POST-SAN DIEGO 2024
Novità dal Meeting della Società Americana di Ematologia

Novità dal Meeting della Società Americana di Ematologia

Bologna
Palazzo Re Enzo
13-15 Febbraio 2025

COORDINATORI
Angelo Michele Carella
Pier Luigi Zinzani

BOARD SCIENTIFICO
Paolo Corradini
Mauro Krampera
Fabrizio Pane
Adriano Venditti

Roberto Mina, MD

Terapia alla prima ricaduta nel MM

Università degli studi di Torino

Disclosures of Name Surname

Company name	Research support	Employee	Consultant	Stockholder	Speakers bureau	Advisory board	Other
Janssen			x			x	x
Sanofi						x	x
BMS						x	x
GSK						x	x
Takeda						x	
Amgen						x	
Pfizer						x	
Menarini Stem-line							x

Frontline therapy

TE patients
DVRd-ASCT-DR

TIE patients
Anti-CD38-VRd / DRd

Len refractory

Anti-CD38 regimens

Isa-Kd
DPd
DVd

Anti-CD38-free regimens

Kd
PVd
Seli-Vd

Anti-CD38 + Len refractory

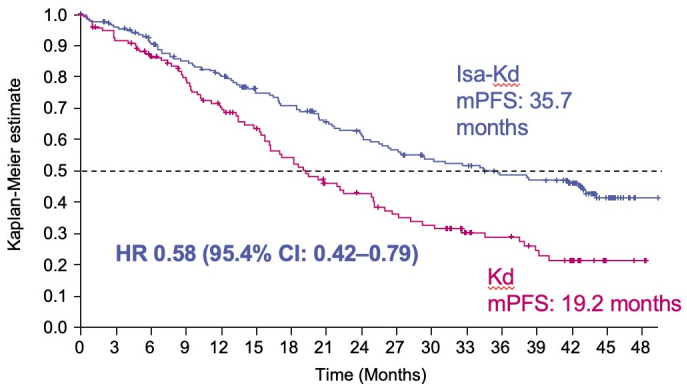
Anti-CD38-free regimens

Kd
PVd
Seli-Vd

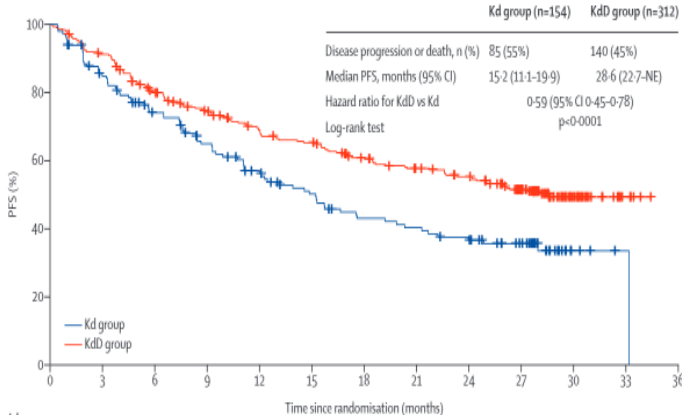
What treatment at relapse for triple-class exposed/refractory patients?

Treatment options at first relapse for daratumumab and lenalidomide refractory patients

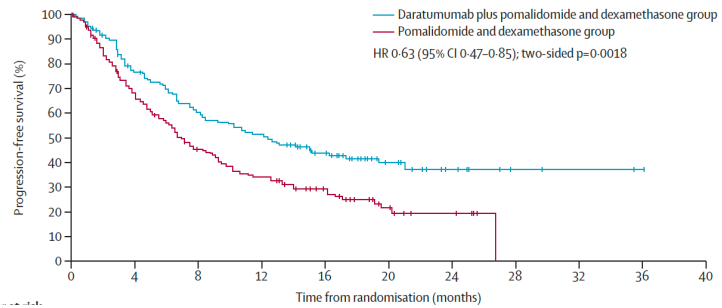
IKEMA: IsaKd vs Kd



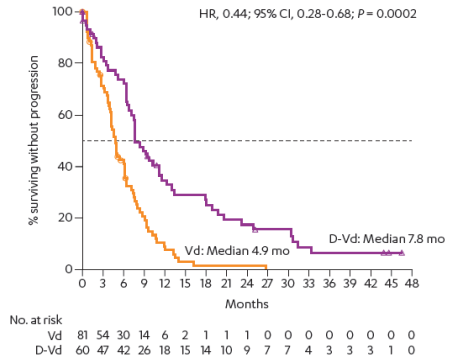
CANDOR: DKd vs Kd



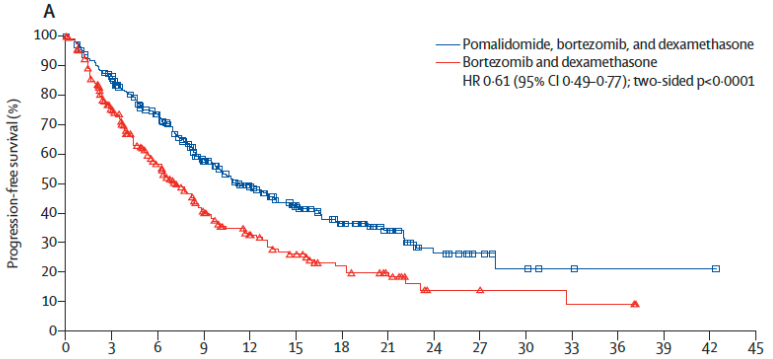
APOLLO: DPd vs Pd



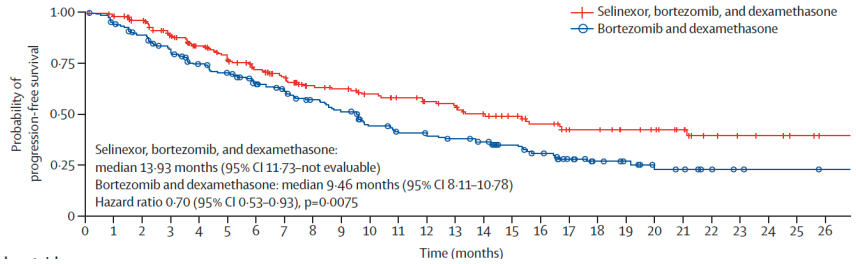
CASTOR: DVd vs Vd



OPTIMISMM: PVd vs Vd



BOSTON: SVd vs Vd



Palumbo A et al, N Engl J Med 2016; Moreau P et al . Lancet 2021; Dimopoulous M et al, EHA 2021; Martin T et al, ASH 2020; Capra M et al, ASH 2020

L’era delle terapie anti-BCMA:
CAR T-cell, anticorpi bispecifici ed anticorpi coniugati

Frontline therapy

TE patients DVRd-ASCT-DR	TIE patients Anti-CD38-VRd / DRd

Len refractory

Anti-CD38 regimens	BCMA-options
Isa-Kd DPd DVd	Cilta-cel Ide-cel Bela-Pd Bela-Vd
Anti-CD38-free regimens	
Kd PVd Seli-Vd	

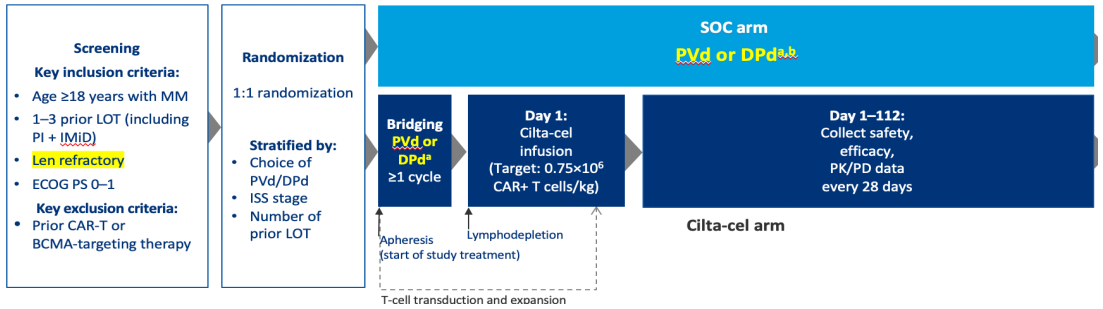
Anti-CD38 + Len refractory

BCMA-options	Non-BCMA options
Cilta-cel Ide-cel Bela-Pd Bela-Vd	Kd PVd Seli-Vd

What treatment at relapse for triple-class exposed/refractory patients?

CARTITUDE-4: Cilta-cel vs SoC in RRMM

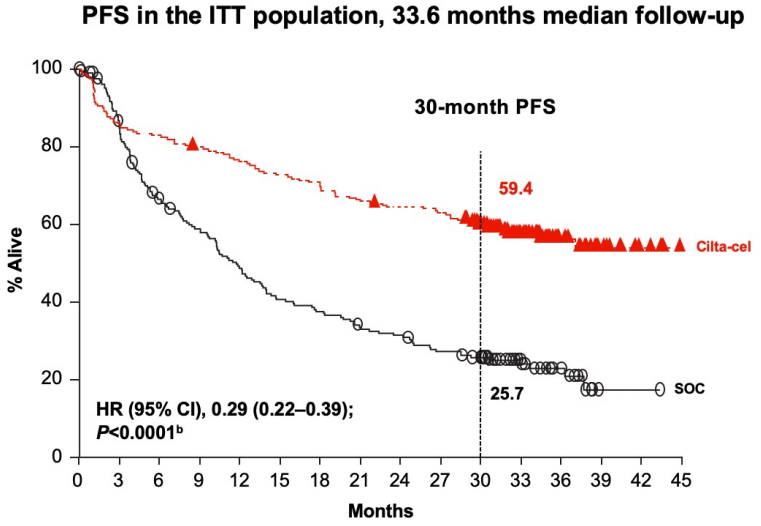
Study design and baseline characteristics

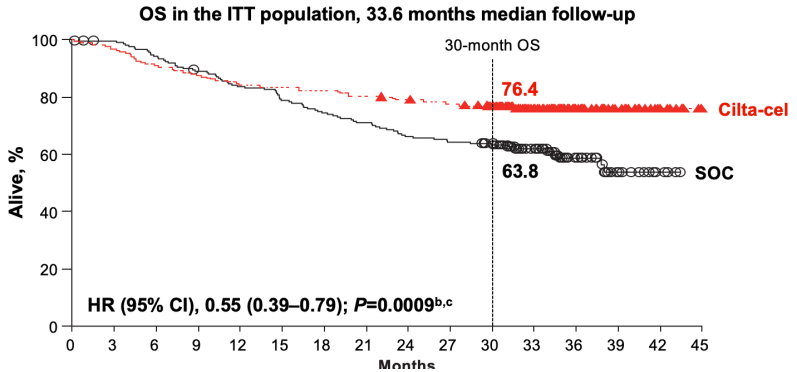


Baseline characteristic	ITT population	
	Cilta-cel (N=208)	SOC (N=211)
Age, median (range), years	61.5 (27–78)	61.0 (35–80)
Male, n (%)	116 (55.8)	124 (58.8)
White, n (%)	157 (75.5)	157 (74.4)
ECOG PS 0 or 1, n (%)[a,b]	207 (99.5)	210 (99.5)
ISS stage, n (%)		
I	136 (65.4)	132 (62.6)
II	60 (28.8)	65 (30.8)
III	12 (5.8)	14 (6.6)
Bone marrow plasma cells ≥60%,[c] n (%)	42 (20.4)	43 (20.7)
Presence of soft tissue plasmacytomas,[d] n (%)	44 (21.2)	35 (16.6)
Years since diagnosis, median (range)	3 (0.3–18.1)	3.4 (0.4–22.1)
Prior LOT, median (range)	2 (1-3)	2 (1-3)
1 prior LOT, n (%)	68 (32.7)	68 (32.2)
2 or 3 prior LOT, n (%)	140 (67.3)	143 (67.8)

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

Progression-free and overall survival

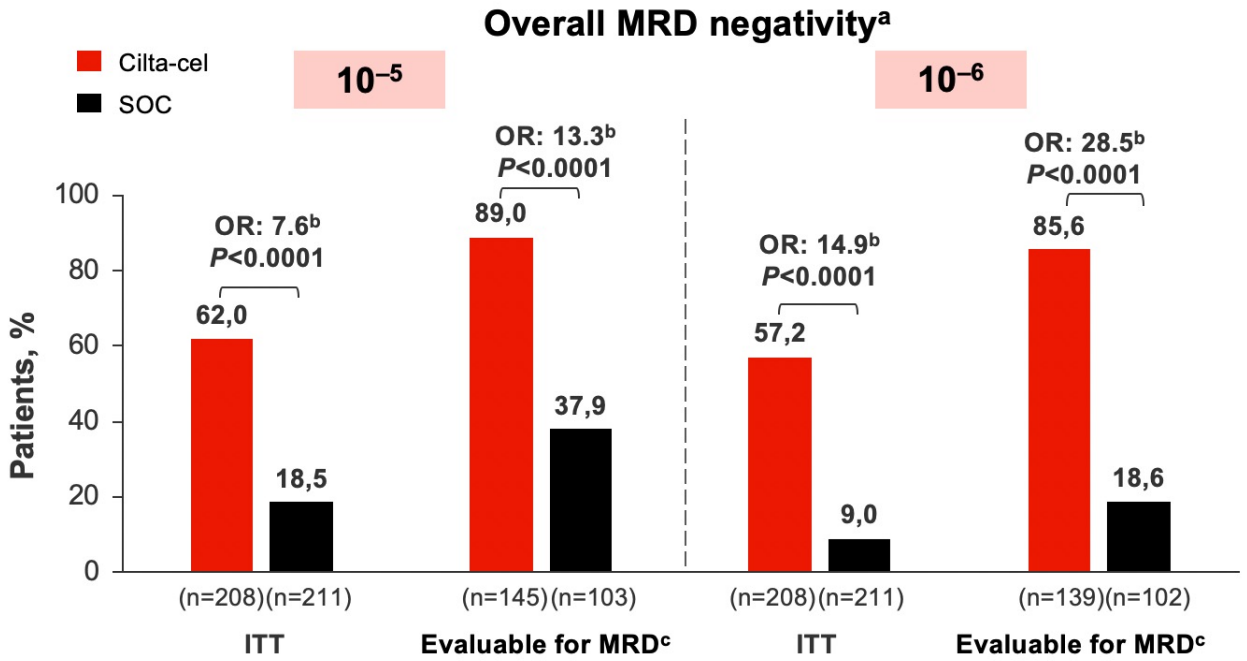


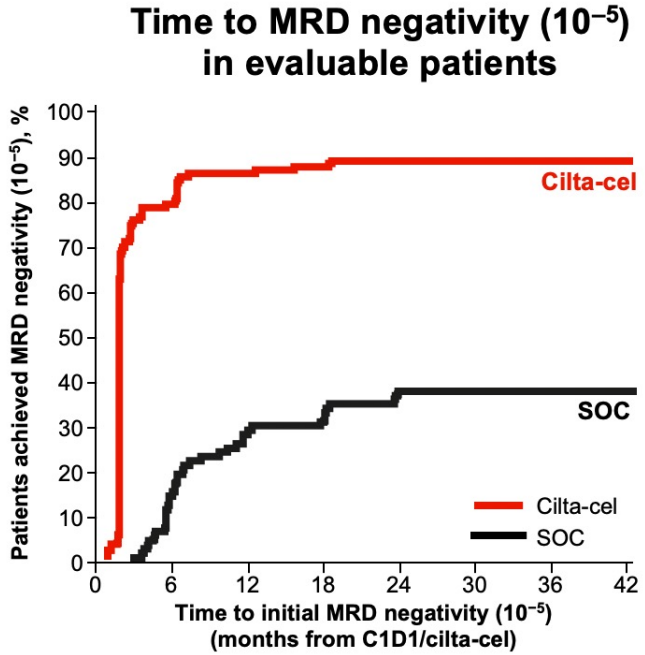


Dhakal, B, et al. ASCO 2023. LBA106; Mateos MV et al, IMS24

CARTITUDE-4 : Cilta-cel vs SoC in RRMM

MRD negativity rates



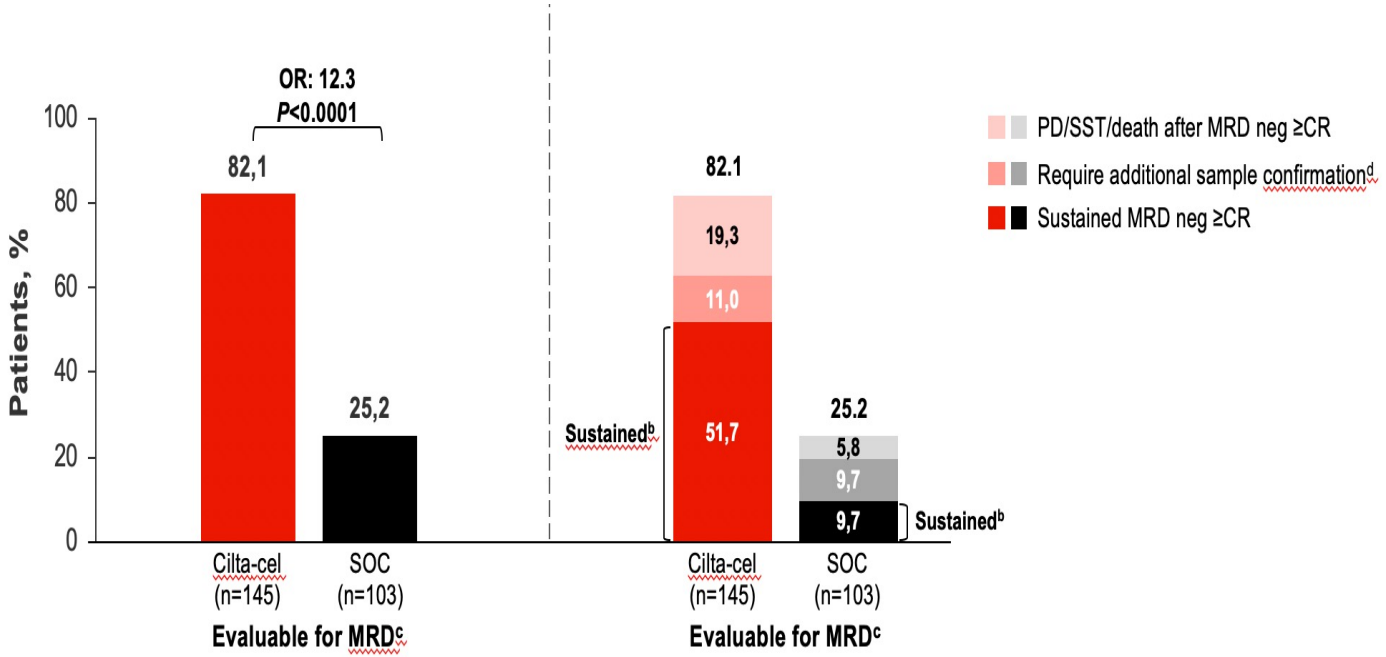


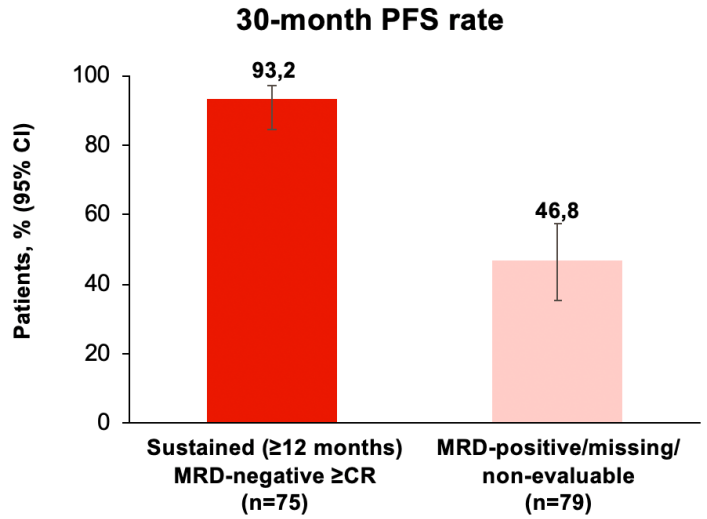
- 69% of evaluable patients achieved MRD negativity (10^{-5}) by day 56 (ITT, 48%), rising to 86% (ITT, 60%) by 6 months post cilta-cel infusion

Popat R. et al, ASH 2024

CARTITUDE-4 : Cilta-cel vs SoC in RRMM

Sustained MRD negativity

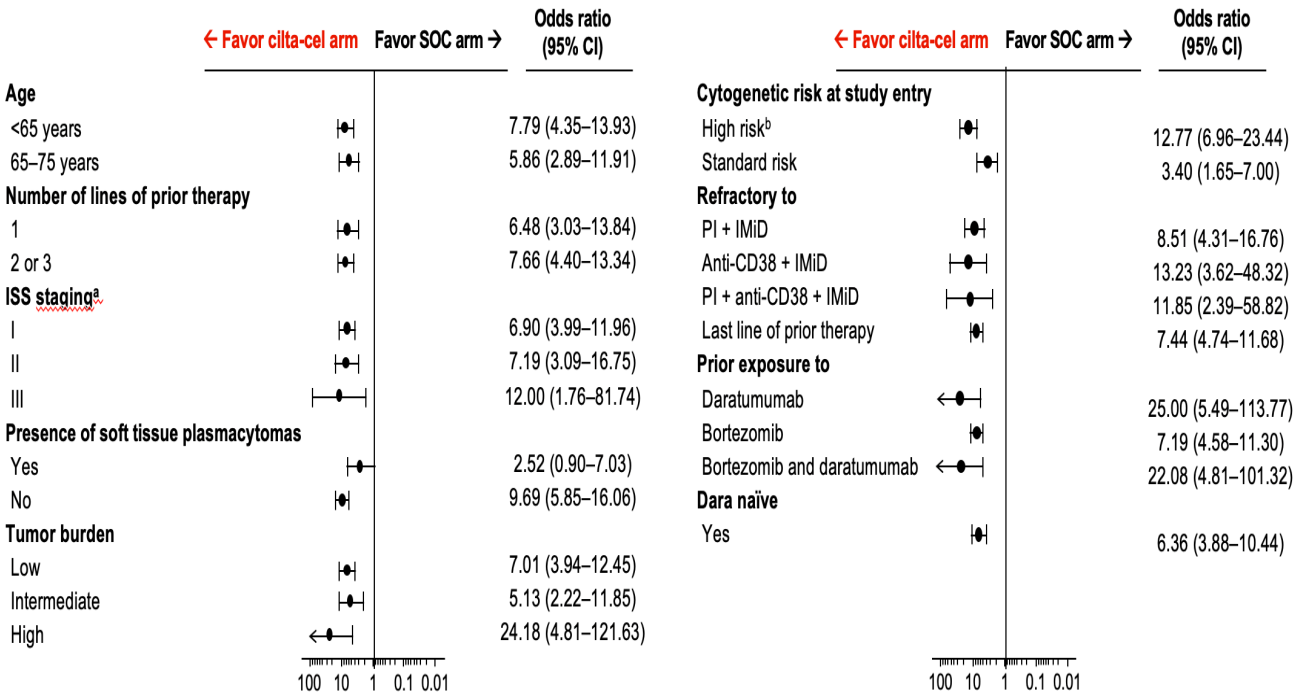




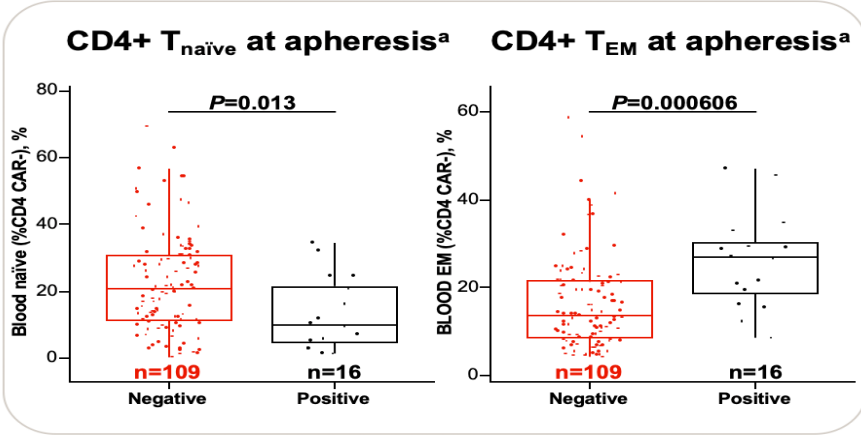
Popat R. et al, ASH 2024

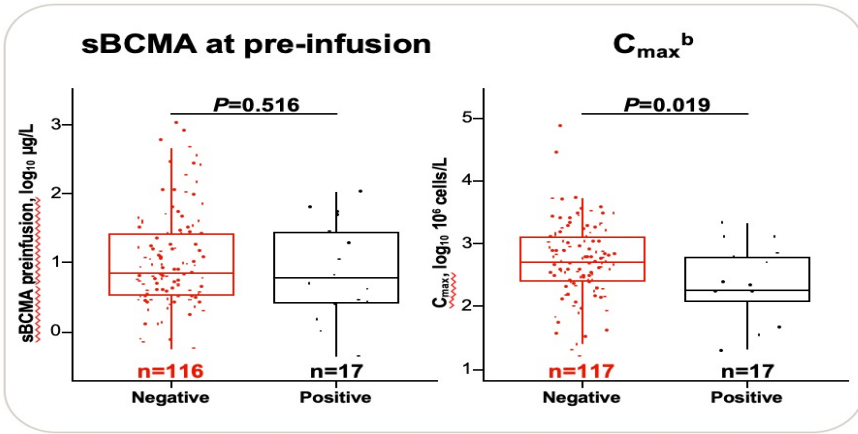
CARTITUDE-4 : Cilta-cel vs SoC in RRMM

MRD negativity rates across subgroups



Biological correlates of MRD status

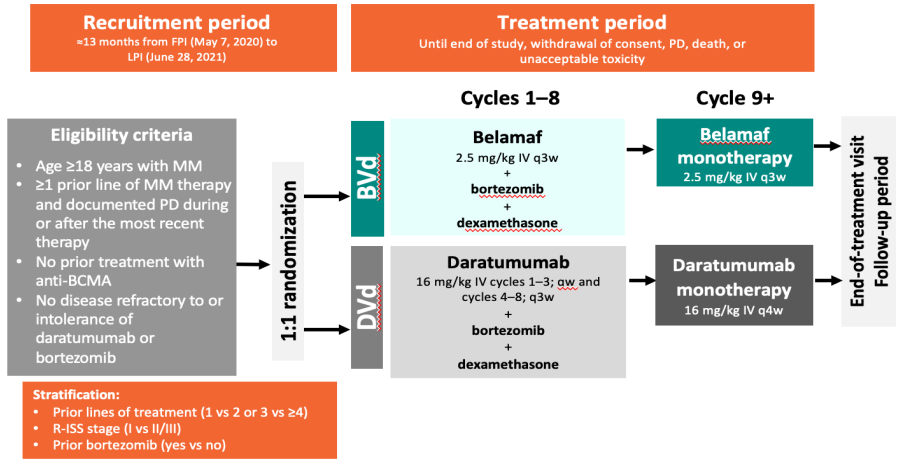




Popat R. et al, ASH 2024

DREAMM-7: BelaVd vs DVd in RRMM

Study design and baseline characteristics

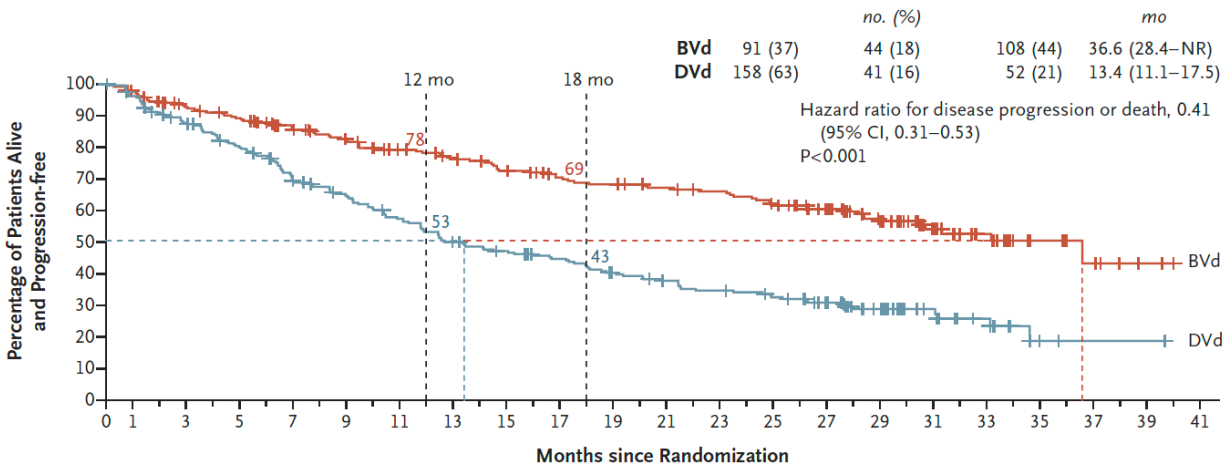


Baseline characteristics	ITT population[a]	
	BVd (N=243)	DVd (N=251)
Age, median (range), years	65.0 (34-86)	64.0 (32-89)
Cytogenetic abnormalities, n (%)		
High risk[d]	67 (28)	69 (27)
Standard risk[e]	175 (72)	175 (70)
Prior lines of therapy		
1	125 (51)	125 (50)
2 or 3	88 (36)	99 (39)
4+	30 (12)	27 (11)
Prior immunomodulatory drugs	198 (81)	216 (86)
Prior lenalidomide	127 (52)	130 (52)
Refractory to lenalidomide	79 (33)	87 (35)
Prior daratumumab	3 (1)	4 (2)

Progression-free survival

Median follow-up: 28.8 months

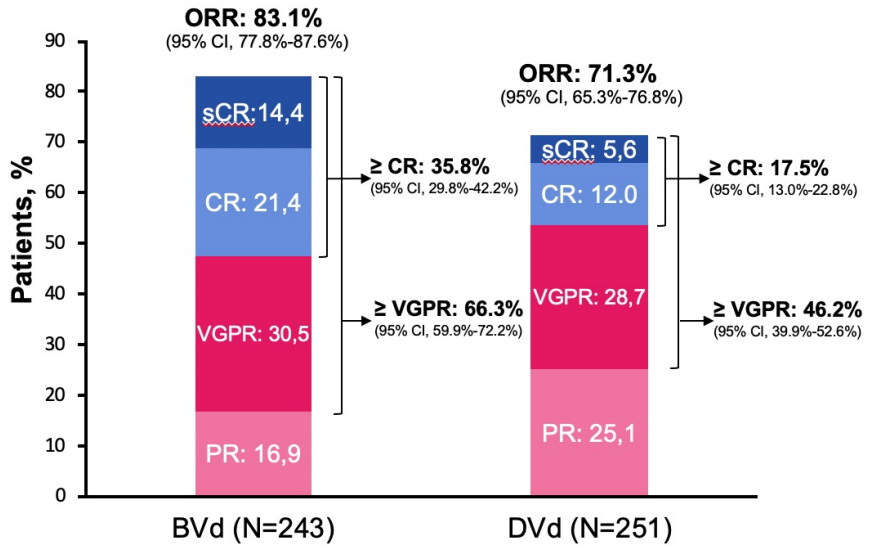
BVd vs DVd: mPFS 36.6 vs 13.4 months



Mateos MV et al, NEJM2024; Mateos MV et al, IMS24

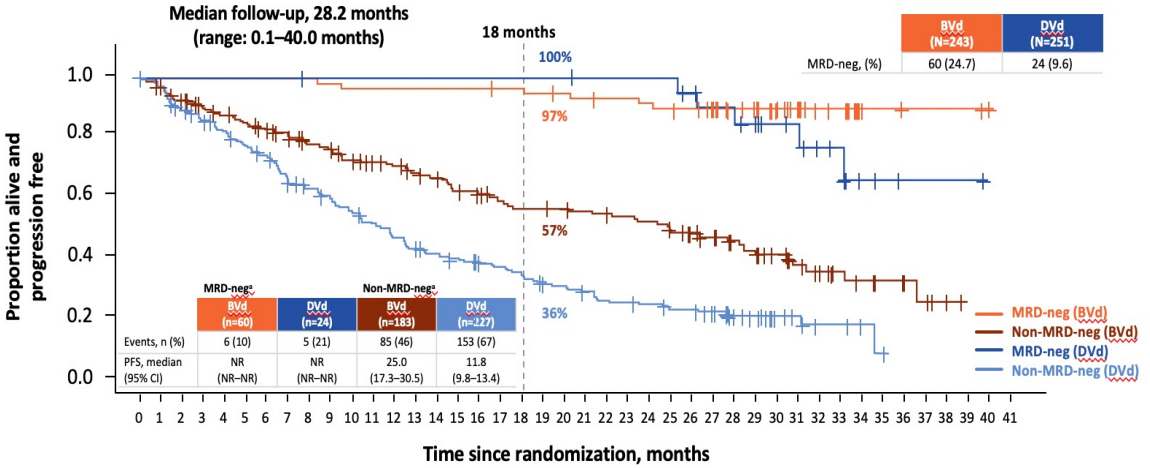
DREAMM-7: BelaVd vs DVd in RRMM

Responsed and MRD status



Responses (95% CI), %	BVd (N=243)	DVd (N=251)
≥ CR and MRD negativity (sensitivity of 10^{-5})[b]	**25.1** (19.8-31.0)	**10.4** (6.9-14.8)
≥ VGPR and MRD negativity (sensitivity of 10^{-5})[b]	**38.7** (32.5-45.1)	**17.9** (13.4-23.2)

Duration of response according to MRD

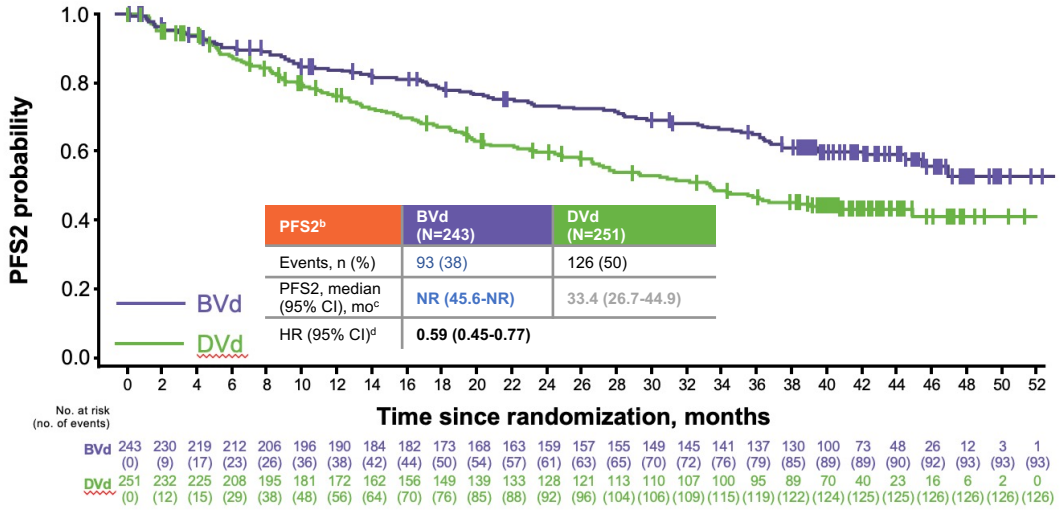


DOR[a]	BVd (N=243)	DVd (N=251)
Responders, n	202	179
DOR, median (95% CI), months[b]	**40.8 (30.5, NR)**	**17.8 (13.8-23.6)**

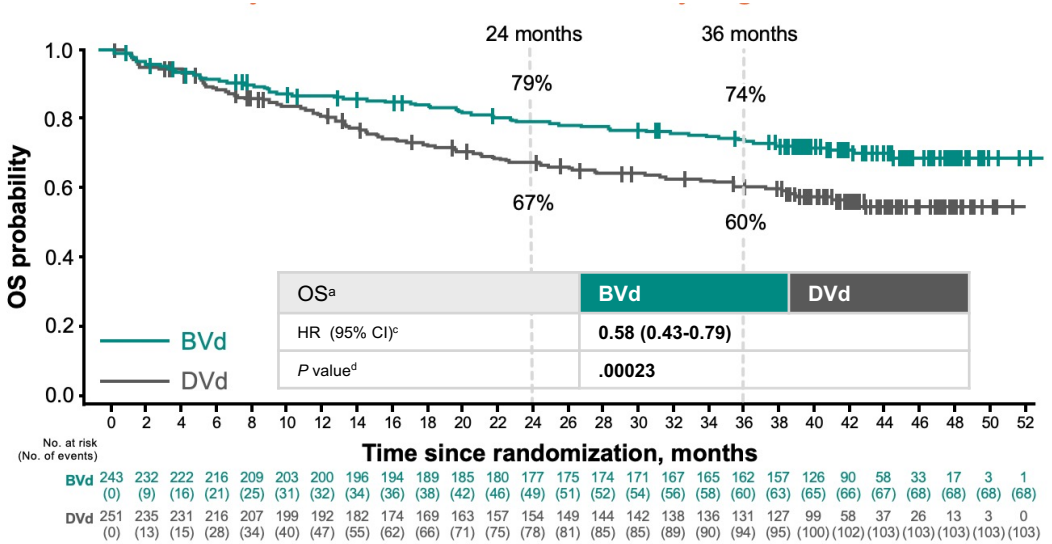
Hungria V. et al, ASH2024

DREAMM-7: BelaVd vs DVd in RRMM

Progression-free survival 2



Overall survival

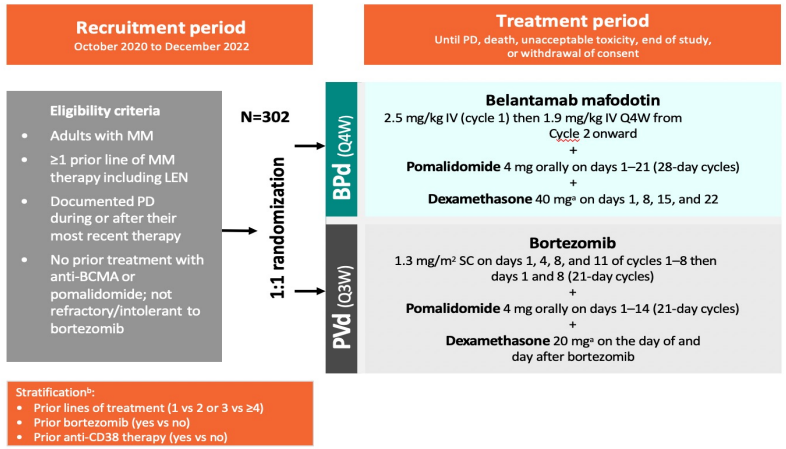


First subsequent antimyeloma therapies/total receiving first subsequent antimyeloma therapy in >10% in either arm, n/N (%)[b]	BVd (N=243)	DVd (N=251)
Any first subsequent antimyeloma therapies	87/243 (36)	130/251 (52)
Lenalidomide	17/87 (20)	40/130 (31)
Pomalidomide	26/87 (30)	25/130 (19)
Carfilzomib	15/87 (17)	39/130 (30)
Daratumumab	30/87 (35)	7/130 (5)
Isatuximab	16/87 (18)	0
Belantamab mafodotin	1/87 (1)	16/130 (12)

Hungria V. et al, ASH2024

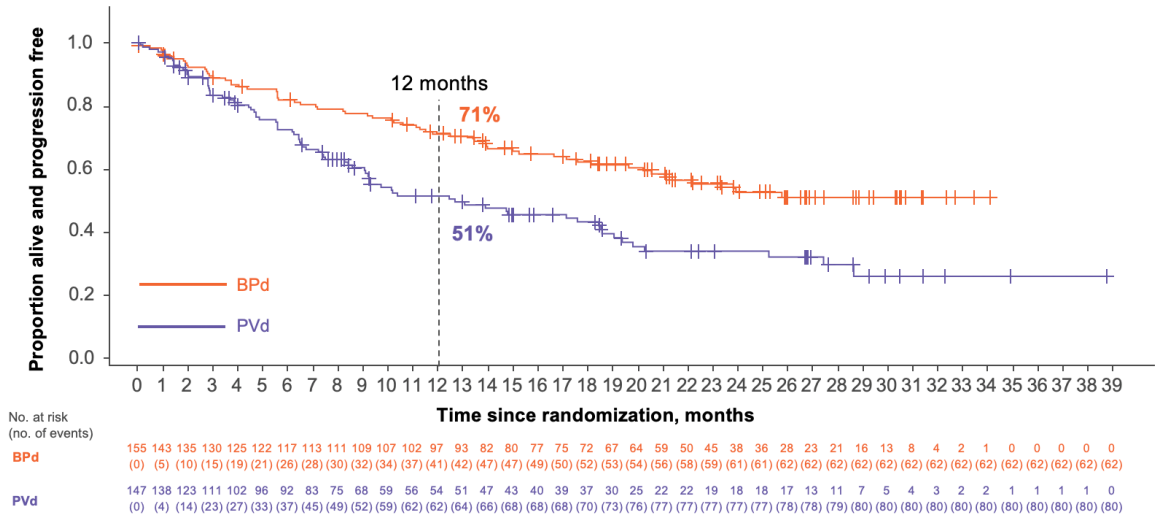
DREAMM-8: BelaPd vs PVd in RRMM

Study design and baseline characteristics



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 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)
Prior immunomodulatory drug[a]	155 (100)	127 (82)	147 (100)	111 (76)
Lenalidomide	**155 (100)**	**125 (81)**	**147 (100)**	**111 (76)**
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)

Progression-free survival



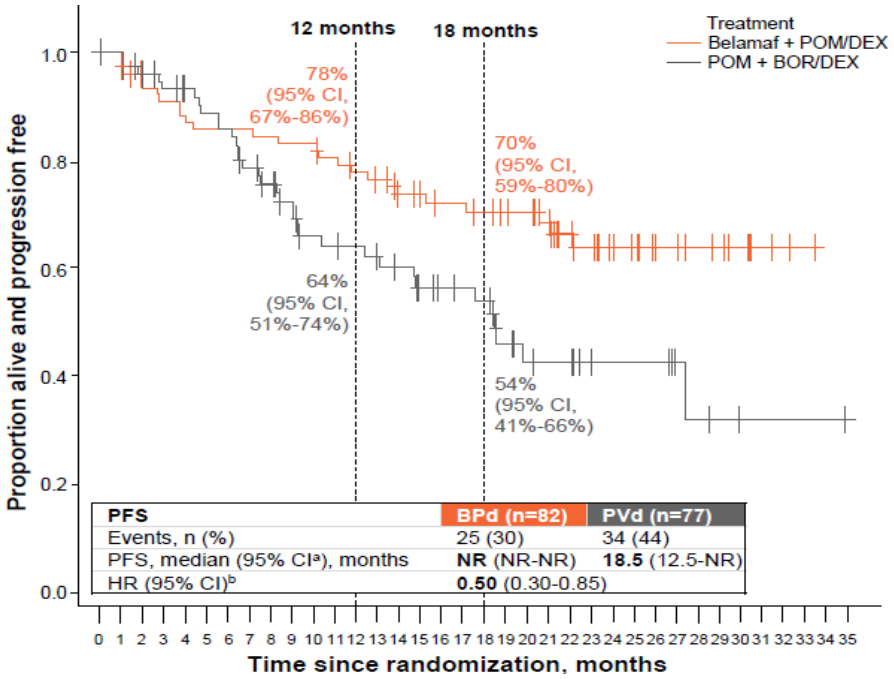
PFS	BPd (N=155)	PVd (N=147)
Events, n (%)	62 (40)	80 (54)
Median PFS (95% CI), months	**NR** (20.6-NR)	**12.7** (9.1-18.5)
HR (95% CI); *P* value	**0.52** (0.37-0.73); **<.001**	

Trudel S, et al. IMS 2024. Oral presentation OA-62; NEJM 2024

DREAMM-8: BelaPd vs PVd as 2° line treatment

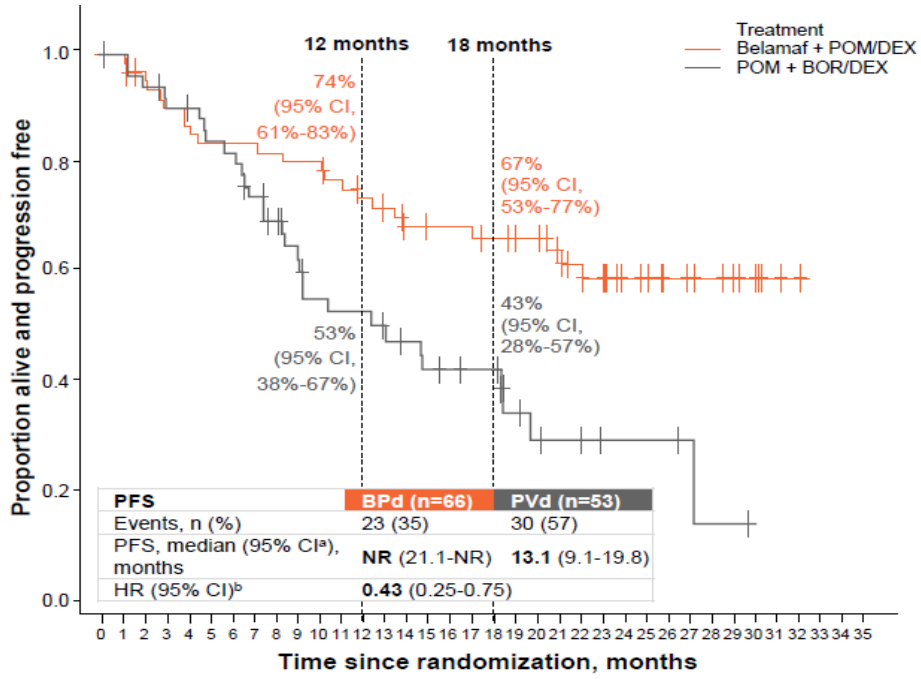
Progression-free survival

All 2L patients



PFS	BPd (n=82)	PVd (n=77)
Events, n (%)	25 (30)	34 (44)
PFS, median (95% CI[a]), months	**NR** (NR-NR)	**18.5** (12.5-NR)
HR (95% CI)[b]	**0.50** (0.30-0.85)	

Len-refractory 2L patients



PFS	BPd (n=66)	PVd (n=53)
Events, n (%)	23 (35)	30 (57)
PFS, median (95% CI[a]), months	**NR** (21.1-NR)	**13.1** (9.1-19.8)
HR (95% CI)[b]	**0.43** (0.25-0.75)	

Beksac M, et al. ASH2024

Ocular toxicity associated with Belantamab-mafodotin combinations

Reprinted from Shi C, et al. *J Vis.* 2020;20(8):29. Copyright © 2020 The Authors.

20/50

20/200

DREAMM-7

BVd	Bilateral worsening of BCVA in patients with normal baseline 20/25 or better	
	20/50 or worse[a]	20/200 or worse[a]
Patients, n/N (%)	84/242 (35)	5/242 (2)
Time to onset of first event, median (range), days	79 (16–1320)	105 (47–304)
Time to resolution of first event to baseline, median (range), days[b]	64 (8–908)	87 (22–194)
Time to improvement of first event, median (range), days[c]	22 (6–257)	19 (8–26)
First event resolved, n/N (%)[b]	78/84 (93)	4/5 (80)
First event improved, n/N (%)[c]	81/84 (96)	5/5 (100)

DREAMM-8

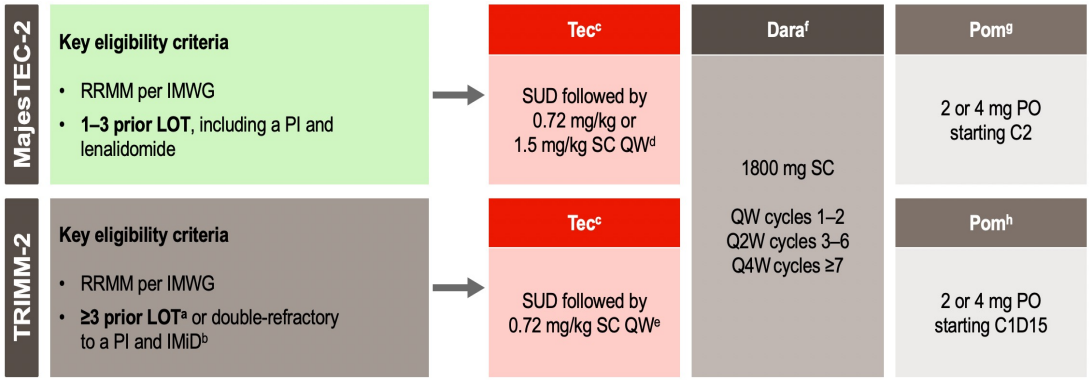
Bilateral worsening of BCVA	20/50 or worse[c]	20/200 or worse[c]
Patients, n/N (%)	24/80 (30)	1/80 (1)
Time to onset of first event, median (range), days	142.0 (28–423)	673.0
Time to resolution of first event, median (range), days[d]	57.0 (14–315)	57.0
First event resolved, n/N (%)[d]	22/24 (92)	1/1 (100)

Hungria V, et al. ASH24; Beksac M. et al, ASH24

Moving bispecific antibodies forward: Majestec-2 study

Teclistamab + daratumumab + lenalidomide

Study design



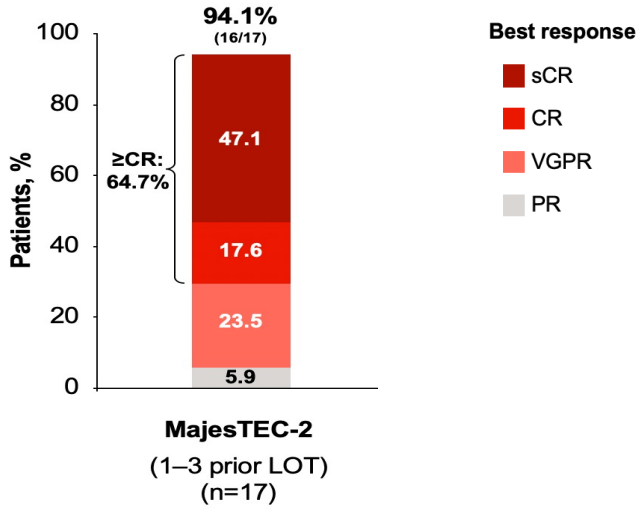
Baseline characteristics

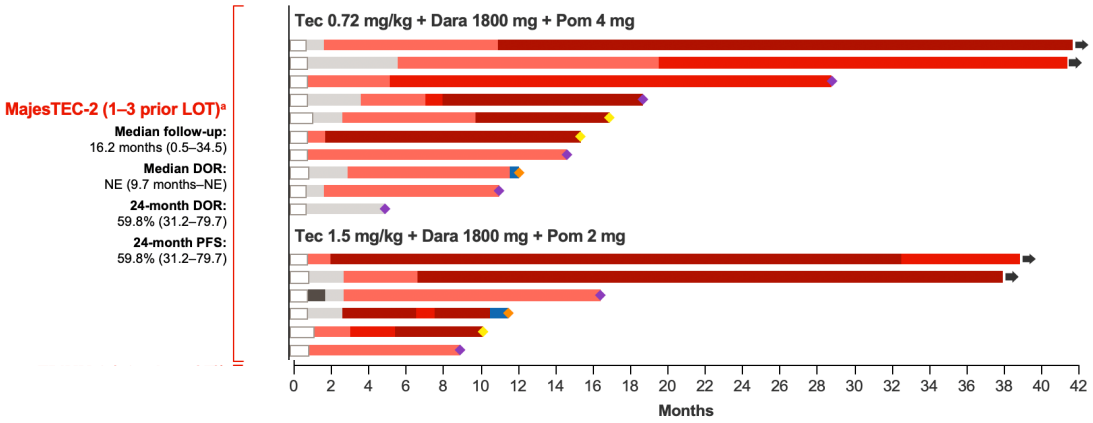
Characteristic	MajesTEC-2 (n=17)
Median age, years (range)	62 (35–74)
EMD, n (%)[a]	0
High cytogenetic risk, n (%)[b]	4 (26.7)
ISS stage, n (%)[c]	
I	9 (56.3)
II	5 (31.3)
III	2 (12.5)
Prior SCT, n (%)	15 (88.2)
Median prior LOT, n (range)	1 (1–4)
Prior anti-CD38, n (%)[d]	3 (17.6)
Prior anti-BCMA, n (%)	0
Triple-class refractory, n (%)[e]	0

D'Souza A. et al ASH2024

Moving bispecific antibodies forward: Majestec-2 study

Responses





Safety

	MajesTEC-2 (1–3 prior LOT) (n=17)	
Median follow-up, months (range)	16.2 (0.5–34.5)	
	Any Grade	Grade 3/4
Neutropenia	15 (88.2)	15 (88.2)
Nonhematologic[a]		
Cough	11 (64.7)	0
CRS	8 (47.1)	0
Any infection	16 (94.1)	11 (64.7)
Upper respiratory tract infection	8 (47.1)	0
Pneumonia	4 (23.5)	1 (5.9)
COVID-19 pneumonia	**4 (23.5)**	**4 (23.5)**
Hypogammaglobulinemia[b]	16 (94.1)	

D'Souza A. et al ASH2024

Conclusions

Patients with NDMM are likely to be triple-class exposed and become refractory to lenalidomide and daratumumab after initial treatment, paving the way to anti-BCMA salvage strategies as early as 2° line:

CAR T-cell therapy → **Cilta-cel:** deeper and sustained responses (MRD negativity) and improved both PFS and OS as compared to standard triplets → new SoC at 1° relapse.

Antibody-drug conjugates → **Belantamab-mafodotin**, in combination with bortezomib or pomalidomide improved MRD negaitivity rates, PFS and OS (BelaVd) as compared to standard triplets; ocular toxicity managable (best schedule for bela TBD)

Bispecific antibodies → **Early use:** improved % and depth of response as comapred to late lines; promising results in combination; continuous administration vs fixed duration?

ACKNOWLEDGEMENTS

Division of Hematology
Department of Molecular Biotechnology and Health Sciences, University of Torino

Azienda Ospedaliero-Universitaria
Città della Salute e della Scienza di Torino, Italy

Prof Benedetto Bruno

Clinical trial and multiple myeloma Unit
Dr Sara Bringhen
Dr Francesca Gay
Dr Giulia Benevolo
Dr Stefania Oliva
Dr Roberto Mina
Dr Mattia D'Agostino
Dr Giuseppe Bertuglia
Dr Lorenzo Cani
Dr Andrea Casson
Dr Tommaso Picardi
Dr Edoardo Marchetti

Laboratory Staff
Transplant Unit
Nurses

Data Managing Staff
Statisticians

European Myeloma Network (EMN)
Prof. Mario Boccadoro

UNIVERSITÀ DI TORINO

AZIENDA OSPEDALIERO - UNIVERSITARIA
Città della Salute e della Scienza di Torino

EMN