

How to treat RRMM with BCMA-directed BsAb therapies

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Patient
Case Poll



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Disclosures

Cyrille Touzeau, University Hospital of Nantes, Nantes, France

- Advisory Boards/Honoraria: Pfizer, Janssen, Sanofi, AbbVie, Amgen, BMS
- Research Funding: Sanofi, GSK
- Travel: Pfizer, Janssen, Sanofi

Patient case*



70-YEAR-OLD MALE

Past Medical History

- Hypertension
- Chronic renal insufficiency

Diagnosis

- IgA multiple myeloma with multiple bone lesions
- No anemia, acute change in renal function, or hypercalcemia
- Baseline cytogenetics: gain(1q); no other chromosomal abnormalities present
- R-ISS stage: 2
- ECOG performance status: 1

Patient case*



70-YEAR-OLD MALE

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- Hypertension
- Chronic renal insufficiency

Diagnosis

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- No anemia, acute change in renal function, or hypercalcemia
- Baseline cytogenetics: gain(1q); no other chromosomal abnormalities present
- R-ISS stage: 2
- ECOG performance status: 1

1L

VRd ASCT VRd
Lenalidomide maintenance

**Best overall
response:
CR**

ASCT, autologous stem cell transplant; CR, complete response; ECOG, Eastern Cooperative Oncology Group; IgA, immunoglobulin A; R-ISS, Revised International Staging System; VRd, bortezomib, lenalidomide, and dexamethasone.

*Fictional case based on clinical practice experience for training purposes.

Patient case*



73-YEAR-OLD MALE

Past Medical History

- Hypertension
- Chronic renal insufficiency

Diagnosis

- IgA multiple myeloma with multiple bone lesions
- No anemia, acute change in renal function, or hypercalcemia
- Baseline cytogenetics: gain(1q); no other chromosomal abnormalities present
- R-ISS stage: 2
- ECOG performance status: 1



VRd ASCT VRd
Lenalidomide maintenance

Best overall
response:
CR

Progression after 3 years on therapy: Biochemical relapse with rapid M spike increase



DaraKd

Best overall
response:
VGPR

Pink=refractory.

ASCT, autologous stem cell transplant; CR, complete response; DaraKd, daratumumab, carfilzomib, and dexamethasone; ECOG, Eastern Cooperative Oncology Group; IgA, immunoglobulin A; R-ISS, Revised International Staging System; VGPR, very good partial response; VRd, bortezomib, lenalidomide, and dexamethasone.

*Fictional case based on clinical practice experience for training purposes.

Patient case*



75-YEAR-OLD MALE

Past Medical History

- Hypertension
- Chronic renal insufficiency

Diagnosis

- IgA multiple myeloma with multiple bone lesions
- No anemia, acute change in renal function, or hypercalcemia
- Baseline cytogenetics: gain(1q); no other chromosomal abnormalities present
- R-ISS stage: 2
- ECOG performance status: 1



VRd ASCT VRd
Lenalidomide maintenance

Best overall response:
CR

Progression after 3 years on therapy: Biochemical relapse with rapid M spike increase



DaraKd

Best overall response:
VGPR

Progression after 2 years on therapy: M spike increase and new bone lesions



PCd

Best overall response:
PR

Pink=refractory.

ASCT, autologous stem cell transplant; CR, complete response; DaraKd, daratumumab, carfilzomib, and dexamethasone; ECOG, Eastern Cooperative Oncology Group; IgA, immunoglobulin A; PCd, pomalidomide, cyclophosphamide, and dexamethasone; PR, partial response; R-ISS, Revised International Staging System; VGPR, very good partial response; VRd, bortezomib, lenalidomide, and dexamethasone.

*Fictional case based on clinical practice experience for training purposes.

Patient case*



75-YEAR-OLD MALE

Past Medical History

- Hypertension
- Chronic renal insufficiency

Diagnosis

- IgA multiple myeloma with multiple bone lesions
- No anemia, acute change in renal function, or hypercalcemia
- Baseline cytogenetics: gain(1q); no other chromosomal abnormalities present
- R-ISS stage: 2
- ECOG performance status: 1

1L VRd ASCT VRd
Lenalidomide maintenance

Best overall response: CR

Progression after 3 years on therapy: Biochemical relapse with rapid M spike increase

2L DaraKd

Best overall response: VGPR

Progression after 2 years on therapy: M spike increase and new bone lesions

3L PCd

Best overall response: PR

Progression after 6 months on therapy: New bone lesions, hypercalcemia, 3% circulating plasma cells, EMD involvement and multiple focal lesions on PET-CT

Pink=refractory.

ASCT, autologous stem cell transplant; CR, complete response; DaraKd, daratumumab, carfilzomib, and dexamethasone; ECOG, Eastern Cooperative Oncology Group; EMD, extramedullary disease; IgA, immunoglobulin A; PCd, pomalidomide, cyclophosphamide, and dexamethasone; PET-CT, positron emission tomography/computerised tomography; PR, partial response; R-ISS, Revised International Staging System; VGPR, very good partial response; VRd, bortezomib, lenalidomide, and dexamethasone.

*Fictional case based on clinical practice experience for training purposes.

Patient Case Recap



- ✓ 75-year-old man
- ✓ RRMM with 3 prior LoT
- ✓ Refractory to: PI (carfilzomib), IMiDs (lenalidomide and pomalidomide) and anti-CD38 mAb (daratumumab)
- ✓ Symptomatic and aggressive disease progression (bone lesions, hypercalcemia, and circulating plasma cells)
- ✓ Chronic renal insufficiency (CrCl: 32 mL/min)

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What would be your preferred therapeutic option for 4L treatment in this patient?

- 1) BCMA bispecific antibody (eg, elranatamab, teclistamab)
- 2) BCMA CAR T (eg, ide-cel, cilta-cel)
- 3) Other

4L, fourth line; BCMA, B-cell maturation antigen; CAR T, chimeric antigen receptor T-cell therapy; CD, cluster of differentiation; cilta-cel, ciltacabtagene autoleuce; CrCl, creatinine clearance; ide-cel, idecabtagene vicleuce; IMiD, immunomodulatory drug; LoT, lines of therapy; mAb, monoclonal antibody; PI, proteasome inhibitor; RRMM, relapsed and/or refractory multiple myeloma.

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What would be your preferred therapeutic option for 4L treatment in this patient?

① Start presenting to display the poll results on this slide.

Patient case*

Patient admitted to the hospital

- ANC: 700/mm³
- Plasma cells: 4%
- Platelets: 75 g/L
- Hemoglobin: 9.2 g/dL
- ALT/AST: within normal limits
- CrCl: 32 mL/min
- COVID-19 test: negative

WEEK 1

DAY
1

Step-up dose 1
elranatamab
12 mg SC

Patient initiated on elranatamab through the early access program

ALT, alanine transaminase; ANC, absolute neutrophil count; AST, aspartate aminotransferase; COVID-19, coronavirus disease 2019; CrCl, creatinine clearance; SC, subcutaneous.

*Fictional case based on clinical practice experience for training purposes.

Patient case*

Patient admitted to the hospital

- ANC: 700/mm³
- Plasma cells: 4%
- Platelets: 75 g/L
- Hemoglobin: 9.2 g/dL
- ALT/AST: within normal limits
- CrCl: 32 mL/min
- COVID-19 test: negative

Patient presents with:

- Temperature: 39°C
- Arterial pressure: 85/65 mmHg
- SpO₂: 95%
- ICE score: 10/10

WEEK 1

DAY
1

DAY
2

Step-up dose 1
elranatamab
12 mg SC

ALT, alanine transaminase; ANC, absolute neutrophil count; AST, aspartate aminotransferase; COVID-19, coronavirus disease 2019; CrCl, creatinine clearance; ICE, immune effector cell encephalopathy; SC, subcutaneous; SpO₂, oxygen saturation.

*Fictional case based on clinical practice experience for training purposes.

Patient Case Recap



On the day after the administration of the first step-up dose of elranatamab, the patient presented with the following:

- ✓ Temperature: 39°C
- ✓ SpO₂: 95%
- ✓ Arterial pressure: 85/65 mmHg
- ✓ ICE score: 10/10

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Based on the patient's presentation, which of the following are correct?

Select all that apply.

- 1) The patient's presentation is consistent with Grade 1 CRS
- 2) The patient's presentation is consistent with Grade 2 CRS
- 3) The patient's presentation is consistent with Grade 2 ICANS
- 4) Sepsis should be considered

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Based on the patient's presentation, which of the following are correct?

① Start presenting to display the poll results on this slide.

ASTCT CRS grading criteria

Grade 1	Grade 2	Grade 3	Grade 4
Fever $\geq 38^{\circ}\text{C}^*$	Fever $\geq 38^{\circ}\text{C}^*$ with: <ul style="list-style-type: none">• Hypotension not requiring vasopressors <i>and/or</i>[†]• Hypoxia requiring ≤ 6 L/min O_2 by NC or blow-by	Fever $\geq 38^{\circ}\text{C}^*$ with: <ul style="list-style-type: none">• Hypotension requiring one vasopressor with or without vasopressin <i>and/or</i>[†]• Hypoxia requiring >6 L/min O_2 by NC, face mask, non-rebreather, or Venturi mask	Fever $\geq 38^{\circ}\text{C}^*$ with: <ul style="list-style-type: none">• Hypotension requiring >1 vasopressors (excluding vasopressin) <i>and/or</i>[†]• Hypoxia requiring O_2 by positive pressure (CPAP, BiPAP, intubation with mechanical ventilation)

Organ toxicities associated with CRS may be graded according to CTCAE V.5.0, but they do not influence CRS grading

**Not attributable to any other cause. In patients who have CRS who then undergo antipyretic or anticytokine therapy such as tocilizumab or steroids, fever is no longer required to grade subsequent CRS severity. In this case, CRS grading is driven by hypotension and/or hypoxia.*

[†]CRS grade is determined by the more severe event: hypotension or hypoxia not attributable to any other cause. For example, a patient with temperature of 39.5°C , hypotension requiring 1 vasopressor, and hypoxia requiring low-flow nasal cannula is classified as grade 3 CRS.

IMWG guideline recommendations for the management of CRS

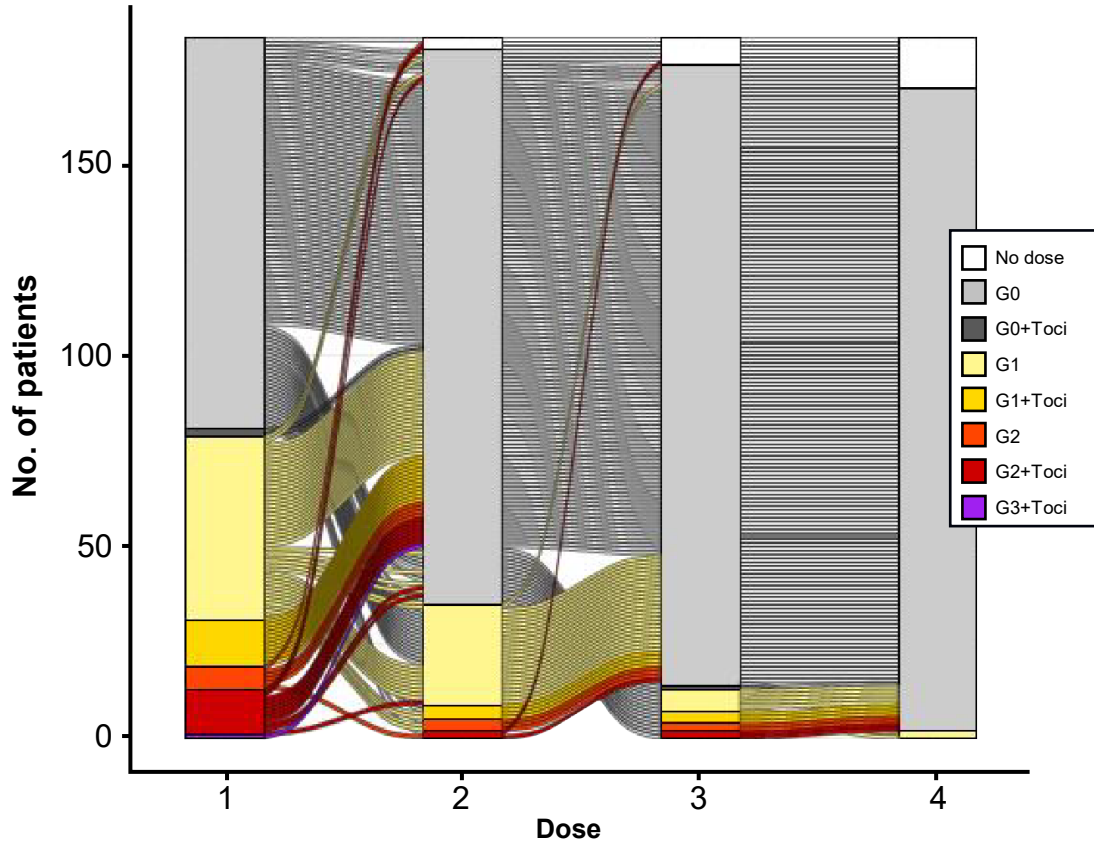
Grade 1	Grade 2	Grade 3	Grade 4
<p>Observation</p> <ul style="list-style-type: none">• Consider early tocilizumab use• If persistent Grade 1 (>24–48 hours), early use of tocilizumab is encouraged	<p>Tocilizumab 8 mg/kg IV</p> <ul style="list-style-type: none">• If no improvement, consider adding second line treatment (ie, steroids)• Supportive care including oxygen supplementation, fluids, should be implemented	<p>Tocilizumab 8 mg/kg IV + dexamethasone 10 mg every 6 hours</p> <ul style="list-style-type: none">• Transfer the patient to ICU• Supportive care as clinically indicated• Consider high-dose steroids and salvage CRS treatment (ie, anakinra)	<p>Tocilizumab + high-dose steroids</p> <ul style="list-style-type: none">• Transfer the patient to ICU• Supportive care as clinically indicated• Consider high-dose steroids and salvage CRS treatment (ie, anakinra)

CRS, cytokine release syndrome; ICU, intensive care unit; IMWG, International Myeloma Working Group; IV intravenously.
Rodriguez-Otero P et al. *Lancet Oncol.* 2024;25:e205–e216.
Table adapted from Rodriguez-Otero P et al. *Lancet Oncol.* 2024;25:e205–e216.

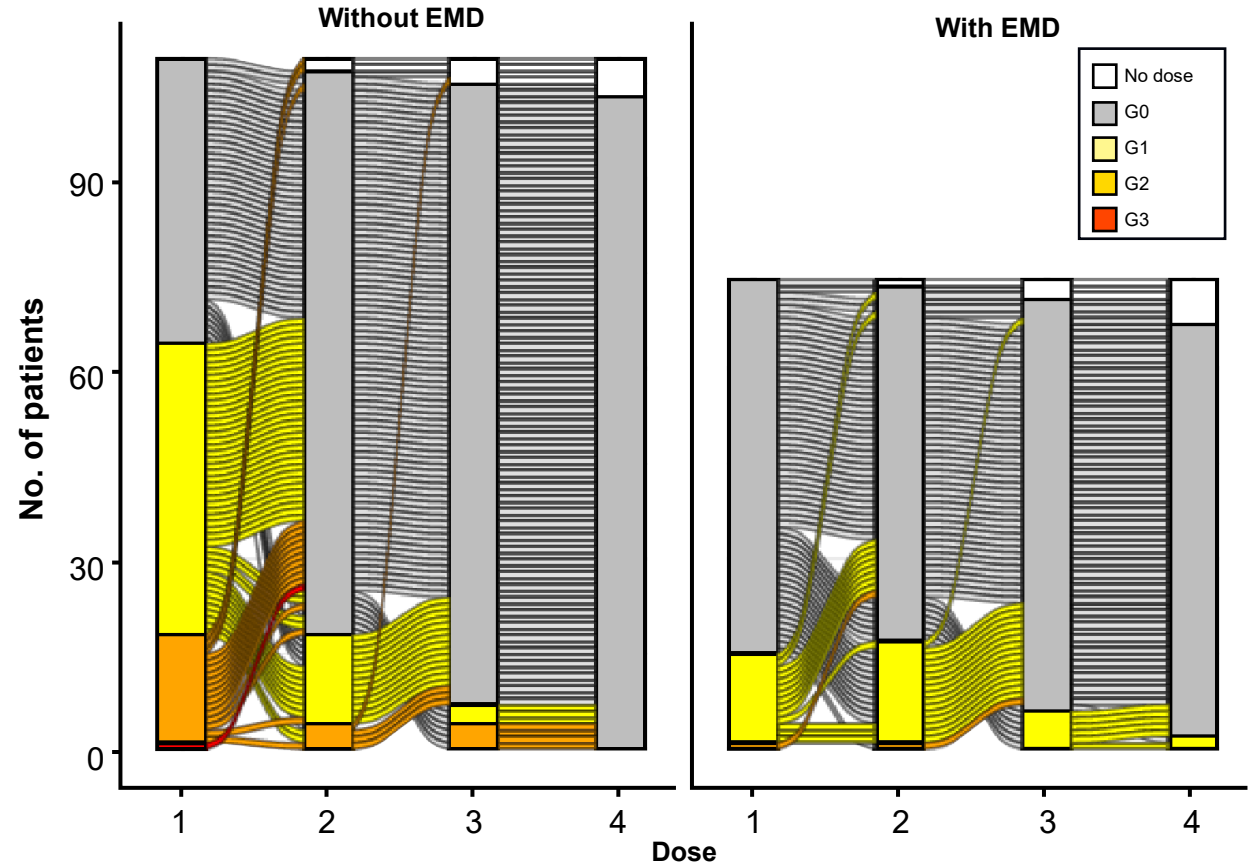
Elranatamab: CRS timing and severity in MagnetisMM-3

RRMM refractory to ≥ 1 of each of the following: PI, IMiD, anti-CD38 mAb
Patients who received the recommended dosing regimen (N=183)

CRS profile after treatment with the 12/32 mg step-up priming doses of elranatamab with or without tocilizumab* treatment



CRS profile in patients without or with baseline EMD by BICR after treatment with the 12/32 mg step-up priming doses of elranatamab



*Tocilizumab or toci refers to both tocilizumab or siltuximab.

BICR, blinded independent central review; CRS= CD, cluster of differentiation; CRS, cytokine release syndrome; EMD, extramedullary disease; G, grade; IMiD, immunomodulatory drug; mAb, monoclonal antibody; PI, proteasome inhibitor; RRMM, relapsed and/or refractory multiple myeloma; toci, tocilizumab.

Niesvizky R et al. ASH 2023. Abstract 3384 (poster presentation). Figures reproduced from Niesvizky R et al. ASH 2023. Abstract 3384 (poster presentation).

Patient case*

Patient admitted to the hospital

- ANC: 700/mm³
- Plasma cells: 4%
- Platelets: 75 g/L
- Hemoglobin: 9.2 g/dL
- ALT/AST: within normal limits
- CrCl: 32 mL/min
- COVID-19 test: negative

Patient presents with:

- Temperature: 39°C
- Arterial pressure: 85/65 mmHg
- SpO₂: 95%
- ICE score: 10/10

WEEK 1

DAY
1

Step-up dose 1
elranatamab
12 mg SC

DAY
2

Patient treated with:

- Tocilizumab
 - Cefepime
-
- CRS resolved within 6 hours
 - No ICANS or infections present

ALT, alanine transaminase; ANC, absolute neutrophil count; AST, aspartate aminotransferase; COVID-19, coronavirus disease 2019; CrCl, creatinine clearance; CRS, cytokine release syndrome; ICANS, immune effector cell-associated neurotoxicity syndrome; ICE, immune effector cell encephalopathy; SC, subcutaneous; SpO₂, oxygen saturation.

*Fictional case based on clinical practice experience for training purposes.

Patient case*

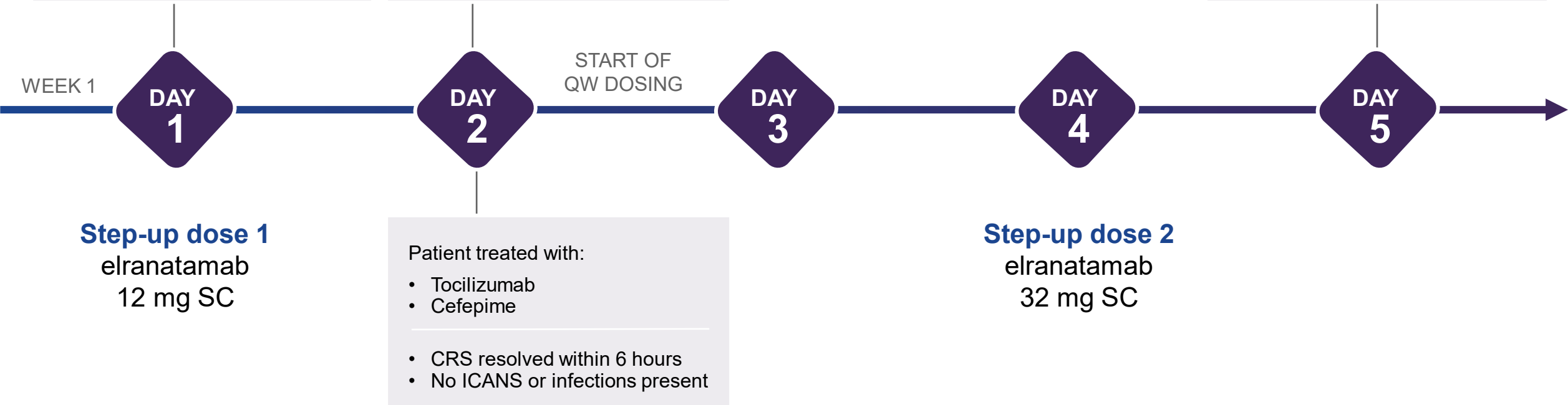
Patient admitted to the hospital

- ANC: 700/mm³
- Plasma cells: 4%
- Platelets: 75 g/L
- Hemoglobin: 9.2 g/dL
- ALT/AST: within normal limits
- CrCl: 32 mL/min
- COVID-19 test: negative

Patient presents with:

- Temperature: 39°C
- Arterial pressure: 85/65 mmHg
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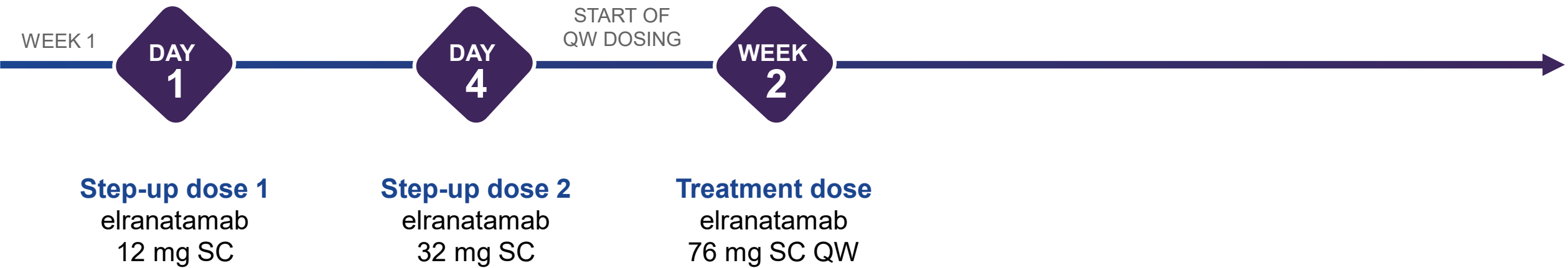
Patient discharged from hospital



ALT, alanine transaminase; ANC, absolute neutrophil count; AST, aspartate aminotransferase; COVID-19, coronavirus disease 2019; CrCl, creatinine clearance; CRS, cytokine release syndrome; ICANS, immune effector cell-associated neurotoxicity syndrome; ICE, immune effector cell encephalopathy; SC, subcutaneous; SpO₂, oxygen saturation.

*Fictional case based on clinical practice experience for training purposes.

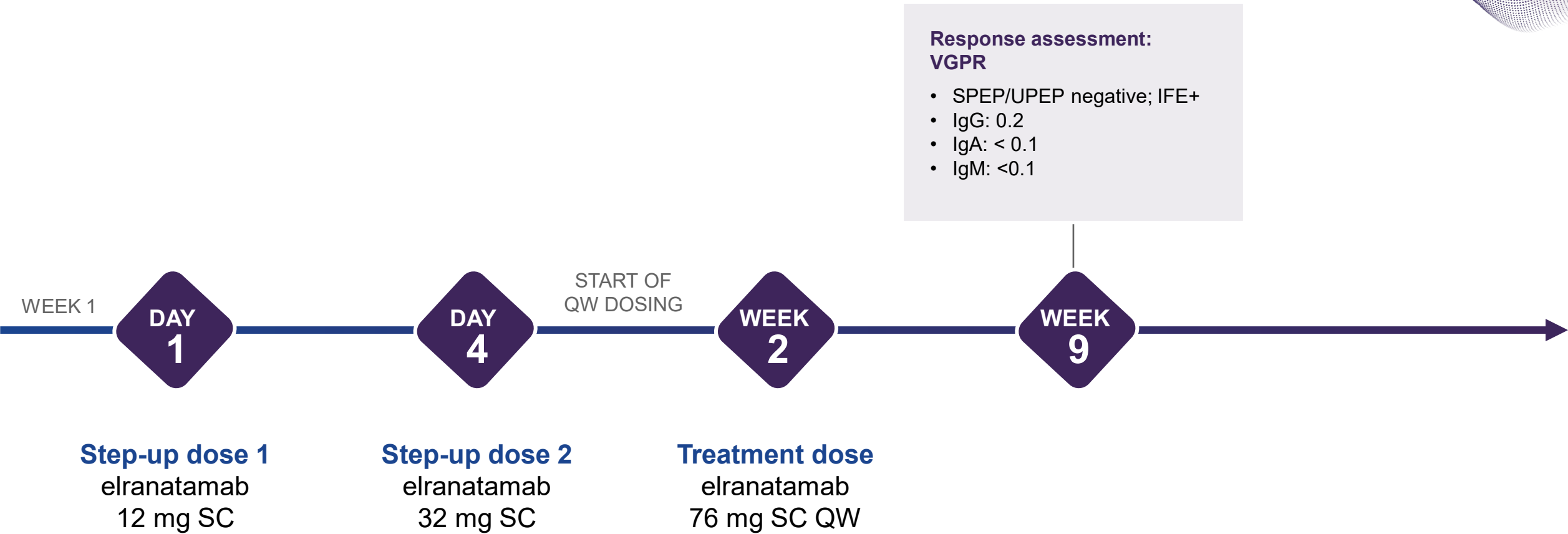
Patient case*



QW, weekly; SC, subcutaneous.

*Fictional case based on clinical practice experience for training purposes.

Patient case*



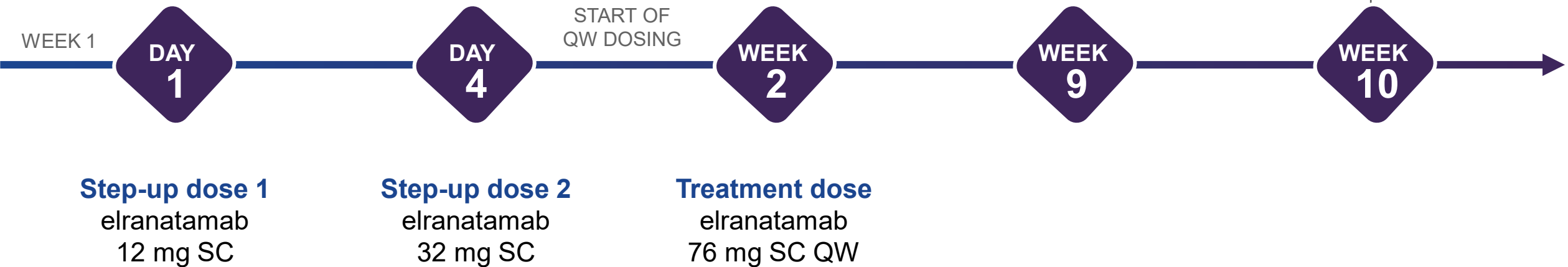
IFE, immunofixation; Ig, immunoglobulin; QW, weekly; SC, subcutaneous; SPEP, serum protein electrophoresis; UPEP, urine protein electrophoresis; VGPR, very good partial response.

*Fictional case based on clinical practice experience for training purposes.

Patient case*

Patient admitted to the ER
for fever and diarrhea

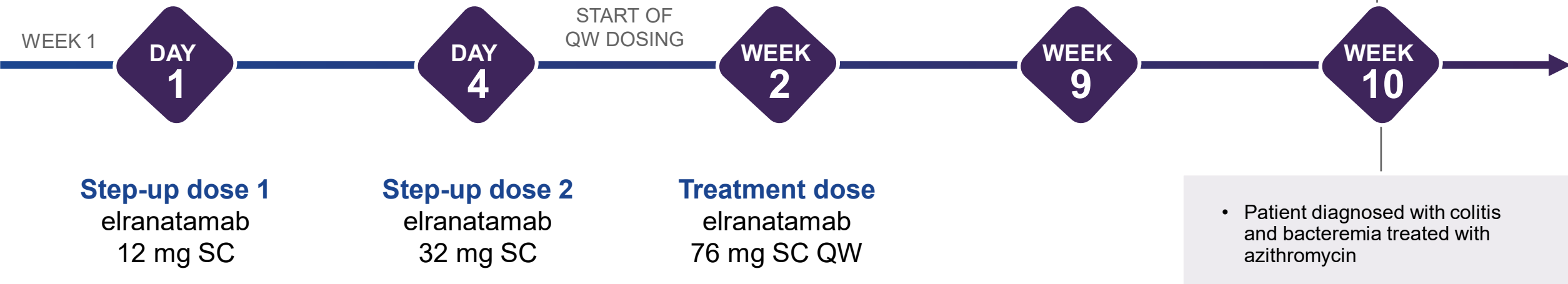
- ANC: 1200/mm³
- No symptoms of severe sepsis
- ALT/AST: within normal limits
- Na: 150 mg/dL
- K⁺: 3.2 mmol/L
- CrCl: 32 mL/min
- Abdomen CT: normal
- Blood culture: *Campylobacter jejuni*
- CMV PCR: negative



ALT, alanine transaminase; ANC, absolute neutrophil count; AST, aspartate aminotransferase; CMV, cytomegalovirus; CrCl, creatinine clearance; CT, computed tomography; ER, emergency room; K, potassium; Na, sodium; PCR, polymerase chain reaction; QW, weekly; SC, subcutaneous.

*Fictional case based on clinical practice experience for training purposes.

Patient case*



ALT, alanine transaminase; ANC, absolute neutrophil count; AST, aspartate aminotransferase; CMV, cytomegalovirus; CrCl, creatinine clearance; CT, computed tomography; ER, emergency room; K, potassium; Na, sodium; PCR, polymerase chain reaction; QW, weekly; SC, subcutaneous.

*Fictional case based on clinical practice experience for training purposes.

Elranatamab: Infection incidence and severity in MagnetisMM-3

RRMM refractory to ≥1 of each of the following: PI, IMiD, anti-CD38 mAb

No prior BCMA-directed therapy (n=123)

Detailed infection data were published in the primary MagnetisMM-3 analysis (median follow-up 14.7 months)

Infections, %	MagnetisMM-3 BCMA-Naïve N=123			Opportunistic infections ^s in <5% of patients, %	MagnetisMM-3 BCMA-Naïve N=123		
	Any grade	Grade 3/4	Grade 5*		Any grade	Grade 3/4	Grade 5*
Any grade	69.9	39.8	6.5				
Infection TEAEs occurring in ≥5% of patients							
COVID-19 related [†]	29.3 [‡]	15.4	1.6	<i>Pneumocystis jirovecii</i> pneumonia	4.9	4.1	0
Pneumonia	16.3	8.1	0	Cytomegalovirus infection	3.3	0	0
Upper respiratory tract infection	16.3	0	0	Adenoviral hepatitis	0.8	0	0.8
Sinusitis	10.6	1.6	0	Adenovirus infection	0.8	0	0.8
Urinary tract infection	9.8	3.3	0	Pneumonia adenoviral	0.8	0	0.8
Sepsis	6.5	6.5	0	Pneumonia cytomegaloviral	0.8	0.8	0
Bacteremia	5.7	1.6	0				
CMV infection reactivation	5.7	1.6	0				

*3 (2.4%) patients had grade 5 septic shock. [†]Includes preferred terms in COVID-19 (narrow) standardized MedDRA queries. [‡]25/36 (69.4%) patients developed COVID-19 or COVID-19 pneumonia and 10/36 (30.6%) only had a positive SARS-CoV-2 test without developing the disease. [§]Opportunistic infection treatment-emergent adverse events includes preferred terms: adenoviral hepatitis, adenovirus infection, cytomegalovirus infection, cytomegalovirus infection reactivation, cytomegalovirus viremia, pneumonia adenoviral, pneumonia cytomegaloviral, Pneumocystis jirovecii pneumonia. ^{||}Preferred terms both reported in the same patient.

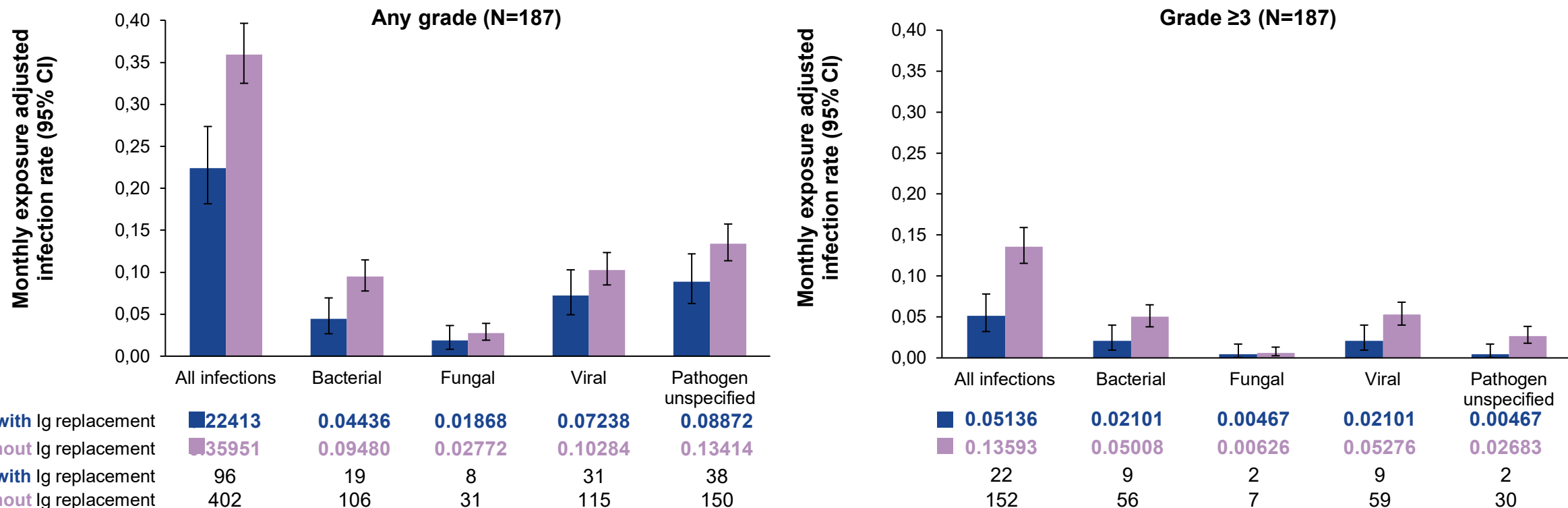
BCMA, B-cell maturation antigen; CD, cluster of differentiation; CMV, cytomegalovirus; COVID-19, coronavirus disease 2019; IMiD, immunomodulatory drug; mAb, monoclonal antibody; MedDRA, Medical Dictionary for Regulatory Activities; PI, proteasome inhibitor; RRMM, relapsed and/or refractory multiple myeloma; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; TEAE, treatment-emergent adverse event.

Lesokhin AM et al. *Nat Med.* 2023;29:2259–2267.

Table adapted from Lesokhin AM et al. *Nat Med.* 2023;29:2259–2267.

MagnetisMM-3: Infections of any grade and Grade ≥ 3 in patients with or without Ig replacement therapy¹

RRMM refractory to ≥ 1 of each of the following: PI, IMiD, and anti-CD38 mAb²



- Lower monthly exposure adjusted infection rates were observed in patients **with** vs **without** Ig replacement (0.22 vs 0.36)
- Similar trends were observed across infection types

CD, cluster of differentiation; CI, confidence interval; Ig, immunoglobulin; IMiD, immunomodulatory drug; mAb, monoclonal antibody; PI, proteasome inhibitor.

1. Leleu X et al. IMS 2023. Abstract S194 (poster presentation). 2. Lesokhin A et al. *Nat Med.* 2023;29:2259–2267.

Figures reproduced from Leleu X et al. IMS 2023. Abstract S194 (poster presentation).

Patient Case Recap

- ✓ 75-year-old man with RRMM
- ✓ Currently receiving treatment with elranatamab
- ✓ History of *Campylobacter jejuni* bacteremia



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What would you recommend to prevent infections in this patient?

Select all that apply.

- 1) Valacyclovir to prevent HSV/VZV
- 2) Valganciclovir to prevent CMV reactivation
- 3) IV or SQ immunoglobulin to prevent bacterial/viral infections
- 4) Cotrimoxazole (or equivalent) to prevent pneumocystis

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What would you recommend to prevent infections in this patient?

① Start presenting to display the poll results on this slide.

IMWG guidelines for infection prevention with BsAbs

	Agent or agents	Timing	Additional comments and recommendations
Antiviral: HSV or VZV	Aciclovir or valacyclovir	Throughout treatment	Continue for 3 months off treatment or until CD4 >200/μL
Pneumocystis	Trimethoprim/sulfamethoxazole, atovaquone	Throughout treatment	Continue until CD4 cell count >200/μL
Antibacterial	Local guidelines or quinolone	Neutropenia	Bacterial infection highest in first few cycles during neutropenia or if prolonged steroids needed
Antifungal	Local guidelines or azole	Neutropenia	Fungal infection risk low, consider during prolonged neutropenia or steroid use
Other viral; CMV, Hepatitis B virus	Entecavir for those at risk of reactivation	Throughout treatment	Cytomegalovirus PCR at start ; if positive consider monitoring; local guidelines for monitoring versus pre-emptive treatment
Polymicrobial	Intravenous immunoglobulin	For IgG concentration <400 mg/dL	Hypogammaglobulinaemia is common throughout treatment; continue even off therapy for IgG concentrations <400 mg/dL

BsAb, bispecific antibody; CD, cluster of differentiation; CMV, cytomegalovirus; HSV, Herpes simplex virus; Ig, immunoglobulin; IMWG, International Myeloma Working Group; PCR, polymerase chain reaction; VZV, varicella zoster virus.
 Rodriguez-Otero P et al. *Lancet Oncol.* 2024;25:e205–e216.
 Table reproduced from Rodriguez-Otero P et al. *Lancet Oncol.* 2024;25:e205–e216.

Patient case*

Patient admitted to the ER
for fever and diarrhea

WEEK
10

- Patient diagnosed with colitis and bacteremia treated with azithromycin

- Infection resolved after treatment with IV fluids and antibiotics
- Patient discharged from hospital on Ig maintenance therapy

WEEK
11

Elranatamab QW dosing
restarted

WEEK
12

Treatment dose
elranatamab
76 mg SC QW

Response assessment:
CR

WEEK
16

CR, complete response; ER, emergency room; Ig, immunoglobulin; IV, intravenous; QW, weekly; SC, subcutaneous.

*Fictional clinical case for training purposes.

Summary



CRS with elranatamab is primarily low grade and most events occur after the first 3 doses¹



Patients receiving treatment with BsAbs should be monitored for infections²



Appropriate prophylaxis to help prevent infections, including immunoglobins, should be used in patients receiving BsAbs²

BCMA-directed BsAbs are an appropriate treatment option with a manageable safety profile for patients with TCE/TCRMM^{3,4}

BCMA, B-cell maturation antigen; BsAbs, bispecific antibodies; CRS, cytokine release syndrome; MM, multiple myeloma; TCE, triple-class exposed; TCR, triple-class refractory.

1. Niesvizky R et al. ASH 2023. Abstract 3384 (poster presentation). 2. Rodriguez-Otero P et al. *Lancet Oncol.* 2024;25:e205–e216. 3. Lesokhin A et al. *Nat Med.* 2023;29:2259–2267. 4. Lee H et al. *Blood.* 2024;143:1211–1217.

Discuss the use of BCMA-directed BsAb therapies in clinical practice

Questions?



Q&A: Please scan the QR code

