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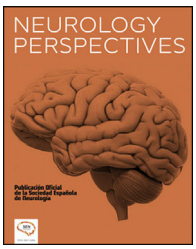

ORIGINAL ARTICLE

Survey on first-line therapeutic management of relapsing–remitting multiple sclerosis in clinical practice in Spain

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KEYWORDS
Relapsing–remitting multiple sclerosis;
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Survey

Abstract
Introduction: Current therapies for relapsing–remitting multiple sclerosis (RRMS) help reduce morbidity and delay disease progression. However, the available information on factors influencing decision-making regarding first-line treatment remain poorly understood.
Methods: Based on a review of the literature and the experience of a scientific committee made up by 2 neurologists, an ad hoc survey was developed and distributed to Spanish neurologists. It included 22 questions related to the first-line therapeutic management of RRMS.
Results: Sixty neurologists (mean age: 45.6 years, 60% women, mean of 16.0 years of experience, mean of 93.8 patients with RRMS attended/month) participated in the study. Neurologists considered that the 3 most important treatment characteristics (1–8 points, with higher scores denoting greater relevance) in treatment decision-making were efficacy in disease control (7.8±0.5), safety/tolerability (6.7±0.9), and improvements in patient quality of life (5.0±1.5); regarding patient characteristics, the 3 most important (1–7 points) were disease activity (6.9±0.5), intention to become pregnant (5.0±1.0), and level of disability (4.3±1.8). Dimethyl fumarate (32.6%) was the most frequently prescribed treatment, followed by teriflunomide (24.8%) and glatiramer acetate (17.6%). According to over 87% of the specialists, the latter drug was considered the most appropriate treatment for patients with liver disorders, who intended to become pregnant, and who presented low disease activity.
Conclusions: Our study provides evidence on the first-line therapeutic management of non-aggressive forms of RRMS and the factors influencing decision-making in routine clinical practice.

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PALABRAS CLAVE
Esclerosis múltiple remitente-recurrente;
Acetato de glatiramero;
Preferencias;
Manejo;
Encuesta

Encuesta sobre el manejo terapéutico en primera línea Para el tratamiento de la esclerosis múltiple recurrente-remitente en práctica clínica española

Resumen
Introducción: Las terapias actuales para la esclerosis múltiple recurrente-remitente (EMRR) ayudan a reducir la morbilidad y retrasar la progresión de la enfermedad. Sin embargo, la información disponible sobre los factores que influyen en la elección de la terapia de primera línea (1 L) es limitada.
Método: Con base a una revisión de la literatura y la experiencia de un Comité científico formado por dos neurólogos se elaboró un cuestionario ad-hoc dirigido a neurólogos españoles que incluía 22 preguntas relacionadas con el abordaje terapéutico en 1 L de la EMRR.
Resultados: Sesenta neurólogos (edad media: 45,6 años, 60% mujeres, experiencia previa: 16,0 años, media de pacientes con EMRR atendidos/mes: 93,8) participaron en la encuesta. Las tres características del tratamiento consideradas más importantes (1 = menos-8 = más importante) para la toma de decisiones fueron la eficacia en el control clínico de la enfermedad (7,8 ± 0,5), la seguridad/tolerabilidad (6,7 ± 0,9) y la mejora de la calidad de vida (5,0 ± 1,5); y del paciente (1 = menos-7 = más importante), la actividad de la enfermedad (6,9 ± 0,5), el deseo gestacional (5,0 ± 1,0) y el grado de discapacidad (4,3 ± 1,8). El dimetil fumarato (32,6%) es el tratamiento más frecuentemente prescrito, seguido de la teriflunomida (24,8%) y el acetato de glatiramero (17,6%). Este último es el considerado más adecuado para pacientes con trastorno hepático, deseo gestacional y una baja actividad de la enfermedad, según más del 87% de los especialistas.
Conclusiones: Nuestro estudio aporta evidencia sobre el manejo terapéutico en 1 L de las formas no agresivas de la EMRR y de los factores que influyen en la toma de decisiones en la práctica clínica habitual.

Introduction

Multiple sclerosis (MS) is an inflammatory neurodegenerative disease characterised by demyelination and the subsequent irreversible axonal damage that occurs as the disease progresses.[1,2] Onset of MS usually occurs in early adulthood, at approximately 25–40 years of age, and the disease more frequently affects women.[1,3]

MS is mediated by an abnormal autoimmune response affecting the central nervous system in genetically predisposed individuals, in whom several environmental factors may influence the development and progression of the disease.[1]

Prevalence studies have shown an overall increase in recent years[3,4]; in Europe, prevalence has increased from 108 cases per 100 000 population in 2013 to 143 cases in 2020.[5] The increase in MS prevalence has also been observed in Spain in the past 2 decades, reaching 80–180 cases per 100 000 population.[6] The most frequent phenotype is relapsing–remitting MS (RRMS), which affects approximately 85% of patients and progresses with relapses and remission periods.[2]

More than 10 disease-modifying therapies (DMT) are currently available for RRMS, including oral and injectable therapies that help delay disease progression and reduce morbidity.[7] Interferon-beta (IFN-β), the first therapy approved for RRMS,[7] and glatiramer acetate (GA) represent the most frequent injectable treatments,[8] showing similar efficacy according to studies directly comparing the 2 drugs.[9,10] Regarding oral treatments, the most frequently used options are teriflunomide and dimethyl fumarate.[3,7] In Spain, clinical practice guidelines[11] and expert consensus documents[8] recommend these drugs as initial treatment for patients with non-aggressive forms of RRMS.

The wide range of first-line therapies available enables tailored treatment and facilitates making switches between drugs where necessary.[12,13] Therefore, decision-making should be based on proper understanding of the action mechanisms of the different drugs and their risk/benefit profiles.[14] In this sense, treatment selection depends on the patient's characteristics, the safety profile of the drug, personal preferences, and clinical data.[8] However, the actual use and main reasons influencing therapeutic decision-making in routine clinical practice are not well understood.

In this context, the main objective of the present study was to explore the current first-line therapeutic management of RRMS in Spanish clinical practice from a neurologist's perspective. Specifically, we aim to describe the use of these drugs, identify the barriers and factors influencing in their selection, determine the most valued characteristics of GA, and establish the profile of patients likely to benefit from this treatment.

Material and methods

Study design and participants

We designed a cross-sectional, observational, descriptive study based on an online survey targeting neurology specialists working at hospitals of all healthcare levels in the Spanish National Healthcare System, which was conducted between September 2022 and February 2023.

An ad hoc survey was designed, based on a literature review on the main aspects related to the first-line therapeutic management of RRMS. The questionnaire was reviewed by 2 neurologists specialising in the management of MS, in order to determine the suitability and comprehensibility of the questions.

Invitations to participate were sent in a personalised e-mail. Using personal and non-transferable access credentials, neurologists could consent to participate in the study, and subsequently access the survey.

Sample size

The sample size was calculated based on the number of neurologists working in the Spanish National Healthcare System (n=1837),[15] and considering that approximately 6% of neurologists are specialists in the management of MS (n=110). Assuming that the majority of the study variables were to be calculated as proportions, and considering the maximum variability criterion,[16] we obtained a minimum sample of 58 specialists.

Survey

The survey included 22 questions (Supplementary Material), addressing: (1) sociodemographic characteristics and professional variables (n=6); (2) decision-making regarding the first-line treatment of MS (n=3); (3) management of RRMS in clinical practice (n=9); and (4) differentiating characteristics of GA (n=4). The majority of questions were closed-ended (dichotomous, polytomous, multiple-choice, 5-point Likert-type, and order of importance). Questions with dichotomous answers were included for such variables as sex, and polytomous questions addressed such variables as autonomous community, level of healthcare, type of consultation, main reason for treatment selection, and treatment of choice with different patient profiles. Multiple-choice questions allowed the selection of several options (3 main reasons for changing treatment, profile of patients benefiting most from treatment with GA, differentiating characteristics of GA with regard to safety profile versus injectable and oral treatments, and most valued characteristics of GA). Likert-type scales were used to grade responses on a scale (frequency of onset of adverse effects, frequency of treatment change, and extent of agreement with certain statements). Questions with answers ranked in order of importance included 7–8 items (treatment and patient characteristics to consider when selecting treatment, and factors influencing the selection of a therapeutic option). Lastly, open-ended questions were used for numerical values (age, years of experience, mean number of patients attended per month, time to diagnosis, time to treatment onset, and percentage of patients switching treatment). Free-text answers were also used (other differentiating characteristics of GA, and an open free-text field for comments).

Statistical analysis

We calculated relative and absolute frequencies for qualitative variables, whereas quantitative variables are expressed as measures of central tendency and dispersion. For both types of variables, we calculated descriptive statistics from the valid data available.

For the statistical analysis of the level of agreement regarding current challenges in the management of RRMS, categories were grouped into disagreement, neutral, and agreement.

Data were analysed using the Stata statistics software, version 14.

Results

Sociodemographic and professional characteristics

A total of 60 neurologists from 13 Spanish autonomous communities and the autonomous city of Ceuta participated in the study. Participants' mean age (SD) was 45.6 (9.5) years, 60% were women, and participants had a mean of 16.0 (9.1) years' experience in the specialty and attended a monthly mean of 93.8 (65.5) patients with RRMS. The majority (81.7%) of neurologists worked at university hospitals. Of all respondents, 38.3% worked at an MS unit, whereas 58.3% worked at specific MS consultations (Table 1).

Decision-making regarding first-line treatment of RRMS

Participants considered that the 3 most relevant characteristics of first-line treatment in the decision-making process were efficacy in the clinical control of the disease, safety/tolerability, and efficacy in reducing the impact on the patient's quality of life (Table 2).

Regarding patient characteristics, neurologists responded that disease activity, intention to become pregnant, and level of disability were the most important characteristics in decision making regarding first-line treatment (Table 2).

Furthermore, respondents suggested that efficacy and safety are the main factors influencing the selection of an alternative drug when a switch in the first-line treatment is required (Table 2).

Management of RRMS in clinical practice

Neurologists estimated that a mean of 3.3 (2.8) months passed between suspicion of RRMS and diagnosis, and 4.8 (3.7) weeks between definitive diagnosis and treatment onset.

Dimethyl fumarate (32.6%) was the most frequently prescribed treatment for non-aggressive forms, and the main reason for prescription of this drug was its efficacy (Table 3). Teriflunomide (24.8%) and GA (17.6%) were

Table 1 Respondents' demographic and professional characteristics.

Variable	
Age in years, mean (SD)	45.6 (9.5)
Sex, *n* (%)	
Men	24 (40.0)
Women	36 (60.0)
Years of specialist experience, mean (SD)	16.0 (9.1)
Patients with RRMS attended per month, mean (SD)	93.8 (65.5)
Type of hospital, *n* (%)	
University hospital (tertiary)	49 (81.7)
Regional hospital (secondary)	9 (15.0)
Community hospital (primary)	2 (3.3)
Type of clinical consultation, *n* (%)	
Specific MS consultation	35 (58.3)
MS unit	23 (38.3)
General neurology	2 (3.3)
Autonomous community, *n* (%)	
Madrid	14 (23.3)
Valencian Community	11 (18.3)
Andalusia	8 (13.3)
Catalonia	6 (10.0)
Galicia	5 (8.3)
Asturias	4 (6.7)
Basque Country	3 (5.0)
Cantabria	2 (3.3)
Castile-Leon	2 (3.3)
Castile-La Mancha	1 (1.7)
Ceuta	1 (1.7)
Canary Islands	1 (1.7)
La Rioja	1 (1.7)
Navarre	1 (1.7)

MS: multiple sclerosis; *n*: sample size; RRMS: relapsing–remitting multiple sclerosis; SD: standard deviation.

Table 2 Order of importance of the treatment and patient characteristics to be considered when selecting a first-line treatment for relapsing–remitting multiple sclerosis, and the most significant factors in the selection of an alternative drug when a treatment switch is required.

	Mean	SD
Treatment characteristics		
Efficacy in the clinical control of the disease	7.8	0.5
Safety/tolerability	6.7	0.9
Efficacy in reducing the impact on the patient's quality of life	5.0	1.5
Speed of action	4.4	2.0
Patient adherence	4.1	1.8
Dosage	3.3	1.3
Administration route	3.0	1.3
Treatment cost	1.8	1.3
Patient characteristics		
Disease activity	6.9	0.5
Intention to become pregnant	5.0	1.0
Level of disability	4.3	1.8
Patient preferences regarding administration route	3.5	1.4
Patient preferences regarding dosage	3.2	1.5
Age	3.1	1.5
Sex	2.0	1.5
Factors influencing the selection of alternative drugs		
Efficacy	8.0	0.2
Safety/tolerability	6.7	1.0
Patient preferences	4.9	1.5
Prior experience	4.6	1.9
Administration route/pharmaceutical formulation	3.9	1.1
Dosage	3.8	1.3
Type of device (pre-filled syringe or pen)	2.2	1.0
Treatment cost	2.1	1.6

Measures of central tendency and dispersion are based on the hierarchy of available options (1: least important; 7–8: most important). SD: standard deviation.

prescribed due to their administration route and safety/tolerability profile, respectively. IFN beta-1a was the most widely used interferon (10.7%). The main reason for prescribing interferons beta-1a and beta-1b was prior experience with these drugs, together with safety in the case of IFN beta-1b, whereas the primary consideration in the case of PEGylated IFN beta-1a was dosage.

Neurologists indicated that a mean of 21.3% (10.6%) of their patients had required a switch of first-line treatment during the year prior to completion of the survey. Of these, a mean of 28.2% (16.7) switched to another first-line treatment, whereas a mean of 71.8% (16.7) switched to a second-line treatment.

Eighty-five percent of participants reported that the main reason for treatment switches was lack of efficacy or inadequate response; other frequent reasons were the onset of adverse effects (76.7%) and lack of tolerability (65.0%) (Fig. 1A). Neurologists reported that the most frequent switches were from injectable treatments (IFN and GA) to oral treatments (dimethyl fumarate and teriflunomide); the least frequent switch was from GA to IFN (Fig. 1B).

A majority of respondents considered that the side effects that occasionally or always/nearly always required

Table 3 Most frequently prescribed treatments and the main reasons for their prescription in patients with relapsing–remitting multiple sclerosis, according to the participating neurologists.

Treatment	Mean	SD	Main reason for prescription
Dimethyl fumarate (%)	32.6	15.1	Efficacy
Teriflunomide (%)	24.8	11.9	Administration route
GA (%)	17.6	13.1	Safety/tolerability
IFN beta-1a (%)	10.7	8.3	Prior experience
PEGylated IFN beta-1a (%)	7.7	7.3	Dosage
IFN beta-1b (%)	4.8	5.3	Safety/tolerability, prior experience
Other (%)	1.8	7.3	Not available

GA: glatiramer acetate; IFN: interferon; SD: standard deviation.

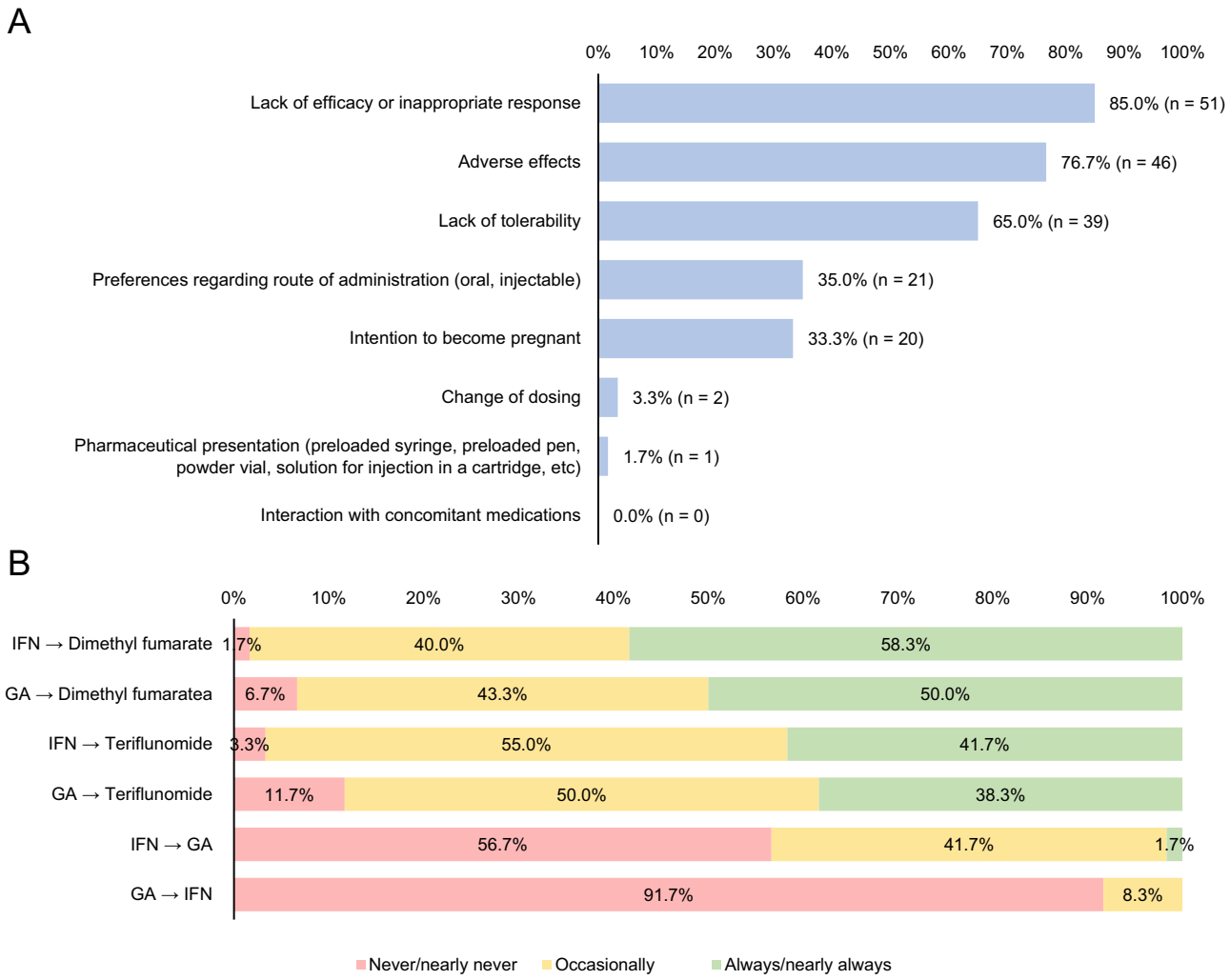

Fig. 1 The main reasons for switching first-line treatments in patients with relapsing–remitting multiple sclerosis (A), and the frequency of treatment switches (B). GA: glatiramer acetate; IFN: interferon.

a treatment switch were lymphocytopenia (83.4%), skin lesions at the injection site (81.7%), gastrointestinal disorders (81.7%), and flu-like symptoms (78.3%). Furthermore, 86.7% of specialists reported that dyspnoea and headache never or nearly never required a treatment switch (Fig. 2).

Participants considered GA to be an adequate treatment for the majority of the patient profiles mentioned, with the drug being especially appropriate for patients with low disease activity (86.7%), who intend to become pregnant (90.0%), and who present liver disorders (91.7%) or other comorbidities (93.3%). Teriflunomide was considered the most appropriate treatment for patients with a high level of fatigue (80.0%) and for those older than 55 years (71.7%) (Fig. 3).

Regarding current challenges in the management of RRMS, neurologists agreed with the majority of statements, underscoring the onset of flu-like symptoms as an obstacle to adherence to first-line treatments (90% agreement) and the low frequency of switches between injectable treatments (80% agreement) (Fig. 4).

Differentiating characteristics of GA

The majority of neurologists reported that the patients benefiting most from treatment with GA are those who intend to become pregnant (95.0%) and those with low disease activity (90.0%) (Fig. 5A).

Regarding safety of treatment, almost all respondents (96.7%) reported that the most distinctive characteristic of GA as compared against the remaining injectable therapeutic options is the lower risk of onset of flu-like symptoms (Fig. 5B). Neurologists also underscored the lower risk of lymphocytopenia (93.3%) with GA, as well as the lower frequency of gastrointestinal problems (91.7%), compared with oral first-line treatments (Fig. 5C).

Lastly, the majority of specialists (96.7%) considered the safety of GA to be its most valued and distinctive characteristics compared with other first-line treatment alternatives. Neurologists also highlighted the cost of GA as a differentiating characteristic, although to a lower extent (65.0%) (Fig. 5D).

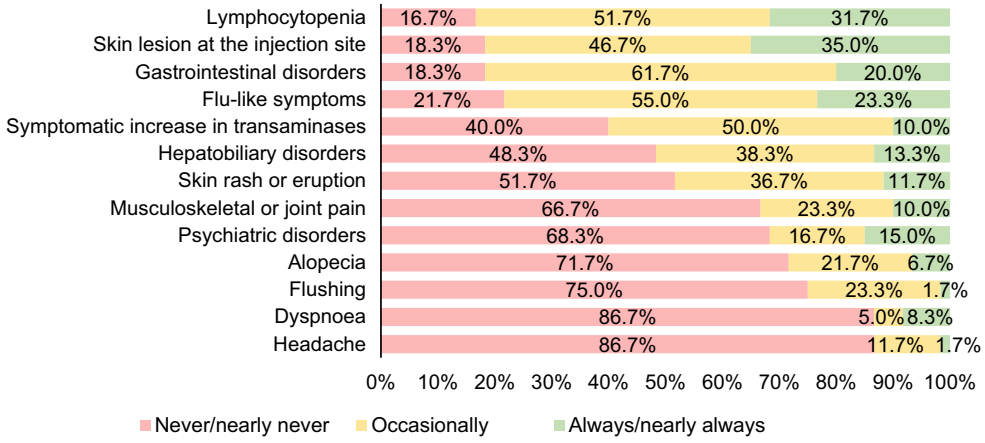

Fig. 2 Frequencies of side effects requiring a first-line treatment switch for relapsing–remitting multiple sclerosis.

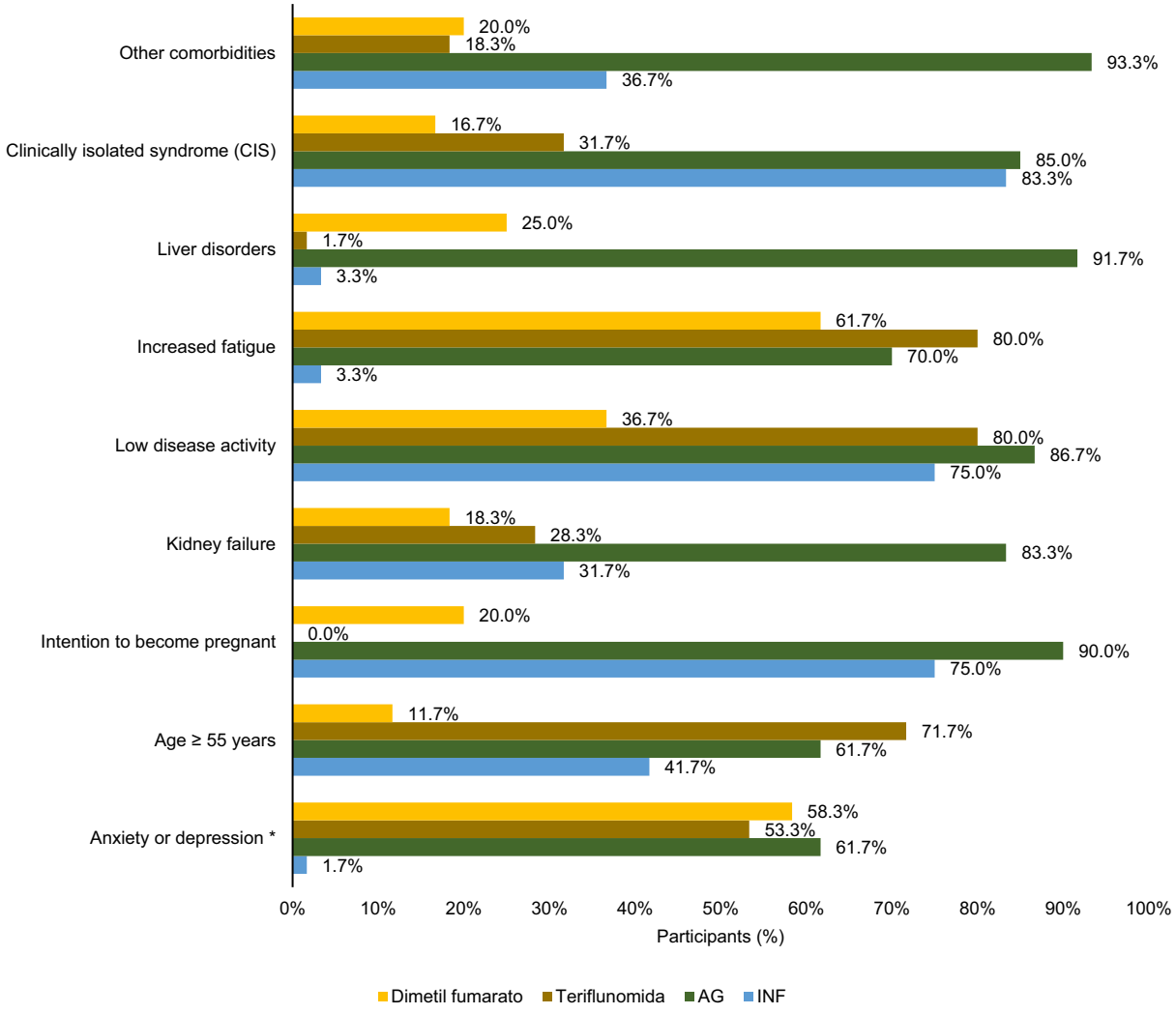

Fig. 3 The most appropriate first-line treatments for different profiles of patients with relapsing–remitting multiple sclerosis.

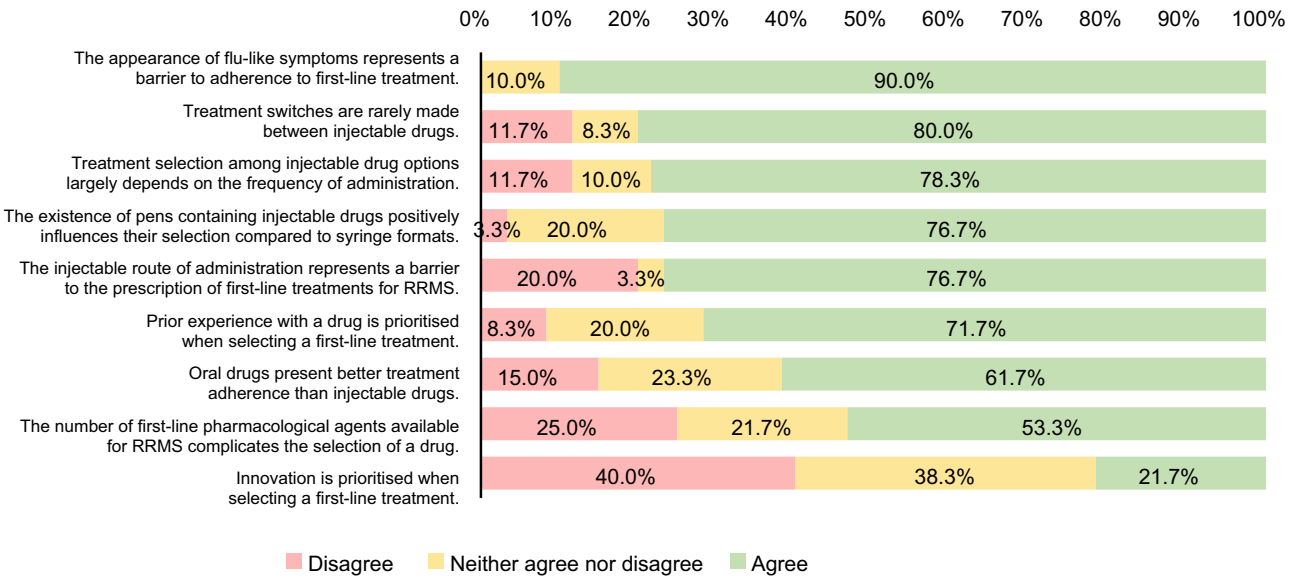

Fig. 4 The levels of agreement regarding the current challenges for the management of relapsing–remitting multiple sclerosis. RRMS: relapsing–remitting multiple sclerosis.

Discussion

This study describes the current management with first-line treatment of non-aggressive forms of RRMS, from the perspectives of 60 neurologists practising in Spain. This is the first study providing evidence on the therapeutic management of this disease in everyday clinical practice in Spain.

In accordance with the recommendations of the British National Institute for Health and Care Excellence (NICE) guidelines for MS, specialists estimated that definitive diagnosis of RRMS is established after a mean delay of approximately 3 months, with a further 5 weeks until treatment is started.[17] These estimations reflect an improvement in healthcare quality for patients with MS with respect to data published in 2010, which showed a median time of 1.6 years from the first clinical manifestation to the first medical consultation, and a further 5.7 months until treatment onset.[18]

European and American guidelines on the management and treatment of MS recommend considering the efficacy and safety of treatment, as well as the characteristics of each patient, before starting or switching treatment.[12,19] In accordance with this, and in line with a similar study performed in the USA,[20] the same characteristics were considered the most important in first-line treatment among the participants in our survey.

Our results suggest that oral treatments are prescribed more frequently than injectable treatments in patients with non-aggressive forms of RRMS, in line with the results of previous studies on the preferred characteristics of DMT.[21-23] Furthermore, respondents estimated that over 20% of their patients had required a treatment switch during the previous year. Although the majority of patients switched to a second-line treatment, the most frequent switch between first-line treatments was from injectable to oral drugs. Although the loss of efficacy and safety/tolerability were the main reasons for switches, preference for an administration route seems also to influence the selection of an alternative treatment.

The majority of specialists agreed that the onset of flu-like symptoms hinders treatment adherence and that the frequency of administration is the main decisive factor in injectable treatments. Similarly, a study of preferences among patients receiving injectable treatments for MS in the United Kingdom and France showed that, for these patients, the decreased frequency of injections and flu-like symptoms were equally as important as treatment efficacy.[21] Similarly, a patient preference study conducted in Spain showed that patients with MS viewed the likelihood of experiencing a lower number of adverse effects as the most important characteristic of a DMT when selecting a treatment.[22] Furthermore, more than half of the surveyed neurologists thought that oral drugs were associated with better treatment adherence than injectable options. The majority believed that the injectable route was an obstacle to their prescription. Contradictory evidence has been reported on the subject: for instance, one previous study showed that patients receiving oral treatment displayed better adherence to treatment than those receiving an injectable treatment, probably due to the greater ease of administration,[23] as previously discussed. On the contrary, other studies conducted in Spain have reported greater adherence in patients receiving intravenous treatment compared with those receiving self-injectable or oral therapies,[24,25] although patients displayed greater satisfaction with oral treatments.[24] These differences may be explained, at least in part, by the fact that intravenous treatments are administered at hospital by a healthcare professional, whereas the other treatments may be administered at home, and therefore present a higher risk of poor adherence due to forgetfulness.[25]

Considering that treatment selection depends on patient characteristics, we asked specialists about the treatment of

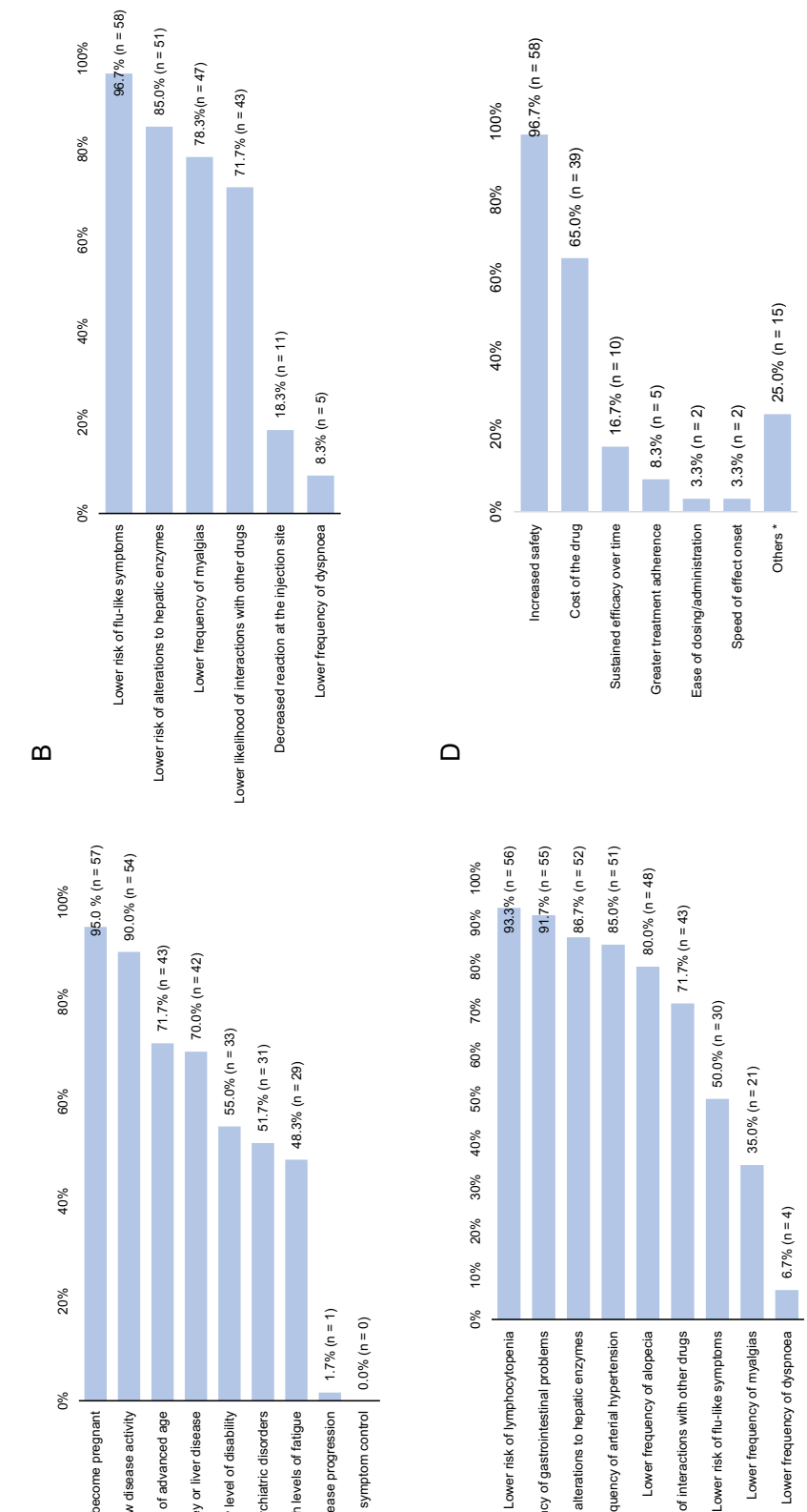

Fig. 5 The differentiating characteristics of glatiramer acetate: patient profiles likely to benefit the most from first-line treatment (A); differentiating characteristics with regard to its safety profile versus the remaining injectable (B) and oral (C) therapeutic options; and differentiating characteristics versus the alternative first-line treatments for relapsing–remitting multiple sclerosis (D). *Other: Possible use in patients intending to become pregnant or breastfeed ($n = 11$); efficacy in patients with IgM oligoclonal bands ($n = 1$); low frequency of side effects ($n = 1$); safety in such other comorbidities as fatigue ($n = 1$), advanced age, and cancer; tolerability ($n = 1$).

choice for certain profiles. The majority of neurologists selected GA as the first therapeutic option for patients with anxiety or depression, and as the second option (after teriflunomide) for patients with a high degree of fatigue; all these symptoms are common in patients with MS and have an impact on their quality of life.[26,27] GA was also the treatment of choice for patients with kidney failure, low disease activity, liver disorders, clinically isolated syndrome, and other comorbidities, as well as the second option (again, after teriflunomide) for patients older than 55 years. Furthermore, in accordance with the recommendations from the European guidelines regarding women of childbearing age,[12] GA was considered the most appropriate treatment for women who intend to become pregnant. Treatment selection for women of childbearing age represents a concern, given the age of onset of MS and its higher prevalence among women.[28] This drug may be used until pregnancy is confirmed, and may be continued during pregnancy, after considering the individual risks and benefits.[29]

One section of the survey aimed specifically to assess the differentiating characteristics of GA. The drug is known to have minimal interactions with certain comorbidities, other drugs, or immune senescence, and may be used in such specific situations as family planning, pregnancy, or vaccination.[30] Therefore, it may be an appropriate treatment option in certain population groups with RRMS, which justifies the importance of knowing the neurologists' opinions in this regard.

As compared with other first-line injectable treatments, the most valued characteristics of GA were the lower risk of flu-like symptoms and liver enzyme alterations, the lower frequency of myalgias, and the lower likelihood of interaction with other drugs. In comparison with oral treatments, important considerations are the lower risk of lymphocytopenia, gastrointestinal problems, arterial hypertension, and alopecia, and once more the lower risk of liver enzyme alterations and the lower likelihood of interaction with concomitant drugs. Accordingly, safety is considered the most valued and distinctive characteristic of GA, in addition to such other characteristics as its low cost, continuous efficacy, and the possibility of using it during pregnancy and breastfeeding. These characteristics of GA, together with lower frequency of flu-like symptoms, favour its use, despite the higher frequency of administration in comparison with other injectable drugs and the increasing number of DMT available.[30,31] Although new therapies may be more efficacious, and aim to prevent disability in the long term in patients with high disease activity, they occasionally represent a risk to patients; in these cases, GA is an appropriate alternative.[30] It should also be considered when implementing a de-escalation strategy after using high-efficacy treatments.

Our study presents certain limitations. Firstly, we cannot establish a causal relationship due to the cross-sectional design of the study. Furthermore, the survey used was specifically created for this purpose, and therefore was not previously validated. The use of closed-ended questions may be a barrier to interpreting the perceptions of the participating neurologists. Finally, caution must be exercised in extrapolating the findings to other contexts, as the management of MS may differ between countries. Despite these limitations, our study presents several strengths: the participating neurologists have extensive experience in the management of MS, and practically the entire Spanish territory was represented. Furthermore, we should underscore the richness of the data of our study, which includes the participation not only of neurologists from specialised units, but also from regional and local hospitals, with or without specific MS consultations. Therefore, the findings of our study reflect the current situation of RRMS in everyday clinical practice in Spain.

In conclusion, our results provide evidence on the first-line therapeutic management of RRMS in everyday clinical practice, and may be useful in optimising the management of the disease and the use of DMT according to patients' profiles. The information obtained, regarding both treatment- and patient-related factors, influences decision-making and may contribute to facilitating and improving the treatment of non-aggressive forms of RRMS.

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Patient informed consent

Not applicable. The study required no patient intervention.

Ethical considerations

As no patient participated in this study, no classification from the Spanish Agency of Medicines and Medical Devices or approval by any clinical research ethics committee was required. The study population included neurology specialists; no patient data are reported. The participants (physicians) were informed about the study through an information sheet and voluntarily consented to participate in the study.

Declaration of competing interest

ML has received fees for consulting on advisory boards and for speaking at meetings, attending congresses, and participating in clinical trials and other research projects sponsored by Almirall, Bayer, Biogen-Idec, Bristol Myers Squibb, Janssen, Merck-Serono, Teva, Novartis, Roche, Sandoz, and Sanofi-Genzyme. GF is an employee of Viatris Pharmaceuticals. LB-P an employee of Outcomes'10, an independent research organisation engaged and funded by Viatris Pharmaceuticals to coordinate the study. EM has received fees for consulting on advisory boards and for speaking at meetings, attending congresses, and participating in clinical trials and other research projects sponsored by Almirall, Bayer, Biogen-Idec, Bristol Myers Squibb, Janssen, Merck-Serono, Teva, Novartis, Roche, Sandoz, and Sanofi-Genzyme.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.neurop.2024.100178.

References

1. Dobson R, Giovannoni G. Multiple sclerosis - a review. Eur J Neurol. 2019;26:27–40. https://doi.org/10.1111/ene.13819.
2. Attia MS, Ewida HA, Abdel Hafez MA, El-Maraghy SA, El-Sawalhi MM. Altered Lnc-EGFR, SNHG1, and LincRNA-Cox2 profiles in patients with relapsing-remitting multiple sclerosis: impact on disease activity and progression. Diagnostics (Basel). 2023:13. https://doi.org/10.3390/diagnostics13081448.
3. Baskaran AB, Grebenciucova E, Shoemaker T, Graham EL. Current updates on the diagnosis and management of multiple sclerosis for the general neurologist. J Clin Neurol. 2023;19:217–29. https://doi.org/10.3988/jcn.2022.0208.
4. Hittle M, Culpepper WJ, Langer-Gould A, Marrie RA, Cutter GR, Kaye WE, et al. Population-based estimates for the prevalence of multiple sclerosis in the United States by race, ethnicity, age, sex, and geographic region. JAMA Neurol. 2023. https://doi.org/10.1001/jamaneurol.2023.1135.
5. The Multiple Sclerosis International Federation. Atlas of MS.3rd Edition. The Multiple Sclerosis International Federation (MSIF); September 2020.
6. Perez-Carmona N, Fernandez-Jover E, Sempere AP. Epidemiology of multiple sclerosis in Spain. Rev Neurol. 2019;69:32–8. https://doi.org/10.33588/rn.6901.2018477.
7. Comi G, Radaelli M, Soelberg Sørensen P. Evolving concepts in the treatment of relapsing multiple sclerosis. Lancet. 2017;389:1347–56. https://doi.org/10.1016/s0140-6736(16)32388-1.
8. García Merino A, Ramón Ara Callizo J, Fernández Fernández O, Landete Pascual L, Moral Torres E, Rodríguez-Antigüedad Zarrantz A. Consensus statement on the treatment of multiple sclerosis by the Spanish Society of Neurology in 2016. Neurologia. 2017;32:113–9. https://doi.org/10.1016/j.nrl.2016.02.026.
9. Mikol DD, Barkhof F, Chang P, Coyle PK, Jeffery DR, Schwid SR, et al. Comparison of subcutaneous interferon beta-1a with glatiramer acetate in patients with relapsing multiple sclerosis (the REbif vs Glatiramer Acetate in Relapsing MS Disease [REGARD] study): a multicentre, randomised, parallel, open-label trial. Lancet Neurol. 2008;7:903–14. https://doi.org/10.1016/s1474-4422(08)70200-x.
10. Lublin FD, Cofield SS, Cutter GR, Conwit R, Narayana PA, Nelson F, et al. Randomized study combining interferon and glatiramer acetate in multiple sclerosis. Ann Neurol. 2013;73:327–40. https://doi.org/10.1002/ana.23863.
11. Grupo de trabajo de la Guía de práctica clínica sobre la atención a las personas con esclerosis múltiple. Guía de práctica clínica sobre la atención a las personas con esclerosis múltiple.Agència d'Informació, Avaluació i Qualitat en Salut. Servei Català de la Salut. Departament de Salut. Generalitat de Catalunya; 2012.
12. Montalban X, Gold R, Thompson AJ, Otero-Romero S, Amato MP, Chandraratna D, et al. ECTRIMS/EAN guideline on the pharmacological treatment of people with multiple sclerosis. Eur J Neurol. 2018;25:215–37. https://doi.org/10.1111/ene.13536.
13. Rotstein D, Montalban X. Reaching an evidence-based prognosis for personalized treatment of multiple sclerosis. Nat Rev Neurol. 2019;15:287–300. https://doi.org/10.1038/s41582-019-0170-8.
14. Winkelmann A, Loebermann M, Reisinger EC, Hartung HP, Zettl UK. Disease-modifying therapies and infectious risks in multiple sclerosis. Nat Rev Neurol. 2016;12:217–33. https://doi.org/10.1038/nrneurol.2016.21.
15. Barber P, González López-Valcárcel B. Estimación de la oferta y demanda de médicos especialistas. España 2018–2030. 2019:61.
16. Marrugat J, Vila J, Pavesi M, Sanz F. Estimation of the sample size in clinical and epidemiological investigations. Med Clin (Barc). 1998;111:267–76.
17. The National Institute for Health and Clinical Excellence. Multiple Sclerosis in Adults: Management; 2022.
18. Fernández O, Fernández V, Arbizu T, Izquierdo G, Bosca I, Arroyo R, et al. Characteristics of multiple sclerosis at onset and delay of diagnosis and treatment in Spain (the Novo Study). J Neurol. 2010;257:1500–7. https://doi.org/10.1007/s00415-010-5560-1.
19. Rae-Grant A, Day GS, Marrie RA, Rabinstein A, Cree BAC, Gronseth GS, et al. Practice guideline recommendations summary: disease-modifying therapies for adults with multiple sclerosis: report of the Guideline Development, Dissemination, and Implementation Subcommittee of the American Academy of Neurology. Neurology. 2018;90:777–88. https://doi.org/10.1212/wnl.0000000000005347.
20. Hanson KA, Agashivala N, Wyrwich KW, Raimundo K, Kim E, Brandes DW. Treatment selection and experience in multiple sclerosis: survey of neurologists. Patient Prefer Adherence. 2014;8:415–22. https://doi.org/10.2147/ppa.S53140.
21. Poulos C, Kinter E, van Beek J, Christensen K, Posner J. Preferences of patients with multiple sclerosis for attributes of injectable multiple sclerosis treatments in the United Kingdom and France. Int J Technol Assess Health Care. 2018;34:425–33. https://doi.org/10.1017/s0266462318000491.
22. Garcia-Dominguez JM, Muñoz D, Comellas M, Gonzalbo I, Lizán L, Polanco Sánchez C. Patient preferences for treatment of multiple sclerosis with disease-modifying therapies: a discrete choice experiment. Patient Prefer Adherence. 2016;10:1945–56. https://doi.org/10.2147/ppa.S114619.
23. Thach AV, Brown CM, Herrera V, Sasane R, Barner JC, Ford KC, et al. Associations between treatment satisfaction, medication beliefs, and adherence to disease-modifying therapies in patients with multiple sclerosis. Int J MS Care. 2018;20:251–9. https://doi.org/10.7224/1537-2073.2017-031.
24. Morillo Verdugo R, Ramírez Herráiz E, Fernández-Del Olmo R, Roig Bonet M, Valdivia García M. Adherence to disease-modifying treatments in patients with multiple sclerosis in Spain. Patient Prefer Adherence. 2019;13:261–72. https://doi.org/10.2147/ppa.S187983.
25. Soria C, Prieto L, Lázaro E, Ubeda A. Factors associated with therapeutic adherence in multiple sclerosis in Spain. Patient Prefer Adherence. 2023;17:679–88. https://doi.org/10.2147/ppa.S401962.
26. Lakin L, Davis BE, Binns CC, Currie KM, Rensel MR. Comprehensive approach to management of multiple sclerosis: addressing invisible symptoms-a narrative review. Neurol Ther. 2021;10:75–98. https://doi.org/10.1007/s40120-021-00239-2.
27. Tervonen T, Fox RJ, Brooks A, Sidorenko T, Boyanova N, Levitan B, et al. Treatment preferences in relation to fatigue of patients with relapsing multiple sclerosis: a discrete choice experiment. Mult Scler J Exp Transl Clin. 2023;9. https://doi.org/10.1177/20552173221150370 20552173221150370.
28. Villaverde-González R. Updated perspectives on the challenges of managing multiple sclerosis during pregnancy. Degener Neurol Neuromuscul Dis. 2022;12:1–21. https://doi.org/10.2147/dnnd.S203406.
29. Canibaño B, Deleu D, Mesraoua B, Melikyan G, Ibrahim F, Hanssens Y. Pregnancy-related issues in women with multiple sclerosis: an evidence-based review with practical recommendations. J Drug Assess. 2020;9:20–36. https://doi.org/10.1080/21556660.2020.1721507.

30. Mirabella M, Annovazzi P, Brownlee W, Cohen JA, Kleinschnitz C, Wolf C. Treatment challenges in multiple sclerosis - a continued role for glatiramer acetate? Front Neurol. 2022;13, 844873. https://doi.org/10.3389/fneur.2022.844873.
31. Zecca C, Disanto G, Sacco R, Riccitelli GC, Gobbi C. Use of glatiramer acetate between 2010-2015: effectiveness, safety and reasons to start GA as first or second line treatment in Swiss multiple sclerosis patients. BMC Neurol. 2019;19:159. https://doi.org/10.1186/s12883-019-1383-6.