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A Real-World Study of Lenalidomide Refractory Multiple Myeloma Patients in Finland: Treatment and Outcomes

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INTRODUCTION

Real-world patients with multiple myeloma (MM) who have 1-3 prior treatment lines, including proteasome inhibitors (PI) and immunomodulatory drugs (IMiD), and are refractory to lenalidomide continue to experience poor outcomes despite advances in MM care.

AIM

This retrospective registry-based study aims to provide real-world data on patients with lenalidomide-refractory MM regarding their characteristics and current treatment outcomes in the Finnish healthcare system.

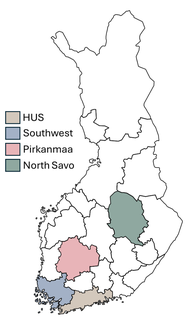

Figure 1. *Map of Finland with included areas highlighted. These regions collectively represent approximately 3 million inhabitants, which corresponds to 54% of the Finnish population.*

METHODS

Data source:
MM patients were identified during 2013-2022 from four hospital district data sources of Helsinki and Uusimaa (HUS), Southwest Finland, Pirkanmaa, and North Savo (Figure 1). Data were collected from hospital electronic health records and the Social Insurance Institution, linked using Finnish social security IDs. For results of the whole MM cohort, see Partanen et al. 2025.

Inclusion Criteria:
- MM patients with 1-3 prior treatment lines.
- Previous exposure to proteasome inhibitors (PI) and immunomodulatory drugs (IMID).
- Refractory to lenalidomide (treatment duration ≤60 days or next treatment started within 60 days, excluding lenalidomide).
- Patients were included at each qualifying treatment line.

Study Design:
- Index date set at initiation of the next treatment line after filling inclusion criteria
- Patients were followed until death or end of the study (EOS; Dec 31, 2022) (Figure 2).
- Cohort divided based on index treatment into:
  - Anti-CD38, carfilzomib, or pomalidomide containing triplet/quadruplet regimens.
  - Other, mainly doublet treatments.

Statistical analyses:
- Overall survival (OS) was analyzed as time from index to death (event) or EOS (censoring)
- Time to next treatment (TTNT) as time from index to start of next treatment line/death (event) or EOS (censoring).

RESULTS

- Out of 1 733 MM patients, altogether 201 filled the criteria at one or more index dates, resulting in 288 included treatment lines (Figure 3). These were further stratified based on treatment regimens used (Figure 4):
  - Modern triplet or quadruplet regimens (n=101, hence forward “triplet or quadruplet”)
  - Other, mainly doublet regimens (n=187, hence forward “doublet”)
- A total of 33 unique treatment combinations were identified. The most common index treatments were:
  - PCd (26%) and DPd (21%) for triplet or quadruplet-group
  - P±d/p (17%) and VC±d/p (12%) for the doublet group.
- Lenalidomide was used as a part of treatment in 9% of the treatment lines after filling the inclusion criteria
- **Median TTNT** (Figure 5):
  - 5.6 months (95% CI: 4.8-7.0) overall
  - 7.7 months (95% CI: 5.4-10.8) for the triplet /quadruplet group
  - 4.9 months (95% CI: 4.0-6.7) for the doublet group
- **Median OS** (Figure 6):
  - 14.9 months (95%: 11.9-18.3) overall
  - 16.3 months (95% CI:12.-22.9) for the triplet / quadruplet group
  - 13.8 months (95% CI: 10.2-20.0) for the doublet group

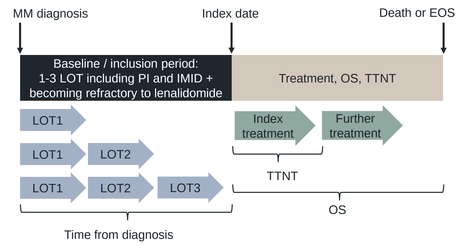

Figure 2. *Study outline. Patients were followed from MM diagnosis onwards. Index was set at the beginning of next treatment line after filling inclusion criteria. LOT: line of treatment.*

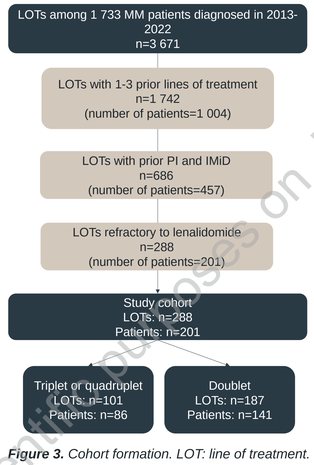

Figure 3. *Cohort formation. LOT: line of treatment.*

Table 1. Characteristics		Overall	Stratification by index treatment: Triplet or quadruplet	Doublet	p- value	Missing %
n		288	101	187		
Age at index, years, median [IQR]		72 [65, 77]	69 [61, 74]	73 [67, 78]	<0.001	0
Follow-up, months, median [IQR]		10 [4, 21]	8 [4, 17]	10 [4, 24]	0.193	0
Time from diagnosis, median [IQR]		31 [17, 46]	36 [21, 55]	28 [14, 43]	0.007	0
Sex, female, N (%)		145 (50)	44 (44)	101 (54)	0.117	0
Index year, N (%)	2013-2017	64 (22)	5 (5)	59 (32)	<0.001	0
	2018-2022	224 (78)	96 (95)	128 (68)		
ECOG, N (%)	0	35 (27)	25 (44)	10 (14)	0.001	56
	1	41 (32)	13 (23)	28 (39)		
	2+	52 (41)	19 (33)	33 (47)		
Cytogenetic profile, N (%)[1]	Standard risk	163 (76)	71 (75)	92 (77)	0.867	25[2]
	High risk	52 (24)	24 (25)	28 (23)		
ISS, N (%)	I	55 (21)	25 (26)	30 (18)	0.318	8
	II	106 (40)	36 (37)	70 (42)		
	III	103 (39)	36 (37)	67 (40)		

Characteristics was determined +/- 3 months from index, except cytogenetic profile that was determined using data from MM diagnosis to index. [1]High risk cytogenetics includes t(4;14), t(14;16), and del(17p). [2]6% for triplet/quadruplet subgroup, 33% for doublet subgroup.

Table 2. Treatment prior to index		Overall	Stratification by index treatment: Triplet or quadruplet	Doublets	p value*
n		288	101	187	
Number of prior treatment lines, median [IQR]		2.0 [2.0, 3.0]	2.0 [2.0, 3.0]	2.0 [2.0, 3.0]	0.118
Number of prior LOTs, N (%)	1	37 (13)	21 (21)	16 (9)	0.011
	2	143 (50)	44 (44)	99 (53)	
	3	108 (38)	36 (36)	72 (39)	
Prior SCT, N (%)		112 (39)	59 (58)	53 (28)	<0.001
Prior PI exposure, N (%)	bortezomib	277 (96)	97 (96)	180 (96)	1.000
	ixazomib	21 (7)	10 (10)	11 (6)	0.310
	carfilzomib	45 (16)	22 (22)	23 (12)	0.052
Prior IMiD exposure, N (%)	lenalidomide	288 (100)	101 (100)	187 (100)	-
	pomalidomide	28 (10)	12 (12)	16 (9)	0.484
	thalidomide	16 (6)	11 (11)	5 (3)	0.008
Prior anti-CD38 exposure, N (%)	daratumumab	23 (8)	18 (18)	5 (3)	<0.001
	isatuximab	0 (0)	0 (0)	0 (0)	-

p-value for difference between triplet or quadruplet and doublet-groups. LOT: line of treatment.

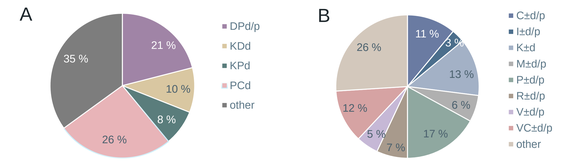

Figure 4. *Treatments used in next line after filling inclusion criteria (index treatment) for those receiving triplet (n=97; 96%) / quadruplet regimens (n=4; 4%) (A) and those receiving mostly doublets (B). C: Cyclophosphamide d: Dexamethasone p: Pomalidomide I: Ixazomib K: Carfilzomib M: Melphalan P: Pomalidomide R: Lenalidomide (Revlimid) V: Bortezomib (Velcade) D: Daratumumab.*

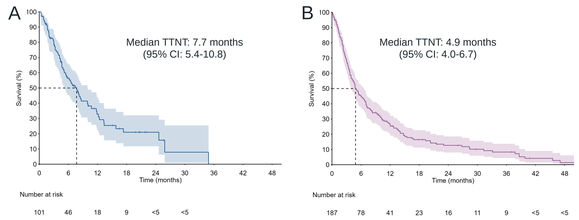

Figure 5. *TTNT for triplet or quadruplet (panel A) and doublet (panel B) treatment groups. TTNT was calculated from the beginning of the index treatment line to the start of next treatment line (event) or death or EOF (censoring events). Shaded areas represent 95% CI.*

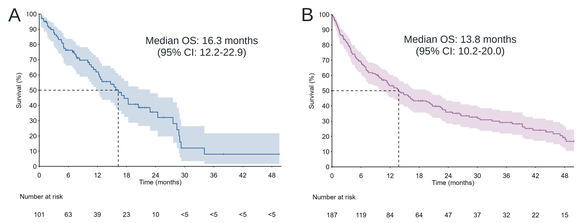

Figure 6. *OS for triplet or quadruplet (panel A) and doublet (panel B) treatment groups. OS was calculated from the beginning of the index treatment line to death (event) or EOS (censoring event). Shaded areas represent 95% CI.*

CONCLUSIONS

- Patients with refractory myeloma to lenalidomide continue to experience suboptimal results, underscoring the limited efficacy of modern triplet and quadruplet therapies.
- The study identified diverse salvage treatment regimens, with triplet and quadruplet combinations showing better outcomes in terms of TTNT and OS compared to doublet regimens.
- Patients treated with doublet therapies were older and had higher ECOG and ISS at index compared to patients with triplet / quadruplet therapies partly explaining their inferior outcomes.
- Due to the numerous index treatments, standard of care for lenalidomide refractory MM cannot be defined
- Due to the increasing use of lenalidomide in earlier treatment lines, the number of lenalidomide refractory patients is expected to increase, highlighting the need for new treatment strategies for this difficult to treat patient population.

FUNDING

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REFERENCE

Partanen, A. et al. 2025. Evolution of treatment practices and outcomes in multiple myeloma during 2013–2022: a Finnish real world registry study. Acta Oncologica. 64, (May 2025), 598–606.

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