A Phase 2 Trial of Elranatamab, a B-Cell Maturation Antigen (BCMA)-CD3 Bispecific Antibody, in Patients With Relapsed/Refractory Multiple Myeloma: Initial Safety Results for MagnetisMM-3

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Objective

- Initial results from the MagnetisMM-3 study in patients with RRMM and no prior BCMA-targeted treatment are presented.

Conclusions

- Results suggest that 76 mg QW elranatamab is efficacious and well tolerated in patients with triple-class refractory MM.
  - Study enrolled, as intended, a diverse population of patients with very advanced MM reflective of a real-world myeloma population, with a high proportion of triple- and penta-refractory disease and unfavorable prognostic factors.
- The 2-step-up priming regimen successfully mitigated the rate and severity of CRS, and the CRS profile was predictable, with the majority of events confined to the first 2 doses (88.4%) and the first 3 doses (98.6%).
- CRS (58.9%) and ICANS (2.2%) were limited to grade 1/2, with no grade ≥3 events.
- Most common grade 3/4 TEAEs were hematologic, with non-hematologic TEAEs predominately low grade (grade 1/2).
- High response rate (ORR, 60.6%) was observed early, with a clinical benefit observed across subgroups.
  - At the data cut-off, 89.5% of objective responders were still ongoing without confirmed progression or death.
- These results support continued development of elranatamab monotherapy for patients with MM.
- The MagnetisMM program continues to evaluate elranatamab alone and in combination with other drugs for the treatment of patients with MM.
  - Phase 3 MagnetisMM-5 trial in patients with RRMM (NCT05020236).
  - Phase 3 MagnetisMM-7 trial in patients with newly diagnosed MM post-transplant maintenance (NCT05317416).

Electronic Poster, Supplementary Material, and Abstract Plain Language Summary

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Disclosures

AC, SS, EL, AV: employee (Pfizer); stocks/ownership (Pfizer). **MR:** honoraria (AbbVie, BMS, GSK, Takeda); consulting/advisory role (Amgen, BMS, GSK, Janssen, Pfizer, Oncopeptides, Sanofi); research funding (BMS, Janssen, Novartis, Sanofi). **NR:** honoraria (Medscape, Research to Practice); consulting/advisory role (Amgen, Bristol Myers Squibb, Celgene, Janssen, Merck, Takeda); research funding (AstraZeneca). **PR-O:** honoraria (Amgen, BMS, GSK, Janssen, Regeneron, Sanofi, Takeda); consulting/advisory role (AbbVie, BMS, GSK, Janssen, Kite Pharma, Oncopeptides, Pfizer, Sanofi, Takeda).

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Background

- B-cell maturation antigen (BCMA) is a member of the tumor necrosis factor receptor superfamily universally expressed on multiple myeloma (MM) cells.[1]
- Elranatamab (PF-06863135) is a humanized bispecific antibody that targets both BCMA-expressing MM cells and CD3-expressing T cells.[1]
- Preliminary data from the ongoing, phase 1 MagnetisMM-1 study (NCT03269136) demonstrated the safety and efficacy of elranatamab in patients with relapsed/refractory MM (RRMM).[2-4]
  - After a median follow-up of 10.6 mo, among responders (overall response rate [ORR]=64%) the 9-mo probability of maintaining a response was 77%.[4]
  - These results support further development of elranatamab both as a monotherapy and in combination with other agents.

Methods

- MagnetisMM-3 (NCT04649359) is an open-label, multicenter, non-randomized, phase 2 study to evaluate the safety and efficacy of elranatamab monotherapy in patients with RRMM (**Figure 1**).
  - Enrolled patients were refractory to at least 1 proteasome inhibitor, 1 immunomodulatory drug, and 1 anti-CD38 antibody.
- Patients were assigned to 1 of 2 independent, parallel cohorts:
  - those naïve to BCMA-directed therapies (Cohort A), and
  - those with previous exposure to BCMA-directed antibody-drug conjugates or CAR-T cells (Cohort B).
- Patients received subcutaneous elranatamab 76 mg QW on a 28-day cycle with a 2-step-up priming dose regimen (12 mg and 32 mg) administered during the first week (**Figure S1**).
  - Dose modifications were permitted for toxicity.
  - **Please scan the QR code to view all Supplementary Material**.
- This interim analysis reports results in the first 94 patients who received ≥1 dose of elranatamab in Cohort A.
  - Data cut-off: March 23, 2022.

Results

PATIENTS AND TREATMENT

Table 1: Baseline demographics and characteristics and prior treatments

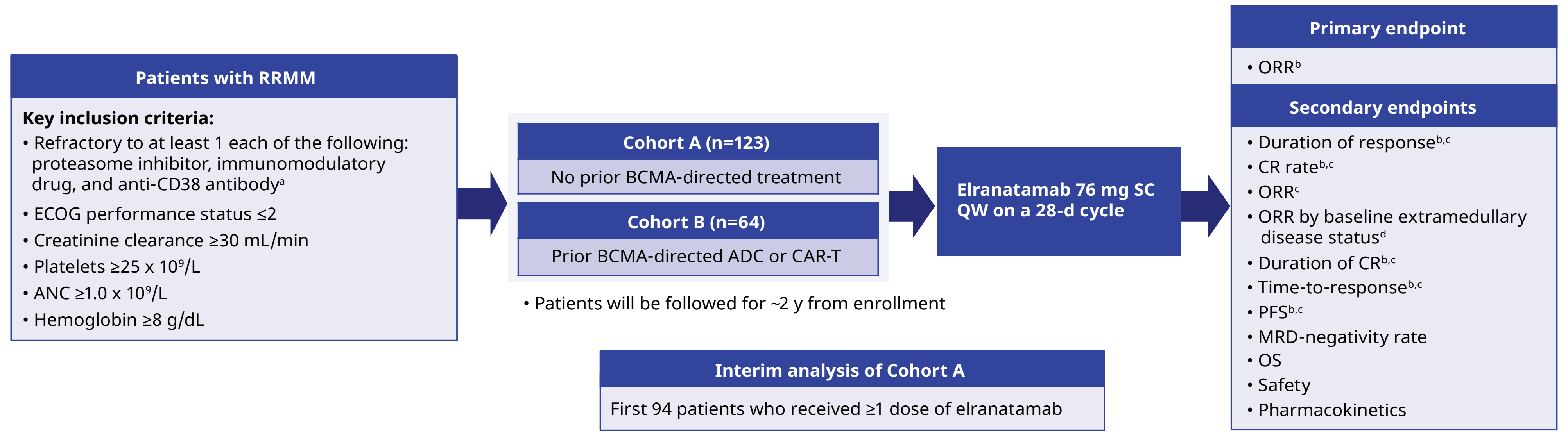
	Cohort A n=94[a]
Age, median (range), y	69 (44–89)
Male, n (%)	50 (53.2)
Race, n (%)	
White	56 (59.6)
Asian	15 (16.0)
Black or African American	7 (7.4)
Not reported or unknown[b]	16 (17.0)
ECOG performance status, n (%)	
0	37 (39.4)
1	51 (54.3)
2	6 (6.4)
R-ISS disease stage, n (%)	
I	20 (21.3)
II	55 (58.5)
II	15 (16.0)
Unknown	4 (4.3)
Extramedullary disease by BICR, n (%)[c]	28 (29.8)
Bone marrow plasma cells, n (%)	
<50%	71 (75.5)
≥50%	18 (19.1)
Missing	5 (5.3)
Prior anti-myeloma therapies, median (range)	5.0 (2–12)
Refractory status, n (%)	
Triple-class[d]	90 (95.7)
Penta-drug[e]	37 (39.4)
Refractory to last line of therapy	89 (94.7)

[a] Includes 4 patients who received 1-step-up priming dose of 44 mg in Week 1. [b] Includes patients recruited in countries where the collection of race is prohibited. [c] Extramedullary disease was defined as presence of any plasmacytoma (extramedullary and/or paramedullary) with a soft-tissue component. [d] Triple-class refers to at least 1 proteosome inhibitor, 1 immunomodulatory drug, and 1 anti-CD38 antibody. [e] Penta-drug refers to at least 2 proteosome inhibitors, 2 immunomodulatory drugs, and 1 anti-CD38 antibody.

Refractory was defined as having disease progression while on therapy or within 60 d of last dose in any line, regardless of response.

BICR=blinded independent review; ECOG=Eastern Cooperative Oncology Group; R-ISS= Revised Multiple Myeloma International Staging System

Figure 1: MagnetisMM-3 study design



Patients with RRMM

Key inclusion criteria:
- Refractory to at least 1 each of the following: proteasome inhibitor, immunomodulatory drug, and anti-CD38 antibody[a]
- ECOG performance status ≤2
- Creatinine clearance ≥30 mL/min
- Platelets ≥25 x 10⁹/L
- ANC ≥1.0 x 10⁹/L
- Hemoglobin ≥8 g/dL

Cohort A (n=123)
No prior BCMA-directed treatment

Cohort B (n=64)
Prior BCMA-directed ADC or CAR-T

- Patients will be followed for ~2 y from enrollment

Elranatamab 76 mg SC QW on a 28-d cycle

Interim analysis of Cohort A
First 94 patients who received ≥1 dose of elranatamab

Primary endpoint
- ORR[b]

Secondary endpoints
- Duration of response[b,c]
- CR rate[b,c]
- ORR[c]
- ORR by baseline extramedullary disease status[d]
- Duration of CR[b,c]
- Time-to-response[b,c]
- PFS[b,c]
- MRD-negativity rate
- OS
- Safety
- Pharmacokinetics

[a] Refractory was defined as having disease progression while on therapy or within 60 d of last dose in any line, regardless of response. [b] By blinded independent central review assessment per IMWG response criteria.[6] [c] By investigator assessment per IMWG response criteria. [d] Includes patients in Cohort A initially dosed at least 4 mo prior to the March 23, 2022 data cut-off date.

ADC=antibody–drug conjugate; ANC=absolute neutrophil count; BCMA=B-cell maturation antigen; CAR-T=chimeric antigen receptor T-cell; CR=complete remission; ECOG=Eastern Cooperative Oncology Group; IMWG= International Myeloma Working Group; MRD=minimal residual disease; ORR=overall response rate; OS=overall survival; PFS=progression-free survival; QW=once weekly; RRMM=relapsed/refractory multiple myeloma; SC=subcutaneous

- Patient demographics and characteristics are shown in **Table 1**.
- Median duration of treatment was 17.4 (range, 0.1–58.1) wk; 55.3% of patients were still receiving treatment at the data cut-off (**Table S1**).

SAFETY

- The most commonly reported treatment-emergent adverse events (TEAEs) are shown in **Table 2**.
- Among patients who received the 2-step-up priming regimen (n=90), cytokine release syndrome (CRS) and immune effector cell-associated neurotoxicity syndrome (ICANS), respectively, were reported in 58.9% and 2.2% of patients (**Table 3**).
  - No patients permanently discontinued treatment due to CRS or ICANS.
- The 2-step-up priming regimen successfully mitigated the rate and severity of CRS, and the CRS profile was predictable with 88.4% of events after the first 2 doses and 98.6% after the first 3 doses (**Figure 2**).
- Infections were reported in 52.1% (grade 3/4, 22.3%) of patients; 24.5% (grade 3/4, 8.5%) were considered to be treatment-related.
  - Most frequently reported were upper respiratory tract infections (10.6% [grade 3/4, 0%]) (**Table S2**).
  - One (1.1%) patient had infection events that led to permanent discontinuation of elranatamab.
- Peripheral neuropathy was reported in 16.0% of patients (grade 3/4, 1.1%); 6.4% (grade 3/4, 1.1%) were considered treatment-related.
- Most common events (≥2% of patients) were peripheral sensory neuropathy (5.3%) and paresthesia (3.2%). All were grade 1/2, except for 1 (1.1%) patient with grade 3 motor neuropathy.
- Two (2.1%) patients had peripheral neuropathy events that led to permanent discontinuation of elranatamab.
- A medical history of peripheral neuropathy was reported by 46.7% of patients with peripheral neuropathy events.

EFFICACY

- After a median follow-up of 3.71 (range, 0.03–12.91) mo, the ORR was 60.6% (95% CI, 50.0–70.6).
  - A clinical benefit was observed across subgroups (**Figure 3**).
- As of the data cut-off, 89.5% of objective responders were ongoing without confirmed progression or death.

Table 2: Most common TEAEs

	Cohort A n=94	
TEAEs in ≥20% of patients, n (%)	Any Grade	Grade 3/4
Hematologic		
Anemia	41 (43.6)	32 (34.0)
Neutropenia	36 (38.3)	35 (37.2)
Thrombocytopenia	27 (28.7)	19 (20.2)
Lymphopenia	24 (25.5)	22 (23.4)
Non-hematologic		
CRS	57 (60.6)	0
Fatigue	29 (30.9)	2 (2.1)
Diarrhea	27 (28.7)	2 (2.1)
Decreased appetite	25 (26.6)	1 (1.1)
Injection site reaction	25 (26.6)	0
Nausea	21 (22.3)	0

AEs were graded by Common Terminology Criteria for Adverse Events v5.0, except for CRS and ICANS, which were graded by American Society for Transplant and Cellular Therapy criteria.[5]

AE=adverse event; CRS=cytokine release syndrome; TEAE=treatment-emergent adverse event

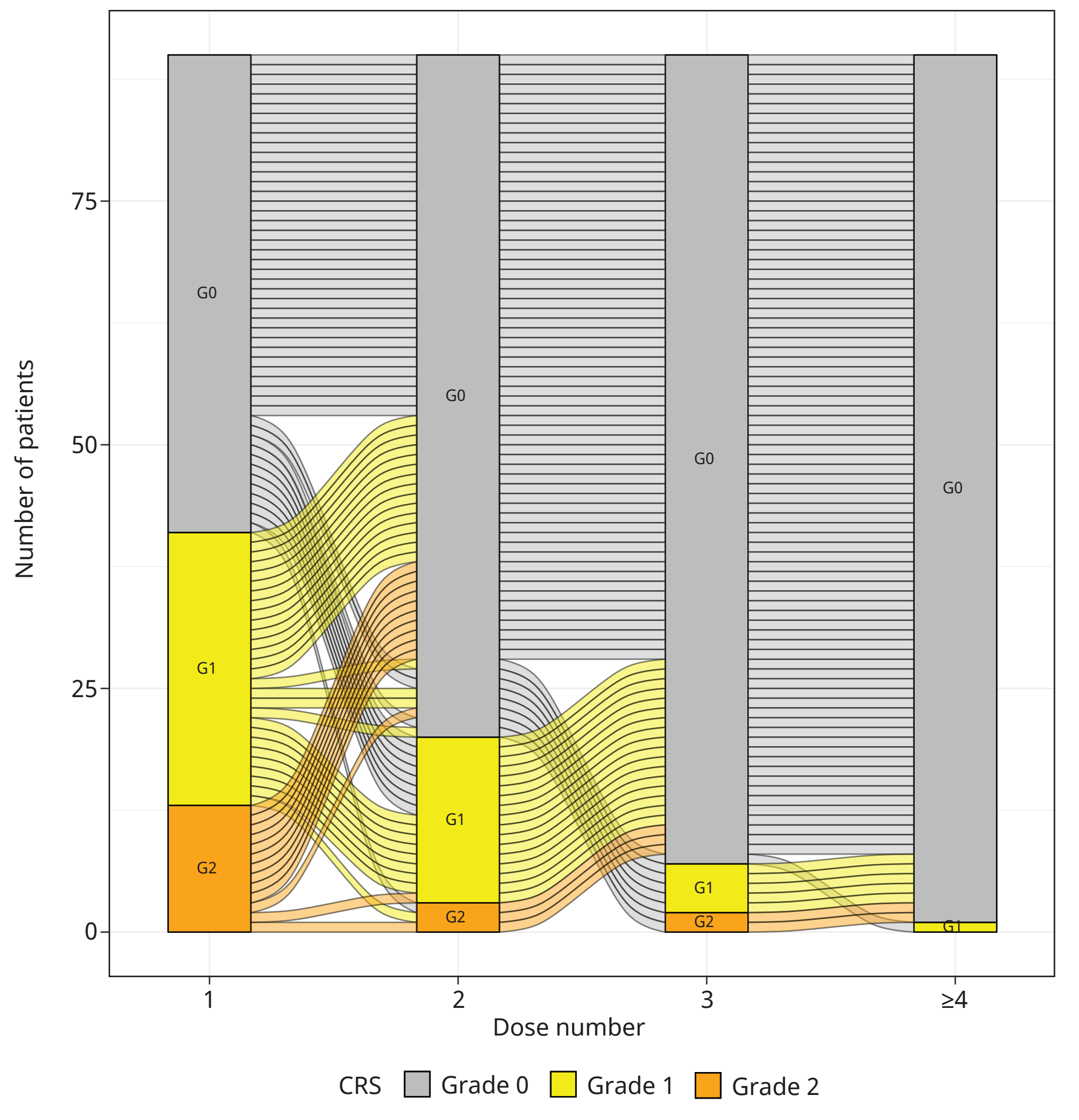
Table 3: AEs of special interest: CRS and ICANS

	12/32 mg 2-step-up regimen n=90[a]	
TEAE of special interest	CRS	ICANS
Patients with TEAE, n (%)	53 (58.9)	2 (2.2)
Maximum grade 1	36 (40.0)	0
Maximum grade 2	17 (18.9)	2 (2.2)
Patients with >1 TEAE, n (%)	16 (17.8)	1 (1.1)
Median time to onset of TEAE, d (range)	2.0 (1.0–9.0)	2.5 (1.0–4.0)
Median time to resolution of TEAE, d (range)	2.0 (1.0–19.0)	3.0 (2.0–6.0)
Patients with TEAE who received tocilizumab[b] or steroids, n (%)	26 (49.1)	2 (100)
Tocilizumab	24 (45.3)	2 (100)
Steroids	7 (13.2)	2 (100)
Permanent discontinuation due to AE, n (%)	0	0

[a] Patients who received 1-step-up priming dose of 44 mg in Week 1 were excluded from this CRS and ICANS analysis (n=4). [b] Includes tocilizumab and siltuximab. CRS and ICANS were graded by American Society for Transplant and Cellular Therapy criteria.[5]

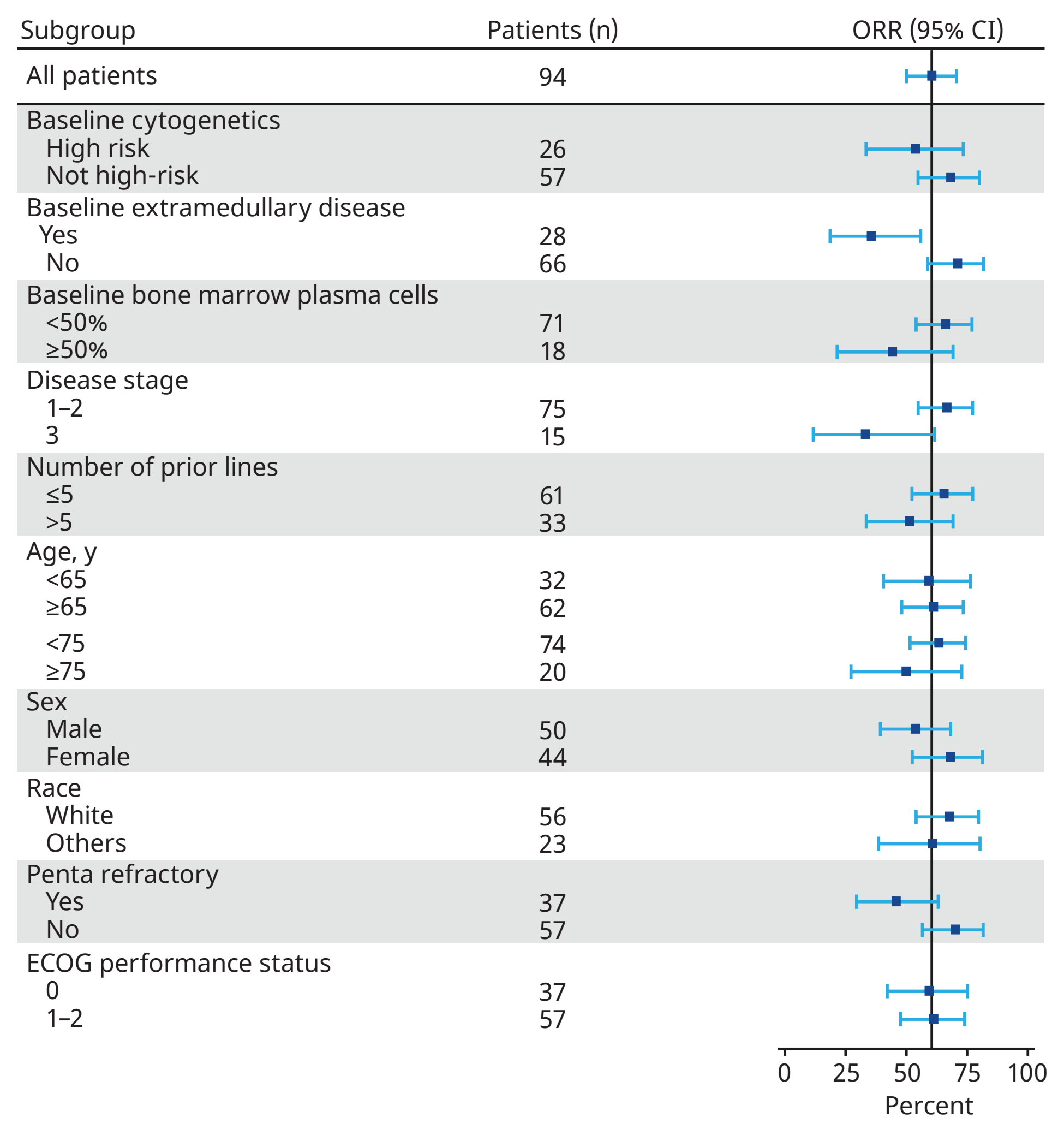
AE=adverse events; CRS=cytokine release syndrome; ICANS=immune effector cell-associated neurotoxicity syndrome; TEAEs=treatment-emergent adverse events

Figure 2: CRS profile by dose



CRS=cytokine release syndrome

Figure 3: Overall response



ORR was defined as confirmed stringent complete response, complete response, very good partial response, or partial response.

ECOG=Eastern Cooperative Oncology Group; ORR=overall response rate