





# Identifying Educational Needs and Practice Gaps of European Hematologists and Hematology Nurses in the Treatment and Management of Multiple Myeloma

Suzanne Murray<sup>1</sup>, Mohamad Mohty<sup>2</sup>, Sophie Peloquin<sup>1</sup>, Niels W. Van de Donk<sup>3</sup>, Sara Leitão<sup>4</sup>, Sara Labbé<sup>1</sup>, Sharon West<sup>5</sup>, Eva Hofstädter-Thalmann<sup>6</sup>, Pieter Sonneveld<sup>7</sup>

Correspondence: Suzanne Murray (e-mail: murrays@axdevgroup.com).

### **Abstract**

This needs-assessment aimed to identify clinical challenges faced by hematologists and hematology nurses in the diagnosis, treatment, and management of multiple myeloma, as well as contextual barriers hindering optimal care of patients with multiple myeloma. This manuscript focuses on key findings in relation to decision-making regarding new treatment options. A mixed methods study consisting of qualitative (from semistructured interviews) and quantitative data (from an online survey) was conducted in 8 European countries among hematologists and hematology nurses. The triangulated data led to the identification of 3 key findings related to decision-making: (1) Educational needs regarding mechanisms of action and side effect profiles of new therapies, (2) educational needs regarding the sequencing and combination of new agents with current therapies, and (3) contextual barriers to the integration of new agents. Specific knowledge and skill gaps were identified as causalities of the educational needs, providing information to guide future educational programs. Of note, 34% of hematologists and 69% of nurses reported suboptimal knowledge of the mechanisms of action of new agents and 30% of hematologists reported suboptimal skills integrating new agents in combination with current treatments. This needs-assessment highlighted the importance to address the educational needs and their underlying causes through medical education activities to ensure hematologists and hematology nurses are up-to-date with the latest treatments in the field as they become available. The contextual barriers identified should be considered when designing the educational programs to ensure content is applicable to the clinical reality of learners.

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Authors' contributions: SM the principal investigator, was involved in the study design, the development of the research tools, and contributed to the analysis plan and interpretation of the findings. She took part in critical discussions around the manuscript content and reviewed the final manuscript. SP, SLa were involved in the study design, led the development of research tools, the data collection, the qualitative and quantitative analyses, the interpretation of findings, and developed a first draft of the manuscript. MM, NWVD, SW, PS were part of an oversight committee which provided clinical expertise to help determine the areas of investigation, refine the study design and the research tools, and contextualize the interpretation of the findings. They critically reviewed content of the manuscript and approved the final version submitted. SLe, ET participated in early discussions on the study design, but the final decision regarding the design was the responsibility of the principal investigator and oversight committee of clinical experts. They critically reviewed content of the manuscript and approved the final version submitted. All coauthors have contributed sufficiently to this article to be considered as authors, as per the authorship requirements detailed by the International Committee of medical Journal Editors (ICMJE). Supplemental Digital Content is available for this article.

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<sup>&</sup>lt;sup>1</sup>AXDEV Group Inc., Brossard, QC, Canada

<sup>&</sup>lt;sup>2</sup>Hematology and Cellular Therapy Department, Hospital St Antoine, University Pierre & Marie Curie, Paris, France

<sup>&</sup>lt;sup>3</sup>Department of Haematology, VU University Medical Center, Amsterdam, the Netherlands

<sup>&</sup>lt;sup>4</sup>Janssen-Cilag Farmacêutica, Barcarena, Portugal

<sup>&</sup>lt;sup>5</sup>Haemato-Oncology Unit, Royal Mardsen Hospital, London, UK

<sup>&</sup>lt;sup>6</sup>Janssen-Cilag, Pharma GmbH, Vienna, Austria

<sup>&</sup>lt;sup>7</sup>Department of Haematology, Erasmus MC, Rotterdam, the Netherlands

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### Introduction

Rapid advances in the last decade in the understanding of multiple myeloma (MM) and the identification of new therapeutic targets have led to drastic changes in the treatment and management of patients, even though MM remains an incurable disease and is considered a chronic condition with relapse being inevitable. MM is a very dynamic scientific area with the arrival of these new treatment options within known therapy classes—such as immunomodulatory drugs (IMiDs) and second-generation of proteasome inhibitors (PIs)—but also treatments with novel modes of action such as the monoclonal antibodies and histone-deacetylase (HDACs) inhibitors. 1-3 The availability of new treatment options in first line and relapse setting has proved to be related to a significant improvement of the survival rate, especially for older patients, and of the early mortality rate. 4-8 In addition, treatment related toxicity has now considerably decreased.<sup>6,9</sup> These fast developments as well as a wealth of clinical data will likely have an impact on healthcare providers' ability to select optimized treatment options, and individualize treatment according to each patient profile.

This study sought to assess and identify practice gaps and educational needs of hematologists and hematology nurses involved in the care of patients with MM, in 8 European countries (Belgium, France, Germany, Italy, the Netherlands, Russia, Spain, and the United Kingdom). The selection of Russia, France, UK, Germany, Italy, and Spain was based on the large population of those nations, and to ensure inclusion of a diversity of health systems. The Netherlands and Belgium were included in this study to reflect the realities of relatively smaller population countries. The authors' goal was to collect evidence of educational gaps that will help tailor the development of medical education interventions to the actual needs of hematologists and hematology nurses, in order to have the greatest impact on optimizing patient care.

This article will present the mixed-methods study findings which pertain specifically to hematologists' and hematology nurses' educational needs and practice gaps in relation to new agents, and their integration into clinical practice in MM.

### **Materials and methods**

This mixed-method study was deployed in 2 consecutive phases between February and June 2016. Mixed-methods studies benefit from both the depth of qualitative exploratory data collection, and the analytical power of quantitative data collection. <sup>10,11</sup> The first phase (qualitative data collection) involved the recruitment and enrolment of participants in 45-minute semistructured interviews. Data collected from the first phase were analyzed and used to inform the design of Phase 2 (quantitative data collection), consisting of a 20-minute online survey deployed to a larger number of participants.

### Ethics approval

An international independent review board (Veritas IRB) provided ethics approval for each country wherein participants were recruited. Participants in this study were offered a financial compensation which was deemed by the ethics board to be fair but not coercive, based on participant's role and country of clinical practice.

### Recruitment and study inclusion criteria

This study targeted hematologists and hematology nurses practicing in one of the 8 targeted countries (Belgium, France, Germany, Italy, the Netherlands, Russia, Spain, and the United Kingdom). Recruitment was done using international online panels that comply with the ESOMAR code of conduct and ethical standards for market and social research. To be eligible to participate in the study, potential participants needed to self-report: (1) being a hematologist or a hematology nurse, (2) having a minimum of 5 years of practice, and (3) having a minimum caseload of 3 patients with MM per month for hematologists, and a minimum of 5 for nurses.

### Qualitative design and data collection

A review of literature was conducted on articles written in English, published after 2013, using key words such as *multiple myeloma*, *needs assessment*, *challenges*, *knowledge*, and *attitude*, to identify practice gaps and potential educational needs in the diagnosis, treatment, and management of MM. The information retrieved was used to determine preliminary areas of exploration for the development of qualitative interview guides. These areas of exploration were reviewed and validated by all coauthors.

The semistructured interview guides were designed to explore and assess a diverse spectrum of issues faced by hematologists and nurses in their practice. The interview guides were developed in English, and then translated into the official languages of each of the targeted countries (Dutch, French, German, Italian, Russian, and Spanish).

Each 45-minute telephone interview was conducted by trained and experienced interviewers in the official language of the participant's country of practice. The interviewers used general open-ended questions along with probes on selected topics targeted for enhanced exploration. Interviews were audiorecorded with the participants' informed consent, for transcription and analysis purposes.

### Quantitative design and data collection

Findings from the analysis of the qualitative data were used by the coauthors to develop 2 20-minute online surveys, 1 for hematologists, and 1 for nurses, with common questions when appropriate. The goal of the surveys was to validate the challenges and practice gaps identified in the interviews with a larger sample, and to identify the educational needs of participants (i.e., knowledge, skills) with greater precision. The surveys used a combination of multiple nominal choices and Likert-type response formats, and were organized into 3 sections. In the first section, participants were asked to select barriers from a list of items that have the most impact on their ability to provide optimal care to MM patients.

In the second section, participants had to reflect and self-report on their level of knowledge and skills ("low," "acceptable," or "optimal") in relation to specific statements. The nurses' survey also included questions on the relevance of various clinical tasks given their role ("not at all relevant," "somewhat relevant," or "very relevant"), as nurses' roles were expected to vary between countries.

The last section of the surveys included questions on specific educational topics that were reported to be relevant for health education in the qualitative interviews of the previous phase. Survey participants were then asked to select the topics they would find most relevant for their own professional development. Both online surveys were also translated from English into the other 6 languages.

### Mixed-methods analysis plan

Interviews were transcribed and coded using NVivo qualitative data analysis software (QSR International, Cambridge, MA) until the coded data reached saturation. Data saturation is reached when no new information is found from additional interviews.<sup>13</sup>

The approach used for the qualitative analysis is derived from the principles of thematic analysis<sup>14</sup> and directed content analysis,<sup>15</sup> and involves the following steps: (1) identification of a coding tree (or coding logic) with predetermined codes based on crucial areas of exploration informed by a review of the pertinent literature and through consultation with clinical experts; (2) coding of data using coding tree; (3) analysis of data that could not be coded using the coding tree and the addition of new codes if needed; (4) identification of emerging themes from the codes with highest data frequency and sources (i.e., reported by multiple participants).

The quantitative data were analyzed using IBM SPSS Statistics for Windows 22.0 software (IBM Corp., Released 2013, Armonk, NY) using frequencies and cross-tabulations. Knowledge and skill answers were recoded into dichotomous variables, either as being a potential educational gap or not. For that purpose, a response from 1 to 3 ("low" to "acceptable") on the 5-point scale was considered to be a potential educational gap. Differences between countries were calculated using analysis of variance (ANOVA) with a significance level of 0.05. The Netherlands and Belgium were excluded from cross-country analysis, due to small sample sizes. Finally, triangulation, which consists of combining different data collection methods (qualita-

tive and quantitative) and data sources (hematologists and hematology nurses), was used to ensure robust and trustworthy findings. <sup>16</sup> Findings presented in this manuscript are those that emerged substantively from both the qualitative and quantitative analyses.

### **Results**

### Sample size and demographics

This study included 364 participants. Thirty-nine interviews were conducted with 28 hematologists and 11 hematology nurses, and 325 participants (253 hematologists and 72 hematology nurses) completed the survey.

A large proportion of the study participants practiced in either an academic setting (49%) or in a specialized cancer centre (18%). The majority of participants also had more than 10 years of experience in their field of practice. Over a third of participants (38% of hematologists and 34% of hematology nurses) had a patient caseload consisting of 20% or more of MM patients. Samples by country, profession, and by study phase, as well as sample demographic characteristics, are presented in Table 1.

### Findings related to treatment decision-making

Triangulation of qualitative (interviews) and quantitative (survey) findings, and data sources (hematologists and nurses) allowed for the identification of practice gaps and educational needs across the continuum of care in MM. Triangulation is used in mixed methods studies to increase validity and trustworthiness of findings. <sup>17</sup> Given the purpose of this manuscript, solely key findings in relation to decision-making regarding new treatment options in the care of MM patients will be presented. Other findings identified by this needs-assessment have been presented elsewhere. <sup>18</sup> No strict definition of new agents was provided

Sample Distribution and Demographic Information

|                       | Hemat             | tologists               | Nu                  | irses                  |           |
|-----------------------|-------------------|-------------------------|---------------------|------------------------|-----------|
| Demographic           | Phase 1:          | Phase 2:                | Phase 1:            | Phase 2:               | Total,    |
| Variables             | Qualitative, n=28 | Quantitative, $n = 253$ | Qualitative, $n=11$ | Quantitative, $n = 72$ | n=364     |
| Country               |                   |                         |                     |                        |           |
| Belgium*              | _                 | 20 (8%)                 | _                   | 5 (7%)                 | 25 (7%)   |
| France                | 5 (18%)           | 41 (16%)                | 2 (19%)             | 10 (14%)               | 58 (16%)  |
| Germany               | 5 (18%)           | 40 (16%)                | 2 (19%)             | 11 (15%)               | 58 (16%)  |
| Italy                 | _                 | 40 (16%)                | _                   | 10 (14%)               | 50 (14%)  |
| Netherlands*          | 3 (11%)           | 9 (4%)                  | _                   | 4 (6%)                 | 16 (4%)   |
| Russia                | 5 (18%)           | 23 (9%)                 | 2 (19%)             | 11 (15%)               | 41 (11%)  |
| Spain                 | 5 (18%)           | 40 (16%)                | 2 (19%)             | 11 (15%)               | 58 (16%)  |
| UK                    | 5 (18%)           | 40 (16%)                | 3 (27%)             | 10 (14%)               | 58 (16%)  |
| Years of practice     |                   |                         |                     |                        |           |
| 5–10                  | 66 (2             | 23%)                    | 12                  | (15%)                  | 78 (22%)  |
| 11-20                 | 145 (5            | 52%)                    | 34                  | (41%)                  | 179 (49%) |
| 21-30                 | 64 (2             | 23%)                    | 30                  | (36%)                  | 94 (26%)  |
| >30                   | 6 (2              | 2%)                     | 7                   | (8%)                   | 13 (4%)   |
| % of patient caseload | with MM           |                         |                     |                        |           |
| <1%                   | 2 (1              | %)                      | 3                   | (4%)                   | 5 (1%)    |
| 1-5%                  | 19 (7             | <b>'%</b> )             | 18                  | (21%)                  | 37 (10%)  |
| 6-10%                 | 56 (2             | 20%)                    | 16                  | (19%)                  | 72 (20%)  |
| 11-20%                | 96 (3             | 34%)                    | 18                  | (22%)                  | 114 (31%) |
| >20%                  | 108 (3            | 38%)                    | 28                  | (34%)                  | 136 (38%) |

MM = multiple myeloma

 $<sup>^{*}</sup>$ The Netherlands and Belgium were excluded from cross-country analysis, due to small sample sizes.

during semistructured interviews since what is considered a new agent might differ according to the country of practice. Concrete examples taken from qualitative data were used to refer to new agents in the quantitative phase. Three main findings that hinder decision-making in relation to new treatments were identified: 2 related to educational needs, and 1 finding related to contextual barriers.

- (1) Educational needs regarding the mechanisms of action and side effect profiles of new therapies.
- (2) Educational needs regarding the sequencing of new agents and their combination with current available therapies (hematologists only).
- (3) Contextual barriers to the integration of new agents in clinical practice.

The following subsections describe each of these findings, as reported by participants in the online survey (n=325), and supported by qualitative data from the semistructured interviews (n = 39).

Educational needs regarding the mechanisms of action and side effect profiles of new therapies. When hematologists were asked in the online survey to rate their overall level of knowledge of the mechanisms of action of new agents, 34% identified their knowledge as "low" to "acceptable" (1–3, on the 5-point scale). Percentages by country are presented in Table 2. Country differences did not reach statistical significance.

For the same item, over two-thirds of nurse participants (69%) reported "low" to "acceptable" knowledge. In addition, 71% of nurses considered this knowledge to be "relevant" or "very relevant" to their practice (4–5 on a 5-point scale), given their role in the clinical practice. Differences between countries did not reach statistical significance (Table 3).

As reported in Table 2, 41% of hematologists and 68% of nurses reported a gap in their knowledge of the safety profile of new agents (1–3 on the 5-point scale). Over three-quarters (78%) of nurses reported this knowledge as "relevant" or "very relevant." Nonsignificant trends between countries were observed regarding the relevance of this clinical knowledge (46% reporting relevance in Germany, vs 90% in France, Italy and the UK and Spain).

As shown in Table 4, of the 5 classes of agents included in the survey, that is, 3rd-generation immunomodulatory drugs (IMiDs), 2nd-generation PIs, HDACs inhibitors, monoclonal antibodies (anti-SLAMF7 (elotuzumab), or anti-CD38 [daratumumab, isatuximab, and MOR202]), the highest proportions of participants reporting gaps in knowledge (63%) of the mechanisms of action, adverse effects and safety profiles, were observed for elotuzumab and the HDACs inhibitors (panobinostat, vorinostat). A statistical difference was observed between countries for elotuzumab (p=0.01) with the knowledge gap being higher among UK hematologists (80%).

Knowledge of mechanism of action, efficacy, side effects, and safety profile of CD38-targeting monoclonal antibodies was reported to be low to acceptable by 59% of hematologist participants. A statistical difference between countries was observed for this item (P = 0.005), with a higher gap in the UK (73%), Russia (78%), and Spain (78%).

When asked to speak openly about their challenges in relation to treating patients with MM, interviewed hematologists and nurses (n=39) explicitly reported desire to increase their knowledge of the mechanisms of action and side-effect profiles of new agents, as mentioned in the following illustrative quotes.

Scale) Among Hematologists on a 5-Point Selected 1 to 3 % Skills ō Self-Reported Gaps in Knowledge

|   |                              | BEL*      | FRA                  | GER       | ITA        | *NTL                            | RUS        | SPA        | Ϋ́           | Total        | Significant |
|---|------------------------------|-----------|----------------------|-----------|------------|---------------------------------|------------|------------|--------------|--------------|-------------|
| Items   | Question                     | (n = 20)  | (n = 41)             | (n = 40)  | (n = 40)   | (b=u)                           | (n=23)     | (n = 40)   | (n = 40)     | (n = 253)    | Difference  |
| The mechanisms of action of new agents (n=253)    | Level of knowledge 30% (n=6) | 30% (n=6) | 46% (n=19) 18% (n=7) | 18% (n=7) | 30% (n=12) | 30% (n=12) 33% (n=3) 48% (n=11) | 48% (n=11) | 35% (n=14) | 33% (n=13)   | 34% (n=85)   | SN          |
| The safety profiles of new agents ( $n=252$ )     | Level of knowledge           | 30% (n=6) | 56% (n=23)           |           | 28% (n=11) | 44% (n=4)                       | 57% (n=13) | 39% (n=15) | 45% (n=18)   |              | NS          |
| New immune-therapies ( $n = 253$ )                | Level of knowledge           | 45% (n=9) | 37% (n=15)           | 20% (n=8) | 38% (n=15) | 44% (n=4)                       | 44% (n=10) | 40% (n=16) | 40% (n = 16) | 37% (n = 93) | NS          |
| Integrating new agents in combination with        | Level of skills              | 25% (n=5) | 38% (n=15)           |           | 39% (n=15) | 11% (n=1)                       | 30% (n=7)  | 21% (n=8)  | 36% (n=14)   |              | NS          |
| current treatment in the first line ( $1 = 240$ ) |                              |           |                      |           |            |                                 |            |            |              |              |             |

t e

Hematologists were asked to select what best describes their current level of knowledge concerning each statement using a 5-point scale (1 = low, 5 = optimal, and N/A). Data presented are the percent of hematologists who responded 1 to 3, which corresponds to a suboptimal level

NTL = Netherlands, NS = not significant, BEL = Belgium, FRA = France,

### Table 3

Self-Reported Gaps in Knowledge (% Selected 1 to 3 on a 5-Point Scale) and High Level of Relevance of That Knowledge (% Selected 4 or 5 on a 5-Point Scale) Among Hematology Nurses Participants Who Self-Reported Knowledge as 1 to 3 (Low to Acceptable): % (n); Participants Who Reported Relevance as 4 to 5 (Relevant-Very Relevant): % (n)

|  |                    | BEL*          | FRA         | GER       | ITA         | * NTL     | RUS        | SPA        | Ϋ́          | Total              | Significant |
|--|--------------------|---------------|-------------|-----------|-------------|-----------|------------|------------|-------------|--------------------|-------------|
| Items  | Question           | (u=2)         | (n=10)      | (n=11)    | (n=10)      | (n=4)     | (n=11)     | (n=11)     | (n = 10)    | (n=72)             | Difference* |
| The mechanisms of action of novel treatments | Level of knowledge | (0.00) (0.00) | (9=u) %09   | 82% (n=9) | 100%        | 100%      | 55% (n=6)  | 64% (n=7)  | 50% (n=5)   | (0 = 0) $(0 = 20)$ | NS          |
|  | Level of relevance | 40% (n=2)     | 80% (n=8)   | 46% (n=5) | (6 = u) %06 | 50% (n=2) | 82% (n=9)  | 73% (n=8)  | 80% (n=8)   | 71% (n=51)         | NS          |
| The safety profiles of novel therapies       | Level of knowledge | 80% (n=4)     | 70% (n=7)   | 73% (n=8) | 80% (n=8)   | 100%      | 55% (n=6)  | 55% (n=6)  | (9 = u) %09 | 68% (n = 49)       | NS          |
|  | Level of relevance | 40% (n=2)     | (6 = u) %06 |           | (6 = u) %06 | 75% (n=3) | 82% (n=9)  | 91% (n=10) | (6 = u) %06 | 78% (n = 56)       | NS          |
| New immune-therapies                         | Level of knowledge | 80% (n=4)     | (9 = u) %09 | 82% (n=9) | 80% (n=8)   | 75% (n=3) | 55% (n=6)  | 64% (n=7)  | (2 = 0) %09 | 67% (n = 48)       | NS          |
|  | Level of relevance | 40% (n=2)     | 80% (n=8)   | 36% (n=4) | (6 = u) %06 | 75% (n=3) | 91% (n=10) | 82% (n=9)  | 80% (n=8)   | 74% (n=53)         | p = 0.003   |

Nurses were asked to select (1) what best describes their current level of knowledge concerning each statement using a 5-points scale (1 = low and 5 = optimal) and (2) considering their role as a nurse, they were asked to indicate how relevant is each statement in the provision of optimal Data presented are the percent of nurses who responded 1 to 3 for the knowledge question (corresponding to a suboptimal level of knowledge), and 4 or 5 for the relevance question (corresponding to a task relevant to the nurse's role in the provision of optimal care to patients care to their patients with MM, using the scale provided (where 1 = not at all and 5 = very relevant).

BEL = Belgium, FRA = France, GER = Germany, ITA = Italy, NS = not significant, NTL = Netherlands, RUS = Russia, SPA = Spain, UK = United Kingdom

with multiple myeloma).

Significant differences between countries using analysis of variance (ANOVA) (p < 0.05). The Netherlands and Belgium were excluded from cross-country analysis, due to small sample sizes.

## Table 4

Percent of Hematologist Participants in Each Country Reporting a Gap in Knowledge for Each of the 5 Classes of New Agents and a Gap in Skills Using These New Agents

Participants Who Self-Reported Knowledge as 1 to 3 (Low to Acceptable): % (n); Participants Who Self-Reported Skill as 1 to 3 (Low to Acceptable): % (n)

|  |                    | BEL*         | FRA        | GER          | ITA        | * NTL       | RUS        | SPA        | NK           | Total       | Significant   |
|--|--------------------|--------------|------------|--------------|------------|-------------|------------|------------|--------------|-------------|---------------|
| New Agents   | Question           | $(n\!=\!20)$ | (n = 41)   | (n = 40)     | (n = 40)   | (b=0)       | (n = 23)   | (n = 40)   | (n = 40)     | (n=253)     | Difference *  |
| Third-generation immunomodulatory drugs (IMiDs)—pomalidomide     | Level of knowledge | 35% (n=7)    | 39% (n=16) | 28% (n=11)   | 33% (n=13) | 26% (n=5)   | 61% (n=14) | 40% (n=16) | 40% (n=16)   | 39% (n=98)  | NS            |
|  | Level of skills    | 45% (n=9)    | 42% (n=17) | 33% (n=13)   | 53% (n=21) | (2 = 1) %82 | 70% (n=16) | 48% (n=19) | 53% (n=21)   | 49% (n=123) | p = 0.02      |
| Second-generation proteasome inhibitors—carfilzomib, ixazomib    | Level of knowledge | 50% (n=10)   | 42% (n=17) | 30% (n=12)   | 45% (n=18) | 11% (n=1)   | 61% (n=14) | 48% (n=19) | 53% (n=53)   | 44% (n=112) | NS            |
|  | Level of skills    | 60% (n=12)   | 44% (n=18) | 40% (n = 16) | 63% (n=25) | (9=u) %29   | 74% (n=17) | 60% (n=24) | 55% (n=22)   | 55% (n=140) | p = 0.031     |
| Histone-deacetylase (HDACs) inhibitors —panobinostat, vorinostat | Level of knowledge | 70% (n=14)   | 68% (n=28) | 50% (n=20)   | 60% (n=24) | 44% (n=4)   | 61% (n=14) | 63% (n=25) | 75% (n=30)   | 63% (n=159) | NS            |
|  | Level of skills    | 75% (n=15)   | 68% (n=28) | 53% (n=21)   | 73% (n=29) | 78% (n=7)   | 78% (n=18) | 68% (n=27) | 80% (n=32)   | 70% (n=177) | NS            |
| Monoclonal antibodies: anti-SLAMF7 (elotuzumab)                  | Level of knowledge | 75% (n=15)   | 59% (n=24) | 48% (n=19)   | 53% (n=21) | 44% (n=4)   | 70% (n=16) | 68% (n=27) | 80% (n=32)   | 63% (n=158) | p = 0.01      |
|  | Level of skills    | 80% (n=16)   | 56% (n=23) | 48% (n=19)   | 65% (n=26) | 78% (n=7)   | 83% (n=19) | 63% (n=25) | 90% (n = 36) | 67% (n=171) | $p \le 0.001$ |
| Monoclonal antibodies: anti-CD38                                 | Level of knowledge | 75% (n=15)   | 46% (n=19) | 40% (n=16)   | 48% (n=19) | 22% (n=2)   | 78% (n=18) | 78% (n=31) | 73% (n=29)   | 59% (n=149) | p = 0.005     |
| (udi attiiliiniau), isatuxiiliau,<br>MOR202)                     |                    |              |            |              |            |             |            |            |              |             |               |
|  | Level of skills    | 80% (n=16)   | 44% (n=18) | 53% (n=21)   | 63% (n=25) | 56% (n=5)   | 83% (n=19) | 63% (n=25) | 83% (n=33)   | 64% (n=162) | $p \le 0.001$ |

For each agents, participants were asked to rate their level of (1) knowledge of the mechanisms of action, efficacy, side effects/sfafety profile of the new agents and (2) their level of skills using the new agents in the clinical practice on a 5-points scale of 1 (low) to 5 (potimal) Data are the percent of oncologists who responded 1 to 3, which corresponds to suboptimal levels of knowledge or skills.

Significant differences between countries using analysis of variance (ANOVA) (p < 0.05). The Netherlands and Belgium were excluded from cross-country analysis, due to small sample sizes. BEL = Belgium, FRA = France, GER = Germany, ITA = Italy, NS = not significant, NTL = Netherlands, RUS = Russia, SPA = Spain, UK = United Kingdom.

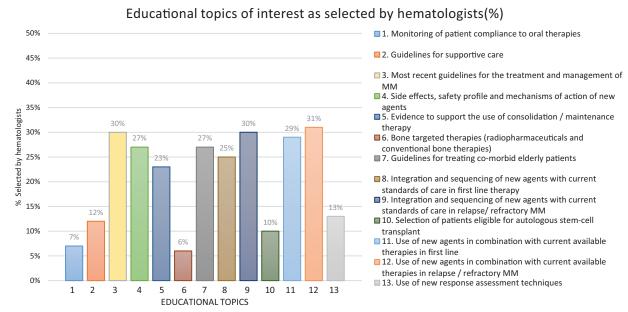


Figure 1. Preferred educational topics of interest as selected by hematologists. Question asked to hematologists: Among the following potential educational program topics, please identify three that you believe would have the most impact on your clinical practice.

Concerning new drugs, we are a bit lost as we hear a lot of things and have high expectations. We like to be informed on these drugs, and especially on the adverse events and long term side effects. (Hematologist, France)

Well for me the treatment regimes are constantly changing, there are new drugs coming onto the market all the time. And often that is dealt with a quite a high level, the doctors and above and it would be good to be able to know what the new treatments are, what they entail. Just very basics about them really. (Hematology nurse, UK)

In addition, when hematologists and nurses were asked to select their 3 most important topics to be addressed in education activities among a list of 13 items, knowledge of the side effects, safety profile, and mechanisms of action of new agents was selected by 27% of hematologists (5th most selected topic; Fig. 1) and 38% of nurses (2nd most selected topic; Fig. 2) selected.

Educational needs on the sequencing of new agents and their combination with current available therapies (hematologists only). As illustrated in Graph 1, among a list of 15 different educational topics that could be covered in education activities, 3 out of 4 topics most selected by hematologists were linked to the sequencing and combination of new agents. Two of those items were related to the use of new agents in combination with current available therapies: in first line (29%) and in relapse setting (31%). In addition, integrating and sequencing of new agents with current standards of care in relapse/refractory MM was selected by 30% of hematologists.

Furthermore, 30% of hematologists reported a gap in their skills integrating new agents in combination with current treatment in the first line. No differences were observed between countries.

Among a list of 5 new agents (Table 4), the gaps in skills using novel agents reported by the highest proportion of hematologists were related to the use of HDACs inhibitors (70%), elotuzumab (67%), and CD38-targeting antibodies (64%). Significant differences between countries were observed for skills using monoclonal antibodies, both elotuzumab ( $p \le 0.001$ ) and CD38 antibodies ( $p \le 0.001$ ). The proportion of participants that reported a gap in skills was higher in the UK and in Russia for elotuzumab (90% and 83%, respectively) and CD38 antibodies (both 83%).

On average, participants tend to report higher levels of skills using the 2nd-generation PIs (carfilzomib, ixazomib) and the 3rd-generation IMiD (pomalidomide). No statistically significant differences were observed between countries (see Table 4).

Treating and managing refractory patients, most specifically when using and sequencing new agents in combination with current available therapies, were topics spontaneously cited as challenging by interview participants.

The most difficult thing is to manage refractory patients because we have tried all the standard treatments and have no more therapeutic options. Managing this type of patients is very complicated. How to use new drugs as well, in combination or monotherapy. Also, improving second line therapies with triple therapy or combinations of drugs so patients respond better and relapse less. (Hematologist, Spain)

I am sure that in the very near future we will be using them [monoclonal antibodies], I can't tell you when and in which patients that it will be reasonable to use, but I think days are not very far when we actually start using them pretty commonly [ . . . ] I would have thought that we will be using them in the relapsed refractory setting. (Hematologist, UK)

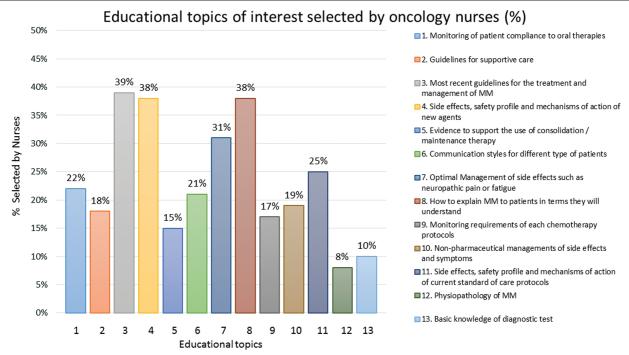


Figure 2. Preferred educational topics of interest as selected by oncology nurses. Question asked to nurses: Among the following potential educational program topics, please identify three that you believe would have the most impact on your clinical practice.

During the interviews, multiple hematologists mentioned the *lack of experience using new agents* as a causality for that challenge, as illustrated by the following quote:

You are always a bit hesitating to use new drugs if you haven't made personal experiences with it so far [...] The more options you have the more difficult it will be to make a choice, but the better will be the overall course, because I will still have something up my sleeve. (Hemato-oncologist, Germany)

Contextual barriers to the integration of new agents into clinical practice. Participants identified contextual barriers that were external to their own role, but did however impact their ability to optimally treat and manage patients with MM.

Among a list of nine different items (see Supplemental Digital Content, http://links.lww.com/HS/A2, for complete list), the *lack* of access to newly approved therapies was the barrier to providing optimal care in MM that was the most frequently selected by hematologists (48%). Statistical differences between countries ( $p \le 0.001$ ) were observed. As illustrated in Table 5, this barrier was selected by 82% of hematologists from the UK, and 65% from Spain, compared to 30% in Germany, and 34% in France.

The *cumbersome drug reimbursement process*, a factor impacting access, was also selected by 26% of hematologists, with significant differences between countries (p=0.016). This barrier was selected by 35% of hematologist participants from the UK, whereas 7% of participants from France selected this same barrier.

The barriers to optimal care reported by nurses differed from the ones reported by hematologists. The 2 most frequently reported barriers for nurses were the lack of trained nurses specialized in MM (38%), followed by the lack of resources in the day care unit (35%). There was no statistical difference between countries.

The *lack of access to new agents due to lack of reimbursement* was also mentioned by hematologists interviewed, as illustrated in the quote below.

I think accessibility is the main thing in the UK, it is not as easily available as you have got in the setting of United States, it's very hard to actually get these drugs freely available to us. (Hematologist, UK)

### **Discussion**

Through this study, the authors conducted an assessment of the current practice gaps and educational needs for hematologists and hematology nurses, collecting evidence that will be used to inform the design of future educational activities. Three specific findings: (1) Educational needs regarding the mechanisms of action and side effect profiles of new therapies, (2) educational needs on the sequencing of new agents and their combination with current available therapies (hematologists only), and (3) contextual barriers to the integration of new agents into clinical practice, were found to hinder decision-making in relation to the use of new treatments, and were thus included within the scope of this manuscript.

Future medical education activities and programs should be developed for hematologists and hematology nurses, based on the first 2 findings of this study, which described 2 educational needs related to new treatments. Although educational activities can not compensate for a lack of access or a cumbersome reimbursement process, these contextual factors must be considered when designing medical education programs, otherwise participants may not perceive the education as applicable to their clinical reality. In addition, programs should consider that

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Percent of Participants (Hematologists and Nurses) in Each Country That Selected the Item as a Barrier to Optimal Care

| Participants Who Selected Item Among Top 2 Barriers: % (n)     | op 2 Barriers: % (n)    |            |            |            |            |            |            |              |            |             |                          |
|--|-------------------------|------------|------------|------------|------------|------------|------------|--------------|------------|-------------|--------------------------|
| Barrier  | Type of Participant     | BEL*       | FRA        | GER        | ITA        | * JIN      | RUS        | SPA          | λU         | Total       | Significan<br>Difference |
| Lack of access to newly approved therapies                     | Hematologists (n = 253) | 45% (n=9)  | 34% (n=14) | 30% (n=12) | 38% (n=15) | 44% (n=4)  | 39% (n=9)  | 65% (n = 26) | 82% (n=33) | 48% (n=122) | p≤0.001                  |
|  | Nurses $(n=72)$         | 20% (n=1)  | 30% (n=3)  | 9% (n=1)   | (0 = u) %0 | 25% (n=1)  | 18% (n=2)  | 18% (n=2)    | 10% (n=1)  | 15% (n=11)  | NS                       |
| Cumbersome process of drug reimbursement Hematologists (n=253) | Hematologists (n = 253) | 35% (n=7)  | 7% (n=3)   | 30% (n=12) | 33% (n=13) | (9=u) % 29 | 17% (n=4)  | 15% (n=6)    | 35% (n=14) | 26% (n=65)  | p = 0.016                |
|  | Nurses $(n=72)$         | (0 = u) %0 | 10% (n=1)  | 27% (n=3)  | 10% (n=1)  | 25% (n=1)  | 18% (n=2)  | (0 = u) %0   | (0 = u) %0 | 11% (n=8)   | SN                       |
| Lack of trained nurses (specialized in MM)                     | Hematologists *(n=253)  | (0 = u) %0 | 22% (n=9)  | 8% (n=3)   | 23% (n=9)  | (0=u) %0   | (0 = u) %0 | 8% (n=3)     | 10% (n=4)  | 11% (n=28)  | p = 0.029                |
|  | Nurses (n=72)           | 60% (n=3)  | 30% (n=3)  | 27% (n=3)  | 50% (n=5)  | 25% (n=1)  | 46% (n=5)  | 36% (n=4)    | 30% (n=3)  | 38% (n=27)  | SN                       |

Among a list of 9 potential barriers, participants were asked to select up to 2 barriers that have the most impact on their ability to provide optimal care to MM patients. Data are the percent of participants who selected the barriers MM=multiple

Significant differences between countries using analysis of variance (ANOVA) (p<0.05). The Netherlands and Belgium were excluded from cross-country analysis, due to small sample sizes

new medications represent only a portion of the global cost of a comprehensive management of patients with MM, and thus should favor a broader view of the issue.

Despite the higher proportion of hematologists who reported knowledge and skill gaps in relation to the 2 most challenging classes (monoclonal antibodies directed against SLAMF7 and CD38, and histone-deacetylase inhibitors), medical education activities should ideally include all the classes surveyed, as there were gaps regarding the integration of all 5 classes of new agents in the MM treatment landscape. Should prioritization be required due to time constraints, the focus of educational interventions should be determined by considering the 2 classes where the highest gaps were observed and the relative clinical utility of the agents.

The identified gaps regarding knowledge and skills of new agents, especially monoclonal antibodies and HDACs, indicate a clear educational need that should be addressed and prioritized by future medical education in MM. The relevance of this topic is supported by the literature, which suggests that the sequencing of agents in MM is crucial due to inevitable relapses. <sup>19</sup>

A trend was observed where gaps in knowledge and skills were found to be greater in the UK and Russia compared those found in Germany and France. An explanation of these differences is suggested in the literature, for example, where Germany is among the European nations most involved in clinical trials, due to strong government support, and an active collaboration with pharmaceutical companies.<sup>20</sup>

Given that a large proportion of the total sample was from academic and specialized cancer centers who often host clinical trials, it is possible that the higher knowledge and skill levels observed in Germany across different topics investigated is a reflection of better access to clinical trials and the dissemination of clinical trial data in that country. This hypothesis is further supported by research suggesting that gaps in skills and knowledge relating to new agents were especially high in the UK, a country where limited access to new cancer medications has been reported. Differences across countries may be further explained by inaccessible best practice guidelines and newly approved therapies caused by language barriers, and distinct national healthcare systems, approval models, and reimbursement schemes.

Gaps in knowledge of the mechanisms of action and safety profile of new agents were higher for nurses due to a presumption that this knowledge is outside their professional responsibilities. Additionally, it has been reported that educational activities offered to nurses generally do not target their specific day-to-day needs.<sup>23,24</sup> Interestingly, a majority of nurses perceived the knowledge of mechanisms of action and the safety profiles of new agents to be highly relevant to their practice. This could be explained by the fact that supportive care in MM patients is highly complex due to the various lines of treatment, and the toxicity that may be generated by pharmaceutical treatments. Nurses working in MM require a highly specialized knowledge of the disease, and rely on a working understanding of mechanisms of action and new agent safety profiles. Is has been reported that specialized nurses in MM do indeed play a crucial role in managing and monitoring treatment toxicity, and therefore influencing the patient's experience and outcomes.<sup>25</sup>

Given the increasing availability of new agents and the highly evolving scientific area of MM, specialized nurses must continuously update their knowledge of the safety profile of new agents. The findings of this study highlight the importance of designing activities that are based on the specific educational needs of specialized nurses. In this study, nurses themselves

reported that the second most often selected barrier to optimal care is a *lack of trained nurses who specialize in MM*, a finding that underscores the need for relevant nurse education.

To our knowledge, this is the first study using a mixed-method design to identify the needs of healthcare professionals working in MM across multiple countries in Europe, with the goal of informing educational interventions and enabling an in-depth understanding of the issues and their potential causalities. Narratives from interview participants are useful for the design of educational programs, as they provide examples of challenging situations or patient cases that can be used to ensure that the program accurately depicts the clinical reality of the targeted learners. The triangulation of sources also allowed for a better understanding of the clinical reality of each targeted professional role and country.

Other studies of the challenges in the field of oncology have reported similar issues facing professionals treating and managing patients with other neoplasms or cancers. As an example, in a previous needs assessment across 7 countries, including 5 of the European countries in this study (France, Germany, Italy, Spain, and the UK), oncologists caring for patients with colorectal cancer reported similar challenges in relation to optimal sequential use of treatment choices as well as challenges accessing emerging treatments.<sup>26</sup>

In the context of a highly dynamic therapeutic area, where several new agents are, or will soon be available, education offerings should target the evidence-based needs of hematologists and specialized nurses. The results of this study provide such evidence to inform medical/health education activities that could be offered by societies, industry, or any other organization aiming to improve the care of patients with MM across Europe. In addition, the findings illustrate differences between countries that should be taken into consideration when designing educational activities and programs at the national level, to ensure adaptation to a local context.

### Limitations

Although purposive sampling was used to obtain participants with a mix of years of practice and different practice settings, the sample contained a large proportion of participants that practiced in academic centers and specialized centers. This may nevertheless adequately represent the breakdown of healthcare practitioners within the MM field, given most patients are being treated in highly specialized centers. It can be hypothesized that broader gaps would have been observed if a larger proportion of the sample would have come from nonacademic affiliated hospitals or community settings.

As with any international cross-cultural study where participants are invited to answer in the language of their choice, it is possible that interview and survey questions were interpreted slightly differently in different countries, due to the variance in language, meaning, or cultural norms. To reduce this risk, study materials were translated by expert medical scientific translators. In addition, all questions were kept simple to reduce the introduction of potential nuances in translation, and each question was formulated with the aim of ensuring understanding in different clinical and cultural contexts.

### Conclusion

With the increasing numbers of new agents available, and constant advances in knowledge about MM pathophysiology,

the treatment options for MM patients have become more complex and challenging. To maintain the highest quality of care possible, hematologists and hematology nurses must not only maintain up-to-date knowledge of most recent clinical advances, but most importantly, enhance their skills to integrate these advances rapidly in their clinical decision-making and clinical practice. The findings from this study, as reported by healthcare providers themselves, indicate how the shift in the current treatment paradigm due to the development of new classes of agents with different mechanisms of action in MM care has increased the perceived complexity of decision making surrounding treatment, and is potentially affecting the hematologists and hematology nurses capacity to provide optimal and personalized treatment to MM patients.

Despite some differences across countries and limitations inherent to any multicountry, multilanguage study, common educational priorities in relation to treatment decision-making with new agents in MM were identified. These findings highlight the key elements needed to support the design of future evidence-based medical education programs and activities, bearing in mind local realities in which they are deployed to ensure the contextual relevance to healthcare providers themselves.

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