ASH 2024 updates
Bi-specific antibodies

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Newly diagnosed

Phase 2 Study of Teclistamab-based Induction Regimens in Patients With Transplant-eligible Newly Diagnosed Multiple Myeloma: Results From the GMMG-HD10/DSMM-XX (MajesTEC-5) Trial*

deutsche studiengruppe multiples myelom

dsmm

doing studies on multiple myeloma

*ClinicalTrials.gov Identifier: NCT05695508; sponsored by the University of Heidelberg Medical Center and is in collaboration with Janssen Research & Development, LLC

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https://www.congresshub.com/ASH2024/Oncology/Teclistamab/Raab

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Presented by MS Raab at the 66th American Society of Hematology (ASH) Annual Meeting and Exposition; December 7-10, 2024; San Diego, CA, USA

GMMG-HD10/DSMM-XX/MajesTEC-5: Introduction

- Teclistamab (Tec), a first-in-class BCMA × CD3 BsAb with weight-based dosing, is approved in TCE RRMM and is being evaluated as monotherapy in early-line RRMM and in daratumumab (Dara)-based combinations in early-line RRMM and NDMM[1-7]
- Dara-based triplet and quadruplet therapies (DRd, DVRd) have extended survival in NDMM[8-10]
  - MRD negativity (10^{-5}) of 57.5% post-consolidation with DVRd in TE NDMM in the PERSEUS study[11]
- Rationale for Tec-DR or Tec-DVR in transplant-eligible NDMM:
  - Target treatment-naive T cells for potential early eradication of all myeloma subclones to further improve rates of MRD-negativity and long-term outcomes
  - Potentially further augment T-cell cytotoxic activity and enhance efficacy by combining Tec with Dara and Len[12,13]
  - Improve patient outcomes with a steroid-sparing regimen
- MajesTEC-5 is the first study to evaluate the efficacy and safety of Tec-DR[a] and Tec-DVR[a] induction in patients with TE NDMM; here, we present initial outcomes from 3 induction cohorts in our phase 2 study

[a]Dexamethasone was also administered in C1 and C2.

BCMA, B-cell maturation antigen; BsAb, bispecific antibody; C, Cycle; D, daratumumab; d, dexamethasone; GMMG/DSMM, German-speaking Myeloma Multicenter Group/Deutsche Studiengruppe Multiples Myelom; MRD, minimal residual disease; NDMM, newly diagnosed multiple myeloma; R, lenalidomide; RRMM, relapsed/refractory multiple myeloma; TCE, triple-class–exposed; TE, transplant-eligible; Tec, teclistamab; V, bortezomib.

1. TECVAYLI® (teclistamab). Summary of product characteristics. Janssen Biologics BV; 2024. 2. TECVAYLI® (teclistamab-cqyv) injection [package insert]. Janssen Biotech, Inc.; 2024. 3. Moreau P, et al. *N Engl J Med*. 2022;387(6):495-505. 4. Garfall AL, et al. *J Clin Oncol*. 2024;42(16 suppl). Abstract 7540. 5. Touzeau C, et al. *J Clin Oncol*. 2024;42(16 suppl). Abstract 7506. 6. Searle E, et al. *Blood*. 2022;140(suppl 1):394-396. 7. Rodriguez-Otero P, et al. *Blood*. 2021;138(suppl 1):1647. 8. Facon T, et al. *Lancet Oncol*. 2021;22(11):1582-1596. 9. Sonneveld P, et al. *N Engl J Med*. 2024;390(4):301-313. 10. Facon T, et al. *N Engl J Med*. 2019;380(22):2104-2115. 11. Rodriguez-Otero P, et al. Presented at: American Society of Clinical Oncology (ASCO) Annual Meeting; May 31-June 4, 2024; Chicago, IL, USA. Abstract 7502. 12. Frerichs KA, et al. *Clin Cancer Res*. 2020:26(9):2203-2215.13. Cho SF, et al. *Blood Adv*. 2020;4(17):4195-4207.

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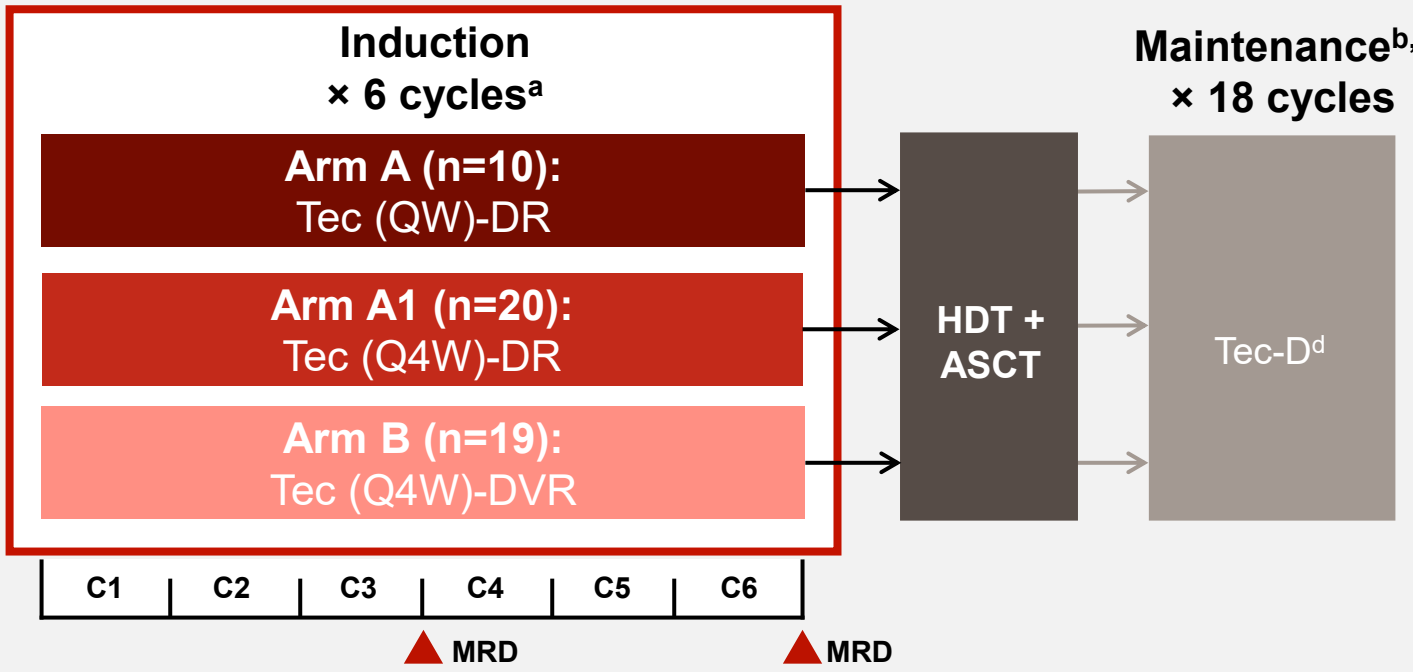
GMMG-HD10/DSMM-XX/MajesTEC-5: Study Design

Key eligibility criteria:

- TE NDMM
- ECOG PS score of 0-2
- Aged 18-70 years



Primary endpoint:
- AEs, SAEs

Select secondary endpoints:
- MRD negativity (10^{-5})
- ORR
- ≥CR
- ≥VGPR
- Stem cell yield

- Per protocol, MRD assessments by NGF were planned following completion of C3 and C6 in all patients
- Additional cohorts evaluating Tal and Tec/Tal combinations are also being investigated as part of this study

[a]Each cycle is 28 days. Dexamethasone was also administered in C1 and C2. Stem cell collection was planned after 3 cycles of induction. [b]Following maintenance therapy, patients could receive additional SoC maintenance treatment per institutional standard and local investigator decision. [c]Maintenance treatment can be discontinued when 12 months of sustained MRD negativity (10^{-5}) have been observed, beginning in induction. [d]Planned maintenance treatment in Arm A was Tec-DR. A protocol amendment permitted patients initially assigned to Tec-DR maintenance to receive Tec-D maintenance per investigator's choice (patients who started Tec-DR may have discontinued Len to receive Tec-D per investigator's choice).
AE, adverse event; ASCT, autologous stem cell transplant; C, Cycle; CR, complete response; D, daratumumab; ECOG PS, Eastern Cooperative Oncology Group performance status; GMMG/DSMM, German-speaking Myeloma Multicenter Group/Deutsche Studiengruppe Multiples Myelom; HDT, high-dose therapy; Len, lenalidomide; MRD, minimal residual disease; NDMM, newly diagnosed multiple myeloma; NGF, next-generation flow cytometry; ORR, overall response rate; QW, weekly; Q4W, every 4 weeks; R, lenalidomide; SAE, serious adverse event; SoC, standard-of-care; Tal, talquetamab; TE, transplant-eligible; Tec, teclistamab; V, bortezomib; VGPR, very good partial response.

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GMMG-HD10/DSMM-XX/MajesTEC-5: Patients With High-risk Disease Were Well Represented

	Arm A: Tec (QW)-DR (n=10)	Arm A1: Tec (Q4W)-DR (n=20)	Arm B: Tec (Q4W)-DVR (n=19)	Total (N=49)
Median age, years (range)	63.0 (54-66)	57.5 (36-65)	56.0 (30-68)	58.0 (30-68)
≥65, n (%)	3 (30)	2 (10)	3 (15.8)	8 (16.3)
Male, n (%)	6 (60)	13 (65)	12 (63.2)	31 (63.3)
Ethnicity, n (%)				
Caucasian	10 (100)	20 (100)	19 (100)	49 (100)
ECOG PS score, n (%)				
≤1	9 (90)	20 (100)	18 (94.7)	47 (95.9)
2	1 (10)	0	1 (5.3)	2 (4.1)
≥60% BMPCs, n (%)	4 (40)	10 (50)	8 (42.1)	22 (44.9)
≥1 soft tissue plasmacytoma,[a] n (%)	0	5 (25)	3 (15.8)	8 (16.3)
ISS disease stage, n (%)				
I	8 (80)	10 (50)	10 (52.6)	28 (57.1)
II	1 (10)	7 (35)	7 (36.8)	15 (30.6)
III	1 (10)	3 (15)	2 (10.5)	6 (12.2)
High cytogenetic risk,[b] n (%)	1 (10)	5 (25)	4 (21.1)	10 (20.4)

Data cutoff: September 30, 2024. [a]All bone-related soft tissue plasmacytomas; no extramedullary soft tissue plasmacytomas. [b]Cytogenetic risk is based on central FISH or local FISH and karyotype testing if central FISH is unavailable. High cytogenetic risk is defined as the presence of ≥1 of the following abnormalities: del(17p), t(4;14), or t(14;16).
BMPC, bone marrow plasma cell; D, daratumumab; ECOG PS, Eastern Cooperative Oncology Group performance status; FISH, fluorescence in situ hybridization; GMMG/DSMM, German-speaking Myeloma Multicenter Group/Deutsche Studiengruppe Multiples Myelom; ISS, International Staging System; QW, weekly; Q4W, every 4 weeks; R, lenalidomide; Tec, teclistamab; V, bortezomib.

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GMMG-HD10/DSMM-XX/MajesTEC-5: Hematologic TEAEs

TEAEs, n (%)[a]	Arm A: Tec (QW)-DR (n=10)		Arm A1: Tec (Q4W)-DR (n=20)		Arm B: Tec (Q4W)-DVR (n=19)		Total (N=49)	
	All grade	Grade 3/4	All grade	Grade 3/4	All grade	Grade 3/4	All grade	Grade 3/4
Hematologic								
Neutropenia	4 (40)	3 (30)	13 (65)	13 (65)	14 (73.7)	12 (63.2)	31 (63.3)	28 (57.1)
Lymphopenia	8 (80)	7 (70)	7 (35)	7 (35)	7 (36.8)	7 (36.8)	22 (44.9)	21 (42.9)
Thrombocytopenia	3 (30)	1 (10)	7 (35)	2 (10)	7 (36.8)	1 (5.3)	17 (34.7)	4 (8.2)
Anemia	5 (50)	0	6 (30)	4 (20)	5 (26.3)	0	16 (32.7)	4 (8.2)
Leukopenia	5 (50)	2 (20)	3 (15)	2 (10)	6 (31.6)	5 (26.3)	14 (28.6)	9 (18.4)

- The most common hematologic TEAE was neutropenia
- Weekly bortezomib did not increase the frequency of thrombocytopenia

Data cutoff: September 30, 2024. [a]TEAEs reported in ≥25% of patients in any arm. AEs are graded according to the NCI-CTCAE Version 5.0.
AE, adverse event; D, daratumumab; GMMG/DSMM, German-speaking Myeloma Multicenter Group/Deutsche Studiengruppe Multiples Myelom; NCI-CTCAE, National Cancer Institute Common Terminology Criteria for Adverse Events; QW, weekly; Q4W, every 4 weeks; R, lenalidomide; TEAE, treatment-emergent adverse event; Tec, teclistamab; V, bortezomib.

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GMMG-HD10/DSMM-XX/MajesTEC-5: Nonhematologic TEAEs

TEAEs, n (%)[a]	Arm A: Tec (QW)-DR (n=10)		Arm A1: Tec (Q4W)-DR (n=20)		Arm B: Tec (Q4W)-DVR (n=19)		Total (N=49)	
	All grade	Grade 3/4	All grade	Grade 3/4	All grade	Grade 3/4	All grade	Grade 3/4
Nonhematologic[b]								
CRS	6 (60)	0	14 (70)	0	12 (63.2)	0	32 (65.3)	0
Pyrexia	6 (60)	1 (10)	9 (45)	2 (10)	7 (36.8)	0	22 (44.9)	3 (6.1)
URTI	6 (60)	0	8 (40)	1 (5)	6 (31.6)	0	20 (40.8)	1 (2)
Rash	5 (50)	2 (20)	5 (25)	0	7 (36.8)	0	17 (34.7)	2 (4.1)
GGT increased	3 (30)	0	6 (30)	3 (15)	5 (26.3)	3 (15.8)	14 (28.6)	6 (12.2)
Diarrhea	6 (60)	0	4 (20)	1 (5)	4 (21.1)	0	14 (28.6)	1 (2)
Hypokalemia	1 (10)	0	8 (40)	2 (10)	4 (21.1)	0	13 (26.5)	2 (4.1)
Nausea	1 (10)	0	4 (20)	0	7 (36.8)	0	12 (24.5)	0
Peripheral sensory neuropathy	1 (10)	0	5 (25)	0	4 (21.1)	0	10 (20.4)	0
BAP increased	4 (40)	0	1 (5)	0	3 (15.8)	1 (5.3)	8 (16.3)	1 (2)
ALT increased	3 (30)	0	2 (10)	1 (5)	2 (10.5)	2 (10.5)	7 (14.3)	3 (6.1)
Nasopharyngitis	3 (30)	0	2 (10)	0	2 (10.5)	0	7 (14.3)	0
Lipase increased	1 (10)	1 (10)	5 (25)	3 (15)	1 (5.3)	1 (5.3)	7 (14.3)	5 (10.2)
Hyperglycemia	3 (30)	0	3 (15)	1 (5)	0	0	6 (12.2)	1 (2)
Constipation	0	0	1 (5)	0	5 (26.3)	0	6 (12.2)	0

- Among the most common nonhematologic TEAEs, rates of grade 3/4 events were low
- All CRS events were grade 1/2
  - Most occurred in C1
  - All resolved; no discontinuations due to CRS
- No ICANS
- No grade 5 TEAEs

Data cutoff: September 30, 2024. [a]TEAEs reported in ≥25% of patients in any arm. AEs are graded according to the NCI-CTCAE Version 5.0. [b]Hypogammaglobulinemia based on TEAE reporting also met the ≥25% threshold and is reported separately.
AE, adverse event; ALT, alanine aminotransferase; BAP, blood alkaline phosphatase; CRS, cytokine release syndrome; D, daratumumab; GGT, gamma-glutamyltransferase; GMMG/DSMM, German-speaking Myeloma Multicenter Group/Deutsche Studiengruppe Multiples Myelom; ICANS, immune effector cell–associated neurotoxicity syndrome; NCI-CTCAE, National Cancer Institute Common Terminology Criteria for Adverse Events; QW, weekly; Q4W, every 4 weeks; R, lenalidomide; TEAE, treatment-emergent adverse event; Tec, teclistamab; URTI, upper respiratory tract infection; V, bortezomib.

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GMMG-HD10/DSMM-XX/MajesTEC-5: Infections

TEAE, n (%)[a]	Arm A: Tec (QW)-DR (n=10)		Arm A1: Tec (Q4W)-DR (n=20)		Arm B: Tec (Q4W)-DVR (n=19)		Total (N=49)	
	All grade	Grade 3/4	All grade	Grade 3/4	All grade	Grade 3/4	All grade	Grade 3/4
Any infection	10 (100)	4 (40)	18 (90)	9 (45)	11 (57.9)	4 (21.1)	39 (79.6)	17 (34.7)
Infections[b]								
URTI	6 (60)	0	8 (40)	1 (5)	6 (31.6)	0	20 (40.8)	1 (2)
COVID-19	2 (20)	0	4 (20)	1 (5)	3 (15.8)	3 (15.8)	9 (18.4)	4 (8.2)
Nasopharyngitis	3 (30)	0	2 (10)	0	2 (10.5)	0	7 (14.3)	0
Bronchitis	2 (20)	0	0	0	0	0	2 (4.1)	0
Infection (NOS)	0	0	1 (5)	1 (5)	2 (10.5)	1 (5.3)	3 (6.1)	2 (4.1)
Pneumonia	1 (10)	1 (10)	1 (5)	0	2 (10.5)	2 (10.5)	4 (8.2)	3 (6.1)

- 17 (34.7%) patients had grade 3/4 infections
  - URTI and COVID-19 were the most common all grade
  - No discontinuations due to infection
  - No grade 5 infections
- Hypogammaglobulinemia[c] was reported in 45 (91.8%) patients
  - 44 (89.8%) received ≥1 dose of IVIg[d]
- Infection prophylaxis, including Ig replacement, was strongly recommended[e]

Data cutoff: September 30, 2024. [a]AEs are graded according to the NCI-CTCAE Version 5.0. [b]Infections reported in >10% of patients in any arm. [c]Includes patients with ≥1 TEAE of hypogammaglobulinemia or post-baseline IgG value <400 mg/dL. [d]Includes patients who started IVIg prior to Tec. [e]Prophylaxis for *Pneumocystis jirovecii* pneumonia and herpes zoster reactivation was also recommended, as well as routine antibiotic prophylaxis.
D, daratumumab; GMMG/DSMM, German-speaking Myeloma Multicenter Group/Deutsche Studiengruppe Multiples Myelom; Ig, immunoglobulin; IgG, immunoglobulin G; IVIg, intravenous immunoglobulin; NCI-CTCAE, National Cancer Institute Common Terminology Criteria for Adverse Events; NOS, not otherwise specified; QW, weekly; Q4W, every 4 weeks; R, lenalidomide; TEAE, treatment-emergent adverse event; Tec, teclistamab; URTI, upper respiratory tract infection; V, bortezomib.

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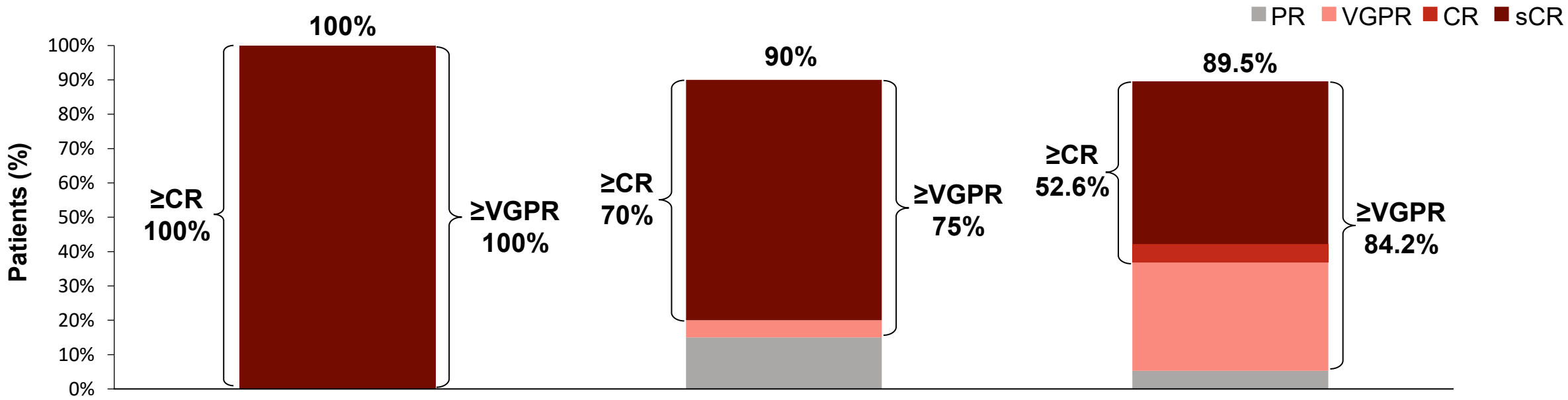
GMMG-HD10/DSMM-XX/MajesTEC-5: Response Rates[a]



	Arm A: Tec (QW)-DR n=10	Arm A1[b]: Tec (Q4W)-DR n=20	Arm B[c]: Tec (Q4W)-DVR n=19
Induction complete, n	10	5[d]	8[e]
Induction ongoing, n	0	14	10

100% sCR observed in Arm A, with deepening responses in maturing cohorts

Data cutoff: September 30, 2024. [a]Response was assessed by investigators based on IMWG criteria. Confirmed response required ≥2 consecutive identical response assessments. Response rates are presented during induction only. [b]2 (10.0%) patients had stable disease. [c]2 (10.5%) patients had stable disease. [d]1 patient discontinued due to refusal of further treatment. [e]1 patient discontinued due to refusal of further treatment.
CR, complete response; D, daratumumab; GMMG/DSMM, German-speaking Myeloma Multicenter Group/Deutsche Studiengruppe Multiples Myelom; IMWG, International Myeloma Working Group; PR, partial response; QW, weekly; Q4W, every 4 weeks; R, lenalidomide; sCR, stringent complete response; Tec, teclistamab; V, bortezomib; VGPR, very good partial response.

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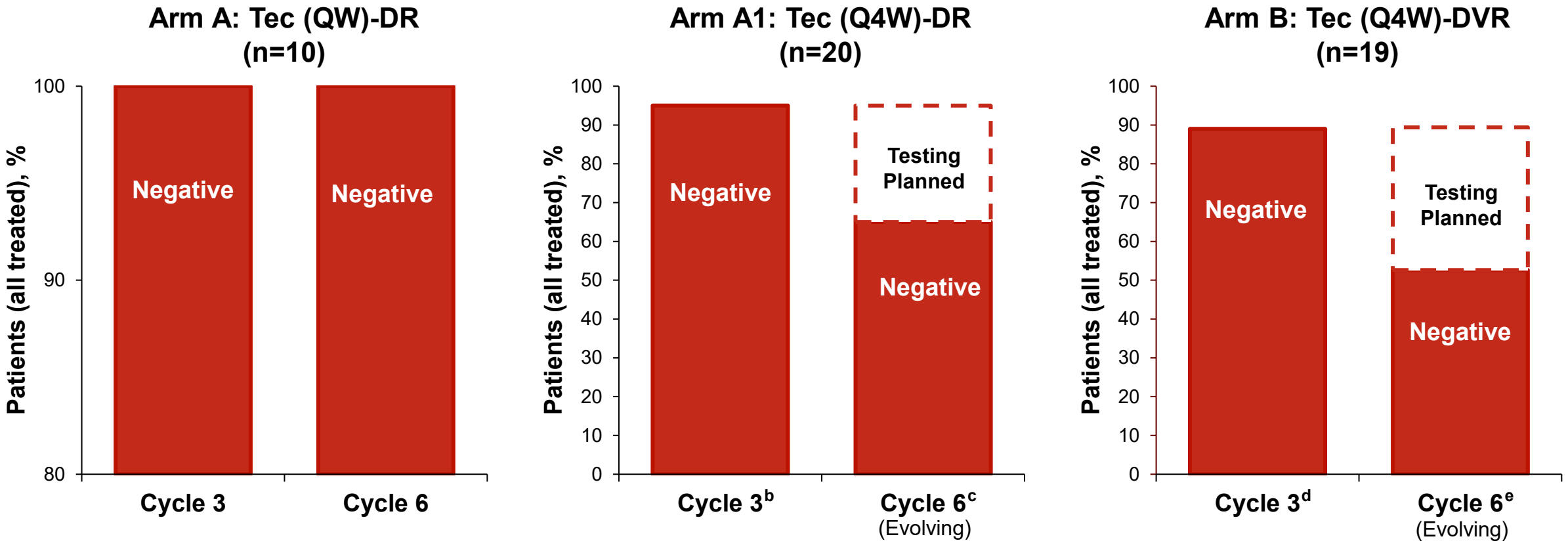
GMMG-HD10/DSMM-XX/MajesTEC-5: MRD Negativity (10^{-5})[a]



100% of evaluable patients achieved MRD negativity by C3; no patients were MRD positive

Data cutoff: September 30, 2024. [a]MRD-negativity rate was defined as the proportion of patients who achieved MRD negativity (10^{-5}), regardless of response. MRD was determined by NGF testing. [b]In Arm A1, 1 patient did not have bone marrow collected after C3. [c]In Arm A1, 1 patient did not have MRD testing (10^{-5}) after C6. [d]In Arm B, 1 patient was not tested at C3, but was MRD-negative at C6; 1 patient discontinued before C3 and had no on-study MRD testing. [e]In Arm B, 1 patient was MRD negative at 10^{-4} after C6 and was considered indeterminate and without available MRD testing (10^{-5}); 1 patient discontinued before C3 and had no on-study MRD testing.
C, Cycle; D, daratumumab; GMMG/DSMM, German-speaking Myeloma Multicenter Group/Deutsche Studiengruppe Multiples Myelom; MRD, minimal residual disease; NGF, next-generation flow cytometry; QW, weekly; Q4W, every 4 weeks; R, lenalidomide; Tec, teclistamab; V, bortezomib.

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GMMG-HD10/DSMM-XX/MajesTEC-5: Conclusions

- Tec-DR[a] and Tec-DVR[a] induction was feasible, with very high and early clinical efficacy in patients with TE NDMM
- MRD negativity (10^{-5}) was achieved in 100% of MRD-evaluable patients after C3 and maintained in evaluable patients through C6
- No TEAE-related discontinuations and no new safety signals compared with individual regimen components
- Infections were common, 34.7% of patients had grade 3/4 infections, and no grade 5 events were reported
  - Infection prophylaxis, including Ig replacement, was adopted
- Stem cell mobilization was feasible with Tec-D(V)R[a]

Teclistamab in combination with daratumumab-based standard of care in patients with transplant-eligible NDMM demonstrates promising efficacy with unprecedented early MRD-negativity rates

[a]Dexamethasone was also administered in C1 and C2.
C, Cycle; D, daratumumab; d, dexamethasone; GMMG/DSMM, German-speaking Myeloma Multicenter Group/Deutsche Studiengruppe Multiples Myelom; Ig, immunoglobulin; MRD, minimal residual disease; NDMM, newly diagnosed multiple myeloma; R, lenalidomide; TE, transplant-eligible; Tec, teclistamab; TEAE, treatment-emergent adverse event; V, bortezomib.

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Phase 3 Study of Teclistamab in Combination With Lenalidomide and Teclistamab Alone vs Lenalidomide Alone in Newly Diagnosed Multiple Myeloma as Maintenance Therapy Following Autologous Stem Cell Transplantation: Safety Run-in Results From the EMN30/MajesTEC-4 Trial*

*ClinicalTrials.gov Identifier: NCT05243797; sponsored by EMN in collaboration with Janssen Research & Development, LLC

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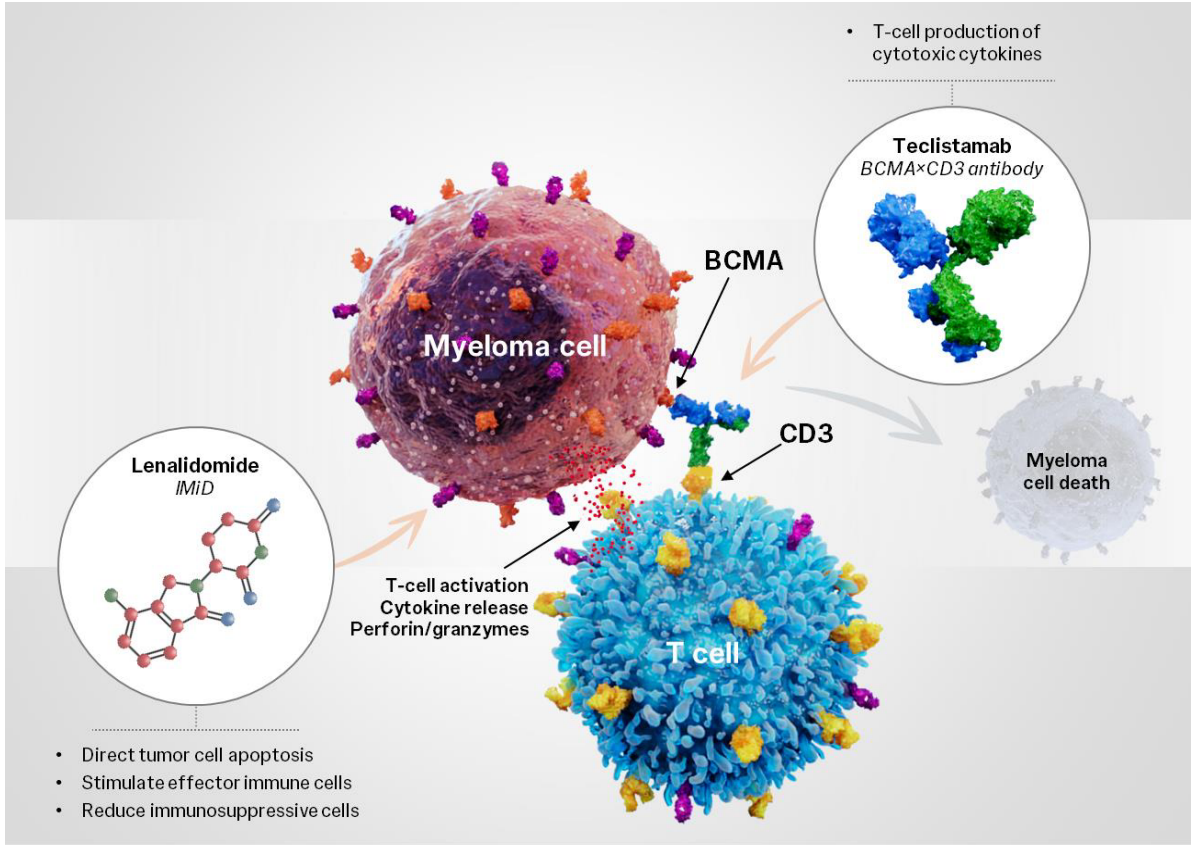
https://www.congresshub.com/ASH2024/Oncology/Teclistamab/Zamagni

EMN30/MajesTEC-4: Introduction

- Lenalidomide (Len) is a SoC maintenance therapy in NDMM following ASCT[1]
- Teclistamab (Tec) is a first-in-class BCMA × CD3 BsAb approved in TCE RRMM, with promising efficacy in earlier-line RRMM[2-7]
- The combined cytotoxic and immunomodulatory properties of Tec and Len may lead to enhanced efficacy[8]
- In MajesTEC-2 (phase 1b), Tec-Len was safely combined and demonstrated promising efficacy in TCE MM[9]
- EMN30/MajesTEC-4 is a multicenter, open-label, phase 3 study evaluating Tec-Len, Tec, and Len maintenance therapy in NDMM
- We report initial results from the SRI



ASCT, autologous stem cell transplantation; BCMA, B-cell maturation antigen; BsAb, bispecific antibody; EMN, Stichting European Myeloma Network; IMiD, immunomodulatory drug; MM, multiple myeloma; NDMM, newly diagnosed multiple myeloma; RRMM, relapsed/refractory multiple myeloma; SoC, standard-of-care; SRI, safety run-in; TCE, triple-class–exposed.

1. McCarthy PL, et al. *J Clin Oncol*. 2017;35(29):3279-3289. 2. Moreau P, et al. *N Engl J Med*. 2022;387(6);495-505. 3. Garfall AL, et al. *J Clin Oncol*. 2024;42(16 suppl). Abstract 7540. 4. Touzeau C, et al. *J Clin Oncol*. 2024;42(16 suppl). Abstract 7506. 5. Raab MS, et al. Presented at: 66th American Society of Hematology (ASH) Annual Meeting and Exposition; December 7-10, 2024; San Diego, CA, USA. Presentation 493. 6. TECVAYLI® (teclistamab). Summary of product characteristics. Janssen Biologics BV; 2024. 7. TECVAYLI® (teclistamab-cqyv) injection [package insert]. Janssen Biotech, Inc.; 2024. 8. Cho SF, et al. *Blood Adv*. 2020;4(17):4195-4207. 9. Tan C, et al. *Hemasphere*. 2023;7(S3):1623-1624.

EMN30/MajesTEC-4: Study Design

Key eligibility criteria:

- NDMM
- ECOG PS score of 0-2
- Received 4-6 cycles of 3- or 4-drug induction therapy (PI and/or IMiD ± anti-CD38 antibody) and ASCT[a] ± consolidation with ≥PR

SRI

SRI Cohort 1: Tec-Len
Tec QW → Q4W

SRI Cohort 2: Tec-Len
Tec Q4W

SRI Cohort 3: Tec
Tec Q4W

Phase 3, randomized study

N≈1500
1:1:1 randomization

→ **Tec-Len**
Tec Q4W

→ **Tec**
Tec Q4W

→ **Len**

Dual primary endpoints:
- PFS
- 12-month MRD-negative CR (by NGF; 10^{-5})

Select secondary endpoints:
- OS
- ≥CR
- CR conversion
- MRD-negative conversion
- MRD negativity/sustained MRD negativity
- PFS2
- TTNT
- Safety

[a]Single or tandem ASCT permitted.
ASCT, autologous stem cell transplantation; CR, complete response; ECOG PS, Eastern Cooperative Oncology Group performance status; EMN, Stichting European Myeloma Network; IMiD, immunomodulatory drug; Len, lenalidomide; MRD, minimal residual disease; NDMM, newly diagnosed multiple myeloma; NGF, next-generation flow cytometry; OS, overall survival; PFS, progression-free survival; PFS2, progression-free survival after next line of therapy; PI, proteosome inhibitor; PR, partial response; QW, weekly; Q4W, every 4 weeks; SRI, safety run-in; Tec, teclistamab; TTNT, time to next treatment.

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EMN30/MajesTEC-4 SRI: Dosing

	Cycle 1	Cycle 2	Cycles 3-6	Cycles 7-26
Cohort 1: Tec-Len Tec QW → Q4W	Tec step up[a] + Tec 1.5 mg/kg on D8, D15, and D22	Tec 1.5 mg/kg QW + Len	Tec 3.0 mg/kg Q2W + Len	Tec 3.0 mg/kg Q4W + Len
Cohort 2: Tec-Len Tec Q4W	Tec step up[a] + Tec 1.5 mg/kg on D8 and D15	Tec 3.0 mg/kg Q4W + Len		
Cohort 3: Tec Tec Q4W	Tec step up[a] + Tec 1.5 mg/kg on D8 and D15	Tec 3.0 mg/kg Q4W		

- Len was initiated at 10 mg/day[b] from Cycles 2 to 4, followed by 15 mg/day in Cycles 5 to 26, if tolerated
- 2-year fixed-duration maintenance regimen[c]

[a]Patients received step-up doses of 0.06 and 0.3 mg/kg. [b]In 28-day cycles. [c]Patients who achieved CR on Tec-Len after 1 year discontinued Tec and continued Len for another year.
CR, complete response; D, Day; EMN, Stichting European Myeloma Network; Len, lenalidomide; QW, weekly; Q2W, every 2 weeks; Q4W, every 4 weeks; SRI, safety run-in; Tec, teclistamab.

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EMN30/MajesTEC-4 SRI: Demographic and Disease Characteristics

Characteristic	Cohort 1: Tec-Len (QW → Q4W) (N=32)	Cohort 2: Tec-Len (Q4W) (N=32)	Cohort 3: Tec (Q4W) (N=30)
Median age, y (range)	58.5 (31-73)	58.0 (38-73)	58.5 (34-72)
≥65, n (%)	12 (37.5)	5 (15.6)	9 (30.0)
Male, n (%)	21 (65.6)	21 (65.6)	22 (73.3)
White race, n (%)	32 (100)	32 (100)	30 (100)
ISS disease stage at diagnosis, n/N (%)			
I	18/32 (56.3)	8/32 (25.0)	9/28 (32.1)
II	7/32 (21.9)	9/32 (28.1)	11/28 (39.3)
III	7/32 (21.9)	15/32 (46.9)	8/28 (28.6)
High cytogenetic risk at diagnosis,[a] n/N (%)	7/25 (28.0)	5/29 (17.2)	6/25 (24.0)
Induction regimen for MM, n (%)			
PI[b] + IMiD[c]	28 (87.5)	28 (87.5)	30 (100)
PI[b] + IMiD[c] + anti-CD38[d]	11 (34.4)	19 (59.4)	20 (66.7)
Prior consolidation, n (%)	6 (18.8)	12 (37.5)	10 (33.3)

- The median time from ASCT to maintenance treatment for all patients was 4.7 months (range, 1.8-7.4)
- All patients had an ECOG PS score of 0 or 1
- More patients in Cohorts 2 and 3 received anti-CD38 during induction compared with in Cohort 1

[a]High cytogenetic risk is defined as the presence of ≥1 of the following abnormalities: del(17p), t(4;14), or t(14;16). [b]93/94 (98.9%) received bortezomib, 3/94 (3.2%) carfilzomib. [c]53/94 (56.4%) received Len, 39/94 (41.5%) thalidomide, 1/94 (1.1%) pomalidomide. [d]49/94 (52.1%) received daratumumab and 1/94 (1.1%) isatuximab as part of a triplet regimen; 1/94 (1.1%) received daratumumab with lenalidomide as part of a doublet regimen.
ASCT, autologous stem cell transplantation; ECOG PS, Eastern Cooperative Oncology Group performance status; EMN, Stichting European Myeloma Network; IMiD, immunomodulatory drug; ISS, International Staging System; Len, lenalidomide; MM, multiple myeloma; PI, proteasome inhibitor; QW, weekly; Q4W, every 4 weeks; SRI, safety run-in; Tec, teclistamab.

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EMN30/MajesTEC-4 SRI: Hematologic TEAEs

	Cohort 1: Tec-Len (QW → Q4W) (N=32)		Cohort 2: Tec-Len (Q4W) (N=32)		Cohort 3: Tec (Q4W) (N=30)	
Median follow-up, mo	21.1		9.2		9.2	
TEAEs,[a] n (%)	**Any grade**	**Grade 3/4**	**Any grade**	**Grade 3/4**	**Any grade**	**Grade 3/4**
Any TEAE	32 (100)	32 (100)	32 (100)	27 (84.4)	30 (100)	17 (56.7)
Hematologic Aes						
Neutropenia	30 (93.8)	30 (93.8)	21 (65.6)	20 (62.5)	17 (56.7)	14 (46.7)
Leukopenia	9 (28.1)	3 (9.4)	1 (3.1)	0	1 (3.3)	1 (3.3)
Lymphopenia	2 (6.3)	1 (3.1)	4 (12.5)	4 (12.5)	4 (13.3)	4 (13.3)
Thrombocytopenia	6 (18.8)	2 (6.2)	0	0	2 (6.7)	0
Febrile neutropenia	3 (9.4)	3 (9.4)	3 (9.4)	3 (9.4)	0	0
Anemia	3 (9.4)	0	1 (3.1)	1 (3.1)	1 (3.3)	0
Eosinophilia	1 (3.1)	1 (3.1)	1 (3.1)	1 (3.1)	0	0

- Cumulative incidence of grade 3/4 neutropenia at 6 months:
  - Cohort 1: 81.3%
  - Cohort 2: 56.3%
  - Cohort 3: 40.0%
- Median relative dose intensity:
  - 95.5% to 99.7% for Tec
  - 58.4% to 61.5% for Len
- Low rates of treatment discontinuation due to TEAEs (5.3% overall)

Teclistamab every 4 weeks from Cycle 2 had a lower cumulative incidence of grade 3/4 neutropenia than teclistamab weekly → every 4 weeks

Data cutoff date: September 9, 2024.

[a]AEs (graded according to the NCI-CTCAE Version 5.0); any grade occurring in >25% of patients or grade 3/4 in >1 patient.

AE, adverse event; EMN, Stichting European Myeloma Network; Len, lenalidomide; NCI-CTCAE, National Cancer Institute Common Terminology Criteria for Adverse Events; QW, weekly; Q4W, every 4 weeks; SRI, safety run-in; TEAE, treatment-emergent adverse event; Tec, teclistamab.

Presented by E Zamagni at the 66th American Society of Hematology (ASH) Annual Meeting and Exposition; December 7-10, 2024; San Diego, CA, USA

EMN30/MajesTEC-4 SRI: Nonhematologic TEAEs

	Cohort 1: Tec-Len (QW → Q4W) (N=32)		Cohort 2: Tec-Len (Q4W) (N=32)		Cohort 3: Tec (Q4W) (N=30)	
Median follow-up, mo	21.1		9.2		9.2	
TEAEs,[a] n (%)	**Any grade**	**Grade 3/4**	**Any grade**	**Grade 3/4**	**Any grade**	**Grade 3/4**
Nonhematologic AEs[b]						
CRS	16 (50.0)	0	13 (40.6)	0	13 (43.3)	0
URTI	20 (62.5)	1 (3.1)	13 (40.6)	0	8 (26.7)	0
Cough	15 (46.9)	0	6 (18.8)	0	8 (26.7)	0
Diarrhea	13 (40.6)	3 (9.4)	9 (28.1)	1 (3.1)	6 (20.0)	0
Injection-site erythema	7 (21.9)	0	12 (37.5)	0	8 (26.7)	0
COVID-19	12 (37.5)	1 (3.1)	5 (15.6)	0	9 (30.0)	1 (3.3)
Fatigue	10 (31.3)	1 (3.1)	8 (25.0)	1 (3.1)	5 (16.7)	0
Pneumonia	9 (28.1)	4 (12.5)	3 (9.4)	0	2 (6.7)	1 (3.3)

- Among the most common nonhematologic TEAEs, rates of grade 3/4 events were low
- All CRS events were grade 1/2, mostly occurring during Tec step-up dosing
  - 37.2% after Step-up Dose 1
  - 8.5% after Step-up Dose 2
  - 5.3% after Treatment Dose 1
  - No discontinuations due to CRS
- No ICANS

Data cutoff date: September 9, 2024.

[a]AEs (graded according to the NCI-CTCAE Version 5.0); any grade occurring in >25% of patients or grade 3/4 in >10% of patients. [b]Hypogammaglobulinemia based on TEAE reporting also met the ≥25% threshold and is reported separately.

AE, adverse event; CRS, cytokine release syndrome; EMN, Stichting European Myeloma Network; ICANS, immune effector cell–associated neurotoxicity syndrome; Len, lenalidomide; QW, weekly; Q4W, every 4 weeks; SRI, safety run-in; TEAE, treatment-emergent adverse event; Tec, teclistamab; URTI, upper respiratory tract infection.

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EMN30/MajesTEC-4 SRI: Infections and Hypogammaglobulinemia

	Cohort 1: Tec-Len (QW → Q4W) (N=32)		Cohort 2: Tec-Len (Q4W) (N=32)		Cohort 3: Tec (Q4W) (N=30)	
Median follow-up, mo	21.1		9.2		9.2	
TEAEs,[a] n (%)	**Any grade**	**Grade 3/4**	**Any grade**	**Grade 3/4**	**Any grade**	**Grade 3/4**
Any infection	30 (93.8)	12 (37.5)	25 (78.1)	9 (28.1)	23 (76.7)	6 (20.0)
Most common infections[b]						
URTI	20 (62.5)	1 (3.1)	13 (40.6)	0	8 (26.7)	0
COVID-19	12 (37.5)	1 (3.1)	5 (15.6)	0	9 (30.0)	1 (3.3)
Pneumonia	9 (28.1)	4 (12.5)	3 (9.4)	0	2 (6.7)	1 (3.3)
Nasopharyngitis	6 (18.8)	0	0	0	3 (10.0)	0

- Hypogammaglobulinemia[c] reported in:
  - Cohort 1: 31 (96.9%) patients
  - Cohort 2: 25 (78.1%) patients
  - Cohort 3: 28 (93.3%) patients
  - All received ≥1 dose of IVIg or SCIg
- One grade 5 COVID-19 TEAE occurred in Cohort 2
- Infection prophylaxis, including Ig replacement, was strongly recommended[d]

Data cutoff date: September 9, 2024.

[a]AEs (graded according to the NCI-CTCAE Version 5.0). [b]Any grade occurring in >10% of patients in any arm. [c]Includes patients with ≥1 TEAE of hypogammaglobulinemia or post-baseline IgG value <400 mg/dL. [d]Prophylactic IVIg replacement advised to maintain serum IgG levels of ≥400 mg/dL. Prophylaxis for *Pneumocystis jirovecii* pneumonia and herpes zoster reactivation was recommended, as well as routine antibiotic and antiviral prophylaxis.

AE, adverse event; EMN, Stichting European Myeloma Network; Ig, immunoglobulin; IgG, immunoglobulin G; IVIg, intravenous immunoglobulin; Len, lenalidomide; QW, weekly; Q4W, every 4 weeks; SCIg, subcutaneous immunoglobulin; SRI, safety run-in; TEAE, treatment-emergent adverse event; Tec, teclistamab; URTI, upper respiratory tract infection.

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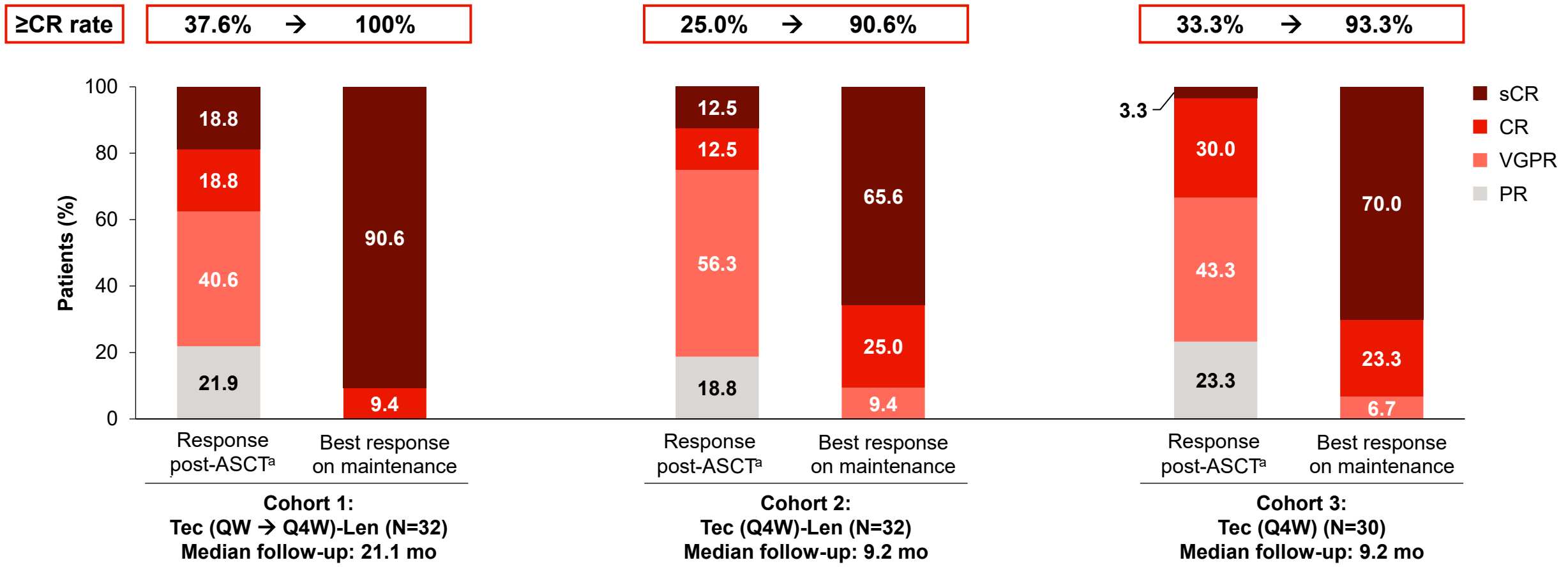
EMN30/MajesTEC-4 SRI: Response Rates Post-ASCT and During Maintenance



Responses deepened during maintenance in all treatment cohorts

Data cutoff date: September 9, 2024.

[a]Post-ASCT ± consolidation.

ASCT, autologous stem cell transplantation; CR, complete response; EMN, Stichting European Myeloma Network; Len, lenalidomide; PR, partial response; QW, weekly; Q4W, every 4 weeks; sCR, stringent complete response; SRI, safety run-in; Tec, teclistamab; VGPR, very good partial response.

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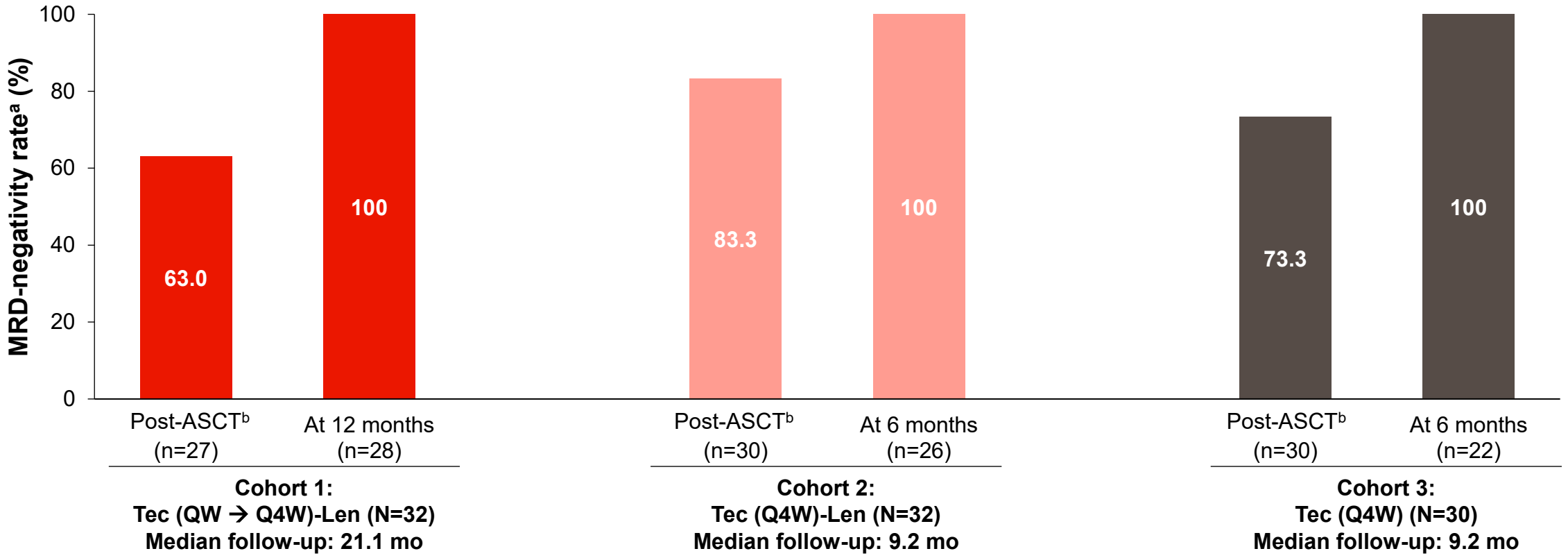
EMN30/MajesTEC-4 SRI: MRD Negativity (10^{-5}) in Evaluable Patients Post-ASCT and During Maintenance



100% of evaluable patients were MRD negative during maintenance

Data cutoff date: September 9, 2024.

[a]MRD-negativity rate was defined as the proportion of patients who achieved MRD negativity (10^{-5}), regardless of response. Percentages are out of evaluable patients. Among 87 evaluable patients, 23 patients were MRD positive at screening (Cohort 1, n=10; Cohort 2, n=5; Cohort 3, n=8). All patients who were MRD positive at study entry and had an assessment during treatment were MRD negative during treatment. One patient in Cohort 1 was MRD positive at 18 months. [b]Post-ASCT ± consolidation.

ASCT, autologous stem cell transplantation; EMN, Stichting European Myeloma Network; Len, lenalidomide; MRD, minimal residual disease; QW, weekly; Q4W, every 4 weeks; SRI, safety run-in; Tec, teclistamab.

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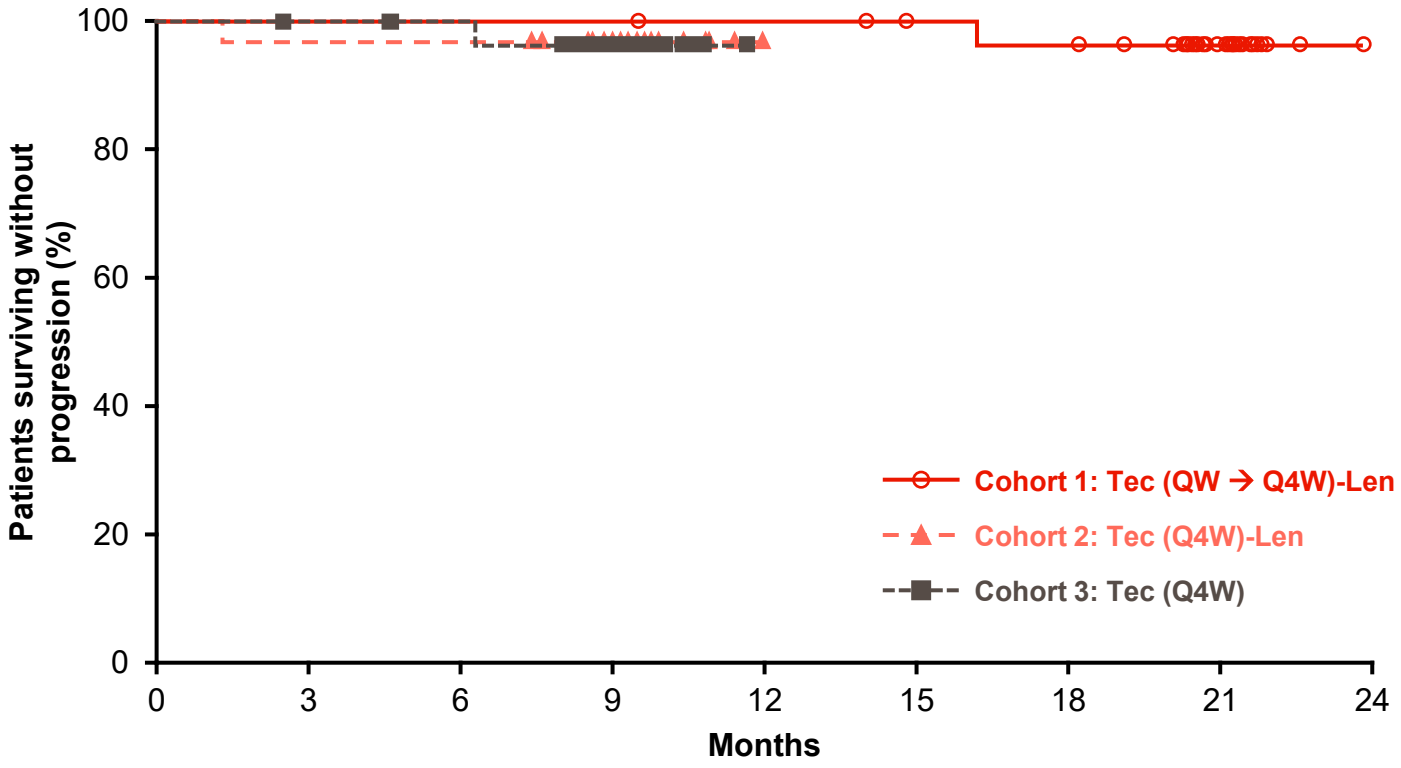
EMN30/MajesTEC-4 SRI: PFS



Patients at risk:									
Cohort 1: Tec (QW → Q4W)-Len	32	32	32	32	31	29	28	14	0
Cohort 2: Tec (Q4W)-Len	32	31	31	17	0	0	0	0	0
Cohort 3: Tec (Q4W)	30	29	28	14	0	0	0	0	0

- Median PFS was not reached in all cohorts

Responses were maintained in all cohorts

EMN, Stichting European Myeloma Network; Len, lenalidomide; PFS, progression-free survival; QW, weekly; Q4W, every 4 weeks; SRI, safety run-in; Tec, teclistamab.

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EMN30/MajesTEC-4 SRI: Conclusions

- Tec as monotherapy or in combination with Len as fixed duration could be safely administered to approximately 90 patients with NDMM following ASCT
- Discontinuation rates due to TEAEs were low
- The most common hematologic toxicity was neutropenia, which was lower with Tec 3.0 mg/kg Q4W from Cycle 2
- Grade 3/4 infections occurred in ~30% of patients, and infection prophylaxis, including Ig replacement, was strongly recommended
- Unprecedented efficacy was observed, with all evaluable patients achieving MRD negativity during maintenance
- The randomized portion of the EMN30/MajesTEC-4 study is evaluating Tec-Len, Tec, and Len as maintenance with Tec dosing at 3 mg/kg Q4W

ASCT, autologous stem cell transplantation; EMN, Stichting European Myeloma Network; Ig, immunoglobulin; Len, lenalidomide; MRD, minimal residual disease; NDMM, newly diagnosed multiple myeloma; Q4W, every 4 weeks; SRI, safety run-in; TEAE, treatment-emergent adverse event; Tec, teclistamab.

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Relapsed - refractory

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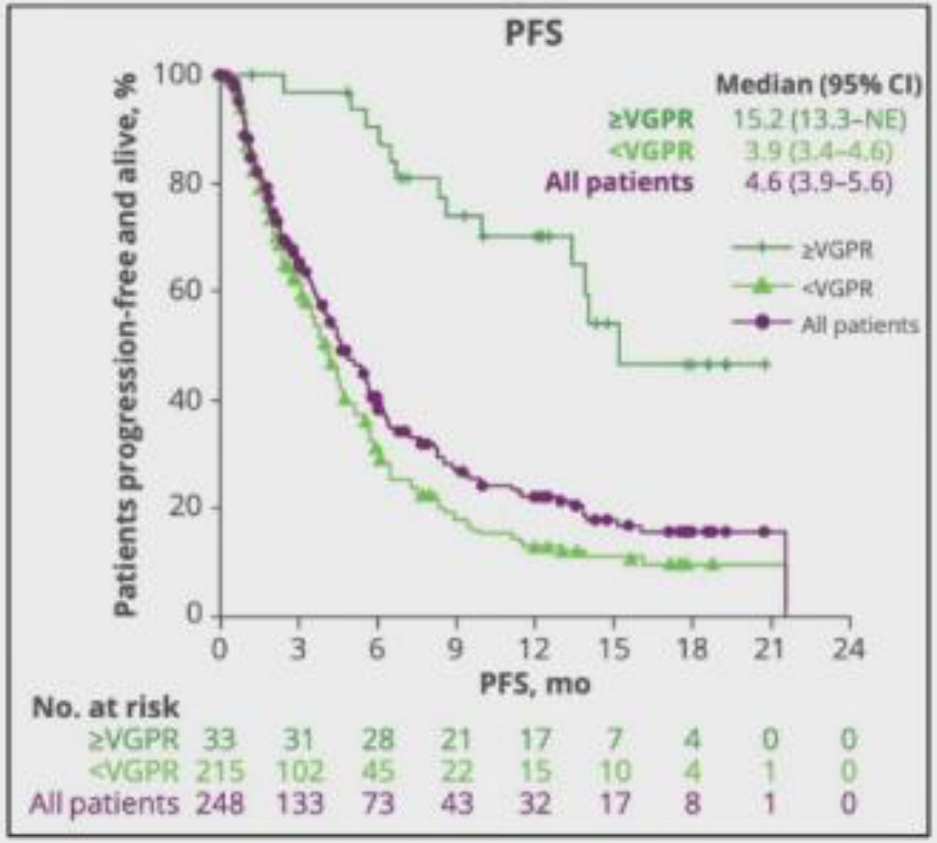
US Multiple Myeloma Immunotherapy Consortium

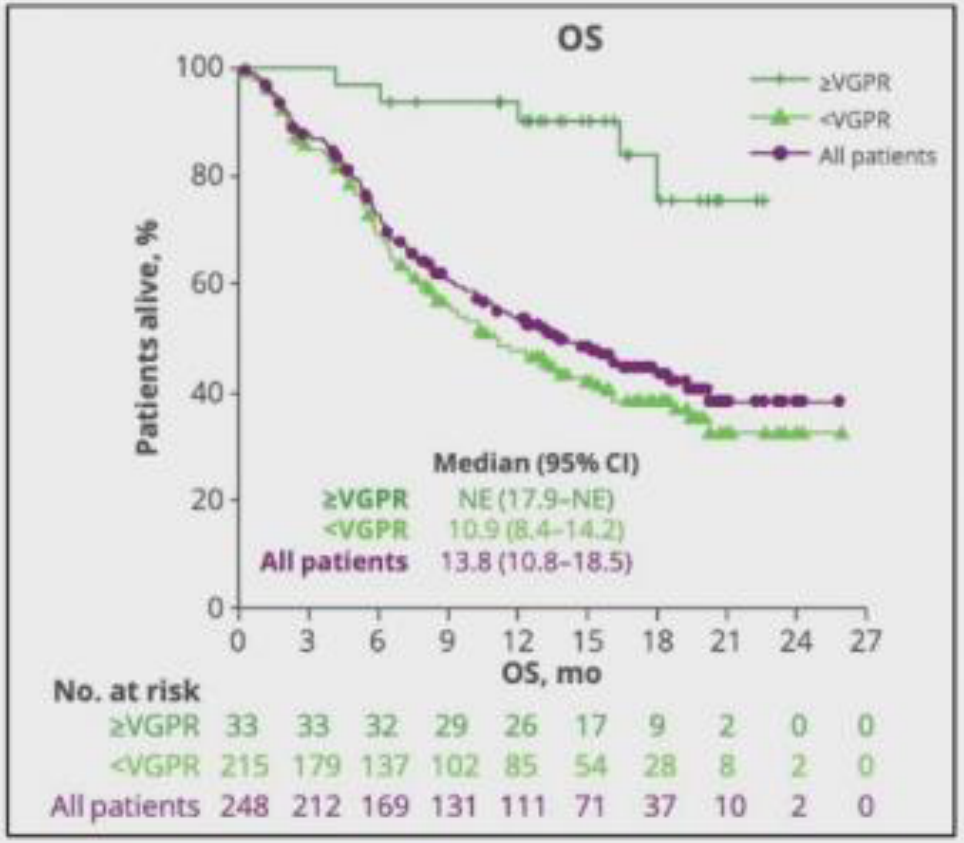
Talquetamab Bridging: Paving the Way to B-cell maturation antigen (BCMA) CAR-T cell Therapy in Relapsed/Refractory Multiple Myeloma (RRMM)

Binod Dhakal, Othman Akhtar, Andrew Cowan, Shambavi Richard, Reed Friend, Matthew Rees, Patrick Costello, Mariola Vazquez, Oren Pasvoslky, Charlotte Wagner, Alexandria Jensen, James Davis, Ran Reshef, Danai Dima, Rahul Banerjee, Manisha Bhutani, Omar Nadeem, Ricardo Porando, Lekha Mikkilineni, Shahzad Raza, Prashant Kapoor, Hitomi Hosoya, Saurabh Chhabra, Ariel Grajales-Cruz, Mahmoud Gaballa, Shonali Midha, Melissa Alsina, Douglas Sborov, Krina Patel, Yi Lin, Christopher Ferreri, Doris Hansen, Luciano J. Costa, Surbhi Sidana

On behalf of US Multiple Myeloma Immunotherapy Consortium

Natural history of triple-class exposed patients prior to approval of T-cell therapy





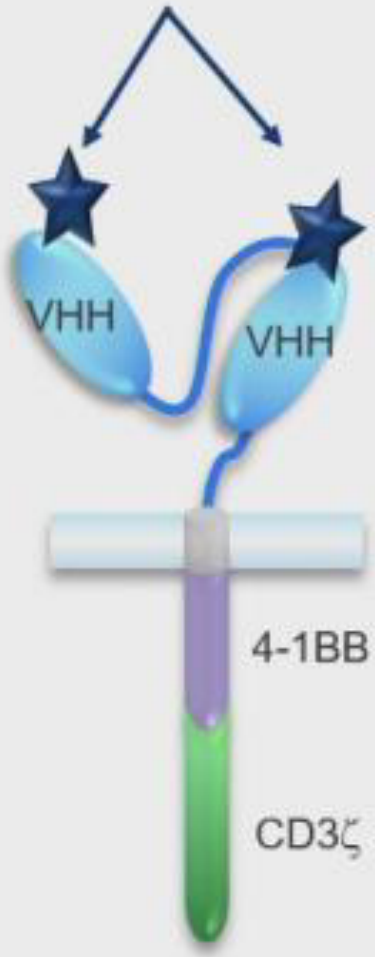
ORR 31.5% (95% CI: 25.7 – 37.6)

Triple-class exposed patients represent an unmet need for transformative therapy

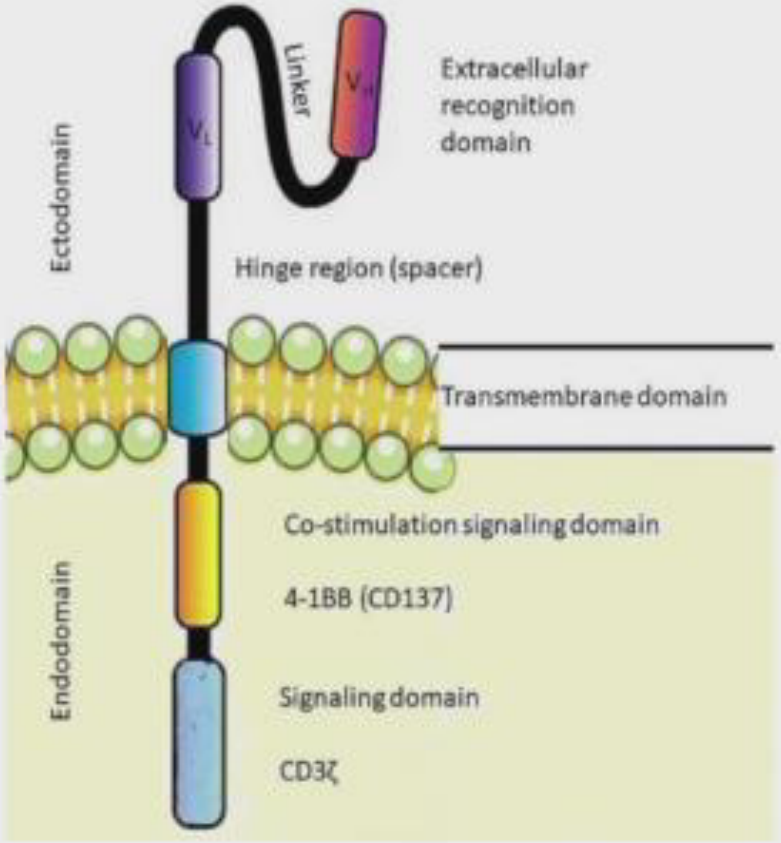
Mateos MV et al. Leukemia 2022;36(5):1371-1376.

Approved anti-BCMA CAR-T therapy in RRMM

Binding domains



	Cilta-cel: CARTITUDE-1 trial	Ide-cel: KarMMa trial
FDA approval	Feb 2022	March 2021
ORR/≥CR	98%/83%	73%/33%
Grade ≥3 CRS	4%	5%
Grade ≥3 ICANS	2%	3%
Median PFS (months)	34.9	8.8



Lin Y et. al ASCO 2023, Munshi NC et. al NEJM 2021

Maintaining disease control while awaiting CAR-T manufacturing is challenging

Clinical trials and Real World: **10-15%**

Do not receive CAR-T due to progression/death while awaiting manufacturing

Manufacturing time for CAR-T: **6-8 weeks**

75% of patients need bridging therapy

Increased disease burden prior to lymphodepletion is associated with

- decreased CAR-T efficacy,
- increased immune-mediated toxicity

There is an urgent need for an effective bridging strategy in these patients

Berdeja et al. Lancet 2021. San Miguel J, Dhakal B; et al. NEJM 2023
Sidana et l. Blood 2024 . Hansen et al JCO 2023

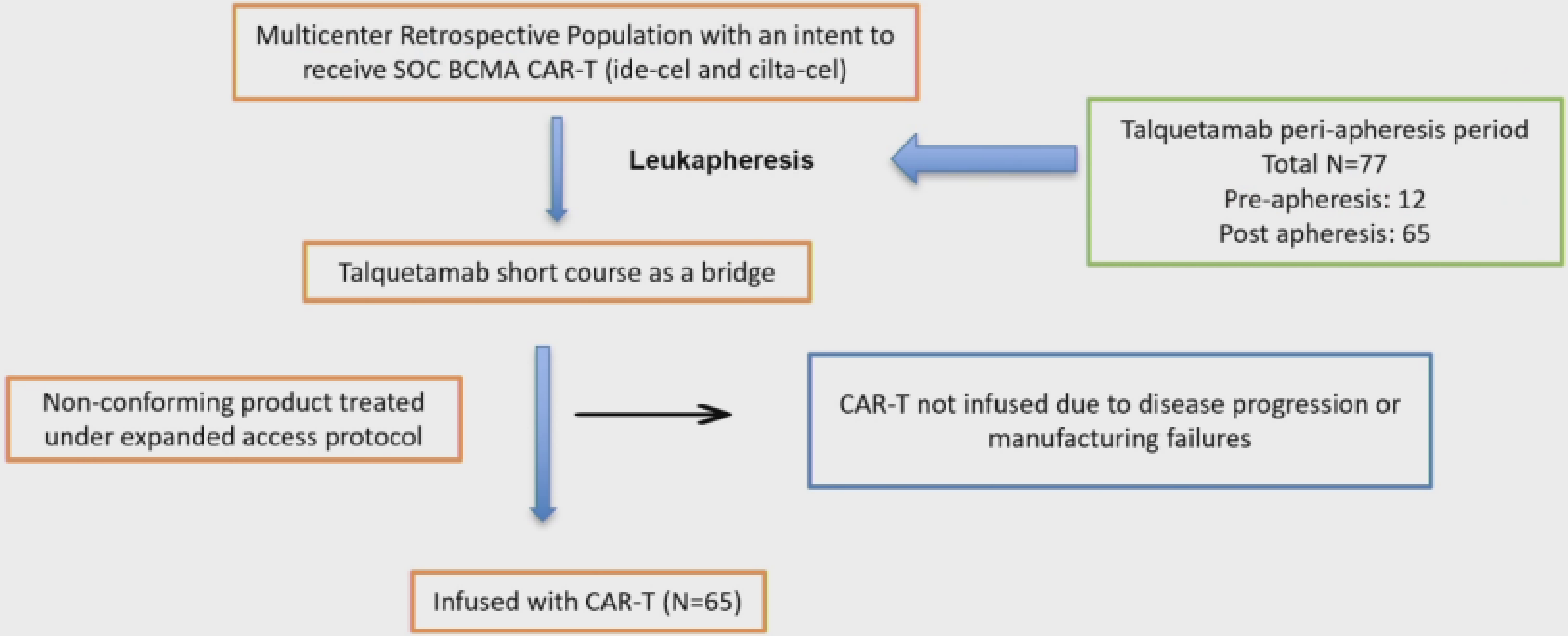
Study Objectives

Safety and feasibility of Talquetamab bridging prior to ide-cel and cilta-cel in the standard of care setting for relapsed and/or refractory multiple myeloma.

Primary outcomes:
Safety: CRS, ICANS, Talq related unique toxicities
Efficacy: Response to Talquetamab bridging, response to CAR-T therapy at different time points

Secondary outcomes:
Survival: Progression-free survival and overall survival
Infections, cytopenia and SPM

Study Design and Methods



Median follow up from Talq 7.5 months, from CAR-T 4.9 months

Patients who did not receive anti-BCMA CAR-T

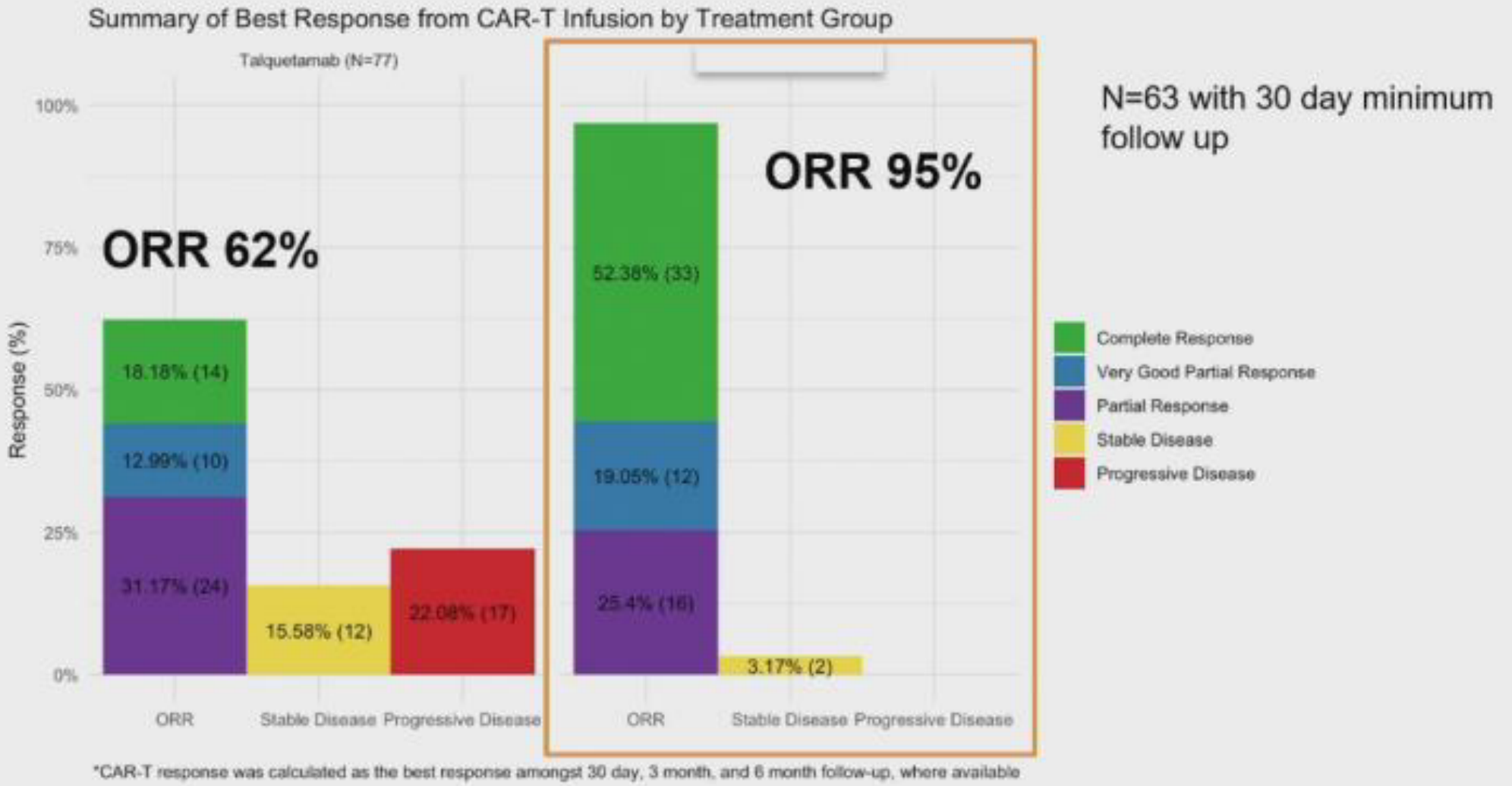
N =12	
Manufacturing failure	5
Disease progression	5
Patient decision	2
First manufacturing unsuccessful	6 (4 had prior BCMA)
Total deaths	8

Baseline Characteristics

Characteristic	Overall (N=77)	No Subsequent CAR (N= 12)	Subsequent CAR (N=65)
Age, years	66 (58-73)	68 (64-72)	65 (58-73)
Male sex	43 (56)	7 (58)	36 (56)
Race, white	57 (74)	8 (67)	49 (75)
Extramedullary disease	33 (43)	4 (33)	29 (45)I
High risk cytogenetics	35 (45)	3 (25)	32 (49)
Prior BCMA	10 (13)	5 (42)	5 (9)
ECOG ≥ 2	15 (19)	3 (16)	12 (21)

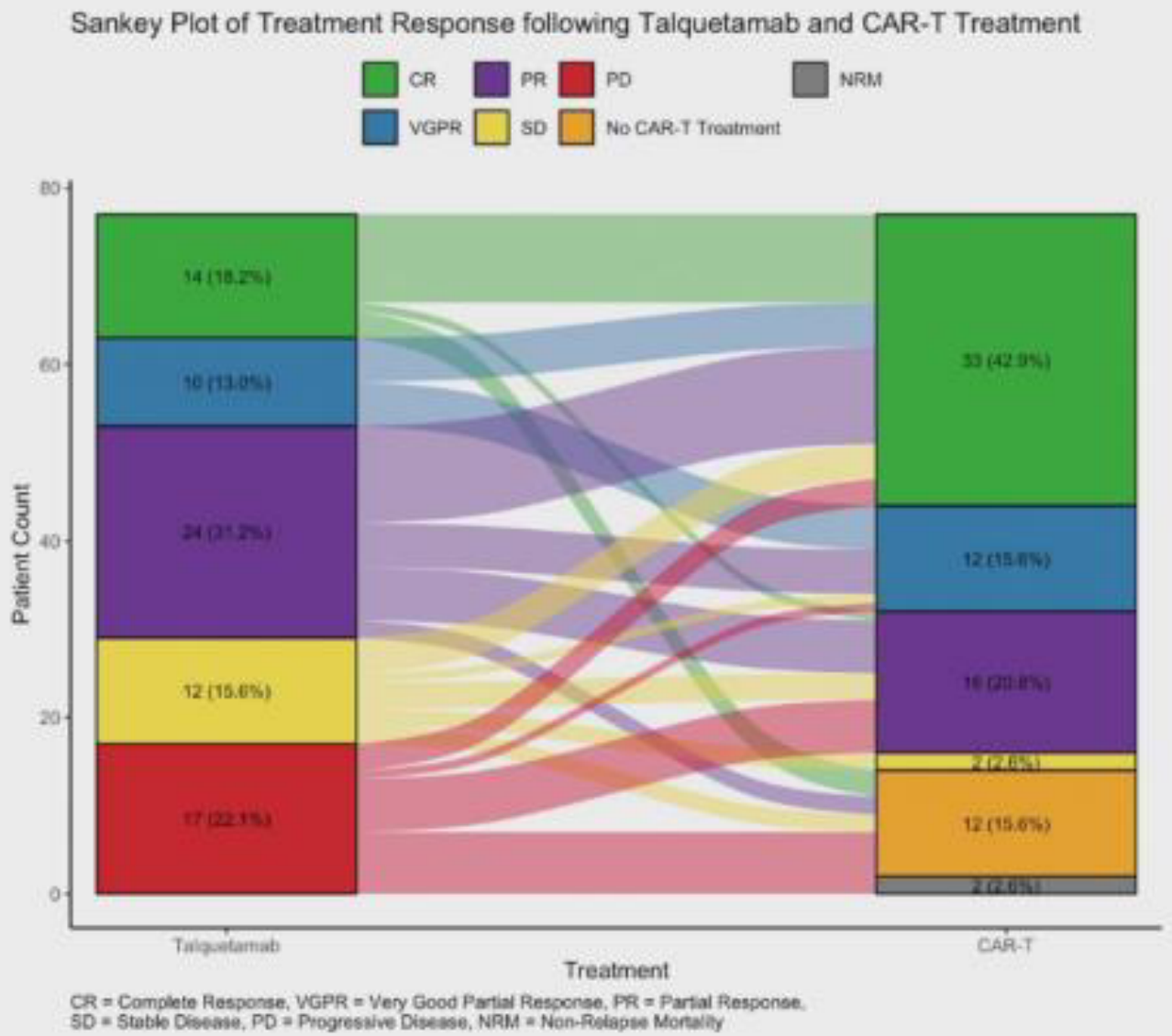
Characteristic	Overall (N=77)	No subsequent CAR (N=12)	Subsequent CAR (N=65)
Prior lines, median	5 (3-11)	5 (3-11)	5 (3-11)
Triple class refractory	56 (73)	13 (68)	43 (74)
Penta class refractory	28 (36)	5 (26)	23 (40)
Prior auto	58 (75)	8 (67)	50 (77)
CAR-T Ide-cel Cilta-cel	 15 50	NA	 15 50
Talq dose 0.8 Q2W 0.4 QW	 59 (77) 18 (23)	 10 (13) 2 (3)	 50 (65) 15 (19)

Best Overall Response to Talq and to CAR-T



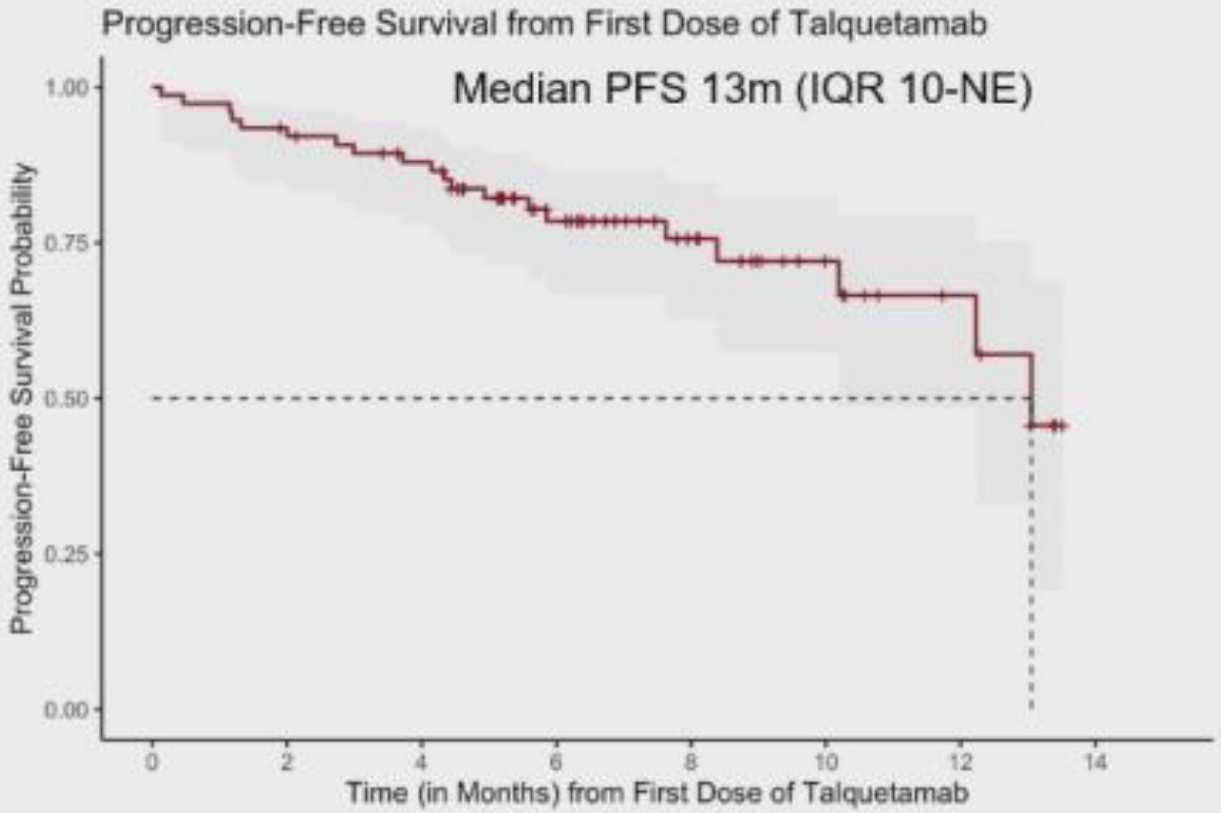
N=63 with 30 day minimum follow up

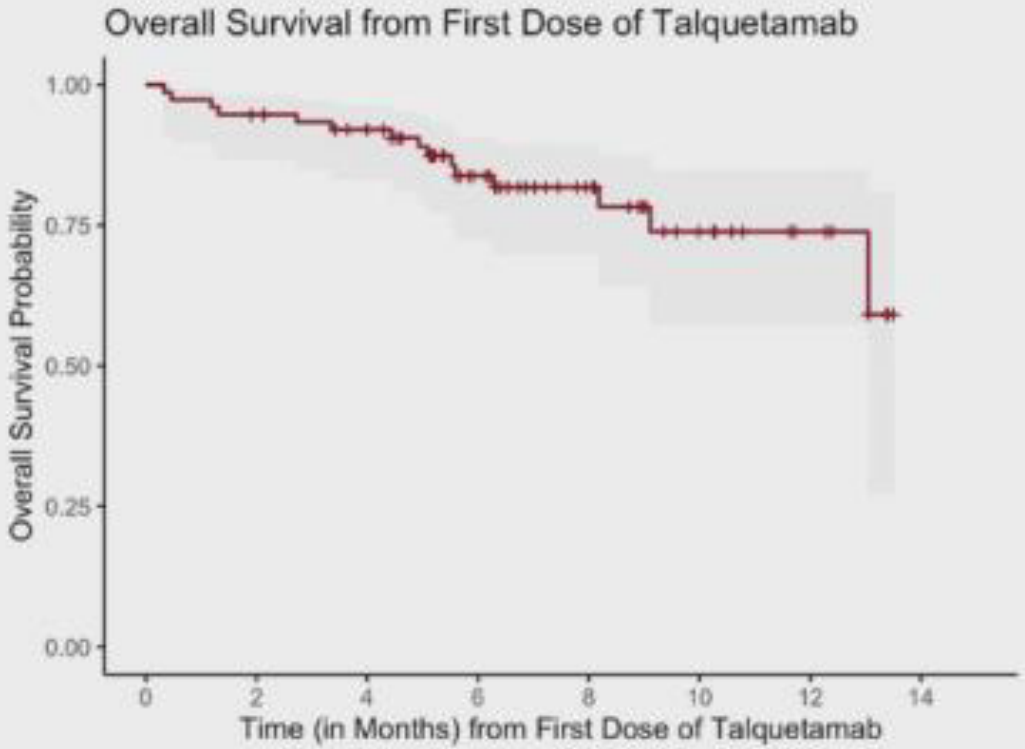
Flow of patient response from Talq to CAR-T



- 49% improved response
- 46% unchanged response
- Higher ORR and deeper response with CAR-T

Talq bridging: PFS and OS





Median follow up time: from Talquetamab first dose 7.5 months (IQR 5.4-10.4)
Median follow up from CAR-T infusion 4.9 months (IQR 3.6- 6.9)

Talquetamab Safety

	N=77	
	Any Grade	Grade 3/4
CRS	52 (68%)	0
ICANS	8 (10%)	2 (2.5%)
Skin toxicities	32 (42%)	0
Nail toxicities	19 (25%)	0
Oral toxicities	43 (56%)	1 (1.2%)
Weight loss	9 (12%)	2 (2.5%)

40/67 (60%) of patients observed complete resolution of Talq related toxicities

CAR-T safety

	N=65	
	All grades	Grade 3/4
CRS	47 (72%)	2 (3%)
ICANS	7 (10%)	1 (2%)
Delayed neurotoxicity	1 (1.5%) (CN VII palsy)	0
Infections	16 (27%)	6 (9%)
Second malignancies	1 (1.5%) (AML TP53 and DNMT3A)	NA
Severe cytopenia (day+60)	7 (10%)	7 (10%)

No cases of Guilian-Barre syndrome and no Parkinsonian-like syndromes
36/59 (61%) showed complete resolution of Talq related toxicities

CAR-T safety

Total deaths overall: 16

Total deaths after CAR-T infusion: 8

Non relapse mortality after CAR:3 (2 sepsis/shock and 1 AML/MDS)

Talquetamab safety and efficacy in different subgroups

	High risk vs. none	Prior BCMA vs none	High ferritin vs. none	Extramedullary dis vs. none
≥ Grade 3 CRS	NA	NA	NA	NA
≥ Grade 3 ICANS	3% vs. 2%	0% vs. 3%	3% vs. 0%	6% vs. 0%
≥ Partial response to Talq	66% vs. 61%	73% vs. 71%	69% vs. 66%	52% vs. 72%

- Median time on Talquetamab 26 days (IQR 10-57)
- Median time from last Talquetamab dose to CAR-T infusion 25 days (IQR 19-35)
- No difference in grade ≥ grade 3 CRS/ICANS by washout period of > or ≤ 4 weeks

Conclusions

- **Talq provided effective disease control in majority of the difficult to treat patients allowing them to proceed to CAR-T including in the peri-apheresis period**
  - CR/sCR rate of 18%, VGPR 31% and ORR 62% in high-risk patients
  - Median PFS 13 months and median OS not reached

- **85% of patients proceed to CAR-T infusion**
  - CR/sCR rate of 52%, >=VGPR 71% and ORR 95%, majority of patients deepened the response
  - Median PFS and OS not reached at the last follow up

- **Both Talq and CAR-T related toxicities were mainly low grade and 60% of the patients had complete resolution of Talq related toxicities**
  - 1 case of CN palsy and no evidence of GBS or parkinsonian like syndrome were observed post CAR-T
  - CRS and ICANS post CAR-T were low grade and manageable

Talq is safe and provides an effective bridging option allowing majority of the patients to safely receive BCMA CAR-T

Abstract #1024

Efficacy of Elranatamab in Combination With Carfilzomib and Dexamethasone in the Phase 1b MagnetisMM-20 Trial in Relapsed or Refractory Multiple Myeloma

Michael H. Tomasson,[1] Eli Gabayan,[2] Syed Abbas Ali,[3] Gabriel Afram,[4] Sona Ghorashi,[5] Trish Creel,[5] Luisa Paccagnella,[6] Carolyn Lou,[5] Ola Landgren[7]

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Presented at the 66th ASH Annual Meeting and Exposition | December 7-10, 2024 | San Diego, CA

MagnetisMM-20

- MagnetisMM-20 (NCT05675449) is an open-label, multicenter, nonrandomized, phase 1b study
- **Part 1 primary objective was to assess the tolerability and safety of elranatamab in combination with carfilzomib and dexamethasone to determine the RP2D of the combination**

Patients with RRMM

Key inclusion criteria
- 1-3 prior lines of therapy
- Relapsed or refractory to last line of therapy[a]
- ECOG PS 0-1
- Prior therapy with carfilzomib allowed if:
  - ≥PR to most recent therapy with carfilzomib
  - Did not relapse within 60 days from discontinuation of carfilzomib
  - ≥6 months carfilzomib treatment–free interval

Key exclusion criterion
- Any previous anti-BCMA–directed therapy

Dose Level 1	Dose Level 2
Elranatamab step-up doses[b] followed by: elranatamab **44 mg** QW + carfilzomib 70 mg/m^2 QW[c] + dexamethasone	Elranatamab step-up doses[b] followed by: elranatamab **76 mg** QW + carfilzomib 70 mg/m^2 QW[c] + dexamethasone

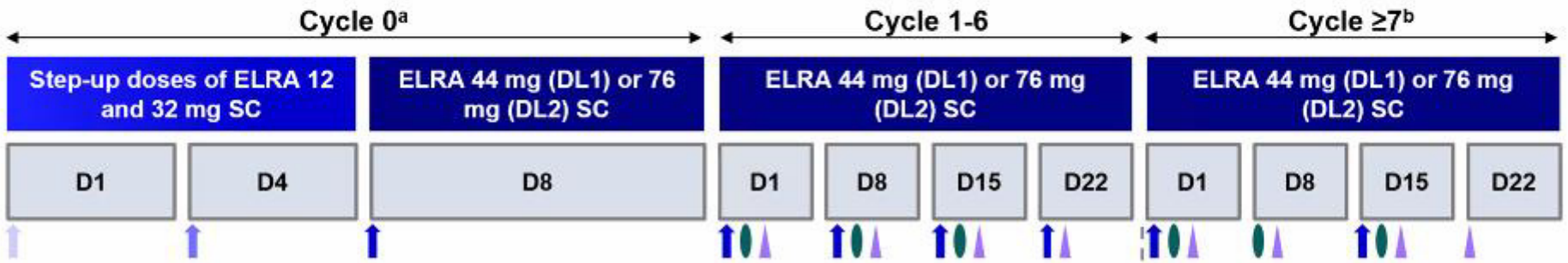
Primary endpoint
- DLTs during DLT observation period

Secondary endpoints
- AEs and laboratory abnormalities
- Best overall response[d]
- ORR[d]
- CR rate[d]
- Time to event endpoints
  - TTR[d]
  - DOR[d]
  - PFS[d]
  - OS

[a] Relapsed MM is the recurrence of disease after a prior response, as defined by IMWG criteria for clinical relapse. Refractory is defined as disease progression while receiving therapy or within 60 days of last dose in any line, regardless of response; [b] 12 mg and 32 mg subcutaneously; [c] Carfilzomib dose on cycle 1, day 1 is 20 mg/m^2 and, if tolerated, is increased to 70 mg/m^2; [d] By investigator assessment per IMWG response criteria (Kumar S, et al. Lancet Oncol 2016;17:e328-e346)

AE=adverse event; BCMA=B-cell maturation antigen; CR=complete response; DLT=dose-limiting toxicity; DOR=duration of response; ECOG PS=Eastern Cooperative Oncology Group performance status; IMWG=International Myeloma Working Group; ORR=objective response rate; OS=overall survival; PFS=progression-free survival; PR=partial response; QW=weekly; RP2D=recommended phase 2 dose; RRMM=relapsed or refractory multiple myeloma; TTR=time to response

MagnetisMM-20 Part 1 Dosing Schedule



Premedication
- Diphenhydramine 25 mg (or equivalent) oral or IV
- Acetaminophen 650 mg (or paracetamol 500 mg) oral
- Dexamethasone 20 mg (or equivalent) oral or IV

[a] Protocol-required hospitalization for elranatamab
- Dose 1: 48 hours
- Dose 2: 24 hours

Cycle length
- Cycle 0: 14 days
- Cyle ≥1: 28 days

Elranatamab 12 mg

Elranatamab 32 mg

Elranatamab 44 mg or 76 mg

Carfilzomib 70 mg/m^2[c]

Dexamethasone 40 mg[d]

If patients received ≥6 months of QW ELRA and achieved ≥PR (lasting ≥2 months), they could change to Q2W dosing at the same DL

[b] Only for patients meeting the criteria for less frequent dosing; [c] Cycle 1, day 1: 20 mg/m^2 IV; thereafter, 70 mg/m^2 for all subsequent doses; [d] 40 mg oral or IV QW. For patients aged ≥75 years, initial dose is 40 mg, and all subsequent doses are 20 mg

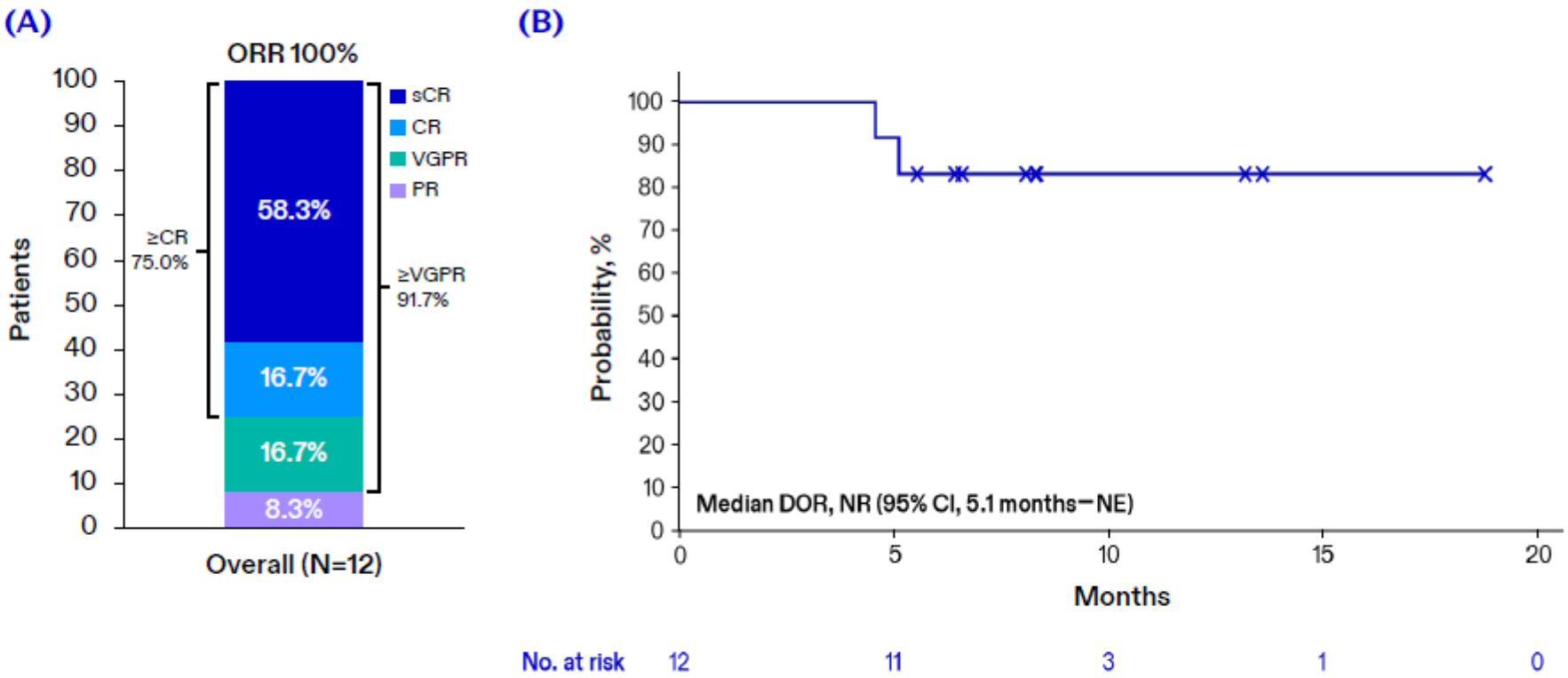
D=day; DL=dose level; ELRA=elranatamab; IV=intravenous; PR=partial response QW=once weekly; Q2W=once every 2 weeks; SC=subcutaneous

Efficacy of Elranatamab in Combination with Carfilzomib and Dexamethasone in the Phase 1b MagnetisMM-20 Trial in Relapsed or Refractory Multiple Myeloma (4/6)

Efficacy

- Confirmed ORR by investigator was 100% (**Figure**)
  - ≥CR 75.0% (95% CI 42.8–94.5)
  - Median time to response was 1.5 (range, 0.5–3.4) months
- First quartile DOR was not reached with a median duration of follow-up of 8.9 (95% CI 7.9–13.7) months* (**Figure**)
  - The probability of maintaining a response at 6 months was 83.3%

Figure. (A) ORR and (B) DOR



*Reverse Kaplan–Meier estimate.
CI = confidence interval; CR = complete response; DOR = duration of response; NE = not evaluable; NR = not reached; ORR = objective response rate; PR = partial response; sCR = stringent complete response; VGPR=very good partial response.

Tomasson MH et al. Oral presentation at ASH 2024 (Abstract 1024).

Efficacy of Elranatamab in Combination with Carfilzomib and Dexamethasone in the Phase 1b MagnetisMM-20 Trial in Relapsed or Refractory Multiple Myeloma (3/6)

Patients, Treatment, and Safety

- 12 patients enrolled at centers in the US
  - 4 patients received elranatamab DL1 and 8 patients received elranatamab DL2
- Median age of participants was 66.0 (range, 45.0–80.0) years and the majority of patients were male (66.7%), White (58.3%), had prior stem cell transplant (66.7%), had standard cytogenic risk (75.0%), and had received a median of 2.0 prior LOTs
  - 33.3%, 50.0%, and 16.7% of patients had R-ISS disease stage I, II, and III, respectively
- Median duration of treatment was 8.4 (range, 0.6–20.1) months
- At the data cutoff date (September 13, 2024):
  - 5 patients (41.7%) were still receiving elranatamab and carfilzomib

Safety

- In 10 evaluable patients, no DLTs were observed at either dose level
- TEAEs are shown in the **Table**
  - Infections were reported in 11 patients (91.7%); 2 patients had grade 3/4 infections†
- No grade 3/4 CRS was reported and no ICANS was reported

Table. TEAEs*

TEAE, n (%)	N=12 Any Grade	N=12 Grade 3/4
Any	12 (100)	11 (91.7)
Hematologic		
Neutropenia	9 (75.0)	9 (75.0)
Thrombocytopenia	9 (75.0)	5 (41.7)
Leukopenia	8 (66.7)	4 (33.3)
Anemia	8 (66.7)	4 (33.3)
Lymphopenia	4 (33.3)	3 (25.0)
Nonhematologic		
Fatigue	10 (83.3)	2 (16.7)
CRS	9 (75.0)	0
Cough	7 (58.3)	0
Diarrhea	6 (50.0)	1 (8.3)
CMV infection reactivation	6 (50.0)	1 (8.3)

TEAE, n (%)	N=12 Any Grade	N=12 Grade 3/4
Nonhematologic Cont'd		
Injection site reaction	6 (50.0)	0
Chills	5 (41.7)	0
Skin exfoliation	5 (41.7)	0
Nausea	5 (41.7)	0
Dizziness	5 (41.7)	0
Dry skin	5 (41.7)	0
Peripheral edema	4 (33.3)	2 (16.7)
Vomiting	4 (33.3)	0
Hypophosphatemia	4 (33.3)	0
Headache	4 (33.3)	0
Blood alkaline phosphatase increase	3 (25.0)	2 (16.7)
Pulmonary embolism	2 (16.7)	2 (16.7)

Please see slide notes for footnotes and abbreviations.

1. Lee DW et al. *Biol Blood Marrow Transplant*. 2019;25:625-638.
Tomasson MH et al. Oral presentation at ASH 2024 (Abstract 1024).

Efficacy of Elranatamab in Combination with Carfilzomib and Dexamethasone in the Phase 1b MagnetisMM-20 Trial in Relapsed or Refractory Multiple Myeloma (6/6)

Authors' Conclusions

- In BCMA-naïve patients with RRMM, with a median of 2 prior lines of therapy, elranatamab in combination with carfilzomib and dexamethasone demonstrated:
  - **Predictable safety profile**
    - No DLTs were observed
    - Hematologic TEAEs were predominantly low grade
    - Most infections were grade ≤2 (75.0%)
  - **Clinical efficacy**
    - At the time of data cutoff, ORR was 100% (confirmed by investigator) and ≥CR rate was 75.0% (95% CI, 42.8-94.5)
    - Median DOR has not been reached
    - Responses deepened over time, and some responses persisted even after treatment discontinuation
- The study is ongoing and will continue to explore the combination of elranatamab, carfilzomib, and dexamethasone in a larger group of patients with RRMM

BCMA = B-cell maturation antigen; CR = complete response; DLT = dose-limiting toxicity; DOR = duration of response; ORR = objective response rate; RRMM = relapsed or refractory multiple myeloma; TEAE = treatment-emergent adverse effect.

Tomasson MH et al. Oral presentation at ASH 2024 (Abstract 1024).

Cevostamab in Patients with Heavily Pretreated Relapsed/Refractory Multiple Myeloma: Updated Results from an Ongoing Phase I Study Demonstrate Clinically Meaningful Activity and Manageable Safety and Inform the Doses and Regimen for Combination Studies

Joshua Richter,[1] Sheeba K Thomas,[2] Amrita Krishnan,[3] Jacob P Laubach,[4] Adam D Cohen,[5] Suzanne Trudel,[6] Luciano J Costa,[7] Nizar J. Bahlis,[8] Peter A Forsberg,[9] Rayan Kaedbey,[10] Rafael Fonseca,[11] Andrew Spencer,[12] Paula Rodriguez-Otero,[13] Maria-Victoria Mateos,[14] Chihunt Wong,[15] James Cooper,[15] Tulika Tyagi,[15] Rin Nakamura,[15] Voleak Choeurng,[15] Alexander Lesokhin[16]

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Presented at the 66th ASH Annual Meeting | December 7–10, 2024

Baseline characteristics

N (%) unless stated	160mg TD (n=167)	C1 0.3/1.2/3.6/160mg TS (n=30)
Age in years, median (range)	66 (40–90)	65 (47–90)
Male	87 (52.1)	19 (63.3)
HR cytogenetics*, n (%) of patients with a conclusive assay result	38/99 (38.4)	6/18 (33.3)
t(4;14)	13/106 (12.3)	4/19 (21.1)
t(14;16)	6/98 (6.1)	2/18 (11.1)
del(17p)	24/124 (19.4)	2/20 (10.0)
Extramedullary disease	47 (28.1)	10 (33.3)
Time since first MM therapy in years, median (range)	6.3 (0.3–21.8)	6.8 (1.8–12.9)

N (%) unless stated	160mg TD (n=167)	C1 0.3/1.2/3.6/160mg TS (n=30)
Number of lines of prior therapy, median (range)	6 (2–18)	7.5 (2–13)
Triple-class refractory†	160 (95.8)	30 (100.0)
Penta-drug refractory‡	123 (73.7)	26 (86.7)
Refractory to last prior therapy	142 (85.0)	29 (96.7)
Any prior BCMA-targeted therapy	96 (57.5)	21 (70.0)
Any prior CAR-T therapy	60 (35.9)	12 (40.0)
Any prior ADC therapy	34 (20.4)	6 (20.0)
Any prior BsAb therapy	40 (24.0)	12 (40.0)

Most patients had heavily pretreated and highly refractory disease; **>50% had received prior BCMA-targeted therapy**

*includes t(4;14), t(14;16) and del(17p); †≥1 IMiD, ≥1 PI and ≥1 anti-CD38 antibody; ‡≥2 IMiDs, ≥2 PIs and ≥1 anti-CD38 antibody; data cut-off: Aug 22, 2024; HR, high risk

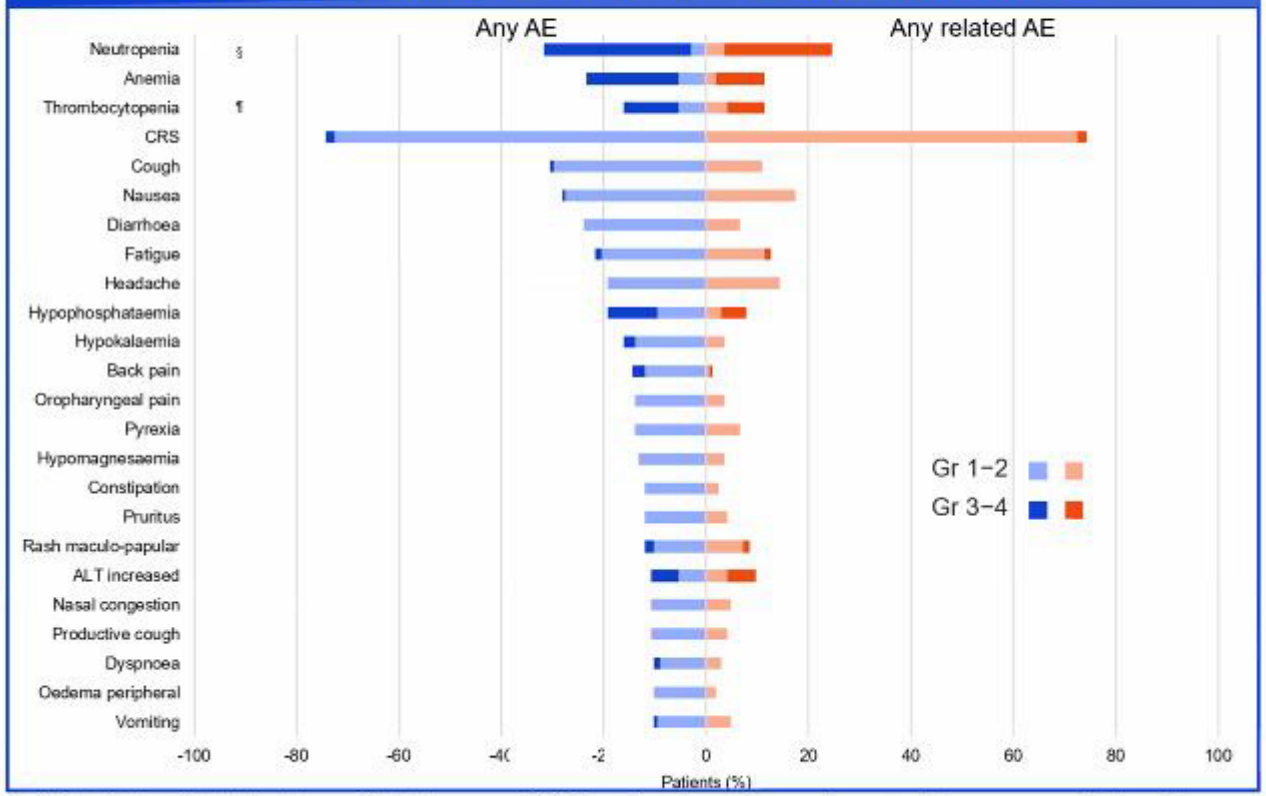
Adverse events at the 160mg TD level (n=167)

N (%) unless stated	Any	Any related
Time on study in months, median (range)*	14.8 (0.5–48.8)	
AE	167 (100)	154 (92.2)
Gr 3–4	96 (57.5)	72 (43.1)
Gr 5 (fatal) excluding PD	10 (6.0)†	3 (1.8)‡
SAE	96 (57.5)	47 (28.1)
AE leading to treatment discontinuation	30 (18.0)	13 (7.8)

Most Gr 3–4 AEs were reversible cytopenias

Almost all CRS was Gr 1–2, with the profile influenced by the step-dosing regimen

AEs (≥10%) and related AEs at the 160mg TD level by PT and Gr



*includes time after completion and/or discontinuation of treatment when AE reporting was limited to 90 days after the last dose of study drug or until initiation of another anti-cancer therapy, whichever occurred first, and to treatment-related SAEs thereafter; †excludes 16 patients with Gr 5 AE of PD; ‡HLH in 2 patients and pseudomonal sepsis in the context of DIC in 1 patient; §group term: neutropenia, neutrophil count decreased and febrile neutropenia; ¶group term: thrombocytopenia and platelet count decreased; data cut-off: Aug 22, 2024; ALT, alanine transaminase; DIC, disseminated intravascular coagulation; Gr, Grade; HLH, hemophagocytic lymphohistiocytosis; PT, Preferred Term; SAE, serious AE

Adverse events of infection at the 160mg TD level (n=167)

AEs of infection summary*

N (%) of patients	n=167
AE of infection	91 (54.5)
Gr 3–5 AE of infection	32 (19.2)
Gr 3	24 (14.4)
Gr 4	2 (1.2)
Gr 5 (fatal)	6 (3.6)
SAE of infection	37 (22.2)
AE of infection leading to treatment discontinuation	10 (6.0)

AEs of infection in ≥2% of patients by PT

N (%) of patients	n=167
Pneumonia	16 (9.6)
URTI	14 (8.4)
UTI	12 (7.2)
Rhinovirus infection	9 (5.4)
COVID-19	8 (4.8)
Sinusitis	6 (3.6)
Viral URTI	6 (3.6)
Pneumonia viral	4 (2.4)
Conjunctivitis	4 (2.4)
Oral candidiasis	4 (2.4)
Skin infection	4 (2.4)

- 29.3% of patients had a medical history of hypogammaglobulinemia; 32.9% received IV immunoglobulin

The majority of infections were Gr 1–2; infections leading to treatment discontinuation were uncommon

*System Organ Class level term; data cut-off: Aug 22, 2024; URTI, upper respiratory tract infection; UTI, urinary tract infection

Adverse events of infection at the 160mg TD level (n=167)

AEs of infection summary*

N (%) of patients	n=167
AE of infection	91 (54.5)
Gr 3–5 AE of infection	32 (19.2)
Gr 3	24 (14.4)
Gr 4	2 (1.2)
Gr 5 (fatal)	6 (3.6)
SAE of infection	37 (22.2)
AE of infection leading to treatment discontinuation	10 (6.0)

AEs of infection in ≥2% of patients by PT

N (%) of patients	n=167
Pneumonia	16 (9.6)
URTI	14 (8.4)
UTI	12 (7.2)
Rhinovirus infection	9 (5.4)
COVID-19	8 (4.8)
Sinusitis	6 (3.6)
Viral URTI	6 (3.6)
Pneumonia viral	4 (2.4)
Conjunctivitis	4 (2.4)
Oral candidiasis	4 (2.4)
Skin infection	4 (2.4)

- 29.3% of patients had a medical history of hypogammaglobulinemia; 32.9% received IV immunoglobulin

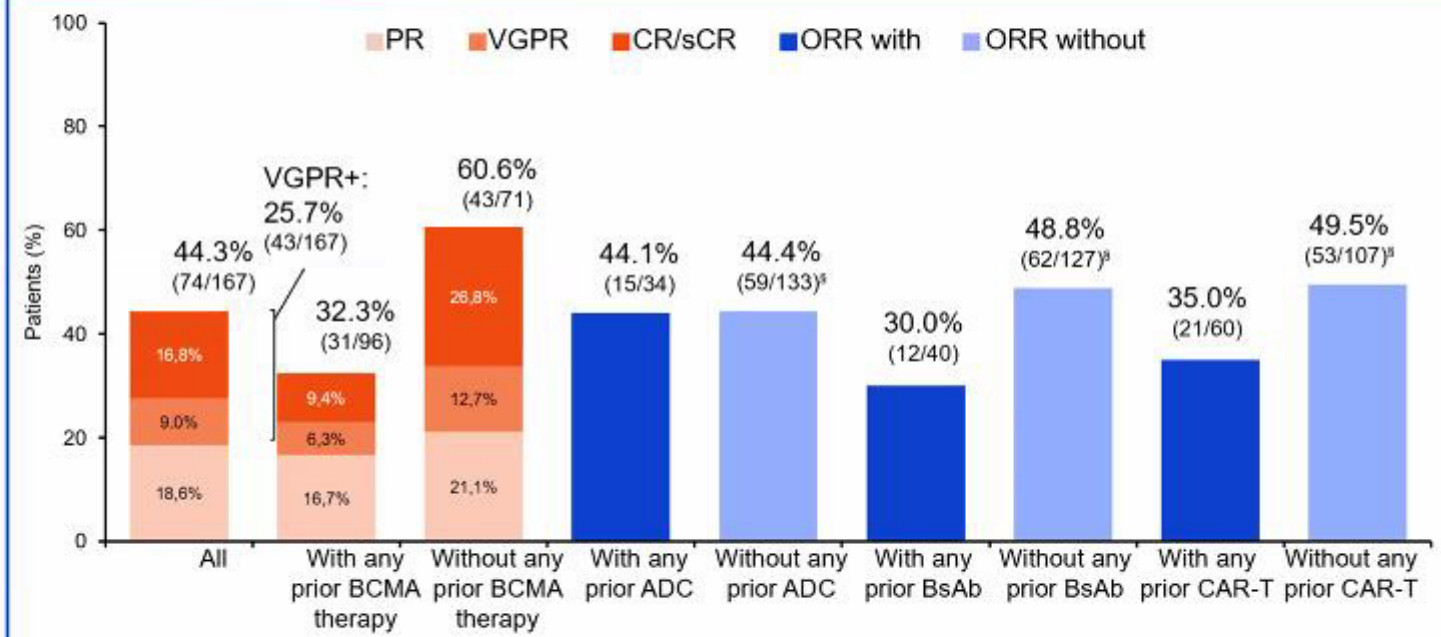
The majority of infections were Gr 1–2; infections leading to treatment discontinuation were uncommon

*System Organ Class level term; data cut-off: Aug 22, 2024; URTI, upper respiratory tract infection; UTI, urinary tract infection

Response at the 160mg TD level (n=167)

- Responses occurred early
  - median time to first response (PR+): 1.4 months (range: 0.5–4.6)
- Responses deepened over time
  - median time to best response: 2.6 months (range: 0.5–13.4)
- MRD negativity* achieved in 11/18 patients evaluated†

ORR at the 160mg TD level in all patients and in patient subgroups by prior treatment‡



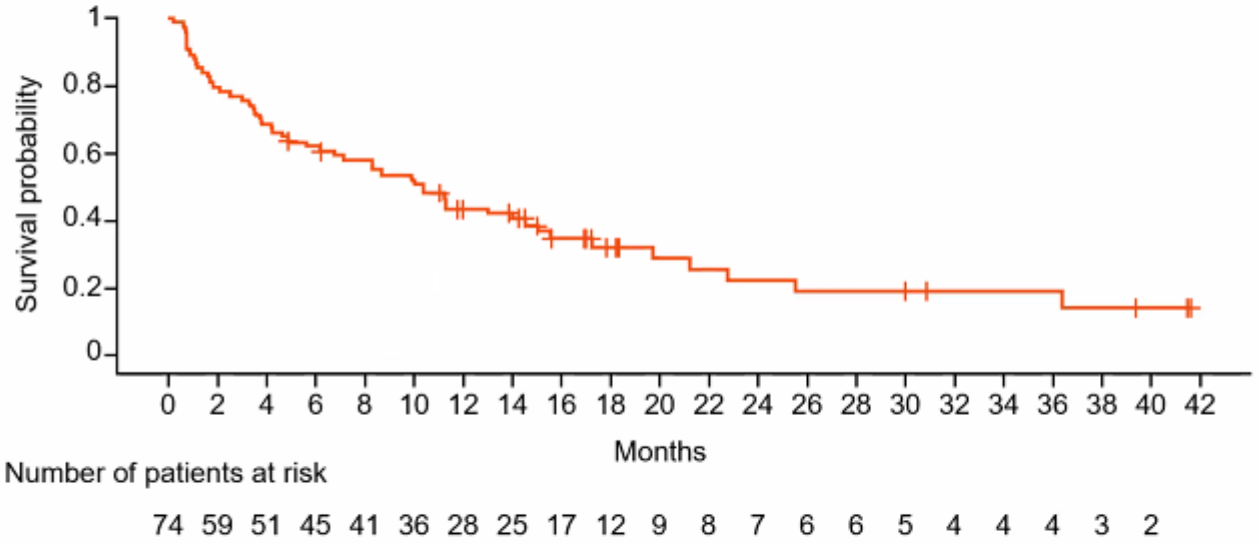
Cevostamab is clinically active in patients with heavily pretreated and highly refractory disease

*<10^{-5} level by NGS; †all patients were in VGPR+; ‡subgroups are not mutually exclusive; §unvalidated analysis; data cut-off: Aug 22, 2024; CR, complete response; MRD, minimal residual disease; NGS, next generation sequencing; ORR, overall response rate; PR, partial response; sCR, stringent CR; VGPR, very good PR

Durability of response at the 160mg TD level (n=167)

- **mDoR in PR+ (n=74): 10.4 months**
- **(95% CI: 6.2, 15.0)**
- **mDoR in VGPR+ (n=43): 21.2 months**
- **(95% CI: 15.0, 36.4)***

DoR at the 160mg TD level among patients in PR+ (n=74)



Cevostamab induces durable responses, especially in patients who achieve VGPR+

*unvalidated analysis; data cut-off: Aug 22, 2024; DoR, duration of response; mDoR, median DoR

First Results of a Phase 1, First-in-Human, Dose-Escalation Study of ISB 2001, a BCMAxCD38xCD3 Targeting Trispecific Antibody in Patients with Relapsed/Refractory Multiple Myeloma (RRMM)

Hang Quach[1], Bradley Augustson[2], Hanlon Sia[3], Nishi Shah[4], Eben Lichtman[5], Michaela Liedtke[6], Camille Martinet[7], Vinu Menon[8], Andrew Garton[9], Maria Pihlgren[10], Beata Holkova[11], Cyril Konto[8], Lida Pacaud[12] and Amit Khot[13]

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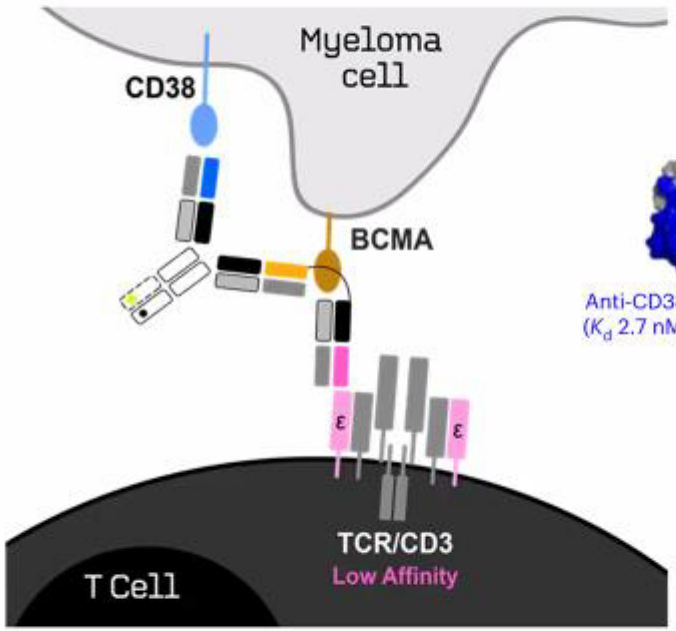
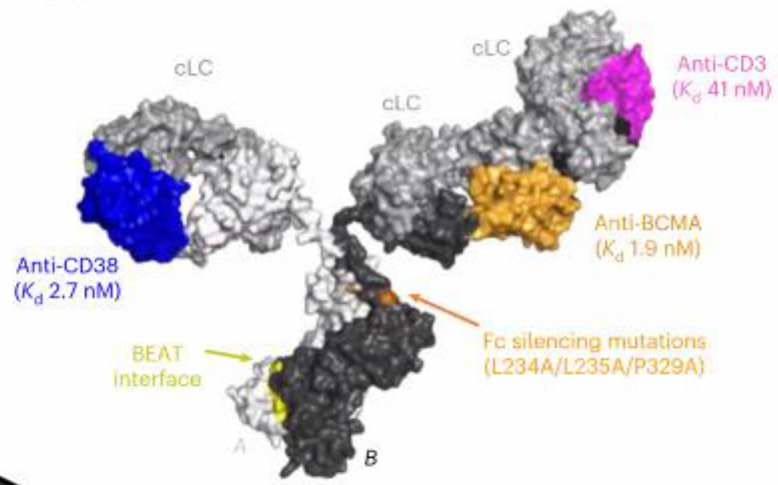
ISB 2001 (BCMAxCD38xCD3): First TREAT ™ Trispecific Antibody for Relapsed/Refractory Multiple Myeloma





Key Attributes

Generated using IGI's proprietary BEAT® protein platform

Enhanced avidity-based binding to myeloma cells with both BCMA and CD38 Fab domains

CD38 Fab domain targets non-overlapping epitopes with Daratumumab

Tuned BCMA>CD38>CD3 binding affinity and distal positioning of the CD38 vs CD3 binders drive potent tumor killing while minimizing CD38-related off-tumor adverse events

TREAT ™, Trispecific Engagement by Antibodies based on the TCR; BEAT®, Bispecific Engagement by Antibodies based on the TCR
Carretero-Iglesia L, et al. *Nat Cancer.* 2024 Oct;5(10):1494-1514. DOI

ISB 2001-101: Demographics and Disease Characteristics

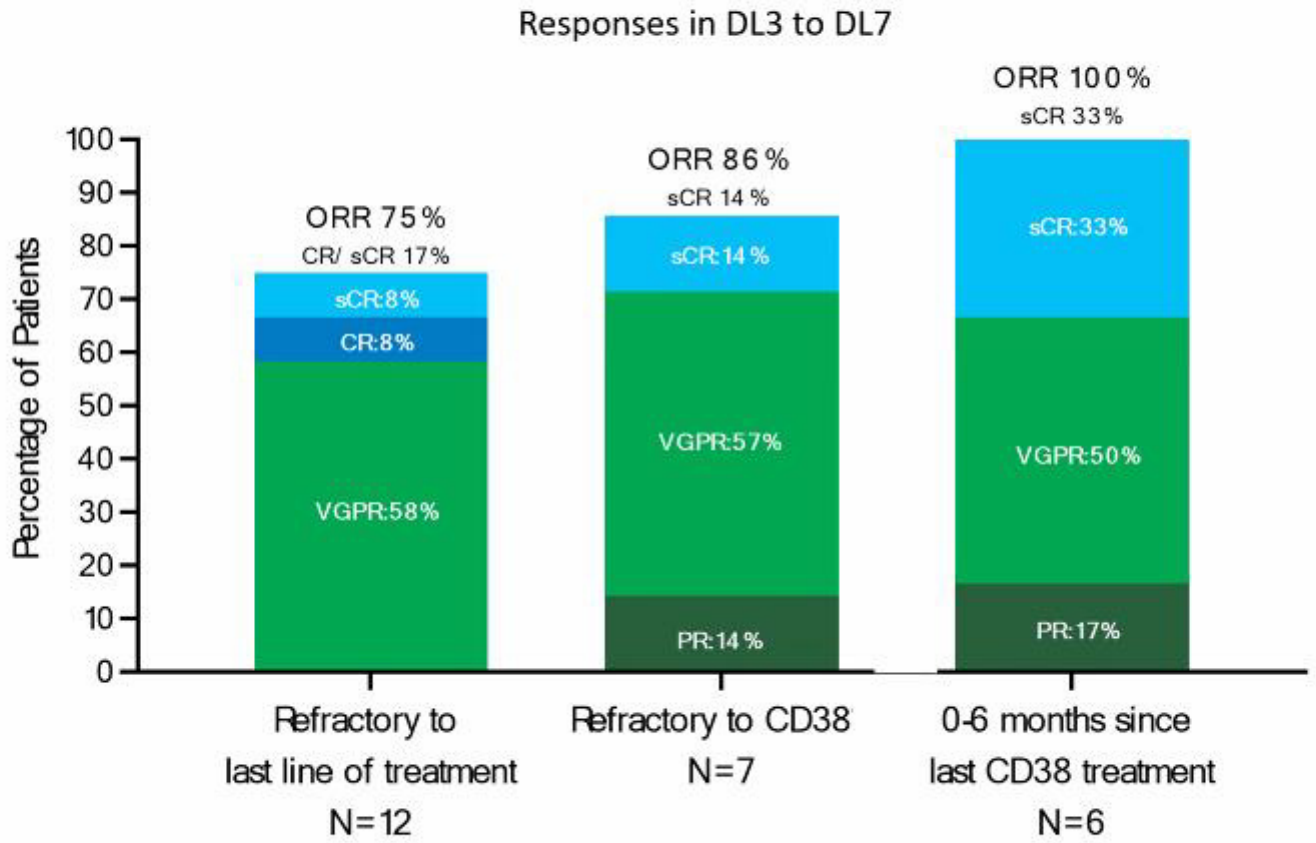
Characteristic	Total (N=20)
Gender	
Female, n (%)	8 (40)
Median Age, range (years)	66 (52; 80)
Race, n (%)	
Black or African American	1 (5)
White	16 (84)
Other	2 (11)
Ethnicity, n (%)	
Not Hispanic or Latino	19 (95)
ECOG performance status, n (%)	
0	15 (75)
1	5 (25)
Lytic Bone Disease, n (%)	15 (75)
Extramedullary Disease, n (%)	6 (30)
Revised ISS, n (%)	
I	11 (55)
II	5 (25)
III	1 (5)
Cytogenetics available, n (%)	12 (60)
High risk cytogenetics	5 (42)
Bone Marrow Myeloma/Plasma cells ≥ 30%, n (%)	5 (25)

Characteristic	Total (N=20)
Median number of lines of previous therapy (range)	6 (3; 11)
Previous therapy exposure, n (%)	
Triple-exposed	20 (100)
Triple-refractory	5 (25)
Penta-exposed	14 (70)
Penta-refractory	2 (10)
Refractory to last line of therapy	13 (65)
ASCT	19 (95)
Anti-BCMA CAR-T	2 (10)
Bispecifics	**9 (45)**
BCMA	1 (5)
FcRH5	6 (30)
GPRC5D	4 (20)
Anti-BCMA ADC	5 (25)

High risk cytogenetics defined as presence of del(17), del(1p), t(14:16), t(14:20), t(4:14) or 1q amp

ECOG, Eastern Cooperative Oncology Group; ISS, International Staging System; ASCT, Autologous stem cell transplantation; FcRH5, Fc receptor-like protein 5; GPRC5D, G-protein coupled receptor family C group 5 member D; ADC, antibody-drug conjugate

ISB 2001: High Response Rates In Patients Refractory to Last Line of Therapy, Refractory or Recently Failing CD38 Therapies



Early Clinical Results of ISB 2001 a novel TREAT ™ Trispecific

Safety:

- No DLTs up to 1200 µg/kg weekly dosing; mild CRS and injection site reactions, no ICANS or neurological Aes; low infection and hematological toxicity rates.

Early and sustained responses were observed across effective dose levels (DL3 to DL7):

- Anti-myeloma activity From 50 µg/kg (MRD-negative sCR) and higher
- 83% ORR overall (22% CR or better, 50% VGP R, 11% PR),
- 90% and 75% ORR in CAR-T/bispecific-naïve or pretreated patients, 86% with prior BCMA therapy, 86% in CD38-refractory patients.

PK and Translational:

- Dose-proportional PK with long half-life supports less-frequent dosing.
- T cell activation observed at effective doses.

Next Steps:

- Escalation continues to 2700 µg/kg, followed by dose-expansion to establish RP2D and best dosing schedule.


Any questions?