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

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HONEUR
Haematological Outcomes Network in Europe

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Introduction

- Survival rates for MM have recently improved,[1,2] thanks to advances in treatment options targeting BCMA[1-4], including:
  - ADCs
  - BsAbs
  - CAR-T cell therapies
- 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
- Therefore, understanding real-world outcomes of BCMA-exposed patients is essential

ADC, antibody-drug conjugate; BCMA, B-cell maturation antigen; BsAb, bispecific antibody; CAR, chimeric antigen receptor; MM, multiple myeloma. 1. National Comprehensive Cancer Network (NCCN). Multiple Myeloma. (Version 2.2026). 2. Jagannath S, et al. *J Clin Oncol* 2025;43:2766-71. 3. Tan CR, et al. *Blood Cancer J* 2025;15:53. 4. Zheng H, et al. *J Hematol Oncol* 2025;18:23.

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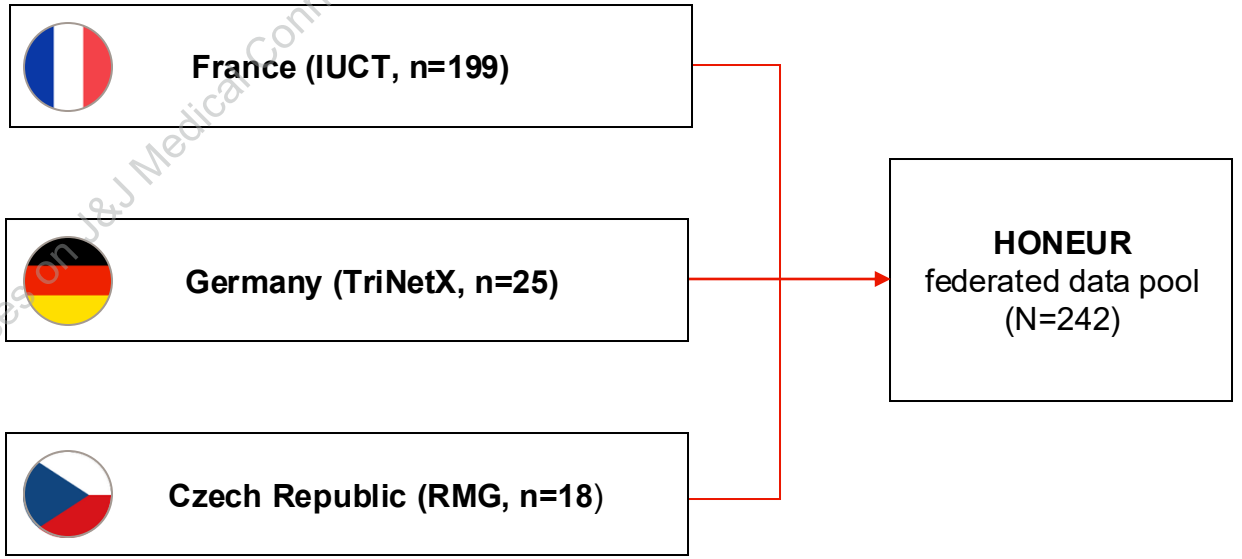
HONEUR: Study Population

- Data from 3 European registries were included in the analysis: IUCT (France), TriNetX (Germany), and RMG (Czech Republic)
- Inclusion criteria:
  - Patients diagnosed with MM
  - ≥18 years of age at start of frontline treatment
  - Received ≥3 prior lines of therapy
  - Quad-class exposed: ≥1 PI, 1 IMiD, and 1 anti-CD38 antibody, and 1 BCMA-targeted therapy
  - First eligible line started ≥2020
- Patients receiving retreatment with anti-BCMA immunotherapy were excluded



BCMA, B-cell maturation antigen; HONEUR, Haematology Outcomes Network in Europe; IMiD, immunomodulatory drug; IUCT, Institut Universitaire du Cancer de Toulouse; MM, multiple myeloma; PI, proteasome inhibitor; RMG, The Registry of Monoclonal Gammopathies.

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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%
  - 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 SCT
  - With a median of 5 prior lines of treatment, only 30.2% of patients received 3 or 4 prior lines of treatment

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; IMiD, immunomodulatory drug; ISS, International Staging System; IUCT, Institut Universitaire du Cancer de Toulouse; LOCF, last observation carried forward; PI, protease inhibitor; RMG, The Registry of Monoclonal Gammopathies; SCT, stem cell transplant.

Baseline Treatment Patterns

- 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
- At BCMA exposure, data reflect the real-world clinical setting, with low CAR-T cell therapy utilization

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.
ADC, antibody-drug conjugate; BCMA, B-cell maturation antigen; BsAb, bispecific antibody; CAR, chimeric antigen receptor; IMiD, immunomodulatory drug; mAb, monoclonal antibody; MM, multiple myeloma; PI, protease inhibitor.

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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

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.
BCMA, B-cell maturation antigen; IMiD, immunomodulatory drug; PI, protease inhibitor.

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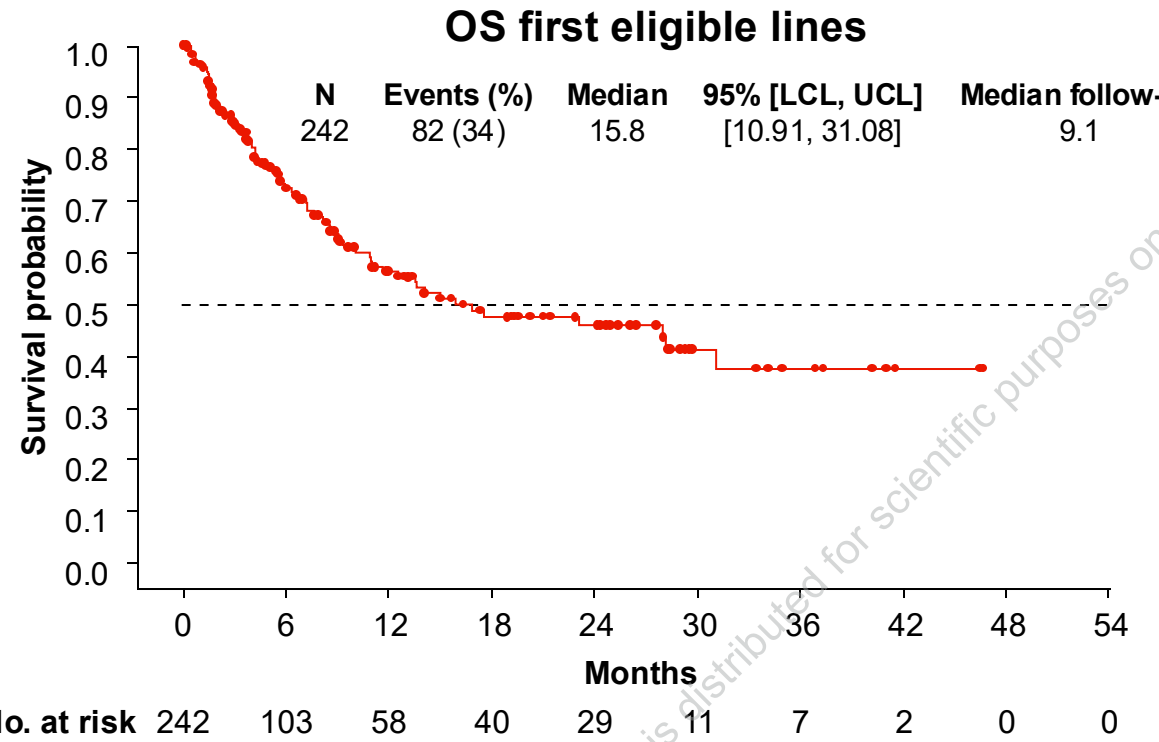
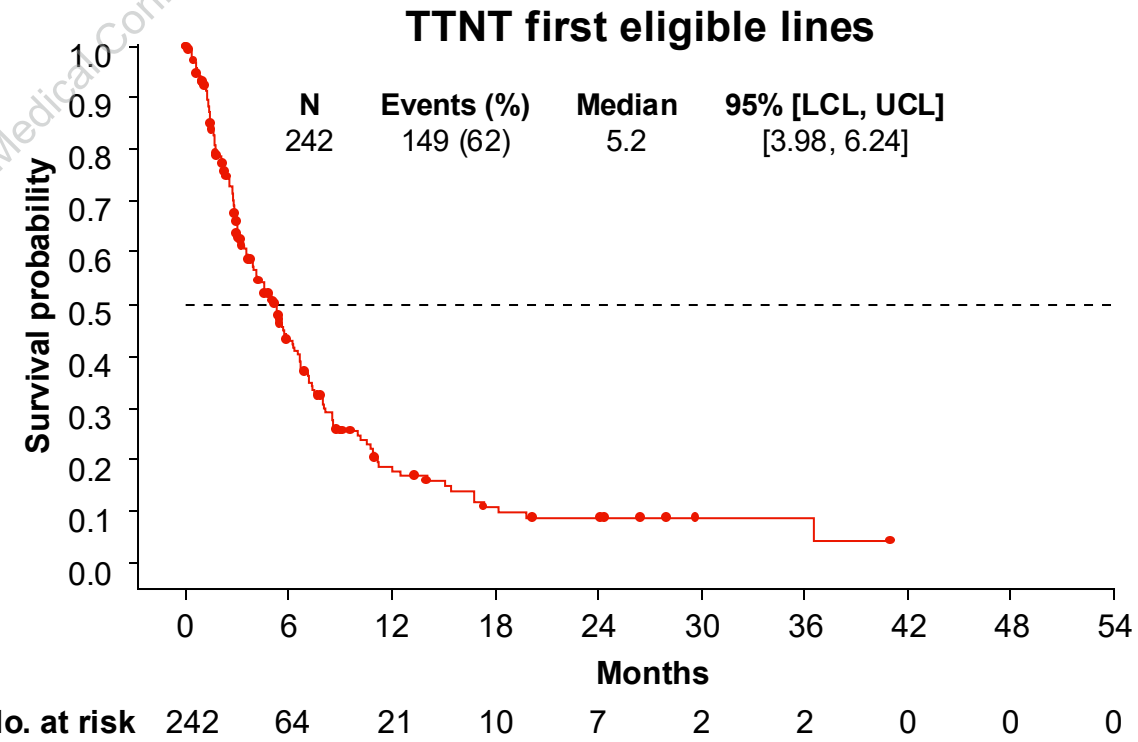
Efficacy Outcomes

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





LCL, lower confidence limit; OS, overall survival; TTNT, time to next treatment; UCL, upper confidence limit.

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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

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

BCMA, B-cell maturation antigen; IMiD, immunomodulatory drug; MM, multiple myeloma; OS, overall survival; PI, proteasome inhibitor; TTNT, time to next treatment.

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