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Neurologist Preferences for New Multiple Sclerosis Treatments: Implications for Market Access Prioritization in the United States and Europe

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INTRODUCTION

- Multiple sclerosis (MS) is a progressive, neurodegenerative, immune-mediated disease characterized by inflammatory lesions in the protective layer surrounding the brain and spinal cord, encompassing relapsing and progressive forms, including relapsing-remitting, secondary progressive, and primary progressive.[1,2]
- While disease modifying therapies for MS have expanded, treatment options for progressive forms of MS (secondary progressive MS [SPMS] and primary-progressive MS [PPMS]) remain limited, with minimal impact on disability progression and cognition. Non-relapsing, nonactive SPMS represents the greatest unmet patient need, with only one treatment currently pending approval for use in this phenotype from the European Medicines Agency's Committee for Medicinal Products for Human Use. Emerging therapies may help address progression earlier in the disease course.
- This study quantified neurologists' market access priorities for MS treatments by assessing how treatment benefits, risks, administration, and cost influence access decisions and the trade-offs neurologists are willing to make to address unmet clinical needs.

OBJECTIVE

- The objective of this study was to determine the relative importance of different aspects of MS treatments to neurologists when prioritizing MS treatments for market access across progressive and relapsing phenotypes, with a focus on addressing unmet needs beyond relapsing disease alone.

METHODS

- An online survey with a discrete-choice experiment was developed using insights from a targeted literature review and dedicated qualitative interviews.
- Board-certified neurologists treating MS patients for at least a year and residing in the US, UK, Germany, Italy, France, and Spain were recruited by a specialized health research organization from February to April 2024 to explore trends and heterogeneity across major access markets.
- Physicians selected their most preferred and second most preferred option for market access between three alternatives: two hypothetical treatments or a "no new treatment" option in each of 12 choice tasks (**Figure 1**).
  - The performance of each hypothetical treatment was described by nine attributes (**Table 1**), for which attribute levels were systematically varied across alternatives and tasks according to an experimental design.

Figure 1. Example Discrete-choice Experiment Task Choice

Imagine that you are being consulted on prioritizing access for new multiple sclerosis treatments. In your first choice, you can recommend making Treatment A available, recommend making Treatment B available, or decide that none of the treatments should receive market access. Afterwards, you are asked to make the same choice but with your preferred choice option being removed. The presented treatments are the only ones available for market authorization; if you decide that neither of them should be made available, the current treatment landscape will remain unchanged. In each choice, features that were the same across Treatment A and Treatment B were shaded in.

Please consider all the presented information within the context of the currently available treatment landscape.

NO NEW TREATMENT	TREATMENT A	TREATMENT B
None of the treatments should receive market access, and the current treatment landscape should **remain the same.**	RRMS / Active SPMS / Non-relapsing SPMS / PPMS; 12m; No confirmed disability worsening/progression; Continuous disability worsening/progression; MONTHS ON TREATMENT; Baseline (treatment initiation)	RRMS / Active SPMS / Non-relapsing SPMS / PPMS; 0m; Continuous disability worsening/progression; MONTHS ON TREATMENT; Baseline (treatment initiation)
	20% reduction in annualized relapse rates	Not applicable
	Cognitive functioning is **maintained**	Cognitive functioning **improves**
	Infusion once every six months (twice a year)	**Oral pill once or twice daily**
	4% (4 out of 100 people) risk of serious infection within two years	**4% (4 out of 100 people)** risk of serious infection within two years
	8% (8 out of 100 people) risk of serious liver event within two years	**4% (4 out of 100 people)** risk of serious liver event within two years
	Cannot be given if planning a pregnancy or during pregnancy	**Cannot be given** if planning a pregnancy or during pregnancy
	20% more expensive to healthcare system than an average branded DMD	**20% less expensive** to healthcare system than an average branded DMD
☐	☐	☐

Abbreviations: DMD = disease-modifying drug; PPMS = primary progressive multiple sclerosis; RRMS = relapsing-remitting multiple sclerosis; SPMS = secondary progressive multiple sclerosis

Note: In each choice scenario, up to two attributes were the same and were highlighted in a different color than the others.

- Data were analyzed using a mixed-logit-model to derive the maximum contribution of improvements in the nine attributes to participants' prioritization decisions conditional on the attribute levels shown (relative attribute importance [RAI]) and the maximum increase in risk participants would accept (maximum acceptable risk) in exchange for improvements in other attributes.

Table 1. Attributes and Levels

Attributes	Levels
Multiple sclerosis indication	· Relapsing-remitting multiple sclerosis · Active secondary progressive multiple sclerosis · Non-relapsing secondary progressive multiple sclerosisa · Primary progressive multiple sclerosis[a] · All multiple sclerosis phenotypes
Time to confirmed disability worsening/progression	· Continuous disability worsening/progression · 6 months until confirmed disability worsening/progression · 12 months until confirmed disability worsening/progression · 24 months until confirmed disability worsening/progression
Reduction in annualized relapse rates	· Not applicable[a] · 20% reduction in annualized relapse rates · 40% reduction in annualized relapse rates · 60% reduction in annualized relapse rates
Impact of treatment on cognitive functioning	· Cognitive functioning improves · Cognitive functioning is maintained · Cognitive function declines
Mode and frequency of administration	· Oral pill once or twice daily · Injection three times a week · Injection once daily · Infusion once every 6 months (twice a year)
Risk of serious infection within 2 years	· 0% risk of serious infection within 2 years · 4% risk of serious infection within 2 years · 8% risk of serious infection within 2 years
Risk of serious liver event within 2 years	· 0% risk of serious liver event within 2 years · 4% risk of serious liver event within 2 years · 8% risk of serious liver event within 2 years
Effect on pregnancy	· Can be given if planning a pregnancy or during pregnancy · Cannot be given if planning a pregnancy or during pregnancy
Cost to the healthcare system	· No change in cost to healthcare system compared to an average branded DMD · 20% more expensive to healthcare system than an average branded DMD · 20% less expensive to healthcare system than an average branded DMD

[a]The levels for "multiple sclerosis indication" and "reduction in annualized relapse rate" were constrained such that: If multiple sclerosis indication = secondary progressive multiple sclerosis or primary progressive multiple sclerosis, then reduction in annualized relapse rate = not applicable;primary progressiveIf multiple sclerosis indication = relapsing-remitting multiple sclerosis, secondary progressive multiple sclerosis, or all multiple sclerosis phenotypes, then reduction in annualized relapse rate = 20%, 40%, or 60%

RESULTS

Participants

- 302 neurologists (US: n=150, 49.67%; UK: n=30, 9.93%; Germany: n=31, 10.26%; Spain: n=31, 10.26%; Italy: n=30, 9.93%; France: n=30, 9.93%) completed the online survey.
- Overall, participating neurologists had 18 years of experience on average treating MS patients. Around half of neurologists practice in university hospital/academic centers and in urban areas. Brief descriptive characteristics are presented in **Table 2**.

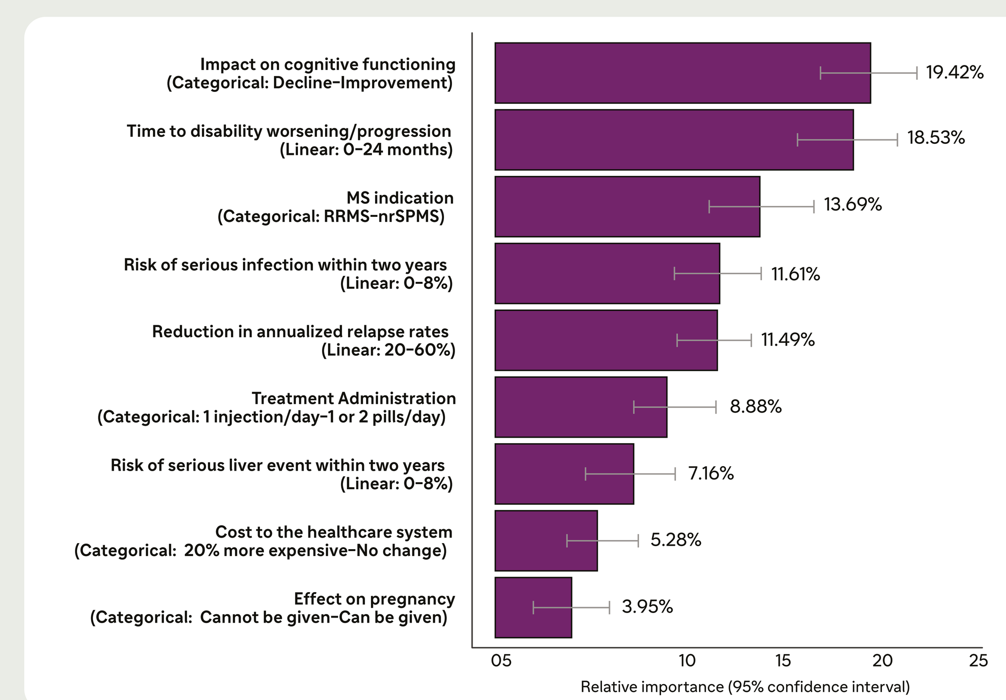
Table 2. Clinical and Sociodemographic Characteristics

Characteristics	Overall (N=302)	US (n=150; 49.67%)	Europe (n=152; 50.33%)
Sex at birth, male, n, (%)	233 (77.15%)	118 (78.67%)	115 (75.66%)
Age (in years), mean (SD)	49.56 (10.03)	48.73 (11.40)	50.38 (8.42)
Years treating multiple sclerosis patients, mean (SD)	18.22 (9.83)	17.40 (12.15)	19.02 (6.74)
Primary type of clinic/facility, n (%)			
Small private practice (five or fewer medical doctors)	51 (16.89%)	36 (24.00%)	15 (9.87%)
Large private practice (over five medical doctors)	52 (17.22%)	45 (30.00%)	7 (4.61%)
Public/community hospital	55 (18.21%)	19 (12.67%)	36 (23.68%)
University hospital/academic center	141 (46.69%)	50 (33.33%)	91 (59.87%)
Other hospital	3 (0.99%)	0 (0.00%)	3 (1.97%)
Primary practice setting, n (%)			
Rural/countryside	23 (7.62%)	10 (6.67%)	13 (8.55%)
Suburban	79 (26.16%)	67 (44.67%)	12 (7.89%)
Urban areas and cities	200 (66.23%)	73 (48.67%)	127 (83.55%)
Number of unique multiple sclerosis patients treated in past year, mean (SD)			
Clinically isolated syndrome	22.94 (33.59)	21.89 (30.53)	23.97 (36.43)
Relapsing-remitting multiple sclerosis	121.48 (145.30)	115.77 (161.29)	127.12 (127.86)
Active secondary progressive multiple sclerosis	33.04 (45.78)	29.99 (48.07)	36.06 (43.34)
Non-relapsing secondary progressive multiple sclerosis	32.44 (47.61)	32.16 (54.05)	32.72 (40.44)
Primary progressive multiple sclerosis	25.81 (37.71)	23.90 (37.58)	27.70 (37.87)
Other phenotypes	10.67 (12.47)	0.40 (0.55)	15.80 (12.41)

Preference Results

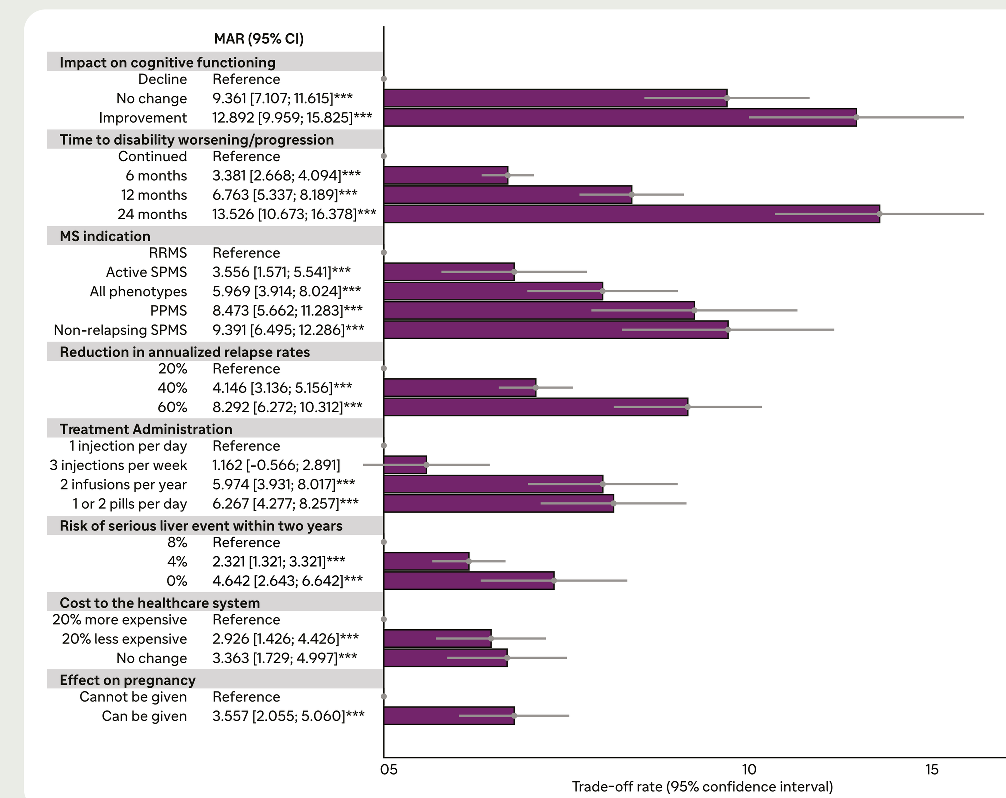
- RAI Scores
  - Achieving improvement instead of a decline in cognitive functioning (RAI=19%) and increasing the time-to-worsening disability from 0 to 24 months (RAI=19%) had the biggest impact on decisions to prioritize market access. Providing market access for treatments addressing progression from early MS stages over those for relapsing-remitting multiple sclerosis (RRMS) alone (RAI=14%) was the third-most important attribute. Achieving a 60% instead of 20% reduction in relapse rate (RAI=11%) was relatively less important.
  - Altogether, benefits accounted for nearly half (∑RAI=49%) of all market access prioritization decisions. Among risks, reducing the risk of serious infection from 8% to 0% within 2 years was considered to be most important (RAI=12%) followed by reducing the risk of serious liver events (RAI=7%).
  - Though relatively less important considerations, physicians prioritized treatments given orally or via infrequent (twice a year) infusions, treatments with lower healthcare costs, and treatments able to be given during pregnancy.
  - Full RAI results outlined in **Figure 2.**
- MAR Trade-offs
  - Maximum acceptable risk was computed as the maximum increase in the 2-year risk of serious liver events or serious infection events that is acceptable to neurologists in exchange for a gain in a benefit, such as an improved clinical outcome, a preferred administration mode, or a reduced risk of another adverse event, when prioritizing market access for treatments.
    - Participants were willing to accept up to 3.56% (95% CI, 1.57–5.54) increase in risk of serious infection for a new treatment indicated for active SPMS, 5.97% (95% CI, 3.91–8.02) increase for a new treatment indicated for all phenotypes, 8.47% (95% CI, 5.66–11.28) increase for a new treatment indicated for PPMS, or 9.39% (95% CI, 6.50–12.29) increase for a new treatment indicated for non-relapsing SPMS rather than prioritizing market access for a new treatment indicated for RRMS (**Figure 3**).
    - Participants were willing to accept up to 4.35% (95% CI, 1.65–7.04) increase in the risk of serious liver events for a new treatment indicated for active SPMS, 7.80% (95% CI, 4.99–10.62) increase for a new treatment indicated for all phenotypes, 12.40% (95% CI, 8.18–16.62) increase for a new treatment indicated for non-relapsing SPMS, or 12.47% (95% CI, 8.18–16.62) increase for a new treatment indicated for PPMS rather than prioritizing market access for a new treatment indicated for RRMS (**Figure 4**).

Figure 2. Relative Attribute Importance



Abbreviations: MS = multiple sclerosis; nrSPMS = non-relapsing secondary progressive multiple sclerosis; RRMS = relapsing-remitting multiple sclerosis

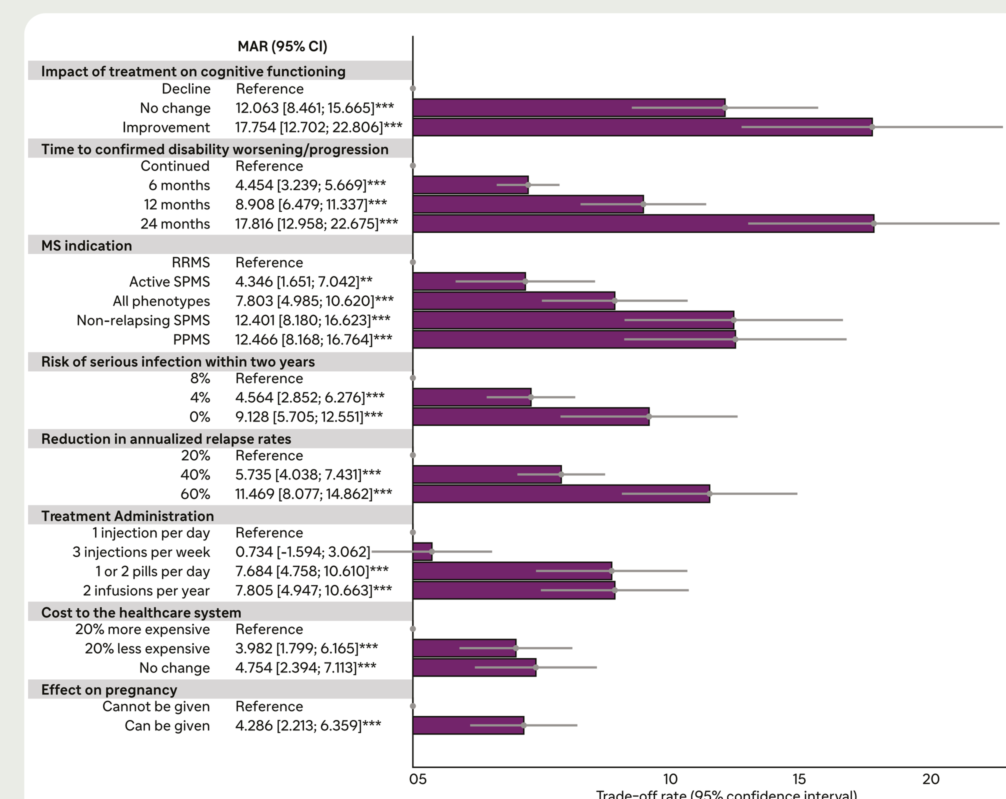
Figure 3. Maximum Acceptable Risk of Serious Infection Within 2 Years



Abbreviations: MAR = maximum acceptable risk; MS = multiple sclerosis; PPMS = primary progressive multiple sclerosis; RRMS = relapsing-remitting multiple sclerosis; SPMS = secondary progressive multiple sclerosis

Significance: *** P<0.001; ** P<0.01; * P<0.05

Figure 4. Maximum Acceptable Risk of Serious Liver Event Within 2 Years



Abbreviations: MAR = maximum acceptable risk; MS = multiple sclerosis; PPMS = primary progressive multiple sclerosis; RRMS = relapsing-remitting multiple sclerosis; SPMS = secondary progressive multiple sclerosis

STRENGTHS & LIMITATIONS

- Key strengths of the study include a best-practice study design involving a dedicated qualitative phase and rigorous testing of the preference survey before fielding for main data collection and a robust physician sample comprising neurologists from a variety of practice types and settings and countries.
- As with all stated preference methods, it is possible that responses to hypothetical scenarios may not reflect participant's actual decisions in a clinical setting. However, carefully designed preference instruments have the potential to predict real-world choices.[3]
- Additionally, participants had to process nine attributes in each choice task, which is more than the five to seven attributes typically included in discrete-choice experiments[4] and represents a substantial amount of information, even for physicians who may be accustomed to handling large volumes of information. However, this study took extensive measures to minimize cognitive burden for participants using illustrative depictions of attributes and levels, which were pilot tested with 20 neurologists.

Main takeaway: Neurologists valued treatments with significant benefits for cognitive functioning and disability progression. When making market access recommendations they prioritized access for phenotypes that currently have limited treatment options.

CONCLUSIONS

- This is the first preference study eliciting neurologists' preferences for prioritizing new MS treatments for market access.
- Neurologists participating in this study demonstrated a clear preference to prioritize market access for treatments for MS phenotypes where there are currently fewer treatment options available, specifically non-relapsing secondary progressive MS, PPMS, and active secondary progressive MS over RRMS.
- Neurologists' treatment choices were most influenced by potential improvements to cognitive functioning, increased time-to-worsening disability, improved options for MS phenotypes other than RRMS, reducing relapse rate, and preventing risks such as serious infection and serious liver events.
- Overall, the study findings highlight the importance of emphasizing disability progression, cognition, and progressive disease benefits in market access submissions for emerging MS therapies.

Disclosures

SM, GF, JW, and SH are employees of PPD™ Evidera™ Patient-Centered Research, Thermo Fisher Scientific, who received funding from Sanofi to conduct this work. JW and SH are minority stockholders of Thermo Fisher Scientific as part of their employment with Thermo Fisher Scientific. JVW and NG are employees of Sanofi and may hold stocks or stock options in the company.

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