PS1941

Real-World Treatment Patterns and Survival Outcomes in Patients With Multiple Myeloma After 1–2 Prior Lines of Therapy From the HONEUR Federated Data Network

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Key Takeaway

This real-world, multiregistry study indicates suboptimal outcomes in earlier lines of therapy and underscores the need to adopt novel combination regimens

Conclusions

Survival outcomes remain limited in 2L and further deteriorate in 3L, underscoring the need to adopt novel combination therapies in the real-world setting that have demonstrated survival benefits in clinical trials as early as 2L therapy

Most patients initiating 2L therapy remain CD38 naive, highlighting an opportunity to improve outcomes by introducing CD38-containing combinations earlier in the treatment sequence

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Poster

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Disclosures

MR is an employee of by TriNetX Oncology.

Introduction

- Treatment decisions following multiple myeloma (MM) relapse have become increasingly complex due to a rapidly evolving therapeutic landscape and changing dynamics based on prior exposure[1-3]
- Understanding real-world outcomes is essential to identify target populations for novel combination therapies that may increase survival
- Here, we describe the baseline characteristics, prior treatment exposure, treatment patterns, and survival outcomes of patients with MM identified at second-line (2L) or third-line (3L) of treatment using the Haematology Outcomes Network in Europe (HONEUR) federated data network[4]

Methods

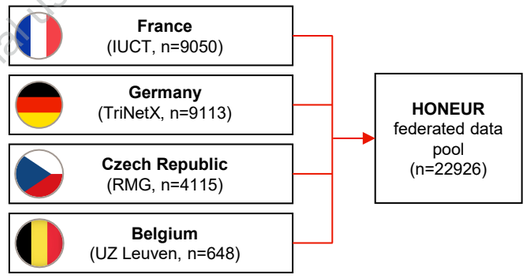
Study design

- Data from patients with MM at 2L and 3L across 4 registries (**Figure 1**) were analyzed between 2016 and 2025
- Locally collected patient-level data were analyzed uniformly; site-specific results were aggregated centrally using the HONEUR federated data network to preserve patient anonymity

Statistical analyses

- The index date was defined as the treatment initiation date
- Baseline characteristics and treatment patterns were descriptively analyzed
- Time to next treatment (TTNT), as a proxy for progression-free survival, and overall survival (OS) were assessed using Kaplan-Meier estimates

Figure 1: European registries included in analysis



IUCT, Institut Universitaire du Cancer de Toulouse; RMG, The Registry of Monoclonal Gammopathies; UZ, Universitair Ziekenhuis.

Results

Study population

- A total of 14104 treatment lines in 2L patients and 8822 treatment lines in 3L patients were examined
- Baseline characteristics of the study population are shown in **Table 1**
  - In the 2L cohort, 31.8% of patients were ≥75 years old, 62.4% had International Staging System (ISS) stage II or III, 17.7% had high-risk cytogenetics, and 30.9% had received stem cell transplantation (SCT)
  - Baseline characteristics were similar in the 3L cohort: 33.6% were ≥75 years old, 63.3% had ISS stage II or III, 18.1% had high-risk cytogenetics, and 33.2% had received frontline SCT

Table 1: Baseline patient characteristics

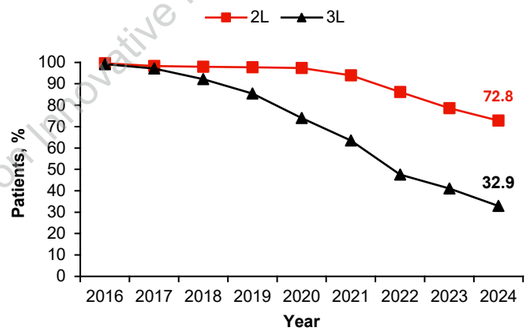
Characteristics, n (%)	2L patients (n=14104)	3L patients (n=8822)
Age at LOT initiation, years		
<65	3577 (25.4)	2070 (23.5)
65–74	6046 (42.9)	3788 (42.9)
≥75	4481 (31.8)	2964 (33.6)
Sex		
Female	6102 (43.3)	3828 (43.4)
Male	8002 (56.7)	4994 (56.6)
ECOG PS category[a,b]		
0–1	5076 (36.0)	2931 (33.2)
≥2	2995 (21.2)	2106 (23.7)
Unavailable	6033 (42.8)	3785 (42.9)
ISS category[a]		
I	2381 (16.9)	1403 (15.9)
II	4087 (29.0)	2220 (25.2)
III	4707 (33.4)	3357 (38.1)
Unavailable	2929 (20.8)	1842 (20.9)
M protein[a]		
IgG	7629 (54.1)	4739 (53.7)
IgA	2693 (19.1)	1686 (19.1)
Other	835 (5.9)	501 (5.7)
Unavailable	2947 (20.9)	1896 (21.5)
Cytogenetic risk profile[a,c]		
High risk	2492 (17.7)	1593 (18.1)
Standard risk	5454 (38.7)	3321 (37.6)
Unavailable	6158 (43.7)	3908 (44.3)
Patient with SCT at 1L		
No	9744 (69.1)	5896 (66.8)
Yes	4360 (30.9)	2926 (33.2)

[a]Missing values were imputed via LOCF. [b]ECOG PS unavailable for both IUCT and UZ Leuven. [c]High risk defined as any presence of del(17p), t(4;14), and/or t(14;16).
1L, first-line; ECOG PS, Eastern Cooperative Oncology Group performance status; Ig, immunoglobulin; LOCF, last observation carried forward; LOT, line of therapy; M, monoclonal.

Evolution of treatment exposure

- The proportion of patients without prior exposure to CD38 (CD38 naive) before starting 2L remained substantial over time from 99.6% in 2016 to 72.8% in 2024. The proportion of CD38-naive patients starting 3L decreased from 99.2% in 2016 to 32.9% in 2024 (**Figure 2**)

Figure 2: Percentage of CD38-naive population over time



Treatment regimens received in 2L and 3L

- At 2L, 44.2% of patients received immunomodulatory drug (IMiD)-based regimens, 39.2% received CD38-based regimens, and 12.3% received proteasome inhibitor (PI)-only regimens (remaining 4.3% others/unknown). At 3L, 42.6% received IMiD-based regimens, 32.4% CD38-based regimens, and 14.8% PI-only regimens (remaining 10.2% others/unknown) (**Table 2**)

Table 2: Regimen used by line of therapy

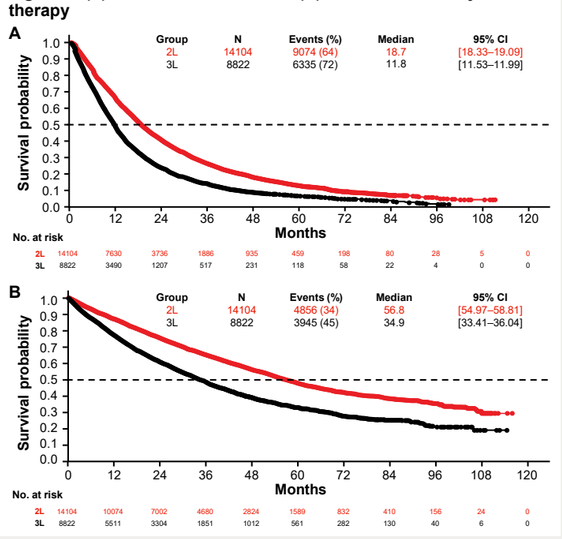
Regimen, n (%)	2L patients (n=14104)	3L patients (n=8822)
PI-only	1740 (12.3)	1302 (14.8)
IMiD-based	6239 (44.2)	3762 (42.6)
CD38-based	5523 (39.2)	2854 (32.4)
Unknown or others[a]	602 (4.3)	904 (10.2)

Treatment regimens: IMiD based includes IMiD and/or IMiD+PI, CD38 based includes CD38 only and/or IMiD+CD38 and/or PI+CD38 and/or IMiD+PI+CD38.
[a]Unknown/others includes chemotherapy, corticosteroids, regimens used in <10 patients or <2% of patients, or where the regimen was unknown.

Survival outcomes in 2L and 3L

- Median follow-up for the 2L cohort was 36.9 months and 31.6 months for the 3L cohort
- Median OS was 56.8 months in the 2L cohort and 34.9 months in the 3L cohort. Median TTNT was 18.7 months in the 2L cohort and 11.8 months in the 3L cohort (**Figure 3**)

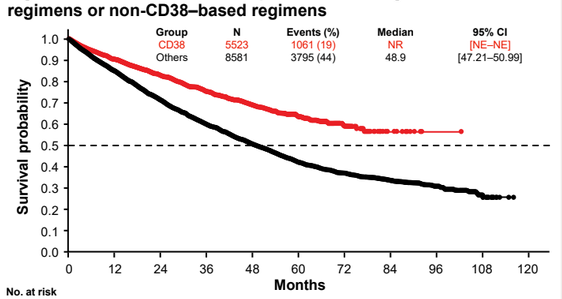
Figure 3: (A) Time to next treatment (B) Overall survival by line of therapy



Overall survival in 2L patients treated with CD38-based regimens or non-CD38–based regimens

- In an unadjusted comparison, median OS was not reached (NR) for patients treated with CD38-based regimens in the 2L setting (median follow-up, 25.4 months). Median OS of 48.9 months was observed for patients receiving other regimens (median follow-up, 46.7 months) (**Figure 4**)

Figure 4: Overall survival in 2L patients receiving CD38-based regimens or non-CD38–based regimens



NE, not estimable.

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Multiple Myeloma