OPTec: A Phase 2 Study to Evaluate Outpatient Step-Up Administration of Teclistamab in Patients With Relapsed/Refractory Multiple Myeloma (RRMM): Updated Results

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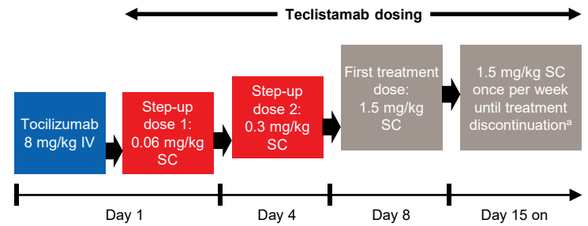
Introduction

- Teclistamab (Tec) is the first approved bispecific antibody targeting CD3 and B-cell maturation antigen for the treatment of adults with relapsed/refractory (RR) multiple myeloma (MM) who have received ≥4 lines of prior therapy[1]
- In the phase 1/2 MajesTEC-1 study (NCT03145181/ NCT04557098), rapid, deep, and durable responses were observed over a median 30.4 months follow-up in patients (pts) with RRMM, with a manageable safety profile[2]
- As all bispecific antibodies for MM can cause cytokine release syndrome (CRS) and neurologic toxicity, US Prescribing Information recommends pts be hospitalized during Tec step-up dosing[1]
- However, CRS occurred less frequently (26% vs 73%)[3] with tocilizumab (Toci) administration before the first Tec step-up dose, with no effect on efficacy or infections[3,4]
- This study assesses the potential benefits of administering Toci before the first step-up dose of Tec to reduce CRS incidence and support safe outpatient administration of Tec

Methods

- This is a phase 2, nonrandomized, single-arm study (NCT05972135) of Tec outpatient administration in pts with RRMM
- Eligible pts are adults who have MM, have received 4 or more prior therapies for MM, are triple-class exposed, and have an Eastern Cooperative Oncology Group performance status (ECOG PS) of 0 or 1
- Tec is administered in the outpatient setting using a step-up dosing schedule, in which pts receive 2 step-up doses of Tec (0.06 mg/kg and 0.3 mg/kg subcutaneously [SC]) before the first full treatment dose (1.5 mg/kg SC), with subsequent doses administered at 1.5 mg/kg SC once weekly and an option to switch to once every 2 weeks based on response (**Figure 1**)
- 2 to 4 hours before the first step-up dose of Tec, all pts receive a single dose of Toci (8 mg/kg intravenously)
- Intravenous (IV) immunoglobulin (IVIG) was strongly recommended for immunoglobulin G (IgG) levels <400 mg/dL
- The primary endpoint is the incidence of any-grade CRS in the first 2 cycles; secondary endpoints include overall response rate and incidence of any-grade recurrent CRS, any-grade infections, any-grade neurotoxicity, and hospitalizations

Figure 1: Study treatment administration



Step-up dose 2 and the first treatment dose may be given between 3 to 5 days after step-up dose 1/2 and up to 7 days after step-up dose 1/2 to allow for resolution of AEs.
[a]Dosing may be reduced to 1.5 mg/kg SC once every 2 weeks in patients who achieve partial response or better after 6 months of study treatment. AE, adverse event.

Results

Demographics

Table 1: Patient demographics (treated population)

Characteristic	Total (N=16)
Age in years, median (range)	74 (53–86)
Sex, n (%)	
Female	9 (56.3)
Male	7 (43.8)
Race, n (%)	
Black or African American	1 (6.3)
White	11 (68.8)
Unknown/unreported	4 (25.0)
Baseline ECOG PS, n (%)	
0	2 (12.5)
1	14 (87.5)
Number of lines of prior therapy, median (range)	4 (4–11)

Patient disposition

Table 2: Patient disposition (treated population)

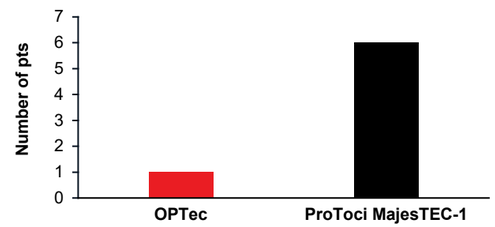
	Total (N=16)
Patient status, n (%)	
On treatment	13 (81.3)
On study	14 (87.5)
Completed study	1 (6.3)
Discontinued study	1 (6.3)
Progressive disease, n (%)	2 (12.5)

- Pts were discontinued from treatment due to progressive disease (2 pts, 12.5%) and completing treatment per protocol (1 pt, 6.3%)
- 1 pt with diffuse bony lesions had a serious AE (SAE) of bilateral leg weakness and pain unrelated to Tec or Toci, was withdrawn from the study, and died 2 weeks later of progressive disease
- The median treatment duration was 9.6 months (range, 0.03–11.08)

Safety

- CRS
  - 1 pt (6.3%) experienced CRS (grade 1, occurring in cycle 1), which was considered related to Tec and which was managed with dexamethasone (**Figure 2**)

Figure 2: CRS in OPTec vs ProToci cohort in MajesTEC-1



CRS occurred in 1 of 16 pts (6.3%) in OPTec and 6 of 24 pts (25.0%) in the ProToci cohort in MajesTEC-1.[3]
ProToci, prophylactic tocilizumab.

- Infections and IgG
  - A total of 7 pts (43.8%) experienced 12 infections, of which 10 infections were grade 2 and 2 infections were considered related to study treatment
  - There were 2 grade ≥3 infections: a grade 3 urinary tract infection and grade 4 sepsis, which was considered an SAE
  - 8 pts (50.0%) experienced quantitative IgG <400 mg/dL, of whom 6 received IVIG
- Neurotoxicity
  - No pts developed immune effector cell–associated neurotoxicity syndrome (ICANS) due to study treatment
- Hospitalizations
  - 1 pt was hospitalized due to treatment-related delirium with febrile neutropenia
- No pts met stopping criteria (grade >3 CRS or neurotoxicity/ICANS)
- A preliminary pharmacokinetics (PK) analysis in pts from this trial showed that observed Toci PK are consistent with the literature[2]
- The most common treatment-related AEs (TRAEs; ≥15% of all pts) were injection site reaction (5 pts, 31.3%; 3 pts, grade 1; 2 pts, grade 2), headache and neutropenia (4 pts each, 25.0%), and fatigue and hypogammaglobulinemia (3 pts each, 18.8%)
- The most common grade ≥3 TRAEs (≥5% of all pts) were neutropenia (4 pts, 25.0%) and febrile neutropenia, increased alanine aminotransferase, anemia, back pain, hypertension, and decreased platelet count (1 pt each, 6.3%)

Table 3: Safety summary (treated population)

	Total (N=16) n (%)
Any TEAE	15 (93.8)
Grade ≥3 TEAE	13 (81.3)
Any-Grade TRAE	12 (75.0)
Grade ≥3 TRAE	8 (50.0)
Any SAE	6 (37.5)
Any treatment-related SAE	1 (6.3)
Any TEAE leading to death	0
Any TEAE leading to treatment discontinuation	0

TEAE, treatment-emergent adverse event.

Efficacy

- Of 11 pts evaluable for response, 100% responded to therapy, with 45% having either stringent complete response (sCR) or complete response (CR) as their best overall response (**Figures 3** and **4**)

Figure 3: Best overall response (evaluable population)

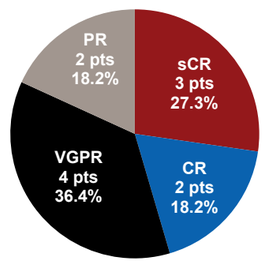
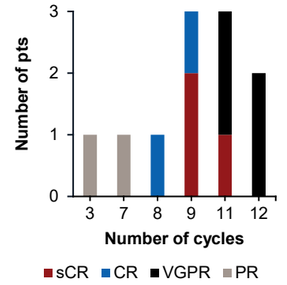


Figure 4: Number of cycles treatment was received



A total of 11 of 16 patients (68.8%) were evaluable for response as of the time of presentation. PR, partial response; VGPR, very good partial response.

Conclusions

- Only 1 of 16 pts experienced a CRS event when tocilizumab was administered before the first step-up dose of teclistamab
- Administering tocilizumab before the first step-up dose of teclistamab reduced the risk of CRS and supports administration of teclistamab in the outpatient setting
- Prophylactic tocilizumab did not appear to increase the risk of serious infections or to reduce the efficacy of teclistamab
- No new safety signals have been observed
- The protocol has been amended to allow pts to receive either teclistamab or talquetamab after 2+ lines of treatment
- The talquetamab arm is now open and enrolling

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Disclosures
RJC is an employee of Johnson & Johnson.

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Multiple Myeloma