OPTec/OPTal: A Phase 2 Study to Evaluate Outpatient Step-up Administration of Teclistamab (Tec) or Talquetamab (Tal) in Participants with RRMM

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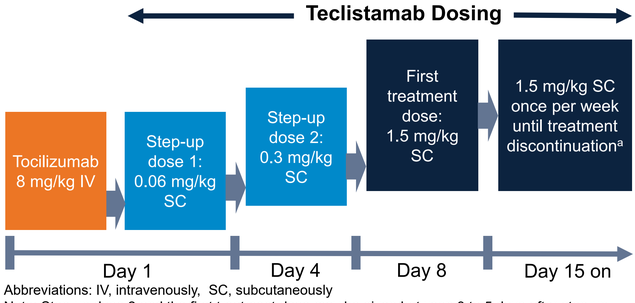
Prophylactic tocilizumab prior to step-up dosing of teclistamab mitigates the risk of cytokine release syndrome (CRS) in the outpatient setting.

Introduction

- Teclistamab (tec), a bispecific antibody targeting CD3 and B-cell maturation antigen, is approved for the treatment of adults with relapsed/refractory (RR) multiple myeloma (MM) who have received at least 4 lines of prior therapy, including a proteasome inhibitor (PI), an immunomodulatory agent (IMiD), and an anti-CD38 monoclonal antibody (mAb).[1]
- Because all bispecific antibodies for MM can cause cytokine release syndrome (CRS) and neurologic toxicity, the US Prescribing Information recommends that patients (pts) be hospitalized during step-up dosing (SUD) of tec.[1]
- However, CRS occurred less frequently (26% vs 73%)[2] when pts were administered tocilizumab (toci), an interleukin-6 receptor antagonist, before the first SUD of tec, with no effect on efficacy or infections.[2,3]
- This study will determine whether administering toci before the first SUD of tec reduces the incidence of CRS and supports safe outpatient (OP) administration of tec SUD, making tec more accessible to pts.

Methods

FIGURE 1. Study treatment administration



Abbreviations: IV, intravenously, SC, subcutaneously
Note: 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 SUD 1/2 to allow for resolution of adverse events.
[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.

- This is a Phase II, nonrandomized, prospective study (NCT05972135) of tec OP administration in pts with RRMM.
- Eligible pts are adults who have MM, have received ≥2 therapies for MM, have received a PI, an IMiD, and an anti-CD38 mAb and have an ECOG performance status of 0 or 1.
- Tec SUD schedule: pts receive 2 SUDs 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 at 1.5 mg/kg SC once weekly and an option to switch to once every 2 weeks based on response (Figure
- Single dose of toci (8 mg/kg IV) 2-4 hrs before the first SUD of tec
- 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.
- Protocol designed pt safety measures:
  - Premedication 1-3 hours before tec SUDs (corticosteroids, H_1 receptor antagonists, or antipyretics)
  - Investigator/staff observation for 2 days after each SUD of tec and after the first full dose (may be by phone during weekends)
  - Home monitoring: measuring and recording of temperature and blood oxygen saturation twice daily [≥8 hours apart]) with immediate reporting of any fever (≥38°C or ≥100.4°F) and subsequent hospitalization for CRS per investigator
  - Recommendation for IV immunoglobulin (IVIG) for IgG levels
  - <400 mg/dL
  - Trained, competent adult companion for 48 hours after each tec SUD and the first full dose of tec.
  - Travel distance restrictions (within 30 minutes of site)

Patient Disposition

TABLE 1. Patient Disposition (treated population)

Patient Status n (%)	Total N=30
Consented	30 (100)
Enrolled and treated	24 (80.0)
On study	8 (26.7)
Completed study	9 (30.0)
Discontinued study	7 (23.3)

- Pts were discontinued from treatment due to completing 12 cycles of treatment per protocol (9, 30%), symptomatic deterioration/clinical disease progression (3, 10.0%), progressive disease (2, 6.7%), withdrawal of consent (1, 3.3%), and a reason listed as “other” (1, 3.3%).
- Median treatment duration was 10.7 months (range: 0.13, 11.77).Zx

References
1. Tecvayli (teclistamab) [package insert]. Horsham, PA: Janssen Biotech, Inc.; 2024.
2. Scott SA, et al. Blood Cancer J. 2023;13(1):191.
3. van de Donk N, et al. J Clin Oncol. 2024;42(16 Suppl):7517.

Results

All results are based on available data as of 01 April 2025.

Demographics

TABLE 2. Patient Demographics (treated population)

Characteristic	Total N=24
Age in years, median (range)	74.5 (53, 86)
Sex, n (%)	
--Female	12 (50)
--Male	12 (50)
Race, n (%)	
--American Indian or Alaskan Native	1 (4.2)
--Black or African American	2 (8.3)
--White	16 (66.7)
--Unknown or Unreported	4 (16.7)
Baseline ECOG Performance Status, n (%)	
--0	3 (12.5)
--1	21 (87.5)
Number of lines of prior therapy, median (range)	5.5 (3, 11)

Safety

CRS:
- Two pts (8%) experienced CRS G1 considered related to tec, one after tec SUD 2 (treated with dexamethasone 20 mg) and the other after tec SUD 1 (treated with dexamethasone 10 mg). These events did not meet stopping criteria (G>3 CRS or neurotoxicity [NT]/immune effector cell-associated neurotoxicity syndrome [ICANS]).

Infections and IgG:
- A total of 11 pts (45.8%) experienced 32 infections (1 G4 [sepsis/not related], 6 G3, 23 G2, and 2 G1). The 7 G ≥3 infections were experienced by 3 (12.5%) pts, none of whom had IgG <400 mg/dL or received IVIG.
- There were14 infections considered related to tec by the investigators experienced by 4 (16.7%) pts.
- Two pts had hypogammaglobulinemia; 1 pt with G2 shingles (related) and 1 pt with 3 G2 events considered by the investigator to be not related.
- Two G3 pneumonia events (related) in the same pt were considered serious adverse events.
- Eleven pts (45.8%) experienced quantitative IgG <400 mg/dL, of whom 5 received IVIG.

Neurotoxicity:
- No pt developed ICANS on treatment.

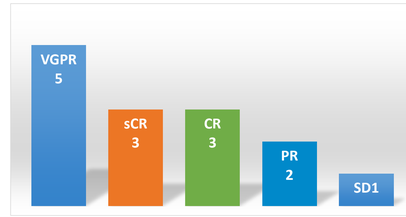
Hospitalizations:
- One pt was hospitalized due to treatment-related delirium, febrile neutropenia, and pneumonia events.

Treatment-related AEs:
- The most common treatment-related AEs (TRAEs; ≥15% of all pts) were injection site reaction (9 pts, 37.5%; 7 pts, G1; 2 pts, G2), neutropenia (6 pts ≥G3, 25.0%), headache (4 pts, 16.7%; 2 pts, G1; 2 pts, G2), and fatigue (4 pts, 16.7%; 1 pt, G1; 3 pts, G2).
- Grade ≥3 TRAEs in addition to neutropenia were seen in 1 pt each (4.2%): pneumonia, back pain, febrile neutropenia, alanine aminotransferase increased, anemia, and platelet and neutrophil counts decreased.
- The 2 deaths on study were due to progressive disease.
- There were no treatment discontinuations due to an AE.

Efficacy

Of 16 evaluable pts, the best overall response rate was 81% (Figure 2).

FIGURE 2. Best Overall Response 81%



Conclusions

- Only 2 of 24 pts experienced a CRS event (both G1) when toci was administered before the first SUD of tec.
- Administering toci before the first SUD of tec reduced the risk of CRS and supports administration of tec in the OP setting.
- Prophylactic toci did not appear to increase the risk of serious infections or to reduce the efficacy of tec.
- No new safety signals have been observed.
- The study is ongoing, and the protocol has been amended to assess toci for outpatient SUD of tec or talquetamab (tal) with a target of 50 tec and 25 tal pts.

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