P962

CURRENT USE OF BCMA-TARGETED AGENTS IN RELAPSED/REFRACTORY MULTIPLE MYELOMA AND KEY DRIVERS WHEN SELECTING CAR-T CELLS VERSUS BISPECIFICS. DATA FROM REAL-WORLD STUDY IN EU5 COUNTRIES AND IN THE US

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BACKGROUND

Treatment of multiple myeloma (MM) has improved due to the use of frontline quadruplets in stem cell transplant (SCT) eligible patients and daratumumab-based triplets in SCT ineligible patients, leading to deeper responses characterized by negative MRD status and prolonged PFS (1). However, most patients eventually relapse, have a poor response or are refractory to the 3 main classes: proteasome inhibitors (PIs), IMiDs and anti-CD38 monoclonal antibodies. New anti-BCMA agents (CAR-T cells and bispecific T-cell engagers, BiTEs) have now been included in international clinical practice guidelines after ≥3 prior lines of therapy including an IMiD, a PI, and an anti-CD38 mAb (2, 3). When deciding between BCMA-targeted CAR-T cells vs. bispecific antibodies/BiTEs, several criteria should be considered: patient/disease stability, logistics, ongoing vs. one-time dosing, response rate, safety, and sequencing (4, 5, 6).

AIMS

Identify patterns and drivers for selecting CAR-T treatment vs. bispecific antibodies in relapsed/refractory MM patients and compare patients' characteristics between those two groups.

METHODS

Anonymized MM patient charts, provided by onco-hematologists in France, Germany, Spain, Italy, UK, and US were analyzed.
The analysis focused on R/R patients receiving a BCMA-targeted agent: CAR-T cells vs. bispecific antibodies.
192 patients receiving a CAR-T (n= 106 ide-cel ; n= 86 cilta-cel) and 210 receiving a bispecific antibody (n= 206 teclistamab ; n= 4 elranatamab) were included in Q4 2023.

RESULTS

In the CAR-T population, the mean age of patients receiving ide-cel was 62 years vs. 61 in the cilta-cel subgroup. As expected in this population of patients receiving a CAR-T treatment, was mostly aged <65 (61% for ide-cel and 64% for cilta-cel). Among patients aged 65-75, 32% received ide-cel and 35% received cilta-cel treatment. The subgroup of patients with an age>75 represented a minority (7% with ide-cel and 1% with cilta-cel). A comparison with the BiTE population can be seen in Figure 1.

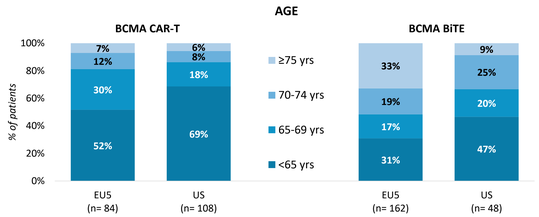

Fig 1. Patients' age in CAR-T and BiTE populations with comparison between EU5 countries and the US

In the ide-cel group, only 6% of patients of patients received the treatment in 2nd line vs. 19% in 3rd line, 43% in 4th line and 32% in 5th line +. These proportions were similar for the cilta-cel group. Notably, patients who received either CAR-T therapy in 2nd line were all from the US, not the EU. Patient disposition by line of therapy in both CAR-T and BCMA BiTE population is seen in Figure 2.

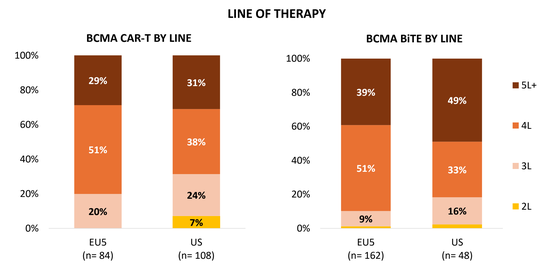

Fig 2. Patients disposition by line of therapy when receiving CAR-T and BCMA BiTE

Breakdown between CAR-T cells and bispecifics in patients receiving their treatment in 4L+ in both European countries and the US can be seen in Figure 3.

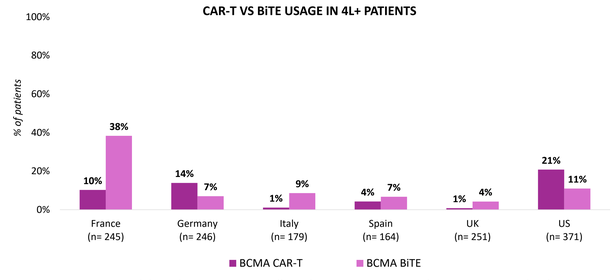

Fig 3. Breakdown between CAR-T cells and BiTE in 4L+ patients (EU5 countries and US)

When considering ECOG status and general fitness in the CAR-T population, the vast majority had an ECOG score between 0 and 1 (80% for ide-cel and 75% for cilta-cel) and 46%/43% of patients were considered to be fit with ide-cel/cilta-cel respectively. There were very few frail patients in the 2 groups (lower than 10%). In patients receiving a bispecific, ECOG status was 0-1 in 70% of patients and 33% were considered fit vs. 57% intermediate fit vs. 9% frail. See Figure 4.

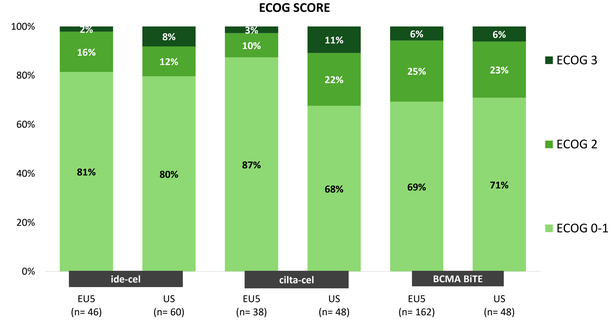

Fig 4. ECOG status at treatment initiation in patients receiving ide-cel, cilta-cel and BCMA BiTE

Analysis of cytogenetic risk profiles revealed no significant difference between ide-cel (31% high-risk) and cilta-cel (20% high-risk) CAR-T subgroups. The BiTE group exhibited a similar distribution (22% high-risk, 36% intermediate, 33% standard risk). Details are provided in Figure 5.

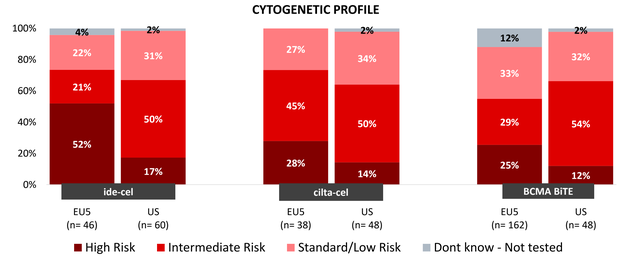

Fig 5. Cytogenetic profile (low, intermediate, high) between different patients subgroups : ide-cel, cilta-cel and BCMA BiTE

Regarding the main co-morbidities, a low proportion (29% and 18% for ide-cel and cilta-cel) had none vs. at least one for ide-cel and cilta-cel at 71% and 82% respectively. The most frequent co-morbidities were mild to moderate renal failure (between 25 to 30%), high blood pressure (between 35 and 40%), dyslipidemia (25%) and diabetes mellitus (25%), with no significant difference between the 2 groups. In the BCMA BiTE group, level of co-morbidities was greater as compared with the CAR-T subgroup as summarized in Table 1.

CAR-T	EU5 (n= 84)	US (n= 108)
Co-morbidities at initiation of current treatment		
None	**21%**	**26%**
At least 1 co-morbidity	**79%**	**74%**
Mild renal insufficiency (ClCr = 50-90 mL/min)	35%	5%
Moderate renal insufficiency (ClCr = 30-49 mL/min)	10%	10%
Severe renal insufficiency (ClCr < 30 mL/min)		1%
Previous Deep Vein Thrombosis	2%	6%
Neuropathy	29%	20%
Hypertension	35%	38%
Dyslipidaemia	20%	26%
Cardiac dysfunction	6%	10%
Diabetes	10%	25%
Cancers	2%	1%
Other co-morbidities	17%	5%

BCMA BiTE	EU5 (n= 162)	US (n= 48)
Co-morbidities at initiation of current treatment		
None	**11%**	**25%**
At least 1 co-morbidity	**89%**	**75%**
Mild renal insufficiency (ClCr = 50-90 mL/min)	31%	8%
Moderate renal insufficiency (ClCr = 30-49 mL/min)	17%	17%
Severe renal insufficiency (ClCr < 30 mL/min)	4%	4%
Previous Deep Vein Thrombosis	8%	2%
Neuropathy	39%	24%
Hypertension	44%	37%
Dyslipidaemia	24%	25%
Cardiac dysfunction	8%	12%
Diabetes	9%	29%
Cancers	3%	
Other co-morbidities	24%	4%

Table 1. Main patients co-morbidities in both CAR-T and BCMA BiTE populations Comparison between EU5 countries and the US

CONCLUSION

The main drivers for treatment selection between BCMA-targeted agents appear to be safety/tolerability based on patient profile and comorbidities, overall convenience, and response rate. BiTEs tend to be preferred in older patients with more comorbidities, especially more severe renal failure, and intermediate fitness.
Future approval by EMA of ide-cel and cilta-cel based on KarMMa-3 (7) and CARTITUDE-4 (8) trials should encourage their use in earlier lines of therapy and current assessment of anti-BCMA bispecifics in 1st and 2nd line of therapy might also enhance their role in the treatment landscape for MM regardless of patient profile.

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