Targeting BCMA in multiple myeloma: Insights from COMy and EHA 2024

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Recorded following **COMy** (23–26 May 2024, Paris, France)
and **EHA** (13–16 June 2024, Madrid, Spain)

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Approved indications for BCMA-targeting agents

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Recorded following **COMy** (23–26 May 2024, Paris, France)
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P942: Long-term follow-up from the phase I/II MajesTEC-1 trial of teclistamab in patients with RRMM

Oriol A, et al.

Study population[1,2]

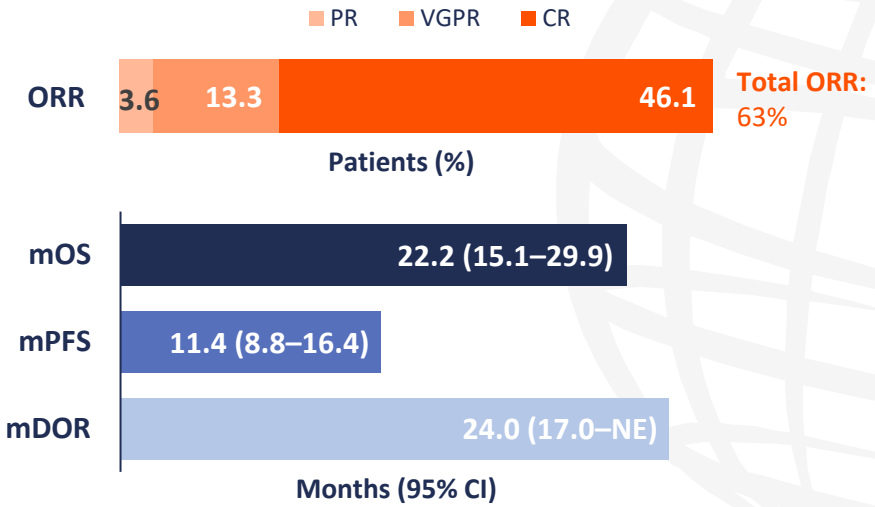
Patient cohort

- Baseline characteristics previously published[2]
- 77.6% triple-class refractory
- Median previous lines of therapy: 5

30.4-month follow-up

- N=165, recommended phase II QW SC dose
  - n=65, transitioned to Q2W dosing
- Patients still on treatment: n=38 (n=37 on Q2W)

Outcomes



Teclistamab continues to demonstrate deep and durable responses, even with less frequent dosing. This is the longest follow-up of any bispecific antibody in RRMM.

CR, complete response; CI, confidence interval; DoR, duration of response; m, median; NE, not estimable; ORR, overall response rate; OS, overall survival; PFS, progression-free survival; PR, partial response; QW, every week; Q2W, every 2 weeks; RRMM, relapsed/refractory multiple myeloma; SC, subcutaneous; VGPR, very good PR.

1. Oriol A, et al. Presented at EHA2024, Madrid, Spain, 13–16 June 2024. Abstr. P942; 2. Moreau P, et al. *N Engl J Med.* 2022;387:495–505.

P942: Long-term follow-up from the phase I/II MajesTEC-1 trial of teclistamab in patients with RRMM

Oriol A, et al.

Safety profile

Grade 3/4 TEAEs, %	N=165
Any	94.5
Haematologic	
Neutropenia	65.5
Anaemia	37.6
Thrombocytopenia	23.0
Lymphopenia	34.5
Leukopenia	9.1

CRS and ICANS

- CRS occurred in **72.1%** of patients (grade 3/4, 0.6%)
- **No changes** at 30.4-month follow-up

Infections

- Occurred in **78.8%** of patients (grade 3/4, 55.2%)
- **18** of 22 grade 5 infections were due to COVID-19
- No new grade 5 COVID-19 TEAEs at 30.4-month follow-up
- Onset of new grade ≥3 infections generally declined over time:
  - Transitioning to Q2W dosing and increasing use of Ig replacement may contribute to this trend

Other

TEAEs leading to:

- dose **reduction** in **one** patient
- **discontinuation** in **eight** patients; five due to infection
- No new safety signals were reported

Teclistamab offers an effective treatment in RRMM with a manageable safety profile and no new safety signals.

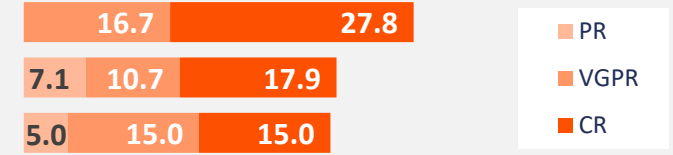
CRS, cytokine release syndrome; ICANS, immune effector cell-associated neurotoxicity syndrome; Ig, immunoglobulin; Q2W, every two weeks; RRMM, relapsed/refractory multiple myeloma; TEAE, treatment-emergent adverse event. Oriol A, et al. Presented at EHA2024, Madrid, Spain, 13–16 June 2024. Abstr. P942.

P923: Efficacy and safety of teclistamab in patients with RRMM with high-risk features: A subgroup analysis from the phase I/II MajesTEC-1 STUDY

Costa LJ, et al.

Outcomes by patient subgroup (~30-month follow-up)

High-risk features	Proportion,% (n/N)	Response rates, %	ORR, %
Total	100.0 (165)	3.6 / 13.3 / 46.1	63.0
Penta-drug refractory	30.3 (50/165)	2.0 / 10.0 / 48.0	60.0
HR cytogenetics	25.7 (38/148)	2.6 / 15.8 / 42.1	60.5
Age ≥75 years	14.5 (24/165)	4.2 / 8.3 / 41.7	54.2
BMPCs ≥60%	11.2 (18/160)	16.7 / 27.8	44.4
Extramedullary disease	17.0 (28/165)	7.1 / 10.7 / 17.9	35.7
ISS stage III	12.3 (20/162)	5.0 / 15.0 / 15.0	35.0



Safety profiles, including grade 3/4 TEAEs and rates of discontinuation and deaths due to AEs, were generally comparable between HR subgroups and the overall population receiving the RP2D

Teclistamab can provide clinical benefit to patients with some HR features historically associated with poorer outcomes. HR subgroups with lower ORRs may benefit from earlier treatment when fewer HR features are present or treating with combinations to enhance antimyeloma activity.

AE, adverse event; BMPC, bone marrow plasma cells; CR, complete response; HR, high risk; ISS, International Staging System; ORR, overall response rate; PR, partial response; RP2D, recommended phase 2 dose; RRMM, relapsed/refractory multiple myeloma; TEAE, treatment-emergent AE; VGPR, very good partial response.

Costa LJ, et al. Presented at EHA2024, Madrid, Spain, 13–16 June 2024. Abstr. P943.

touch HAEMATOLOGY

P932: MagnetisMM-3: Long-term survival after elranatamab monotherapy in patients with RRMM

Mohty M, et al.

Baseline characteristics and treatment schedule

• Refractory to ≥1 PI, ≥1 IMiD, and ≥1 anti-CD38 antibody	BCMA-naive (N=123)
Median age, years (range)	68.0 (36–89)
Median prior lines of therapy, n (range)	5.0 (2–22)
Prior stem cell transplant, %	70.7
Triple-class exposed/refractory, %	100/96.7
Penta-class exposed/refractory, %	70.7/42.3
Extramedullary disease, %	31.7
R-ISS III, %	15.4
High-risk cytogenetics, %	25.2
Refractory to last line of therapy, %	95.9

Treatment schedule

Patients received SC elranatamab as 2 step-up priming doses followed by 76 mg QW

Patients with ≥6 months of QW dosing achieving ≥PR for ≥2 months were transitioned to

Q2W dosing schedule and to a Q4W dosing schedule after ≥6 Q2W cycles

BCMA, B-cell maturation antigen; IMiD, immunomodulatory drug; PI, proteasome inhibitor; PR, partial response; QW, once weekly; Q2W, every 2 weeks; Q4W, every 4 weeks; R-ISS, Revised Multiple Myeloma International Staging System; RRMM, relapsed/refractory multiple myeloma; SC, subcutaneous.

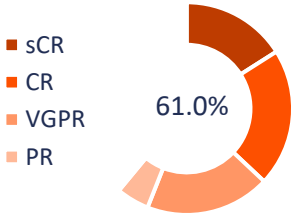
Mohty M, et al. Presented at EHA2024, Madrid, Spain, 13–16 June 2024. Abstr. P932.

P932: MagnetisMM-3: Long-term survival after elranatamab monotherapy in patients with RRMM

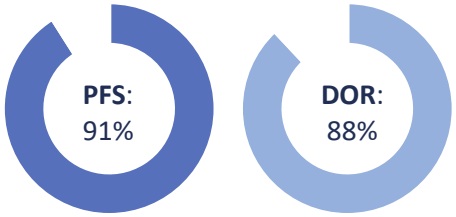
Mohty M, et al.

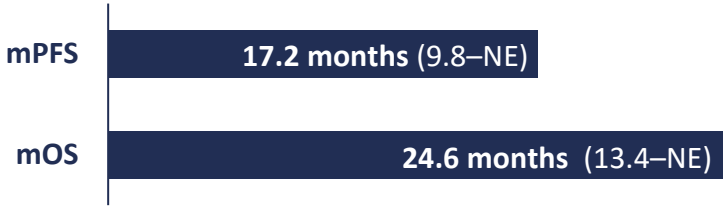
Efficacy and safety outcomes

ORR per BICR



24-month rates for ≥CR





No new safety signals were observed with extended follow-up

With an additional 6 months' follow-up:

- **Four new deaths** had occurred
  - **Two** patients with **disease under study**
  - **One** patient **each** with **unknown reason** and **septic shock**
- **Five patients** had **secondary primary malignancies (SPMs)**
  - **All** were cutaneous squamous cell carcinoma
  - **All** received prior lenalidomide and a stem cell transplant
  - **No haematological** SPMs were observed

Elranatamab continued to demonstrate deep and durable responses in heavily pretreated BCMA-naive patients with RRMM, with no new safety signals observed with extended follow-up.

BCMA, B-cell maturation antigen; CR, complete response; DOR, duration of response; m, median; NE, not estimable; ORR, overall response rate; OS, overall survival; PFS, progression-free survival; PR, partial response; RRMM, relapsed/refractory multiple myeloma; sCR, stringent CR; VGPR, very good partial response.

Mohty M, et al. Presented at EHA2024, Madrid, Spain, 13–16 June 2024. Abstr. P932.

P959: CARTITUDE-4 subgroup analysis: Ciltacabtagene autoleucel (cilta-cel) vs SOC in patients with functionally high-risk (fHR) MM

Weisel K, et al.

Baseline characteristics

- Adults with MM and ECOG PS ≤1
- 1–3 prior LOT including PI + IMiD
- Lenalidomide refractory
- No prior CAR T or anti-BCMA

	1 prior LOT		1 prior LOT + fHR	
	Cilta-cel (n=68)	SOC (n=68)	Cilta-cel (n=40)	SOC (n=39)
Median age, years (range)	60.5 (27–78)	60.0 (35–78)	60.0 (27–71)	60.0 (40–78)
ISS stage II/III, %	29.4	32.4	30.0	35.9
High-risk cytogenetics*, %	57.4	66.2	55.0	69.2
With ≥2 high-risk abnormalities	29.4	29.4	32.5	30.8
Prior ASCT, %	82.4	88.2	82.5	84.6
Prior anti-CD38 antibody, %	2.9	4.4	5.0	2.6
High tumour burden, %	13.2	11.8	12.5	10.3
Soft tissue plasmacytoma, %	17.6	10.3	15.0	10.3

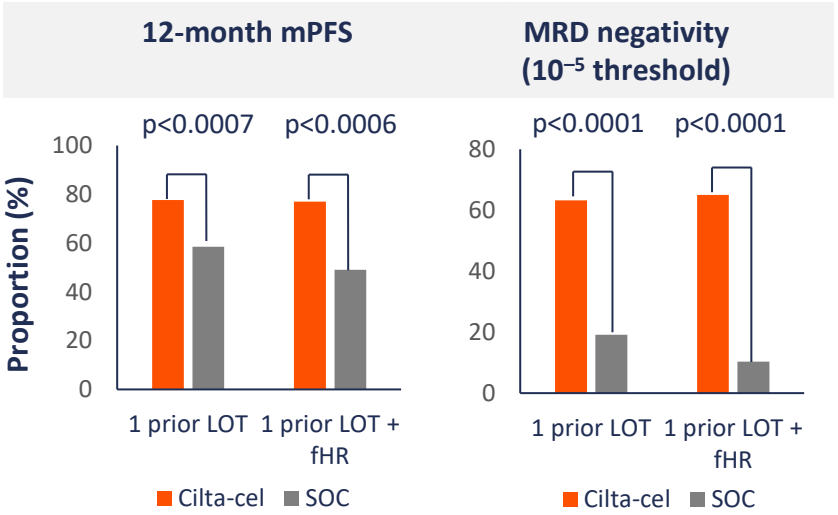
*High-risk cytogenetics defined as any of the following cytogenetic features: del17p, t(14;16), t(4;14), or gain/amp(1q).
ASCT, autologous stem cell transplant; BCMA, B-cell maturation antigen; CAR, chimeric antigen receptor; ECOG PS, Eastern Cooperative Oncology Group Performance Status; fHR, functionally high risk; IMiD, immunomodulatory drug; ISS, International Staging System; LOT, line of therapy; MM, multiple myeloma; PI, proteasome inhibitor; SOC, standard of care.
Weisel K, et al. Presented at EHA2024, Madrid, Spain, 13–16 June 2024. Abstr. P959.

P959: CARTITUDE-4 subgroup analysis: Ciltacabtagene autoleucel (cilta-cel) vs SOC in patients with functionally high-risk (fHR) MM

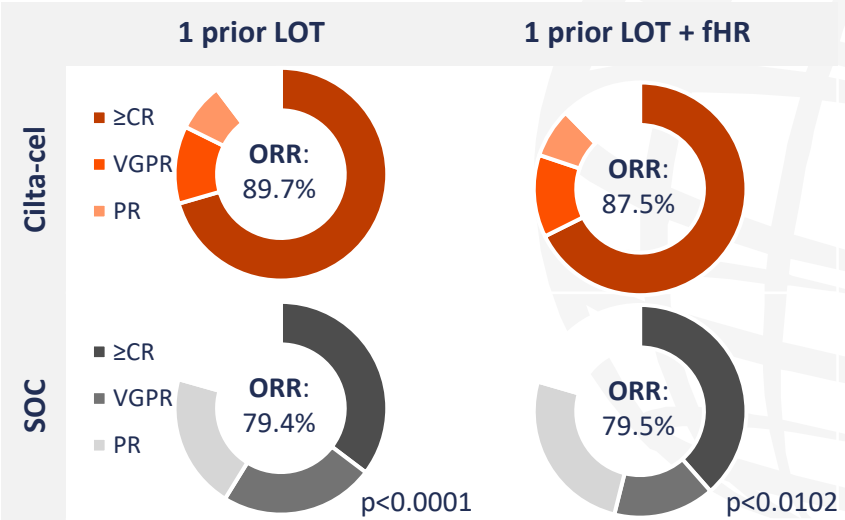
Weisel K, et al.

Efficacy outcomes

PFS and MRD-negativity



ORR



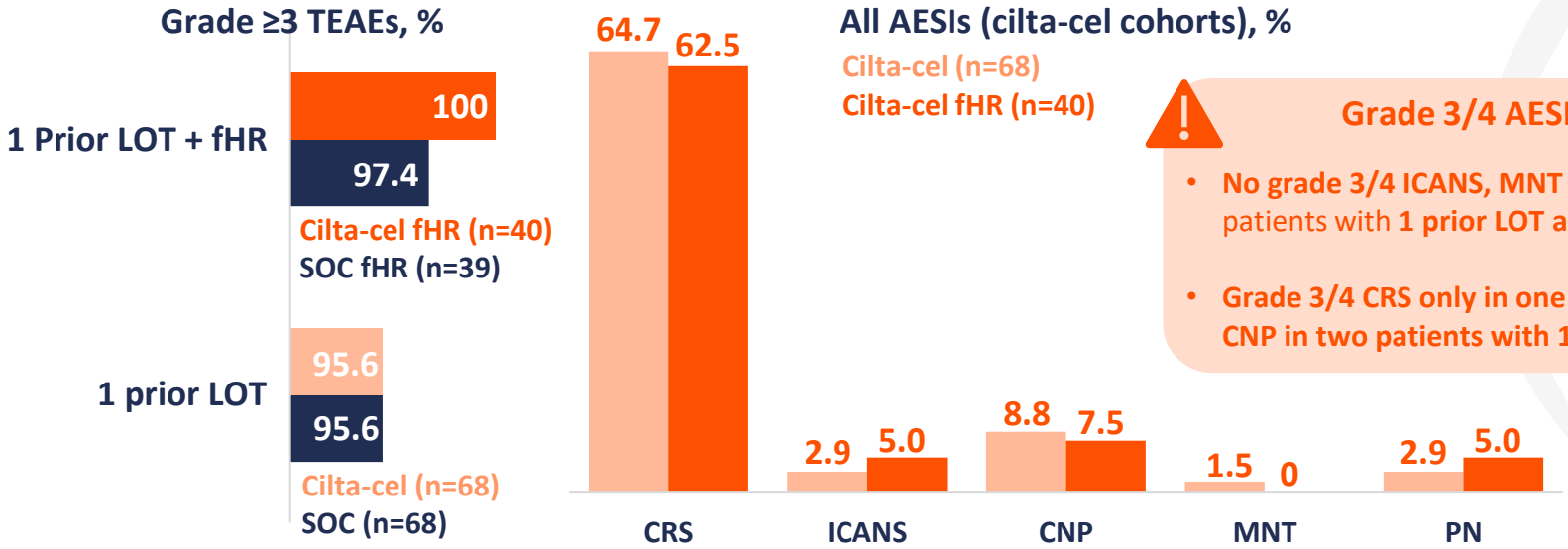
Regardless of functional risk strata, after 1 prior line of therapy, a single cilta-cel infusion substantially improved PFS and depth of response vs SOC in lenalidomide-refractory patients with MM.

CR, complete response; fHR, functionally high-risk; LOT, line of therapy; m, median; MM, multiple myeloma; MRD, minimal residual disease; ORR, overall response rate; PFS, progression-free survival; PR, partial response; SOC, standard of care; VGPR, very good PR. Weisel K, et al. Presented at EHA2024, Madrid, Spain, 13–16 June 2024. Abstr. P959.

P959: CARTITUDE-4 subgroup analysis: Ciltacabtagene autoleucel (cilta-cel) vs SOC in patients with functionally high-risk (fHR) MM

Weisel K, et al.

Safety profile



Grade 3/4 AESIs

- **No grade 3/4 ICANS, MNT or PN** in patients with **1 prior LOT and fHR**
- **Grade 3/4 CRS only in one patient,** and **CNP in two patients with 1 prior LOT**

AEs were generally similar in patients with 1 prior LOT and those with 1 prior LOT and functionally high-risk MM.

AE, adverse event; AESI, AE of special interest; CNP, cranial nerve palsy; CRS, cytokine release syndrome; fHR, functionally high-risk; ICANS, immune effector cell-associated neurotoxicity syndrome; LOT, line of therapy; MM, multiple myeloma; MNT, movement and neurocognitive TEAE; PN, peripheral neuropathy; SOC, standard of care; TEAE; treatment-emergent AE.

Weisel K, et al. Presented at EHA2024, Madrid, Spain, 13–16 June 2024. Abstr. P959.

P978: Phase III CARTITUDE-4 analysis by cytogenetic risk: Ciltacabtagene autoleucel (cilta-cel) vs standard of care in lenalidomide-refractory MM

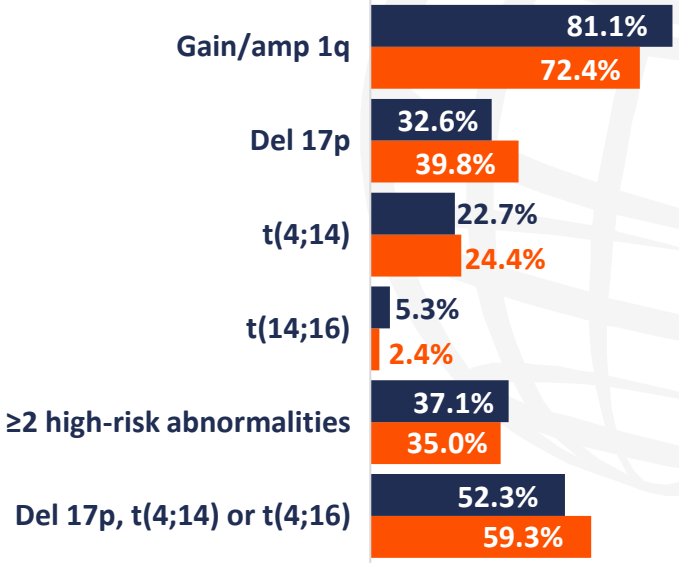
Mina R, et al.

Baseline characteristics and cytogenetic status

- Adults with MM and ECOG PS ≤1
- 1–3 prior lines including PI + IMiD
- Lenalidomide refractory
- No prior CAR T or anti-BCMA

	15.9 months median follow-up	
	High-risk	
	Cilta-cel (n=123)	SOC (n=132)
Median age, years (range)	62 (40–78)	62 (35–80)
Time since diagnosis, years (range)	3.2 (0.5–12.1)	3.4 (0.5–13.2)
Median prior lines of therapy, %		
1	31.7	34.1
2–3	68.3	65.9
Prior ASCT, %	84.6	90.9
Triple-class exposed, %	26.8	25.8
Soft tissue plasmacytomas, %	22.0	15.2

High-risk cytogenetics status

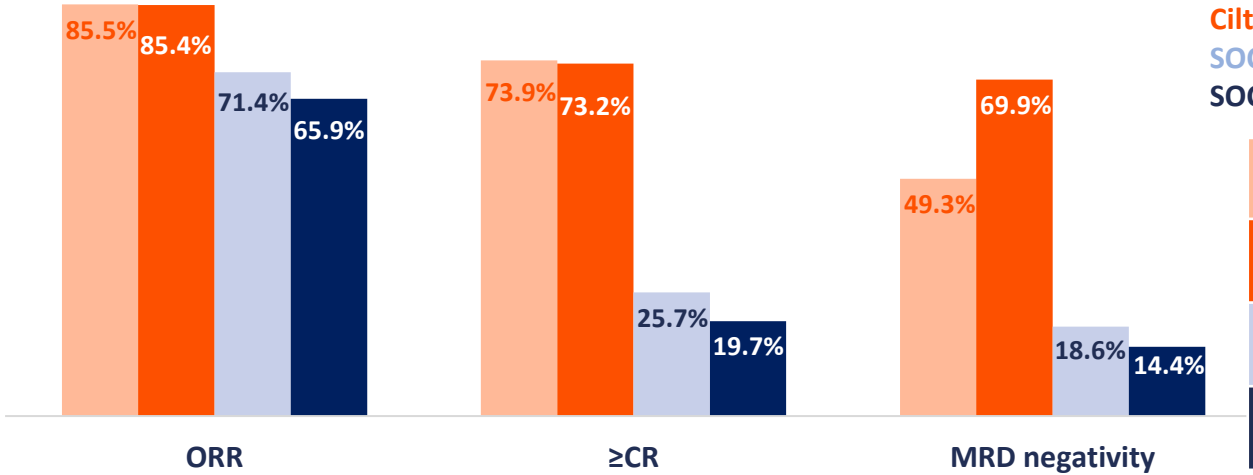


ASCT, autologous stem cell transplant; BCMA, B cell maturation antigen; CAR, chimeric antigen receptor; ECOG PS, Eastern Cooperative Oncology Group Performance Status; IMiD, immunomodulatory drug; MM, multiple myeloma; PI, proteasome inhibitor; SOC, standard of care. Mina R, et al. Presented at EHA2024, Madrid, Spain, 13–16 June 2024. Abstr. P978.

P978: Phase III CARTITUDE-4 analysis by cytogenetic risk: Ciltacabtagene autoleucel (cilta-cel) vs standard of care in lenalidomide-refractory MM

Mina R, et al.

Efficacy outcomes by cytogenetic risk*



Cilta-cel standard risk (n=69)
Cilta-cel high risk (n=123)
SOC standard risk (n=70)
SOC high risk (n=132)

	Median PFS, months (range)
Cilta-cel standard risk	NE (NE–NE)
Cilta-cel high risk	NE (18.4–NE)
SOC standard risk	20.6 (11.2–NE)
SOC high risk	10.3 (7.6–12.5)

Cilta-cel demonstrated favourable efficacy outcomes vs SOC in patients with high-risk and standard-risk cytogenetics.

*High-risk cytogenetic abnormalities, including t(4;14), del(17p), t(14;16), and gain/amp(1q).

CR, complete response; MM, multiple myeloma; MRD, minimal residual disease ($x10^{-5}$); NE, not evaluable; ORR, objective response rate; PFS, progression free survival; SOC, standard of care.

Mina R, et al. Presented at EHA2024, Madrid, Spain, 13–16 June 2024. Abstr. P978.

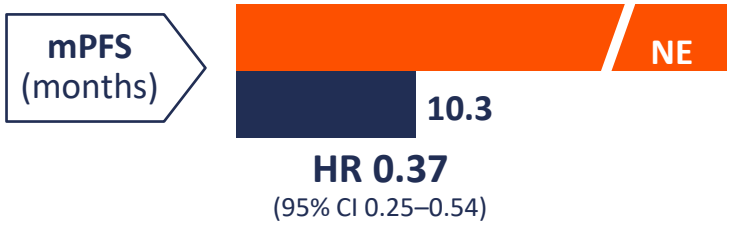
P978: Phase III CARTITUDE-4 analysis by cytogenetic risk: Ciltacabtagene autoleucel (cilta-cel) vs standard of care in lenalidomide-refractory MM

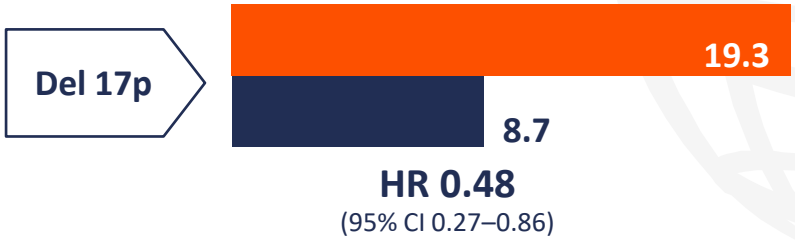
Mina R, et al.

mPFS by cytogenetic status and abnormalities

Cilta-cel high-risk (n=123)
SOC high-risk (n=132)

High-risk cytogenetics*





Cilta-cel lessens the impact of high-risk cytogenetics on PFS, and improved PFS compared with SOC.

*High-risk cytogenetic abnormalities, including t(4;14), del(17p), t(14;16), and gain/amp(1q).
CI, confidence interval; HR, hazard ratio; m, median; MM, multiple myeloma; NE, not evaluable; PFS, progression-free survival; SOC, standard of care.
Mina R, et al. Presented at EHA2024, Madrid, Spain, 13–16 June 2024. Abstr. P978.

New approaches to the use of existing BCMA-targeting agents

Prof. María-Victoria Mateos
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Recorded following **COMy** (23–26 May 2024, Paris, France)
and **EHA** (13–16 June 2024, Madrid, Spain)

LB3440: Phase III DREAMM-8 trial: Belantamab mafodotin plus pomalidomide and dexamethasone (BPd) vs PVd in RRMM

Dimopoulos MA, et al.

Baseline characteristics and treatment status

- Adults with MM
- Anti-BCMA and pomalidomide naive
- ≥1 prior line including lenalidomide
- PD on/after latest therapy
- Not refractory/intolerant to bortezomib

21.8 months' median follow-up
(0.03–39.23)

	Randomized (N=302)	
	BPd (ITT n=155)	PVd (ITT n=147)
Age, years (range)	67 (40–82)	68 (34–86)
Time since diagnosis, years (range)	4.04 (0.4–16.7)	3.43 (0.4–17.7)
Time to relapse after 1L therapy initiation, %		
≤12 months	14	14
>12 months	86	86
Extramedullary disease, %	13	7
PI exposed/refractory, %	90/26	93/24
Lenalidomide exposed/refractory, %	100/81	100/76
Anti-CD38 mAb exposed/refractory, %	25/23	29/24
Ongoing treatment	**36%**	**21%**

1L, first-line; BCMA, B cell maturation antigen; B, belantamab mafodotin; d, dexamethasone; ITT, intention-to-treat; P, pomalidomide; PD, progressive disease; PI, proteasome inhibitor; RRMM, relapsed/refractory multiple myeloma; V, bortezomib. Dimopoulos MA, et al. Presented at EHA2024, Madrid, Spain (June 13–16). Abstract: LB3440.

LB3440: Phase III DREAMM-8 trial: Belantamab mafodotin plus pomalidomide and dexamethasone (BPd) vs PVd in RRMM

Dimopoulos MA, et al.

Primary endpoint and key secondary endpoints

mPFS (months)

HR 0.52
(95% CI 0.37–0.73); p<0.001

PFS benefit seen consistently across all prespecified subgroups

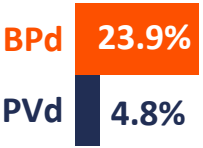
mDOR (months)

Ongoing response (% patients) **55%** vs **31%**

12-month OS

Median OS was NR in both arms (HR 0.77; 95% CI 0.53–1.14)

MRD negativity*



Favourable survival outcomes and treatment response with BPd vs PVd; additional OS follow-up is ongoing.

*Percentage of total ITT patients who were MRD negative by NGS based on sensitivity of 10^{-5}. Data shown for patients with complete response or better.
B, belantamab mafodotin; CI, confidence interval; d, dexamethasone; DOR, duration of response; HR, hazard ratio; ITT, intent-to-treat; m, median; MRD, minimal residual disease; NGS, next-generation sequencing; NR, not reached; OS, overall survival; P, pomalidomide; PFS, progression-free survival; RRMM, relapsed/refractory multiple myeloma; V, bortezomib.
Dimopoulos MA, et al. Presented at EHA2024, Madrid, Spain (June 13–16). Abstract: LB3440.

LB3440: Phase III DREAMM-8 trial: Belantamab mafodotin plus pomalidomide and dexamethasone (BPd) vs PVd in RRMM

Dimopoulos MA, et al.

Safety profile

Grade 3/4 AEs, %	BPd (n=150)	PVd (n=145)
Any	91	73
Neutropenia	57	39
Infections (grade ≥3)	49	26
Thrombocytopenia	38	29
Any ocular AESI	43	2
Blurred vision	17	0
Dry eye	8	0

Bilateral BCVA worsening in patients with normal baseline (20/25 or better in ≥1 eye)

BPd	20/50 or worse	20/200 or worse
Patients, %	34	1
Median time to first event, days (range)	112 (28–761)	351 (29–673)
First event resolved to normal baseline, %	84	50

Management of ocular AEs → 83% dose holds and 59% reduced dosing frequency → 9% discontinuation rate

Safety profile broadly consistent with known profiles of individual regimen components.
Visual acuity changes that could affect daily living were reversible in most BPd-treated patients.

AE, adverse event; AESI, AE of special interest; B, belantamab mafodotin; BCVA, best-corrected visual acuity; d, dexamethasone; P, pomalidomide; RRMM, relapsed/refractory multiple myeloma; V, bortezomib. Dimopoulos MA, et al. Presented at EHA2024, Madrid, Spain (June 13–16). Abstract: LB3440.

S214: Phase III DREAMM-7 trial: Belantamab mafodotin plus bortezomib and dexamethasone (BVd) vs DVd in RRMM

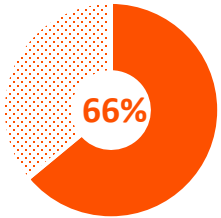
Mateos MV, et al.

Baseline characteristics and treatment status

- Anti-BCMA-naive adults with MM
- ≥1 prior line of therapy
- PD on/after latest therapy
- Not refractory/intolerant to bortezomib or daratumumab

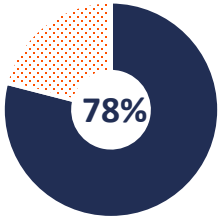
	Randomized (N=494)	
	BVd ITT n=243 (treated, n=242)	**DVd ITT n=251** (treated, n=246)
Age, years (range)	65 (34–86)	64 (32–89)
1 prior line of therapy, %	51	50
≥2 prior lines of therapy, %	48	50
Prior bortezomib, %	86	84
Prior lenalidomide, %	52	52
Lenalidomide refractory, %	33	35
Prior daratumumab, %	1	2
28.2 months median follow-up (0.1–40.0) / **Ongoing treatment**	**33%**	**20%**

Belantamab mafodotin discontinued (n=161)



- Progressive disease: 24%
- AE: 19%
- Physician decision: 14%
- Patient withdrawal: 9%
- Loss to follow up: <1%
- Protocol-defined stopping criteria reached: <1%

Daratumumab discontinued (n=195)



- Progressive disease: 59%
- AE: 9%
- Patient withdrawal: 5%
- Physician decision: 4%
- Loss to follow up: <1%
- Protocol deviation: <1%

AE, adverse event; B, belantamab mafodotin; BCMA, B cell maturation antigen; D, daratumumab; d, dexamethasone; ITT, intent-to-treat; PD, progressive disease; P, pomalidomide; RRMM, relapsed/refractory multiple myeloma; V, bortezomib. Mateos MV, et al. Presented at EHA2024, Madrid, Spain (June 13–16). Abstract: S214.

S214: Phase III DREAMM-7 trial: Belantamab mafodotin plus bortezomib and dexamethasone (BVd) vs DVd in RRMM

Mateos MV, et al.

Primary endpoint and key secondary endpoints

mPFS (months)

HR 0.41
(95% CI 0.31–0.53); p<0.00001

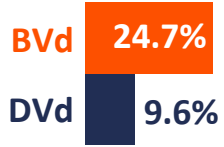
PFS benefit seen consistently across all prespecified subgroups

mDOR (months)

Ongoing response (% patients) **53%** vs **29%**

18-month OS

MRD negativity†



Median OS was NR in both arms (HR 0.57; 95% CI 0.4–0.8; p=0.00049*)

Favourable survival outcomes and treatment response with BVd vs DVd; additional OS follow-up is ongoing.

*The P value has not yet reached criteria for statistical significance (p≤0.00037) at interim analysis. †MRD negativity rate defined as percentage of patients who were MRD negative by NGS based on a sensitivity of 10^{-5}. B, belantamab mafodotin; CI, confidence interval; D, daratumumab; d, dexamethasone; DOR, duration of response; HR, hazard ratio; m, median; MRD, minimal residual disease; NR, not reached; OS, overall survival; PFS, progression-free survival; RRMM, relapsed/refractory multiple myeloma; V, bortezomib. Mateos MV, et al. Presented at EHA2024, Madrid, Spain (June 13–16). Abstract: S214.

S214: Phase III DREAMM-7 trial: Belantamab mafodotin plus bortezomib and dexamethasone (BVd) vs DVd in RRMM

Mateos MV, et al.

Safety profile

AEs (% patients)	BVd (N=242)	DVd (N=246)
Any grade 3/4	95	76
Leading to dose reduction	75	59
Leading to dose interruption/delay	94	75
Leading to discontinuation	31	19

Any grade ocular AEs (% patients)

Bilateral BCVA worsening in patients with normal baseline (20/25 or better in ≥1 eye)

BVd	20/50 or worse	20/200 or worse
Patients, %	34	2
Median time to first event, days (range)	73.5 (16–753)	105 (47–304)
First event resolved to normal baseline, % (n/N)	94 (77/82)	80 (4/5)

In BVd-treated patients with ocular events, 44% had dose reductions; 78% had dose delays/interruptions | 9% discontinuation rate

Safety profile broadly consistent with known profiles of individual regimen components.
Among all BVd-treated patients, ocular AEs led to low treatment discontinuations.

AE, adverse event; B, belantamab mafodotin; BCVA, best-corrected visual acuity; D, daratumumab; d, dexamethasone; RRMM, relapsed/refractory multiple myeloma; V, bortezomib.
Mateos MV, et al. Presented at EHA2024, Madrid, Spain (June 13–16). Abstract: S214.

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Phase III DREAMM-7 trial — additional analyses

P938: Subgroup analyses; Mateos MV, et al.

P945: PRO analyses; Hungria V, et al.

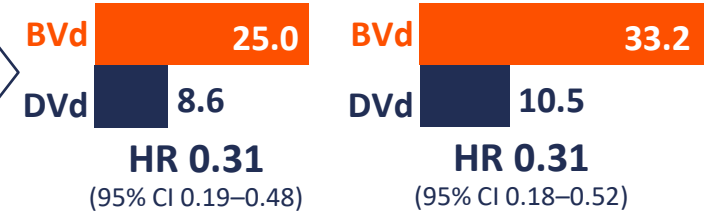
Efficacy in subgroups[1]

- Refractory to prior lenalidomide
- ≥1 high-risk cytogenetic abnormality

PROs[2]

- QoL, vision and functioning measures

mPFS (months)



ORR

N=494

BVd=243

DVd=251

>90% adherence to PRO assessments

PROs were stable over time and consistent between treatment arms, e.g.

- Global health/QoL assessments
- Role/physical functioning
- Fatigue
- Pain

- Eye-related side effects manageable with dose and schedule changes
- In patients with clinically meaningful deterioration in vision-related function, overall QoL comparable to that in all patients receiving DVd

B, belantamab mafodotin; CI, confidence interval; D, daratumumab; d, dexamethasone; HR, hazard ratio; LEN, lenalidomide; mPFS, median progression-free survival; ORR, objective response rate; PRO, patient-reported outcomes; QoL, quality of life; V, bortezomib.

1. Mateos MV, et al. Presented at EHA2024, Madrid, Spain (June 13–16). Abstract: P938; 2. Hungria V, et al. Presented at EHA2024, Madrid, Spain (June 13–16). Abstract: P945.

S205: CARTITUDE-2 trial Cohort D: Ciltacabtagene autoleucel (cilta-cel) ± LEN maintenance in newly diagnosed MM with suboptimal response to frontline ASCT

Roeloffzen W, et al.

Baseline characteristics and LEN maintenance status

- History of 4–8 cycles of initial therapy including induction, high-dose ChT and ASCT ± consolidation
- Overall best response <CR

	22.4 months median follow-up (4.7–39.3) N=17
Age, years (range)	54 (37–69)
Time from initial diagnosis to enrolment, years (range)	0.9 (0.6–1.4)
Prior PI and IMiD, %	100
Prior anti-CD38 mAb, %	17.6
High-risk cytogenetics, %	5.9

	10 mg daily LEN maintenance n=12
Time to LEN initiation, days (range)	51 (21–214)
Median duration, days (range)	426.5 (70–716)
Median cycles (range)	15 (3–26)
Median overall relative dose intensity (range)	93.4 (68–100)

ASCT, autologous stem cell transplant; ChT, chemotherapy; CR, complete response; IMiD, immunomodulatory drug; LEN, lenalidomide; mAb, monoclonal antibody; MM, multiple myeloma; PI, proteasome inhibitor.

Roeloffzen W, et al. Presented at EHA2024, Madrid, Spain (June 13–16). Abstract: S205.

S205: CARTITUDE-2 trial Cohort D: Ciltacabtagene autoleucel (cilta-cel) ± LEN maintenance in newly diagnosed MM with suboptimal response to frontline ASCT

Roeloffzen W, et al.

Key safety and efficacy outcomes

18-month DOR rate 93.3% (95% CI 61.3–99.0)

18-month PFS rate 93.8% (95% CI 63.2–99.1)

18-month OS rate 93.8% (95% CI 63.2–99.1)

Select TEAEs	Grade 3/4, %
Any	100
Neutropenia	82.4
Lymphopenia	58.8
Leukopenia	35.3
Infections	29.4
Thrombocytopenia	23.5

No cases of MNT/ parkinsonism were observed

One patient with ICANS, which resolved; six patients with other neurotoxicities (mostly grade 1/2)

No grade 3/4 CRS (82.4% grade 1/2)

Cilta-cel ± LEN maintenance is promising in patients with poor response to frontline ASCT, especially given the historically poorer clinical outcomes in this population.

ASCT, autologous stem cell transplant; CI, confidence interval; CR, complete response; CRS, cytokine release syndrome; DOR, duration of response; ICANS, immune effector cell-associated neurotoxicity syndrome; LEN, lenalidomide; MM, multiple myeloma; MNT, movement and neurocognitive TEAE; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; sCR, stringent CR; TEAE, treatment emergent adverse event. Roeloffzen W, et al. Presented at EHA2024, Madrid, Spain (June 13–16). Abstract: S205.

touch HAEMATOLOGY

S208: KarMMa-2 trial Cohort 2b: Idecabtagene vicleucel (ide-cel) in clinical high-risk early relapse MM without frontline ASCT

Leleu X, et al.

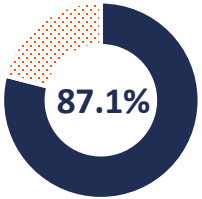
Baseline characteristics and frontline and/or bridging therapy status

- Early relapse (PD <18 months from frontline therapy without ASCT)
- Frontline therapy included PI, IMiD and dexamethasone
- Measurable disease
- ECOG PS ≤1

	30.1 months median follow-up (1.0–51.4) Treated (n=31)
Age, years (range)	60 (32–77)
Median time to progression on frontline tx, months (range)	7.1 (1.7–16.5)
High tumour burden, %	45.2
High-risk cytogenetics, %	38.7
Extramedullary disease, %	12.9
Double-class refractory, %	67.7
Triple-class refractory, %	16.1

Frontline therapy (%)	Treated (n=31)
VRd/VTd	38.7
KRd	9.7
Ixad	3.2
Rd	3.2
DRd	3.2
Other	41.9

Bridging therapy



Regimen type

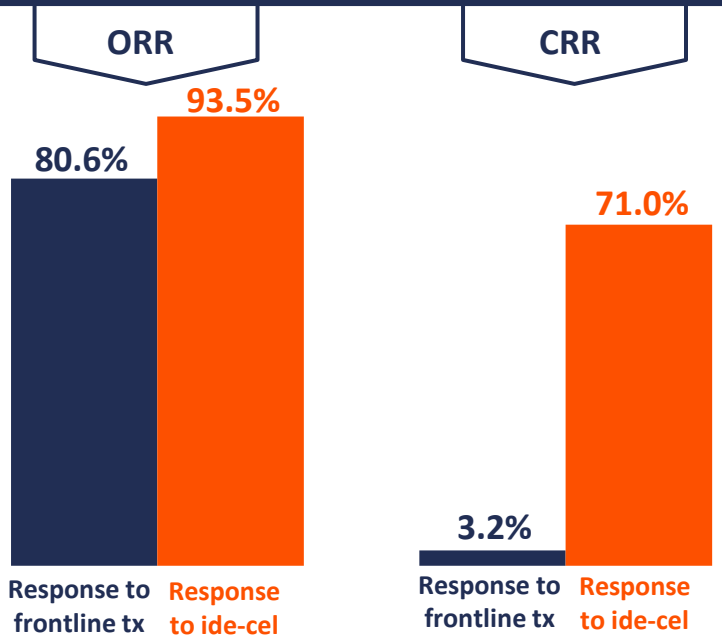
- Bortezomib: 25.9%
- Carfilzomib: 44.4%
- Daratumumab: 11.1%
- Other: 18.5%

ASCT, autologous stem cell transplant; D, daratumumab; d, dexamethosone; ECOG PS, European Cooperative Oncology Group Performance Status; IMiD, immunomodulatory drug; Ixa, ixazomib; K, carfilzomib; MM, multiple myeloma; PD, progressive disease; PI, proteasome inhibitor; R, lenalidomide; T, thalidomide; tx, treatment; V, bortezomib. Leleu X, et al. Presented at EHA2024, Madrid, Spain (June 13–16). Abstract: S208.

S208: KarMMa-2 trial Cohort 2b: Idecabtagene vicleucel (ide-cel) in clinical high-risk early relapse MM without frontline ASCT

Leleu X, et al.

Key efficacy outcomes



DOR rate at 24 months

With response	65.3%	n = 29
With ≥CR	75.7%	n = 22

Median DOR was not reached

Survival rates at 12 and 24 months (n=31)

PFS

12 months	70.0%
24 months	63.3%

Median PFS was not reached

OS

12 months	89.9%
24 months	78.9%

Median OS was not reached

ASCT, autologous stem cell transplant; CR, complete response; CRR, CR rate; DOR, duration of response; MM, multiple myeloma; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; tx, treatment.

Leleu X, et al. Presented at EHA2024, Madrid, Spain (June 13–16). Abstract: S208.

S208: KarMMa-2 trial Cohort 2b: Idecabtagene vicleucel (ide-cel) in clinical high-risk early relapse MM without frontline ASCT

Leleu X, et al.

Safety profile

Grade ≥3 AEs, %	n=31
Any AE	93.5
Haematologic AEs	
Neutropenia	93.5
Anaemia	54.8
Lymphopenia	45.2
Leukopenia	38.7
Thrombocytopenia	35.5

- Grade 3/4 infection and infestations occurred in 19.4% of patients

CRS	n=31
Grade 1/2	83.9%
Median time to onset, days (range)	1.0 (1–9)
Median duration, days (range)	3.0 (1–16)

94.4% of CRS events were managed with tocilizumab

iiNT	n=31
Grade 1/2	9.7%
Median time to onset, days (range)	2.0 (1–16)
Median duration, days (range)	6.0 (1–11)

Events were managed with:
- Tocilizumab (33.3%)
- Steroids (33.3%)
- Anakinra (33.3%)

⚠ No grade 3/4 CRS or iiNT events were observed

Ide-cel showed a favourable risk–benefit profile in clinical high-risk patients with MM who experienced relapse on frontline therapy (excluding ASCT), highlighting potential use in earlier lines of therapy

AE, adverse event; ASCT, autologous stem cell transplant; CRS, cytokine release syndrome; iiNT, investigator-identified neurotoxicity; MM, multiple myeloma.
Leleu X, et al. Presented at EHA2024, Madrid, Spain (June 13–16). Abstract: S208.

Emerging BCMA-targeting agents

Prof. María-Victoria Mateos
University of Salamanca
Spain

Recorded following **COMy** (23–26 May 2024, Paris, France)
and **EHA** (13–16 June 2024, Madrid, Spain)

COMy Oral: LINKER-MM1 trial: Efficacy and safety of 200 mg linvoseltamab – a CD3 x BCMA bispecific antibody – in RRMM, including difficult-to-treat subgroups

Jagannath S, et al.

Baseline characteristics and treatment schedule

- Active MM that progressed on/after ≥3 lines of therapy including a PI, IMiD and anti-CD38 antibody
- Double- or triple-class refractory

11.1 months median follow-up

200 mg (N=117)

Patient characteristics

Median age, years (range)	70 (37–91)
Extramedullary plasmacytomas per IRC, %	16.2
Prior autologous transplant, %	65.0
Number of prior lines, median (range)	5 (2–16)
At least triple-class exposed/refractory, %	100/82.1
Refractory to last line of therapy, %	85.5
High-risk cytogenetics, %	39.3
ISS stage I–II, %	76.9
ISS stage III, %	17.9

IV dosing: Phase II expansion cohort

Weeks 1–2 Step-up doses	5 mg → Day 1 25 mg → Day 8
Weeks 3–14 200 mg	Once a week
Weeks 16–23 200 mg	Every 2 weeks
Week 24 onward 200 mg	≥ VGPR → every 4 weeks < VGPR → every 2 weeks

Primary

- Ph I: Safety
- Ph 2: ORR by IRC

Secondary

- Ph I: ORR
- Ph 2: Safety, DOR, PFS, OS

BCMA, B-cell maturation antigen; DOR, duration of response; IMiD, immunomodulatory drug; IRC, independent review committee; ISS, International Staging System; IV, intravenous; ORR, objective response rate; OS, overall survival; PFS, progression free survival; PI, proteasome inhibitor; RRMM, relapsed/refractory multiple myeloma; VGPR, very good partial response.

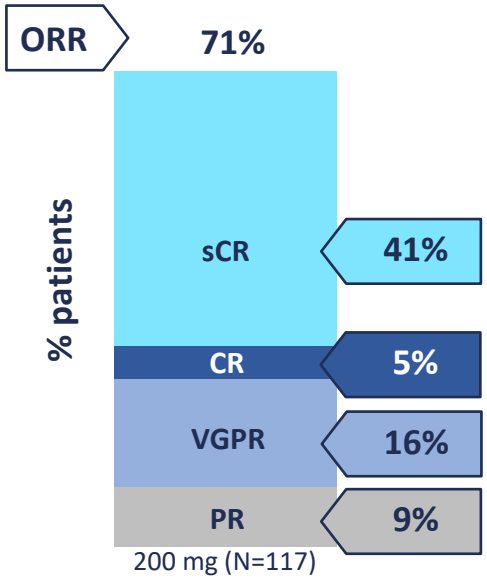
Jagannath S, et al. Presented at COMy, Paris, France, 23–26 May 2024. Available On-Demand at: https://comylive.cme-congresses.com/ (accessed 06 August 2024).

COMy Oral: LINKER-MM1 trial: Efficacy and safety of 200 mg linvoseltamab – a CD3 x BCMA bispecific antibody – in RRMM, including difficult-to-treat subgroups

Jagannath S, et al.

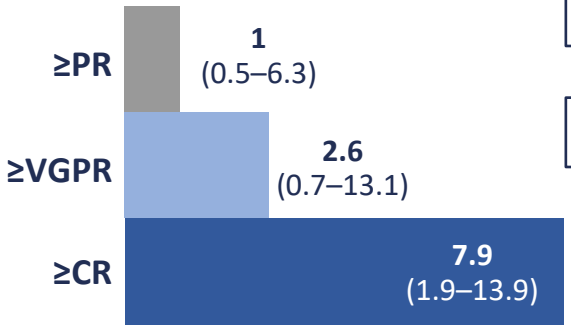
Results

IRC-assessed ORR



Median time to response

months (range)



Responses continued to deepen after switch to once every 4 weeks dosing:
48% (n/N=14/29) in VGPR achieved ≥CR after dosing switch

Response by cytogenetics

mDOR: **Not reached** (95% CI 14.2 months–NE)

Estimated probability at 12 months of:

- **78%** maintaining a response
- **68.8%** being progression-free
- **74.5%** survival

BCMA, B-cell maturation antigen; CI, confidence interval; CR, complete response; IRC, independent review committee; mDOR, median duration of response; NE, not evaluable; ORR, objective response rate; PR, partial response; RRMM, relapsed/refractory multiple myeloma; sCR, stringent CR; VGPR, very good partial response.

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COMy Oral: LINKER-MM1 trial: Efficacy and safety of 200 mg linvoseltamab – a CD3 x BCMA bispecific antibody – in RRMM, including difficult-to-treat subgroups

Jagannath S, et al.

Safety profile

Grade 3/4 TEAEs, %	N=117
Any	72.6
Haematologic	
Neutropenia	40.2
Anaemia	30.8
Non-haematologic	
COVID-19	8.5
Hypokalaemia	3.4
Diarrhoea	1.7
CRS	0.9
Headache	0.9

Median exposure to treatment (200 mg): **47.4 weeks**

CRS
- Occurred in **46.2%** of patients (any grade)

ICANS
- Occurred in **7.7%** of patients
- All events concurrent with CRS or immune-related reactions

Infections
- Occurred in **73%** of patients
- Grade 3/4 in **34%** of patients

TEAEs

Six patients experienced TEAEs leading to death within 30 days of the last treatment doses:
- Five due to infection
- One due to renal failure

Linvoseltamab demonstrated high efficacy in late-stage RRMM, including in pre-specified high-risk subgroups, and with an acceptable safety profile.

BCMA, B-cell maturation antigen; CRS, cytokine release syndrome; ICANs, immune effector cell-associated neurotoxicity syndrome; RRMM, relapsed/refractory multiple myeloma; TEAE, treatment emergent adverse event.

Jagannath S, et al. Presented at COMy, Paris, France, 23–26 May 2024. Available On-Demand at: https://comylive.cme-congresses.com/ (accessed 06 August 2024).

S211: Efficacy, safety and recommended phase II dose finding for the BCMA bispecific antibody ABBV-383 in RRMM

Weisel K, et al.

Baseline characteristics

- Adult patients with RRMM who received ≥3 prior lines of therapy
- Prior exposure to PI, IMiD and anti-CD38 mAb
- ECOG PS 0–2
- No prior BCMA-targeted therapy

12.1 months median follow-up (0.8–13.0)

	Q4W 60 mg (n=21)
Median age, years (range)	67 (51–87)
Median prior lines of therapy, (range)	4 (3–23)
Extramedullary disease, %	19
Triple-class refractory, %	81
Penta-class refractory, %	38
Treatment ongoing	48%

Primary reason for treatment discontinuation

- **29%** Disease progression
- **14%** DLT/TEAE
- **10%** Withdrawal of consent

Deaths following last dose:

- Two patients died within 30 days
- Two patients died within 90 days

BCMA, B-cell maturation antigen; DLT, dose-limiting toxicity; ECOG PS, Eastern Cooperative Oncology Working Group Performance Status; IMiD, immunomodulatory drug; mAb, monoclonal antibody; PI, proteasome inhibitor; Q4W, every 4 weeks; RRMM, relapsed/refractory multiple myeloma; TEAE, treatment emergent adverse event.

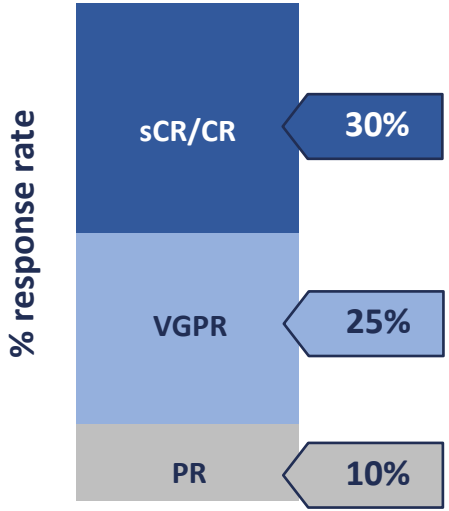
Weisel K, et al. Presented at EHA2024, Madrid, Spain, 13–16 June 2024. Abstr. S211.

S211: Efficacy, safety and recommended phase II dose finding for the BCMA bispecific antibody ABBV-383 in RRMM

Weisel K, et al.

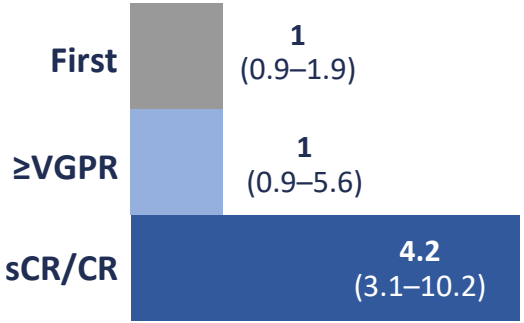
Efficacy

ORR 65% ≥VGPR 55%



Median time to response

months (range), n=13



Median DOR: **months** (95% CI)

- PR or better (n=13): **NR** (4.6–NR)
- CR or better (n=6): **NR** (NR–NR)

Survival outcomes

	Q4W 60 mg (n=21)
mPFS, months (95% CI)	NR (2.8–NR)
PFS at 12 months, % (95% CI)	54.8 (30.5–73.2)

BCMA, B-cell maturation antigen; CI, confidence interval; CR, complete response; DOR, duration of response; m, median; NR, not reached; ORR, objective response rate; PFS, progression-free survival; PR, partial response; Q4W, every 4 weeks; RRMM, relapsed/refractory multiple myeloma; sCR, stringent CR; VGPR, very good partial response.

Weisel K, et al. Presented at EHA2024, Madrid, Spain, 13–16 June 2024. Abstr. S211.

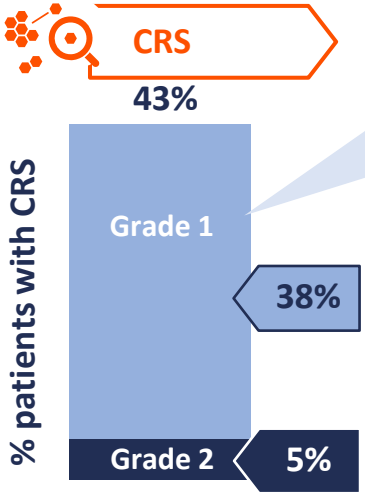
S211: Efficacy, safety and recommended phase II dose finding for the BCMA bispecific antibody ABBV-383 in RRMM

Weisel K, et al.

Safety profile

Grade 3/4 TEAEs, %	Q4W 60 mg (n=21)
Any	86
Haematologic	
Lymphopenia	43
Neutropenia	29
Anaemia	29
Thrombocytopenia	19

No non-haematologic grade 3/4 TEAEs



- CRS onset typically occurred on the same day following first dose
- Quick recovery with standard care
- Most events were grade 1 and did not recur

ICANS

- One patient experienced grade 2 ICANS
- No other ICANS events reported

Optimal dose of Q4W 60 mg ABBV-383 monotherapy was selected on the basis of safety and efficacy, resulting in deep, durable responses.

BCMA, B-cell maturation antigen; CRS, cytokine release syndrome; ICANs, immune effector cell-associated neurotoxicity syndrome; Q4W, every 4 weeks; RRMM, relapsed/refractory multiple myeloma; TEAE, treatment emergent adverse event.

Weisel K, et al. Presented at EHA2024, Madrid, Spain, 13–16 June 2024. Abstr. S211.

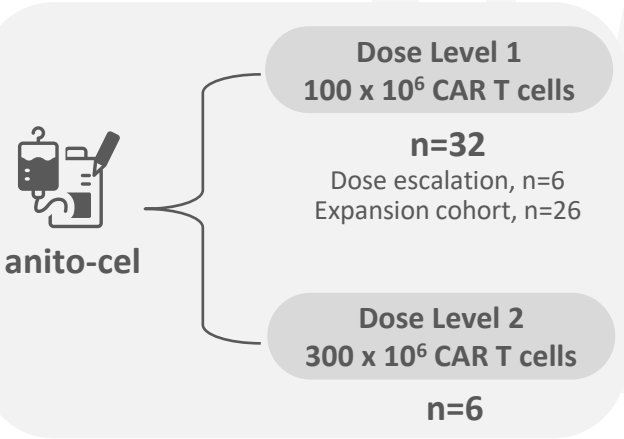
S207: ≥1 year follow-up phase I data: Anitocabtagene autoleucel (anito-cel) in RRMM

Frigault M, et al.

Baseline characteristics

- Received ≥3 prior lines of therapy or triple-refractory
- Prior PI, IMiD and CD38-targeted therapy

	26.5 months median follow-up (14–44)
	All (N=38)
Median age, years (range)	66 (44–76)
Median prior lines of therapy, (range)	4 (3–16)
Extramedullary disease, %	34
High-risk cytogenetics, %	29
Triple refractory, %	100
Penta refractory, %	68



ASCT, autologous stem cell transplant; CAR, chimeric antigen receptor; IMiD, immunomodulatory drug; PI, proteasome inhibitor; RRMM, relapsed/refractory multiple myeloma.

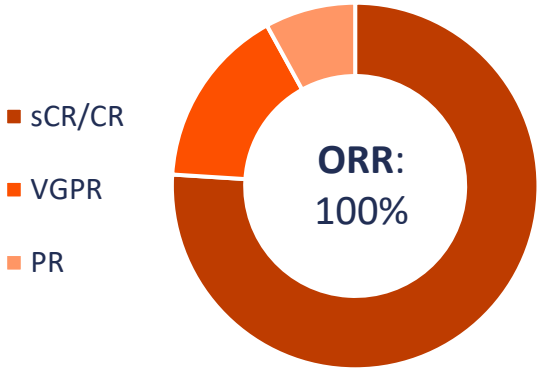
Frigault M, et al. Presented at EHA2024 by Dhakal B, Madrid, Spain, 13–16 June 2024. Abstr. S207.

S207: ≥1 year follow-up phase I data: Anitocabtagene autoleucel (anito-cel) in RRMM

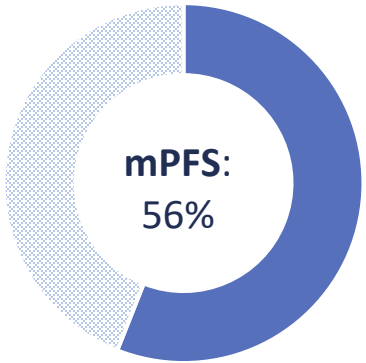
Frigault M, et al.

Efficacy outcomes (N=38)

Best overall response



PFS rate at 24 months



- **sCR/CR rates** >80% in all sub-groups including high-risk (EMD, high-risk cytogenetics, age ≥65 years)
- 89% of MRD evaluable patients (n=25/28) MRD negative
- **Median PFS, DOR** and **OS** not reached at 2 years of follow-up (median 26.5 months)
- Similar deep and durable efficacy observed in high-risk patient sub-groups

CR, complete response; DOR, duration of response; EMD, extramedullary disease; m, median; MRD, minimal residual disease; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; PR, partial response; RRMM, relapsed/refractory multiple myeloma; sCR, stringent CR; VGPR, very good partial response.

Frigault M, et al. Presented at EHA2024 by Dhakal B, Madrid, Spain, 13–16 June 2024. Abstr. S207.

S207: ≥1 year follow-up phase I data: Anitocabtagene autoleucel (anito-cel) in RRMM

Frigault M, et al.

Safety profile

Grade 3/4 haematologic AEs ≥5% after cell infusion, %	N=38
Neutropenia	81.6
Anaemia	57.9
Thrombocytopenia	42.1
Lymphopenia	39.5
Leukopenia	18.4
Febrile neutropenia	13.2

Non haematologic AEs (non-CRS/ICANS) all ≤7.9%

Grade 3 CRS

- Dose level 1: Occurred in **0** patients
- Dose level 2: Occurred in **1** patient

Grade 3 ICANS

- Dose level 1: Occurred in **1** patient
- Dose level 2: Occurred in **1** patient

Other

During follow-up period:

- No delayed neurotoxicities
- No Guillan–Barré syndrome
- No cranial nerve palsies
- No parkinsonian-like syndromes

Anito-cel showed efficacy even in high-risk subgroups, and with a manageable safety profile
A phase II study (iMMagine-1) is now enrolling.

Dose level 1: 100 x 10^6 CAR T cells (n=32); dose level 2 300 x 10^6 CAR T cells (n=6).
AE, adverse events; CRS, cytokine release syndrome; ICANS, immune effector cell-associated neurotoxicity syndrome; RRMM, relapsed/refractory multiple myeloma.
Frigault M, et al. Presented at EHA2024, Madrid, Spain, 13–16 June 2024. Abstr. S207.

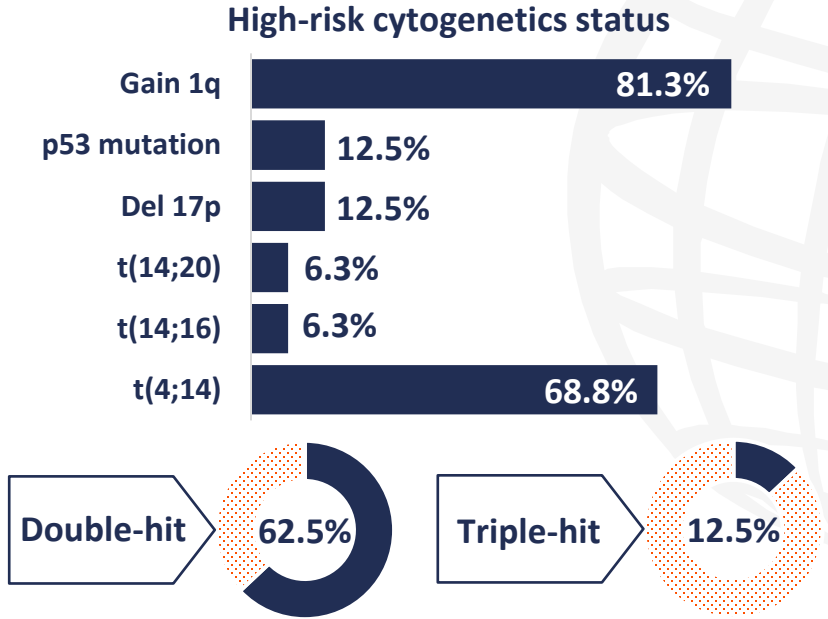
S206: FUMANBA-2: Equecabtagene autoleucel (eque-cel) in high-risk newly diagnosed MM

Chen L, et al.

Baseline characteristics and cytogenetic status

- Adults with newly diagnosed MM
- Ineligible for ASCT
- ECOG PS 0–1
- High-risk features (R-ISS stage III; mSMART 3.0 criteria)

	13.1 months median follow-up
	All (N=16)
Median age, years (range)	58.5 (51–69)
Extramedullary disease, %	25
R-ISS Stage II, %	62.5
R-ISS Stage III, %	37.5
High-risk cytogenetics, %	100
Double-hit and R-ISS III, %	6.3
Triple-hit and R-ISS III, %	6.3



ASCT, autologous stem cell transplant; ECOG PS, Eastern Cooperative Oncology Group Performance Status; MM, multiple myeloma; mSMART, Stratification for Myeloma and Risk-Adapted Therapy; R-ISS, Revised-International Staging System.

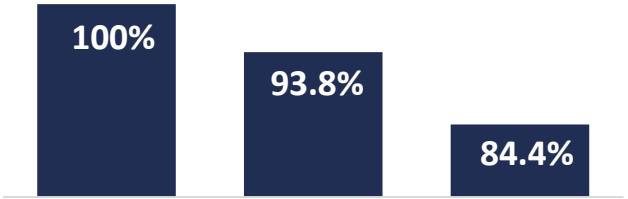
Chen L, et al. Presented at EHA2024, Madrid, Spain, 13–16 June 2024. Abstr. S206.

S206: FUMANBA-2: Equecabtagene autoleucel (eque-cel) in high-risk newly diagnosed MM

Chen L, et al.

Efficacy outcomes (N=16)

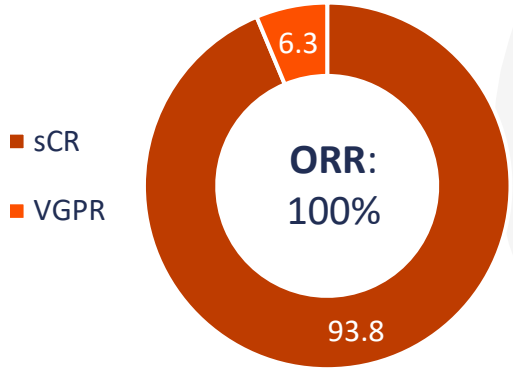
PFS rates



NB: median PFS not yet reached

Sustained MRD negativity rates

Best overall response



sCR rates similar in patients with high-risk features:

- **EMD:** 100% (n=4)
- **R-ISS stage III:** 83.3% (n=6)
- **Double/triple-hit:** 100% (n=10)

EMD, extramedullary disease; MM, multiple myeloma; MRD, minimal residual disease; ORR, objective response rate; PFS, progression-free survival; R-ISS, Revised-International Staging System; sCR, stringent complete response; VGPR, very good partial response.

Chen L, et al. Presented at EHA2024, Madrid, Spain, 13–16 June 2024. Abstr. S206.

S206: FUMANBA-2: Equecabtagene autoleucel (eque-cel) in high-risk newly diagnosed MM

Chen L, et al.

Safety profile

Grade ≥3 TRAEs, %	N=16
Any TRAE	100
Haematologic	
Neutropenia	81.3
Lymphocytopenia	68.8
Leukopenia	62.5
Infections	
Pneumonia	18.8
COVID-19 pneumonia	6.3
Hepatitis B	6.3

No grade ≥3 CRS and no ICANS or neurotoxicity were observed

CRS

- Any grade: **11** (68.8%) patients
- Grade 1: **8** (50.0%) patients
- Grade 2: **3** (18.8%) patients
- Median time of onset: **7 days**
- Median duration: **3 days**

Other

- No extra safety signals observed
- One death due to COVID-19 infection; not attributed to eque-cel

Eque-cel showed efficacy and favourable safety in transplant-ineligible subjects with high-risk newly diagnosed MM

CRS, cytokine release syndrome; ICANS, immune effector cell-associated neurotoxicity syndrome; MM, multiple myeloma; TRAE, treatment-related adverse event.

Chen L, et al. Presented at EHA2024, Madrid, Spain, 13–16 June 2024. Abstr. S206.