Preferences of Patients for Features of Injectable, Oral, and Infused Disease-Modifying Treatments for Relapse-Remitting Multiple Sclerosis

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CONCLUSION

- Patient preferences for MS treatments are diverse, reflecting the heterogeneity of the MS disease course and underscoring the importance of a shared-decision framework in which patients share information about the outcomes and features they value most with physicians.

BACKGROUND

- Patients with multiple sclerosis (MS) exhibit considerable heterogeneity in terms of clinical features, pathogenesis, and response to treatment.[1]
- Consequently, clinical guidelines for MS do not recommend a single treatment pathway; instead, individualized treatment decisions should consider an individual patient's clinical profile, the benefits and risks of the available therapies, and patient preference.[2,3]

OBJECTIVE

- To quantify the preferences of German patients with MS for attributes of disease-modifying treatments and examine subgroups with distinct preferences.

METHODS

- A discrete-choice experiment (DCE) survey was developed following best practices,[4] pretested, and administered online.
- Respondents were recruited from an Internet panel of people who were willing to participate in online surveys.
- Eligibility criteria: self-reported physician diagnosis of MS, at least 18 years of age, and able to read and understand German to provide informed consent and complete the survey instrument.
- Each respondent was asked to answer the treatment choice questions as if their health status was one of two randomly assigned baseline health conditions to ensure that treatment benefit was described consistently across respondents (Table 1). One of the randomly assigned baseline health conditions represented a less advanced disease status than the other (Table 1).
- Each choice question (Figure 1) asked the respondent to choose between a pair of hypothetical disease-modifying therapies, where each therapy is characterized by 7 attributes with varying levels (Table 2).
- Latent-class logit regression analysis[5] was used to analyze the choice data.
  - This model probabilistically identifies classes in the sample without having to rely on preidentified subgroups.
  - Information criteria (i.e., Bayesian information criterion, Akaike's information criterion, and modified Akaike's information criterion [AIC3]) were evaluated and then plotted to understand the number of classes.[6]
  - For each latent segment, the latent-class model yields log-odds relative preference weights for each attribute level in Table 1. The weights indicate the strength of preference for the corresponding level.
  - Logit regression analysis examined respondent characteristics associated with likely class membership.
  - Prior to the implementation of the latent-class logit regression analysis, a subgroup analysis examined whether preferences varied systematically by assigned baseline health condition.
- Conditional relative importance—the maximum change in utility achievable with any attribute, conditional on the levels chosen for the attributes in the study—was calculated as the difference between the preference weight for the attribute level with the highest preference weight and the preference weight for the level of the same attribute with the lowest preference weight.

Table 1. Patient Reference Conditions

Better Reference Condition	Worse Reference Condition
No walking problems	Need cane only for long distances
• You have mild symptoms, and some are noticeable to others. • They do limit your activities or lifestyle a little bit. • You do not have any problems with your walking that are noticeable to others.	• You have problems with your walking that are noticeable to others. You can walk at least 8 meters without a cane or crutch. You often need a cane, crutch or some other form of support to walk longer distances, especially when walking outside.

Note: Each respondent was randomly assigned to one of the reference conditions before answering the choice questions.

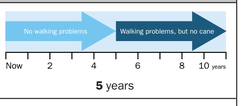
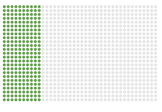
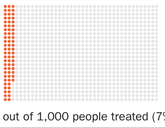
Table 2. Attributes and Attribute Levels for DCE

Type of Attribute	Attribute	Level
Treatment benefit	Number of years until disability progression	2 years 5 years 8 years 10 years
	Number of relapses in the next 10 years	3 relapses in the next 10 years 5 relapses in the next 10 years 8 relapses in the next 10 years
Treatment administration	Mode of administration	Oral tablet Subcutaneous injection Intramuscular injection IV infusion[a]
	Dosing frequency	2 times per year (once every 6 months) 12 times per year (once a month) 52 times per year (once a week) 730 times per year (twice a day)
Treatment risks	Risk of mild side effect	None 100 out of 1,000 people treated (10%) 250 out of 1,000 people treated (25%) 400 out of 1,000 people treated (40%)
	Risk of moderate side effect	None 50 out of 1,000 people treated (5%) 200 out of 1,000 people treated (20%) 300 out of 1,000 people treated (30%)
	Risk of severe side effect	None 10 out of 1,000 people treated (1%) 70 out of 1,000 people treated (7%) 100 out of 1,000 people treated (10%) 150 out of 1,000 people treated (15%)

IV = intravenous.

[a] The experimental design was restricted such that IV infusions could be administered only 2 or 12 times per year and would not be taken 52 or 730 times per year. This restriction was based on pretest interview findings that physicians believed that more frequent IV dosing is not feasible or realistic.

Figure 1. Sample Choice Question

Medicine Feature	Medication A	Medication B
Number of years until MS symptoms progress	 **5** years	 **5** years
Number of relapses in the next 10 years	**3** relapses in the next 10 years	**8** relapses in the next 10 years
How you take the medicine	Oral tablet	Intravenous infusion
How often you take the medicine	52 times per year (once every week)	2 times per year (once every 6 months)
Risk of a mild side effect	 100 out of 1,000 people treated (10%)	 250 out of 1,000 people treated (25%)
Risk of a moderate side effect	 50 out of 1,000 people treated (5%)	0 out of 1,000 people treated (0%)
Risk of a severe side effect	0 out of 1,000 people treated (0%)	 70 out of 1,000 people treated (7%)
Which medicine would you choose if these were the only two medicines available?		

RESULTS

- 301 patients completed the survey. Average respondent age was 46 years; 60% were female, 52% reported having relapsing-remitting MS, and 70% did not need a walking aid on most days. Approximately 8% of respondents were first diagnosed with MS less than a year before taking the survey. Of those who were diagnosed more than a year before taking the survey, the median time since diagnosis was 10 years.
- Subgroup analysis indicated that patient preferences did not vary systematically across assigned baseline health conditions. Consequently, the respondents assigned to the 2 baseline health conditions were pooled in the patient preference analysis.
- All three information criteria indicated that there were two classes with distinct preferences.

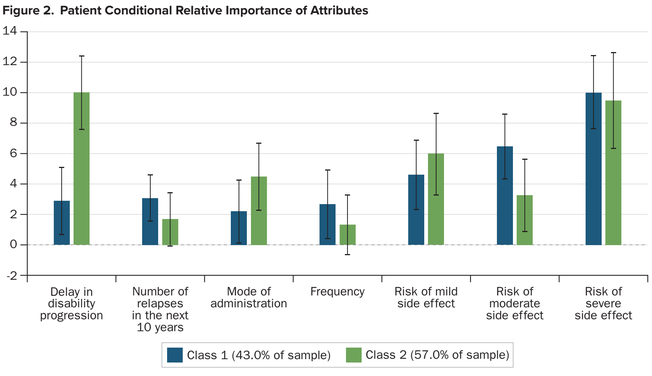
Class 1: Side Effect Risk Minimizing

- Members of this class (43% of the sample) were risk-focused and placed greatest importance (conditional on levels in the study) on minimizing risks of severe, moderate, and mild adverse events (AEs), followed by avoiding relapses and delaying progression. Dosing frequency and mode were least important to this subgroup (Figure 2).
- Members of this class were more likely to be female (odds ratio [OR] = 2.151; P = 0.017) and more likely to have children (OR = 2.065; P = 0.019).

Class 2: Delay Maximizing and Severe Risk Minimizing

- Members of this class (57% of the sample) were efficacy and severe AE focused and placed the greatest importance on delaying progression and minimizing risks of severe AEs. The next most important attributes were risks of mild AEs and mode of administration. Dosing frequency and avoiding relapses were least important to this subgroup (Figure 2).
- Members of this class were less likely to be female (P = 0.017) and less likely to have children (P = 0.019).

Figure 2. Patient Conditional Relative Importance of Attributes



DISCLOSURES This study was sponsored by Biogen (Cambridge, MA, USA). CP and BM are employees of RTI Health Solutions, and RTI Health Solutions was paid to conduct the research. CW and EK are employees of and stockholders of Biogen. TS was a paid consultant to Biogen. **REFERENCES** **1.** Disanto G, Berlanga AJ, Handel AE, Para AE, Burrell AM, Fries A, et al. Heterogeneity in multiple sclerosis: scratching the surface of a complex disease. Autoimmune Dis. 2010 Dec 9;2011:932351. **2.** 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. Mult Scler. 2018 Feb;24(2):96-120. **3.** 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 Apr 24;90(17):777-88. **4.** Bridges JF, Hauber AB, Marshall D, Lloyd A, Prosser LA, Regier DA, Johnson FR, Mauskopf J. Conjoint analysis applications in health—a checklist: a report of the ISPOR Good Research Practices for Conjoint Analysis Task Force. Value Health. 2011;14(4):403-13. **5.** Greene WH, Hensher DA. A latent class model for discrete choice analysis: contrasts with mixed logit. Transp Res Part B Methodological. 2003;37(8):681-98. **6.** Thiene M, Galletto L, Scarpa R, Boatto V. Determinants of WTP for Prosecco wine: a latent class regression with attitudinal responses. Brit Food J. 2013 Feb 8;115(2):279-99. **CONTACT INFORMATION** Christine Poulos, PhD; Senior Economist; RTI Health Solutions, 3040 East Cornwallis Road, Research Triangle Park, NC 27709; Phone: +1.919.541.7130, Fax: +1.919.541.7222, E-mail: cpoulos@rti.org

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