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Real-world treatment patterns for teclistamab and talquetamab in multiple myeloma (MM): experience from 609 patients

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The bispecific antibodies (bsAbs) teclistamab and talquetamab have received United States Food and Drug Administration (FDA) approval for use in relapsed/refractory multiple myeloma (MM) following remarkable single-agent activity in early-phase clinical trials [1–3].The FDA-approved treatment schedule for teclistamab involves initial step-up dosing (SUD) followed by 1.5 mg per kilogram (mg/kg) dosed once per week (Q1W) with the option of 1.5 mg/kg dosing every two weeks (Q2W) in patients who have maintained a complete response (CR) for at least 6 months. The FDA-approved treatment schedule for talquetamab consists of either 0.4 mg/kg Q1W or 0.8 mg/kg Q2W dosed until progression.

Bispecific antibodies uniquely induce rapid and deep remission in responding patients, with some maintaining a response for over two years, even after treatment has been discontinued [3]. This brings up the question of whether alternative dosing and/or fixed-duration therapy may be preferred in the long term [3, 4]. Moreover, there is significant interest in investigating alternative dosing schedules to reduce T-cell exhaustion, reduce long-term toxicities such as infectious complications, minimize costs of care, and maximize clinical efficacy. Herein, we examine real-world (RW) treatment patterns of these two agents in patients with MM with an emphasis on the initial SUD and long-term treatment schedule.

The TriNetX dataset used for this particular analysis contains aggregate data from 134 million patients treated across 40 healthcare organizations in the US, 90% of which are academic centers. This database was used to identify patients with MM treated with at least one dose of teclistamab or talquetamab before the data cutoff (July 31, 2024). Day 0 (D0) refers to the first SUD of the drug, and the first three doses were assumed to be SUD as well. Dosing frequency was categorized by the time between two consecutive doses as follows: Q1W (4–10 days), Q2W (11 to 17 days), once every 3 weeks (Q3W [18–25 days]), once every 4 weeks (Q4W [26 to 31 days]), and >Q4W (32 days or more). These were weighted by the inverse frequency of expected doses per month, i.e., ¼, ½, ¾, 1, and 2, respectively, to adjust for the over-representation of high-frequency dosing schedule and estimate the proportion of patients using each schedule. The duration of treatment was evaluated using the Kaplan-Meier estimator from the date of the first dose to the date of the last dose recorded. Treatment was considered completed at the last recorded dose if the patient had a bsAb-free period of 60 days before the last encounter for any reason, or if the patient died within 60 days from the last dose.

A total of 609 individual patients received teclistamab ($n = 501$) or talquetamab ($n = 108$). For teclistamab, the median age was 70 years (range 31–90) with 21% ($n = 91$) of patients being African American. Of note, 9% of patients ($n = 43$) had received prior talquetamab. The median duration of teclistamab therapy was 3.9 [95% confidence interval (CI) 2.8–5.0] months. Teclistamab SUD comprised 17% of doses, typically in a D0-D2-D4 schedule or D0-D3-D6 as shown in Fig. 1A. Of patients who remained on teclistamab as of the data cutoff (82% [$n = 4970$] doses), 54% of the doses were administered Q1W, 16% Q2W, 2% Q3W, 3% Q4W, and 1% at intervals >Q4W. The use of second SUD was rare, accounting for only 0.7% of events ($n = 44$).

Next, we analyzed the dosing patterns of teclistamab across different treatment intervals from start of treatment such as <3 months, 3–6 months, and >6 months from D0. During the first 3 months, 83% of doses were administered Q1W, 9.6% Q2W, and less than 1% at Q4W or >Q4W. For the 3–6-month interval, the most common dosing schedule was Q1W (61%), followed by Q2W (28%). About 4% and 2.5% of teclistamab doses were administered at Q4W and >Q4W, respectively. Beyond 6 months, Q2W dosing predominated (44%) with 33% at Q1W intervals. Further, there was also an increase in Q4W dosing to 13%, and nearly 4% of doses were administered at intervals greater than four weeks (>Q4W) in patients on teclistamab for more than 6 months (Fig. 2A). The observed weighted dosing frequency of teclistamab remained largely consistent across different time periods during the first 3 months, from 3 to 6 months, and beyond 6 months of therapy (Supplement Table 1). The median overall survival (OS) for recipients of teclistamab therapy was 22 months (95% CI 16.3-Not Reached [NR]) in this cohort.

Of 108 patients who received talquetamab, the median age was 66 years (range 34–90) with 22% ($n = 21$) being African American. Most patients (60%, $n = 65$) had not previously received teclistamab. The median duration of talquetamab therapy was NR at last data cut off. SUD accounted for 29% of occurrences, with the most common schedules being D0-D2-D4 (33%) and D0-D3-D6 (21%) with rare use of second SUD (0.64%) (Fig. 1B). Of patients who were still on talquetamab as of the data cutoff (70% [$n = 548$] doses), Q2W dosing was the most common followed by Q1W. Q4W and >Q4W dosing were rare, occurring in 6.5% and less than 1% of events respectively. Q2W talquetamab was the predominant dosing schedule regardless of timeframe: <3 months of initiation (49%), 3–6 months (70%), and >6 months (79%). The dosing frequencies for Q4W and >Q4W were observed to range from 2% to 6% and 1% to 5%, respectively, at the three time points (Fig. 2B). The weighted distribution of dosing frequency was consistent, with Q2W being the most common as shown in Supplement Table 1. The median OS was NR in this cohort.

Overall, this analysis provides the largest RW data on treatment patterns with teclistamab and talquetamab to date. Our study highlights two important findings, one with regard to step-up dosing and one with regard to long-term dosing. In terms of SUD, majority of the patients treated with either bsAb were able to safely complete this period with a minimum of 48 h between doses on a D0-D2-D4 schedule. While the uptake of outpatient SUD is increasing, many centers are still admitting for a median of 7–10 days for this period [5]. For centers where step-up dosing is

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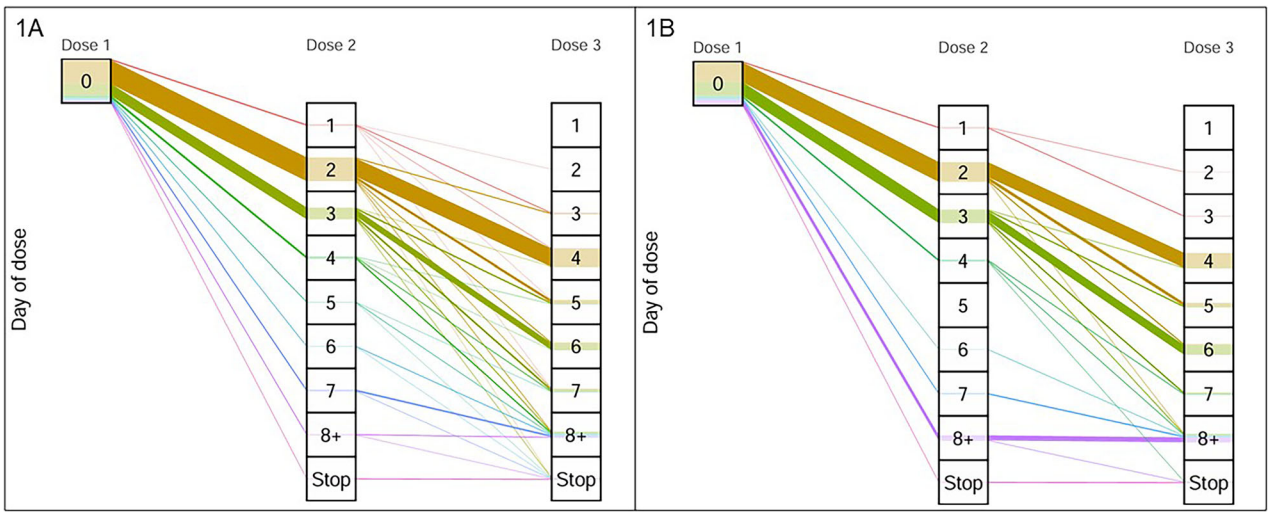

Fig. 1 Step-up Dosing Schedules. Patterns of step-up dosing schedules with teclistamab (**1A**) and talquetamab (**1B**).

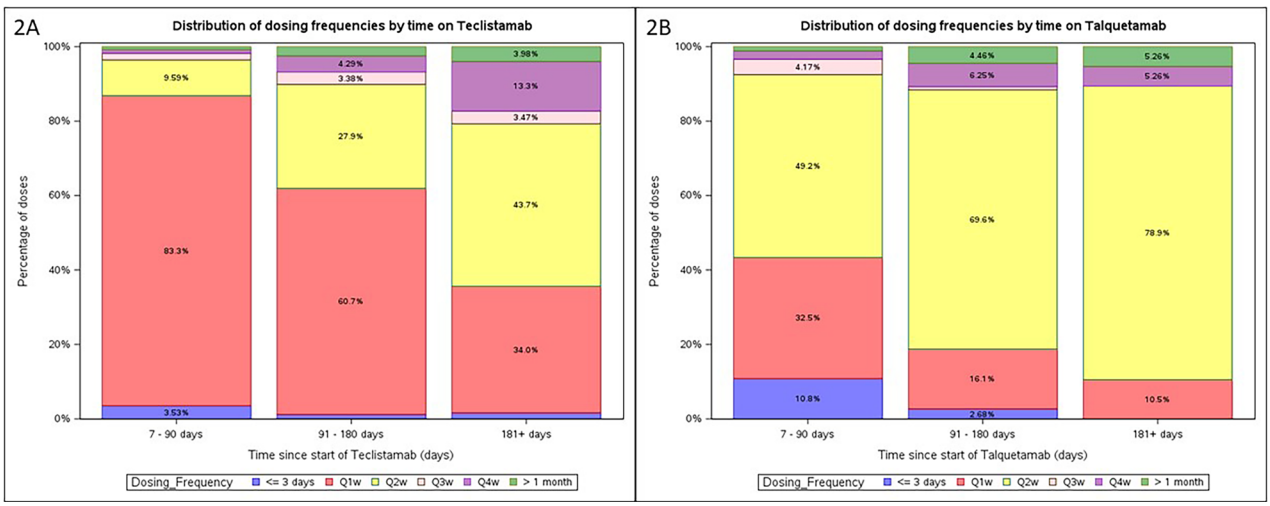

Fig. 2 Dosing Frequencies. Distribution of dosing frequencies by time with teclistamab (**2A**) and talquetamab (**2B**).

performed in the inpatient setting, minimizing the time between doses to exactly 48 h (rather than rounding up to the next day) could further minimize the length of inpatient stays, thereby reducing the burden on both patients and healthcare resources alike. Importantly, there were very few instances of second step-up dosing in this real-world experience. This point is very relevant given the prevalence of dose de-escalation as noted below. The FDA package insert for teclistamab recommend re-initiation of SUD if the interval between bsAb doses exceeds 28 days for weekly dosing, or if there a gap exceeds 63 days between doses for those on biweekly dosing. Similar for talquetamab, SUD is recommended for >28 days between doses. The rationale for this recommendation for a patient in disease response with likely low tumor burden and thus a low risk of cytokine release syndrome or immune effector cell associated neurotoxicity syndrome especially where treatment has been de-escalated or paused for toxicities is unclear. Indeed, our data suggest that continued treatment-level dosing without repeating SUD may be the norm in these cases.

A second key finding of our study is the considerable dosing heterogeneity in bsAb dosing patterns. After 3 months of teclistamab treatment, for instance, a third of the doses were being administered Q2W. This matches updated findings from MajesTEC-1, where 37 of the 38 patients who remained on teclistamab at a follow up of nearly 30 months were switched to Q2W dosing while maintaining clinical responses [6]. In our study, nearly 4–13% of doses were administered Q4W beyond 3 months of teclistamab therapy. Further research is needed to better understand the long-term clinical efficacy of less frequent dosing (every 4 week or longer) of single-agent teclistamab therapy although existing data suggest lower incidence of high-grade infections with such an approach [7]. Ongoing MajesTEC-7 and MajesTEC-5 studies are exploring teclistamab combination therapy with less frequent monthly dosing in newly diagnosed MM [8, 9].

Talquetamab was similarly administered at a Q2W dosing schedule as well. While high-grade infections are less common with talquetamab than with teclistamab, dysgeusia and epithelial toxicities are frequent causes of treatment modification [10]. In recently presented results of a dose de-escalation cohort of MounmenTAL-1, reducing the dose or frequency of talquetamab further (e.g., to 0.8 mg/kg Q4W rather than Q2W) led to maintained durations of responses and improvements in most toxicities except weight loss [11]. We expect the RW prevalence of Q4W dosing (or even less frequently) to increase in coming years with both bsAbs.

This analysis offers an overview of the treatment patterns of teclistamab and talquetamab across a large sample of patients, but we had several limitations. We lack data on reasons for

choosing a preferred dosing schedule, whether less frequent or more frequent, during treatment, and did not have patient-level data or data on toxicities including infections. Additionally, in this database, drugs are recorded as concentration of medications dispense rather than exact weight-based doses. Overall, there is an unmet need to optimize dosing schedules, particularly for novel bsAb therapies, where responses if they occur—are usually rapid and deep allowing for a possible response-adapted dosing based on minimal residual disease.

In conclusion, this analysis offers an overview of the treatment patterns of teclistamab and talquetamab across a large RW sample of patients in the US. Our findings demonstrate considerable heterogeneity with bsAb dosing in MM, both in SUD and in long-term dosing. However, our data also highlight potential areas for improvement in the future: namely, strategies to accelerate bsAb step-up dosing and de-escalate maintenance dosing to improve outcomes and patient quality of life.

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DATA AVAILABILITY

The data will be made available upon reasonable request to the corresponding author.

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AUTHOR CONTRIBUTIONS

Authorship was determined using ICMJE recommendations. Conception and design: MM; AS; FC. Provision of study materials for patients: MM; AS; FC; CL; KO. Collection and assembly of data: MM; AS; FC; CL; KO. Manuscript writing: MM.; AS.; FC. Final approval of manuscript: FC; CL; KO; MS; NS; JK; GRM; SVR; GK; RC; RB; LR; CS; AD; AS; MM.

COMPETING INTERESTS

The authors declare no competing interests.

ADDITIONAL INFORMATION

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