P-089

Impact of COVID-19 on Outcomes With Teclistamab in the Phase 1/2 MajesTEC-1 Study in Patients With Relapsed/Refractory Multiple Myeloma

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Key Takeaway

Median PFS, OS, and DOR in MajesTEC-1 were prolonged when censored for COVID-19 deaths. Appropriate infection prevention, monitoring, and management are of critical importance in optimizing outcomes for patients with RRMM treated with teclistamab

Conclusions

The COVID-19 pandemic placed healthcare systems globally under unprecedented pressure, creating a unique set of circumstances for all healthcare professionals and patients involved in clinical studies at the time

Published consensus guidelines and expert recommendations should be used to guide infection management with BCMA bispecific antibodies such as teclistamab, with vaccination and Ig replacement playing key roles in mitigating infection risk[18-21]

More than 10,000 patients worldwide have been treated with teclistamab since the first patient was dosed in clinical trials. The rates of infection, including COVID-19, and efficacy outcomes seen in MajesTEC-1 should be viewed in the context of the timing of the study, with future studies likely to provide a more representative clinical picture for teclistamab[22]

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Poster

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Disclosures

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Introduction

- The COVID-19 pandemic had a disproportionate effect on patients with multiple myeloma (MM)
  - Higher infection risk, higher excess mortality rate, and decreased survival[1]
  - COVID-19 mortality rates of up to 57% among patients with MM in 2020,[2-4] with worse outcomes in hematologic cancers vs other tumor types[5]
- The onset of the pandemic immediately placed hospitals and healthcare systems under immense pressure,[6,7] with:
  - No approved COVID-19 treatments or vaccines
  - No unified approach to managing MM in the COVID-19 setting
- This created an extraordinary set of circumstances for all clinical studies ongoing at the time, including the MajesTEC-1 study of teclistamab in relapsed/refractory MM (RRMM)
  - Teclistamab is the first approved B-cell maturation antigen (BCMA) × CD3 bispecific antibody with weight-based dosing for the treatment of triple-class exposed RRMM[8,9]
- MajesTEC-1 recruitment ran concurrently with the pandemic, beginning March 2020 and overlapping with peak infection and death rates worldwide based on World Health Organization data[10]
  - There was little knowledge of, and no published consensus guidelines on, infection prophylaxis and management with BCMA bispecific antibodies at that time
  - Implementation of preventive strategies varied widely across institutional protocols
- Access to routine healthcare was severely disrupted during the pandemic, especially for patients with MM for whom active treatment was critical for disease control[4,11,12]
  - Continuing active treatment was particularly important for the heavily pretreated, highly refractory MajesTEC-1 population, who had poor outcomes with standard treatments[13]
- To evaluate the potential impact of COVID-19 on outcomes with teclistamab, we undertook a post hoc analysis of MajesTEC-1 in patients receiving the recommended phase 2 dose (RP2D)

Methods

- Full details of MajesTEC-1 (NCT03145181/NCT04557098) have been published previously[14]
- Per protocol, relevant precautions to mitigate infection risk were taken and evolved over time as appropriate. Infections were managed per institutional guidelines (eg, use of immunoglobulin [Ig] replacement) and/or teclistamab interruption.[15] Vaccination (including booster doses) was recommended when available[15]
- Patients with grade 5 COVID-19 infection were censored at the time of last disease evaluation for analyses of progression-free survival (PFS) and duration of response (DOR) and at time of death for overall survival (OS; **Figure 1**)

FIGURE 1: Post hoc analysis of impact of COVID-19 on outcomes in MajesTEC-1

Data cut-off: January 4, 2023 (median follow-up 22.8 months). N=165 (RP2D cohort). PD, disease progression.

- Outcomes were analyzed overall by number of prior lines of therapy (≤3 or >3) and in the phase 2 efficacy population subgroup (110 patients enrolled on or before March 18, 2021)

Results

Baseline characteristics

- The MajesTEC-1 population of 165 patients had a median age of 64 years (range, 33–84) and had previously received a median of 5 prior lines of therapy (range, 2–14)[14]
  - 77.6% of patients were triple-class refractory and 30.3% were penta-drug refractory (≥2 immunomodulatory drugs, ≥2 proteasome inhibitors, and ≥1 anti-CD38 antibody) at study entry[14]

COVID-19 incidence, management, and vaccination

- COVID-19 infections of any grade occurred in 29.1% of patients (**Table 1**)
- 7.9% of patients were vaccinated prior to starting teclistamab; 60.0% received ≥1 COVID-19 vaccination on-study (**Table 1**)
  - Depending on country, the first COVID-19 vaccines were not approved until the end of 2020 through early 2021,[16] at least 9 months into MajesTEC-1 enrollment
  - Patients who had never been vaccinated tended to die of COVID-19 earlier during teclistamab treatment than those who had received ≥1 vaccine dose (between 0.7–5.9 vs 2.4–25.9 months, respectively, after starting teclistamab), reflecting the timing of global vaccine rollout

TABLE 1: COVID-19 infections in MajesTEC-1

Patients, n (%)	N=165
Incidence and severity	
Any Grade	48 (29.1)
Grade 3/4	35 (21.2)
Death	18 (10.9)
Management	
Supportive therapies	40 (24.2)
Glucocorticoids	26 (15.8)
Tocilizumab	8 (4.8)
Anti-infectives	38 (23.0)
Monoclonal antibodies	17 (10.3)
Hyperimmune plasma COVID-19	9 (5.5)
Other	31 (18.8)
Teclistamab interruption	29 (17.6)
COVID-19 vaccination (≥1 dose)	
Prior to starting teclistamab[a]	13 (7.9)
On-study[b]	99 (60.0)

[a]Including 1/18 patients who died of COVID-19 (received 2 vaccine doses before starting teclistamab). [b]Including 13/18 patients who died of COVID-19 (1 dose, n=3; 2 doses, n=4; 3 doses, n=3; 4 doses, n=3 [the patient vaccinated prior to starting teclistamab received their third dose on-study]).

Impact of COVID-19 on outcomes with teclistamab

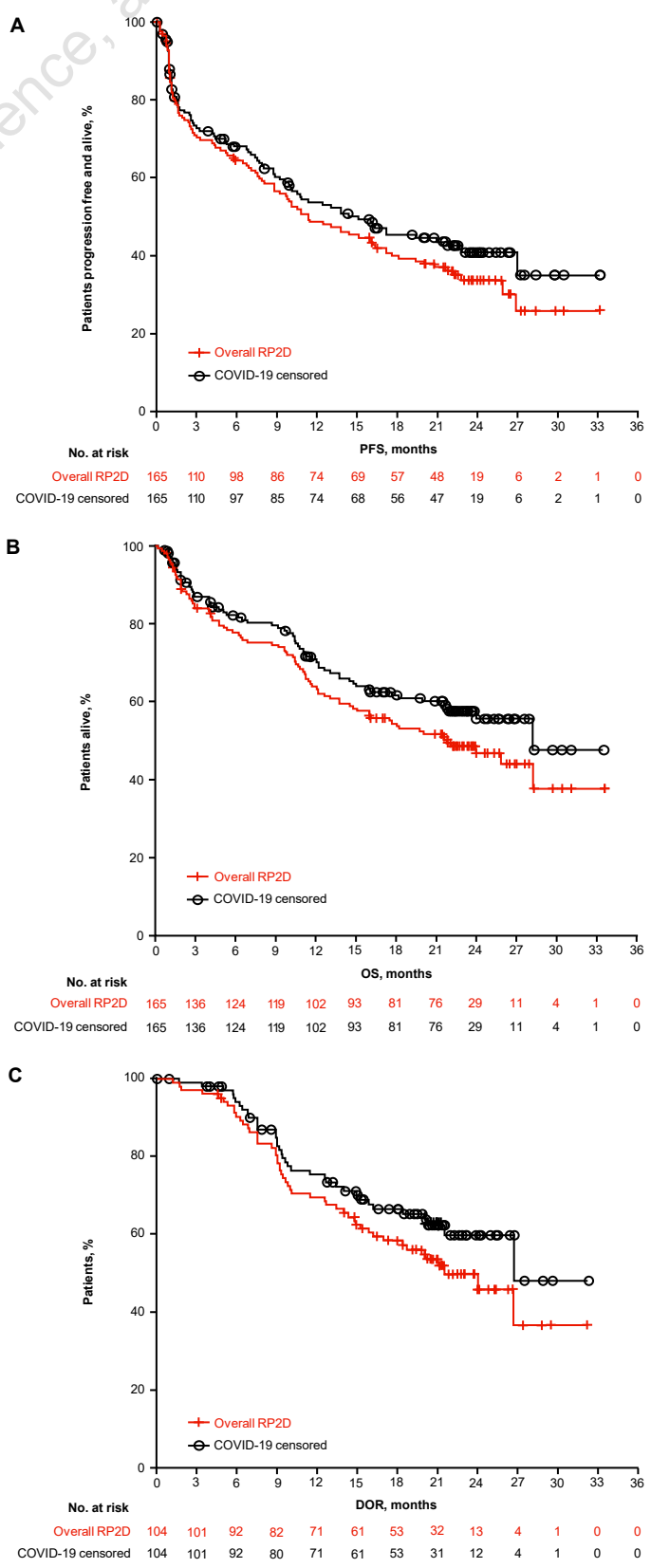
- When censored for COVID-19 deaths, median PFS, OS, and DOR were prolonged compared with the overall MajesTEC-1 analysis (**Table 2** and **Figure 2**)
- Median PFS was 15.1 months when censored for COVID-19 deaths, compared with 11.3 months in the overall analysis

TABLE 2: Median PFS, OS, and DOR with teclistamab in MajesTEC-1 in the overall study analysis and when censored for COVID-19 deaths

Outcome	Overall analysis (uncensored)[a]	Censored for COVID-19 deaths[a]
Median PFS, months (95% CI)		
All patients (N=165)[b]	11.3 (8.8–16.4)	15.1 (9.9–22.8)
≤3 prior lines of therapy (n=43)	18.1 (13.8–26.9)	26.9 (13.8–NE)
>3 prior lines of therapy (n=122)	9.7 (6.4–13.1)	10.8 (7.1–21.0)
Phase 2 efficacy population (n=110)	10.8 (7.4–16.4)	13.8 (8.8–NE)
Median OS, months (95% CI)		
All patients (N=165)[b]	21.9 (15.1–NE)	28.3 (21.9–NE)
≤3 prior lines of therapy (n=43)	25.9 (18.3–NE)	NE (21.7–NE)
>3 prior lines of therapy (n=122)	17.7 (12.2–NE)	28.3 (16.0–NE)
Phase 2 efficacy population (n=110)	21.7 (12.7–NE)	NE (21.7–NE)
Median DOR, months (95% CI)		
All patients (N=104)[b]	21.6 (16.2–NE)	26.7 (21.6–NE)
≤3 prior lines of therapy (n=32)	21.1 (14.0–NE)	26.7 (15.9–NE)
>3 prior lines of therapy (n=72)	NE (14.9–NE)	NE (20.1–NE)
Phase 2 efficacy population (n=68)	21.6 (14.9–NE)	NE (21.6–NE)

[a]Estimated median follow-up 22.8 months. [b]18 patients died from COVID-19 in the RP2D cohort of MajesTEC-1 (N=165); 17 were censored in the PFS analysis, 13 in the DOR analysis, and 18 in the OS analysis. CI, confidence interval; NE, not estimable.

FIGURE 2: (A) PFS, (B) OS, and (C) DOR with teclistamab in the RP2D cohort of MajesTEC-1 in the overall study analysis and when censored for COVID-19 deaths[a,b]



[a]Estimated median follow-up 22.8 months. [b]18 patients died from COVID-19 in the RP2D cohort of MajesTEC-1 (N=165); 17 were censored in the PFS analysis, 13 in the DOR analysis, and 18 in the OS analysis.

- The same trends toward prolonged survival and DOR were observed when evaluated by number of lines of prior therapy and in the phase 2 efficacy population (**Table 2**)
  - This included the subgroup who had received ≤3 prior lines of therapy; these patients were earlier in their treatment journey and may likely have had more favorable baseline immune fitness, which is important in achieving a response to teclistamab[17]

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