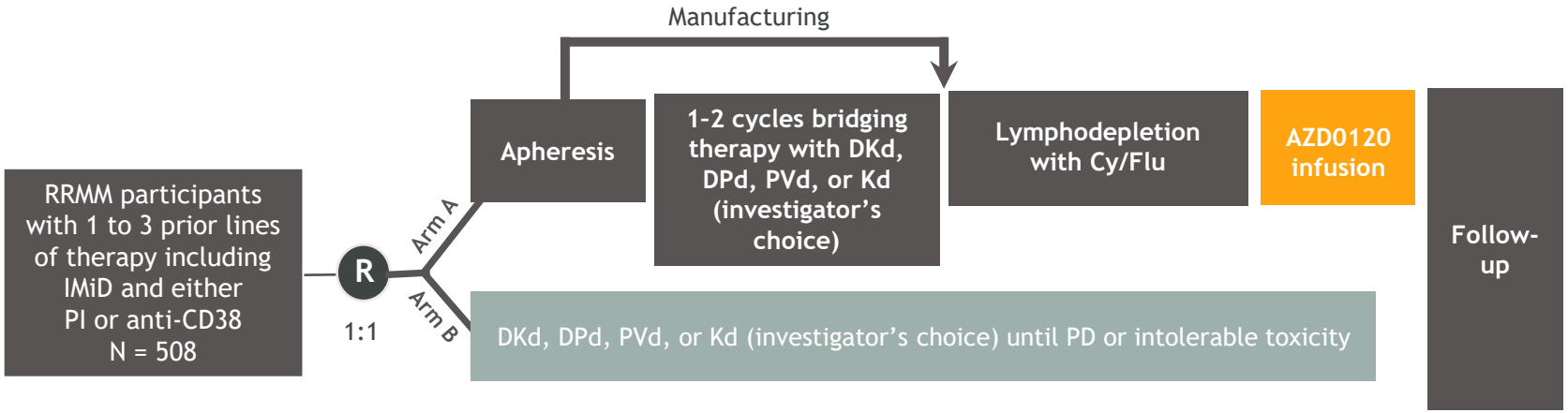


ORR in subgroups of interest (all dose levels)

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

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

DURGA-4: Study Design



Stratification

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

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

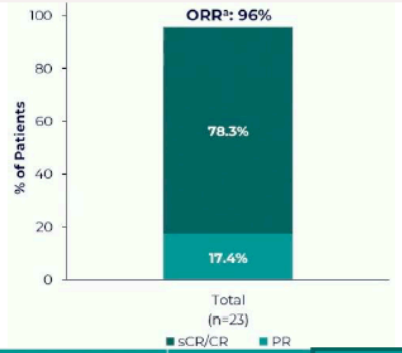
DURGA-4

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

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

ORR (n=23)

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



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

Overall Safety

n=26

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

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

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

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

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

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

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

Treatment Landscape in Multiple Myeloma: First Take-Home Message

First line

ASCT eligible

Anti-CD38 + PI + IMiD + Dex

ASCT

Len/Dara-Len

ASCT ineligible

Anti-CD38 + PI + IMiD + Dex

Dara-Len-Dex

Dara-VMP/RVd

Second line

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

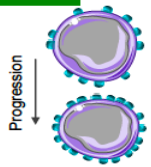
BCMA presents a clinically meaningful and well-validated target in MM

Cell specificity

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

Expression level

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

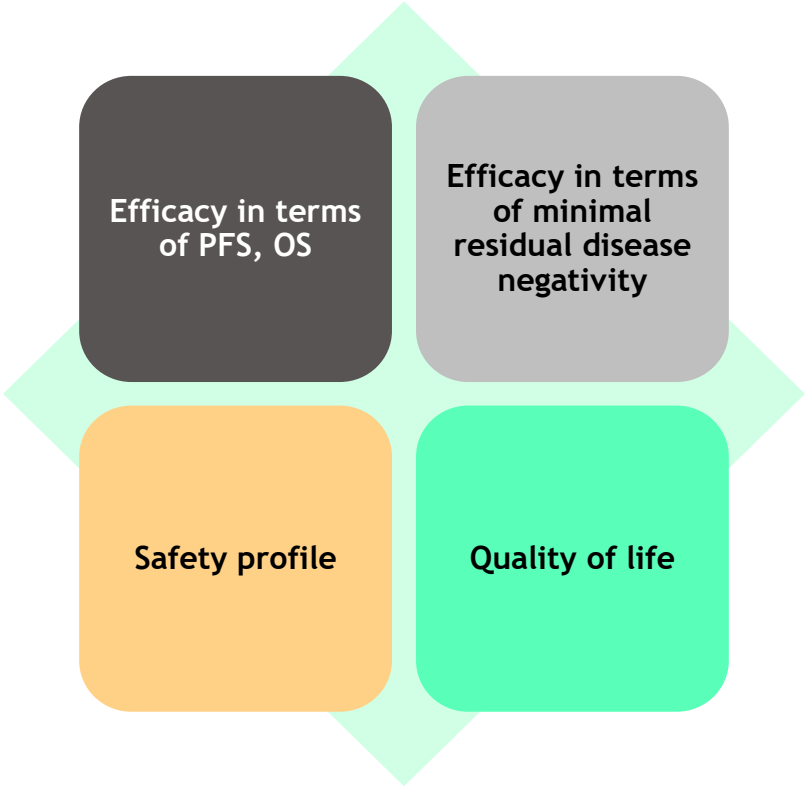


Mateos MV, personal communication; Dimopoulos MA, et al. *Ann Oncol*. 2021;32:309-322.

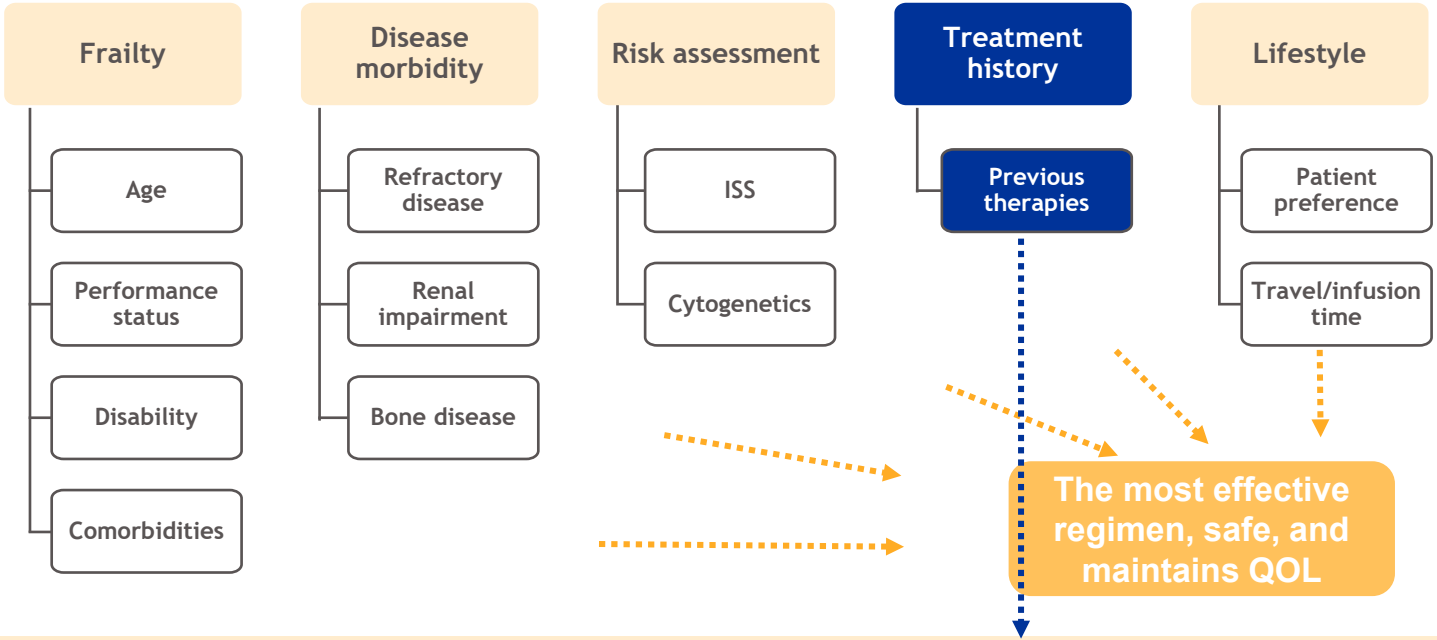
What Are the Key Administration Considerations for Anti-BCMA Therapies?

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

What Is Relevant for Treatment Decision-Making?

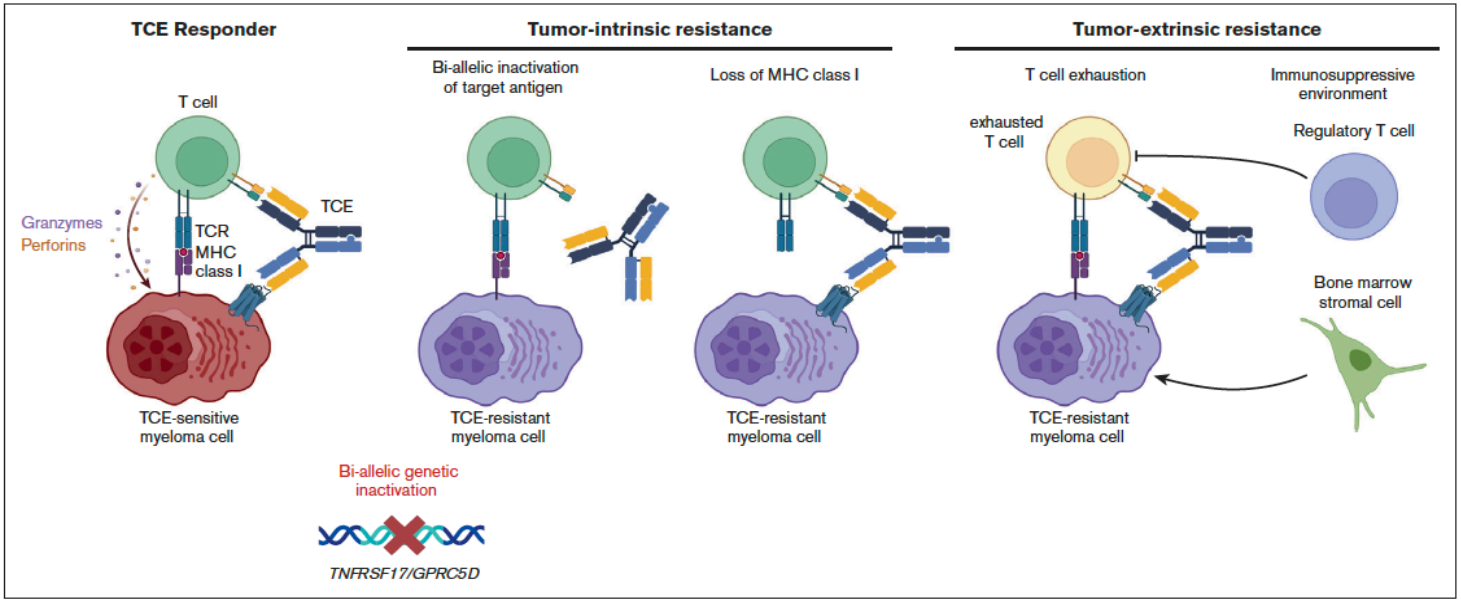


Disease and Patient-Based Factors Influencing Treatment Decision-Making in the Relapse Setting



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

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



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

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

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

Mechanisms of Resistance and Clinical Implications

Table 1. Clinical impact of resistance mechanisms

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

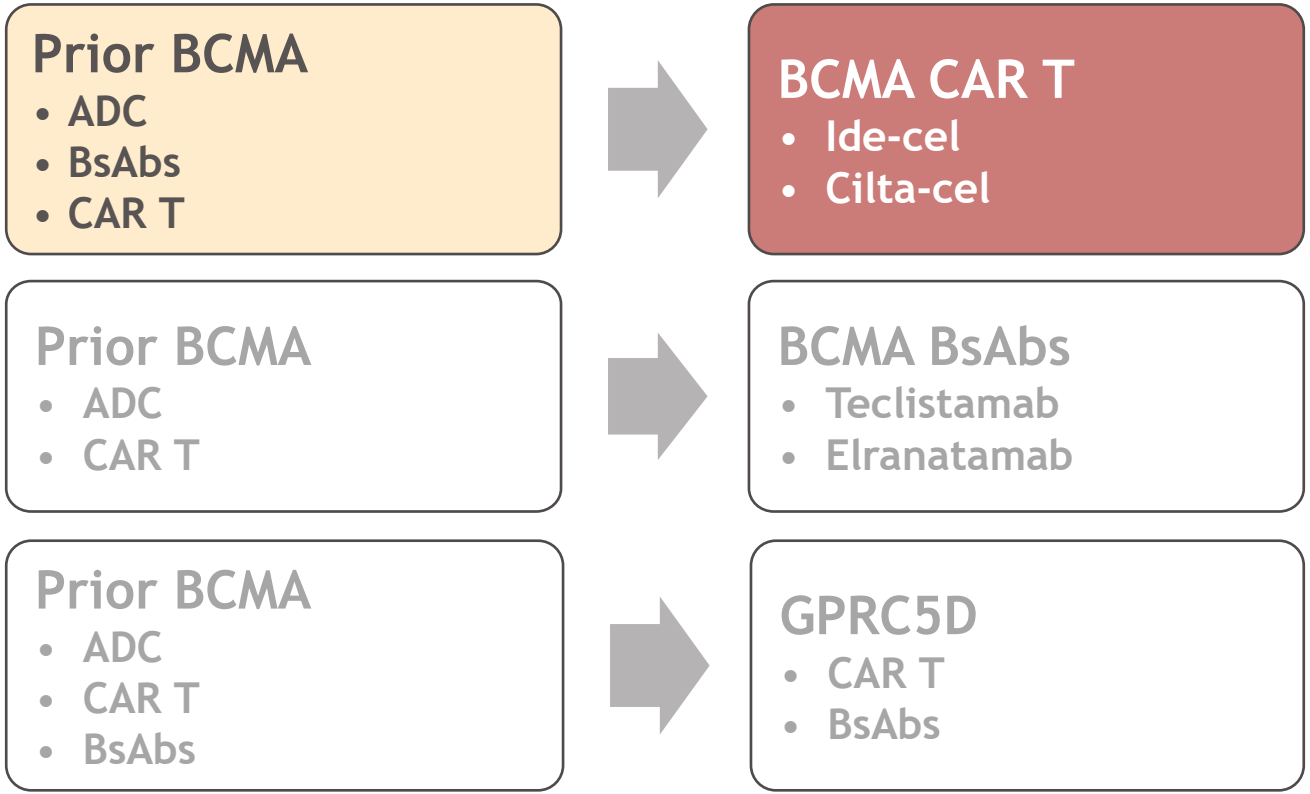
BCMA antigen escape via biallelic TNFRSF17 loss has been observed at relapse after BCMA-directed therapies in up to 14%–15% of the patients

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

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

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

Would It Be Possible to Sequence Both Approaches?

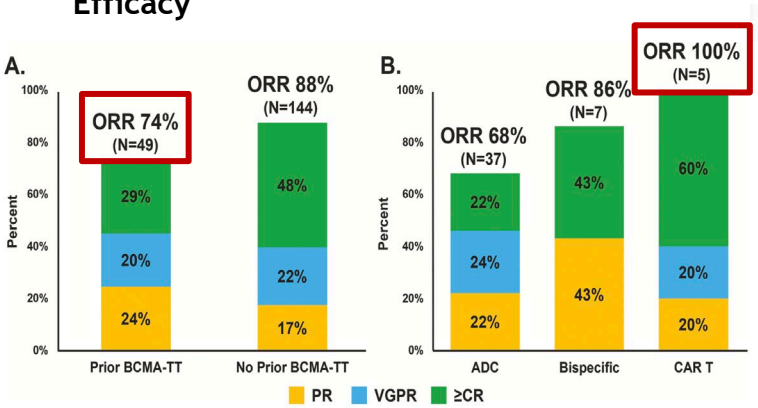


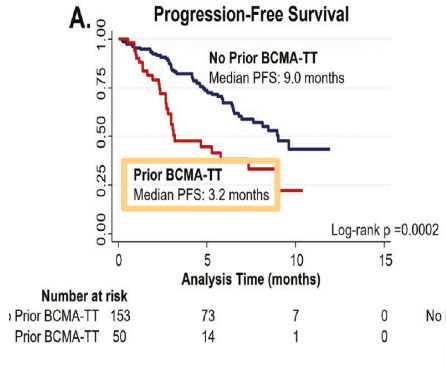
Ide-Cel for RRMM: Real-World Experience in Patients Previously Exposed to BCMA-Targeted Therapy

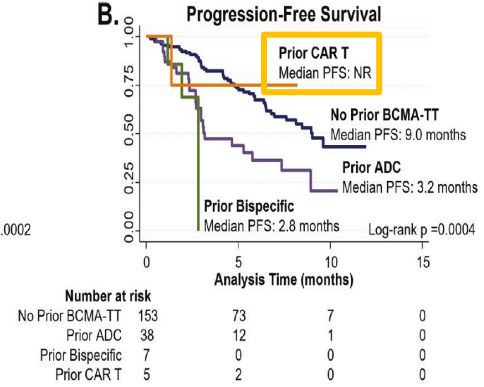
50 patients treated with Ide-cel after prior BCMA-TT (ADC 76%/BsAbs 14%/CAR T 10%); timing of prior BCMA TT: 40% <6 months

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

Efficacy







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

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

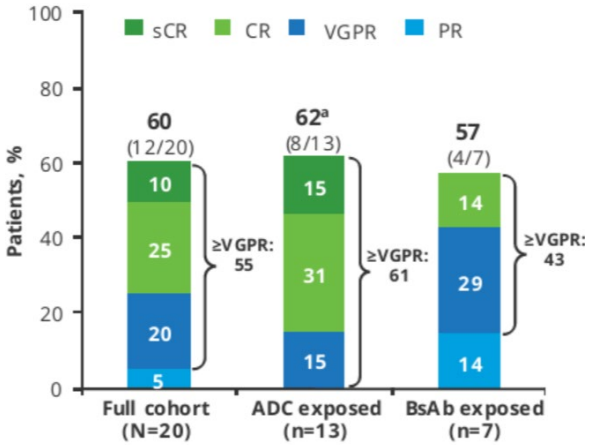
Shorter PFS in prior BCMA-TT than that observed in BCMA-naive patients

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

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

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

FIGURE 2: Overall response rate



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

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

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

TABLE: Median DOR, PFS, and OS

Estimate, months (95% CI)	Full cohort (N=20)	ADC exposed (n=13)	BsAb exposed (n=7)
DOR	12.3 (7.2–NE)	13.3 (7.2–NE)	8.2 (4.4–NE)
PFS	9.1 (1.5–13.2)	9.5 (1.0–15.2)	5.3 (0.6–NE)
OS	16.0 (8.3–NE)	21.0 (9.4–NE)	13.2 (0.6–NE)

NE, not estimable.

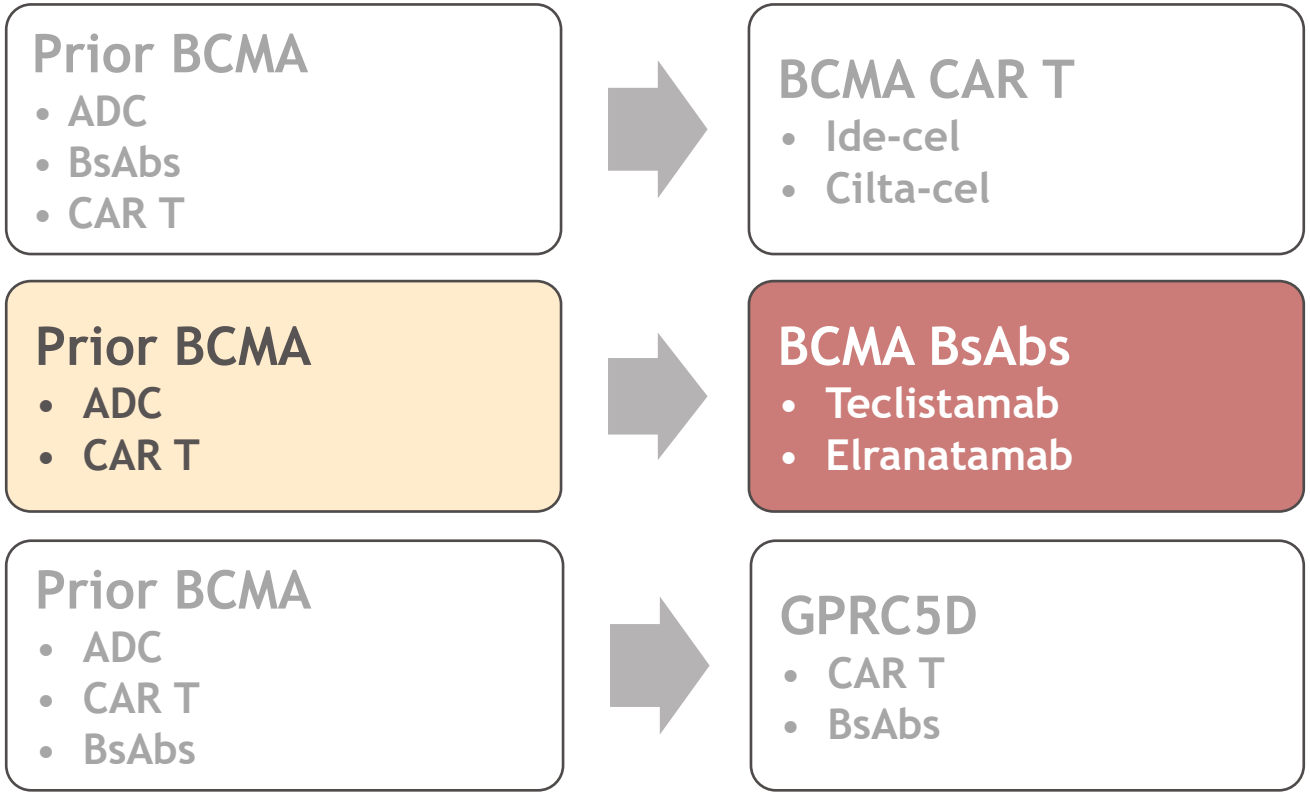
Cilta-cel induced favorable responses in highly pretreated patients with MM with prior exposure to anti-BCMAs[1,2]

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

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

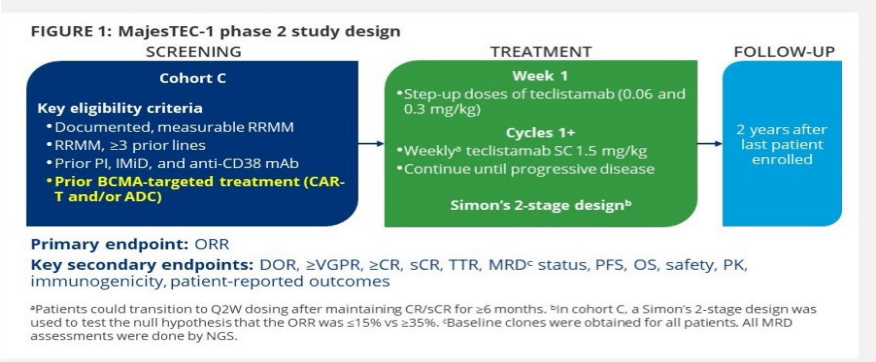
1. Cohen AD, et al. *Blood*. 2023;141:219-230; 2. Cohen AD, et al. IMS 2023. Abstract P-240.

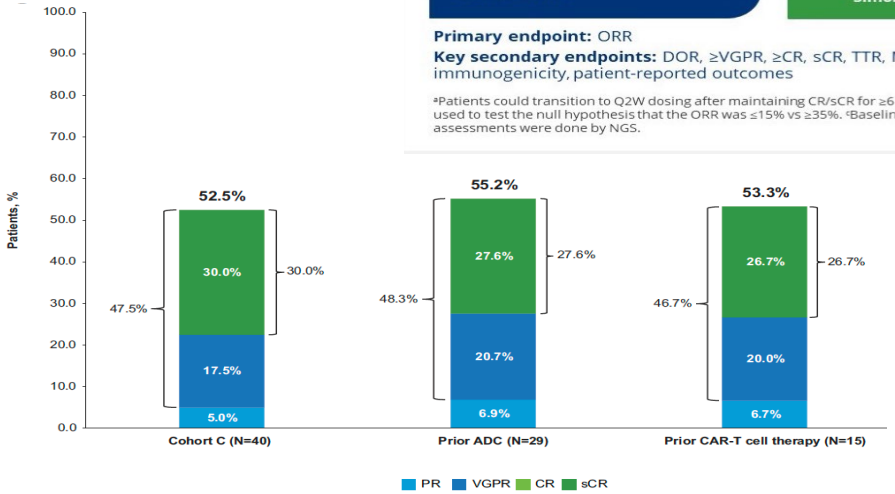
Would It Be Possible to Sequence Both Approaches?



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

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





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

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

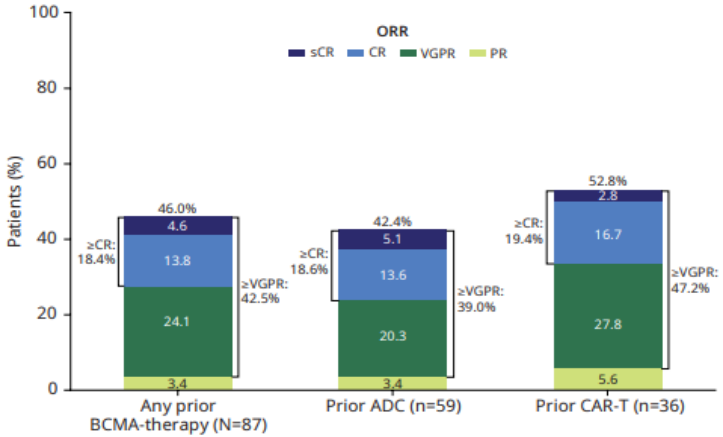
Elranatamab: Outcomes in RRMM With Prior BCMA-Directed Therapy

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

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

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

Primary endpoint: ORR



PFS

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

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

Elranatamab: Outcomes in RRMM With Prior BCMA-Directed Therapy

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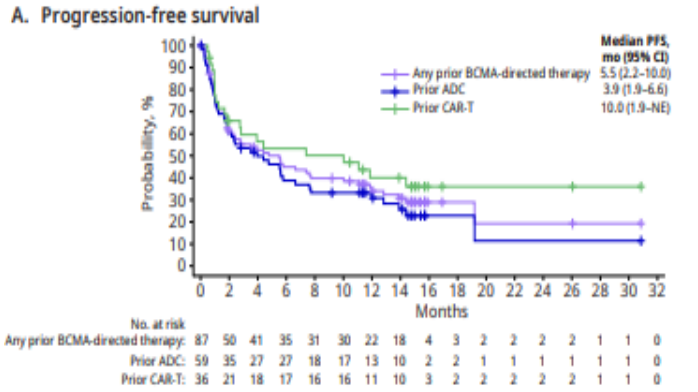
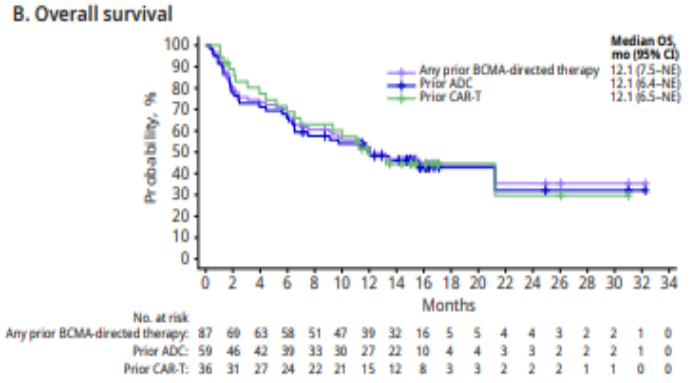
PFS



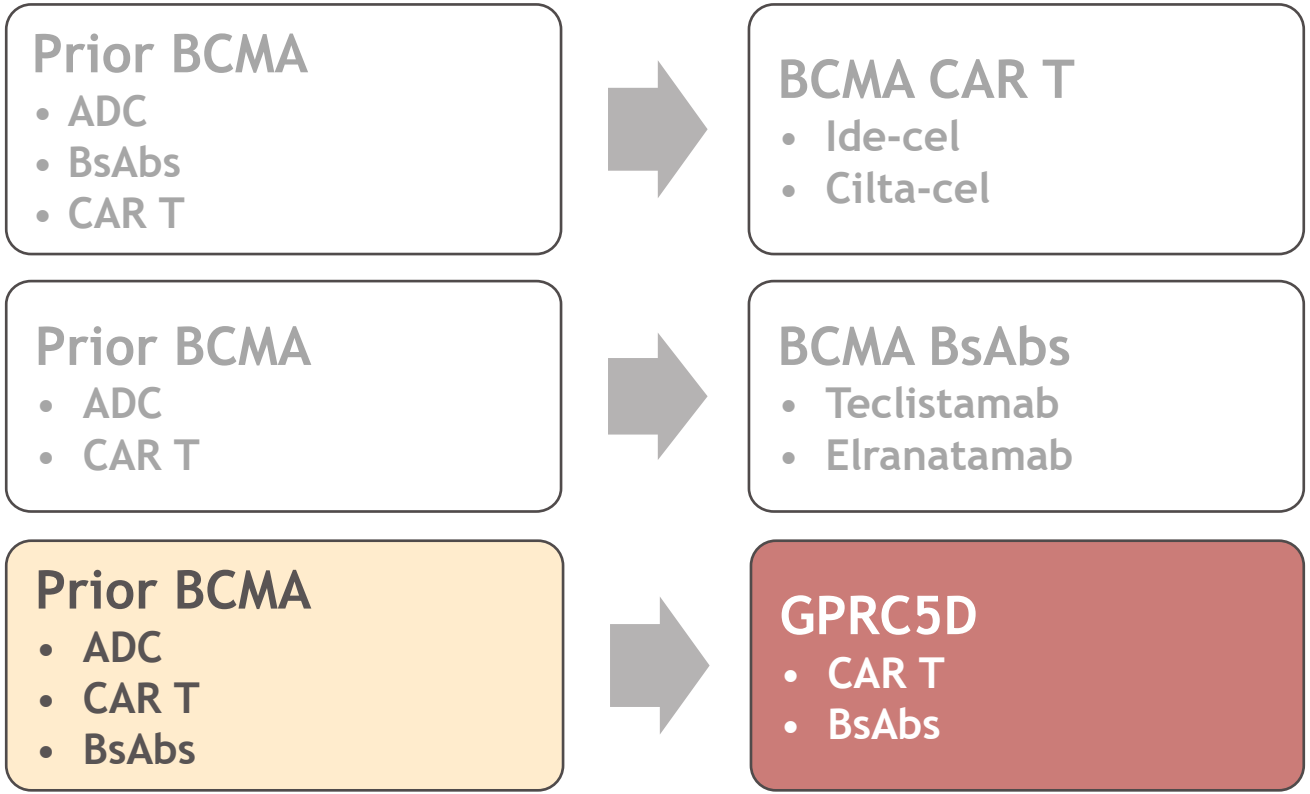
OS



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

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

Would It Be Possible to Sequence Both Approaches?

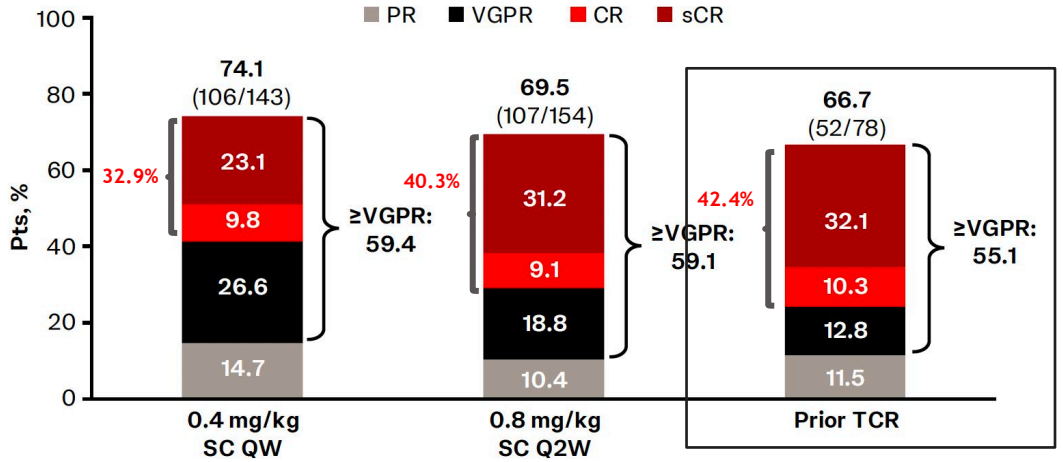


MonumenTAL-1 First-in-Human Phase I Trial: Talquetamab (GPRC5D/CD3 duo Ab) for RRMM – Efficacy With Longer FU

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

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

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



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

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

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

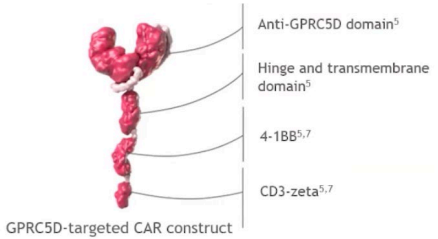
Touzeau C, et al. EHA 2023. Abstract S191; Rasche L, et al. EHA 2024. Abstract P915.

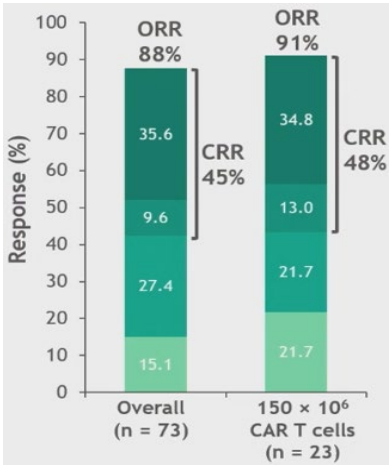
BMS-986393 (CC-95266), a GPRC5D CAR T for RRMM: Updated Results From a Phase I Study

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

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

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





ORR in subgroups of interest (all dose levels)

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

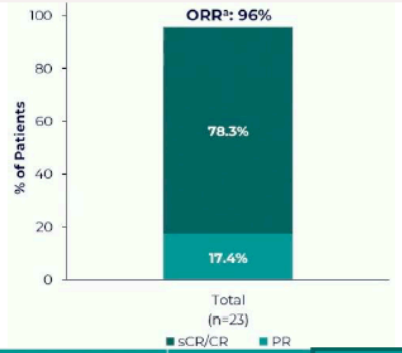
Promising efficacy and safety data even in patients previously exposed to BCMA-TT

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

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

ORR (n=23)

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



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

Overall Safety

n=26

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

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

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

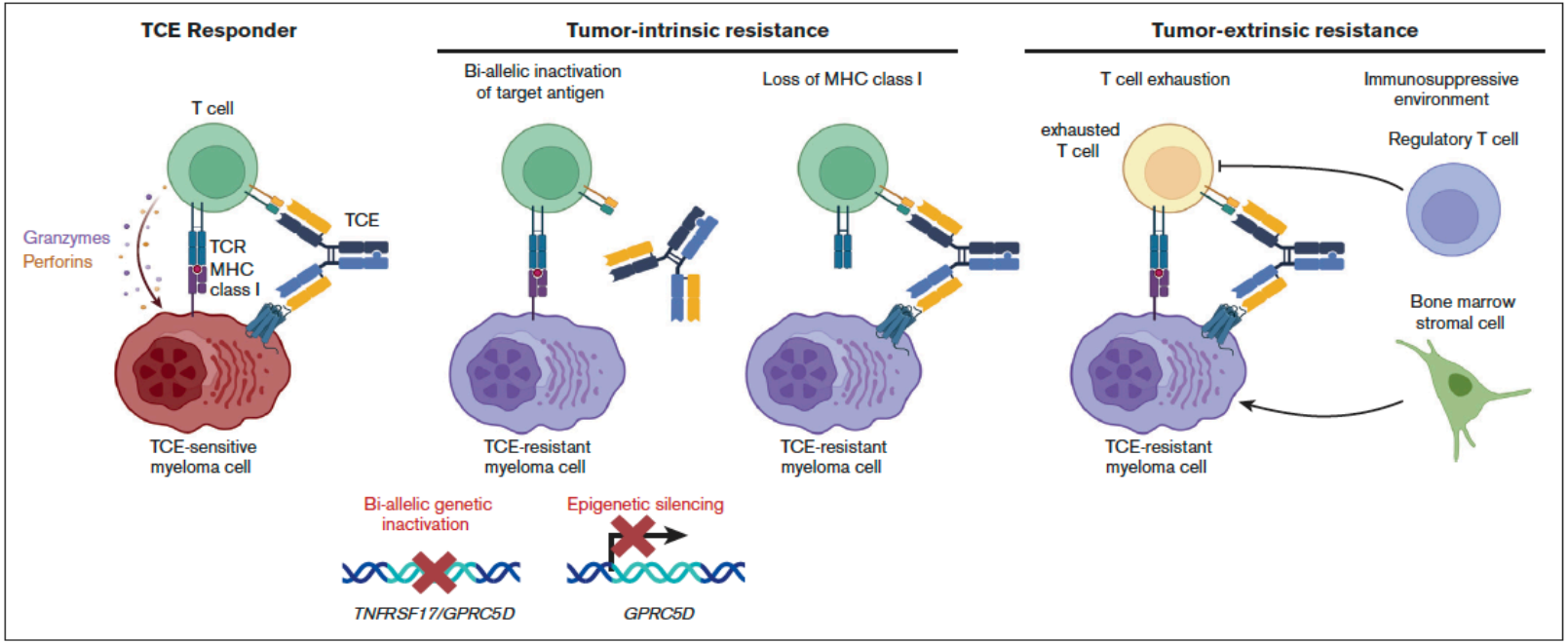
- No delayed neurotoxicities, including no Parkinsonism, no cranial nerve palsies, and no Guillain-Barré syndrome reported
- No IEC-associated colitis reported
- Only one grade 1 ICANS event
- One patient with IEC-HS (DL1, grade 2); resolved within 7 days

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

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

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

Mechanisms of Resistance and Clinical Implications for BCMA-TT



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

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

Mechanisms of Resistance and Clinical Implications

Table 1. Clinical impact of resistance mechanisms

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

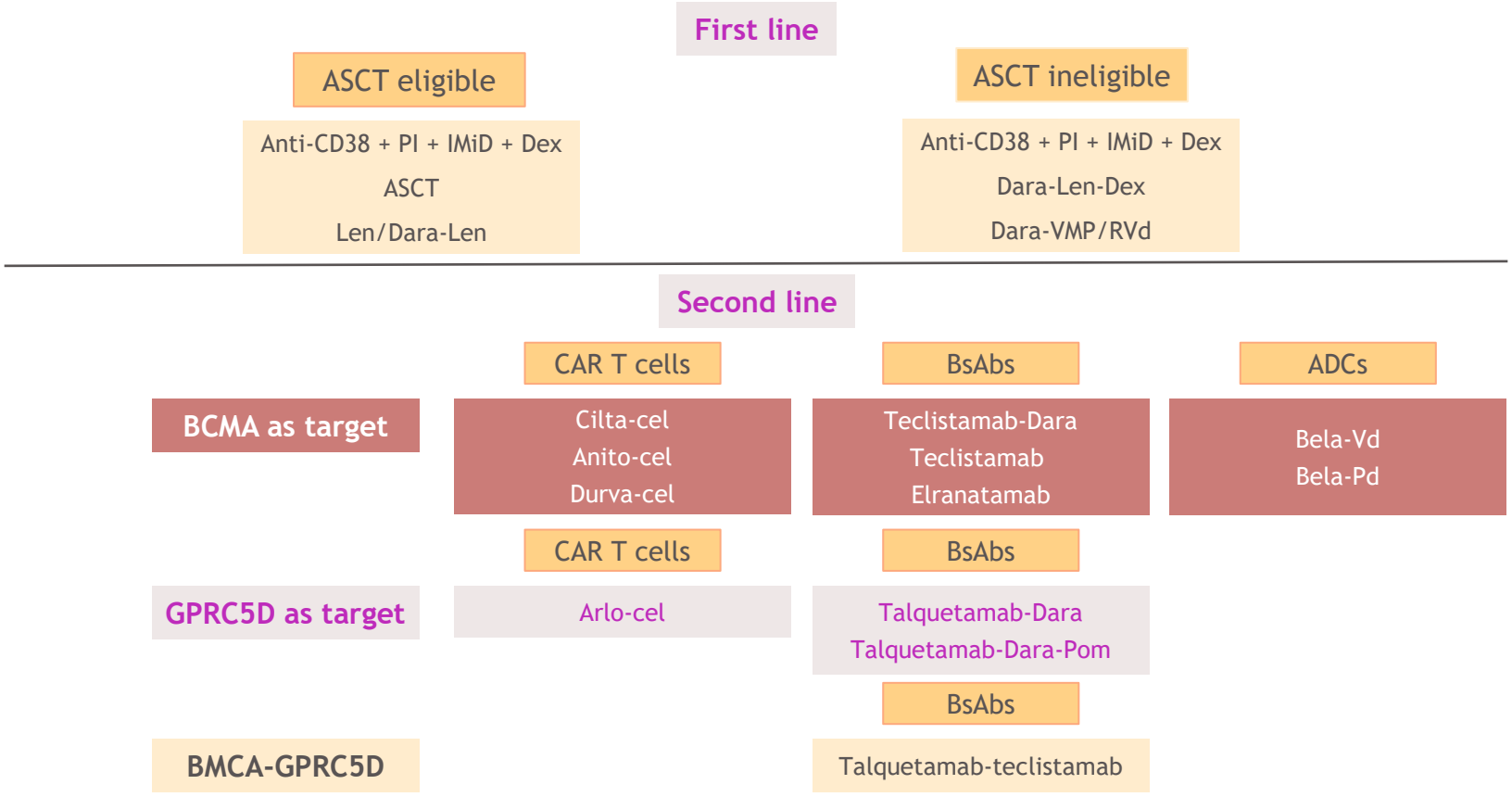
GPRC5D antigen escape via mutations has been observed at relapse after GPRC5D-directed therapies in up to 50% of the patients

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

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

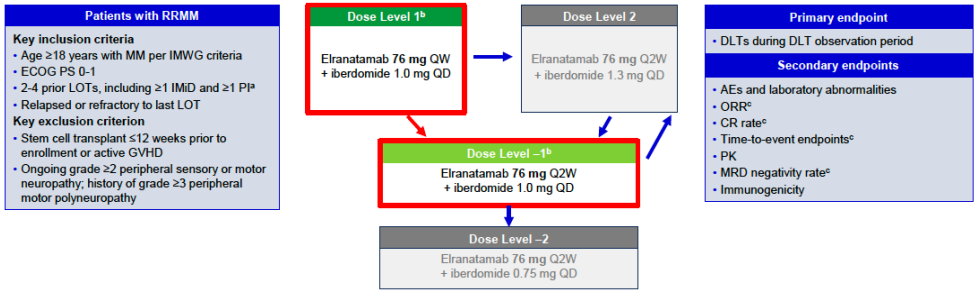
Letouzé E, et al. *Blood Adv*. 2024;8:2952-2959; Lee H, et al. *Nat Med*. 2023;29:2295-2306.

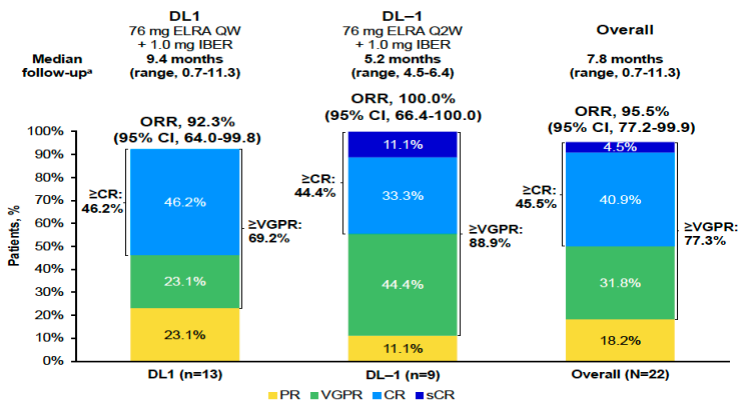
Treatment Landscape in Multiple Myeloma in Early Relapse in the Future



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

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





Responses are expected to deepen with further follow-up

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

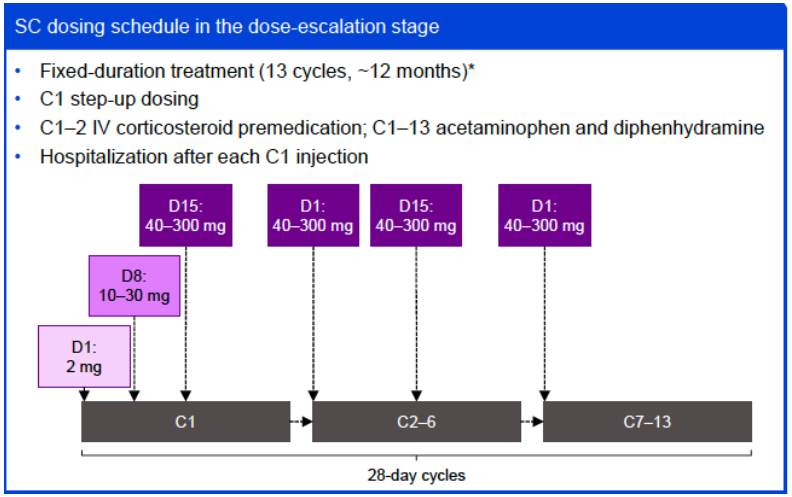
	N=22	
TEAE, n (%)[a]	**Any grade**	**Grade 3/4**
Any	22 (100.0)	19 (86.4)
Hematologic		
Neutropenia	17 (77.3)	16 (72.7)
Anemia	7 (31.8)	3 (13.6)
Lymphopenia	4 (18.2)	4 (18.2)
Nonhematologic		
CRS	15 (68.2)	0
Fatigue	14 (63.6)	0
Diarrhea	11 (50.0)	0
Headache	10 (45.5)	0
Cough	10 (45.5)	0
Nausea	9 (40.9)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

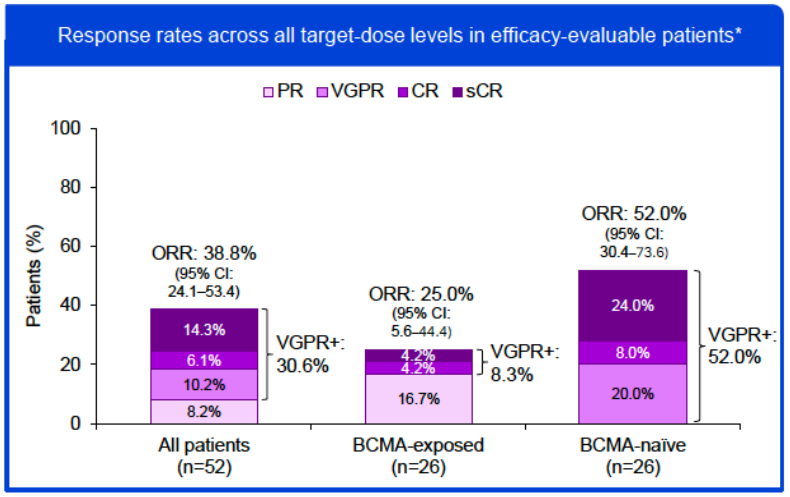
Infections occurring in >5% of patients	**N=22**	
TEAE, n (%)[a]	**Any grade**	**Grade 3**
Infections[b]	9 (40.9)	2 (9.1)
Upper respiratory tract infection	6 (27.3)	0
Candida infection	3 (13.6)	0
Urinary tract infection	2 (9.1)	0

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

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

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

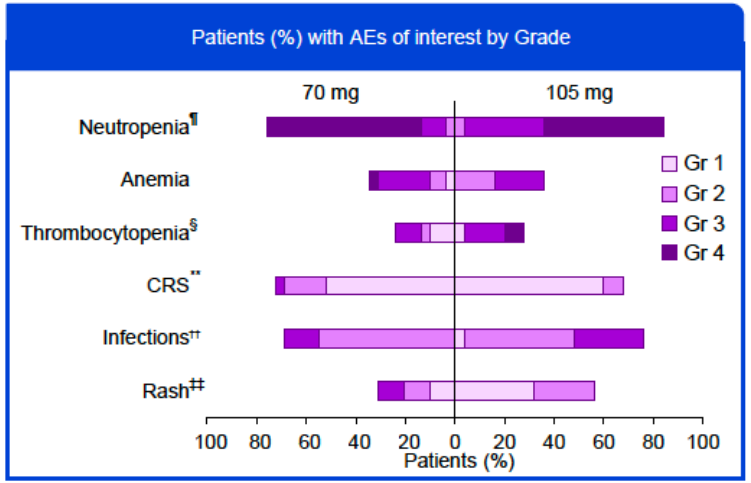




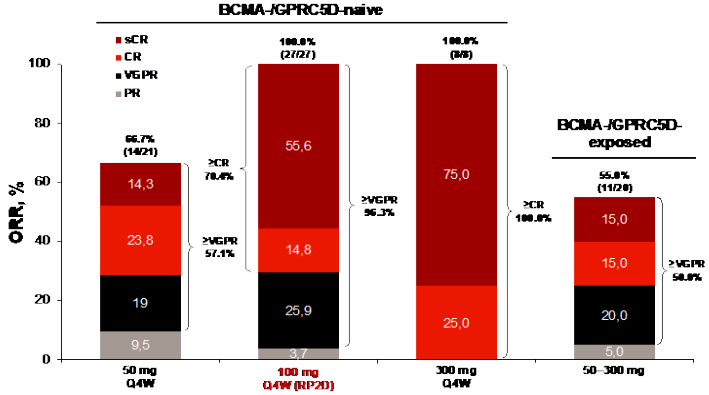
- Median DOR was 12 months, NR in BCMA-naive, and 8.3 months in BCMA-exposed patients
- CRS in 69% (G3 in 1 patient); infections in 45% (G3–5 in 15%); IVIG administration in 41% of patients

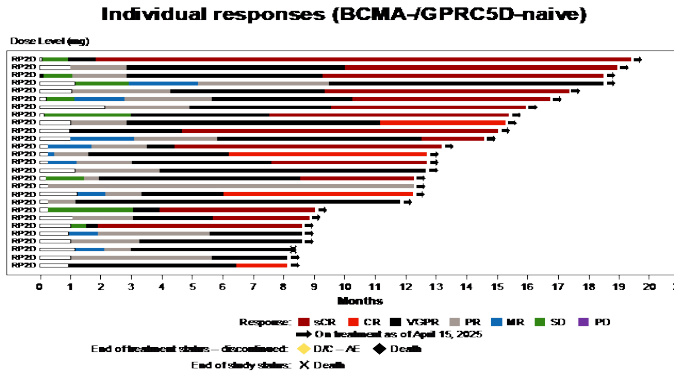
Cevostamab Plus Pomalidomide-Dex in Patients With RRMM

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

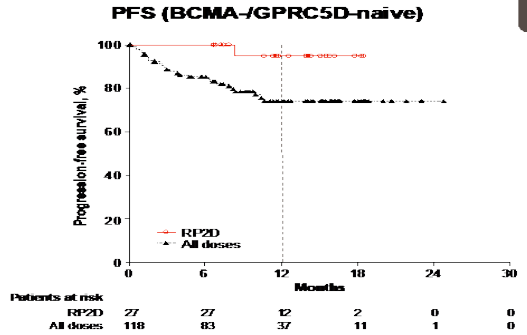


First-in-Human Study of JNJ-79635322 (JNJ-5322): Ramantamig, a BCMA-GPRC5D-CD3 mAb and Novel Next-Generation Trispecific Antibody, in Patients With RRMM – Initial Phase I Results





Only one discontinuation to date at the RP2D



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

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

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

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

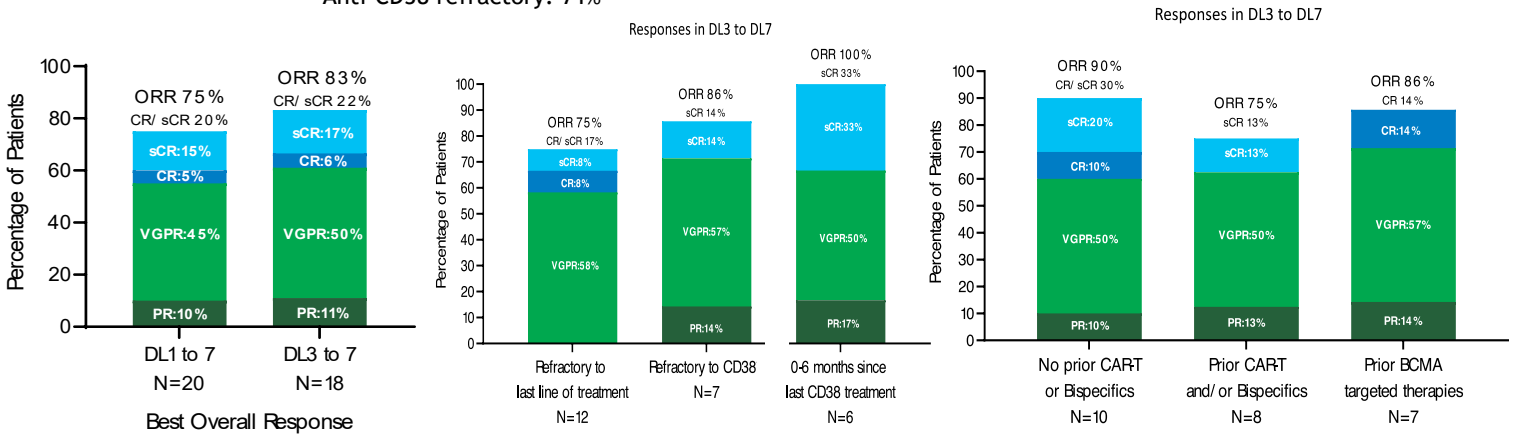
Dose escalation/expansion study in dose escalation. ISB 2001 is administered SC QW in 28-day cycles, starting with 2 step-up doses on days 1 and 4, followed by the full target dose from day 8 onward

Population (n = 40)

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

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

Anti-CD38 refractory: 71%



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

Trial is ongoing to define the RP2D

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

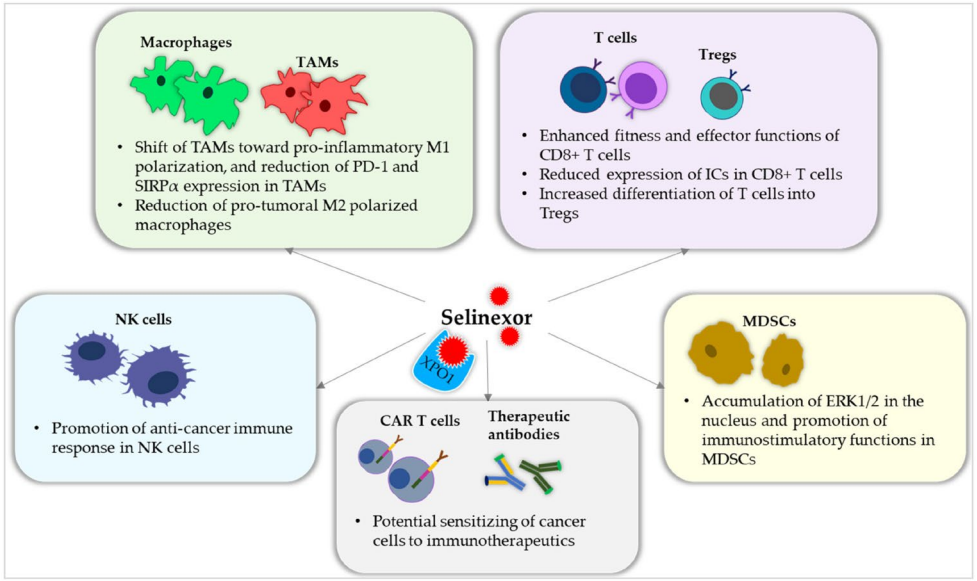
Carretero-Iglesia L, et al. *Nat Cancer*. 2024;5:1494-1514; Quach H, et al. ASH 2024. Abstract P898.

And Beyond the T-Cell Redirecting Therapies . . .

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

Selinexor Influences Multiple Immune Cells Pathways

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



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

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

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

UPREGULATION OF BCMA EXPRESSION BY SELINEXOR

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

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

Abstract # 6102

INTRODUCTION

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

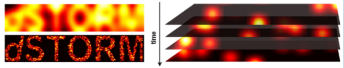
AIM

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

METHOD

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

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



RESULTS

1. BCMA GENE EXPRESSION INCREASED BY SELINEXOR TREATMENT

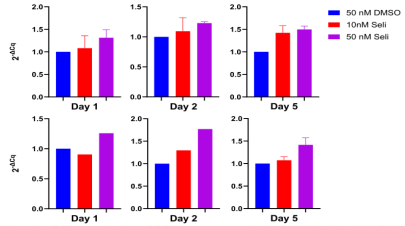


Figure 1. qPCR quantification of BCMA gene expression in OPM-2 (top) and AMO1 (bottom) cells treated with 50 nM DMSO (blue), 10 nM Selinexor (red) or 50 nM Selinexor (magenta) for 1, 2 and 5 days. OPM-2 cells showed a 1.2- and 1.5-fold increase and AMO1 cells revealed a 1.8- and 1.5-fold increase in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

2. SELINEXOR CONCENTRATIONS DO NOT IMPACT CELL VIABILITY

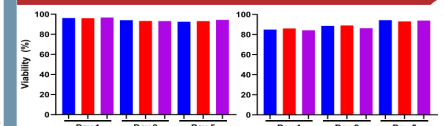


Figure 2. Cell viability of OPM-2 (left) and AMO1 (right) cells when treated with 50 nM DMSO (blue), 10 nM Seli (red) or 50 nM Seli (magenta). Viability of OPM-2 cells remained above 90% and AMO1 cell viability even improved from 84% to 93% by day 5

3. BCMA RECEPTOR EXPRESSION INCREASED BY SELINEXOR TREATMENT

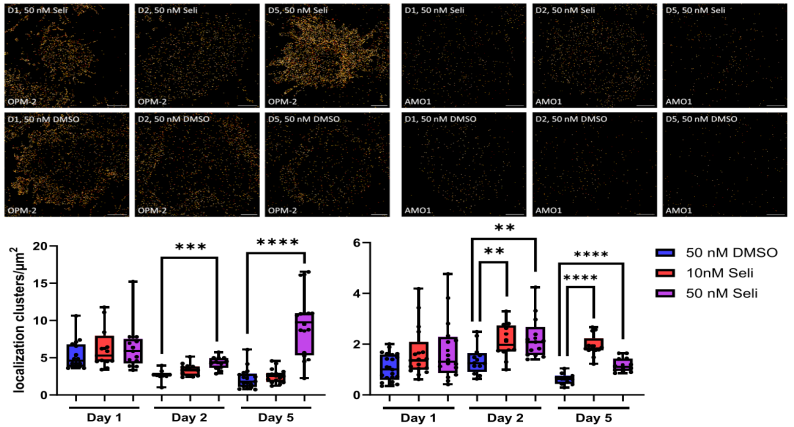


Figure 3. Top: *d*STORM images of OPM-2 (first three columns) and AMO1 (last three columns) after respectively 1, 2 and 5 days of treatment. Top panels show 50 nM Selinexor treated cells, bottom panel 50 nM DMSO. Scale bars, 3 µm. Each yellow dot corresponds to one BCMA receptor, an increase in signal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

CONCLUSIONS

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

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

OUTLOOK

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

CONTACT INFORMATION

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Summary

- Treatment is rapidly evolving
- The first line of therapy seems to be now well established with PIs, IMiDs, and anti-CD38 mAbs
- BCMA-targeted therapies are options at early relapse: today with Cilta-cel and Belamaf-based combinations, and BCMA BsAbs are coming
- CELMoDs will be also be available soon, with 2 combinations based on Iber-Dara-Dex and mezigdomide-carfilzomib-Dex
- The availability of all these options may allow for a more individualized therapy based on the disease and patient-based characteristics
- T-cell redirecting therapies against other targets are coming and will facilitate the sequencing
- Sequencing is also a challenge, and we should generate information from the real-world experiences

Global Multiple Myeloma Academy

Discussion

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Session Close – Audience Response Questions

Rafael Fonseca, MD

APTITUDE HEALTH

Question 10

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

1. True
2. False

Question 11

[REPEATED]: What is the primary mechanism of action for CELMoDs?

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

Thank You!

- Please complete the **evaluation survey** that will be sent to you via chat
- The meeting recording and slides presented today will be shared on the www.globalmmacademy.com website

THANK YOU!

Global Multiple Myeloma Academy

Global Multiple Myeloma Academy: Emerging and Practical Concepts in RRMM

Thank you for your participation!

Pfizer

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