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Efficacy and Safety of Teclistamab in Patients With Relapsed/Refractory Multiple Myeloma With High-Risk Features: A Subgroup Analysis From the Phase 1/2 MajesTEC-1 Study

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Key Takeaway

Teclistamab provides clinical benefit to patients with TCE RRMM with some of the HR features that have been historically associated with poorer outcomes and limited effective treatment options. This is further supported by emerging real-world data

Conclusions

Patients who are penta-drug refractory, have HR cytogenetics, or are age ≥75 years had ORR and ≥CR rates comparable with the overall RP2D MajesTEC-1 population; patients with BMPCs ≥60%, EMD, or ISS stage III disease also derived benefit but remain difficult to treat

Safety profiles, including grade 3/4 TEAEs and rates of discontinuation and deaths due to AEs, were generally comparable between HR subgroups and the overall RP2D population

An opportunity remains to further improve outcomes by treating earlier in the disease course, when fewer HR features are present, or treating with teclistamab-based combinations to enhance antimyeloma activity

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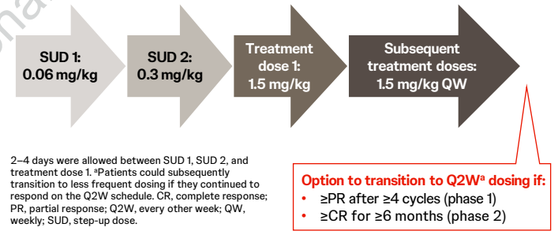
Introduction

- Teclistamab is the first approved B-cell maturation antigen (BCMA) × CD3 bispecific antibody (BsAb) for the treatment of triple-class exposed (TCE) relapsed/refractory multiple myeloma (RRMM), with weight-based dosing and the longest study follow-up of any BsAb in MM[1,2]
- In the pivotal phase 1/2 MajesTEC-1 study, rapid, deep, and durable responses were observed in patients treated with the recommended phase 2 dose (RP2D) of teclistamab[3-5]
- High-risk (HR) features of MM, such as older age, HR cytogenetics, and extramedullary disease (EMD), have been historically associated with poorer outcomes and fewer treatment options[6,7]
  - Emerging real-world data suggest teclistamab may provide meaningful clinical benefit for some of these patients[8,9]
- Here, we present a subgroup analysis of patients from MajesTEC-1 with HR features

Methods

- All patients provided informed consent and received teclistamab at the RP2D (**Figure 1**)
- HR subgroups included:
  - Penta-drug refractory (≥2 proteasome inhibitors, ≥2 immunomodulatory drugs, ≥1 anti-CD38 monoclonal antibodies)
  - HR cytogenetics (del[17p], t[4:14], t[14;16])
  - Age ≥75 years
  - Bone marrow plasma cells (BMPCs) ≥60%
  - EMD (≥1 soft tissue plasmacytoma with no contact with bony structures, a stricter definition than used in other clinical trials)
  - International Staging System (ISS) stage III

Figure 1: Teclistamab dosing schedule



2–4 days were allowed between SUD 1, SUD 2, and treatment dose 1. [a]Patients could subsequently transition to less frequent dosing if they continued to respond on the Q2W schedule. CR, complete response; PR, partial response; Q2W, every other week; QW, weekly; SUD, step-up dose.

Results

Patients

- As of Aug 22, 2023, 165 patients had received teclistamab at the RP2D (**Table 1**)

Table 1: Patients with HR features in MajesTEC-1

Characteristic	n/N	%
Penta-drug refractory	50/165	30.3
HR cytogenetics	38/148	25.7
Age ≥75 years	24/165	14.5
BMPCs ≥60%	18/160	11.2
EMD	28/165	17.0
ISS stage III	20/162	12.3

Efficacy

- Patients who were penta-drug refractory, had HR cytogenetics, or were aged ≥75 years had similar response rates to the overall RP2D population (**Figure 2**)
- Duration of response (DOR) was generally comparable with the overall RP2D population across most subgroups (**Figure 3**)

Safety

- The safety profile across subgroups was generally consistent with the overall RP2D population, including incidence and severity of adverse events (AEs), deaths due to AEs, and low rates of discontinuation due to AEs (**Table 2**)
  - Rates of death due to disease progression were comparable or higher in most subgroups compared with the overall RP2D population, highlighting the poor outcomes associated with these HR features

Figure 3: DOR to teclistamab in patients with HR features in MajesTEC-1

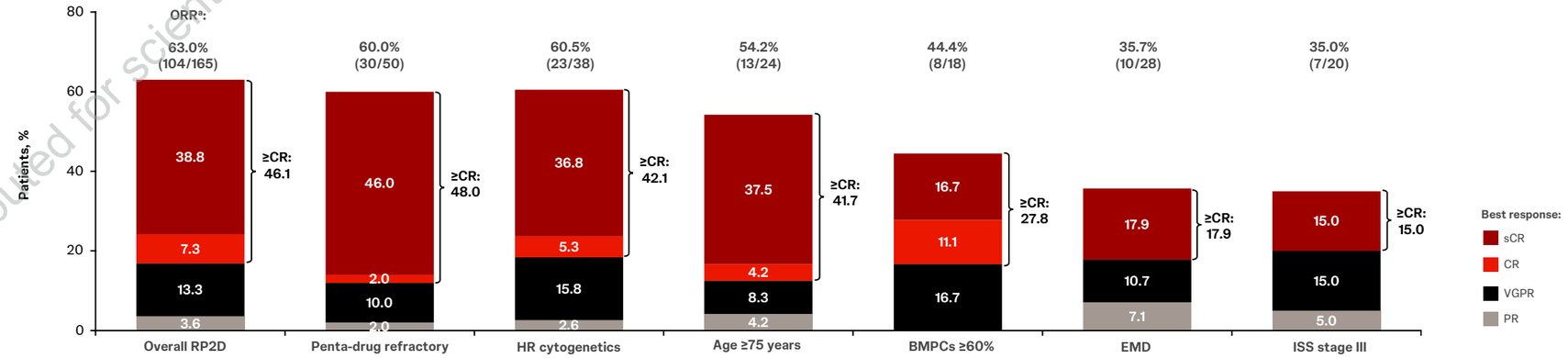
Results should be interpreted with caution due to small patient numbers. mFU, median follow-up; NE, not estimable; NR, not reached.

Table 2: Summary of safety outcomes in patients with HR features in MajesTEC-1

	Overall RP2D (N=165)	Penta-drug refractory (N=50)	HR cytogenetics (N=38)	Age ≥75 y (N=24)	BMPCs ≥60% (N=18)	EMD (N=28)	ISS stage III (N=20)
Any grade TEAE, n (%)	165 (100)	50 (100)	38 (100)	24 (100)	18 (100)	28 (100)	20 (100)
Grade 3/4 TEAE	156 (94.5)	48 (96.0)	37 (97.4)	21 (87.5)	18 (100)	26 (92.9)	18 (90.0)
Discontinuation due to TEAE, n (%)	8 (4.8)	4 (8.0)	0	0	1 (5.6)	1 (3.6)	1 (5.0)
Deaths, n (%)	94 (57.0)	28 (56.0)	26 (68.4)	15 (62.5)	11 (61.1)	20 (71.4)	12 (60.0)
Due to AE	26 (15.8)	10 (20.0)	6 (15.8)	5 (20.8)	1 (5.6)	2 (7.1)	3 (15.0)
Due to disease progression	56 (33.9)	17 (34.0)	17 (44.7)	9 (37.5)	10 (55.6)	15 (53.6)	7 (35.0)

TEAE, treatment-emergent adverse event.

Figure 2: ORR in patients with HR features in MajesTEC-1



[a]Response assessed by independent review committee. sCR, stringent complete response; VGPR, very good partial response.

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Multiple Myeloma