Treatment Patterns, Outcomes, and Physician Decision-Making in Multiple Myeloma: A Real-World European Study

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BACKGROUND

- Multiple myeloma (MM) is a clonal plasma cell neoplasm accounting for ≈10% of haematologic malignancies[1]
- Despite the approval of multiple agents, MM remains incurable[2]
  - The approval of first- and second-generation proteasome inhibitors, immunomodulatory agents, and anti-CD38 monoclonal antibodies (mAbs) has improved patient outcomes, but over time, patients become refractory to one or more classes and outcomes are increasingly poor in later lines[2,3]
- Patients with relapsed or refractory MM (RRMM) often receive multiple lines of therapy (LOTs) in a rapidly evolving treatment landscape[2]
- Multiple factors, including patient and physician preferences and country of residence, may impact the regimens used, particularly in later LOTs[4-6]
- Real-world data on treatment patterns can provide insight into the complexity of therapeutic choices, usage, and decision making and help inform patient treatment options during the MM journey

OBJECTIVES

- To describe current real-world treatment patterns, outcomes, and physician decision-making for patients with MM in France, Germany, Italy, Spain, and the United Kingdom (UK)

METHODS

- Real-world data were derived from the Adelphi MM Disease Specific Programme™,[7-9] a point-in-time survey of haematologists and haemato-oncologists conducted from May to November 2021 in France, Germany, Italy, Spain, and the UK
  - The surveys collected data on both physician and patient experiences
- Physicians completed online patient record forms for 8 consecutive consulting patients with MM with a quota of ≥2 patients for each LOT (1L, 2L, 3L, 4L) and for the triple-class exposed (PI/IMiD/anti-CD38 mAb) cohort
  - Physicians were presented with a predefined list of 31 possible reasons for treatment choice on the line received at the time of data collection
- Descriptive information on demographics, current MM treatment patterns, and physician decision-making were collated and analyzed for each LOT from first-line (1L) to fourth-line (4L) therapy at the time of data collection and historically (back to diagnosis of MM)
  - Missing data were not imputed; therefore, the base of patients could differ from variable to variable
  - All analyses were descriptive in nature; no statistical comparisons were made
  - The same patient may be captured under multiple LOTs
- Limitation: results may not be representative of the full MM population, because only patients seeking care for MM and actively on treatment were included

Key physician inclusion criteria	Key patient inclusion criteria
▪ A specialty in haematology or haem-oncology ▪ Seeing ≥6 patients with RRMM per month ▪ Personal responsibility for prescribing decisions for patients with MM ▪ Acceptance of all survey rules and responsibilities	▪ ≥18 years of age ▪ A confirmed medical diagnosis of MM ▪ Receiving an active drug treatment for MM ▪ No current involvement in a clinical trial ▪ Not receiving only best supportive care

RESULTS

Patient demographics and clinical characteristics

- A total of 256 physicians provided data for 2179 patients; at the time of data collection, 18%, 23%, 29%, and 25% of patients were on their 1L, second-line (2L), third-line (3L), and 4L of treatment, respectively
  - Of the 256 physicians, 51, 52, 51, 48, and 54 were from France, Germany, Italy, Spain, and the UK, respectively
- Patient and disease characteristics were generally similar across countries, although France had a high percentage of patients with International Staging System stage III MM, Spain had a high percentage of patients who were eligible for and received a stem cell transplant (SCT), and the UK had a low percentage of patients who were anti-CD38 mAb exposed (**Table 1**)
- Across all countries combined, 29.8% (650/2179), 46.3% (301/650), and 26.9% (156/581) of patients were anti-CD38 mAb exposed, anti-CD38 mAb refractory, and triple-class refractory, respectively

Table 1. Patient and Disease Characteristics by Country

		Total (n=2179)	France (n=483)	Germany (n=421)	Italy (n=449)	Spain (n=411)	UK (n=415)
	Age, median (IQR), y	72 (65-77)	74 (68-78)	71 (67-74)	70 (63-77)	72 (65-78)	72 (64-77)
	Male, n (%)	1255 (58)	253 (52)	261 (62)	260 (58)	229 (56)	252 (61)
	Stage at data collection, n (%)						
	I	225 (10)	24 (5)	52 (12)	54 (12)	56 (14)	39 (9)
	II	517 (24)	79 (16)	157 (37)	90 (20)	114 (28)	77 (19)
	III	1161 (53)	342 (71)	184 (44)	254 (57)	172 (42)	209 (50)
	Unknown/not assessed	276 (13)	38 (8)	28 (7)	51 (11)	69 (17)	90 (22)
	ECOG PS at data collection, n (%)						
	0	403 (18)	75 (16)	34 (8)	91 (20)	90 (22)	113 (27)
	1	1136 (52)	286 (59)	223 (53)	204 (45)	204 (50)	219 (53)
	≥2	638 (29)	122 (25)	164 (39)	153 (34)	116 (28)	83 (20)
	Unknown/not assessed	2 (<1)	0	0	1 (<1)	1 (<1)	0
	Line of therapy, n (%)						
	1	401 (18)	106 (22)	82 (19)	61 (14)	78 (19)	74 (18)
	2	508 (23)	141 (29)	70 (17)	138 (31)	87 (21)	72 (17)
	3	637 (29)	124 (26)	157 (37)	119 (27)	114 (28)	123 (30)
	4	555 (25)	96 (20)	108 (26)	115 (26)	112 (27)	124 (30)
	≥5	78 (4)	16 (3)	4 (1)	16 (4)	20 (5)	22 (5)
	SCT, n (%)						
	Eligible	386 (18)	77 (16)	58 (14)	75 (17)	108 (26)	68 (16)
	Received	558 (26)	126 (26)	81 (19)	109 (24)	147 (36)	95 (23)
	Received at 1L[a]	506 (91)	118 (94)	56 (69)	104 (95)	137 (93)	91 (96)
	Anti-CD38 mAb exposed, n (%)[b]	650 (30)	134 (28)	136 (32)	158 (35)	116 (28)	106 (26)
	Anti-CD38 mAb refractory, n (%)[b, c]	301 (46)	86 (64)	54 (40)	63 (40)	55 (47)	43 (41)
	Triple-class exposed, n (%)[b]	581 (27)	123 (25)	118 (28)	145 (32)	105 (26)	90 (22)
	Triple-class refractory, n (%)[d]	156 (27)	47 (38)	26 (22)	35 (24)	31 (30)	17 (19)

ECOG PS, Eastern Cooperative Oncology Group performance status; IQR, interquartile range.
[a] Percentage based on patients who received SCT. [b] Exposed/refractory at previous line of therapy. [c] Percentage based on patients who received an anti-CD38 mAb. [d] All patients with disease refractory to a proteasome inhibitor, immunomodulatory agent, and anti-CD38 agent.

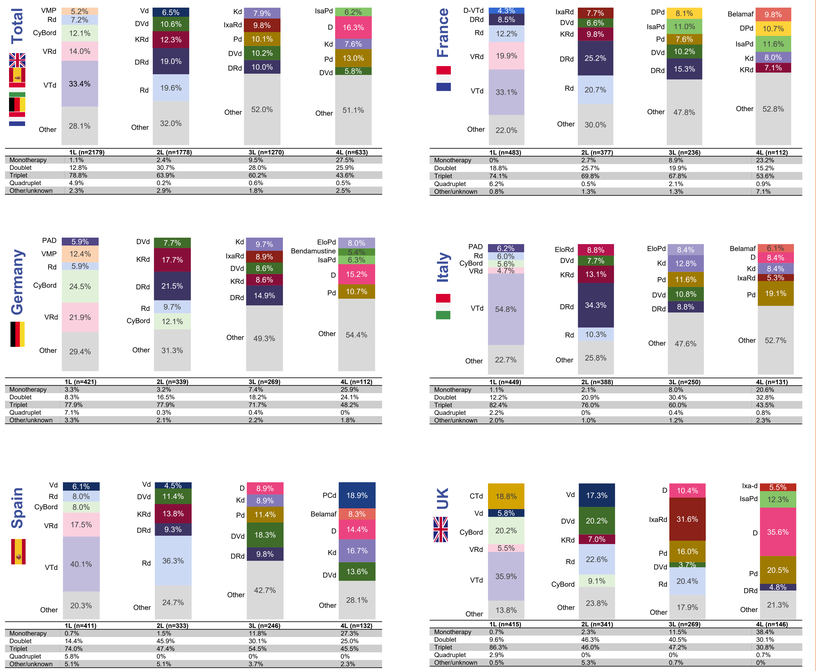
Treatment regimens across all countries (total population)

- Bortezomib-based regimens were more commonly seen in 1L (79.0%) (**Figure 1**)
  - Bortezomib-based triplets were common in 1L (VTd, VRd, and VMP use was 33.4%, 14.0%, and 5.2%, respectively)
- Lenalidomide-based regimens were more commonly seen in 2L (57.4%)
  - Rd, DRd, and KRd use was 19.6%, 19.0%, and 12.3%, respectively
- Pomalidomide-based regimens were more commonly seen in 3L and 4L (25.4% and 34.9%, respectively)
  - Pd use was 10.1% and 13.0% in 3L and 4L, respectively
- Daratumumab-based regimens were commonly seen in 2L to 4L (30.5%-32.5%)
  - Daratumumab-based triplets were used as early as 2L (DRd and DVd use was 19.0% and 10.6% in 2L and 10.0% and 10.2% in 3L, respectively)
  - Daratumumab monotherapy was the most common regimen in 4L (16.3%)
  - DRd use was 19.0% in 2L and DVd use was 10.2% in 3L
- The use of specific regimens varied more greatly in 3L and 4L
- Triplet regimens were more common than monotherapy or doublet regimens, regardless of LOT

Highlighted observations on treatment regimens by country

- France
  - Daratumumab monotherapy was not highly used in any LOT
  - Anti-CD38 mAb-based triplets were common in 2L and 3L
  - Belamaf use was high in 4L
- Germany
  - The top 5 regimens in 3L were daratumumab- or carfilzomib-based
  - Despite high daratumumab use observed in 2L and 3L, daratumumab monotherapy was still the most common regimen in 4L
- Italy
  - In 3L, use of triplet regimens was most common and predominantly anti-CD38 mAb-based
  - Doublet use in 3L was also common, with Kd (12.8%) and Pd (11.6%) being the highest used doublet regimens
  - Belamaf was a top 5 regimen in 4L
- Spain
  - Similar to Italy, triplets and doublets were common in 3L
  - Daratumumab monotherapy was a common regimen in both 3L and 4L
- UK
  - Across all countries, the UK had the highest use of daratumumab monotherapy and Pd use in both 3L and 4L
  - In 2L and beyond, the use of triplets appeared to be lower and the use of doublets appeared to be higher in the UK vs other countries

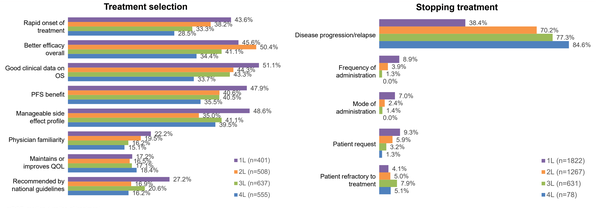
Figure 1. Top 5 Regimens Received by Country and LOT



Physician reasons for starting and stopping treatment

- Efficacy- and safety-based characteristics were common reasons for selecting treatment (**Figure 2**)
  - Efficacy-based characteristics were more common in earlier LOTs
  - Quality of life (QOL), physician familiarity, and treatment guideline recommendations were less-common reasons for selecting treatment
- Disease progression/relapse was a key reason physicians stopped treatment and it increased from 1L to 4L
  - Frequency and mode of administration decreased in importance from 1L to 4L
  - Patient request to stop treatment also decreased in importance from 1L to 4L

Figure 2. Selected Physician Reasons for Selecting and Stopping Treatment[a]

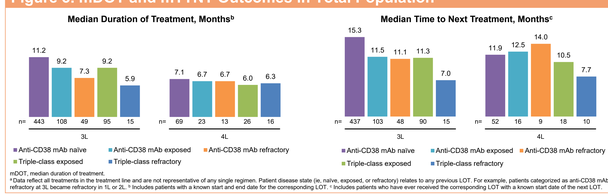


mDOT, median duration of treatment.
[a] Data reflect all treatments in the treatment line and are not representative of any single regimen. Physicians could choose more than one reason for selecting and stopping treatment; therefore, variables may not add to 100%.

LOT outcomes

- Overall, patients with anti-CD38 mAb–refractory or triple-refractory disease had a short median duration of treatment (mDOT) in 3L with a similar trend also in 4L (**Figure 3**)
- Although limited by small numbers, patients with triple-refractory disease had a short median time to next treatment (mTTNT) in 3L and 4L

Figure 3. mDOT and mTTNT Outcomes in Total Population[a]



mDOT, median duration of treatment.
[a] Data reflect all treatments in the treatment line and are not representative of any single regimen. Patient disease state (ie, naïve, exposed, or refractory) relates to any previous LOT. For example, patients categorized as anti-CD38 mAb refractory at 3L became refractory in 1L or 2L. [b] Includes patients with a known start and end date for the corresponding LOT. [c] Includes patients who have ever received the corresponding LOT with a known start date of the next LOT.

CONCLUSIONS

- In France, Germany, Italy, Spain, and the UK, there were large variances in MM treatment regimens used by LOT, especially in 3L and beyond
  - Triplet treatment regimens were the most common, regardless of LOT; however, in the UK, the use of triplets was lower in 2L and beyond
  - Kd and Pd doublets were the common doublets in 3L and 4L
  - Given the recent 1L approval for daratumumab, future analyses may show different patterns of overall daratumumab use
  - Belamaf use in 4L in Spain, Italy, and France may reflect treatment in the early access program or real-world utilisation patterns
- Efficacy and safety were the main reasons for prescribing treatment, and disease progression was the main reason to stop treatment
- Lack of standard care after 2L demonstrates an unmet need exists in these patients

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AR, AB, and EL are employees of Adelphi Real World.
SP, Td'E, and PFW are employees of GSK.

Abbreviations
Belamaf, belantamab mafodotin; CTd, cyclophosphamide + thalidomide + dexamethasone; CyBord, cyclophosphamide + bortezomib + dexamethasone; D, daratumumab; DPd, daratumumab + pomalidomide + dexamethasone; DRd, daratumumab + lenalidomide + dexamethasone; DVd, daratumumab + bortezomib + dexamethasone; DVTd, daratumumab + bortezomib + thalidomide + dexamethasone; EloPd, elotuzumab + pomalidomide + dexamethasone; EloRd, elotuzumab + lenalidomide + dexamethasone; IsaPd, isatuximab + pomalidomide + dexamethasone; Ixa-d, ixazomib + dexamethasone; IxaRd, ixazomib + lenalidomide + dexamethasone; Kd, carfilzomib + dexamethasone; KRd, carfilzomib + lenalidomide + dexamethasone; OS, overall survival; PAD, bortezomib + doxorubicin + dexamethasone; PCd, pomalidomide + cyclophosphamide + dexamethasone; Pd, pomalidomide + dexamethasone; PFS, progression-free survival; Rd, lenalidomide + dexamethasone; Vd, bortezomib + dexamethasone; VMP, bortezomib + melphalan + prednisone; VRd, bortezomib + lenalidomide + dexamethasone; VTd, bortezomib + thalidomide + dexamethasone.

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