Patient Preference and Adherence

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ORIGINAL RESEARCH

Description of Feelings, Perception, and Experience Before and After Switching from IV Daratumumab to the SC Form: A Mixed-Method, Cross-Sectional Survey in Multiple Myeloma Patients in Europe

Valeria Magarotto[1], Julien Thevenon[2], Kate Morgan[3], Silene ten Seldam[3], Wafae Iraqi[4], Xavier Guillaume[5], Marjorie Leclerc[5], Claire Graziani-Taugeron[5], Bleuenn Rault[5], Dahbia Horchi[5]

[1]MD, Janssen-Cilag, Cologno Monzese, MI, Italy; [2]Medical Affairs, Janssen Pharmaceuticals, Issy-les-Moulineaux, France; [3]Myeloma Patients Europe, Brussels, Belgium; [4]Patient Engagement, Janssen Pharmaceuticals, Issy-les-Moulineaux, France; [5]RWE Data & Analytics, Oracle Life Sciences, Paris, France

Correspondence: Xavier Guillaume; Claire Graziani-Taugeron, Oracle France, 198 Avenue de France, Paris, 75013, France, Email xavier.guillaume@oracle.com; claire.graziani-taugeron@oracle.com

Purpose: To provide real-world data on patient perceptions and experiences with subcutaneous (SC) versus intravenous (IV) daratumumab.

Patients and Methods: This was a cross-sectional, mixed-method (qualitative/quantitative) survey conducted in France, Germany, Spain and the United Kingdom involving multiple myeloma (MM) patients who switched from IV to SC daratumumab in the last 12 months (qualitative phase) or 24 months (quantitative phase [26 months in the UK]) prior to enrollment in the study.

Results: Nine patients (mean age 65 years) participated in the qualitative phase and 113 patients (mean age 65.1 years) in the quantitative phase. Qualitative study results provided insights for the quantitative study and highlighted the benefits of switching from daratumumab IV to daratumumab SC as an improvement and a satisfactory change in patients' treatment journey. Quantitative survey showed that patients were significantly less anxious, stressed and nervous before SC injections than IV infusions (mean score: 1.3, 1.1, 1.4 versus 2.1, 2.0, 2.0 respectively, $p<0.001$), and significantly more reassured, ready/well-prepared, usual self and relieved (mean score: 3.8, 4.3, 3.7, 3.6 versus 3.0, 3.6, 3.1, 3.0 respectively, $p<0.001$). Immediately after SC first injection, 96.5% patients were feeling well or very well versus 77.9% immediately after IV first infusion ($p<0.001$). 97.3% patients were satisfied with their SC treatment versus 89.4% for the IV injection ($p<0.001$). Patients spent significantly less time in hospital for an SC injection of daratumumab than for an IV infusion, 1.5 hours and 5.0 hours respectively ($p<0.001$). In the UK, the differences between the two administration forms were less visible, likely because of confounding factors including a longer time passed since the switch from the IV to the SC form and administration of the survey.

Conclusion: In line with results from other studies, the SC form of daratumumab had less impact on patients' emotional burden than the IV form.

Keywords: multiple myeloma, daratumumab, mode of administration, patients' emotional burden, mixed method

Introduction

Multiple myeloma (MM) is a progressive, incurable haematological malignancy of plasma cells. The disease is the second most prevalent blood cancer, with an incidence that increases with age.[1] It accounts for more than 10% of all blood cancers and 1% of cancers in total.[2] MM symptoms can vary from physical[3] to psychological[4] impairment;

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from pain, anaemia, bone lesions and renal dysfunction, to anxiety and depression. Patients experience periods of inactivity of the disease amidst active periods requiring systemic therapy.[5]

Advancements in treatment options over the past 10 years have increased overall survival from months to years.[6] Daratumumab is a fully human monoclonal antibody targeting CD38 that has shown encouraging results both as monotherapy and in combination with other regimens in both R/R MM and frontline populations.[7] It was first developed for intravenous (IV) administration, a subcutaneous (SC) form has recently been launched with no inferiority in terms of efficacy and pharmacokinetics and with an improved safety profile in patients compared to the IV administration.[8] One of the major improvements for patients is a reduced administration time for Daratumumab SC compared with IV administration. Indeed, in COLUMBA clinical trial, the median duration of injection for the SC form was 5 minutes compared with 421 minutes for the first infusion of IV daratumumab, 255 minutes for the second infusion, and 205 minutes for the third infusion.[8]

A recent study has shown that the SC form is associated with less health-care providers involvement compared with the IV form, since the SC form does not require an installation of a peripheral cannula, an injection line connection and discontinuation or a monitoring during the injection.[9] This time savings reduces the patients and caregivers' s burden and creates efficiencies for the healthcare-providers allowing more patients access to care.[9] On top of that, reducing the treatment duration is associated with lessening the time spent in hospital or clinical setting, resulting thereby in minimizing the patient's risk of healthcare associated infections.[9] This benefit is particularly relevant at this present time; after the COVID-19 pandemic.

Additionally, reducing the treatment time includes the increase of patient satisfaction and improves health-related quality of life.[21] Those findings have been demonstrated in the COLUMBA trial where a specific questionnaire evaluating patient satisfaction showed that patients assigned to the SC form were more satisfied with their cancer therapy than patients on daratumumab IV.[8] Similarly, a recent meta-analysis of studies comparing oncology patients treated with IV versus SC forms found significant improvement in health-related quality of life, healthcare resource utilization, and economic outcomes (including time away from work and decreased productivity) with SC administration.[10] Finally, increasing the patient's satisfaction by reducing the treatment duration may be related to a greater patient compliance and therefore improving the overall treatment outcomes.[10] Nevertheless, given the recent approval daratumumab SC, there is a need to provide data to the different stakeholders (eg, clinicians, payers and the MM patients community) on the real-world experience of daratumumab SC administration.

This mixed-methods study aimed to understand how daratumumab SC is being perceived and experienced in the real-world clinical setting versus the IV form. The qualitative phase aimed to describe the patient's experience, exploring perception, feelings, and attitude towards switching from daratumumab IV to SC. The quantitative phase aimed at quantifying the patient's experience, perception, feelings, and attitudes.

Materials and Methods

This was a multi-country (France, Germany, Spain, United Kingdom [UK]), cross-sectional, mixed-method (qualitative and quantitative) survey involving MM patients, currently receiving daratumumab as part of their frontline, second- or third-line treatment regimen, and who had switched from IV to SC administration (index event) in the last 12 months (qualitative phase) or 24 months (quantitative phase [26 months in the UK]). The study was conducted sequentially, with the qualitative part (Figure 1) run prior to the quantitative (Figure 2) one, to design the quantitative questionnaire based on the qualitative findings. The qualitative data was also used to provide context to numerical values derived from the quantitative survey, enhancing the relevance of findings. All procedures in the study complied with General Data Protection Regulation (GDPR) guidelines and with the European Society for Opinion and Marketing Research (ESOMAR) and European Pharmaceutical Market Research Association (EphMRA) ethical codes of conduct that guarantee the anonymity of the respondents and of the responses that they give. Anonymity of patient respondents was also ensured by ascertaining that responses could not be directly linked to the respondent, and no survey responses identified respondents individually.

This research did not focus on measuring medical outcomes, and no individual medical data about the patient was abstracted from patient medical records. Furthermore, data was completely anonymized with no possibility for

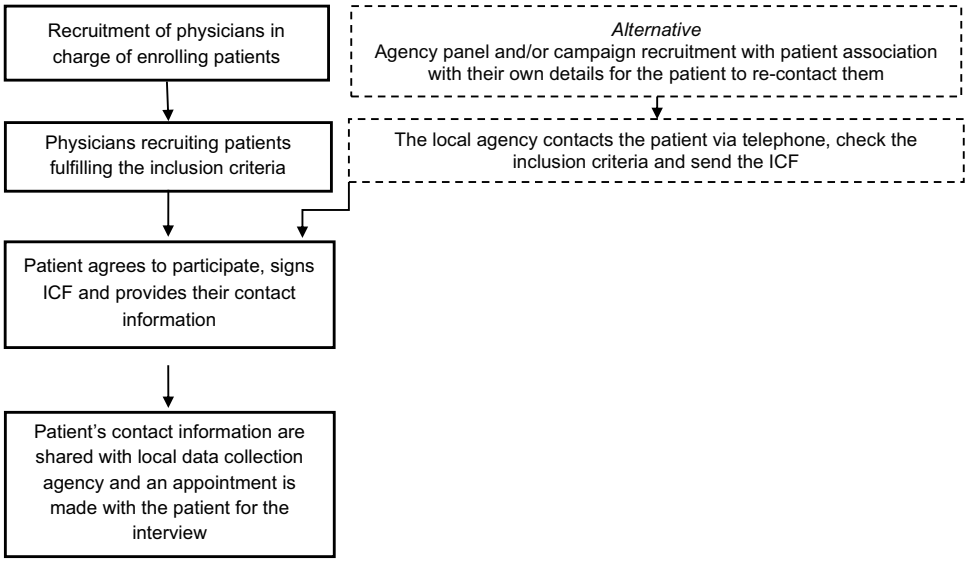

Figure 1 Schematic overview of the survey administrative procedures for patients for the qualitative phase (n = 9 patients; mean age: 65 years).

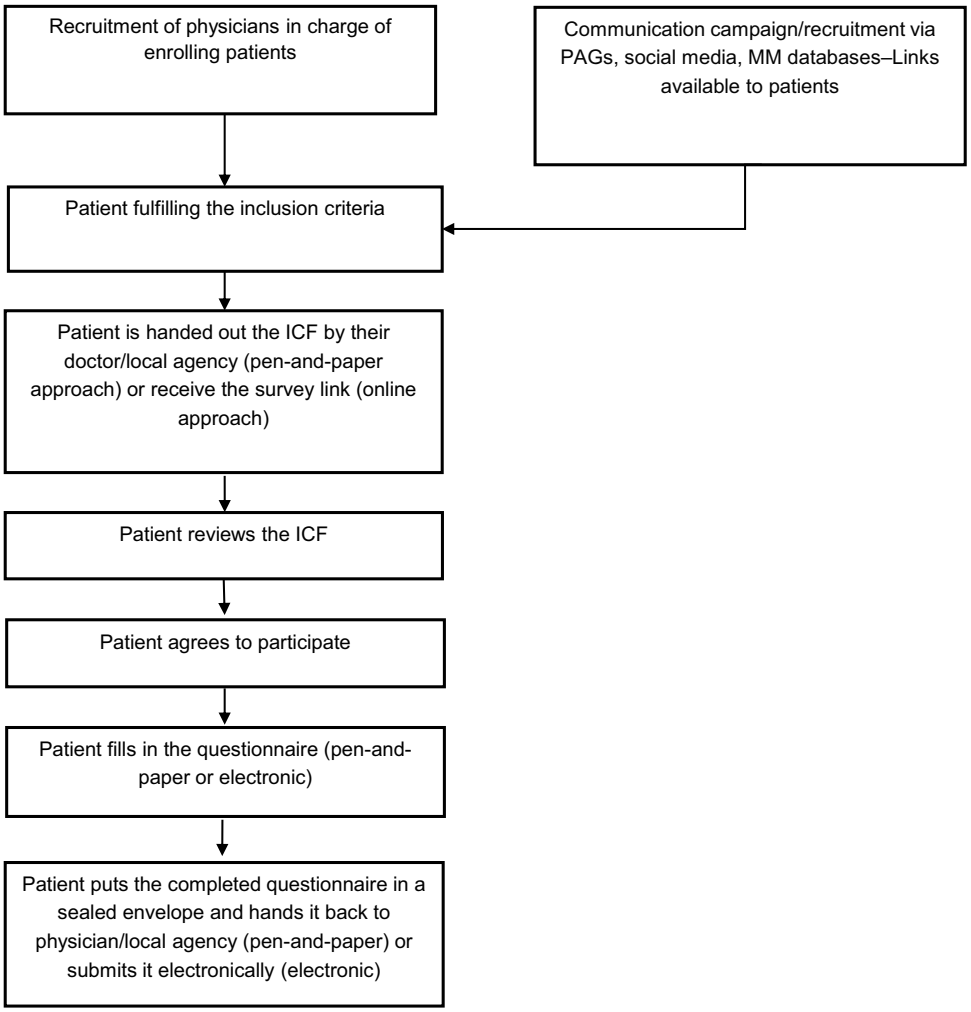

Figure 2 Schematic overview of the survey administrative procedures for patients for the quantitative phase (n = 113 patients; mean age: 65.1 years).

reidentification of the patients. Therefore, this study could not be classified as a Human Subject Research as defined in the Helsinki declaration. The study was submitted and approved by an Independent Review Board (Oracle Life Sciences IRB, 15 December 2021). All participants provided informed consent prior to participation in the study which included consenting to publication of anonymized responses.

The inclusion criteria were: (1) an MM diagnosis, (2) daratumumab SC as part of the first-, second- or third-line treatment, either alone or in combination with other oral or subcutaneous products, (3) daratumumab IV received within the past 12 months (qualitative phase) or 24 months (quantitative phase [26 months in the UK]) prior to participation in the survey (either started the line with daratumumab IV and switched to daratumumab SC or received daratumumab IV in a previous line), (4) >18 and <80 years of age when the interviews were conducted, (5) understanding, ability and willingness to fully comply with survey procedures. In terms of exclusion criteria: patients should not have received daratumumab as part of an interventional clinical trial.

Qualitative Phase Procedures

Data collection: All participants were recruited by physician referral. Data collection (recruitment and interviewing) lasted from February until April 2022. The qualitative phase consisted of a 45-minute in-depth telephone or web assisted telephone interview. All interviews were conducted in local language and recorded; all audio recordings were transcribed in full verbatims, and the non-English ones were translated into English for analysis purposes.

Data analysis and interpretation: A qualitative thematic analysis of the interview data was performed. The transcripts were exhaustively coded using NVivo (v.12 Plus, QSR International), a computer-assisted qualitative data analysis software (CAQDAS), which enables the assignment of codes to discourse segment to facilitate interpretation and classification into themes. Codes were identified by the researchers from raw data as well as from the interview guide, structuring the discussion and regrouped by categories (descriptive association of coded segment of interviews) and themes (interpretative abstraction from the researcher). Codes, categories and themes were critically investigated and discussed among the two principal researchers until an agreement was reached to ensure consistency and reliability. Interview transcripts were reviewed throughout the coding process to ensure that themes reflect the original data and their context.

Recruitment during the qualitative study was limited by growing proportion of patients treated with daratumumab SC, resulting in the majority of patients being treated with daratumumab SC at the time of the interviews. To overcome this, the 12-month period was extended to 24 months for the quantitative study which was started almost 6 months after the start of the qualitative study. The qualitative study was mainly exploratory and aimed to highlight the key aspects of the patient's experience, perception, feelings, and attitude towards switching from daratumumab IV to SC. Thus, the study results provided context and insights that were used in the quantitative study, such as in the material development.

Quantitative Survey Procedures

Data collection: Data collection (recruitment and interviewing) lasted from August until December 2022. In France and Germany, patients were recruited by physician referral and pre-screened by physicians before being able to complete the survey. In the UK and Spain, patients were recruited by multimodal ad hoc approaches (physician referral, patient database, social media, patient association's referral) and pre-screened via phone by the recruiting agency (Global Prospective) prior to accessing the survey. Patients meeting the selection criteria were invited to complete a 20-minute questionnaire administered in pen-and-paper (France and Germany) or electronic form (Spain and UK). The questionnaire was developed following insights from prior qualitative interviews.

Sample size: As the nature of qualitative research means that there are no calculations per se, the numbers are influenced by resources available and when the data saturation point is reached. Thus, the sample size for the qualitative phase was determined by the survey scope and objectives. Regarding the quantitative phase, there were no a priori hypotheses and the objectives were descriptive in nature. The sample size for the quantitative phase was therefore based on statistical robustness, feasibility and practical considerations.

Data analysis and interpretation: Analyses were conducted using the R software (version 3.5.1) and descriptive statistics. Mean scores were calculated from Likert scales. Administration form differences (IV versus SC) were analysed

using paired *T*-test for comparison of numerical variables and paired Wilcoxon test for comparison of categorical variables. Country differences were analysed using Kruskal–Wallis rank sum test for comparison of numerical variables, Fisher's exact test (small sample) and Pearson's Chi-squared test for comparison of categorical variables. All tests were two tailed, and a value of P values <0.05, two tailed was considered statistically significant, without adjustment for multiplicity.

Results

Patient Demographics and Baseline Characteristics

Qualitative Phase

Nine participants (France, 3; Germany, 2; Spain, 1; UK, 3) were recruited for qualitative interviews; 7 were male (78%) and the mean age was of 65 years (range 43–79 years). At the time of the interview, 1 patient was treated in first-line, 6 in second-line and 2 in third-line. Six respondents had a stem cell transplant, and one had one scheduled at the time of the interview.

Quantitative Survey

Overall, 113 patients (France, 30; Germany, 30; Spain, 23; UK, 30) with MM participated in the quantitative phase. Patients' demographics and baseline characteristics are summarised in Table 1. The average age of the patients at the time of recruitment was 65.1 years old. In Spain, patients were on average younger than in the three other countries (Spain: 56.6 vs UK: 65.5, Germany: 66.9 and France: 69.7). Overall, 54.9% patients switched within the last 12 months, 31.9% between 12 and 24 months and 13.3% between 24 and 26 months. In the UK, 50.0% switched after 24 months (26 months was set as the maximum). The mean age at MM diagnosis was 59.7 years old (52.3 in Spain, 59.2 in the UK, 62.2 in France and 64.4 in Germany). The average time between diagnosis and the start of IV daratumumab infusions was 2.9 years. The average time between the start of IV daratumumab and the start of SC daratumumab was 9.4 months. The average time between the start of SC daratumumab and the informed consent form signature to participate in this survey was 11.7 months. The cut-off for inclusion in the study was 24 months and 26 months for the UK.

Regarding the number of lines of therapy, of the 113 patients included, 15.9% were in first-line, 54.9% in second line and 27.4% in third line. In Spain and UK, all patients were treated in second-line and over. In Germany and France, 46.7% and 13.3% of patients were treated in first-line, respectively. Overall, almost half of patients (48.7%) received stem-cell transplants.

Perception of Health Status and Most Bothering Symptoms

In the quantitative survey, respondents considered their overall health as good with 84.1% being ECOG 0–1 ("normal with no limitation"/ "not my normal self, but able to be up and about with fairly normal activities"), which is in line with what was previously observed in the qualitative phase.

> Considering the myeloma and the chronic kidney disease, I'm in a very good place at the moment. I'm in good health, but obviously having the myeloma and the kidney disease, I am not as fit and healthy as I was pre-diagnosis. UK

This proportion is significantly lower in Spain (65.2% versus 90.0% in France, 90.0% in the UK, 86.7% in Germany, p<0.05) (Table 1). In the qualitative interviews, the most bothering symptoms stated by the majority were pain and fatigue, and a few of the participants mentioned they had to adapt their leisure activities since MM diagnosis because of these symptoms. Regarding their mental health, patients declared feeling good and grateful to be alive despite their disease.

> The most bothering symptom [is] fatigue. Fatigue. Without a doubt, fatigue. Definitely. UK

> Before I was never tired, now I am tired, I told you I was doing the garden, I work in the morning but in the afternoon I rest. France

Table 1 Patient Demographics and Baseline Characteristics

	Total (n=113)	France (n=30)	Germany (n=30)	Spain (n=23)	UK (n=30)
Gender, n (%)					
Male	63 (55.8)	19 (63.3)	16 (53.3)	13 (56.5)	15 (50.0)
Female	50 (44.2)	11 (36.7)	14 (46.7)	10 (43.5)	15 (50.0)
Age, mean (SD); years	65.1 (10.6)	69.7 (10.2)	66.9 (8.3)	56.6 (12.9)	65.5 (7.3)
Age at diagnosis, mean (SD); years	59.7 (11.9)	62.2 (13.5)	64.4 (9.4)	52.3 (13.8)	59.2 (7.8)
ECOG PS, n (%)					
0–1	95 (84.1)	27 (90.0)	26 (86.7)	15 (65.2)	27 (90.0)
≥2	17 (15.0)	2 (6.7)	4 (13.3)	8 (34.8)	3 (10.0)
Unknown	1 (0.9)	1 (3.3)	0 (0)	0 (0)	0 (0)
Duration between the first diagnosis of MM and the starting date of IV daratumumab, mean (SD); years	2.9 (3.1)	4.1 (4.4)	1.0 (1.5)	3.6 (2.9)	2.8 (1.9)
Duration between starting date of IV daratumumab and starting date of SC daratumumab, mean (SD); months	9.4 (6.9)	6.8 (4.8)	6.8 (7.0)	9.8 (8.4)	14.2 (4.4)
Duration between the start of SC daratumumab and study enrolment, months (%)					
≤12 months	62 (54.9)	12 (40.0)	27 (90.0)	21 (91.3)	2 (6.7)
>12 and ≤24 months	36 (31.9)	18 (60.0)	3 (10.0)	2 (8.7)	13 (43.3)
>24 and ≤26 months	15 (13.3)	0 (0)	0 (0)	0 (0)	15 (50.0)
Line of therapy, n (%)					
Front line (1st line)	18 (15.9)	4 (13.3)	14 (46.7)	0 (0)	0 (0)
2nd line	62 (54.9)	15 (50.0)	13 (43.3)	14 (60.9)	20 (66.7)
3rd line	31 (27.4)	9 (30.0)	3 (10.0)	9 (39.1)	10 (33.3)
4th line	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Unknown	2 (1.8)	2 (6.7)	0 (0)	0 (0)	0 (0)
Current treatment, n (%)					
Daratumumab monotherapy	20 (17.7)	5 (16.7)	0 (0)	11 (47.8)	4 (13.3)
Daratumumab - Bortezomib – Dexamethasone	12 (10.6)	2 (6.7)	2 (6.7)	0 (0)	8 (26.7)
Daratumumab – Dexamethasone	22 (19.5)	0 (0.0)	2 (6.7)	2 (8.7)	18 (60.0)
Daratumumab - Lenalidomide - Dexamethasone	24 (21.2)	8 (26.7)	15 (50.0)	1 (4.3)	0 (0.0)
Other regimens	35 (31.0)	15 (49.9)	11 (36.6)	9 (39.2)	0 (0.0)
Stem-cell transplant status for MM, n (%)					
Yes	55 (48.7)	11 (36.7)	6 (20.0)	12 (52.2)	26 (86.7)
No	55 (48.7)	19 (63.3)	23 (76.7)	9 (39.1)	4 (13.3)
Unknown	3 (2.6)	0 (0)	1 (3.3)	2 (8.7)	0 (0)

Abbreviations: ECOG PS, Eastern Cooperative Oncology Group Performance Status; IV, intravenous; SC, subcutaneous; SD, Standard Deviation; MM, Multiple Myeloma; n, number of patients.

Emotional Burden Related to the Administration of Daratumumab IV versus SC

Overall, before receiving daratumumab, patients were significantly less anxious, stressed and nervous before SC injections than IV infusions (mean score: 1.3, 1.1, 1.4 versus 2.1, 2.0, 2.0 respectively, $p<0.001$). On the contrary they were significantly more reassured, ready/well-prepared, usual self and relieved (mean score: 3.8, 4.3, 3.7, 3.6 versus 3.0, 3.6, 3.1, 3.0 respectively, $p<0.001$). The UK was the only country where the form of administration had no impact on the emotional burden of patients before receiving daratumumab injections, except for stress. Patients in the UK were significantly less stressed (mean score: 0.6 versus 0.9, $p<0.05$) before IV infusions than SC injections (Figure 3).

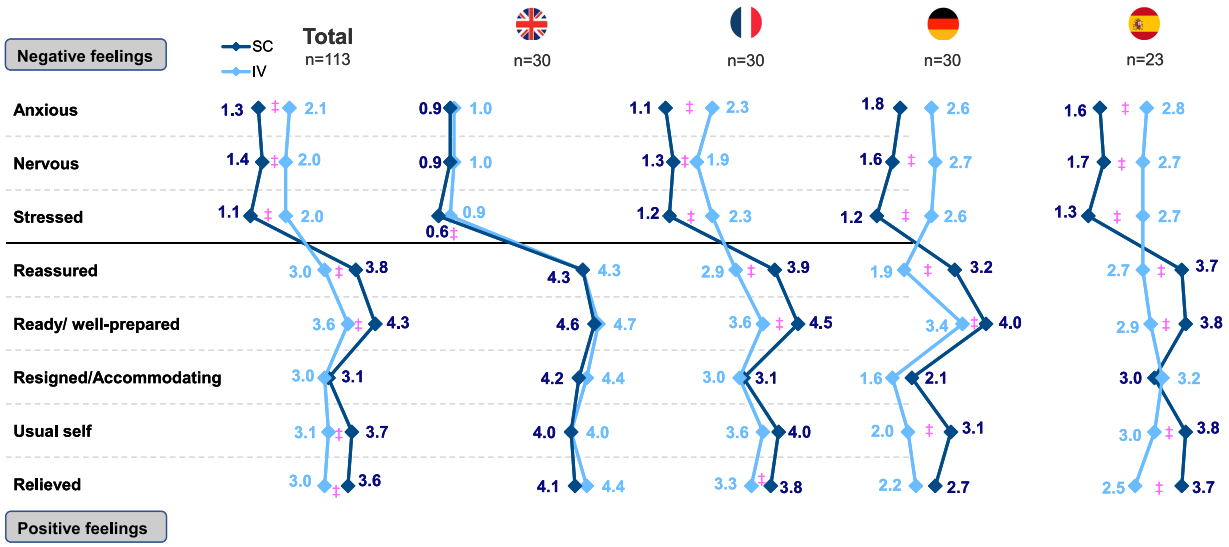

Figure 3 Patients' feelings before receiving injection of daratumumab. Mean score calculated from five-point Likert scale where 0 means "Not all" and 5 means "Yes totally". ‡Indicates a significant difference (p<0.05) between the intravenous (IV) and the subcutaneous (SC) modes of administration.

Overall, while receiving daratumumab, patients were significantly less anxious, stressed, bored, constrained, tired and impatient (mean score: 1.1, 1.1, 1.2, 1.1, 1.8, 1.1 versus 1.8, 1.9, 1.8, 1.7, 2.6, 1.8 respectively, p<0.001) before SC injections than IV infusions. On the contrary they were significantly more reassured, comfortable and relaxed (mean score: 4.0, 4.1, 3.7 versus 3.4, 3.4, 2.9, p<0.001) before SC injections than IV infusions (Figure 4).

Confirming these results, almost all participants to the qualitative study stated they were happy/glad to switch from IV to SC.

> It [SC injection] was an easier, happier change. The truth is that I was glad because […] it's easier. Spain

Even though a few participants still expressed concern over the change.

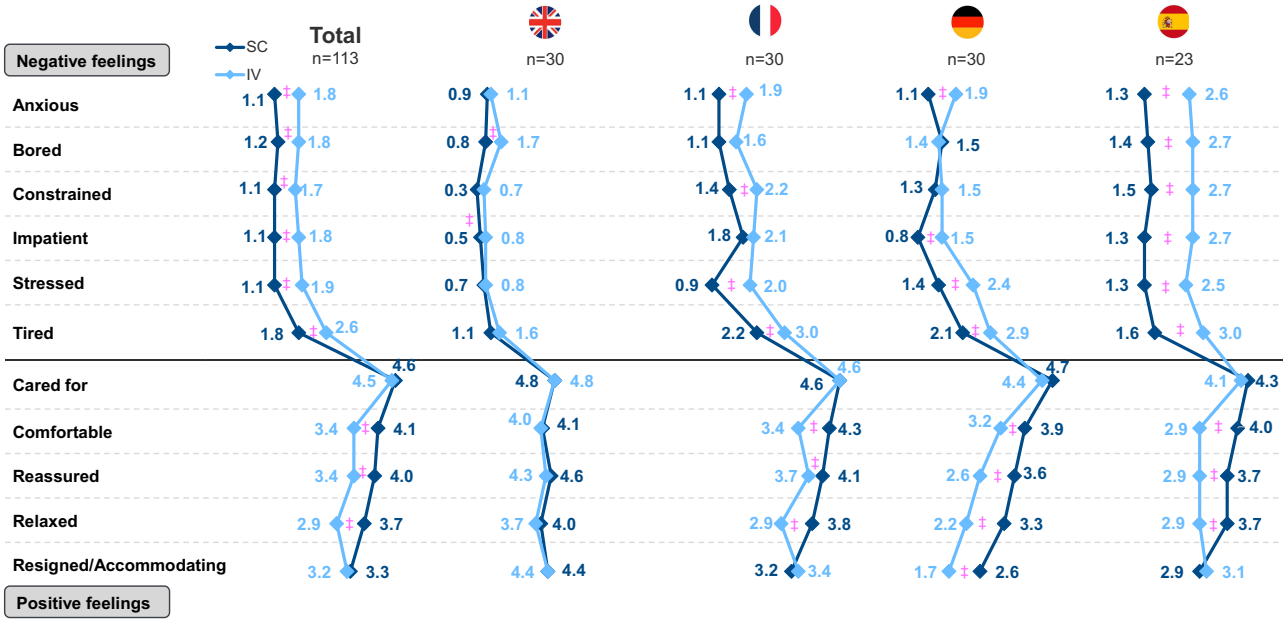

Figure 4 Patients' feelings while receiving injection of daratumumab. Mean score calculated from five-point Likert scale where 0 means "Not all" and 5 means "Yes totally". ‡Indicates a significant difference (p<0.05) between the intravenous (IV) and the subcutaneous (SC) modes of administration.

I was a bit worried about having an injection in my stomach 'cause [the injection takes] quite a long period of time. UK

Level of Well-Being After Receiving Daratumumab

In the quantitative survey, almost all (96.5%) patients were feeling well or very well right immediately after SC first injection versus 77.9% right immediately after their IV first infusion (Figure 5). Almost all (97.3%) patients were feeling well or very well on average right immediately after their SC injections versus 82.3% for the IV infusions (Figure 6). German patients have a better level of well-being immediately after receiving their first SC injection than the overall population (56.7% were feeling very well versus 32.7%; Figure 5) and on average after receiving SC injection (50.0% were feeling very well versus 31.9%; Figure 6).

Patients were in a better shape after receiving their SC injection than after receiving their IV infusion (Figure 7A). More than three quarter (79.6%) patients agreed that they were fit enough to do other activities after receiving their SC injection versus 38.9% after receiving their IV infusion ($p<0.001$). More patients agreed that they recovered quickly after receiving their SC injection than after receiving their IV infusion, 85.8% and 71.7% respectively ($p<0.001$). Only one third (33.6%) agreed that they felt tired after receiving their SC injection versus 65.5% after receiving their IV infusion ($p<0.001$; Figure 7A). These differences between SC and IV in overall state after the injection are less pronounced among UK patients: one third (33.3%) agreed that they felt tired after receiving their SC injection versus 43.3% after receiving their IV infusion. The same proportion of UK patients (83.3%) agreed that they recovered quickly after receiving their SC injection and after receiving their IV infusion.

Illustrating these results, the qualitative study participants expressed the burden of receiving IV and a swifter recovery after switching to SC.

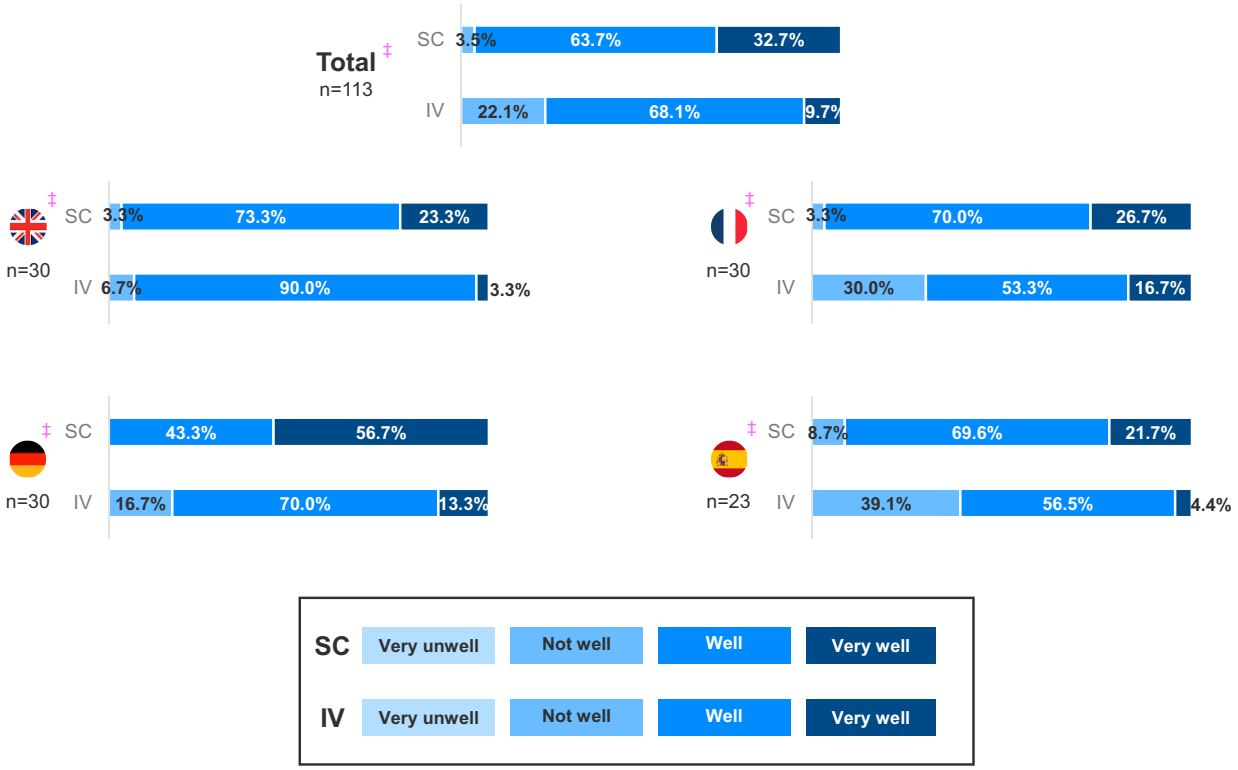

Figure 5 Level of well-being immediately after receiving first injection of daratumumab. ‡Indicates a significant difference ($p<0.05$) between the intravenous (IV) and the subcutaneous (SC) modes of administration.

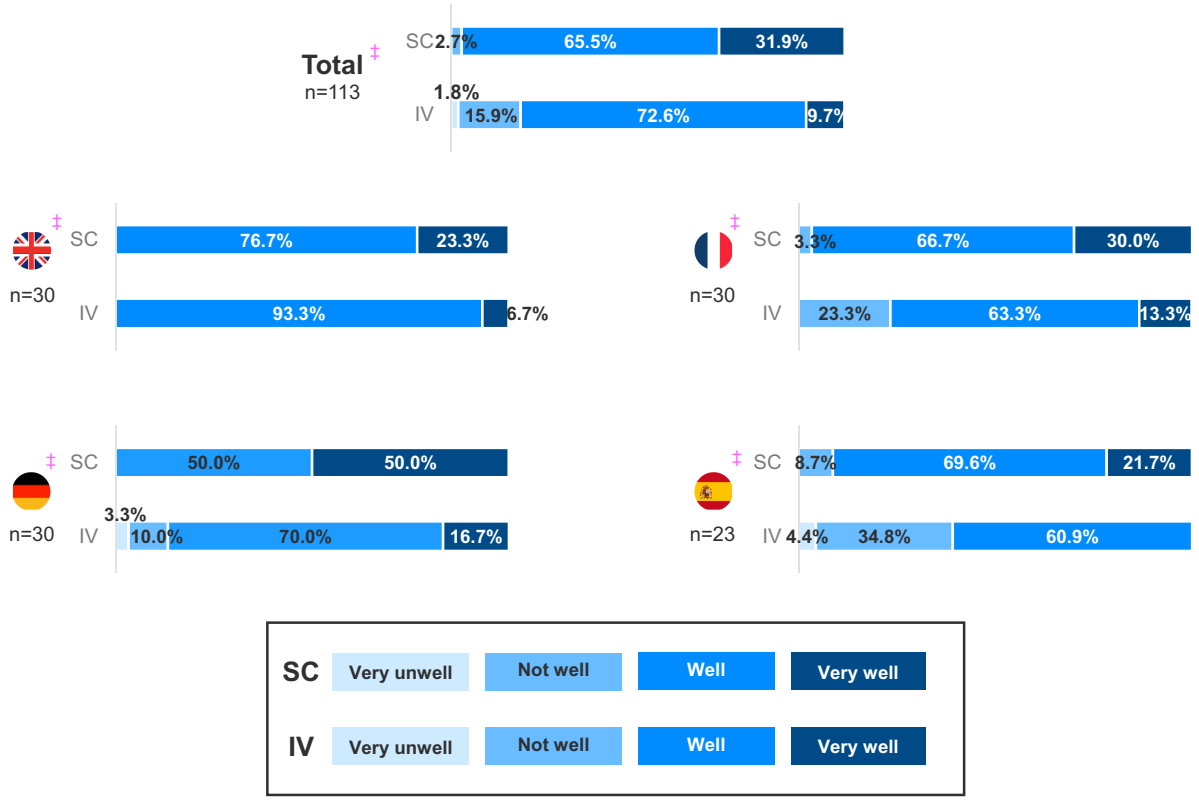

Figure 6 Level of well-being immediately after receiving injections of daratumumab on average. ‡Indicates a significant difference (p<0.05) between the intravenous (IV) and the subcutaneous (SC) modes of administration.

The very first session that I had of the daratumumab [IV], I didn't feel very well at all. I didn't cope with it very well. I couldn't have what they call rapid rate, I had to have it, IV every however many days it was, over a period of four to five hours, I believe. That was a long time. UK

"[With SC] you get back on your feet much quicker, I was able to bake a cake or help with preparing dinner because we have our main meal at night. Often, that wasn't possible after IV administration". Germany

Patient's Perceptions of Daratumumab Route of Administration

Patients perceived their treatment route of administration more positively when it comes to SC form compared to when it comes to IV form (Figure 7B). The overall satisfaction with treatment is very high for both forms but significantly higher for the SC injection: almost all (97.3%) patients agreed that they were satisfied with their SC treatment versus 89.4% when they received their IV infusion (p<0.001). Almost all patients (91.2%) agreed that they were comfortable with their treatment's route of administration when they received their SC injection versus 54.9% for the IV infusion (p<0.001). The patients agreed that their SC treatment was invasive and caused discomfort and/or pain for 21.2% of them (versus 51.3% for IV infusion, p<0.001) and 24.8% of them (versus 30.1% for IV infusion) respectively (Figure 7A). Only 22.1% patients agreed that the whole process of their treatment administration (including pre-tests, pre-medication administration, daratumumab (Darzalex®) infusion, etc.) was burdensome to them when they received their SC injection versus 44.2% for the IV infusion (p<0.001; Figure 7A). These differences on patients' perceptions with daratumumab route of administration between SC and IV injection are less pronounced in the UK (Figures 7A).

Terms such as hassle and hard time were used in the qualitative interviews to describe the IV administration whereas not painful and convenient were used for the SC injection.

About IV: "[I think it's] just the soreness really. It's invasive, isn't it? You know, having to have a needle in your arm and like I say, because you're having all the fluids all the time, and you're drinking lots of water, you go to the loo all the time, so you've got to take your trolley with you, you know. That's a big bit of a hassle. UK

I have very tiny veins, they are very small, they are not visible, and it hurts, I have a hard time. Spain

SC: When the nurse comes the injection she can't do it very quickly, it normally lasts three minutes as the liquid is quite viscous, she can't go any faster, she has to press slowly. But it's not painful at all. France

About SC versus IV: [I said:] Yes, great! Convenient. Long infusion duration is gone. And of course, it also shortens my stay at the outpatient clinic. Germany

This contrast between perceptions of the SC form versus the IV form was somewhat nuanced in the qualitative interviews. For the vast majority of patients, the reassurance of benefiting from having a treatment option available outweighed the invasive route of administration. These patients tended to trust their medical team to give them the best option. As well, for most respondents, efficacy of the treatment comes before administration form.

About IV: It's always annoying but you have no choice. We can't say we are wasting time, it was getting better and better, the pain was going away, it's positive. (…) We have no choice [to go to the hospital], we must take care of ourselves. But I am always trusting, I don't worry. France

After a while I came to terms with [going to the hospital] and eventually came to cope with my changed routines. Things got better then. I was able to live my life. Germany

Time in Hospital

The median time spent in the hospital/clinic when patients received one injection of daratumumab was significantly lower with the SC injection (1.5 hours [IQR: 1.0–2.8]) than with IV infusion (5.0 hours [3.5–7.0]), $p<0.001$. Five German patients, enrolled by the same physician, who answered a duration of 24 hours or more for both IV and SC administration have been excluded from this analysis as they are probably due to a local practice not representative of national practice. The median time spent in the hospital/clinic was higher in the UK for both the SC injection (3.1 hours [2.5–4.0]) and IV infusion (8.5 hours [6.0–9.2]).

Overall, one patient out of ten (11.5%) agreed that the treatment administration process was too long when receiving the SC injection versus 57.5% ($p<001$) when receiving the IV infusion (Figure 7A).

This time saving allowed patients to have more free time: 84.1% patients agreed that they have the time to do other activities immediately after receiving their SC injection versus 29.2% ($p<0.001$) when it comes to the IV infusion (Figure 7B). This has been highlighted in the qualitative interviews too:

[I feel] much better, I get my life back. I don't have to spend so much time in the waiting room and in a hospital. With the current situation now, it has improved quite a bit, to be honest. Spain

[The benefit is] the reduced time, you spend much less time in hospital and the fact that you can go home, you can eat at home, you can have your day, the whole day is not obsessed with the hospital actually. France

It's not a whole day that's taken up by the hospital, I go in my morning like when you go shopping, you come home and you're at home, you eat, and you have your day to yourself. France

Mode of Transport and Indirect Resource Use/Costs of Drug Administration

Patients were asked to rate the financial burden related to the mode of transport from 0 to 6 where 0 means "Not at all a burden" and 5 "A great burden". This financial burden is minimal (0–1) (France, 93.3%; Germany, 76.7%; UK, 76.7%) except in Spain where 21.7% of the participants regarded it as an important burden (4–5). The main mode of transport is the taxi in France (76.7%) and Germany (60.0%). In Spain, 39.1% of the patients have a family member/friend/caregiver who drives them. In the UK, the majority (56.7%) drive themselves.

Figure 7 Administration of daratumumab – Total (n=113) – (**A**) Negative points, (**B**) Positive points. ‡Indicates a significant difference ($p<0.05$) between the intravenous (IV) and the subcutaneous (SC) modes of administration.

The choice of the taxi was confirmed and explained by French respondents during the qualitative phase:

I don't [go to the hospital myself] with the Polaramine that puts me to sleep, most of the time when the taxi comes to pick me up, I'm drowsy. I was a little less sleepy when I was on the infusion because it had time to wear off during the 3.5 hours of infusion, now as I leave immediately afterwards, I am completely asleep and, in the afternoon, I sleep, I might be a danger in the car. France

In the morning the taxi is there, everything is fine. It's very convenient for me because if I had to drive, now that I don't like driving so much, it would be a problem for me. France

Discussion

Following the recent approval of daratumumab SC, there is a lack of data on the real-world experience of patients who received SC treatment to supplement data from randomised clinical trials and to provide insights into the patient experience before and after switching from IV daratumumab to the SC form. Herein, we conducted a mixed-method study, with a qualitative phase followed by a quantitative one, to highlight the experience of MM patients treated with the SC form of daratumumab in four European countries in a real-world setting.

Perception of Health Status and Most Bothering Symptoms

In general, the participants tended to cope well with their MM diagnosis and expressed a positive perception of their health status. However, symptoms such as pain and fatigue forced them to adapt their daily lives and limit their activities.

Overall Perception on the Switch from the IV to the SC Administration

The IV treatment was well accepted, as all patients felt relieved to receive a treatment for the underlying condition and knew that IV administration was a part of their cancer treatment and hence perceived normal. However, IV administration had a clear impact on their lives in terms of organisation and treatment burden. Given its invasive form, the overall IV process timing was mentioned as the most burdensome characteristics of the treatment. Although most patients were used to the process, it clearly affected their daily activities.

All participants welcomed the switch to SC administration as a positive change. While a few patients mentioned experiencing some pain and/or swelling at the injection site, all expressed their high satisfaction with the switch from IV to SC form. In particular, SC treatment was less invasive, not painful and more convenient, and considerably decreased the time spent at the hospital as compared to the IV form. Some participants found SC treatment as less tiring, both physically and mentally, and more comfortable and reassuring than the IV treatment, which allowed them to enjoy their saved time. All participants confirmed that they would rather retain their SC treatment, if given a choice, than switching back to the IV administration.

The preference of patients for the SC form of daratumumab over the IV form observed in this real-world study is in line with results reported from the Phase III COLUMBA study.[11] Based on a survey using a modified version of the Cancer Therapy Satisfaction Questionnaire (CTSQ), the COLUMBA study demonstrated consistently higher mean modified CTSQ scores for the SWT domain over time in the daratumumab SC group in comparison to the daratumumab IV group, and thus an overall higher satisfaction with therapy in the daratumumab SC group. The findings of the present study are also comparable to data reported for other biologic treatments like trastuzumab for HER2-positive breast cancer or rituximab for non-Hodgkin's lymphoma.[12]

Impact of Switching from IV to SC Administration on the Emotional Burden and Quality of Life

In general, patients were willing to go through the tedious treatment procedure and had experienced the benefits of the switch to SC administration. This observation was consistent with high satisfaction among participants, as it improved their treatment journey. They described having more time to themselves and being able to perform more daily activities, which offered them improved quality of life.

In comparison with the IV form, the SC form of daratumumab had a lower impact on the emotional burden of patients both before and while receiving injections in all countries except the UK. In general, patients reported to be significantly less anxious, stressed, and nervous and more reassured, prepared, and relieved prior to receiving SC injections. Further, patients were significantly less anxious, stressed, and tired and more comfortable, reassured, and relaxed while receiving SC injections. The UK was the only country where the differences between the effects of the two forms of administration on the emotional burden were less visible. In the UK, patients were significantly less stressed before receiving IV

infusions than SC injections. Also, they were less bored and impatient while receiving SC injections than IV infusions. Compared with the other countries, patients in the UK had an overall higher level of education (college/ university completed: 63% in the UK vs 7% in France, 20% in Germany and 26% in Spain). A higher level of education might be associated with higher expectations which in turn influence the perception of the quality of life before and after the switch. Furthermore, 50% of the patients in the UK switched to the SC form between 24 and 26 months prior to taking the survey while this proportion was 0% in the other countries. Vice versa, only 7% of the UK patients switched less than 12 months prior to taking the survey while this proportion was considerably higher in the other countries (40% in France, 90% in Germany: 90%, 91% in Spain). The time passed since the switch could also influence how patients feel about the impact of the switch on their quality of life.

Additionally, we observed improvement in patients' health-related quality of life following their switch to the SC form of daratumumab. The time spent at the hospital reduced for SC injection (median of 1.5 hours with SC form vs 5.0 hours with IV form). Patients also reported to recover more quickly from SC treatment, have more time to do other activities immediately after receiving their treatment, and feel less tired and more fit to do other activities. In comparison to the IV administration process, the SC treatment process was reported to be less burdensome and the appointments were easier to schedule.

Remaining Burden with SC Administration

Patients expressed some burden related to the SC form of daratumumab treatment. Overall, 11.5% of patients agreed that the treatment administration process was too long, and 23.9% were uncomfortable with having to go to the hospital for their treatment administration. In addition, 24.8% of patients reported that the treatment caused discomfort and/or pain. In Spain, the financial burden related to the mode of transport was moderate to important for 52.1% of patients.

Study Limitations

Although our study provides a meaningful contribution into the real-world experience of patients switching from IV to SC daratumumab, it is not without certain limitations. The self-reported nature of the survey is associated with potential response biases, such as inaccurate recall and false reporting (whether intentional or unintentional). The online approach in the UK and Spain is subject to selection bias (under-representation of people without access to or comfortable with computers, as well as less healthy, older people, and institutionalized patients, and those with the more severe comorbidities and disabilities). Some patients were not recruited through physician's referral but self-reported their profile. However, they were screened over the phone by a trained recruiter to mitigate this shortcoming. As we asked patients to recall their perception and experience of IV daratumumab, there is a risk of cognitive bias either due to the time elapsed since they had treatment or owing to the fact that the good experience with SC treatment may retrospectively impact their perception of IV daratumumab. However, this can be an advantage, as the study cannot be suspected to overestimate the difference in the perception between daratumumab IV and SC, meaning that the differences observed in our study are a "best case scenario". Further, because of the sampling approach used, our results might not be fully generalizable to the global population of MM patients who switched from IV to SC daratumumab.

Measuring perceptions when patients are receiving daratumumab IV and then when they are receiving daratumumab SC would have been the design with the least possible bias. However, this would not have been possible as most patients treated with daratumumab had already switched to the SC form. Furthermore, such a design – if it were feasible – would have involved higher costs and a more complex logistic compared with a cross-sectional study. In order to limit the recall bias, the delay between the treatment switch and administration of the survey has been limited.

Study Strengths

Despite these limitations, our study has some considerable strengths. Qualitative description offers a minimal theoretical bias by staying close to the real-world data produced by respondents' discourses. Content analysis using a coding structure arising from the data and being refined during analysis offers a dynamic and iterative approach to qualitative data analysis.[13,20] There is no numerical regulation in sample size for in-depth interview studies, apart from the theoretical saturation requirement.[14,15,19,20] Based on previous studies using similar design,[16,17] it was assumed that 9

interviews were an appropriate sample size for the purpose of this survey. It is of note that data saturation was assessed with each additional interview to ensure maximum reliability and validity. The nature of qualitative research means that there are no calculations per se, and the numbers are influenced by resources available and when the data saturation point is reached. One of the main strengths of the survey is the mixed qualitative and quantitative approach. Feeding the quantitative phase with qualitative insights is an ideal method to ensure measurement of the relevant parameters in the quantitative phase and not missing anything important. In-depth interviews are a well-known and proven methodology for collecting personal experiences and meaningful insights on why and how individuals organize their preferences and opinion.[18,22] Qualitative studies analyse phenomena, which can be observed but not measured, highlighting behaviours and actions that might not have been explained with the use of another methodology. Hence, qualitative results are appropriate to determine variables and inform subsequent quantitative studies. Another strength of the survey is the multi-country scope that improves the generalisation of the results. The sample size is robust given the rarity of the condition. The patients were mostly recruited through physician's referral confirming diagnosis and eligibility.

Conclusion

In this study, the SC form of daratumumab had a lower impact on the emotional burden of patients both before and while receiving injections compared to the IV form in all countries except the UK. Although some burden regarding the SC form of daratumumab prevails, we observed an improvement in patients' health-related quality of life following their switch to the SC form of daratumumab. These findings clearly support the SC form as the preferable choice of daratumumab treatment for multiple myeloma patients in clinical practice.

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

Julien Thevenon, Wafae Iraqi and Valeria Magarotto are employees/ shareholders of Janssen. Mrs Valeria Magarotto reports being an employee of Johnson and Johnson outside the submitted work. Xavier Guillaume, Dahbia Horchi, Bleuenn Rault, Marjorie Leclerc and Claire Graziani Taugeron are employees of Oracle France. Kate Morgan and Silene Ten Seldam are employees of Myeloma Patient Europe (MPE) which receives funding from the following sponsors: AbbVie, Amgen, Alexion, BeiGene, Binding Site, Bristol Myers Squibb, GlaxoSmithKline, Janssen, Novartis, Oncopeptides, Pfizer, Regeneron, Roche, Sanofi, Stemline Therapeutics, Takeda, Sebia, Prothena, SkylineDx, Sandoz. Kate Morgan has been a member of the Janssen Global MM Collaboration Council since 2021. The authors report no other conflicts of interest in this work.

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