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Clinical Unmet Need of Lenalidomide-Refractory vs Non–Lenalidomide-Refractory Patients With Multiple Myeloma in the HONEUR Federated Data Network

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Key Takeaway

This real-world study confirms that Len-refractory patients with MM are harder to treat, with generally poorer clinical outcomes, indicating a need for more effective therapies to improve their survival

Conclusions

- This updated analysis indicates an increased proportion of patients with Len-refractory MM, which is associated with a higher risk of death
- In the 2L population, Len-refractory patients had an 84% higher mortality risk compared with non–Len-refractory patients
- Among 2L patients with ECOG PS ≤1, Len- vs non–Len-refractory patients had a 73% higher mortality risk, despite this subgroup having better functional status than the overall 2L population

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Disclosures

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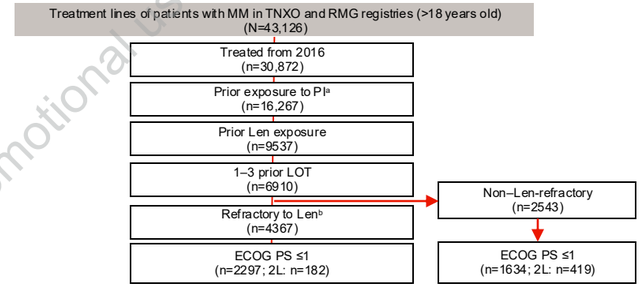
Introduction

- Lenalidomide (Len) is a cornerstone in multiple myeloma (MM) treatment across various lines of therapies[1]
- The widespread use of Len has led to an increasing population of Len-refractory patients with MM, who face limited treatment options and poorer prognosis than non–Len-refractory patients[2-4]
  - Real-world data on the management and outcomes of Len-refractory patients, especially outside clinical trials, remain limited
- This study evaluates real-world characteristics and outcomes of Len-refractory and non–Len-refractory patients with MM and 1–3 prior lines of therapy (LOT), including a subgroup analysis of those patients with Eastern Cooperative Oncology Group performance status (ECOG PS) ≤1

Methods

- Patients with MM treated from 2016–2024 were identified from 2 registries: TriNetX Oncology (TNXO, Germany) and Registry of Monoclonal Gammopathies (RMG; Czech Republic)
- Locally stored patient-level data were converted into Observational Medical Outcomes Partnership format and were analyzed using uniform coding run locally at each data source site
- Site-specific aggregate results were pooled at a central level using the Haematology Outcomes Network in Europe (HONEUR) network
- Eligible patients had 1–3 prior LOT and received both a proteasome inhibitor (PI) and Len; each LOT was treated as a separate observation if eligibility criteria were met at multiple timepoints
- Len-refractory status was defined as disease progression on Len or initiation of a new LOT within 60 days of discontinuation of Len

Figure 1: Patient inclusion criteria



[a]Bortezomib, carfilzomib, and ixazomib. [b]Len-refractory status was defined as disease progression on Len and/or start of a new LOT that does not contain Len ≤60 days of discontinuation of Len.

Results

Study population

- A total of 6910 treatment lines were examined across both registries (TNXO, n=5069; RMG, n=1841)
- In the overall population (patients with 1–3 prior LOT), 63.2% of treatment lines were from Len-refractory patients; among them, 52.6% had ECOG PS ≤1
- The proportion of Len-refractory patients increased from 30% in second-line therapy (2L) to 65% in third-line therapy and to 71% in fourth-line therapy
- Patient characteristics were largely similar between Len- and non–Len-refractory groups, except ECOG PS ≤1 frequency was higher in non–Len-refractory vs Len-refractory patients (64.3% vs 52.6%) in the overall population (**Table 1**)
- Among 2L patients with ECOG PS ≤1, baseline characteristics were otherwise generally well balanced between Len and non–Len-refractory groups

Overall survival

- Len- vs non–Len-refractory patients had shorter OS, with a 57% higher risk of death in the overall population (**Figure 2A**)
  - In 2L, risk of death increased to 84% with a median OS of 44.5 vs 57.4 months, respectively
- For the overall population with ECOG PS ≤1, median OS in the Len- vs non–Len-refractory group was 27.8 vs 37.1 months, respectively, with a 46% increased risk of death (**Figure 2B**)
- In the 2L ECOG PS ≤1 subgroup, mortality risk rose further to 73% with an observed median OS of 49.8 vs 63.0 months in the Len- vs non–Len-refractory group, respectively (**Figure 2C**)

Time to next treatment

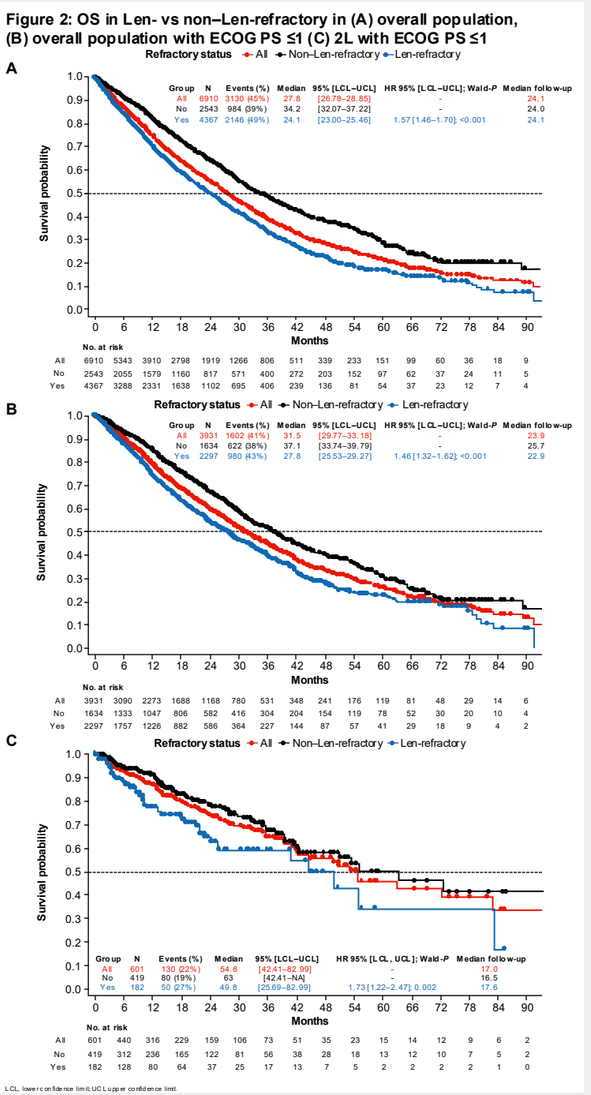
- In the overall population, median TTNT (mTTNT) was shorter in the Len- vs non–Len-refractory group (10.1 vs 13.0 months, respectively) with a 37% increased risk of initiating next treatment (hazard ratio [HR], 1.37 [95% CI, 1.29–1.45]; *P*<0.001)
- For the overall population with ECOG PS ≤1, mTTNT was 11.1 vs 13.2 months in the Len- vs non–Len-refractory patients (HR, 1.33 [95% CI, 1.23–1.44]; *P*<0.001)
- In the 2L ECOG PS ≤1 subgroup, mTTNT in the Len- and non–Len-refractory group was 15.9 vs 15.7 months (HR, 1.31; 95% CI, 1.02–1.67; *P*=0.032)

Table 1: Baseline demographics and disease characteristics

Characteristic, n (%)	Len-refractory (n=4367)			Non–Len-refractory (n=2543)		
	Overall (n=4367)	All lines ECOG PS ≤1 (n=2297)	2L and ECOG PS ≤1 (n=182)	Overall (n=2543)	All lines ECOG PS ≤1 (n=1634)	2L and ECOG PS ≤1 (n=419)
Age, years						
<60	413 (9.5)	289 (12.6)	47 (25.8)	269 (10.6)	212 (13)	72 (17.2)
60–64	347 (7.9)	242 (10.5)	26 (14.3)	235 (9.2)	165 (10.1)	55 (13.1)
65–69	902 (20.7)	443 (19.3)	29 (15.9)	402 (15.8)	276 (16.9)	70 (16.7)
70–74	1248 (28.6)	587 (25.6)	44 (24.2)	688 (27.1)	430 (26.3)	120 (28.6)
75–79	929 (21.3)	459 (20)	24 (13.2)	556 (21.9)	331 (20.3)	69 (16.5)
≥80	528 (12.1)	277 (12.1)	12 (6.6)	393 (15.5)	220 (13.5)	33 (7.9)
ECOG PS, n (%)						
0	350 (8)	350 (15.2)	40 (22)	332 (13.1)	332 (20.3)	98 (23.4)
1	1947 (44.6)	1947 (84.8)	142 (78)	1302 (51.2)	1302 (79.7)	321 (76.6)
2	1551 (35.5)	NA	NA	713 (28.0)	NA	NA
3	339 (7.8)	NA	NA	53 (2.1)	NA	NA
4	28 (0.6)	NA	NA	7 (0.3)	NA	NA
Unavailable	152 (3.5)	NA	NA	136 (5.3)	NA	NA
Male, n (%)	2515 (57.6)	1334 (58.1)	94 (51.6)	1505 (59.2)	971 (59.4)	267 (63.7)
M protein, n (%)						
IgG	2984 (68.3)	1600 (69.7)	113 (62.1)	1685 (66.3)	1074 (65.7)	270 (64.4)
non-IgG[a]	1282 (29.4)	660 (28.7)	64 (35.2)	737 (29)	489 (29.9)	129 (30.8)
Unavailable	101 (2.3)	37 (1.6)	≤5	121 (4.8)	71 (4.3)	20 (4.8)
ISS stage, n (%)						
I	307 (7)	241 (10.5)	39 (21.4)	236 (9.3)	194 (11.9)	49 (11.7)
II	375 (8.6)	275 (12)	25 (13.7)	285 (11.2)	234 (14.3)	42 (10)
III	779 (17.8)	392 (17.1)	38 (20.9)	510 (20.1)	331 (20.3)	103 (24.6)
Unavailable	2906 (66.5)	1389 (60.5)	80 (44)	1512 (59.5)	875 (53.5)	225 (53.7)
Prior stem cell transplant, n (%)	934 (21.4)	681 (29.6)	102 (56)	734 (28.9)	564 (34.5)	156 (37.2)

[a]Includes IgA and other M protein types. Ig, immunoglobulin; ISS, International Staging System; NA, not applicable.

Figure 2: OS in Len- vs non–Len-refractory in (A) overall population, (B) overall population with ECOG PS ≤1 (C) 2L with ECOG PS ≤1



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

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HONEUR Haematological Outcomes Network in Europe

Multiple Myeloma