BiTE’s and Trispecific in Myeloma
IMS 2025
Toronto

Miri Zektser
Soroka Medical Centre

And the winner is....

לא מוצגים	מוצגים
Trispecific- anti BCMA+CD 38	Teclistamab+DaraRD in TE
Cevostamab Pom Dex in relapse	Elranatamab+DaraR in TIE
BiTEs consolidation post CART	Limited duration of BiTEs
Linvo in SMM, frail patients	IVIg
	Outpatient step-up dose

Post-Induction Outcomes and Updated Minimal Residual Disease Analysis From GMMG-HD10/DSMM-XX (MajesTEC-5): a Study of Teclistamab-Based Induction Regimens in Newly Diagnosed Multiple Myeloma (NDMM)*

*ClinicalTrials.gov Identifier: NCT05695508; sponsored by the University of Heidelberg Medical Center and in collaboration with Johnson & Johnson

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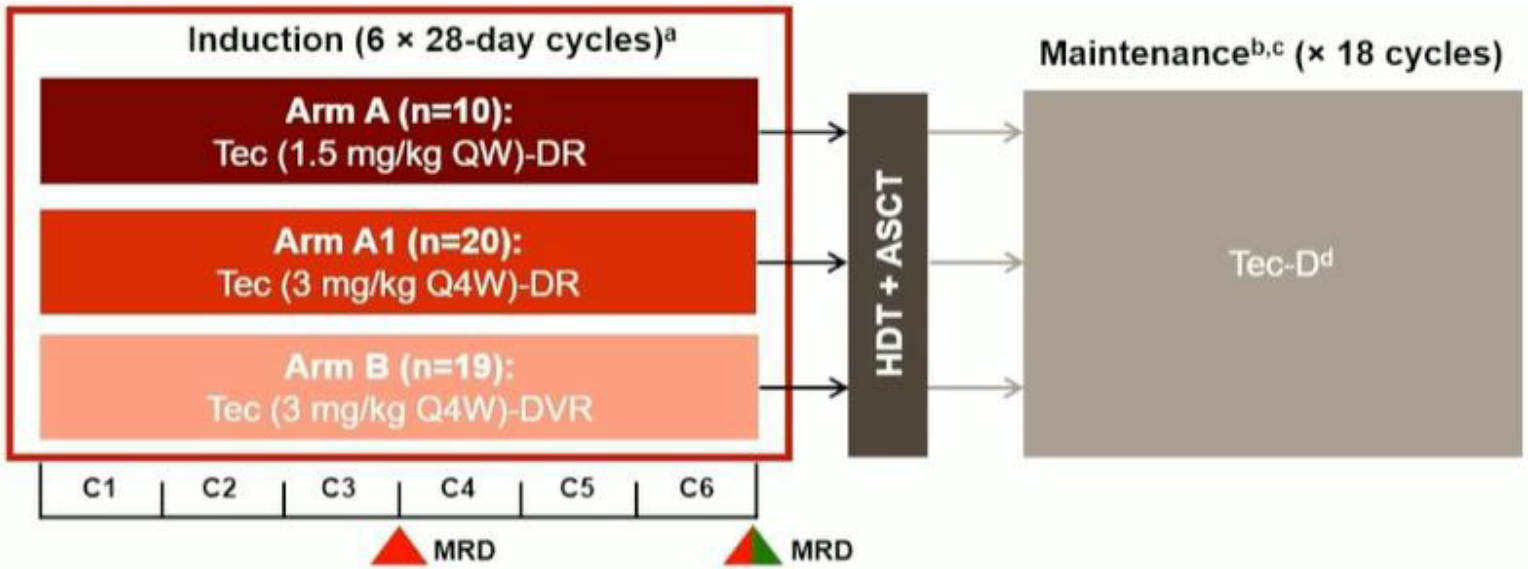
GMMG-HD10/DSMM-XX/MajesTEC-5: Study Design

Key eligibility criteria:

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



Primary endpoints:

- AEs, SAEs

Select secondary endpoints:

- MRD negativity (10^{-5} and 10^{-6})
- ORR
- ≥CR
- ≥VGPR
- Stem cell yield

MRD 10^{-5} via NGF

MRD 10^{-6} via NGS

- **Tec (Cycle 1):** Tec step-up dosing (0.06 and 0.3 mg/kg on Days 2 and 4) + 1.5 mg/kg on Days 8 and 15[e]
  - **Tec (Cycles 2-6):** 1.5 mg/kg QW on Day 1 (Arm A); 3 mg/kg Q4W on Day 1 (Arm A1 and B)
- **D:** 1800 mg SC per label (QW for Cycles 1-2; Q2W for Cycles 3-6)
- **V:** 1.3 mg/m^2 SC QW
- **R:** 25 mg PO daily starting in Cycle 2 (Days 1-21)
- **d:** 20 mg (PO or IV) in Cycles 1-4 (Arm A) or Cycles 1-2 (Arm A1/B) only

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	9 (90)	8 (80)	9 (45)	9 (45)	12 (63.2)	12 (63.2)	30 (61.2)	29 (59.2)
Anemia	5 (50)	0	8 (40)	4 (20)	7 (36.8)	1 (5.3)	20 (40.8)	5 (10.2)
Thrombocytopenia	3 (30)	1 (10)	7 (35)	2 (10)	7 (36.8)	1 (5.3)	17 (34.7)	4 (8.2)
Leukopenia	5 (50)	2 (20)	3 (15)	2 (10)	6 (31.6)	5 (26.3)	14 (28.6)	9 (18.4)

Neutropenia was the most common all grade hematologic TEAE.
The addition of weekly bortezomib did not increase the rate of thrombocytopenia

[a]TEAEs reported in ≥25% of patients in any arm. AEs are graded according to the NCI-CTCAE Version 5.0. The median follow-up was 7.3 (3.1-14.5) months.
AE, adverse event; D, daratumumab; DSMM, Deutsche Studiengruppe Multiples Myelom; GMMG, German-speaking Myeloma Multicenter Group; 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	7 (70)	1 (10)	10 (50)	2 (10)	8 (42.1)	0	25 (51.0)	3 (6.1)
URTI	6 (60)	0	8 (40)	1 (5)	6 (31.6)	0	20 (40.8)	1 (2)
Rash	6 (60)	2 (20)	5 (25)	0	8 (42.1)	0	19 (38.8)	2 (4.1)
GGT increased	3 (30)	0	6 (30)	3 (15)	5 (26.3)	4 (21.1)	14 (28.6)	7 (14.3)
Hypokalemia	1 (10)	0	9 (45)	2 (10)	4 (21.1)	0	14 (28.6)	2 (4.1)
Diarrhea	6 (60)	0	4 (20)	1 (5)	4 (21.1)	0	14 (28.6)	1 (2)
Nausea	1 (10)	0	4 (20)	0	8 (42.1)	0	13 (26.5)	0
PN	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)
Lipase increased	1 (10)	1 (10)	5 (25)	3 (15)	1 (5.3)	1 (5.3)	7 (14.3)	5 (10.2)
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
Hyperglycemia	3 (30)	0	3 (15)	1 (5)	0	0	6 (12.2)	1 (2)

- Safety consistent with individual treatment components
- All CRS events were grade 1/2 and resolved
  - 10 (20.4%) were grade 2
  - Most occurred in Cycle 1
  - No discontinuations due to CRS
- No ICANS reported
- No grade 5 TEAEs
- No increase in PN with bortezomib

[a]TEAEs reported in ≥25% of patients in any arm. AEs are graded according to the NCI-CTCAE Version 5.0. The median follow-up was 7.3 (3.1-14.5) months. [b]Constipation and hypogammaglobulinemia based on TEAE reporting also met the ≥25% threshold. Hypogammaglobulinemia is reported separately. AE, adverse event; ALT, alanine aminotransferase; BAP, blood alkaline phosphatase; CRS, cytokine release syndrome; D, daratumumab; DSMM, Deutsche Studiengruppe Multiples Myelom; GGT, gamma-glutamyl transferase; GMMG, German-speaking Myeloma Multicenter Group; ICANS, immune effector cell–associated neurotoxicity syndrome; NCI-CTCAE, National Cancer Institute Common Terminology Criteria for Adverse Events; PN, peripheral sensory neuropathy; 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)	10 (50)	11 (57.9)	4 (21.1)[b]	39 (79.6)	18 (36.7)[b]
Infections[c]								
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)	2 (10.5)	9 (18.4)	3 (6.1)
Nasopharyngitis	3 (30)	0	2 (10)	0	2 (10.5)	0	7 (14.3)	0
Pneumonia	1 (10)	1 (10)	0	0	2 (10.5)	2 (10.5)	3 (6.1)	3 (6.1)
RTI	0	0	1 (5)	0	2 (10.5)	0	3 (6.1)	0
Bronchitis	2 (20)	0	0	0	0	0	2 (4.1)	0

- 18 (36.7%) patients had grade 3/4 infections[b]
  - No discontinuations due to infection
  - No grade 5 infections
- Hypogammaglobulinemia[d] reported in 45 (91.8%) patients
  - 44 (89.8%) patients received ≥1 dose of IVIg
- Stringent infection prophylaxis was strongly recommended,[e] including Ig replacement
- Low patient numbers and relatively short follow-up time may account for differing infection rates across arms

[a]AEs are graded according to the NCI-CTCAE Version 5.0. The median follow-up was 7.3 (3.1-14.5) months. [b]One patient had a grade 3 "unknown" infection that was reported under the "uncoded" category. [c]Infections reported in >10% of patients in any arm. [d]Includes patients with ≥1 TEAE of hypogammaglobulinemia or a post-baseline IgG value <400 mg/dL. [e]Additional recommended measures included prophylaxis for Pneumocystis jirovecii pneumonia and herpes zoster reactivation as well as routine antibiotic prophylaxis. D, daratumumab; DSMM, Deutsche Studiengruppe Multiples Myelom; GMMG, German-speaking Myeloma Multicenter Group; Ig, immunoglobulin; IVIg, intravenous immunoglobulin; NCI-CTCAE, National Cancer Institute Common Terminology Criteria for Adverse Events; QW, weekly; Q4W, every 4 weeks; R, lenalidomide; RTI, respiratory tract infection; TEAE, treatment-emergent adverse event; Tec, teclistamab; URTI, upper respiratory tract infection; V, bortezomib.

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GMMG-HD10/DSMM-XX/MajesTEC-5: Stem Cell Mobilization[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)
Undergone stem cell mobilization,[b] n (%)	10 (100)	20 (100)	17 (89.5)[c]	47 (95.9)
Received plerixafor[d]	2 (20)	11 (55)	7 (41.2)	20 (42.6)
Received cyclophosphamide and G-CSF[d]	10 (100)	15 (75)	14 (82.4)	39 (83)
Stem cell yield (10^6 CD34 cells/kg)				
Median (range)	8.6 (5.7-14.9)	7.7 (2.6-15.1)	7.5 (2.9-15.9)	8.1 (2.6-15.9)

Tec-D(V)R enabled successful stem cell mobilization (~96% of patients) with total median stem cell yield surpassing minimum protocol requirements[e]

[a]Stem cell collection was planned after 3 cycles of induction. [b]Percentages are calculated based on the number of patients in each treatment group as the denominator. [c]2 patients in the Tec-DVR group did not undergo mobilization; 1 patient withdrew consent after Cycle 3 and 1 patient failed to proceed to mobilization due to cytopenia and insufficient circulation of CD34+ cells. [d]Percentages are calculated based on the number of patients who underwent stem cell mobilization as the denominator. [e]Per protocol minimum, defined as 2.5×10^6/kg CD34+ cells. In addition, an ideal target was also identified as a yield of 5×10^6/kg CD34+ cells.
D, daratumumab; DSMM, Deutsche Studiengruppe Multiples Myelom; G-CSF, granulocyte-colony stimulating factor; GMMG, German-speaking Myeloma Multicenter Group; QW, weekly; Q4W, every 4 weeks; R, lenalidomide; Tec, teclistamab; V, bortezomib.

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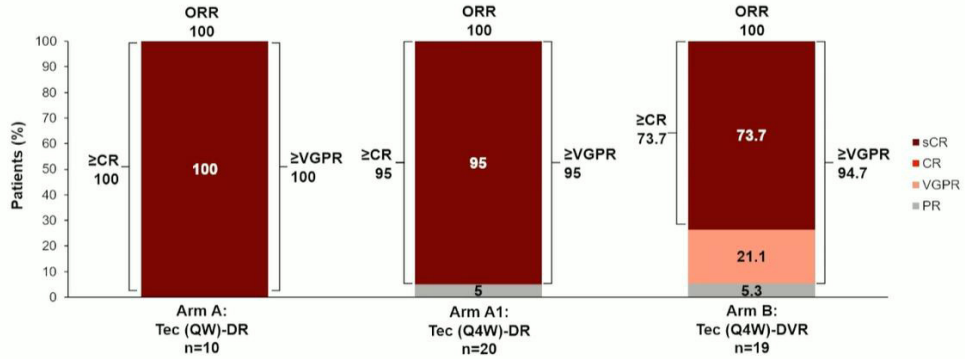
GMMG-HD10/DSMM-XX/MajesTEC-5: Response Rates[a]



100% of patients responded by the end of induction

[a]Response was assessed by investigators based on IMWG criteria, with a confirmed response requiring ≥2 consecutive identical response assessments. ORR was defined as ≥PR. CR, complete response; D, daratumumab; DSMM, Deutsche Studiengruppe Multiples Myelom; GMMG, German-speaking Myeloma Multicenter Group; IMWG, International Myeloma Working Group; ORR, overall response rate; 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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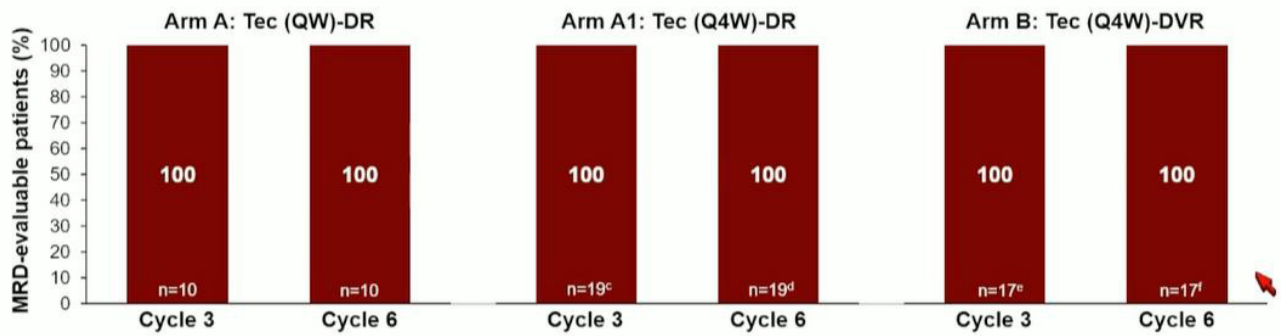
GMMG-HD10/DSMM-XX/MajesTEC-5: MRD Negativity (10^{-5})[a] in the MRD-Evaluable Analysis Set

- MRD-evaluable population: all patients with an available MRD test (positive or negative)[b]
  - Only 1 patient was not evaluable for MRD throughout induction (Cycle 3 or 6) due to discontinuation before Cycle 3



With completion of induction, 100% MRD negativity (10^{-5}) continues to be observed in MRD-evaluable patients, regardless of depth of response

[a]MRD-negativity rate was defined as the proportion of patients who achieved MRD negativity (10^{-5}) per NGF, regardless of response (ie, not all patients achieved CR). [b]Excluding those who were not tested, indeterminate, or had no baseline clone detected (NGS). [c]One patient was not tested. [d]One patient had discontinued after completing Cycle 3. [e]One patient was not tested, and 1 had discontinued before completing Cycle 3. [f]One patient had discontinued before completing Cycle 3, and 1 had an indeterminate result. CR, complete response; D, daratumumab; DSMM, Deutsche Studiengruppe Multiples Myelom; GMMG, German-speaking Myeloma Multicenter Group; MRD, minimal residual disease; NGF, next-generation flow cytometry; NGS, next-generation sequencing; QW, weekly; Q4W, every 4 weeks; R, lenalidomide; Tec, teclistamab; V, bortezomib.

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Elranatamab in Combination With Daratumumab and Lenalidomide in Patients With Newly Diagnosed Multiple Myeloma Not Eligible for Transplant: Initial Results from MagnetisMM-6 Part 1

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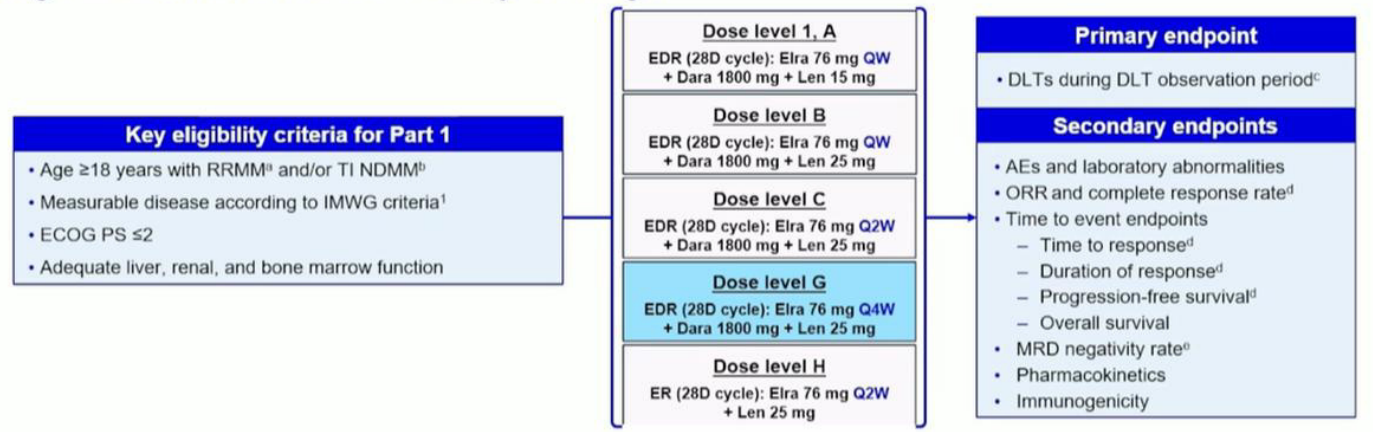
Previously presented at the 2025 ASCO Annual Meeting | May 30-June 3, 2025 | Chicago, IL and the EHA 2025 Congress | June 12-15, 2025 | Milan, Italy

Objectives

- MagnetisMM-6 (NCT05623020) is designed to:
  - Evaluate the efficacy and safety of elranatamab + lenalidomide ± daratumumab (EDR or ER) vs daratumumab + lenalidomide + dexamethasone (DRd) in patients with transplant-ineligible NDMM
  - Part 1 of the study evaluates the optimal dose of EDR or ER in patients with RRMM or NDMM to determine the recommended phase 3 dose for Part 2

MagnetisMM-6 Part 1 Study Design



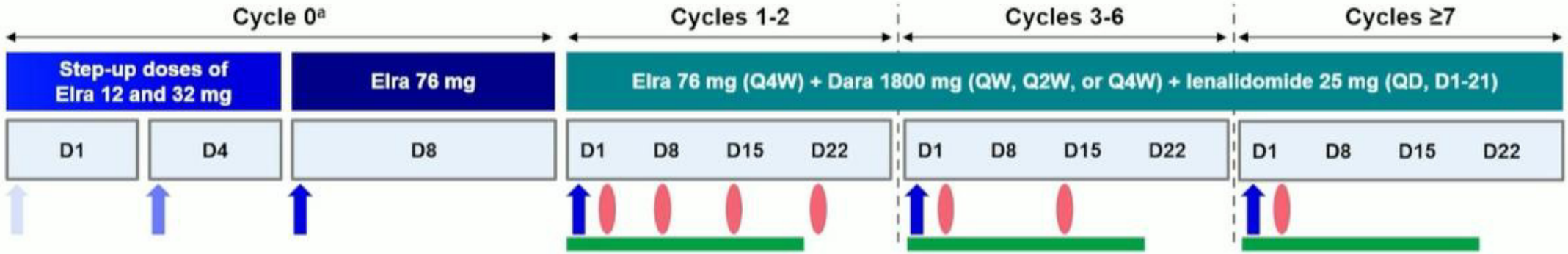
MagnetisMM-6 Part 1 **dose level G** is evaluating the combination of **elranatamab 76 mg SC Q4W**, **daratumumab 1800 mg SC**, and **lenalidomide 25 mg PO** in patients with transplant-ineligible **NDMM** (Data cutoff: April 1, 2025)

1. Kumar S, et al. Lancet Oncol 2016;17:e328-e346.

[a] Must have received 1 or 2 prior lines of MM therapy including ≥1 IMiD and ≥1 PI; [b] Defined as age ≥65 years or <65 years with comorbidities impacting the possibility of transplant; [c] DLTs will not be assessed in any DL that represents a lower dose than an already cleared DL, or where the initial DLT period is the same as an already cleared DL; [d] Per IMWG response criteria; [e] Per IMWG sequencing criteria

AE=adverse event; D=day; Dara=daratumumab; DL=dose level; DLT=dose-limiting toxicity; ECOG PS=Eastern Cooperative Oncology Group performance status; EDR=elranatamab + daratumumab + lenalidomide; Elra=elranatamab; ER=elranatamab + lenalidomide; IMiD=immunomodulatory drug; IMWG=International Myeloma Working Group; Len=lenalidomide; MRD=minimal residual disease; NDMM=newly diagnosed multiple myeloma; ORR=objective response rate; PI=proteasome inhibitor; PO=orally; RRMM=relapsed or refractory multiple myeloma; SC=subcutaneously; TI=transplant ineligible; QW=once weekly; Q2W=every 2 weeks; Q4W=every 4 weeks

MagnetisMM-6 Part 1 Dose Level G Dosing Schedule



Elranatamab 12 mg SC

Elranatamab 32 mg SC

Elranatamab 76 mg SC

Daratumumab 1800 mg SC

Lenalidomide 25 mg PO

Elranatamab premedication
- Diphenhydramine 25 mg (or equivalent) PO or IV
- Acetaminophen 650 mg (or paracetamol 500 mg) PO
- Dexamethasone 20 mg (or equivalent) PO or IV

Daratumumab premedication
- Diphenhydramine 25-50 mg (or equivalent) PO or IV
- Acetaminophen 650-1000 mg (or paracetamol 500) PO
- Dexamethasone 20 mg (or equivalent) PO 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

D=day; Dara=daratumumab; Elra=elranatamab; IV=intravenously; PO=orally; QD=daily; QW=once weekly; Q2W=every 2 weeks; Q4W=every 4 weeks; SC=subcutaneously

Baseline Characteristics

- All patients (100%) had NDMM

	N=37
Age, median (range), years	75.0 (67-83)
Female, n (%)	23 (62.2)
Race, n (%)	
Asian	5 (13.5)
White	32 (86.5)
ECOG PS, n (%)	
0	22 (59.5)
1	14 (37.8)
2	1 (2.7)

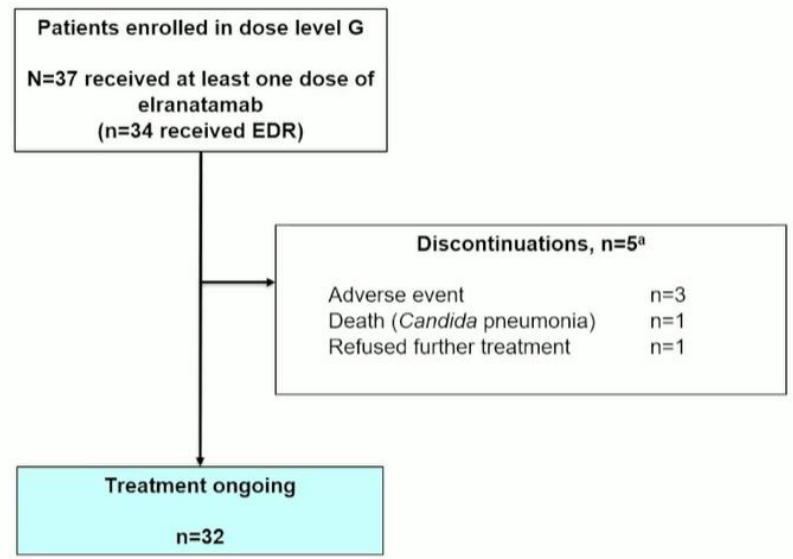
	N=37
R-ISS disease stage by investigator, n (%)	
I	9 (24.3)
II	20 (54.1)
III	5 (13.5)
Unknown	3 (8.1)
Baseline bone marrow plasma cells, n (%)	
<50%	28 (75.7)
≥50%	9 (24.3)
Frail status, n (%)[a]	
Yes	9 (24.3)
No	28 (75.7)

[a] According to the simplified IMWG scale using scores for ECOG PS, Charlson Comorbidity Index, and age

ECOG PS=Eastern Cooperative Oncology Group performance status; IMWG=International Myeloma Working Group; NDMM=newly diagnosed multiple myeloma; R-ISS=Revised Int

Patient Disposition

- 37 patients with TI NDMM enrolled and received at least one dose of elranatamab
  - 34 patients received the EDR regimen
  - 3 patients received only elranatamab and discontinued during the step-up period
- As of the data cutoff (Apr 1, 2025), median follow-up was 7.9 (range, 1.2-9.5) months
  - 32 (86.5%) patients were still on treatment



[a] 3 patients received only elranatamab and discontinued during the step-up dose period

Treatment-Emergent Adverse Events ≥15%

- The most frequent (≥50%) TEAEs were hematologic (83.8%; grade 3/4 78.4%), infections (70.3%; grade 3/4 18.9%), and CRS (62.2%, grade 3/4 0%)
- All CRS events were grade ≤2
  - 45.9% grade 1, 16.2% grade 2
- One grade 2 ICANS event was reported

	N=37	
TEAE, n (%)[a]	**Any grade**	**Grade 3/4**
Any	37 (100)	35 (94.6)
Hematologic		
Neutropenia[b]	28 (75.7)	27 (73.0)
Anemia[c]	13 (35.1)	7 (18.9)
Thrombocytopenia[d]	6 (16.2)	4 (10.8)
Nonhematologic		
CRS	23 (62.2)	0
Pyrexia	14 (37.8)	0
Cough	11 (29.7)	0
Injection site reaction	11 (29.7)	0
Nausea	11 (29.7)	0
Rash	11 (29.7)	3 (8.1)
Diarrhea	9 (24.3)	1 (2.7)
Hypogammaglobulinemia	9 (24.3)	1 (2.7)
Constipation	8 (21.6)	0
Decreased appetite	8 (21.6)	2 (5.4)
Fatigue	7 (18.9)	0
Peripheral sensory neuropathy	7 (18.9)	0
Asthenia	6 (16.2)	4 (10.8)
Cytomegalovirus test positive	6 (16.2)	0
Edema peripheral	6 (16.2)	

1. Lee DW, et al. Biol Blood Marrow Transplant 2019;25:625-638.

[a] TEAEs according to the Medical Dictionary for Regulatory Activities v27.1 and Common Terminology Criteria for Adverse Events v5; severity of CRS and ICANS was assessed according to the American Society for Transplantation and Cellular Therapy criteria[1]; [b] Including neutrophil count decreased, neutrophil percentage decreased, cyclic neutropenia, agranulocytosis, granulocytopenia, and granulocyte count decreased; [c] Includes hemoglobin decreased, red blood cell count decreased, hematocrit decreased, normochromic anemia, normocytic anemia, and normochromic normocytic anemia; [d] Includes platelet count decreased

CRS=cytokine release syndrome; ICANS=immune effector cell-associated neurotoxicity syndrome; TEAE=treatment-emergent adverse event

TEAEs: Infections ≥5%

- Any-grade infections were reported in 70.3% of patients (grade 3/4, 18.9%)
  - One case of grade 5 *Candida* pneumonia was reported
- Frequent (any grade >10%) infections included upper respiratory tract infection and *Escherichia* urinary tract infection
- Anti-infective prophylaxis was given
  - 91.9% received immunoglobulin replacement therapy
  - 81.1% received anti-viral prophylaxis
  - 83.8% received anti-*Pneumocystis jirovecii* prophylaxis

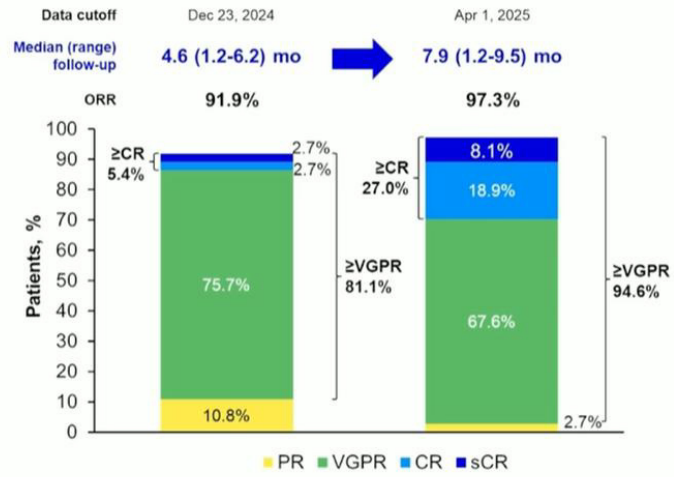
	N=37	
TEAE, n (%)[a]	**Any grade**	**Grade 3/4**
Infections[b]	26 (70.3)	7 (18.9)
Upper respiratory tract infection	8 (21.6)	0
Escherichia urinary tract infection	4 (10.8)	1 (2.7)
Bronchitis	3 (8.1)	0
Cytomegalovirus reactivation*	4 (10.8)	1 (2.7)
Rhinitis	3 (8.1)	0
Viral upper respiratory tract infection	3 (8.1)	0
Pneumonia	2 (5.4)	1 (2.7)
Urinary tract infection	2 (5.4)	0

* 3 patients with cytomegalovirus infection reactivation, 1 patient with cytomegalovirus viremia and pneumonia cytomegaloviral (grade 3)

[a] TEAEs according to the Medical Dictionary for Regulatory Activities v27.1 and Common Terminology Criteria for Adverse Events v5; [b] Infections include preferred terms in the system organ class of infections and infestations
TEAE=treatment-emergent adverse event

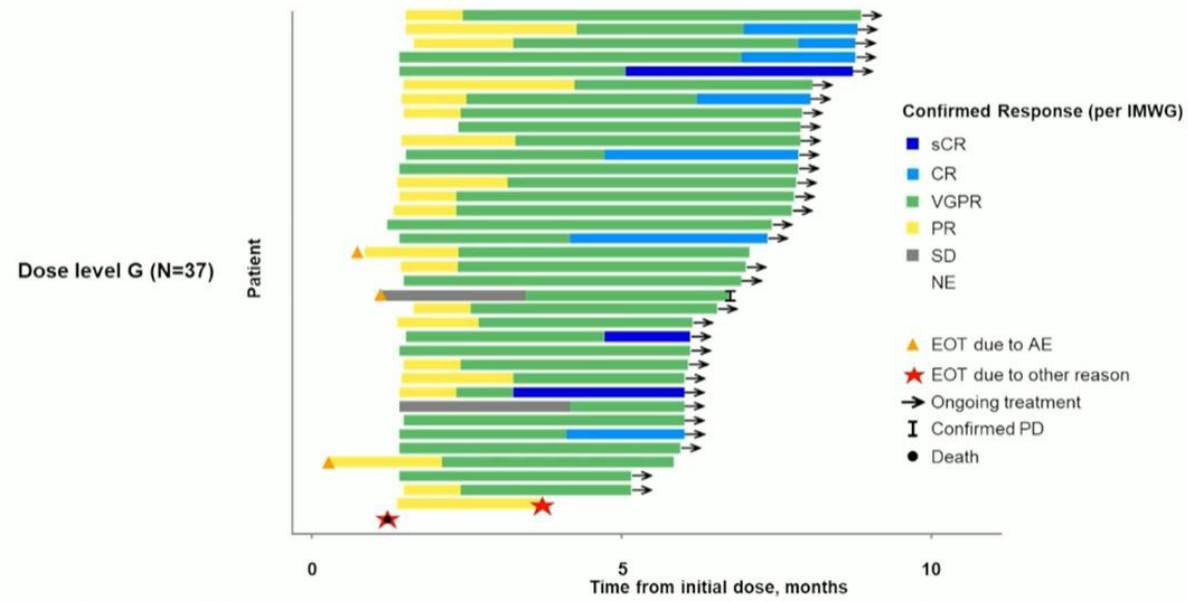
Early Emerging Response Data

- The confirmed ORR (ITT, N=37) by investigator was 97.3% (95% CI, 85.8-99.9)
  - 94.6% had VGPR or better
  - 27.0% had CR or better
- Responses occurred early
  - Median time to response of 1.5 (range, 0.3-4.2) months
- Median follow-up was short
  - CR rate will increase over time



CR=complete response; mo=months, ORR=objective response rate; PR=partial response; sCR=stringent complete response; VGPR=very good partial response

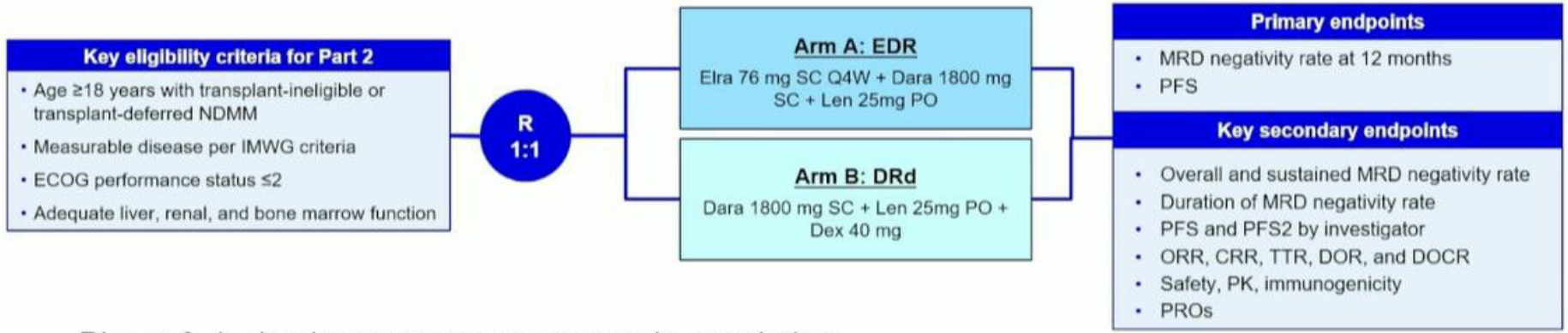
Duration of Progression-Free Survival



AE=adverse event; CR=complete response; EOT=end of trial; IMWG=International Myeloma Working Group; NE=not evaluable; PD=progressive disease; PR=partial response; sCR=stringent complete response; SD=stable disease; VGPR=very good partial response

MagnetisMM-6 Phase 3 – Enrolling

- Phase 3 MagnetisMM-6 Part 2 evaluates EDR (elranatamab 76 mg SC Q4W + daratumumab 1800 mg SC + lenalidomide 25 mg PO) vs DRd (daratumumab + lenalidomide + dexamethasone) in transplant-ineligible and transplant-deferred patients with NDMM



– Phase 3 design incorporates treatment de-escalation

Acknowledgments

- We thank the MagnetisMM-6 trial patients and their families, as well as the study investigators, nurses, and site staff
- This study was sponsored by Pfizer. Medical writing support was provided by William Clafshenkel, PharmD, PhD, of Nucleus Global, and was funded by Pfizer

Sustained Remission Following Limited Duration of Bispecific Antibody Therapy in Patients with Relapsed/Refractory Multiple Myeloma

22nd International Myeloma Society Annual Meeting
Toronto, Canada

MEDICAL COLLEGE OF WISCONSIN
knowledge changing life
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Methods

Inclusion criteria

- Patients treated with bispecific or multispecific antibodies targeting BCMA and/or GPRC5D (either standard of care or an investigational drug)
- Stopped treatment for reasons other than progression or death
- Remained in remission ≥3 months post-discontinuation

Outcomes of interest

- Relapse-free survival
- Relapse and non-relapse mortality
- Cumulative incidence of ≥ grade 3
- Kinetics of humoral immunodeficiency (assuming an IgG level of >700 mg/dL as normal)
- Utilization of intravenous immunoglobulin supplementation

Patient Characteristics

78 out of 720 patients treated with a bispecific antibody were included

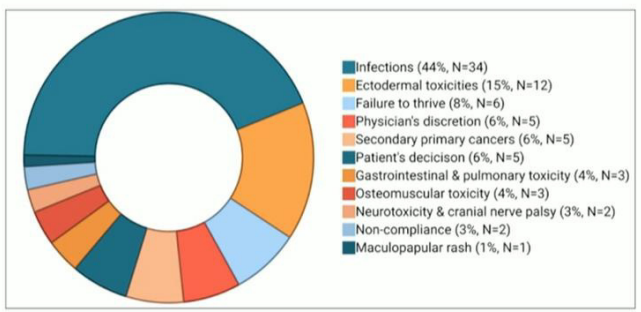
- Median prior lines of therapy: 4 (range 1-9)
- Median total duration of bispecific antibody before treatment discontinuation: 7 (range 1-40) months
- 97% of patients attained a ≥VGPR at treatment discontinuation
- 72% of patients were treated with a BCMA-directed bispecific antibody

Characteristics	N = 78[1]
Age at initiation of bispecific antibody therapy	70 (26 - 86)
Sex	
Female	43 (55%)
Male	35 (45%)
Race	
Asian	2 (2.9%)
Black	14 (18%)
Caucasian	57 (73%)
Hispanic	3 (3.8%)
Others	2 (2.6%)
Subtype of myeloma	
IgA Kappa	12 (15%)
IgA Lambda	5 (6%)
IgG Kappa	19 (24%)
IgG Lambda	20 (26%)
Kappa light chain	16 (21.3%)
Lambda light chain	6 (7.7%)
High-risk cytogenetics#	35 (47%)
Extraosseous extramedullary disease#	6 (8%)
[1] Median (Min-Max); n (%)	

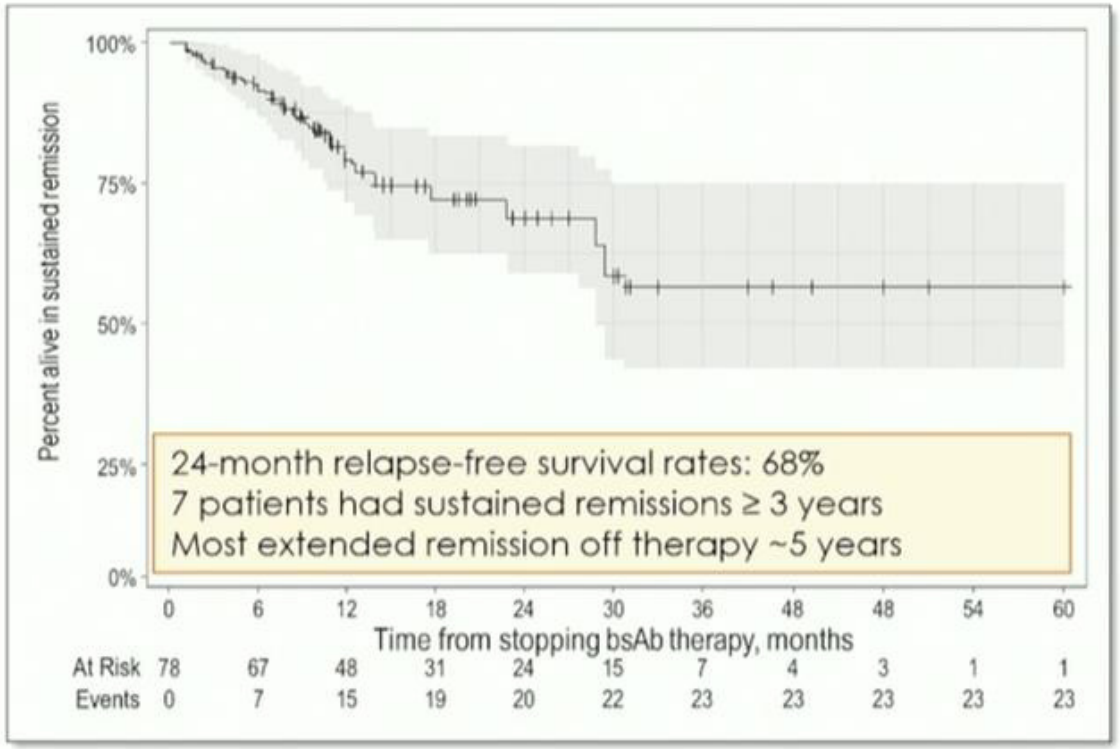
Data is available in 75 patients. High-risk cytogenetics is defined by the presence of any one of these abnormalities on bone marrow FISH studies: t(4;14), t(14;16), t(14;20), gain/amp(1q), del(1p), or del(17p)

Causes For Treatment Discontinuation

The most common reason for treatment discontinuation was infections



Relapse-Free Survival and Its Predictive Factors

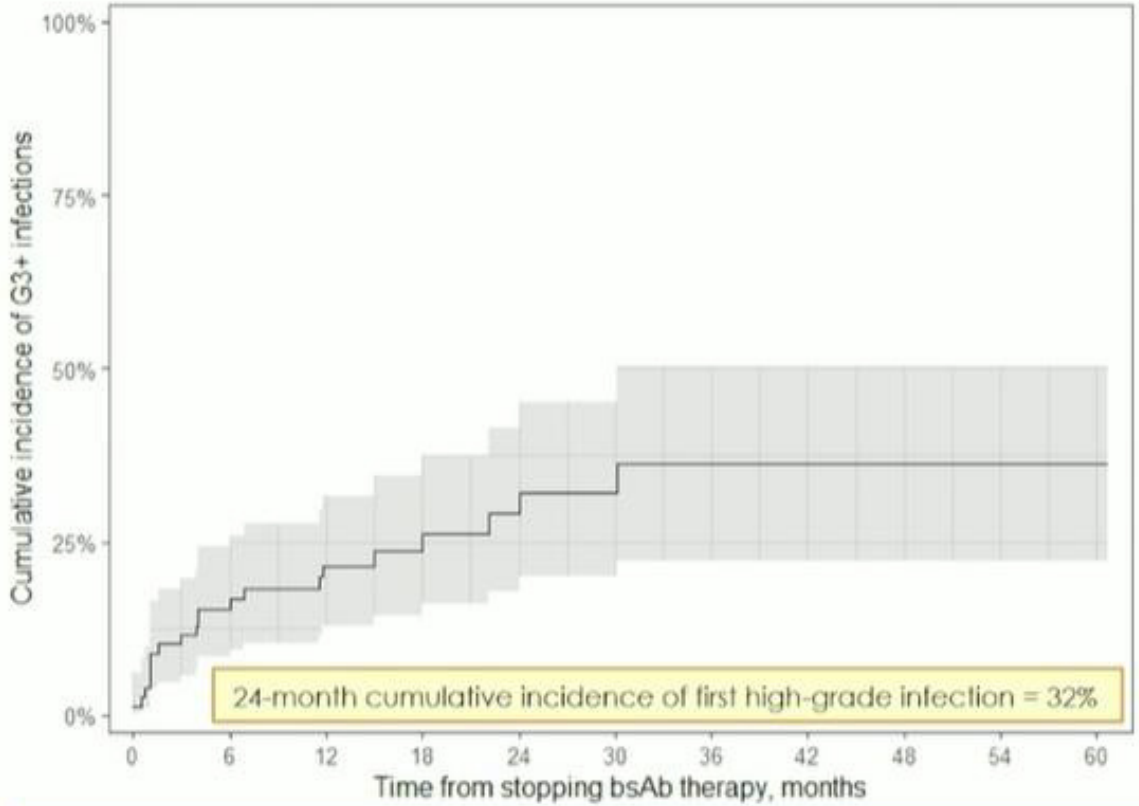


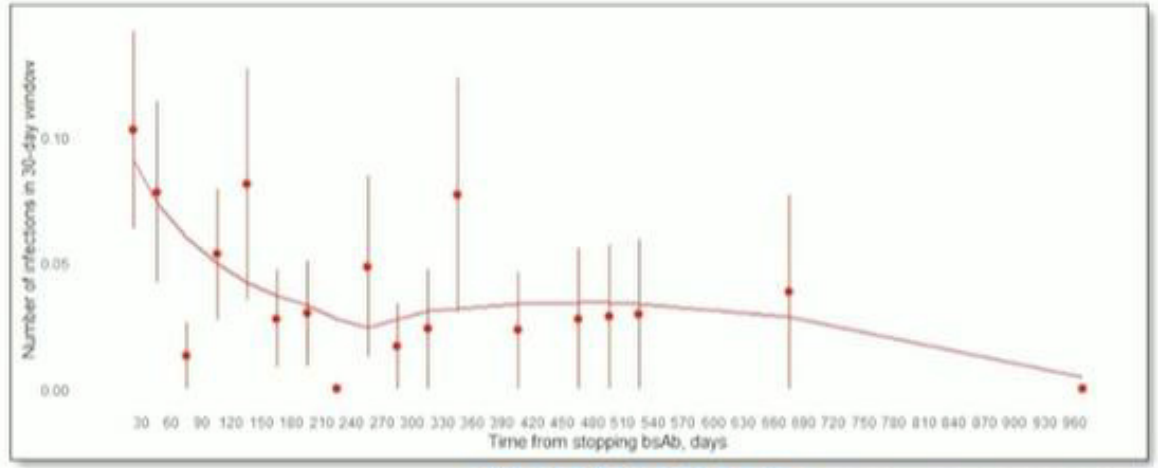
Factors associated with inferior relapse-free survival

- Presence of EMD (HR = 7.88; 95% CI: 1.95–31.8; p < 0.004)
- Higher number of prior lines of therapy (HR = 1.79; 95% CI: 1.32–2.43; p < 0.001)
- Partial remission at time of treatment discontinuation (HR = 28.3; 95% CI: 2.03–390; p = 0.012)

EMD: extramedullary disease; HR: hazard ratio
AIC-guided backward model selection was used to select a parsimonious model for predicting relapse-free survival from the following predictors: Age at bispecific antibody (bsAb) initiation, sex, high-risk cytogenetics, EMD at initiation of bsAb, number of prior lines of therapy, number of prior ASCT, target of bsAb, time from myeloma diagnosis to the start of bsAb (grouped), best disease response (grouped), IMWG response at bsAb discontinuation (grouped), and total duration of bsAb therapy (grouped).

Risk of ≥ Grade 3 Infection Following Discontinuation of Treatment



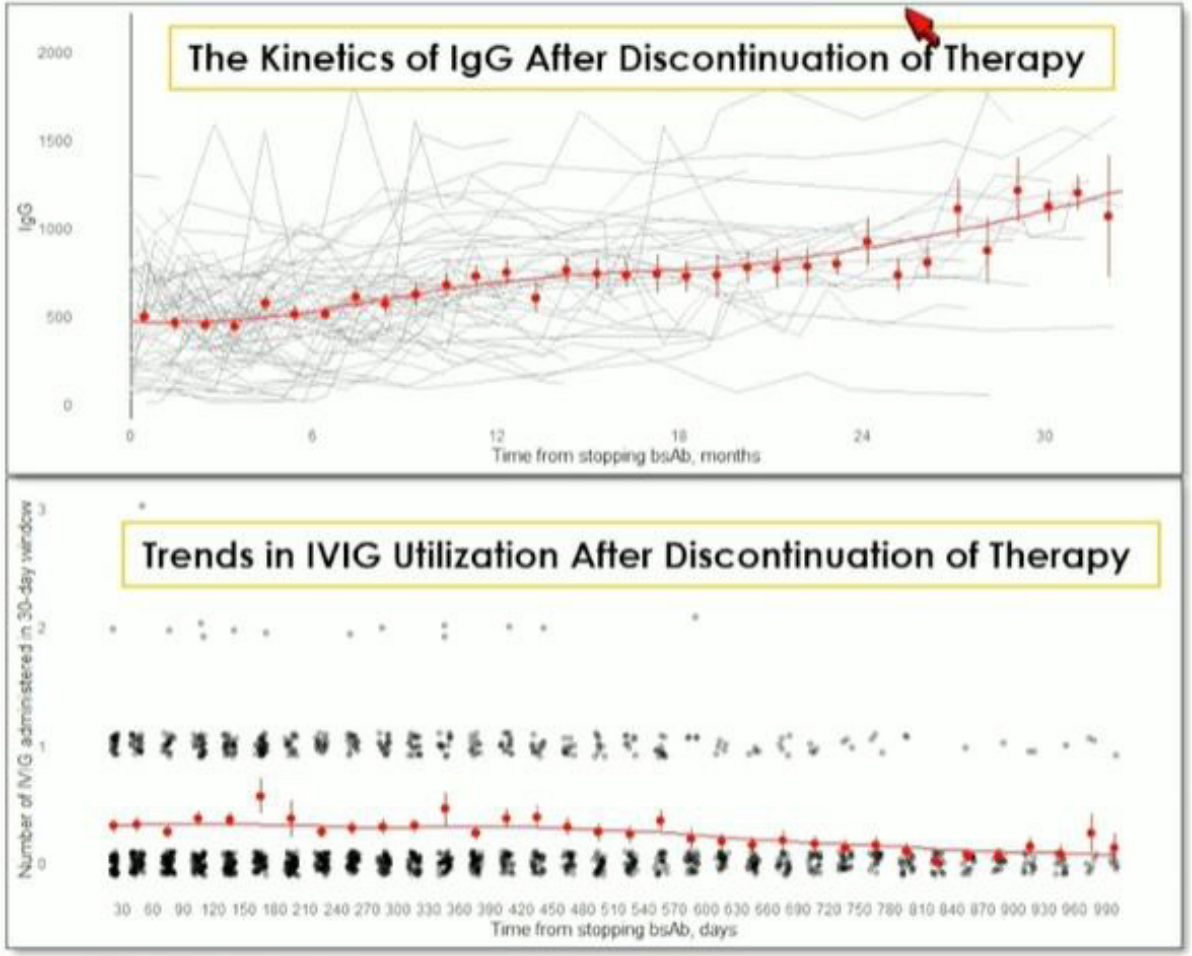


Characteristic	n N = 222	≥ Grade 3 Infections per month N = 222	Any ≥ grade 3 infection in 30-day window N = 222
Window			
D0 - 179	78	0.07 (0.16)	5.21%
D180 - 359	67	0.04 (0.14)	2.79%
D360 - 539	43	0.04 (0.16)	4.07%
D540 - 719	26	0.04 (0.20)	3.85%
D900 - 1079	8	0.00 (0.00)	0%

n; Mean (SD); Mean

The rates of high-grade infection improve with time off therapy, with no infection reported beyond 900 days after ceasing all treatment

Immune Reconstitution and IVIG Utilization



Characteristic	n N = 2051	Mean IgG N = 2052	IgG<700 N = 2053
Window			
D0 - 179	64	495 (255)	74.90%
D180 - 359	51	595 (265)	70.90%
D360 - 539	39	745 (317)	46.90%
D540 - 719	25	759 (339)	44.90%
D720 - 899	17	943 (390)	22.50%
D900 - 1079	9	1,110 (368)	11.10%
1 n; 2 Mean (SD); 3 Mean			

Normal IgG level of >700 mg/dL

Characteristic	n N = 2641	IVIGs per month N = 2642	Any IVIG in 30-day window N = 2643
Window			
D0 - 179	78	0.35 (0.36)	32.90%
D180 - 359	67	0.42 (1.25)	26.80%
D360 - 539	49	0.28 (0.39)	26.50%
D540 - 719	31	0.25 (0.35)	22.60%
D720 - 899	24	0.12 (0.29)	10.80%
D900 - 1079	15	0.11 (0.29)	10.00%
1 n; 2 Mean (SD);3 Mean			

Slow but steady improvement in serum IgG levels, with 13 mg/dL increments each month off therapy, along with a significant decrease in IVIG supplementation over time, nearly 2.5 years after stopping treatment

Amsterdam UMC
Universitair Medische Centra

IVIG and longer dosing intervals reduce risk of infections in patients with RRMM treated with teclistamab

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1. Amsterdam UMC location Vrije Universiteit Amsterdam; 2. Cancer Center Amsterdam, Cancer Biology and Immunology, Amsterdam;
3. Haga Hospital, The Hague, The Netherlands; 4. HOVON Data Center, Rotterdam, The Netherlands; 5. Erasmus MC Cancer Institute, Rotterdam, The Netherlands

September 20th, 2025

Retrospective, single center cohort study

- All patients with RRMM who were treated with teclistamab in Amsterdam University Medical Center, The Netherlands
- Antimicrobial prophylaxis: cotrimoxazole and valaciclovir
- IVIG as primary prophylaxis when polyclonal IgG was <4 g/L or as secondary prophylaxis in patients who developed a severe infection (CTC grade ≥3) with polyclonal IgG <4 g/L
  - Patients more often received primary prophylaxis due to increasing evidence on the benefit of IVIG
- Infections documented from start of treatment until disease progression, death or the date of last follow-up

17% never received IVIG, 90% due to early progression

Patient characteristics

- 80 patients with RRMM
  - 51/80 (64%) in clinical trial
  - 29/80 (36%) in compassionate use program
- ISS III in 17% of patients
- High-risk cytogenetic abnormalities in 40%
- Extra-medullary disease in 23%
- Median 5 prior lines of therapy
- 52% triple-class refractory

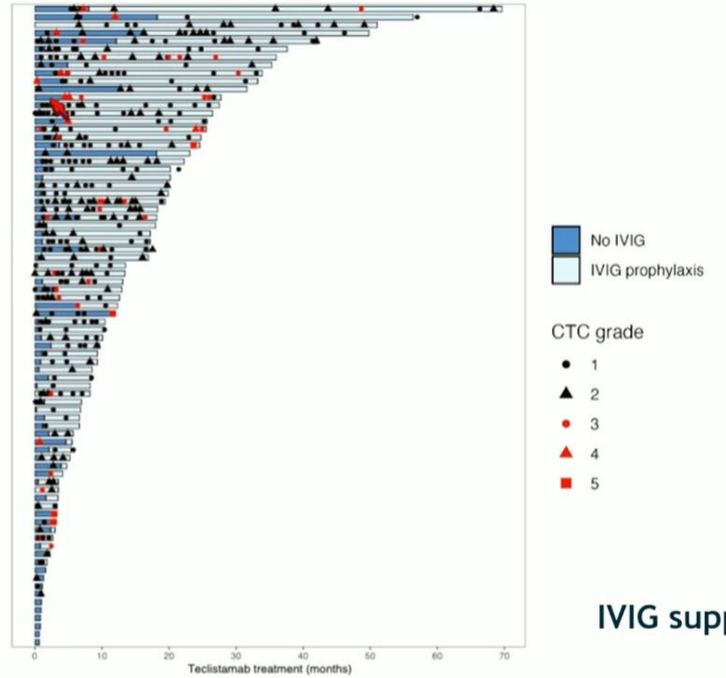
High incidence of infections

Incidence

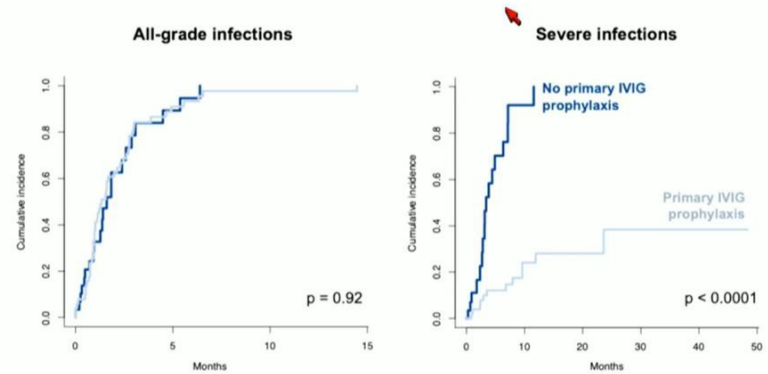
- 72/80 (90%) patients experienced >1 infection (all grades)
- 30/80 (38%) patients experienced >1 severe infection
- 4/80 (5%) died due to infection

Total

- 390 infections occurred, of which 48 (12%) were severe

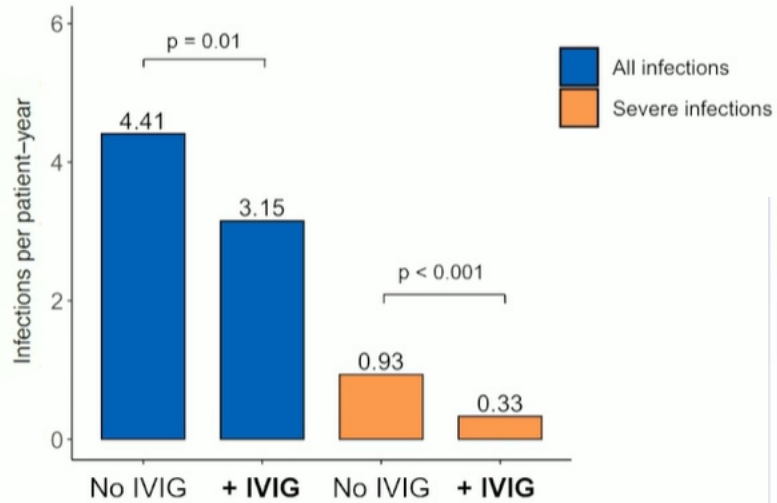


IVIG supplementation prolonged the time to first severe infections



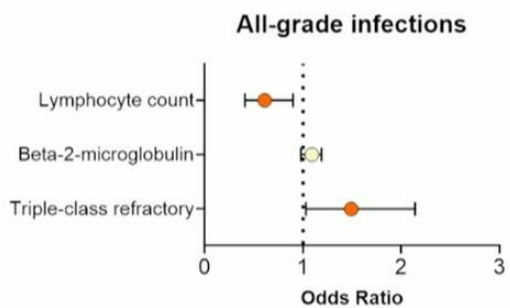
IVIG reduced annualized rates of both all-grade and severe infections

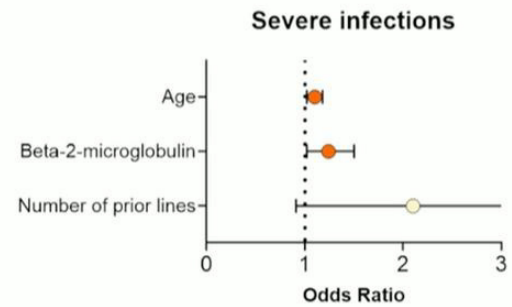
- Annualized infection rate = total number of infections per patient-year



Risk factors associated with infections during IVIG supplementation

Multivariate analysis including all variables with p<0.10 in univariate analysis

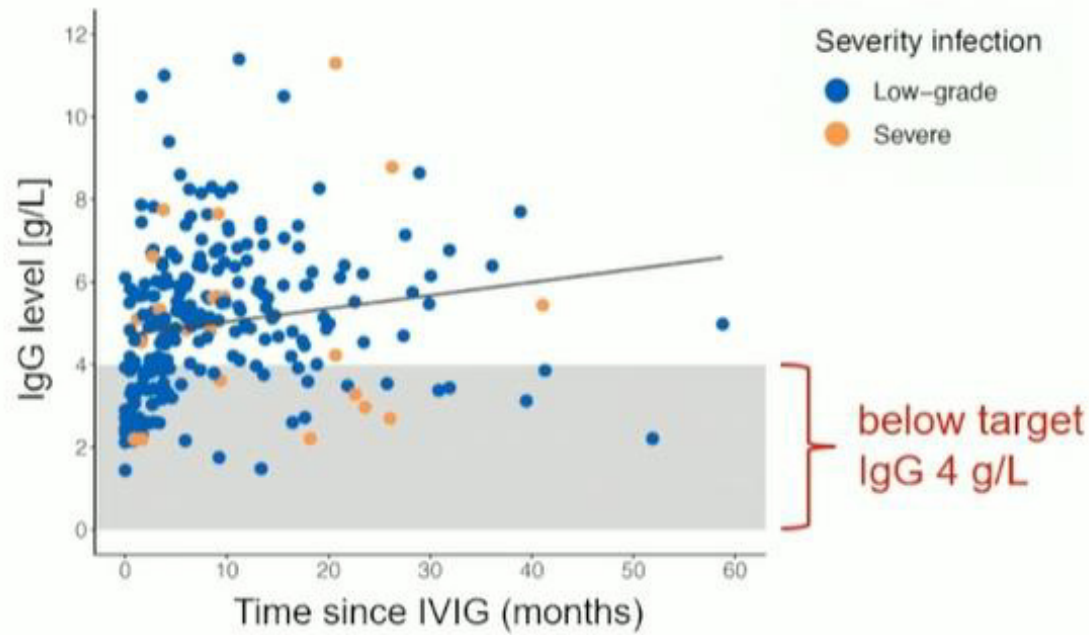




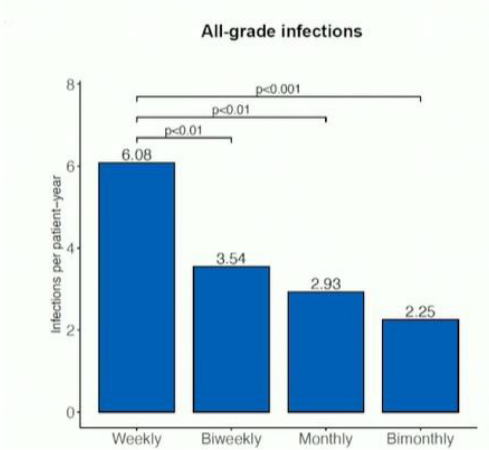
Suboptimal IgG levels may have contributed to infections during IVIG supplementation

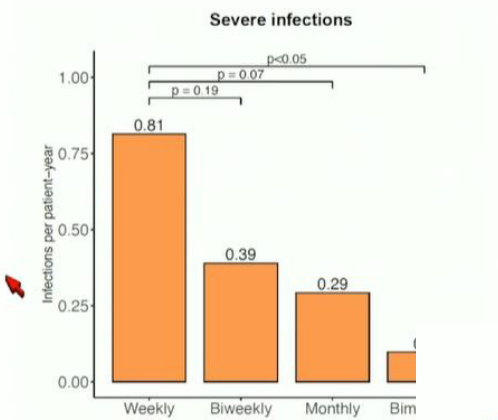
- In 82/265 (31%) infections that occurred during IVIG supplementation patients had IgG levels below 4 g/L

- Most infections during IVIG supplementation with suboptimal IgG levels occurred early after start of IVIG (56% in first 3 months, 73% in first 6 months)

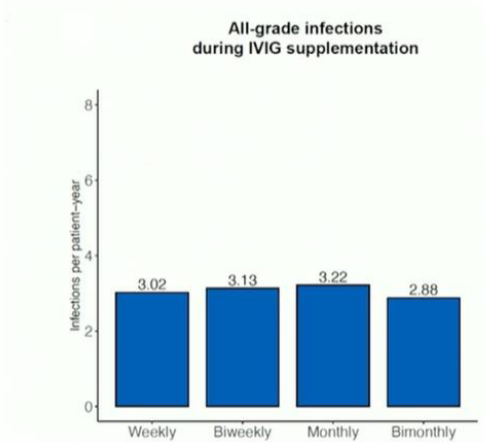


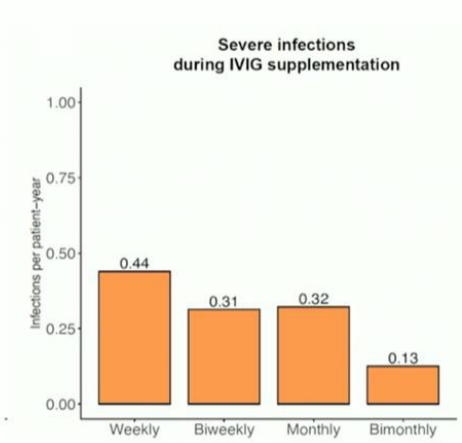
Longer dosing intervals reduced annualized rates of infections





During IVIG a reduced risk for severe infections was still observed





Negative binomial models for statistical comparisons could not be estimated due to limited patient numbers

Outpatient dosing of BiTEs

(PA-008) Economic Value of Tocilizumab Prophylaxis to Prevent Cytokine Release Syndrome (CRS) During Outpatient Teclistamab (Tec) or Talquetamab (Tal) Initiation for Relapsed/refractory Multiple Myeloma (RRMM)

(PA-058) Real-world Safety Outcomes and Healthcare Resource Utilization (HCRU) During Outpatient, Inpatient, and Hybrid Step-up Dosing (SUD) of Teclistamab (Tec) and Talquetamab (Tal): A Chart Review Study

(PA-014) Outpatient Step-up Dosing of Teclistamab (TEC): An Implementation Process Shifting from the Academic Inpatient (IP) to Community Outpatient (OP) Setting

(PA-037) Real World Accelerated Step-up Dosing of Teclistamab and Talquetamab in the Outpatient Setting Is Feasible and Associated with Low Incidence of Cytokine Release Syndrome

Real-World Experiences Demonstrated Feasibility of Managing CRS and ICANS Associated With Outpatient Step-Up Dosing

- Of 65 patients with MM treated with teclistamab at Mayo Clinic, Rochester, between October 2022 and October 2023, 57 (**89%**) initiated step-up dosing in **outpatient setting**:[1]
  - All patients received **premedication** per label recommendations[1]
  - Patients with grade 1 CRS were treated with dexamethasone 10 mg and acetaminophen 1000 mg and admitted to hospital if there was no improvement or new symptoms[2]
  - Patients with grade ≥2 CRS or ICANS of any grade were admitted to hospital[2]
- 18 (**31.6%**) developed **CRS** and were admitted to hospital (median hospitalization: 2 days)[1]
- 2 (**3.5%**) had **ICANS**[1]
- **All CRS and ICANS resolved**, and patients continued on therapy[1]
- At Massachusetts General Hospital, Boston, eligibility for outpatient step-up dosing determined based on patient fitness, disease extent, LDH, ferritin, cytopenia, and proximity to hospital[3]
- Of 43 patients with MM treated with elranatamab at MGH, 9 (**20.9%**) initiated step-up dosing in outpatient setting[3]
- **CRS** occurred in **33%** of those initiated in **outpatient setting** vs. 71% in inpatient setting[3]
  - Tocilizumab administered to all outpatients who experienced CRS
  - Median hospitalization: 3 days
- **ICANS** occurred in **11%** of those initiated in **outpatient** setting vs. 27% in inpatient setting[3]

CRS, cytokine release syndrome; ICANS, immune effector cell-associated neurotoxicity syndrome; LDH, lactate dehydrogenase; MGH, Massachusetts General Hospital; MM, multiple myeloma.

1. Sandahl TB et al. JCO Oncol Pract. 2025;21:702-707. 2. Sandahl TB et al. ASH 2024. Poster MON-5047. 3. Cirstea et al. ASCO 2025. Abstract e19507.

ICO Institut Català d'Oncologia

(PA-018) Severe Tumor Flare Pain Syndrome During Step-Up Dosing of Teclistamab in High-Risk Relapsed/Refractory Multiple Myeloma

Introduction: 3.6% of patients complaining debilitating bone pain episodes. In contrast, we have observed a higher frequency of such events in our outpatient setting, particularly during the step-up dosing (SUD) phase. This study aimed to assess the incidence, presentation, and outcomes of tumor flare pain syndrome associated with TEC.

Methods: We conducted a retrospective, single-center analysis of patients ≥18 years of age with RRMM treated with TEC in the outpatient setting. Tocilizumab prophylaxis 8 mg/kg was administered before SUD 1 of TEC. The SUD regimen consisted of 0.06 mg/kg subcutaneously (SC) on day 1, 0.3 mg/kg SC on day 3, and 1.5 mg/kg SC on day 5. TEC 1.5 mg/kg SC was then given weekly, until MM progression or unacceptable toxicity. The primary endpoint was the incidence of severe tumor flare pain syndrome occurring during SUD (equivalent to bone pain grade ≥3 per CTCAE v5.0).

Results: A total of 49 patients who received teclistamab were reviewed. Among them, we identified 7 subjects (5 males, 2 females) who developed tumor flare pain syndrome during SUD, including 3 patients with plasmablastic myeloma and 1 with plasma cell leukemia**.** Median age was 63 years (39-79 years). Each of these patients had extramedullary disease at the beginning of TEC administration. One patient experienced grade 2 CRS, none had ICANS. Median time until the onset of tumor flare pain syndrome was 3 days (range: 2-4) after the first TEC dose, and the median duration was 5 days (range: 2 to 7). Tumor flare pain syndrome only occurred during SUD. Imaging finding on PET-CT or CT-scan included (in contrast with baseline imaging) progression of bone lesions (n=4), progression of extramedullary plasmacytomas (lung and peritoneum; n=2) and a new muscular lesion in one patient. Four patients required hospitalization for pain control. All received opioids, and 4 (n=4/7) were relieved by dexamethasone 10 mg PO/IV q 6h. All 7 patients were evaluable for clinical response; with complete response in 2, partial response in 2, and stable disease in 3.

Conclusions: Clinicians should be aware that tumor flare pain syndrome is an underreported manifestation occurring during the SUD phase of T-cell redirected therapies. It is associated with intense pain sometimes requiring hospitalization and may mimic disease progression radiographically (pseudoprogression). Dexamethasone seems most beneficial for pain management, but prospective studies are needed to guide optimal relief strategies**.**