REAL-WORLD SEQUENCING OF ANTI-BCMA CAR T-CELLS AND BISPECIFIC T-CELL ENGAGERS IN RELAPSED/REFRACTORY MULTIPLE MYELOMA: A MULTI-COUNTRY ANALYSIS

Poster # 2287

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INTRODUCTION

Multiple myeloma (MM) is the second most common hematologic malignancy, driven by uncontrolled plasma cell proliferation (1,2).
While recent advances with combinations of proteasome inhibitors, IMiDs, corticosteroids, and anti-CD38 monoclonal antibodies have improved 5-year survival rates to 60%, most patients eventually relapse and become triple-class refractory (3).

B-cell maturation antigen (BCMA) has emerged as a key therapeutic target in this setting. Novel BCMA-targeted therapies, including CAR T-cells and bispecific T-cell engagers, offer new hope (4,5).
Despite targeting the same antigen, their mechanisms, efficacy, and safety profiles vary, and head-to-head comparisons are lacking 6,7).

As a result, the optimal sequencing of these powerful new therapies in clinical practice remains a significant challenge.

AIM

This real-world study aimed to identify the typical treatment sequencing and key drivers for selecting **anti-BCMA CAR T-cells** versus **bispecific T-cell engagers** in triple-class exposed patients with relapsed/refractory MM.

The analysis focused on treatments administered outside of clinical trials across a broad international cohort.

METHOD

- We conducted a retrospective analysis of anonymous patient charts based on data reported by onco-hematologists making treatment decisions for MM patients in the EU5 countries (France, Germany, Italy, Spain, UK), the US, Japan, and China.
- The dataset included 341 unique patient charts for patients treated with an anti-BCMA CAR T-cell product (including ide-cel and cilta-cel) and 570 unique patient charts for patients treated with a bispecific antibody (including teclistamab and elranatamab).
- Data collection took place over three distinct periods: October–December 2022, October–December 2023, and January–March 2025.
- The analysis focused on comparing typical lines of therapy, disease characteristics (ISS score, cytogenetic profile), and patient profiles (mean age, ECOG status, and comorbidities) between the two treatment groups.

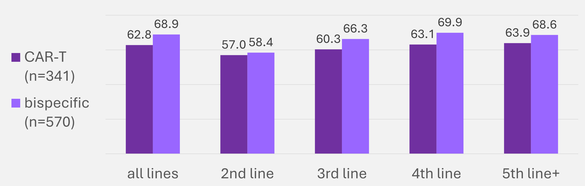
RESULTS

Patient demographics and line of therapy

A total of 911 patient charts were included in the analysis.
The CAR T-cell population (n = 341) had a mean age of 62.8 years, whereas the bispecific T-cell engager population (n = 570) had a significantly higher mean age of 68.9 years ($p < 0.05$). (**Fig. 1**).
Of the patients receiving CAR-T treatment, 206 received ide-cel and 135 received cilta-cel as second- to fifth-line therapy.
In the bispecific population, 105 unique patients received elranatamab and 465 received teclistamab.

CAR T-cell therapy was used for a greater proportion of patients in earlier lines of therapy (22% in second/third lines) compared to bispecifics (14%).
When stratified by line of therapy, the mean age of CAR T-cell patients was 57.0 years in second line, 60.3 years in third line, 63.1 years in fourth line and 63.9 years in fifth line and beyond. In the bispecific cohort, the mean age was 58.4 years in second line, 66.3 years in third line, 69.9 years in fourth line and 68.6 years in fifth line and beyond. (**Fig. 1**).

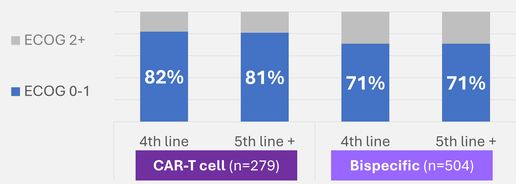
Fig.1. mean age by line of therapy (n= 911)



Disease characteristics, fitness and sequencing

Patient fitness, as assessed by ECOG status, revealed a distinct pattern: 82% of CAR T-cell patients in fourth line and 81% of those in fifth line and above had an ECOG of 0–1, compared to 71% of bispecific patients in both fourth and fifth lines (**Fig. 2**). This suggests that fitter patients are selected for CAR T-cell therapy, even in later lines.
Analysis of comorbidities in the CAR-T subgroup revealed that 23% of patients had no comorbidities, compared to 77% who had at least one, as opposed to 14% with no comorbidities and 86% with at least one in the bispecific arm.
The most frequent comorbidities in both patient groups were mild renal failure (21% in the CAR-T group vs. 28% in the bispecific group), high blood pressure (36% in the CAR-T group vs. 43% in the bispecific group) and diabetes (16% in the CAR-T group vs. 22% in the bispecific group), with no significant differences observed after statistical analysis ($p = 0.25$, 0.18 and 0.19, respectively).

Fig. 2. percentage of patients presenting with ECOG 0-1 (n=537)



Analysis of disease characteristics among the CAR-T cell therapy population revealed the following breakdown of International Staging System (ISS) scores: 8% stage I, 30% stage II and 59% stage III (not tested in 3%) versus 7% stage I, 30% stage II and 57% stage III in the bispecific T-cell engager (BiTE) antibody therapy population, with no significant difference between the two groups (**Fig. 3**).
The cytogenetic profile of the CAR-T cell therapy population showed 32% high-risk, 37% intermediate-risk and 28% low-risk, compared to 26% high-risk, 31% intermediate-risk and 33% low-risk in the BiTE antibody therapy population. There was a slight trend towards a higher proportion of high-risk cytogenetics in the CAR-T cell therapy group across all lines of therapy (**Fig. 4**).
The most frequent cytogenetic abnormalities in the CAR-T cell therapy group were t(4;14) in 18%, 15% had del17p, 13% had t(11;14), 10% had t(14;16). By way of comparison, the most frequent abnormalities in the bispecific group were del17p in 12% of cases, t(4;14) in 9%, t(11;14) in 9%, and t(14;16) in 5%.

Fig. 3. percentage of ISS among patients

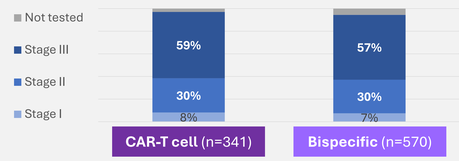
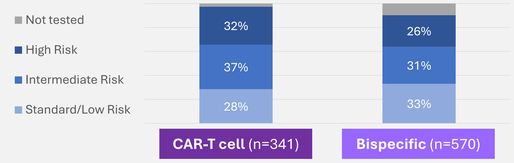


Fig. 4. percentage of cytogenetic risks among patients



Thirty-one patients received a BCMA bispecific antibody after previous exposure to CAR T cells, primarily in fourth (n = 8) and fifth (n = 23) lines of therapy. Their mean age was 65.4 years, and their general fitness and comorbidity status were similar to those of the overall CAR T-cell population (66% ECOG 0–1 and 77% with at least one comorbidity).

CONCLUSIONS

- This real-world study reveals **distinct treatment selection patterns** for anti-BCMA therapies in relapsed/refractory Multiple Myeloma.
- **CAR T-cells** are preferentially used in **younger, fitter patients** (ECOG 0-1) and in **earlier lines of therapy**.
- Conversely, **bispecific antibodies** are more often prescribed to **older, less fit patients** , including those who have previously been treated with a CAR T-cell agent.
- The use of a BCMA bispecific after CAR T-cell exposure remains uncommon, occurring primarily in 4th (n=8) and 5th lines (n=23) of therapy. The profile of these patients was comparable to that of the overall CAR T-cell population.
- These real-world data are crucial and provide valuable insights for developing **optimal sequencing strategies** for these novel therapies in clinical practice

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