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A Clinical Overview of Infections in Patients Receiving Elranatamab in Combination With Daratumumab and Lenalidomide for Newly Diagnosed Multiple Myeloma in the MagnetisMM-6 Trial

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Objective

To describe the characteristics of infection AEs observed in patients who received the RP3D of EDR during the dose-finding Part 1 of MagnetisMM-6

Conclusions

- Patients with NDMM receiving EDR are at risk of developing infections, especially early in the treatment course, highlighting the need for early and proactive screening, anti-infective prophylaxis (including Ig replacement), and close monitoring
- Infections predominantly occurred during the initial treatment period and coincided with the lowest levels of functional IgG
  - Early intravenous Ig replacement use is important during the initial cycles to avoid IgG levels <400 mg/dL
  - Prompt intervention for suspected infections should be prioritized

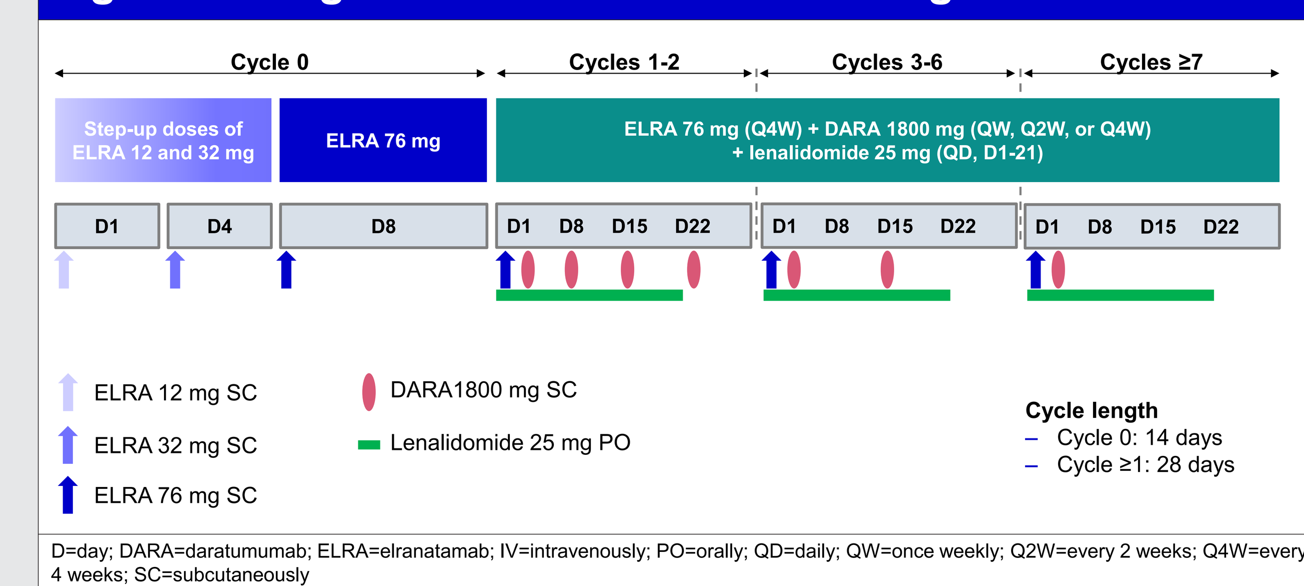
Background

- Initial results from the dose-finding phase of MagnetisMM-6 (NCT05623020), evaluating elranatamab (ELRA) + daratumumab (DARA) + lenalidomide (R) (EDR), showed early and promising efficacy with a predictable safety profile in transplant-ineligible (TI) patients with newly diagnosed multiple myeloma (NDMM)[1]
- Patients with MM are at increased risk of developing infections due to the immunosuppressive nature of the disease and the host factors[2]
- Given the potential overlapping infectious and hematologic adverse events (AEs) with the EDR combination, a comprehensive understanding of the infection profile is needed to guide prophylaxis and risk-management strategies in the randomized phase 3 portion of MagnetisMM-6

Methods

- In dose level G (DLG), eligible patients had TI (age ≥65 or <65 years with comorbidities impacting the possibility of transplant) NDMM per International Myeloma Working Group criteria; Eastern Cooperative Oncology Group performance status ≤2; and adequate liver, renal, and bone marrow function
- DLG dosing schedule (**Figure 1**) is the recommended phase 3 dose (RP3D) for MagnetisMM-6
- Patients should receive antiviral, anti-*Pneumocystis jirovecii* pneumonia (PJP), antibacterial and antifungal prophylaxis as clinically indicated
- Immunoglobulin (Ig) replacement should be administered when functional (ie, excluding the M-spike in patients with IgG myeloma) IgG levels are <400 mg/dL
- Data cutoff was September 25, 2025
  - The median (range) follow-up was 13.7 (1.2-15.2) months

Figure 1. MagnetisMM-6 Part 1 DLG dosing schedule



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

Results

PATIENTS AND TREATMENT

- In Part 1 DLG of MagnetisMM-6, 37 patients with TI NDMM received ≥1 dose of ELRA
  - 34 patients received the EDR combination

INFECTIONS

- Infections were reported in 78.4% of patients (**Table 1**)
  - The most frequent (≥10%) infections (any grade; grade 3) were upper respiratory tract infection (24.3%; 0%), pneumonias (clustered) (16.2%; 8.1%), *Escherichia* urinary tract infection (13.5%; 2.7%), viral upper respiratory tract infection (13.5%; 0%), and bronchitis (10.8%; 0%)
  - There were no grade 4 infections
  - One patient (2.7%) had a grade 5 AE of *Candida* pneumonia in cycle 1
- Infections by pathogen type were 35.1% bacterial, 35.1% viral, and 13.5% fungal; the pathogen was unspecified in 51.4% of infections (**Figure 2**)
  - Cytomegalovirus-related AEs occurred in 10 patients (27.0%; 4 [10.8%] grade 2 and 1 [2.7%] grade 3)
  - There were 2 (5.4%) COVID-19 infections (both grade 2) and 1 (2.7%) SARS-CoV-2 positive test (grade 1)
- The overall exposure-adjusted event rate (95% CI) of grade ≥3 infections was 0.04 (0.03-0.07) events per month
  - Rates without and with hypogammaglobulinemia (ie, IgG <400 mg/dL) were 0.03 (0.01-0.06) and 0.07 (0.04-0.12), respectively
  - Rates with and without Ig replacement were 0.02 (0.01-0.04) and 0.08 (0.05-0.14), respectively
  - The grade 5 infection occurred in a patient who did not receive Ig replacement

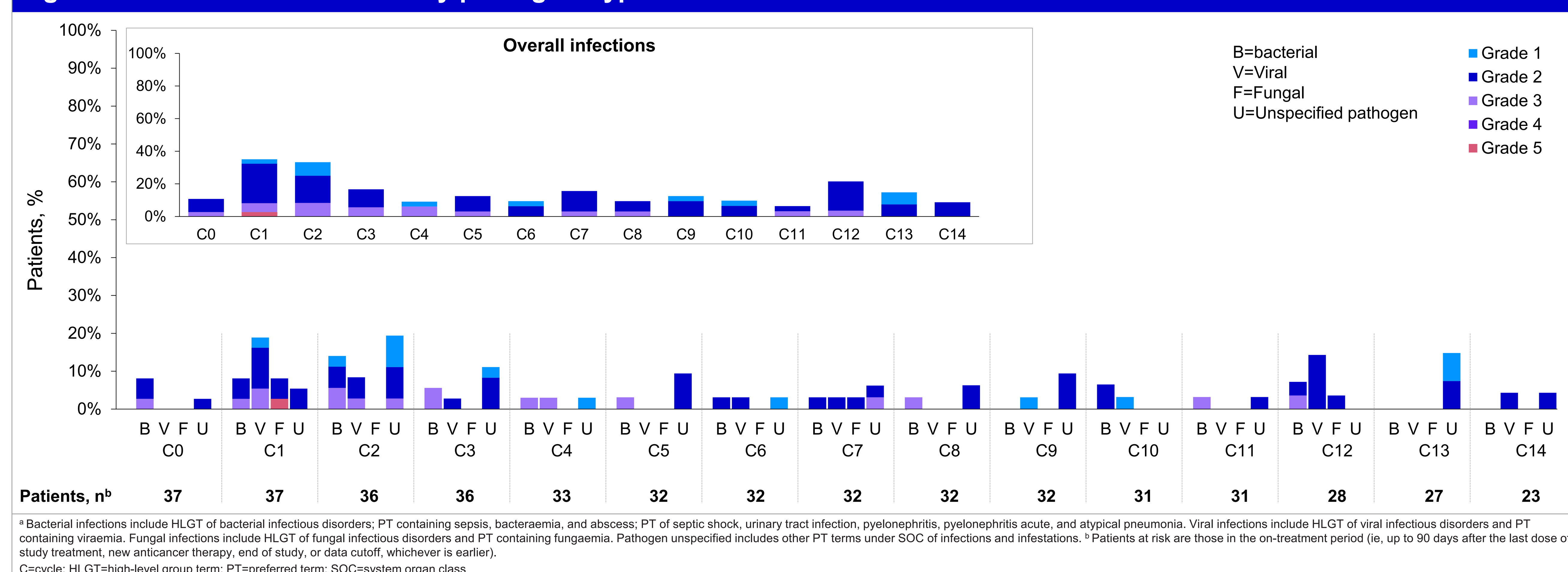
Table 1. Infections occurring in ≥5% of patients

	N=37	
Infections, n (%)	**Any grade**	**Grade 3**
Any	29 (78.4)	9 (24.3)
Upper respiratory tract infection	9 (24.3)	0
Pneumonias (clustered)	6 (16.2)	3 (8.1)
Escherichia urinary tract infection	5 (13.5)	1 (2.7)
Viral upper respiratory tract infection	5 (13.5)	0
Bronchitis	4 (10.8)	0
Cytomegalovirus infection reactivation	3 (8.1)	0
Rhinitis	3 (8.1)	0
Urosepsis	2 (5.4)	2 (5.4)
Campylobacter bacteremia	2 (5.4)	1 (2.7)
Infection	2 (5.4)	1 (2.7)
Salmonellosis	2 (5.4)	1 (2.7)
COVID-19	2 (5.4)	0
Sinusitis	2 (5.4)	0
Urinary tract infection	2 (5.4)	0

TIMING OF INFECTIONS

- Median time (range) to onset of any-grade and grade ≥3 infection was 40.0 (1-317) and 63.0 (4-321) days, respectively
- Overall, infections occurred early after treatment initiation (**Figure 2**) and tended to decrease over time in those still being followed up for AEs in each cycle

Figure 2. Infections overall and by pathogen[a] type over time

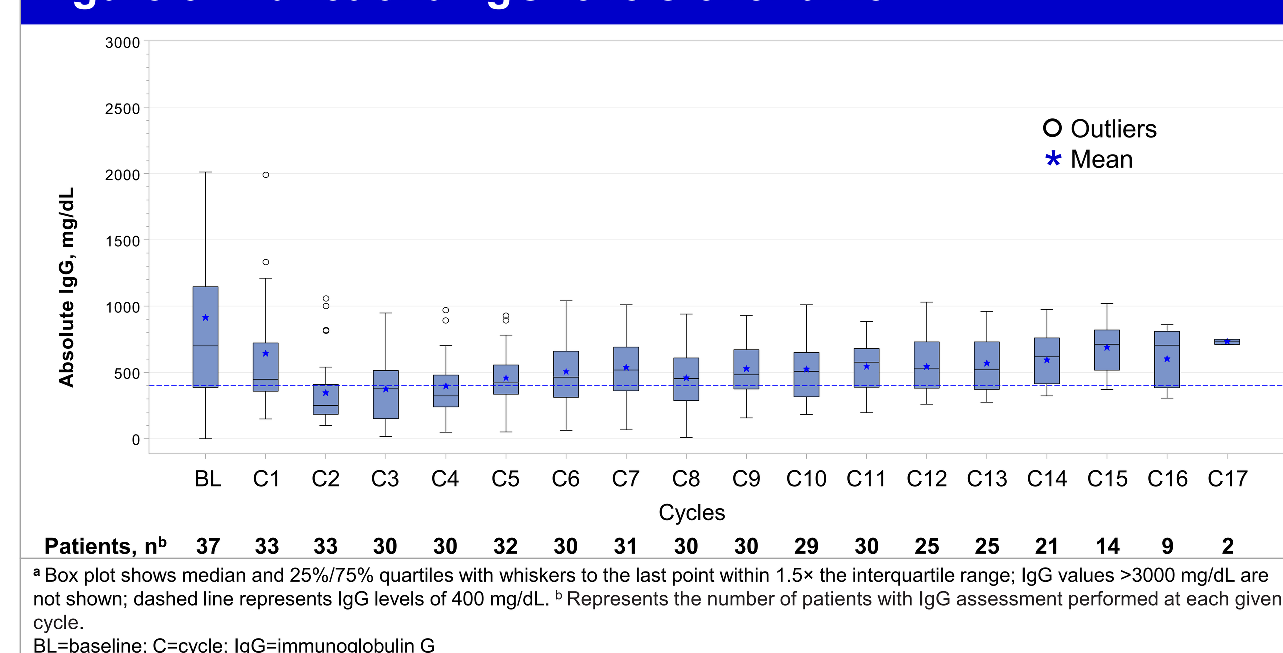


[a] Bacterial infections include HLGT of bacterial infectious disorders; PT containing sepsis, bacteraemia, and abscess; PT of septic shock, urinary tract infection, pyelonephritis, pyelonephritis acute, and atypical pneumonia. Viral infections include HLGT of viral infectious disorders and PT containing viraemia. Fungal infections include HLGT of fungal infectious disorders and PT containing fungaemia. Pathogen unspecified includes other PT terms under SOC of infections and infestations. [b] Patients at risk are those in the on-treatment period (ie, up to 90 days after the last dose of study treatment, new anticancer therapy, end of study, or data cutoff, whichever is earlier).
C=cycle; HLGT=high-level group term; PT=preferred term; SOC=system organ class

SUPPORTING TREATMENTS

- Viral, PJP, fungal, and bacterial anti-infectious prophylaxis was given to 94.6%, 94.6%, 13.5%, and 13.5% of patients, respectively
- Overall, 83.8% of patients had ≥1 postbaseline IgG level <400 mg/dL and 91.9% received Ig replacement (**Figure 3**)
  - At baseline, 29.7% of patients already had functional IgG levels <400 mg/dL
  - In patients with functional IgG >400 mg/dL at baseline, the median (range) time to IgG <400 mg/dL prior to Ig replacement was 44.0 (14-73) days
- The median (range) time to the first Ig replacement administration was 52.5 (9-219) days

Figure 3. Functional IgG levels over time[a]



[a] Box plot shows median and 25%/75% quartiles with whiskers to the last point within 1.5× the interquartile range; IgG values >3000 mg/dL are not shown; dashed line represents IgG levels of 400 mg/dL. [b] Represents the number of patients with IgG assessment performed at each given cycle.
BL=baseline; C=cycle; IgG=immunoglobulin G

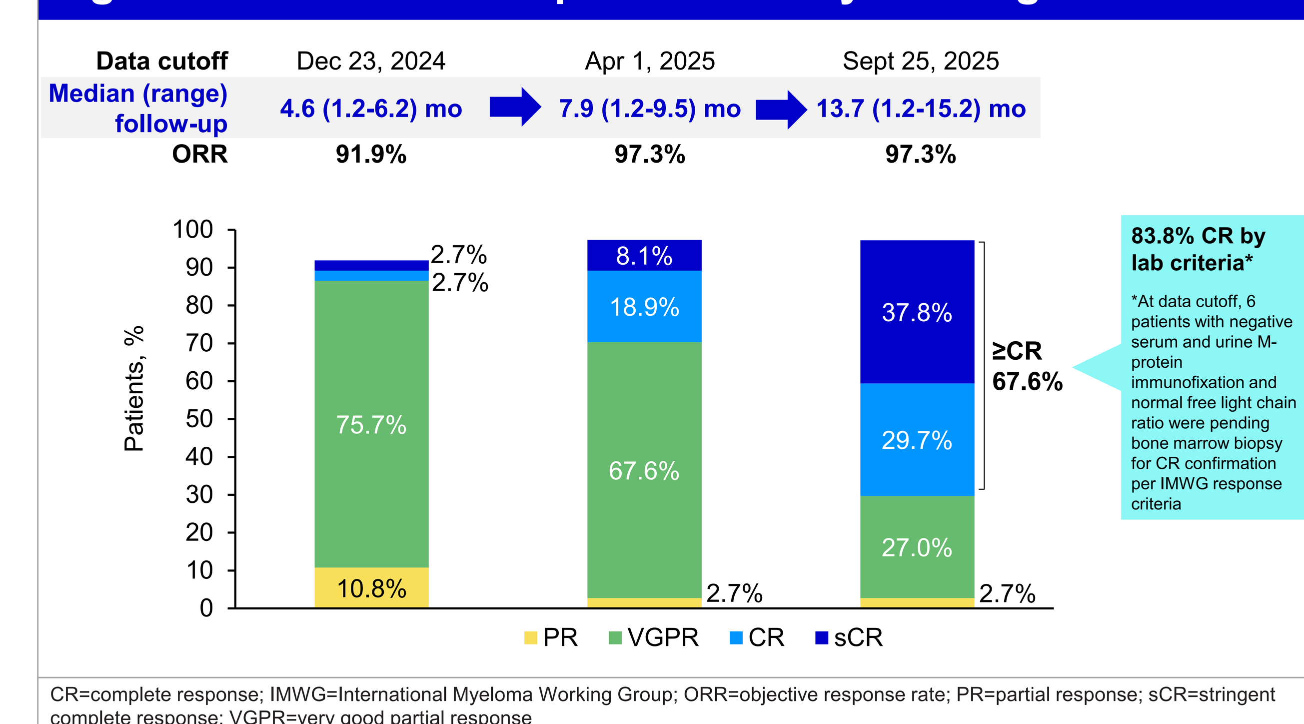
NEUTROPENIA

- Grade 3/4 neutropenia and febrile neutropenia were reported in 78.4% and 8.1% of patients, respectively
  - The median (range) time to onset of the first grade ≥3 neutropenia event was 57.0 (3-407) days
- 73.0% of patients received granulocyte colony-stimulating factor (G-CSF)
  - The median (range) time to first G-CSF administration was 36.0 (3-169) days

EFFICACY

- Responses continued to deepen with additional follow-up (**Figure 4**)

Figure 4. Confirmed response rates by investigator



CR=complete response; IMWG=International Myeloma Working Group; ORR=objective response rate; PR=partial response; sCR=stringent complete response; VGPR=very good partial response

Supplementary Materials

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References: 1. Quach H, et al. J Clin Oncol 2025;43(16 suppl):7504. **2.** Blimark CH, et al. Haematologica 2014;100:107-113.

Acknowledgments: We thank the MagnetisMM-6 trial patients and their families, as well as the study investigators, nurses, and site staff. The study was sponsored by Pfizer. Medical writing support was provided by Robyn Roth, PhD, of Nucleus Global and was funded by Pfizer.

Presented at the 67th ASH Annual Meeting and Exposition
December 6-9, 2025 | Orlando, FL, USA