Real-World Treatment Outcomes of Teclistamab Under an Outpatient Model for Step-Up Dosing Administration

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BACKGROUND

- Multiple myeloma (MM), a plasma cell malignancy, is the second most common hematologic cancer with an estimated 35,730 new cases in 2023 in the United States.[1] Despite advances in treatment, most patients with MM will eventually experience disease relapse or become refractory to therapy. Relapsed/refractory multiple myeloma (RRMM) has poor prognosis and limited treatment options[2]
- Teclistamab, a first-in-class B-cell maturation antigen (BCMA)-directed CD3 bispecific therapy, was approved by the US Food and Drug Administration (FDA) on October 25, 2022, for the treatment of RRMM after ≥4 prior lines of therapy, including a proteasome inhibitor, an immunomodulatory agent, and an anti-CD38 monoclonal antibody[3]
- Early adverse events of teclistamab include cytokine release syndrome (CRS) and immune effector cell-associated neurotoxicity syndrome (ICANS). To mitigate the risk of these adverse events, teclistamab is initiated with step-up dosing (SUD)[4]
- Although SUD is commonly administered in an inpatient setting, healthcare institutions have begun exploring outpatient administration of SUD to reduce resource utilization[5,6]
- Since FDA approval, teclistamab SUD has been administered as part of Mayo Clinic's hospital-based outpatient program for immunotherapies. Under this program, each dose of the teclistamab SUD is administered in an outpatient setting. Patients are given a remote monitoring kit to regularly measure vital signs and stay connected with the command center for signs and symptoms of CRS and ICANS throughout the SUD period[5]

OBJECTIVE

- To evaluate early safety outcomes and healthcare resource utilization during SUD in real-world (RW) patients who initiated teclistamab under an outpatient administration model

METHODS

- This was a retrospective observational study using Mayo Clinic's electronic medical records. The study was approved by the Institutional Review Board

Study population

- Adult patients (≥18 years) with RRMM who initiated commercial teclistamab at any of the 3 Mayo Clinic locations (Rochester, MN; Phoenix/Scottsdale, AZ; Jacksonville, FL) between October 26, 2022, and September 16, 2023, were included
- Patients who received teclistamab in a clinical trial setting were excluded

Data analysis

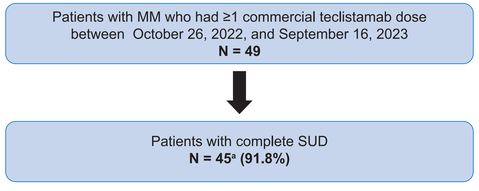
- Patients were indexed on the date of the first teclistamab dose
- Baseline demographic and clinical characteristics were captured during the 6 months period prior to or on the index date. Genetic abnormalities were captured any time before the index date
- Safety outcomes (CRS and ICANS) and healthcare resource utilization (hospital admission rate, length of stay, supportive care use, emergency room visits, and intensive care unit use) during SUD were captured using structured and unstructured electronic medical record data
- Clinic time between teclistamab administration and patient check-out was reported for doses during SUD and full treatment doses, respectively
  - SUD is defined as the 2 initial step-up doses plus the first full treatment dose (first 3 doses)
  - Treatment dose refers to full treatment doses after completing SUD (dose 4 and beyond)
- All variables were analyzed descriptively
  - Mean, standard deviation (SD), and median were reported for continuous variables; numbers and percentages were reported for categorical variables

RESULTS

Patient demographics

- At the time of data cutoff, 49 patients received ≥1 teclistamab dose across the 3 locations, including 45 patients (91.8%) who initiated teclistamab SUD directly in an outpatient setting; 45 patients (91.8%) completed SUD as of data cutoff (**Figure 1**)
- Among the 49 patients who received ≥1 teclistamab dose, the median (min, max) age was 67.2 (38, 84) years, and the majority of patients were male (63.3%). Most patients were White (87.8%) and non-Hispanic (93.9%) (**Table 1**)
- A total of 42 patients (85.7%) received ≥1 teclistamab full treatment dose after the SUD period as of data cutoff. The mean (SD) number of doses received per patient as of data cutoff was 8.1 (5.4)

FIGURE 1. PATIENT ATTRITION



MM, multiple myeloma; SUD, step-up dosing.
[a]Includes 41 patients who initiated and completed teclistamab SUD directly in an outpatient setting.

Patient clinical characteristics

- A total of 31 patients (63.3%) had MM with high-risk cytogenetics. 17 patients (34.7%) had prior exposure to other BCMA-targeted therapies
  - High-risk cytogenetics was defined as having ≥1 of the following abnormalities: del(17p), t(4;14), t(14;16); t(14;20), and gain or amp(1q)
- Prevalent comorbidities of interest prior to receiving teclistamab included peripheral neuropathy (57.1%), anemia (55.1%), hypogammaglobulinemia (40.8%), neutropenia (28.6%), and hypertension (26.5%)
- Renal impairment or failure was observed in 30.6% of patients (**Table 1**)

TABLE 1. BASELINE PATIENT DEMOGRAPHIC AND CLINICAL CHARACTERISTICS

Patient demographics	
Site of administration, n (%)	
Rochester, MN	32 (65.3)
Phoenix/Scottsdale, AZ	12 (24.5)
Jacksonville, FL	5 (10.2)
Age at the first teclistamab dose, years	
Median, (min, max)	67.2 (38.7, 84.2)
≥75 years, n (%)	7 (14)
Sex, n (%)	
Male	31 (63.3)
Female	18 (36.7)
Race, n (%)	
White	43 (87.8)
Black or African American	3 (6.1)
Asian	1 (2.0)
Other	2 (4.1)
Ethnicity, n (%)	
Hispanic	2 (4.1)
Non-Hispanic	46 (93.9)
Unknown	1 (2.0)
Patient clinical characteristics, n (%)	
MM with high-risk cytogenetics[a]	31 (63.3)
Prior BCMA exposure	17 (34.7)
CAR-T therapy (ide-cel)	10 (20.4)
ADC (belantamab)	5 (10.2)
Other BCMA bispecific therapy from clinical trials	3 (6.1)
Comorbidities of interest within 6 months before initiating teclistamab	
Peripheral neuropathy	28 (57.1)
Anemia	27 (55.1)
Hypogammaglobulinemia	20 (40.8)
Renal impairment/failure[b]	15 (30.6)
Neutropenia	14 (28.6)
Hypertension	13 (26.5)
Lytic bone lesions	7 (14.3)
Hypercalcemia	4 (8.2)
Extramedullary plasmacytomas	3 (6.1)

ADC, antibody-drug conjugate; BCMA, B-cell maturation antigen; CAR-T, chimeric antigen receptor T-cell; MM, multiple myeloma.
[a]Defined having ≥1 of the following abnormalities: del(17p), t(4;14), t(14;16); t(14;20), and gain or amp(1q).
[b]Renal impairment/failure includes all stage chronic kidney disease, dialysis, end stage renal disease, kidney transplant, and kidney failure.

SUD schedule

- Among 45 patients with complete SUD as of data cutoff, 56% received the SUD on a 3-day dose interval (i.e., day 1, 4, 7). The mean time between the first and third doses was 7.8 days

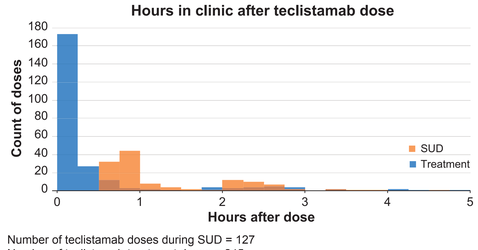
Safety outcomes

- All patients received acetaminophen (100%) and diphenhydramine (100%) and almost all patients received dexamethasone (97.8%) as pre-medications on the same day as teclistamab administrations during SUD (**Table 2**)
- Among the 45 patients with complete SUD, 13 patients (28.9%) developed CRS. The highest CRS grade was grade 1 for 10 patients (22.2%); 2 patients (4.4%) had a grade 2 CRS, and 1 patient (2.2%) had a grade 4 CRS (**Table 2**)
  - The patient with grade 4 CRS concurrently decompensated during a dialysis session and all symptoms were considered for CRS grading. This patient was managed in an intensive care unit for a length of 3 days
  - 6 patients (13.3%) were admitted from emergency rooms for CRS management
- A total of 7 patients (15.6%) had recurrent CRS, including 2 patients with 3 events during SUD (**Table 2**)

Healthcare resource utilization

- All patients who developed CRS (N = 13) during SUD were admitted to a hospital for treatment, with a total of 22 admissions across all patients with CRS and a median length of stay of 1.7 days per admission
- Among patients who were admitted for CRS (N = 13), the majority were treated with acetaminophen (100%) and dexamethasone (92.3%); tocilizumab was given to the 5 patients (38.5%) for CRS treatment (**Table 2**)
- A total of 2 patients (4.4%) developed ICANS during SUD. Both were admitted to the hospital for treatment and were resolved to continue the treatment of teclistamab (**Table 2**)
- Among doses with clinic time data (99%), the majority (60%) of doses during SUD required 30 minutes to 1 hour of clinic time for monitoring between administration and check-out
- After SUD, the clinic time for weekly treatment doses decreased to less than 30 minutes for most doses (82%) (**Figure 2**)

FIGURE 2. TIME BETWEEN TECLISTAMAB ADMINISTRATION AND CHECK-OUT DURING STEP-UP DOSING AND FOR TREATMENT DOSES



Number of teclistamab doses during SUD = 127
Number of teclistamab treatment doses = 245

TABLE 2. CYTOKINE RELEASE SYNDROME AND NEUROTOXICITY OUTCOMES IN PATIENTS WITH COMPLETE SUD (N = 45)

CRS during SUD (highest grade), n (%)	13 (28.9)
Grade 1	10 (22.2)
Grade 2	2 (4.4)
Grade 3	0 (0)
Grade 4	1 (2.2)
Patients with only 1 CRS event	6 (13.3)
Patients with 2 CRS events	5 (11.1)
Patients with 3 CRS events	2 (4.4)
Number of patients admitted due to CRS	13 (28.9)
Length of stay per admission, days, median (IQR)	1.7 (1.4, 3.4)
Pretreatment given on the same day as teclistamab dose, n (%)	
Acetaminophen	45 (100.0)
Diphenhydramine	45 (100.0)
Dexamethasone	44 (97.8)
Tocilizumab	5 (38.5)
Prochlorperazine	1 (2.2)
Supportive care for CRS treatment during admission, n (%)[a]	
Acetaminophen	13 (100)
Dexamethasone	12 (92.3)
Prochlorperazine	3 (23.1)
Meperidine	1 (7.7)
Methylprednisolone	1 (7.7)
ICANS during SUD, n (%)	2 (4.4)
Number of patients admitted due to ICANS	2 (4.4)

CRS, cytokine release syndrome; ICANS, immune effector cell-associated neurotoxicity syndrome; IQR, interquartile range; SUD, step-up dosing.
[a]Among the 13 patients admitted for CRS.

CONCLUSIONS

- This study evaluated early RW safety outcomes of teclistamab under an outpatient administration model and found the CRS rate and severity to be comparable with other RW evidence generated from various data sources
- Outcomes related to teclistamab SUD from Mayo Clinic supported the safety and feasibility of the outpatient administration model as a potential option to reduce healthcare resource utilization and improve patient treatment experiences

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IRB INFORMATION

This study was reviewed and approved by the Mayo Clinic Institutional Review Board (IRB 23-000267)

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