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Survival Outcomes of Multiple Myeloma Patients Previously Exposed to BCMA-Targeted Therapies in the HONEUR European Network

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Key Takeaway

Despite new treatment advances, such as anti-BCMA therapy, this real-world analysis indicates that there is still an unmet need in heavily pretreated patients with MM

Conclusions

Real-world data from 3 European registries indicate that BCMA-exposed patients are heavily pretreated and have limited survival outcomes, with a median OS of 15.8 months and a median TTNT of 5.2 months

With a median of 5 prior lines, 93% were triple-class refractory and 54.5% were penta-drug refractory, highlighting significant treatment resistance within this relapsed/refractory MM population

The persistent prescription of chemotherapy and IMiD/PI triplets as subsequent treatment underscores a critical gap in treatment options and the need for new therapeutic targets to be adopted in clinical practice

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Disclosures
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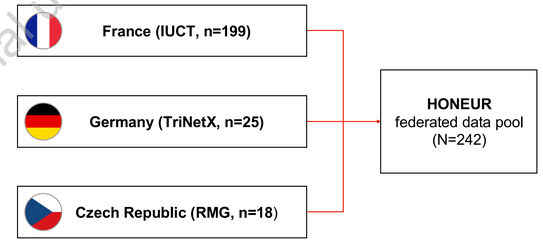
Introduction

- Survival rates for patients with multiple myeloma (MM) have recently improved,[1,2] thanks to advances in treatment options that target B-cell maturation antigen (BCMA) receptors, including antibody-drug conjugates (ADCs), bispecific antibodies (BsAbs), and chimeric antigen receptor (CAR)-T cell therapies[1-4]
- However, this progress introduces a new population of patients with disease refractory to both standard-of-care and novel BCMA therapies, thereby limiting treatment options at relapse
- Therefore, understanding real-world outcomes of BCMA-exposed patients is essential

Methods

- Data from 3 MM European registries were included in the analysis: IUCT (France), TriNetX (Germany), and RMG (Czech Republic) (**Figure 1**)
- Locally collected patient-level data were analyzed uniformly and site-specific results were aggregated centrally using the HONEUR federated data network
- Inclusion criteria:
  - Patients diagnosed with MM
  - At least 18 years of age at start of frontline treatment
  - Received ≥3 prior lines
  - Quad-class exposed (received at least 1 proteosome inhibitor [PI], 1 immunomodulatory drug ([MiD], 1 anti-CD38 antibody, and 1 BCMA-targeted therapy)
  - First eligible line started ≥2020
- Exclusion criteria: Patients receiving retreatment with anti-BCMA immunotherapy were excluded from the analysis
- Statistical analyses:
  - Patient characteristics and treatment patterns were descriptively analyzed
  - Index date was considered as the date of initiating the subsequent therapy after anti-BCMA treatment
  - Time to next treatment (TTNT), used as a proxy for progression-free survival, and overall survival (OS) were analyzed using the Kaplan-Meier method
  - The last observation carried forward (LOCF) method was employed for the International Staging System (ISS), M protein, and cytogenetics data

Figure 1: European registries included in analysis



HONEUR, Haematology Outcomes Network in Europe; IUCT, Institut Universitaire du Cancer de Toulouse; RMG, The Registry of Monoclonal Gammopathies.

Results

Study population

- A total of 242 patients with MM who had received an anti-BCMA–based regimen were analyzed from 3 European registries
  - Most cases came from IUCT (82.2%), with TriNetX contributing to 10.3% of cases and RMG contributing to 7.4%
- Baseline characteristics are shown in **Table 1**
  - Most patients were ≥65 years of age
  - Half of patients (51.2%) were ISS stage II/III, and 23.6% presented with high-risk cytogenetics
  - Most patients (70.2%) had previously undergone stem cell transplant (SCT)

Table 1: Baseline patient characteristics

Characteristics, n (%)	N=242
Sex	
Female	115 (47.5)
Male	127 (52.5)
Age at line of treatment initiation, years	
Median (range)	68 (43–88)
≤64 years	78 (32.2)
65–74 years	109 (45)
≥75 years	55 (22.7)
ISS stage[a]	
I	35 (14.5)
II	68 (28.1)
III	56 (23.1)
Unavailable	83 (34.3)
M protein[a]	
Non-IgG positive	50 (20.7)
IgG positive	88 (36.4)
Unavailable	104 (43)
Cytogenetic risk[a,b]	
High risk	57 (23.6)
Standard risk	122 (50.4)
Unavailable	63 (26)
Prior line received SCT	
No	72 (29.8)
Yes	170 (70.2)
Prior lines	
Median (range)	5 (3–12)
3 or 4 lines	73 (30.2)
>4 lines	169 (69.8)

[a]LOCF values used. [b]High risk defined as any presence of del(17p), and/or t(4;14), and/or t(14;16). Standard risk=no high risk. Ig, immunoglobulin.

Baseline treatment patterns

- With a median of 5 prior lines of treatment, only 30.2% of patients received 3 or 4 prior lines of treatment (**Table 1**)
- Regarding refractoriness, 93% of patients were triple-class refractory and 54.5% were penta-drug refractory, highlighting the significant treatment resistance within this relapsed/refractory MM population observed in real-world clinical practice (**Table 2**)
- At BCMA exposure, data reflect the real-world clinical setting, with low CAR-T cell therapy utilization (**Table 2**)

Table 2: Baseline treatment characteristics

Characteristics, n (%)	N=242
Exposed to 2 PIs, 2 IMiDs, and 1 anti-CD38 antibody	
No	66 (27.3)
Yes	176 (72.7)
Exposed to CAR-T	
No	223 (92.1)
Yes	19 (7.9)
Exposed to BsAb	
No	140 (57.9)
Yes	102 (42.1)
Exposed to ADC	
No	119 (49.2)
Yes	123 (50.8)
Refractory status	
Triple-refractory[a]	16 (6.6)
Quad-refractory[b]	65 (26.9)
Penta-refractory[c]	132 (54.5)
Other	29 (12.0)
Triple-class refractory	
No	17 (7.0)
Yes	225 (93.0)

[a]Refractory to 1 IMiD, 1 PI, and 1 anti-CD38 mAb. [b]Refractory to ≥2 IMiDs, 1 PI, and 1 anti-CD38 mAb or ≥2 PIs, 1 IMiD, and 1 anti-CD38 mAb. [c]Refractory to ≥2 IMiDs, ≥2 PIs, and 1 anti-CD38 mAb. mAb, monoclonal antibody.

Post-BCMA treatment

- Following BCMA exposure, the available treatment regimens predominantly included chemotherapy doublet (34.7%) IMiD/PI-based triplet (17.8%), IMiD/PI-based doublet (12.4%), and 4.1% anti-CD38–based triplet (**Table 3**)

Efficacy outcomes

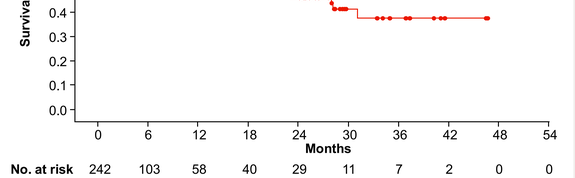
- With a median follow-up of 9.1 months, median OS was 15.8 months (95% CI, 10.91–31.08 months) (**Figure 2**), and median TTNT was 5.2 months (95% CI, 3.98–6.24 months) (**Figure 3**)

Table 3: Post-BCMA treatment

Drug combination, n (%)	N=242
Chemotherapy doublet[a]	84 (34.7)
PI/IMiDs doublet[b]	30 (12.4)
PI/IMiDs triplet[c]	43 (17.8)
CD38 triplet[d]	10 (4.1)
Unknown or Others	75 (31.0)

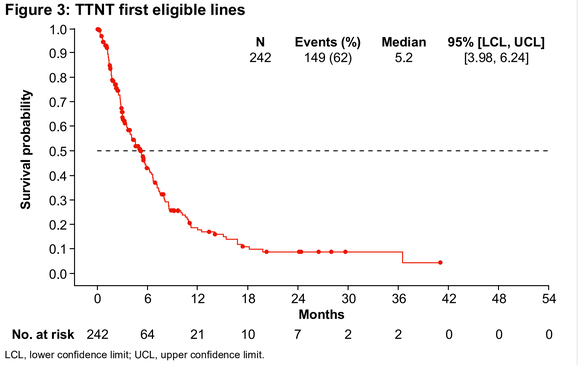
[a]Cyclophosphamide/dexamethasone; bendamustine/dexamethasone; melphalan/prednisone; vincristine/dexamethasone; cyclophosphamide/doxorubicin. [b]Bortezomib/dexamethasone; carfilzomib/dexamethasone; pomalidomide/dexamethasone; thalidomide/dexamethasone. [c]Carfilzomib/cyclophosphamide/dexamethasone; bortezomib/cyclophosphamide/dexamethasone; bortezomib/melphalan/prednisone; ixazomib/cyclophosphamide/dexamethasone; ixazomib/lenalidomide/dexamethasone; cyclophosphamide/pomalidomide/dexamethasone; cyclophosphamide/thalidomide/dexamethasone; elotuzumab/pomalidomide/dexamethasone; ixazomib/pomalidomide/dexamethasone; melphalan/pomalidomide/dexamethasone; carfilzomib/lenalidomide/dexamethasone; bortezomib/lenalidomide/dexamethasone; selinexor/bortezomib/dexamethasone; bortezomib/cyclophosphamide/thalidomide; bortezomib/pomalidomide/dexamethasone. [d]Daratumumab/pomalidomide/dexamethasone; daratumumab/lenalidomide/dexamethasone; daratumumab/carfilzomib/dexamethasone; isatuximab/pomalidomide/dexamethasone; isatuximab/thalidomide/dexamethasone; isatuximab/carfilzomib/dexamethasone.

Figure 2: OS first eligible lines



LCL, lower confidence limit; UCL, upper confidence limit.

Figure 3: TTNT first eligible lines



LCL, lower confidence limit; UCL, upper confidence limit.

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HONEUR Haematological Outcomes Network in Europe

Multiple Myeloma

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