

The triple-exposed patient with progressing multiple myeloma: what are my antibody-based options?

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Disclosures

- I have received honoraria for lectures and participation in advisory boards from: Amgen, Celgene-BMS, Johnson&Johnson, Kite, GSK, Sanofi, Pfizer and Thermofisher



Treatment landscape in Multiple Myeloma

1st line

ASCT eligible

AntiCD38 + PI + IMiD + Dex

ASCT

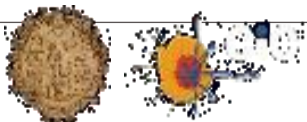
Len/Dara-Len

ASCT ineligible

Dara-Len-dex

Dara-VMP/RVd

AntiCD38 + PI + IMiD + Dex



Treatment landscape in Multiple Myeloma

1st line

ASCT eligible

AntiCD38 + PI + IMiD + Dex

ASCT

Len/Dara-Len

ASCT ineligible

Dara-Len-dex

Dara-VMP/RVd

AntiCD38 + PI + IMiD + Dex

2nd 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)

New combinations:

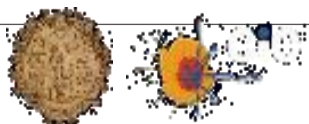
Teclistamab-Dara /Elra

Talquetamab-Pom or Tec-Tal

Linvoseltamab

Enentamig

If all options are available, how to select the best option?



Treatment landscape in Multiple Myeloma in the future

1st line

ASCT eligible

AntiCD38 + PI + IMiD + Dex
ASCT
Dara-Len x 2 years or Len s/a

ASCT ineligible

Dara-Len-dex
Dara-VMP/RVd
AntiCD38 + PI + IMiD + Dex

2nd line

Relapse during Dara-R or early after stopping Dara:
young pts, early relapses

Cilta-cel

Elranatamab s/a
Tec or Tal-based combos
Linvo/Enentamig
Belamaf-Vd/Belamaf-Pd

Late relapse after Dara stopped and
continued with R/ R s/a

Cilta-cel
Elranatamab s/a
Belamaf-Vd/Belamaf-Pd
BCMA-BsAb plus dara
GPC5D-BsAb plus dara
Kd AntiCD38/ Pd AntiCD38

Patients refractory to Dara and
Len

Cilta-cel
Elranatamab s/a
Belamaf-Vd/Belamaf-Pd
PVd /Selinexor-Vd



Treatment landscape in Multiple Myeloma in the future

1st line

ASCT eligible

AntiCD38 + PI + IMiD + Dex
ASCT
Dara-Len x 2 years or Len s/a

ASCT ineligible

Dara-Len-dex
Dara-VMP/RVd
AntiCD38 + PI + IMiD + Dex

2nd line

Relapse during Dara-R or early after stopping Dara:
young pts, early relapses

Cilta-cel
Elranatamab s/a
Tec or Tal-based combos
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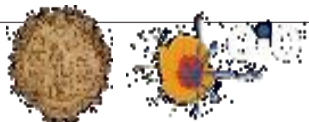
Late relapse after Dara stopped and
continued with R/ R s/a

Cilta-cel
Elranatamab s/a
Belamaf-Vd/Belamaf-Pd
BCMA-BsAb plus dara
GPRC5D-BsAb plus dara
Kd AntiCD38/ Pd AntiCD38

Patients refractory to Dara and
Len

Cilta-cel
Elranatamab s/a
Belamaf-Vd/Belamaf-Pd
PVd /Selinexor-Vd

If the pt is eligible for antiCD38 plus Kd/Pd, we can potentially reserve the BCMA-TT for 3rd line



Treatment landscape in Multiple Myeloma in the future

1st line

ASCT eligible

AntiCD38 + PI + IMiD + Dex

ASCT

Dara-Len x 2 years or Len s/a

ASCT ineligible

Dara-Len-dex

Dara-VMP/RVd

AntiCD38 + PI + IMiD + Dex

2nd line

Relapse during Dara-R or early after stopping Dara:
young pts, early relapses

Cilta-cel
Elranatamab s/a
Tec or Tal-based combos
Linvo/Enentamig
Belamaf-Vd/Belamaf-Pd

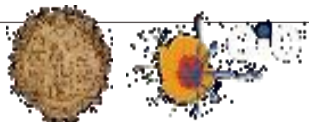
Late relapse after Dara stopped and
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Cilta-cel
Elranatamab s/a
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BCMA-BsAb plus dara
GPC5D-BsAb plus dara
Kd AntiCD38/ Pd AntiCD38

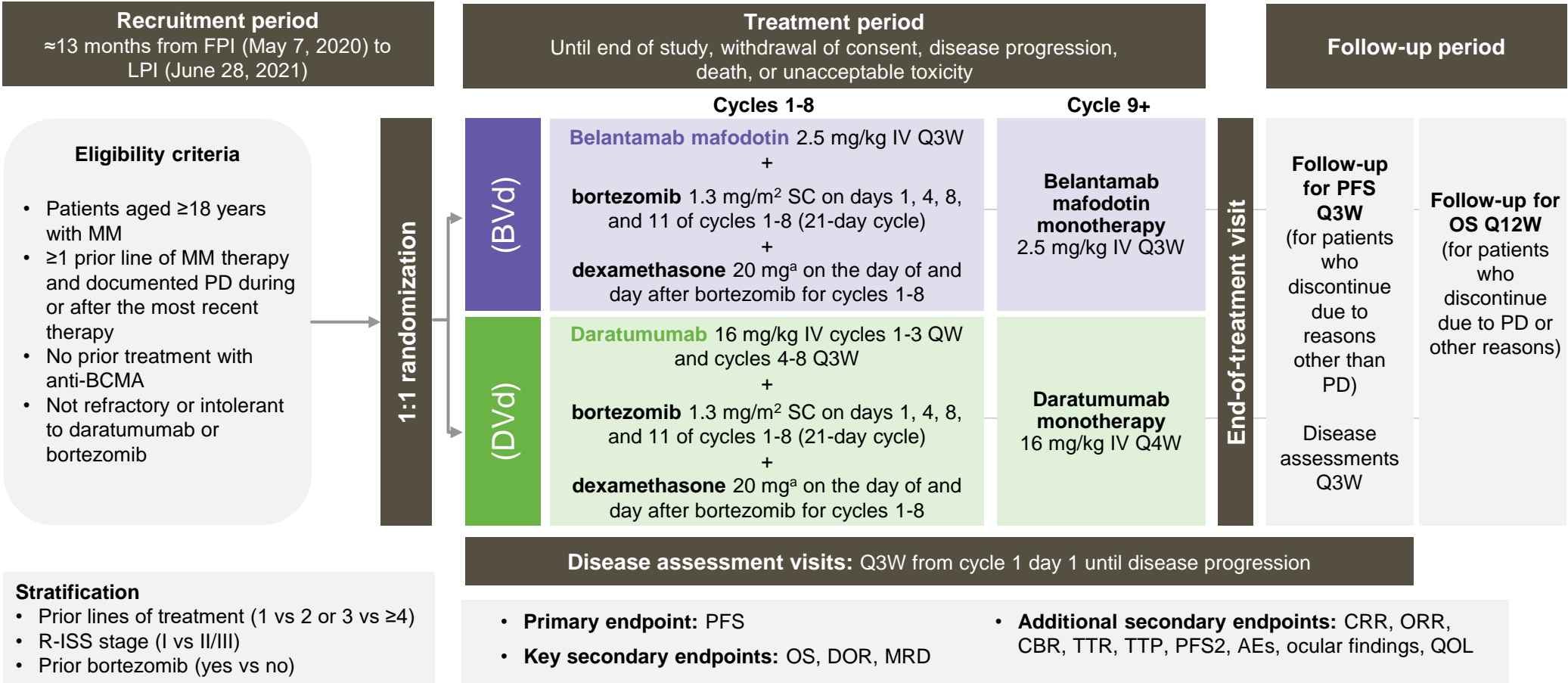
Patients refractory to Dara and
Len

Cilta-cel
Elranatamab s/a
Belamaf-Vd/Belamaf-Pd
PVd /Selinexor-Vd

It is maybe more clear the role of Belab-based combos in this population although efficacy and safety for BsAb are pending



DREAMM-7 Is a Phase 3 Study Examining a Belantamab Mafodotin–Based Combination in RRMM in 2L+ (NCT04246047)



2L, second line; AE, adverse event; BCMA, B-cell maturation antigen; Bvd, belantamab mafodotin, bortezomib, and dexamethasone; CBR, clinical benefit rate; CRR, complete response rate; DOR, duration of response; Dvd, daratumumab, bortezomib, and dexamethasone; FPI, first patient in; IV, intravenous; LPI, last patient in; MM, multiple myeloma; MRD, minimal residual disease; ORR, overall response rate; OS, overall survival; PD, progressive disease; PFS, progression-free survival; PFS2, time from randomization to disease progression after initiation of new antimyeloma therapy or death from any cause; Q3W, every 3 weeks; Q4W, every 4 weeks; Q12W, every 12 weeks; QOL, quality of life; QW, once weekly; R-ISS, Revised International Staging System; RRMM, relapsed/refractory multiple myeloma; SC, subcutaneous; TTP, time to progression; TTR, time to response.

^a Reduce starting dose of dexamethasone to 10 mg for patients aged >75 years who have a body mass index of <18.5 kg/m², previous unacceptable AE associated with glucocorticoid therapy, or inability to tolerate the starting dose. Hungria V, et al. *N Engl J Med.* 2024;391(5):393-407.

Baseline Disease Characteristics and Prior Treatments Were Generally Well Balanced Across Both Groups



Baseline characteristics	ITT population	
	BVd (N=243)	DVd (N=251)
Age, median (range), years	65.0 (34-86)	64.0 (32-89)
<65 years, n (%)	121 (50)	126 (50)
65 to <75 years, n (%)	85 (35)	95 (38)
≥75 years, n (%)	37 (15)	30 (12)
Male/female, n (%)	128 (53)/115 (47)	144 (57)/107 (43)
White/Black or African American/Asian, n (%)^a	206 (85)/8 (3)/28 (12)	203 (81)/12 (5)/33 (13)
ECOG PS ≤1, n/N (%)	232/242 (96)	235/246 (96)
Revised ISS stage at screening, n (%)		
I	102 (42)	103 (41)
II	130 (53)	132 (53)
III	9 (4)	14 (6)
Unknown	2 (<1)	2 (<1)
Time since diagnosis, median (range), years	4.3 (0.2-26.0)	3.9 (0.1-23.4)
Cytogenetic abnormalities, n (%)		
High risk ^b	67 (28)	69 (27)
Standard risk ^c	175 (72)	175 (70)
Missing or nonevaluable	1 (<1)	7 (3)
Extramedullary disease, n (%)		
Yes ^d	13 (5)	25 (10)
No	230 (95)	226 (90)

Prior treatments, n (%)	ITT population	
	BVd (N=243)	DVd (N=251)
Prior LOTs		
1	125 (51)	125 (50)
2 or 3	88 (36)	99 (39)
4+	30 (12)	27 (11)
Prior PI	218 (90)	216 (86)
Prior bortezomib	210 (86)	211 (84)
Prior immunomodulatory drug	198 (81)	216 (86)
Prior thalidomide	121 (50)	144 (57)
Prior lenalidomide	127 (52)	130 (52)
Refractory to lenalidomide	79 (33)	87 (35)
Prior daratumumab	3 (1)	4 (2)
Prior ASCT	164 (67)	173 (69)

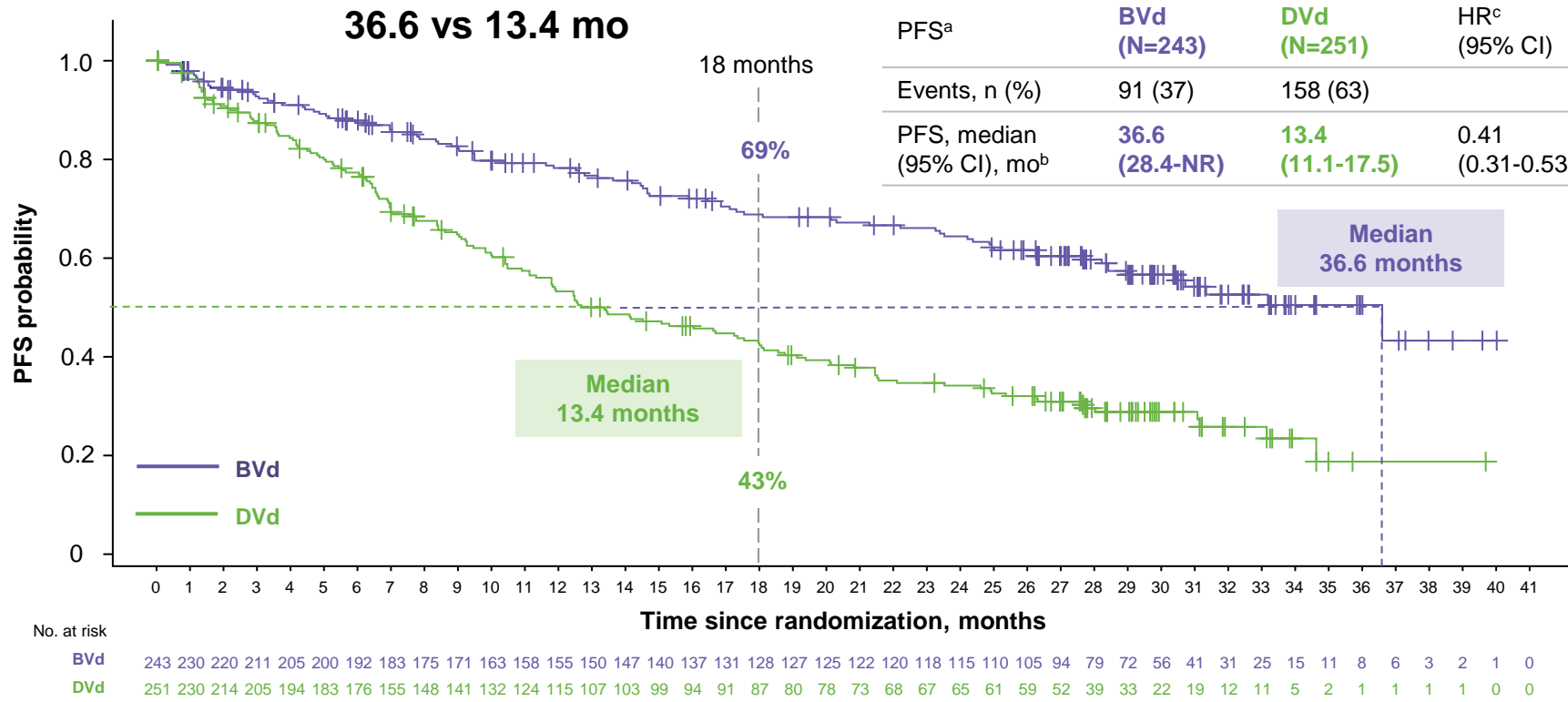
Hungria V, et al. *N Engl J Med.* 2024;doi: 10.1056/NEJMoa2405090. Copyright © 2024 Massachusetts Medical Society. Reprinted with permission from Massachusetts Medical Society.

ASCT, autologous stem cell transplant; BVd, belantamab mafodotin, bortezomib, and dexamethasone; DVd, daratumumab, bortezomib, and dexamethasone; ECOG PS, Eastern Cooperative Oncology Group performance status; ISS, International Staging System; ITT, intention to treat; LOT, line of therapy; PI, proteasome inhibitor.

^a Race was reported by the investigators. ^b High-risk cytogenetics was defined as the presence of ≥1 of the following: t(4;14), t(14;16), or del(17p13). ^c Standard-risk cytogenetics was defined as having negative results for all high-risk abnormalities: t(4;14), t(14;16), or del(17p13). ^d Since the trial was not stratified for extramedullary disease status, the difference between arms occurred by chance during randomization.

Hungria V, et al. *N Engl J Med.* 2024;391(5):393-407.

BVd Significantly Extended the Time to Disease Progression or Death vs DVd



Hungria V, et al. *N Engl J Med.* 2024;doi: 10.1056/NEJMoa2405090. Copyright © 2024 Massachusetts Medical Society. Reprinted with permission from Massachusetts Medical Society.

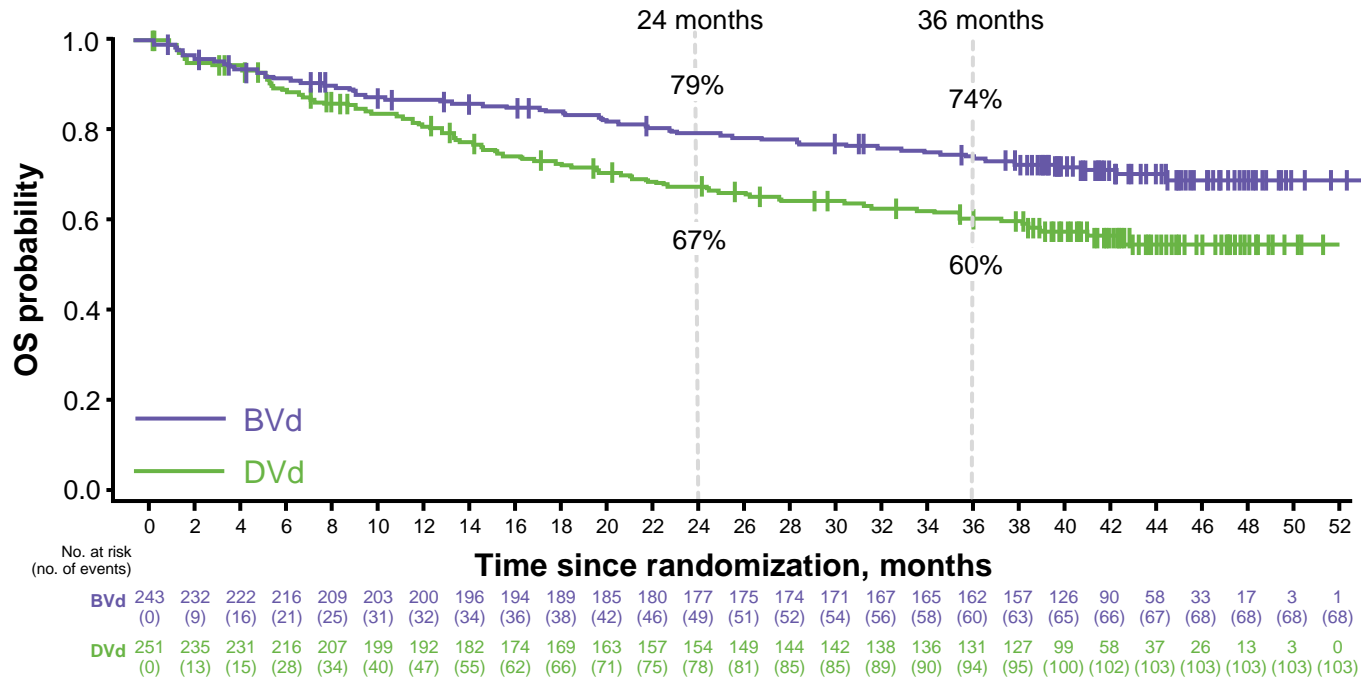


BVd demonstrated statistically significant and clinically meaningful PFS benefit (HR, 0.41; 95% CI, 0.31-0.53; P<.001), with a median PFS that was 23 months longer than that with DVd (36.6 vs 13.4 months)

BVd, belantamab mafodotin, bortezomib, and dexamethasone; DVd, daratumumab, bortezomib, and dexamethasone; HR, hazard ratio; ITT, intention to treat; NR, not reached; PFS, progression-free survival; R-ISS, Revised International Staging System.
^aTwo patients in the ITT population were randomized, not treated, rescreened, and rerandomized. They are counted as 4 unique patients in this output. ^b CIs estimated using the Brookmeyer-Crowley method. ^c HRs estimated using a Cox proportional hazards model stratified by the number of lines of prior therapy (1 vs 2 or 3 vs ≥4), prior bortezomib, and R-ISS stage at screening (I vs II/III), with a covariate of treatment. ^d P value from 1-sided stratified log-rank test.
 Hungria V, et al. *N Engl J Med.* 2024;391(5):393-407.

BVd Had an Early, Sustained, and Statistically Significant OS Benefit vs DVd

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



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)

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Median OS was not reached. Predicted median OS based on modeling is 84 months with BVd and 51 months with DVd.^e

BVd, belantamab mafodotin, bortezomib, and dexamethasone; DVd, daratumumab, bortezomib, and dexamethasone; HR, hazard ratio; ITT, intention to treat; NR, not reached; OS, overall survival; R-ISS, Revised International Staging System.

^a Two patients in the ITT population were randomized, not treated, rescreened, and rerandomized. They are counted as 4 unique patients in this output. ^b CIs were estimated using the Brookmeyer-Crowley method. ^c HRs were estimated using a Cox proportional hazards model stratified by the number of lines of prior therapy (1 vs 2 or 3 vs ≥4), prior bortezomib (no vs yes), and R-ISS stage at screening (I vs II or III), with a covariate of treatment. ^d P value is from 1-sided stratified log-rank test. At 171 actual events (48.2% OS information fraction), OS was declared significant if the P value was <.00112. ^e Post hoc analysis was performed with simulation using an exponential distribution to predict median OS values in each arm using the observed data at this interim analysis 2, with a 39.4-month median follow-up, to extrapolate time to death in ongoing censored patients.

Predicted median OS values are subject to change as data mature.

Hungria V, et al. ASH 2024. Oral 772.

Safety Was Consistent With Known Safety Profile of the Individual Agents^{1,2}

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



n (%)	BVd (N=242)	DVd (N=246)
Any AE	242 (100)	246 (100)
Related to any study treatment ^a	242 (100)	234 (95)
Grade 3/4 AE	230 (95)	191 (78)
Related to any study treatment ^a	222 (92)	166 (67)
AEs leading to permanent discontinuation of any study treatment	77 (32)	47 (19)
Related to any study treatment leading to permanent discontinuation of any study treatment ^a	67 (28)	36 (15)
AEs leading to dose reduction	181 (75)	146 (59)
AEs leading to dose interruption/delay	229 (95)	186 (76)
Any SAE	129 (53)	94 (38)
Related to any study treatment ^a	50 (21)	32 (13)
Fatal SAEs	26 (11)	20 (8)
Related to any study treatment ^a	7 (3)	2 (<1)

Exposure-adjusted rate (per 100 person-years) ^b	BVd (N=242)	DVd (N=246)
Grade 3/4 AE	57.17	55.71
AEs leading to permanent discontinuation of any study treatment	19.14	13.71
AEs leading to dose reduction^c	44.99	42.58
AEs leading to dose interruption/delay^c	56.92	54.25
Any SAE	32.07	27.42

	BVd (N=242)	DVd (N=246)
Deaths	69 (29)	101 (41)
Primary cause of death^d		
Cancer	23 (10)	53 (22)
Equivocally due to myeloma	3 (1)	7 (3)
Unequivocally due to myeloma	19 (8)	44 (18)
Other cancer	1 (<1)	2 (<1)
Cardiovascular^e	8 (3)	4 (2)
Sepsis	8 (3)	4 (2)
Stroke	0	1 (<1)
Trauma	0	1 (<1)
Other noncardiovascular	24 (10)	25 (10)

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The safety and tolerability of the BVd regimen were consistent with those in the primary analysis.¹ More deaths due to myeloma were observed in the DVd vs the BVd arm; rates of fatal SAEs related to treatment were low

AE, adverse event; BVd, belantamab mafodotin, bortezomib, and dexamethasone; DVd, daratumumab, bortezomib, and dexamethasone; SAE, serious adverse event.

^a "Related to any study treatment" includes responses of "yes" and missing responses to the following question: "Is there a reasonable possibility that the AE may have been caused by the study treatment?"

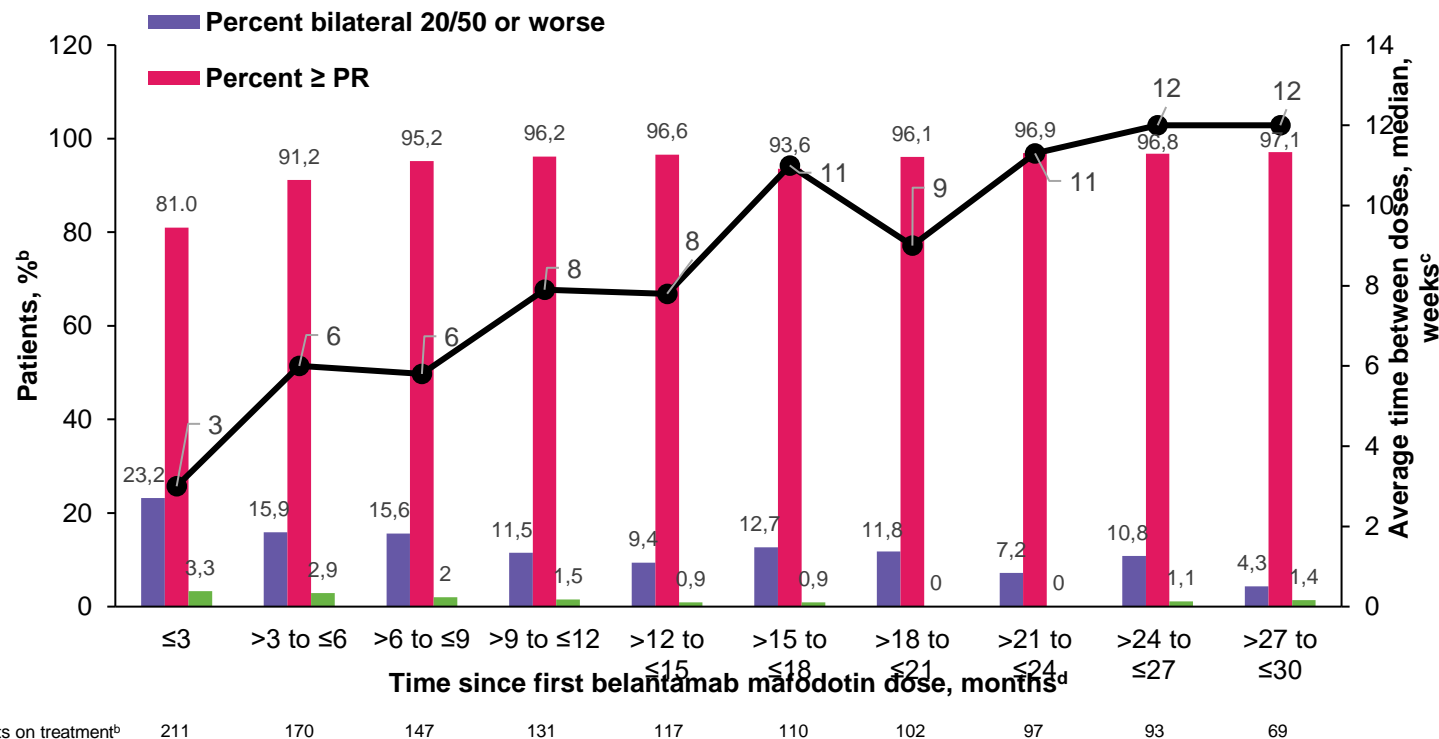
^b Exposure-adjusted rates were calculated as the total number of patients with an event divided by the total exposure time in person-years (per 100 person-years). Total person-years is the sum of all patient exposure calculated as (last dose - first dose + 1) / 365.25. ^c Post hoc exposure-adjusted rates. ^d The primary cause of death was unknown for 6 patients in the BVd arm and 13 patients in the DVd arm.

^e Cardiovascular includes hemorrhage, heart failure, myocardial infarction, and other cardiovascular diagnosis.

1. Hungria V, et al. *N Engl J Med*. 2024;391(5):393-407. 2. Hungria V, et al. *ASH* 2024. Oral 772.



Prevalence of Bilateral BCVA 20/50 or Worse, Median Dosing Interval, and Response Rates by Time on Treatment^{1-4,a}



- Median time between doses increased with treatment duration
- Response rates (best confirmed response ≥ PR in each interval) remained high throughout treatment
- 23% of patients experienced 20/50 or worse events in the first 3 months; prevalence generally decreased thereafter
- The rate of treatment discontinuation due to ocular events was low

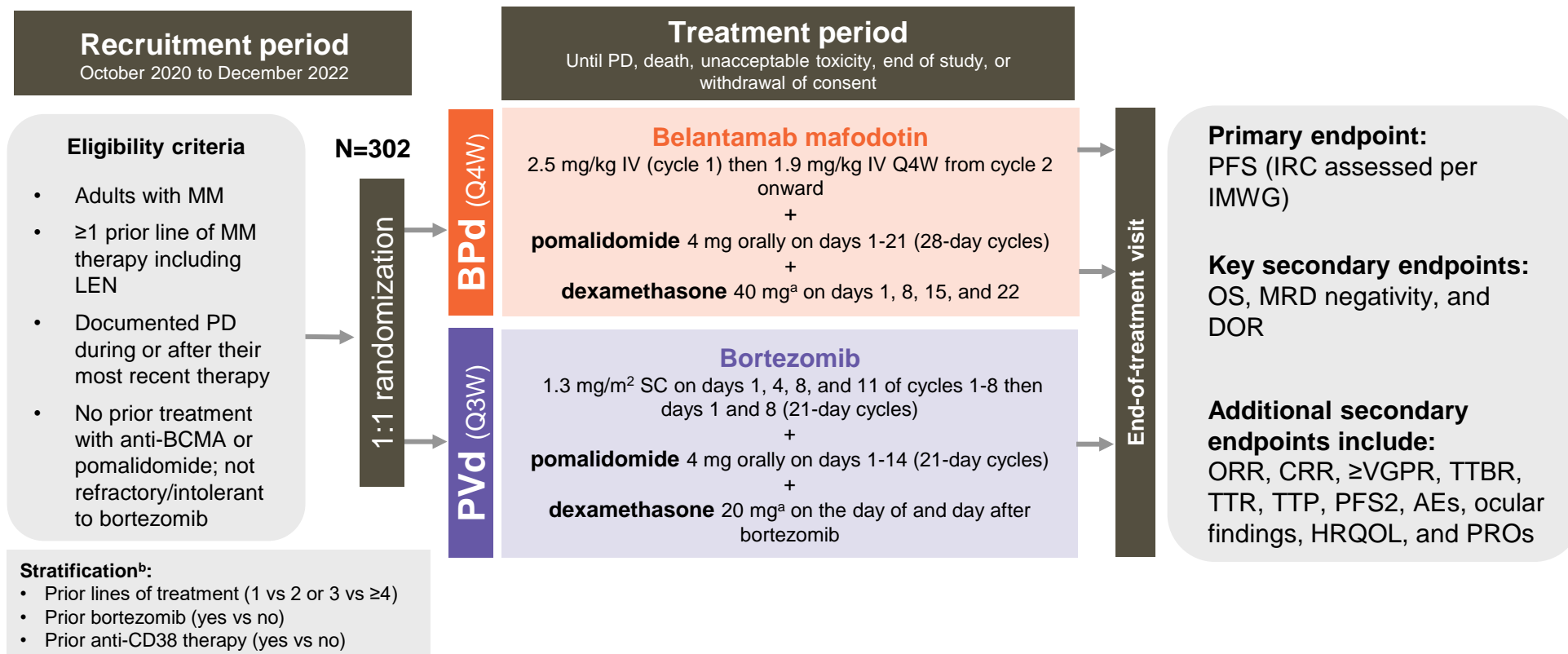
Results from the primary analysis (data cutoff: October 2, 2023)

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AR, adverse reaction; BCVA, best-corrected visual acuity; PR, partial response.
^a Only the belantamab mafodotin treatment period was considered in these post hoc analyses. ^b Only patients with 20/25 or better in ≥1 eye at baseline are considered. ^c Mean of days between doses for each patient per interval is used. ^d Graph is truncated at 30 months because data beyond 30 months represented low number of patients on treatment (>30 to ≤33 months, n= 42; >33 to ≤36 months, n=20; >36 to ≤39 months, n=8; >39 to ≤42 months, n=3).
 1. Mateos MV, et al. ASCO 2024. Updates to abstract 439572. 2. Mateos MV, et al. EHA 2024. Abstract S214. 3. Hungria V, et al. IMS 2024. Poster P-396. 4. Hungria V, et al. ASH 2024. Oral 772.



DREAMM-8 is a phase 3 study examining a belantamab mafodotin–based combination in 2L+ RRMM (NCT04484623)^{1,2}



2L, second line; AE, adverse event; BCMA, B-cell maturation antigen; BPd, belantamab mafodotin, 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.

^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).

1. Trudel S, et al. ASCO Annual Meeting 2024. Abstract LBA105; 2. Dimopoulos MA, et al. *N Engl J Med*. 2024;391:408-421.

DREAMM-8 Baseline disease characteristics and clinical characteristics

Baseline characteristics	ITT population		Prior treatments, n (%)	ITT population			
	BPd (N=155)	PVd (N=147)		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 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	Refrac	Exposed	Refrac
			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	43 (32)	3 (6)	46 (33)	0 (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.

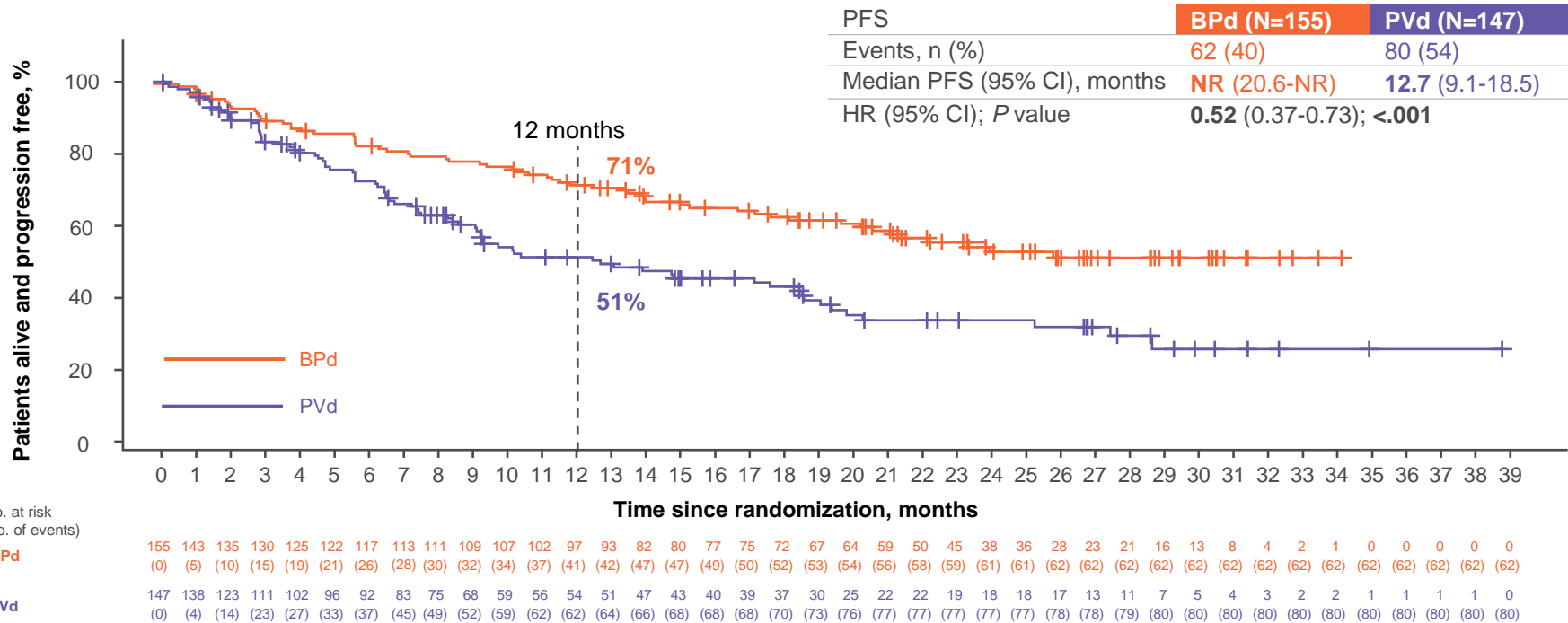
Pd, belamaf, pomalidomide, and dexamethasone; ECOG PS, Eastern Cooperative Oncology Group performance status; ISS, International Staging System; ITT, intent to treat; PVd, pomalidomide, bortezomib, and dexamethasone.

Trudel S et al. Presented at the 2024 ASCO Annual Meeting. May 31 – June 4, 2024. Abstract LBA105.

Primary endpoint: PFS^{1,2}



NR vs 12.7 mo



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

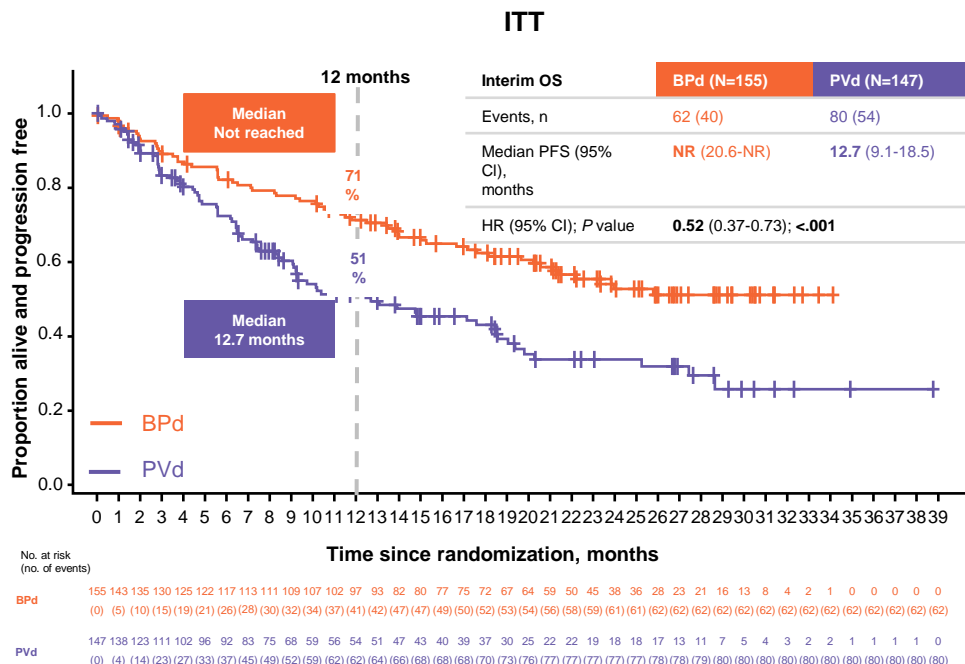
Median follow-up, 21.8 months (range, 0.03-39.23 months).

The treatment effect (HR and corresponding 95% CIs) was estimated using the stratified Cox proportional hazards model, and the P value was produced based on the 1-sided stratified log-rank test. Stratified analyses were adjusted for number of prior lines of therapy and prior bortezomib use.

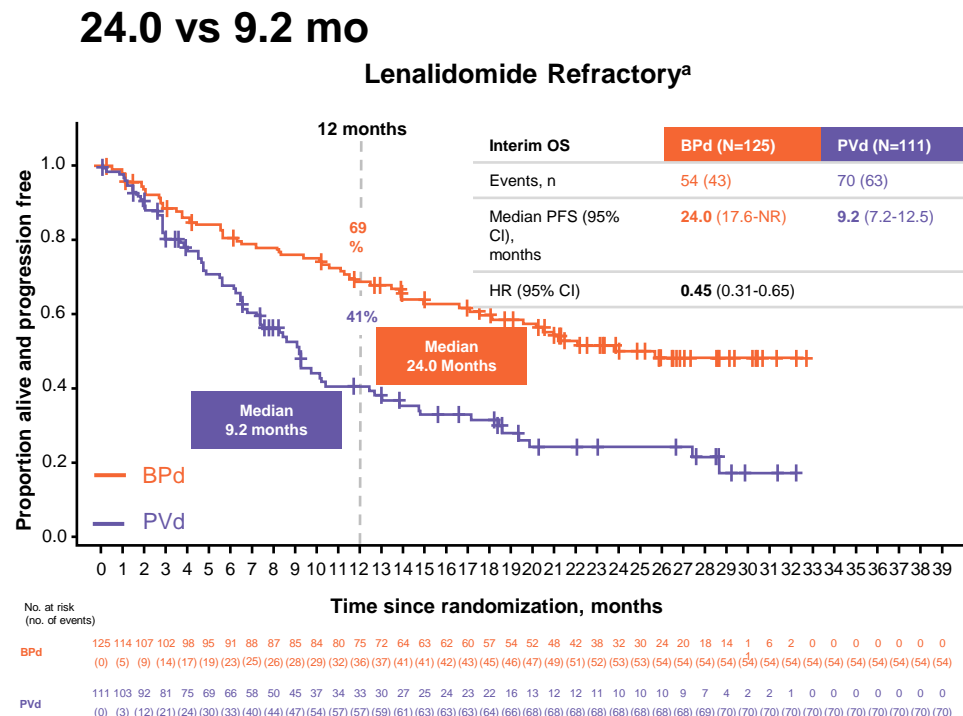
BPd, belamaf, pomalidomide, and dexamethasone; HR, hazard ratio; NR, not reached; PFS, progression-free survival; PVd, pomalidomide, bortezomib, and dexamethasone; RRMM, relapsed or refractory multiple myeloma.

1. Trudel S, et al. 2024 ASCO Annual Meeting 2024. Abstract LBA105; 2. Dimopoulos MA, et al. *N Engl J Med.* 2024;391:408-421.

PFS outcomes in len-refractory population



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Trudel S, et al. Presented at the International Myeloma Society Annual Meeting 2024. Abstract OA-62. Reprinted with permission by the author.



- PFS benefit seen in the len-refractory subgroup is consistent with that in the overall study population
- BPd led to a statistically significant and clinically meaningful reduction in risk of disease progression or death vs PVd in ITT

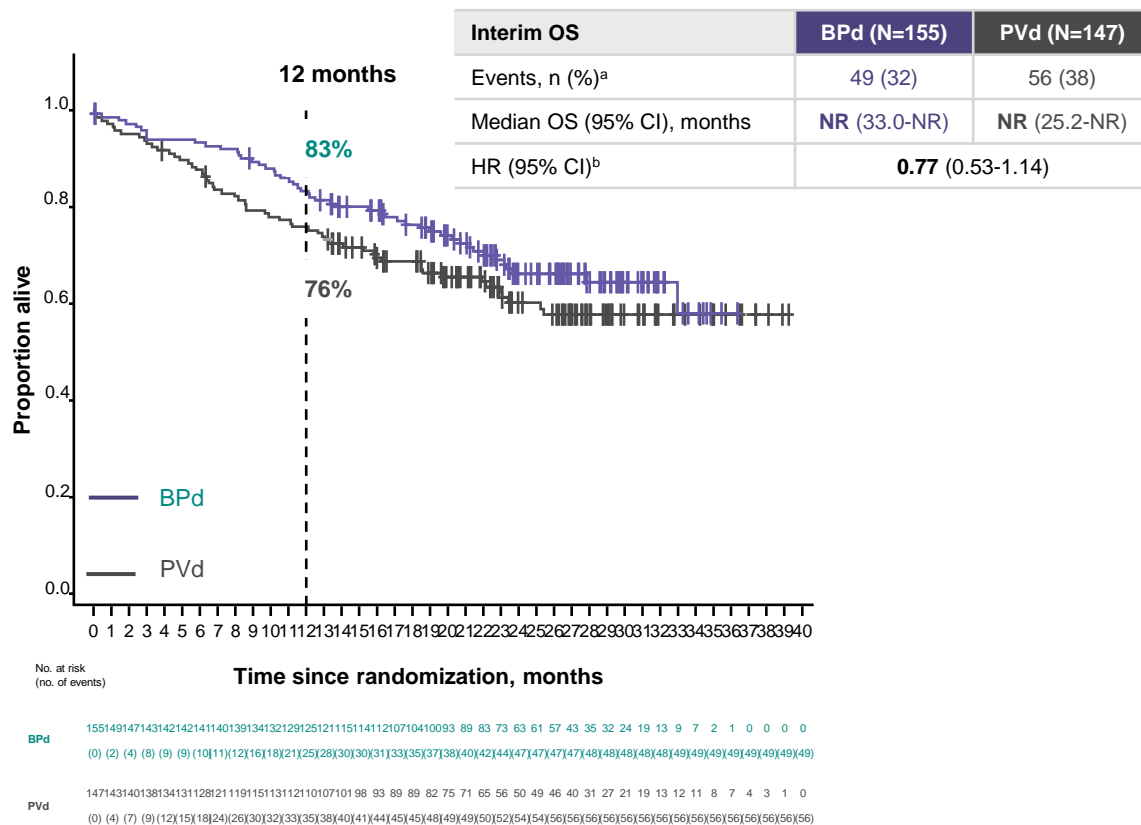
Median follow-up, 21.8 months (range, 0.03-39.23 months). The treatment effect (HR and corresponding 95% CIs) was estimated using the stratified Cox proportional hazards model, and the P value was produced based on the 1-sided stratified log-rank test. Stratified analyses were adjusted for number of prior lines of therapy and prior bortezomib use.

^a Post-hoc analysis.

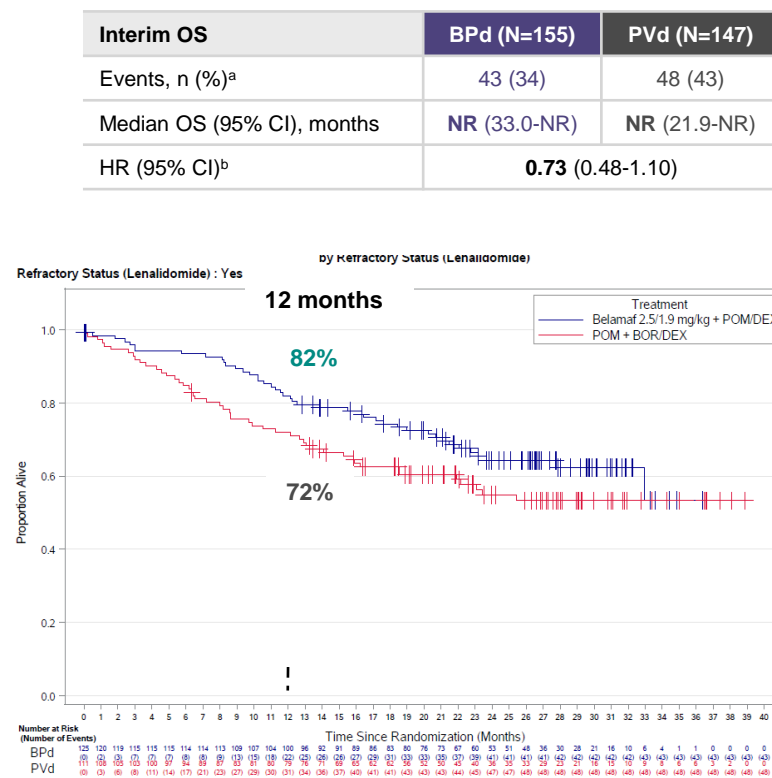
BPd, belamaf, pomalidomide, and dexamethasone; HR, hazard ratio; ITT, intent to treat; len, lenalidomide; NR, not reached; PFS, progression-free survival; PVd, pomalidomide, bortezomib, and dexamethasone.

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

Positive OS Trend Favoring BPd vs PVd



Lenalidomide Refractory



Positive OS trend favoring BPd was seen despite the use of effective anti-MM therapies after progression with PVd; similar trend favoring BPd was also seen in len-refractory population

From Dimopoulos M, et al. N Engl J Med. 2024; doi: 10.1056/NEJMoa2403407. Copyright © 2024 Massachusetts Medical Society. Reprinted with permission from Massachusetts Medical Society.

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



AEs of clinical interest

Grouped term, n (%) ^a	Safety population			
	BPd (N=150)		PVd (N=145)	
	n (%)	Patients/100-person years	n (%)	Patients/100-person years
Thrombocytopenia^b				
Any event	82 (55)	40	60 (41)	44
Grade 3 or 4	57 (38)	28	42 (29)	31
Neutropenia^c				
Any event	95 (63)	46	66 (46)	49
Grade ≥3	86 (57)	42	57 (39)	42
Infections^d				
Any event	123 (82)	59	99 (68)	73
Grade ≥3	73 (49)	35	38 (26)	28
Ocular AESIs (by CTCAE) preferred terms, n (%)				
≥30% of patients in either treatment group				
	Any grade	Grade ≥3	Any grade	Grade ≥3
Any event	133 (89)	65 (43)	44 (30)	3 (2)
Vision blurred	119 (79)	26 (17)	22 (15)	0
Dry eye	91 (61)	12 (8)	14 (10)	0
Foreign body sensation in eye	91 (61)	9 (6)	9 (6)	0
Eye irritation	75 (50)	6 (4)	13 (9)	0
Photophobia	66 (44)	5 (3)	6 (4)	0
Eye pain	49 (33)	3 (2)	7 (5)	0



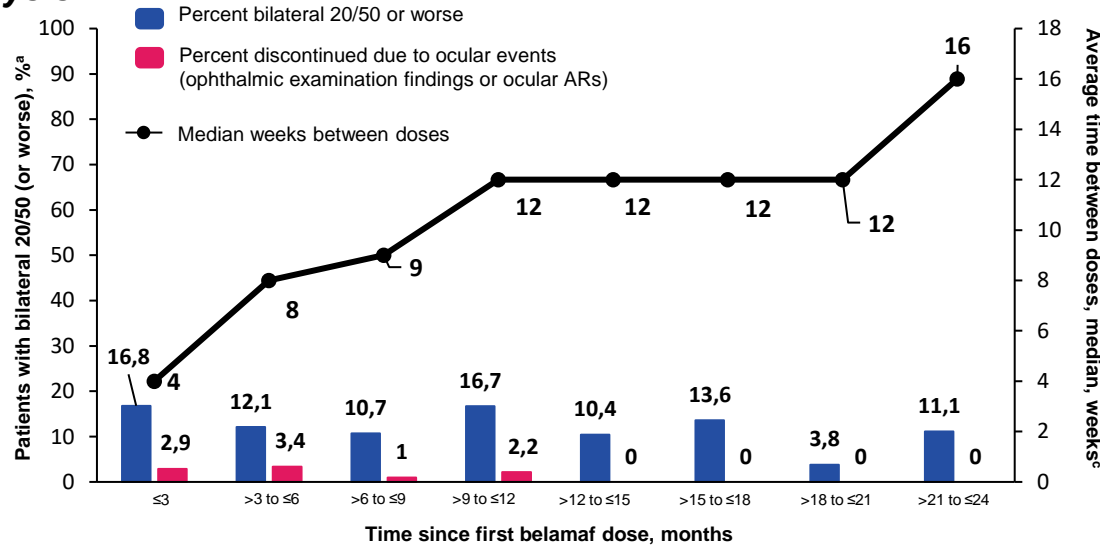
- In the BPd and PVd arms, exposure-adjusted rates of infections were 59 and 73 (all grades) and 35 and 28 (grade ≥3), respectively
- There was low usage of immunoglobulin replacement in both arms (BPd, 18%; PVd, 9%). Exposure-adjusted rates of IVIG replacement were 13% vs 10% (BPd vs PVd)

^a posthoc analysis. ^b Thrombocytopenia includes events identified by site or preferred terms thrombocytopenia or platelet count decreased. ^c Neutropenia includes preferred terms febrile neutropenia, neutropenia, and neutrophil count decreased. ^d Infections are based on all preferred terms included in the system organ class of infections and infestations. AE, adverse event; AESI, adverse event of special interest; BPd, belamaf, pomalidomide, and dexamethasone; CTCAE, Common Terminology Criteria for Adverse Events; PVd, pomalidomide, bortezomib, and dexamethasone. Trudel S et al. Presented at the 2024 ASCO Annual Meeting, May 31 – June 4, 2024. Abstract LBA105.

Prevalence of bilateral BCVA 20/50 or worse and time interval between doses by time period on treatment^{a,b}



Post hoc analysis



No. of patients on treatment, n ^d	137	116	103	90	77	59	52	45
No. of patients with bilateral 20/50 or worse, n ^d	23	14	11	15	8	8	2	5
Median days between doses ^d	28.5	56	63.5	84	84	86	84	111
No. of patients who discontinued due to ocular event, n ^d	4	4	1	2	0	0	0	0

Quach H, et al. Presented at the International Myeloma Society Annual Meeting 2024. Poster P-413. Reprinted with permission by the author.



The median time between doses increased with time on treatment while the rate of bilateral 20/50 worsening events and discontinuations remained low throughout

AR, adverse reaction; belamaf, belantamab mafodotin; BCVA, best-corrected visual acuity.

^a Only the belamaf treatment period was considered in these post hoc analyses. ^b First 2 years of treatment shown due to limited patients at risk beyond this time point. ^c Mean of days between doses for each patient per interval is used. ^d Only patients with 20/25 or better in either or both eyes at baseline are considered. ^e Only patients receiving ≥6 months of treatment included in analysis to exclude early discontinuations (eg, rapid PD).

Quach H, et al. International Myeloma Society Annual Meeting 2024. Poster P-413.

Ocular events resolved with adequate follow-up, allowing patients to resume belamaf



- At data cutoff, ocular events had resolved as follows:
 - 91% of all ARs resolved
 - The first occurrence of an ophthalmic examination finding resolved in 89% of patients
 - The first occurrence of bilateral BCVA 20/50 or worse resolved in 84% of patients
 - The event resolved in all 14 patients (9%) who discontinued belamaf due to an ocular event

Efficacy was maintained in patients requiring extended belamaf dosing intervals^e

Treatment landscape in Multiple Myeloma today: realistic situation

1st line

ASCT eligible

AntiCD38 + PI + IMiD + Dex

ASCT

Len/Dara-Len

ASCT ineligible

Dara-Len-dex

Dara-VMP/RVd

AntiCD38 + PI + IMiD + Dex

2nd 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

3rd line

Anti-CD38 + Pomalidomide-dex

Elotuzumab-Pomalidomide-dex

Previous combos if pt eligible

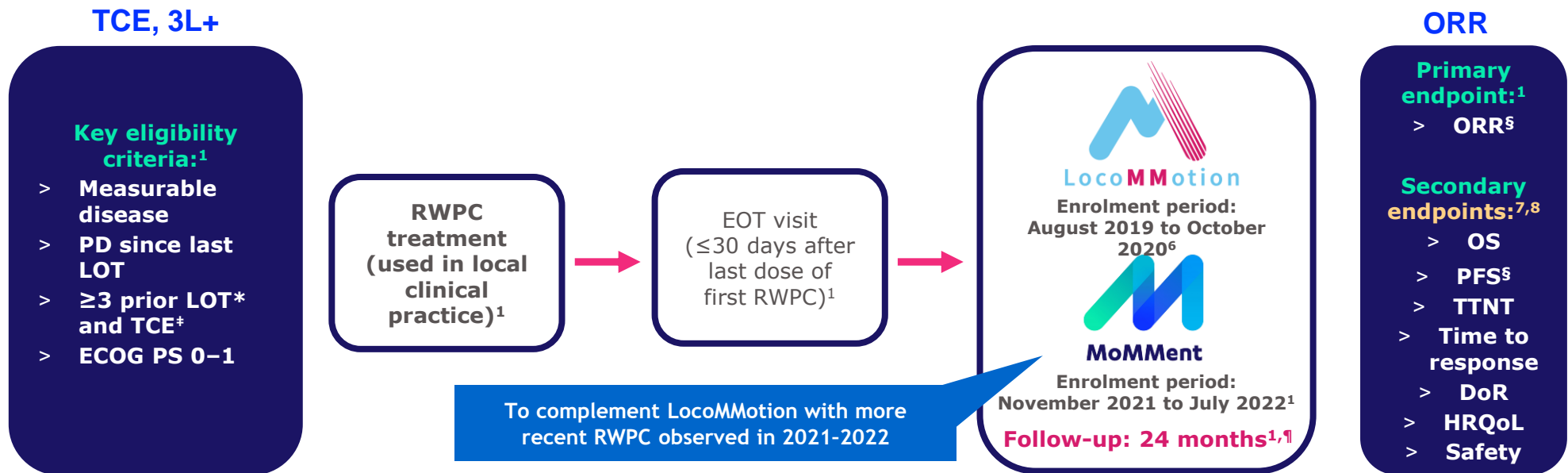
After 2nd and especially 3rd line of therapy majority of MM patients have been exposed to PIs, IMiDs and anti-CD38 mABs

In this population an unmet medical need?

LocoMMotion and MoMMent were designed to mimic single-arm trials in triple-class exposed RRMM¹



- Prospective design allowed collection of data from patients that would balance well with baseline characteristics in the single-arm trials²
- LocoMMotion and MoMMent were specifically designed as external control arms mimicking the ongoing MajesTEC-1, CARTITUDE-1 and MonumentAL-1 trials¹⁻⁵



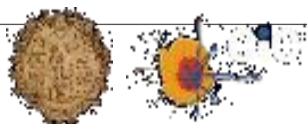
*LocoMMotion allowed <3 prior LOT if patients were double refractory to a PI and IMiD.^{1 †1 PI + 1 IMiD + 1 anti-CD38 mAb.^{1 ¶}After last patient in.^{1 §}Assessed by the same RRC across both studies per IMWG guidelines.}

1. Weisel K, et al. IMS 2023: poster [325]. 2. Mateos M-V, et al. IMS 2023: poster [294]. 3. NCT04557098. Available at: <https://www.clinicaltrials.gov/study/NCT04557098>.

4. NCT03548207. Available at: <https://www.clinicaltrials.gov/study/NCT03548207>. 5. NCT04634552. Available at: <https://www.clinicaltrials.gov/study/NCT04634552>.

6. Mateos M-V, et al. Leukemia 2022;36:1371-6. 7. NCT04035226. Available at: <https://classic.clinicaltrials.gov/ct2/show/NCT04035226>.




8. NCT05160584. Available at: <https://classic.clinicaltrials.gov/ct2/show/NCT05160584>. ClinicalTrials.gov accessed in September 2023.



2 Current real-world physician's choice leads to poor outcomes in patients with triple-class exposed RRMM



- The **poor efficacy and QoL outcomes**, seen in patients with TCE RRMM receiving RWPC, demonstrate that there is an **urgent need for new therapy options** to improve outcomes in this patient population¹⁻⁴
- More than 100 different regimens were used to rescue to these patients highlighting the lack of standard of care for these patients

	 (N=248) ¹	 (N=54) ²	 Pooled analysis (N=302) ²
ORR (95% CI), %	31.9 (26.1–38.0)	31.5 (19.5–45.6)	31.8 (26.6–37.4)
CR, %	0.4 ²	0	0.3
VGPR, %	12.9 ²	11.1	12.6
Median DoR (95% CI), months	7.4 (4.9–11.1)	-	-
Median PFS (95% CI), months	4.6 (3.9–5.6)	4.6 (3.4–9.0)	4.6 (4.1–5.6)
Median OS (95% CI), months	13.8 (10.8–17.0)	NE (10.5–NE)	14.5 (11.1–17.9)



> **Patients experienced rapid disease progression** and poor survival despite wide range of RWPC treatments¹

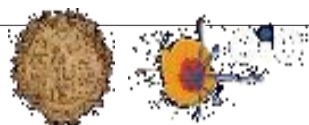


> ORR and median PFS were consistent between LocoMMotion and MoMMent²

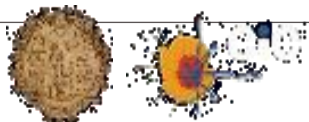
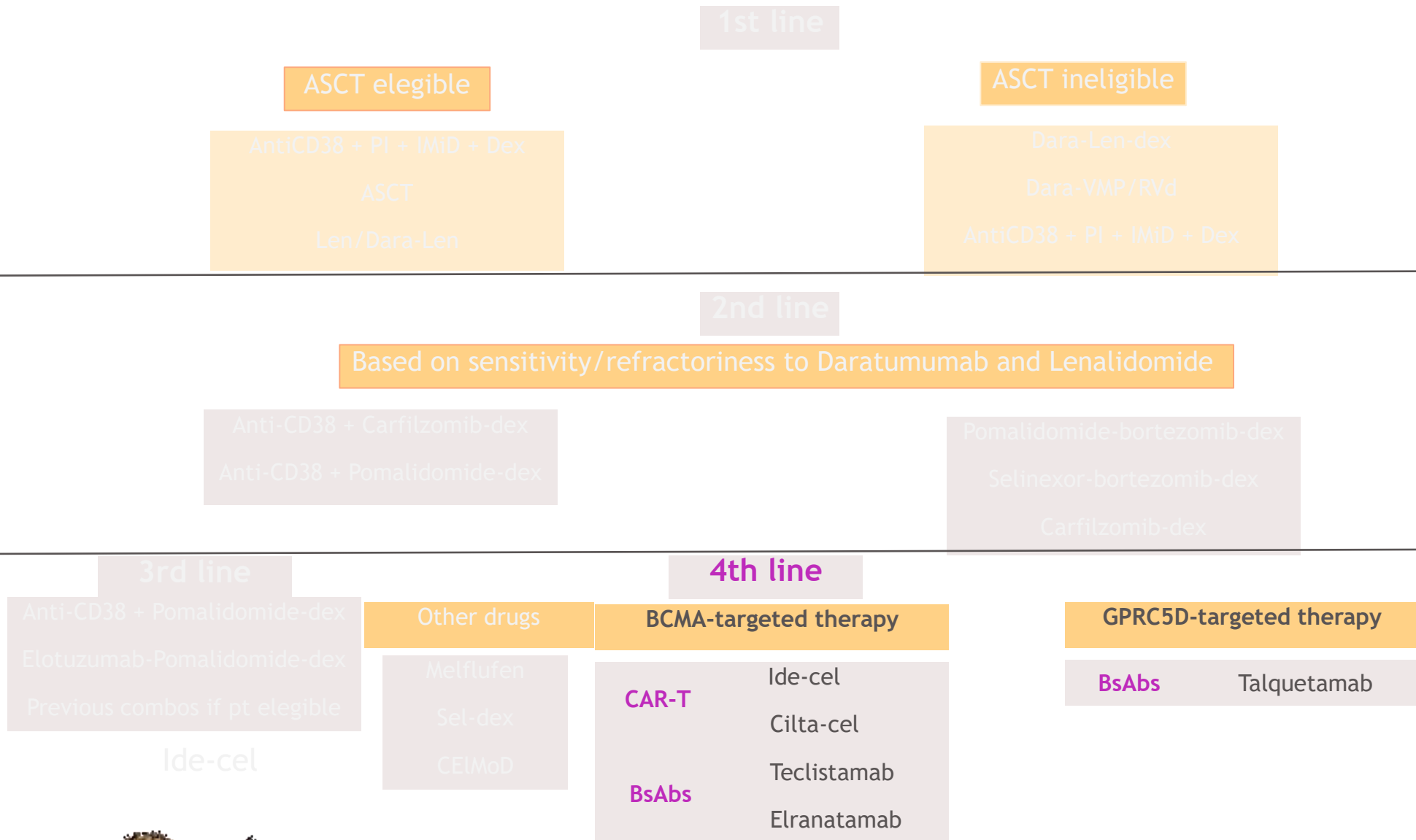


> Existing RWPC treatments do not substantially **improve QoL**, particularly in non-responders³

Median follow-up was 26.4 months for LocoMMotion at the final analysis and 9.3 months for MoMMent (data cut-off, 13 March, 2023).^{1,2}



Treatment landscape in Multiple Myeloma today: realistic situation



BCMA-targeting bsAbs: Efficacy

Product	n	PL/TCR	Efficacy at the RP2D	PFS/DoR/OS (m)	Schedule of administration
Teclistamab ²	165	5PL/ 77.6%	ORR 63% ≥CR: 45.5%	11.4/24/22.2 months	0.06–0.3–1.5 mg/kg QW SC; switch to Q2W/Q4W dosing (under investigation)
Elranatamab ³	123	5PL/ 96.7%	ORR 61% ≥CR: 35.0%	17.2m/69% at 12m/24.6m	12–32–76 mg SC QW Option to switch to Q2W dosing after ≥2 months if ≥PR and to Q4W dosing after ≥6 Q2W cycles
Linvoseltamab ⁴	117 at 200mg	5–6PL/ 80%	ORR 71% (46% ≥CR) (n=117)	69% /87% /75% at 12m	5–25–200 mg IV C1–C3 QW C4–C5 Q2W Q4W later if ≥VGPR
Etentamig ⁵	124	5PL/ 82%	ORR 65% (27% ≥CR) @ 40mg ORR 64% (35% ≥CR) @ 60mg	10.4 months/NR in all patients @10.8 month follow-up	60 mg IV Q3W

**Most BCMA×CD3 bispecific antibodies have been evaluated in TCR MM patients.
ORR ranges from 50–71% and covers the unmet need. PFS is approx 1 year for most bsAbs**

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. BCMA, B-cell maturation antigen; bsAb, bispecific antibody; C, Cycle; CR, complete response; DoR, duration of response; IV, intravenous; mAb, monoclonal antibody; MM, multiple myeloma; MTD, maximum tolerated dose; NR, not reported; ORR, overall response rate; PFS, progression-free survival; PL, prior lines; QW, every week; Q2W, every other week; Q3W, every three weeks; Q4W, every four weeks; RP2D, recommended phase II dose; SC, subcutaneous; sCR, stringent complete response; TCR, triple-class refractory; VGPR, very good partial response.
2. Van de Donk NWCJ, et al. ASCO 2023 (Abstract No. 8011 - presentation); 387:495-505; 3. Tomasson et al. ASH 2023 (Abstract No. 3385 - oral presentation);
4. Lee HC, et al. ASCO 2023 (Abstract No. 8006 - presentation); 5. Vij R et al. ASH 2023 (Abstract No. 3378 - poster).

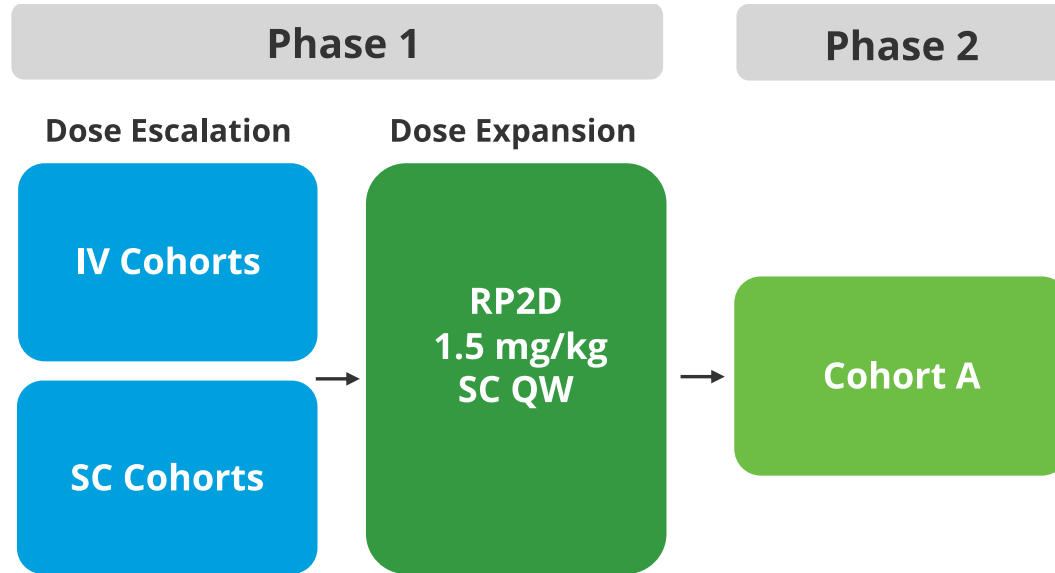


Majestec-1 clinical trial: Teclistamab monotherapy in RRMM patients

TCE, 3L+

Key Eligibility Criteria:

- RRMM per IMWG 2016 criteria¹
- ECOG PS 0-1
- Prior PI, IMiD, anti-CD38 mAb
- ≥3 prior LOT (phase 2)
- No prior BCMA-directed therapy



Primary Endpoint

- ORR

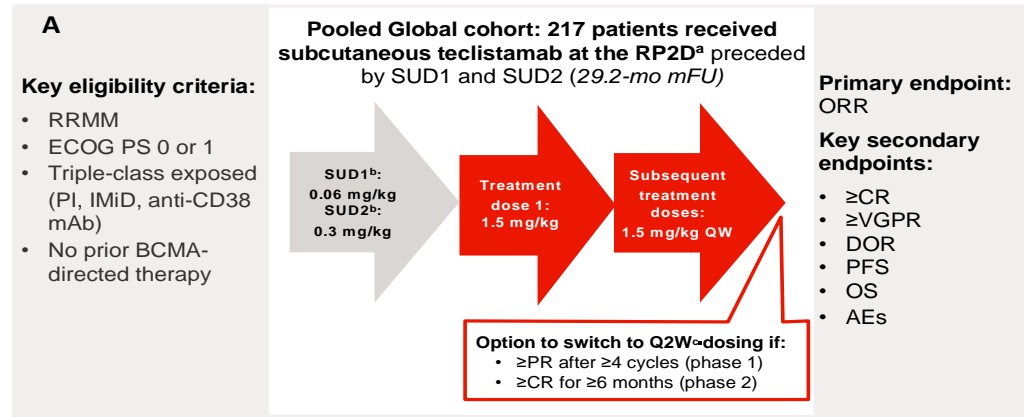
Key Secondary Endpoints

- PK/PD
- DOR
- PFS
- OS
- MRD negativity
- Safety
- HRQoL

q2w si ≥RP tras C4 or
≥RC durante 6 o más ciclos

Pooled Efficacy and Safety of Teclistamab in 217 Patients With Triple-Class Exposed Relapsed/Refractory Multiple Myeloma From 3 Registrational Clinical Studies

Figure 1: Study design (A) and enrollment periods relative to COVID-19



^a1.5 mg/kg subcutaneously QW. ^b2–4 days were allowed between SUD1, SUD2, and treatment dose 1. ^cPatients in the Japan study could switch to Q2W dosing if they achieved ≥PR for ≥6 months. AE, adverse event; CR, complete response; DOR, duration of response; EGOG, Eastern Cooperative Oncology Group; IMiD, immunomodulatory drug; mAb, monoclonal antibody; mFU, median follow-up; ORR, overall response rate; OS, overall survival; PFS, progression-free survival; PI, proteasome inhibitor; PR, partial response; PS, performance status; QW, weekly; Q2W, every other week; SUD, step-up dosing; VGPR, very good partial response.

Table 1: Patient baseline demographics and characteristics

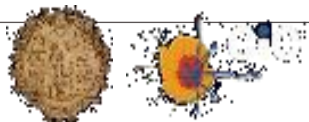
Characteristic	Global cohort (N=217)	Asian cohort (n=52)
Male, n (%)	117 (53.9)	21 (40.4)
Age (years), median (range)	65 (33–84)	67 (42–84)
Race, n (%)		
Asian	55 (25.3)	52 (100.0)
Black or African American	21 (9.7)	0
White	134 (61.8)	0
Other	7 (3.2)	0
Weight (kg), median (range), n (%)	69 (37.5–138.9)	58 (37.5–86.4)
Extramedullary plasmacytomas, ≥1, n (%)	41 (18.9)	13 (25.0)
ECOG PS at baseline, n (%)		
0	79 (36.4)	24 (46.2)
≥1	138 (63.6)	28 (53.8)
ISS stage at study entry, n (%)		
I	110 (51.4)	25 (48.1)
II	74 (34.6)	17 (32.7)
III	30 (14.0)	10 (19.2)
High-risk cytogenetics, n (%)	58 (29.0)	20 (38.5)
Number of prior LOT, median (range)	5 (2–14)	5 (3–12)
Prior exposure, n (%)		
Triple-class	217 (100)	52 (100)
Penta-drug	142 (65.4)	26 (50.0)
Refractory status, n (%)		
Triple-class	161 (74.2)	33 (63.5)
Penta-drug	59 (27.2)	9 (17.3)

ISS, International Staging System; LOT, line of therapy.

3 pandemic (B)

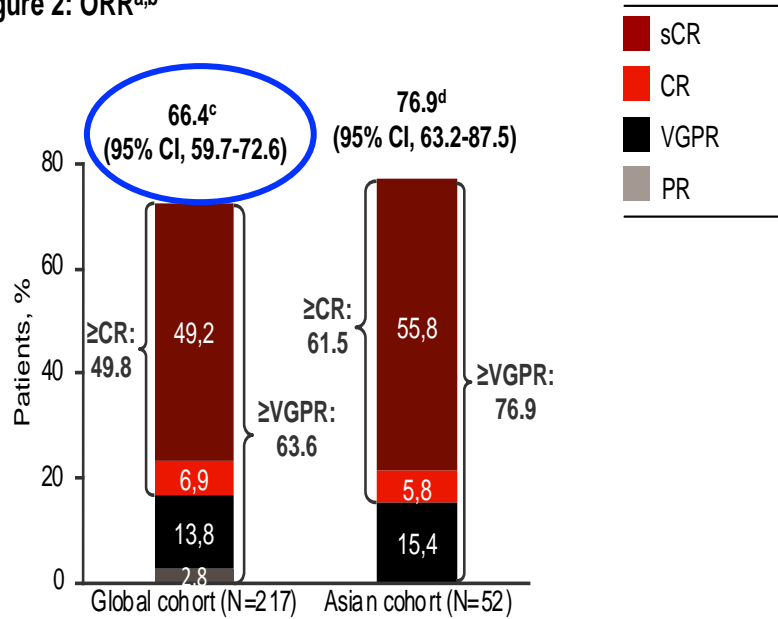


could switch to Q2W dosing if they achieved ≥PR for ≥6 months. AE, adverse event; CR, complete response; DOR, duration of response; EGOG, Eastern Cooperative Oncology Group; IMiD, immunomodulatory drug; mAb, monoclonal antibody; mFU, median follow-up; ORR, overall response rate; OS, overall survival; PFS, progression-free survival; PI, proteasome inhibitor; PR, partial response; PS, performance status; QW, weekly; Q2W, every other week; SUD, step-up dosing; VGPR, very good partial response.

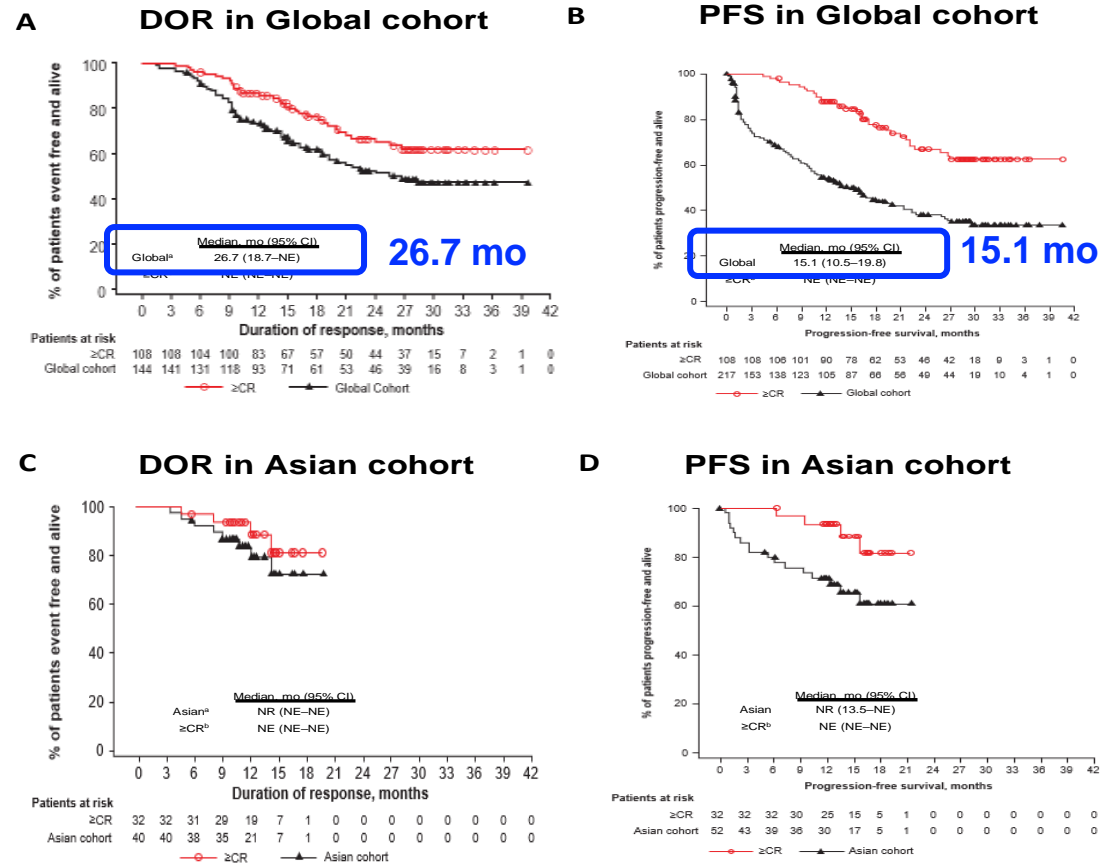


Pooled Efficacy and Safety of Teclistamab in 217 Patients With Triple-Class Exposed Relapsed/Refractory Multiple Myeloma From 3 Registrational Clinical Studies

Figure 2: ORR^{a,b}



^aResponse assessed by independent review committee in the MajesTEC-1 study. ^bResponse in the Japan study was assessed using a computerized algorithm. ^cmFU, 29.2 months. ^dmFU, 14.9 months. sCR, stringent complete response.



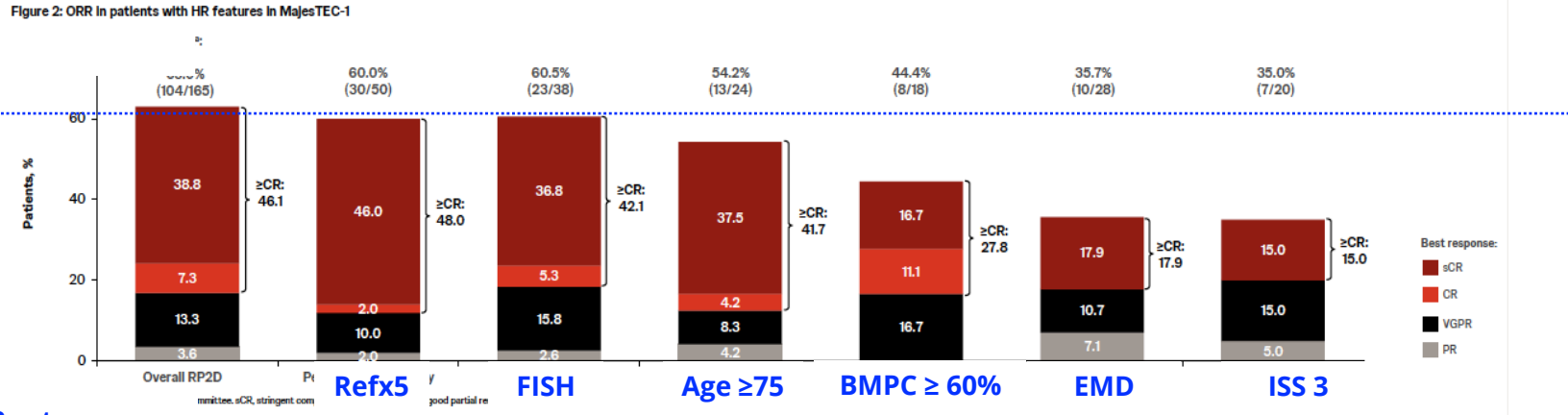
Median follow-up 29.2 months



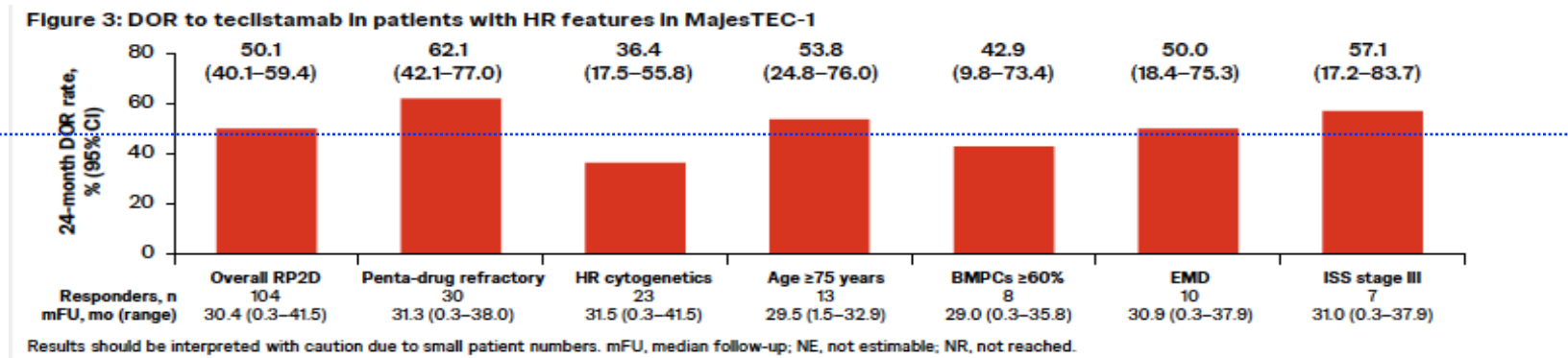
Efficacy of Teclistamab in subgroup of patients with **high-risk features**: results from the Majestic-1

Penta-drug refractory patients: 30.3%; HR cytogenetics: 25.7%; Older than 75 years: 14.5%; BMPCs \geq 60%: 11.2%; Extramedullary disease: 17% and ISS-3: 12.3%

ORR



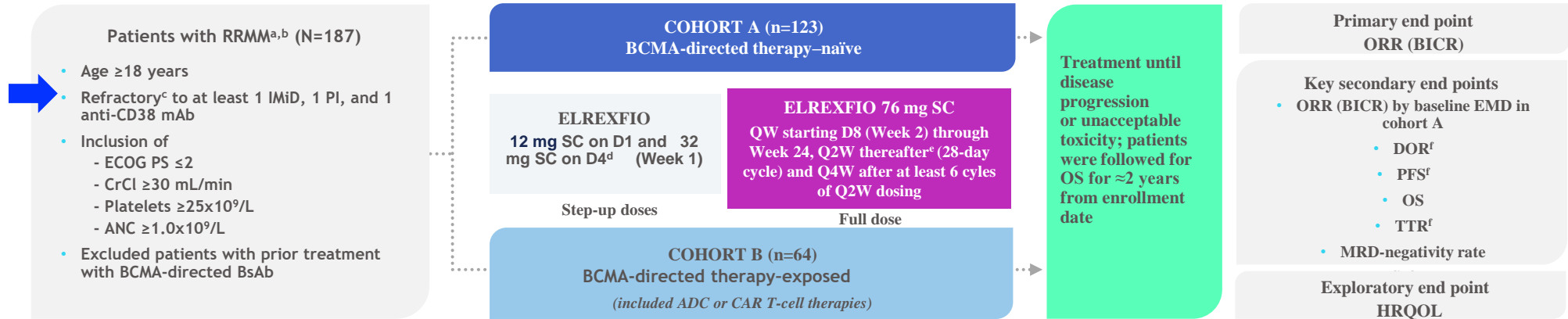
24-mo DOR rate



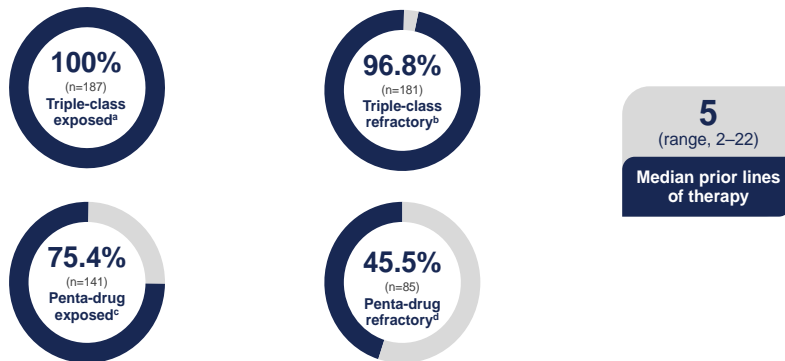
Patients who are penta-drug refractory, have HR cytogenetics, or are age \geq 75 years had ORR and \geq CR rates comparable with the overall RP2D Majestic-1 population; patients with BMPCs \geq 60%, EMD, or ISS stage III disease also derived benefit but remain difficult to treat



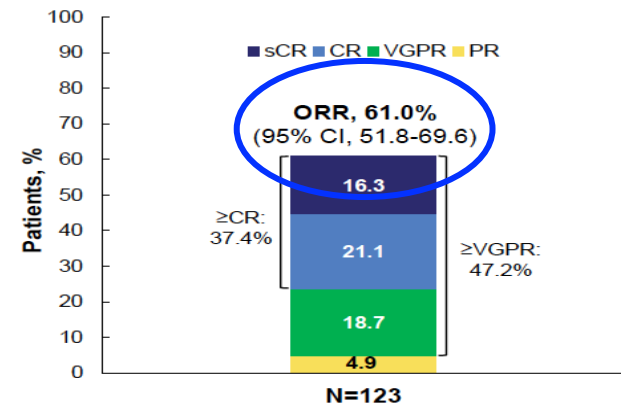
MagnetisMM-3: an open-label, global, multicenter, single-arm, phase 2 study: **update** on efficacy and safety (median f/u: 33 months)



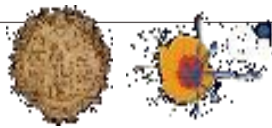
Treatment-related factors (N=187)



ORR and CR rate



Teclis: 66.4/49.8

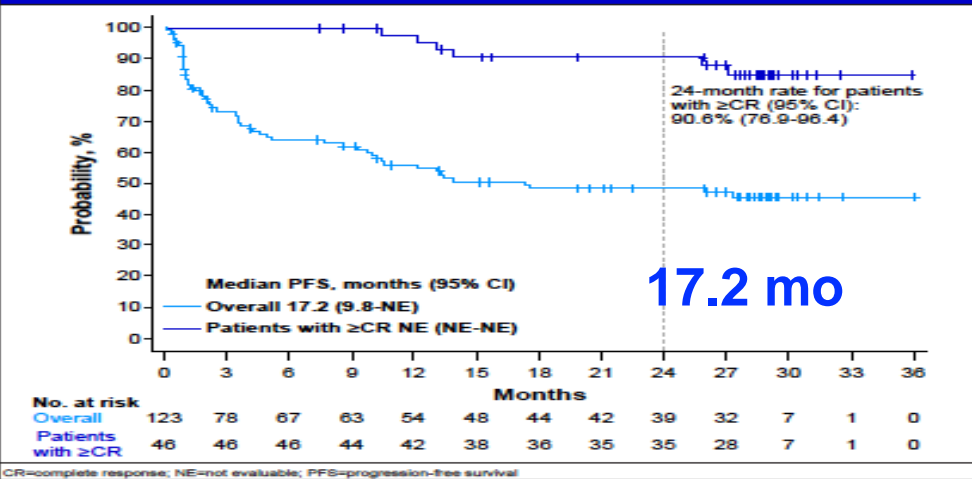


Treatment with Elranatamab led to durable PFS

Secondary end point: PFS and OS

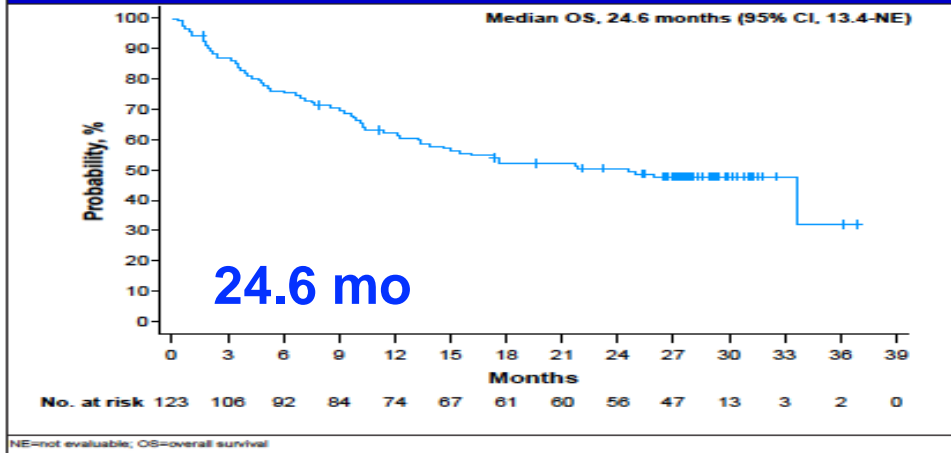
Efficacy: PFS and OS

Figure 2. Progression-free survival



Kaplan-Meier median PFS 17.2 months

Figure 3. Overall survival



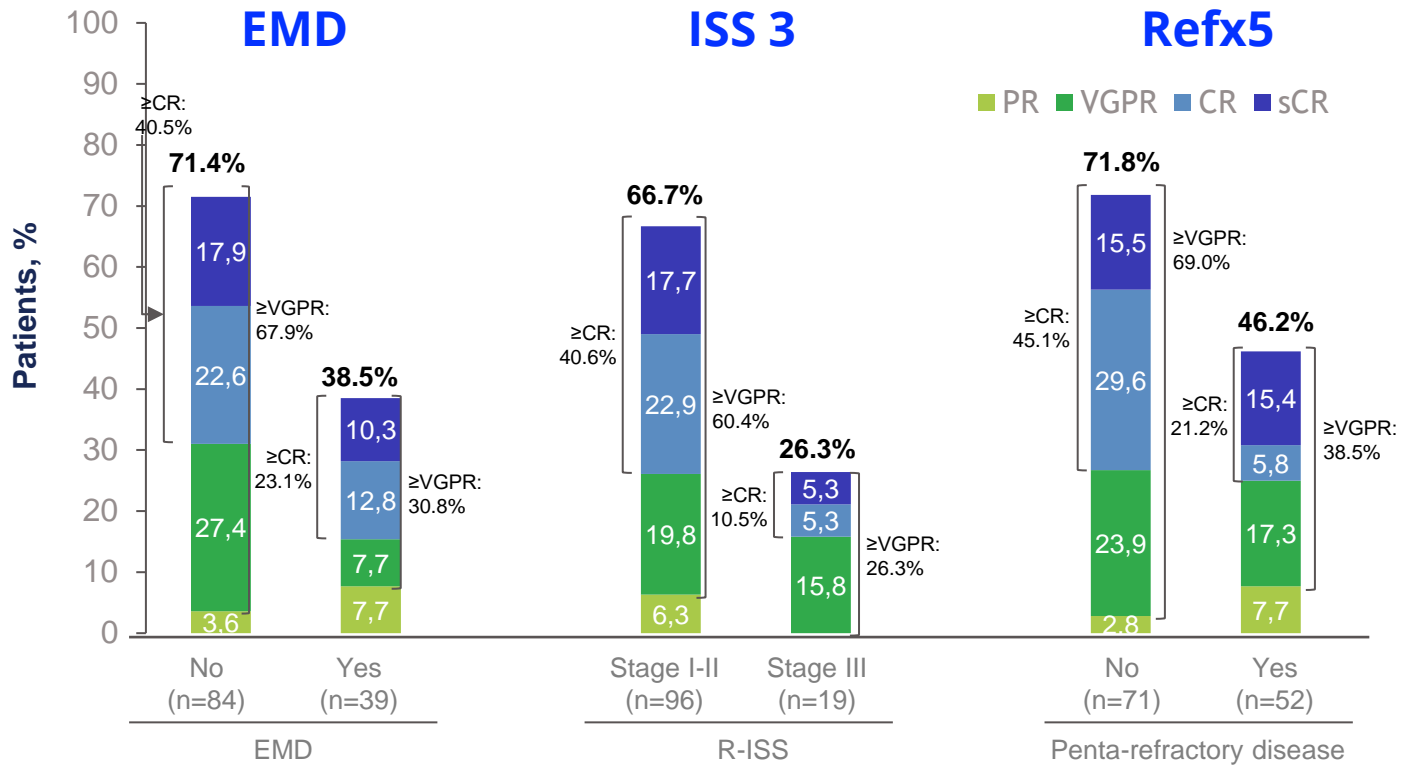
Kaplan-Meier median OS 24.6 months
 Median OS was not yet mature as >50% of pts were still censored

^aPFS was assessed by BICR.

BCMA, B-cell maturation antigen; BICR, blinded independent central review; NE, not estimable; PFS, progression-free survival.

1- Mohty M et al. Long-Term Efficacy and Safety of Monotherapy in the Phase 2 MagnetisMM-3 Trial in Relapsed or Refractory Multiple Myeloma, Poster presented at EHA 2024.

ORR and DOR by BICR in select **poor prognosis subgroups**

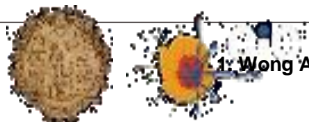


ORR were higher in patients with **R-ISS stage I-II disease** and in those **without EMD or penta-refractory disease**

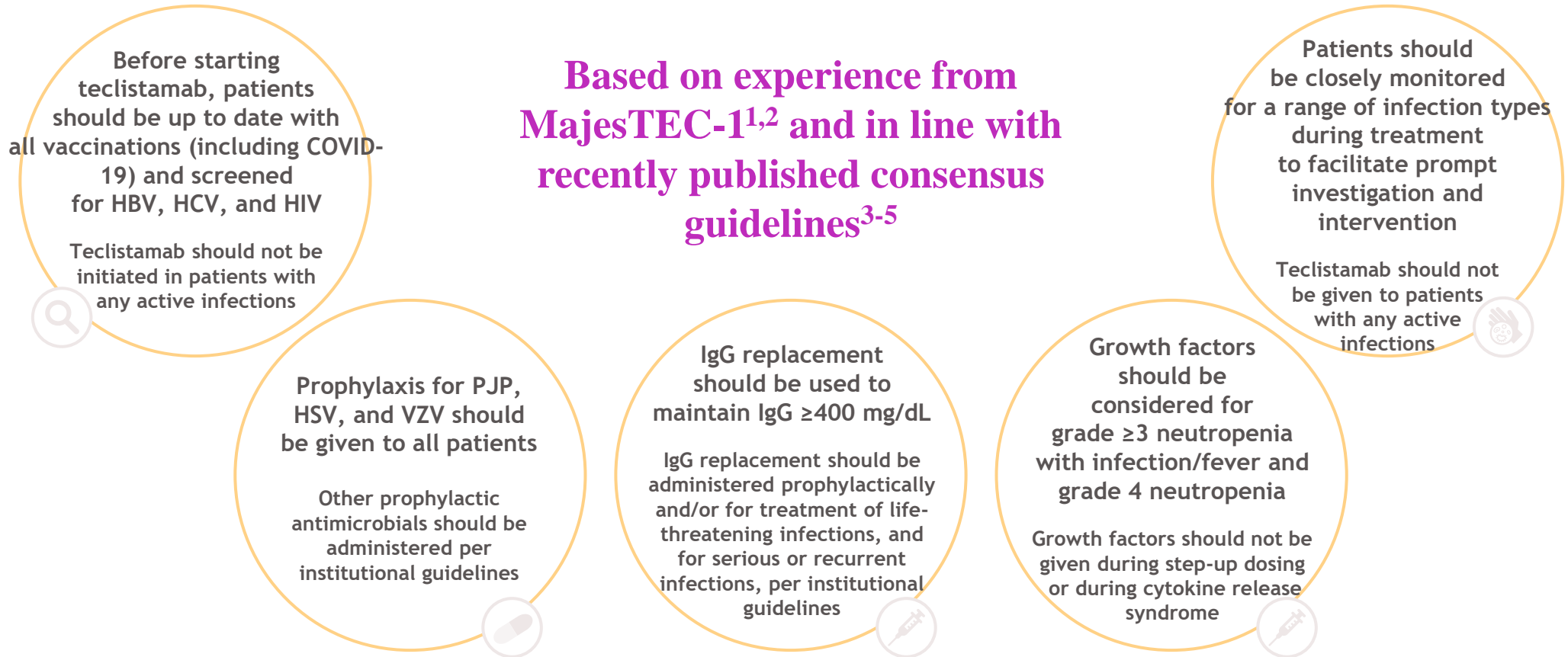
mFU: 14.7 months

BCMA-bispecific mAbs: Safety profile

	Teclistamab	Elranatamab	Linvoseltamab	ABVV-3883
CRS (G 3-4)	71.5% (0.6%)	56.3% (0%)	46.2% (0%)	43% (1%)
Median onset	2(1-6)	2	11 hours	1(1-2)
Duration	2(1-9)	2	15 hours	1(1-8)
Tocilizumab	36.4%	40%	18%	NR
NTS	14.5%	NR	NR	NR
ICANS	3%	4%	7.7%	5%
Grade 3-4	0	0	2.6%	0.5%
Median onset	3 days	2.5 days	NR	NR
Duration	7 days	2 days	NR	NR
Treatment required	8.5%	3%	NR	NR
Cytopenias				
Grade 3-4				
Neutropenia	64%	48%	22%	26%
Anemia	37%	36%	23%	18%
Thrombopenia	21%	22%	13%	11%
Infections	76%	66%	75%	NR
Grade 3-4	44%	35%	36.8%	22%
Hypogammaglobulinemia as AEs observed in most patients treated with BCMA-CD3 mAbs along the therapy				



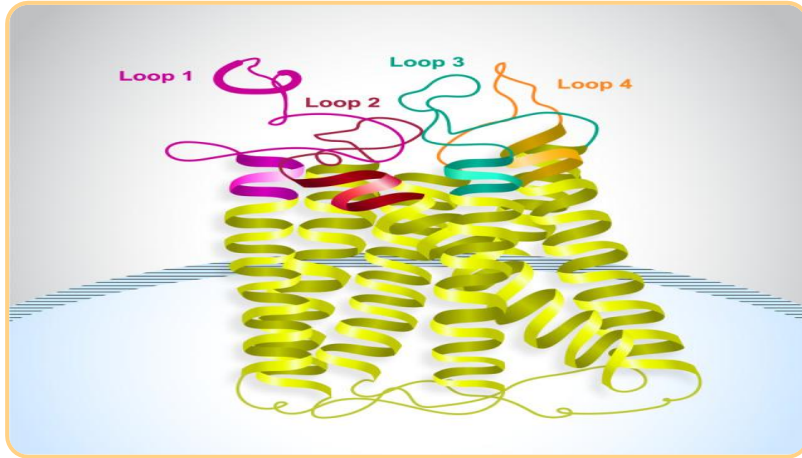
Summary of Key Recommendations for Managing Infections During Teclistamab Treatment



HBV, hepatitis B virus; HCV, hepatitis C virus; HSV, herpes simplex virus; IgG, immunoglobulin G; PJP, *Pneumocystis jirovecii* pneumonia; VZV, varicella-zoster virus. 1. Moreau P, et al. *N Engl J Med* 2022;387:495-505. 2. van de Donk NWCJ, et al. *J Clin Oncol* 2023;41(16 Suppl):8011. 3. Rajc N, et al. *Lancet Haematol* 2022;9:143-61. 4. Ludwig H, et al. *Lancet Oncol* 2023;24:e255-69. 5. Rajc N, et al. *Blood Cancer J* 2023;13:116.



GPRC5D: G Protein-coupled Receptor (class C group 5 member D)



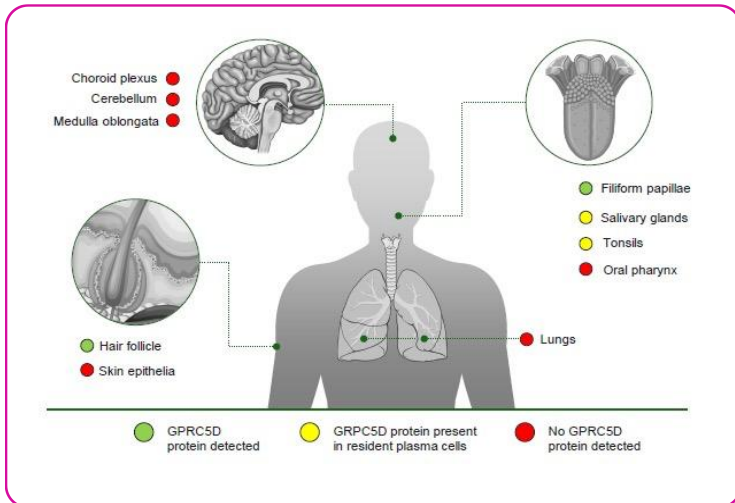
GPRC5D is a type-C 7-pass transmembrane receptor protein that is predominantly expressed in cells with a plasma-cell phenotype^{1,2}

It is an **orphan receptor**, which means that its ligand, signaling mechanism and function have not yet been established^{3,4}

As a 7-pass transmembrane protein, GPRC5D is **unlikely to be shed into the serum**^{3,5}

GPRC5D is highly expressed in MM cells and is abundant in bone marrow from patients with MM^{1,2}

In contrast, GPRC5D has relatively **limited expression in healthy tissues**²



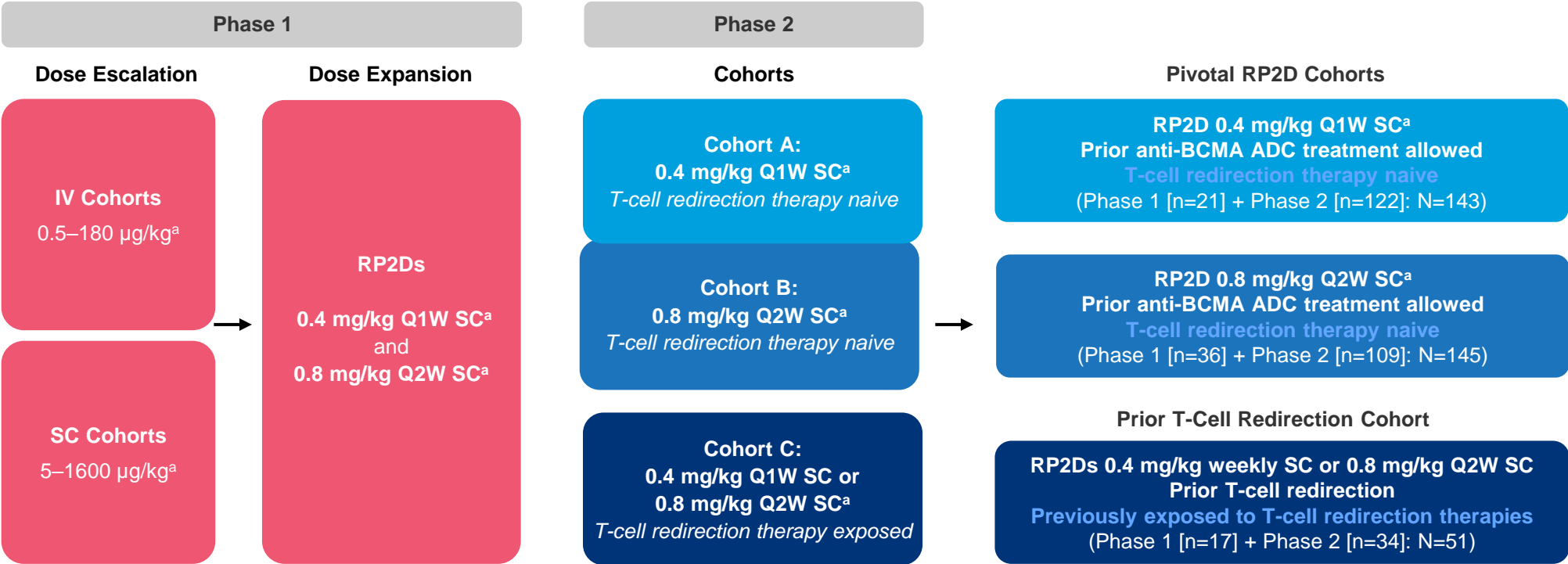
GPRC5D, G protein-coupled receptor class C group 5 member D.

1. Atamaniuk J, et al. Eur J Clin Invest 2012; 42:953-60. 2. Frigyesi I, et al. Blood 2014; 123:1336-40. 3. Pillarisetti K, et al. Blood 2020; 135:1232-43. 4. Verkleij CPM, et al. Blood Adv 2021; 5:2196-215. 5. Hipp S, et al. Leukemia 2017; 31:1743.



MomumenTAL-1 is a pivotal Phase 1/2 trial evaluating the efficacy and safety of talquetamab monotherapy in the treatment of TCE RRMM

MonumentTAL-1 is an ongoing, first-in-human, Phase 1/2, open-label, multicenter clinical trial evaluating the safety, tolerability, anti-myeloma activity, and pharmacokinetics of talquetamab monotherapy in the treatment of adult patients with TCE RRMM.¹



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^a1–3 step-up doses given within 1 week before a full dose.

1. Chari 2022.



Baseline characteristics of patients included in the MonumenTAL-1

We report pivotal phase 2 results from MonumenTAL-1 in pts with and without prior T-cell redirection therapy.

Patients enrolled in MonumenTAL-1 were heavily pre-treated, and many had high-risk features and/or features associated with a poor prognosis.^{1,a}

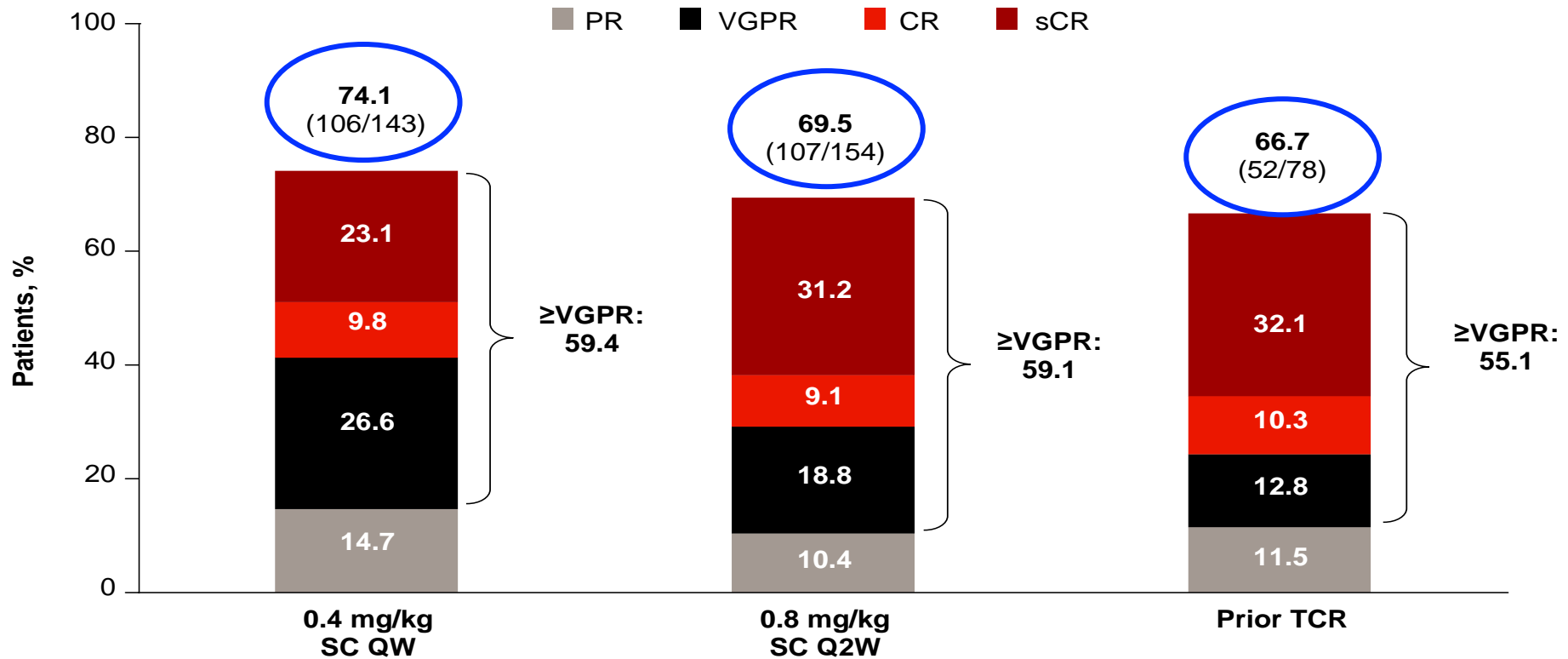
Characteristic	0.4 mg/kg SC Q1W ^a	0.8 mg/kg SC Q2W ^a	Characteristic	0.4 mg/kg SC Q1W ^a	0.8 mg/kg SC Q2W ^a
	n=143	n=145		n=143	n=145
Age (years), median (range)	67.0 (46-86)	67.0 (38-84)	Time since diagnosis (years), median (range)	6.7 (1.4-20.8)	6.4 (0.8-25.4)
Male, n (%)	78 (54.5)	83 (57.2)	Prior lines of therapy, median (range)	5 (2-13)	5 (2-17)
Race, n (%)			Prior stem cell transplantation, n (%)	113 (79.0)	114 (78.6)
White	128 (89.5)	125 (86.2)	Exposure status, n (%)		
Black/African American	12 (8.4)	9 (6.2)	Triple-class ^f	143 (100)	145 (100)
Asian	1 (0.7)	6 (4.1)	Penta-drug ^g	105 (73.4)	101 (69.7)
Not reported	2 (1.4)	2 (1.4)	Belantamab	22 (15.4)	16 (11.0)
Bone marrow plasma cells ≥60%, ^b n (%)	17 (12.3)	32 (22.7)	Refractory status, n (%)		
Extramedullary plasmacytomas ≥1, ^c n (%)	33 (23.1)	37 (25.5)	PI ^h	114 (79.7)	120 (82.8)
High-risk cytogenetics, ^d n (%)	41 (31.1)	37 (28.9)	IMiD ⁱ	133 (93.0)	130 (89.7)
ISS stage, n (%) ^e			Anti-CD38 mAb ^j	133 (93.0)	134 (92.4)
I	62 (43.4)	64 (44.4)	Triple-class ^f	106 (74.1)	100 (69.0)
II	53 (37.1)	45 (31.3)	Penta-drug ^g	42 (29.4)	34 (23.4)
III	28 (19.6)	35 (24.3)	Belantamab	18 (12.6)	13 (9.0)
			To last line of therapy	134 (93.7)	137 (94.5)

^aWith 2-3 step-up doses. ^bPercentages calculated from n= 138 for 0.4 mg/kg QW, and n= 141 for 0.8 mg/kg Q2W. ^cSoft tissue plasmacytomas not associated with the bone were included. ^ddel(17p), t(4:14), and/or t(14;16); calculated from n=132 for 0.4 mg/kg SC QW, and n=128 for 0.8 mg/kg SC Q2W. ^ePercentages calculated from n=144 for 0.8 mg/kg Q2W. ^f≥1 PI, ≥1 IMiD, and ≥1 anti-CD38 mAb. ^g≥2 PIs, ≥2 IMiDs, and ≥1 anti-CD38 mAb. ^hBortezomib, carfilzomib, and/or ixazomib. ⁱThalidomide, lenalidomide, and/or pomalidomide. ^jDaratumumab, isatuximab, and/or an investigational anti-CD38 mAb. ADC = antibody drug conjugate; IMiD = immunomodulatory drug; ISS = International Staging System; mAb = monoclonal antibody; PI = proteasome inhibitor; Q2W = once every two weeks; QW = once every week; SC = subcutaneous.

1. Schinke 2023.



MonumenTAL-1 study: Talquetamab, GPRC5D-CD3 bsAb in RRMM patients¹



ADC, antibody-drug conjugate; BCMA, B-cell maturation antigen; BsAb, bispecific antibody; CD, cluster of differentiation; CI, confidence interval; CR, complete response; DOR, duration of response; EMD, extramedullary disease; FU, follow-up; GPRC5D, G protein coupled-receptor Class 5 group 5; NE, not evaluable; ORR, overall response rate; OS, overall survival; PFS, progression-free survival; PL, prior lines; PR, partial response; Q2W, every 2 weeks; QW, weekly; RRMM, relapsed/refractory multiple myeloma; SC, subcutaneous; sCR, stringent complete response; TCR, T-cell redirection; VGPR, very good partial response.

1. Yen Cristine et al. IMS 2024



MonumenTAL-1: Outcomes

Table 1: Efficacy outcomes

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, mo (95% CI) ^a	9.5 (6.7–13.4)	17.5 (12.5–NE)	N/A ^b
→ mDOR in patients with ≥CR, mo (95% CI)	28.6 (19.4–NE)	NR (21.2–NE)	N/A ^b
→ mPFS, mo (95% CI)	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)

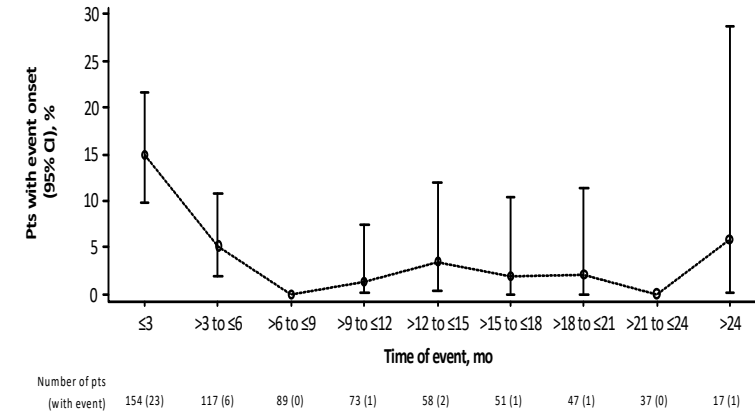
^an=106 (QW), n=107 (Q2W), and n=52 (prior TCR). ^bNot reported due to heavy censoring from 12 to 20 mo; the estimate may not be reliable at this time point. See **Supplemental Table 2** for efficacy outcomes in the USPI population (≥4 prior LOT). mDOR, median duration of response; mFU, median follow-up; NA, not available; NE, not estimable; NR, not reached; USPI, United States prescribing information.



Talquetamab Safety

Bispecific antibody	Talquetamab Phase 1/2 MonumentAL-1 Study GPRC x CD3		
	QW	Q2W	overall
AEs, all (G 3+)			
CRS	79% (2%)	75% (0.7%)	77% (2.0%)
Infections	59% (20%)	66% (15%)	73% (28%)
Neutropenia	35% (31%)	28% (22%)	55% (53%)
Anemia	45% (32%)	39% (25%)	39% (25%)
Thrombocytopenia	27% (20%)	30% (19%)	37% (29%)
ICANS	11% (1.6%)	10% (1.8%)	10% (1.8%)
# Deaths	0 due to AEs	0 due to AEs	0 due to AEs
Hypogamma/IVIg	NR/13%	NR/10%	NR/10%
Other	Dysgeusia 72% (N/A) Skin 56% (0%) Nail 55% (0%)	Dysgeusia 71% (N/A) Skin 73% (0.7%) Nail 54% (0%)	Dysgeusia 77% (N/A) Skin 69% (0%) Nail 63% (0%)

Figure 5: New-onset grade ≥3 infections over time in the Q2W cohort



The safety profile was clinically manageable with low rates of high-grade infections and tal discontinuations

94 ataxia events have been reported among 79 study participants in all studies with Talquetamab. Most of them G1-2 and none of them resulted in death

AE, adverse event; CD, cluster of differentiation; CRS, cytokines release syndrome; GPRC, G protein-coupled receptor Class C; ICANS, immune effector cell-associated neurotoxicity syndrome; IVIg, intravenous immunoglobulin; LOT, line of therapy; N/A, not applicable; NR, not reported; QW, once weekly; Q2W, every 2 weeks; SC, subcutaneous.
Chari A, et al. ASH 2022: Abstract 157; Touzeau C, et al. EHA 2023; Abstract S191.



The future: Bispecific Combinations in TCE/TCR patients



Attribute	Key Data Element	Talquetamab + Dara ² TRIMM-2 (N=65)	Talquetamab + POM ³ MonumentAL-2 (N=35)		Tecl+ Tal ⁴ (N=93)	Tal+Pom+Dara (N=77)		Elnentamig+Dara+ Dex (N=86)
		Talquetamab 0.8 mg/kg, Q2W n=51	Talquetamab 0.4 mg/kg, QW n=16	Talquetamab 0.8 mg/kg, Q2W n=19	Teclistamab 3.0 mg/kg + Talquetamab 0.8 mg/kg, Q2W (n=34)	Talquetamab 0.4 mg/kg, QW n=18	Talquetamab 0.8 mg/kg, Q2W n=59	Elnentamig at dose of 20/40 and 60 mg Q4W
Patient Characteristics	High-Risk, %	21.2	31.3	21.1	33.3	NR		40
	Median prior LoT, n (range)	5 (2-14)	3 (2-12)	3 (2-5)	4 (2-10)	6		4 (3-10)
	Prior PI / IMiD / Anti-CD38, %	- / - / 90.2	- / - / 75.0	- / - / 73.7	- / - / -	80 and 70% Dara and Pom- refractory		70 TCE/45 TCR (46% antiCD38 refractory)
	Extramedullary Disease, %	25.5	12.5	15.8	32.4	-		-
	Prior BCMA, %	52.9	25.1	0	-	70		-
	Prior CAR T / ADC / Bispecific, %	17.6 / 21.6 / 19.6	18.8 / - / 6.3	0 / - / 0	2.9 ^d /11.8/0	-		-
Efficacy	Median Follow-Up, mo (range)	15.0 (1.0-25.3)	15.0 (1.2-19.0)	11.1 (1.2-14.8)	8.1 (0.7-15.0)	10		7
	ORR, %	84.0 [42/50] 82.2 [37/45] (prior anti-CD38) 88.9 [8/9] (prior CAR T) 70.0 [7/10] (prior bispecific)	93.8 (all patients) 100 [3/3] (prior CAR T) 50.0 [1/2] (EMD) 80.0 [4/5] (HR cytogenetics)	84.2 (all patients) No prior CAR T 67.0 [2/3] (EMD) 75.0 [3/4] (HR cytogenetics)	96.3	100 (0.4 mg/Kg) 82 (0.8 mg/Kg) 100% overall in the antiCD38 naïve/sensitive 82 overall in the Pom naïve/sensitive 78 in the antiCD38 ref 81 in the Pom ref 82.8 in the BsAb ref 83% in the CAR-T		71 Overall 82 in the cohort at 60 mg
	2vORR, %	74.0	87.5	88.4	88.8	77.5		53 overall /45 at the 60 mg
	mDoR, mo	20.3	NR (12.0-NR)	NR (7.4-NR)	NE (NE-NE)	14 (0.4 mg/Kg) 26 (0.8 mg/Kg)		-





^aThe median duration range was confounded by ongoing infection. ^bICANS in 4.6% of patients (QW and Q2W). ^c76.9% had dysgeusia (QW and Q2W). ^dIncludes ide-cel. ^eIncludes ageusia, dysgeusia, hypogeusia, and taste disorder. NE, not estimable. NR, not reached.

. Dholaria et al. ASCO 2023. Abstract 8003. 3. Matous et al. ASH 2023. Abstract 1014. 4. Cohen et al. ASCO 2023. Abstract 8002.



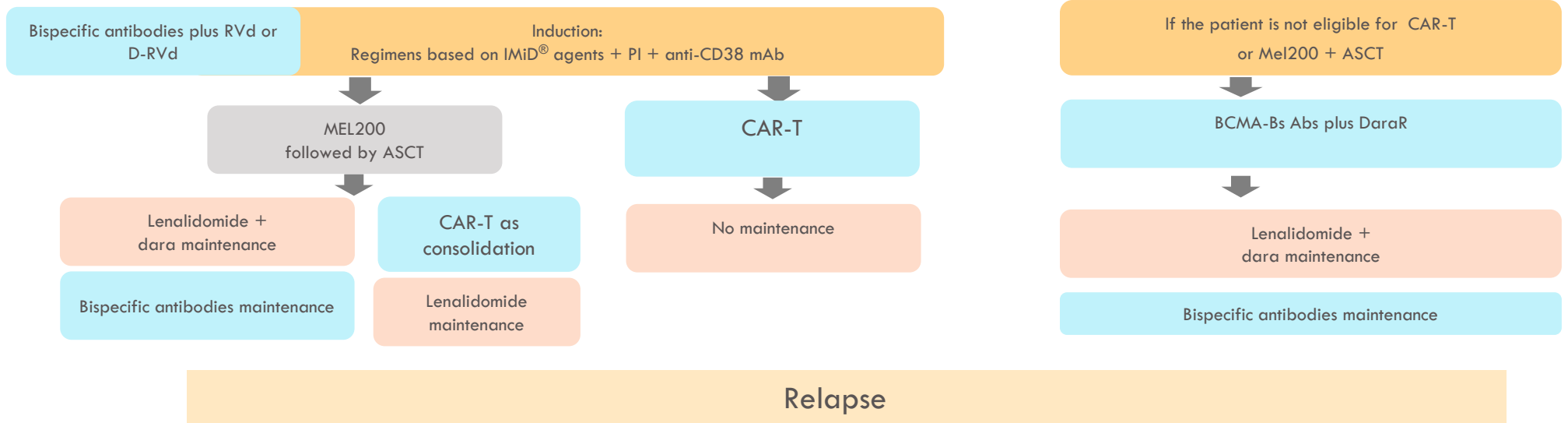
The future: Bispecific Combinations in earlier lines of therapy

Attribute	Key Data Element	Teclistamab + Dara + Len ¹ MajesTEC-2 (Cohort E, N=32)		Elranatamab + Carfilzomib (N=12)
		Teclistamab 0.72 mg/kg, SC n=13	Teclistamab 1.5 mg/kg, SC n=19	Elranamab at dose of 12/32/76 mg QW and Q2W from C7
 Patient Characteristics	High-Risk, %	25	46.7	25
	Median prior LoT, n (range)	2 (1-3)	2 (1-3)	2 (1-3)
	Prior PI / IMiD / Anti-CD38, %	100 / 100 / 38.5	100 / 100 / 26.3	91/83/58
	Extramedullary Disease, %	7.7	5.3	-
	Prior BCMA, %	-	-	-
	Prior CAR T / ADC / Bispecific, %	-	-	-
 Efficacy	Median Follow-Up, mo (range)	8.4 (1.1-12.9)		9
	ORR, %	100	81	100
	≥VGPR, %	92	Not mature	92
	mDoR, mo	NR	NR	83% at 6m

^aThe median duration range was confounded by ongoing infection. ^bICANS in 4.6% of patients (QW and Q2W). ^c76.9% had dysgeusia (QW and Q2W). ^dIncludes ide-cel. ^eIncludes ageusia, dysgeusia, hypogeusia, and taste disorder. NE, not estimable. NR, not reached.

1. Searle et al. ASH 2022. Abstract 160. 2. Tomasson et al. ASH 2024: oral presentaion

The future: Bispecifics/ADC in earlier and first line/s of therapy



Summary

- BsAbs and ADC targeting BCMA and GPRC5D **cover the unmet medical need** for the Triple Class Exposed/Refractory population and some are already approved and being used in the clinical practice
 - **Patient and disease-based factors** together with availability, **access**,.... will drive the selection amongst the different BsAbs and also if it is better to start with BCMA or GPRC5D as target...
 - **Sequencing** is the challenging situation but we will have more information in the future about mechanisms of resistance and how to overcome them
 - In spite of all these problems, we have never seen these efficacy data in a population of MM patients already exposed to PIs, IMiD's and antiCD38 mAbs and deserve to be available for our MM patients and to move to earlier lines of therapy.
 - The future are **combinations and in earlier lines of therapy**
-