Relationship Between Treatment Satisfaction and Other Patient-Reported Outcomes

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CONCLUSIONS

- **In patients with relapsing MS switching to fingolimod or remaining on SoC DMT, treatment satisfaction (TSQM Global Satisfaction) correlated consistently with all PROs, including TSQM Effectiveness, Convenience, and Side Effects subscales, activities of daily living (PRIMUS-Activities), fatigue (FSS), depression (BDI-II), and quality of life (SF-36).**
  - **Correlations were strongest for the TSQM Effectiveness subscale.**
- **These results suggest that patient satisfaction with MS therapy may reflect a variety of improvements, therapy effectiveness being a primary factor.**

INTRODUCTION

- Fingolimod, a first-in-class sphingosine 1-phosphate receptor modulator, was the first oral therapy approved in the United States and more than 60 other countries for treatment of relapsing multiple sclerosis (MS).[a]
- Fingolimod 0.5 mg demonstrated superior efficacy vs intramuscular (IM) interferon (IFN) β-1a in the pivotal phase 3 Trial Assessing Injectable Interferon Versus Oral Fingolimod in Relapsing-Remitting Multiple Sclerosis (TRANSFORMS), with a 52% reduction in annualized relapse rate (ARR; fingolimod, 0.16; IFNβ-1a IM, 0.33; $P<0.001$).[1]
- In a 1-year extension, patients switching from IFNβ-1a IM to fingolimod 0.5 or 1.25 mg exhibited within-group ARR reductions of 30% and 36%, respectively, vs the core phase.[2]
- There are no data on patient satisfaction after switching to fingolimod, although numerous patient-reported outcomes (PROs) are available to assess patient perspectives on treatment efficacy in MS.[3]
- The phase 4 study to Evaluate Patient Outcomes, Safety, and Tolerability of Fingolimod (EPOC; NCT01216072) sought to assess PROs and physician assessments of a change in therapy to fingolimod 0.5 mg once daily vs standard-of-care (SoC) disease-modifying therapy (DMT) in patients with relapsing forms of MS who are candidates for change in DMT.
  - This post hoc analysis assessed the relationship between patient satisfaction and other PROs after 3 or 6 months of randomized treatment.

METHODS

Study Design

- EPOC was a 6-month, randomized, open-label, multicenter study in the United States and Canada.
- Patients were randomized 3:1 to fingolimod or SoC DMT for 6 months with no washout period.
- The protocol and informed consent forms were reviewed and approved by an institutional review board or independent ethics committee at each study center, and each patient provided written informed consent.

Patients

- Patients were 18–65 years of age with relapsing forms of MS (2005 revised McDonald criteria[4]) and an Expanded Disability Status Scale (EDSS) score of 0–5.5.
- Patients were required to be fingolimod-naive, to have received continual treatment for ≥6 months with a single SoC DMT (IFNβ-1b subcutaneous [SC] 0.25 mg every other day, IFNβ-1a IM 30 µg once weekly, IFNβ-1a SC 22 or 44 µg 3 times weekly, or glatiramer acetate [GA] SC 20 mg once daily), and to be candidates for therapy change.
- Key exclusion criteria were significant cardiac history; macular edema; active infection; treatment with natalizumab, immunosuppressants, immunoglobulins, or monoclonal antibodies ≤6 months before screening; live or live attenuated vaccines ≤1 month before screening; treatment with cladribine, cyclophosphamide, or mitoxantrone at any time; and current treatment with class Ia or class III antiarrhythmic drugs.

[a]*The approved indication may vary from country to country. In the United States, it is approved for the treatment of patients with relapsing forms of MS. In the EU, fingolimod is approved for treatment of patients with highly active relapsing-remitting MS.*

Patient-Reported Outcomes

- Screening and months 3 and 6
  - The Treatment Satisfaction Questionnaire for Medication (TSQM) Global Satisfaction, Effectiveness, Convenience, and Side Effects scales[5]
  - The Fatigue Severity Scale (FSS)[6]
  - The Beck Depression Inventory (BDI)-II[7]
- Screening and month 6
  - The Patient-Reported Indices for Multiple Sclerosis (PRIMUS)–Activities scale, an assessment of activities of daily living[3]
  - The Short Form Health Survey (SF)–36 v2 standard mental and physical health summary scores

Statistical Analysis

- This post hoc analysis assessed cross-sectional correlations between the TSQM Global Satisfaction scale, the primary study endpoint, and secondary PROs at 3 months (TSQM, FSS, and BDI-II) and 6 months (all) using Spearman rank-order correlation.

RESULTS

Patients

- 1053 patients were randomized, 790 (75.0%) to fingolimod 0.5 mg and 263 (25.0%) to SoC DMT; demographics and clinical characteristics are shown in **Table 1**.

Table 1. Patient demographics and clinical characteristics (randomized set)

Characteristic	Fingolimod 0.5 mg (n=790)	SoC DMT (n=263)
Mean (SD) age, y	46.0 (9.8)	45.1 (9.8)
Women, n (%)	601 (76.1)	208 (79.1)
Race, n (%)		
White	642 (81.3)	211 (80.2)
Black	113 (14.3)	43 (16.3)
Native American	4 (0.5)	1 (0.4)
Asian	3 (0.4)	0
Other	28 (3.5)	8 (3.0)
Mean (SD) duration of MS symptoms, y	12.1 (8.4)	11.7 (8.4)
Mean (SD) number of relapses		
Past year	0.8 (1.2)	0.8 (1.3)
Past 2 years	1.4 (2.0)	1.4 (1.9)
Mean (SD) EDSS score	2.4 (1.3)	2.4 (1.3)
Previous MS treatments, n (%)		
Glatiramer acetate	263 (33.3)	92 (35.0)
IFNβ-1a IM	205 (25.9)	60 (22.8)
IFNβ-1a SC	196 (24.8)	65 (24.7)
IFNβ-1b	125 (15.8)	46 (17.5)
Other	1 (0.1)	0

DMT=disease-modifying therapy; EDSS=Expanded Disability Status Scale; IFN=interferon; IM=intramuscular; MS=multiple sclerosis; SC=subcutaneous; SoC=standard of care.

Patient-Reported Outcomes Assessed at Months 3 and 6

- In the fingolimod and SoC DMT groups, TSQM Global Satisfaction score significantly correlated with TSQM Effectiveness, Convenience, and Side Effects scale scores at months 3 and 6 (**Table 2**; each $P<0.001$).
  - Correlations were strongest for the TSQM Effectiveness subscale (month 3: fingolimod, $r=0.70$; SoC DMT, $r=0.71$; month 6: fingolimod, $r=0.68$; SoC DMT, $r=0.71$).
  - Correlations were of similar magnitude in each treatment arm with the exception of Convenience scale scores, for which the correlation was lower for fingolimod (month 3, $r=0.39$; month 6, $r=0.31$) than SoC DMT (month 3, $r=0.54$; month 6, $r=0.53$).

Table 2. Spearman rank-order correlation coefficients* for TSQM Effectiveness, Convenience, and Side Effects scale scores vs TSQM Global Satisfaction score at months 3 and 6 (full-analysis set, LOCF)

Subscale	Fingolimod 0.5 mg (n=789)	SoC DMT (n=263)
TSQM Effectiveness		
Month 3	0.70	0.71
Month 6	0.68	0.71
TSQM Convenience		
Month 3	0.39	0.54
Month 6	0.31	0.53
TSQM Side Effects		
Month 3	0.35	0.31
Month 6	0.33	0.33

DMT=disease-modifying therapy; LOCF=last observation carried forward; SoC=standard of care; TSQM=Treatment Satisfaction Questionnaire for Medication.
**All correlations were statistically significant at $P<0.001$.*

- The correlations between TSQM Global Satisfaction score and fatigue (FSS) and depression (BDI-II) total scores were also significant in both treatment groups at months 3 and 6 (**Table 3**; $P<0.001$).
  - The *r* values for FSS at 3 and 6 months were –0.26 and –0.24 for fingolimod and –0.38 and –0.36 for SoC DMT, respectively.
  - The *r* values for BDI-II at 3 and 6 months were –0.29 and –0.33 for fingolimod and –0.32 and –0.28 for SoC DMT, respectively.

Table 3. Spearman rank-order correlation coefficients* for FSS and BDI-II scores vs TSQM Global Satisfaction score at months 3 and 6 (full-analysis set, LOCF)

	Fingolimod 0.5 mg (n=789)	SoC DMT (n=263)
FSS total score		
Month 3	–0.26	–0.38
Month 6	–0.24	–0.36
BDI-II total score		
Month 3	–0.29	–0.32
Month 6	–0.33	–0.28

BDI-II=Beck Depression Inventory-II; DMT=disease-modifying therapy; FSS=Fatigue Severity Scale; LOCF=last observation carried forward; SoC=standard of care; TSQM=Treatment Satisfaction Questionnaire for Medication.
**All correlations were statistically significant at $P<0.001$.*

Patient-Reported Outcomes Assessed at Month 6

- In both treatment groups, TSQM Global Satisfaction score significantly correlated with the PRIMUS-Activities score and the SF-36 physical and mental health component summary measures (**Table 4**; $P<0.001$; last observation carried forward).
  - The *r* values for PRIMUS-Activities were –0.28 for fingolimod and –0.27 for SoC DMT.
  - The *r* values for the SF-36 physical and mental health summary scores were 0.29 and 0.29, respectively, for fingolimod and 0.25 and 0.31 for SoC DMT, respectively.

Table 4. Spearman rank-order correlation coefficients* for PRIMUS-Activities and SF-36 scores vs TSQM Global Satisfaction score at month 6 (full-analysis set, LOCF)

Outcome	Fingolimod 0.5 mg (n=789)	SoC DMT (n=263)
PRIMUS-Activities	–0.28	–0.27
SF-36 physical health summary score	0.29	0.25
SF-36 mental health summary score	0.29	0.31

DMT=disease-modifying therapy; LOCF=last observation carried forward; PRIMUS=Patient-Reported Indices for Multiple Sclerosis; SF-36=Short Form Health Survey-36; SoC=standard of care; TSQM=Treatment Satisfaction Questionnaire for Medication.
**Statistically significant at $P<0.001$ except for bodily pain scale in the SoC DMT group, which was $P=0.02$.*

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Disclosures

D. Kantor has served as a director, officer, partner, employee, advisor, consultant, or trustee for Allergan, Acorda, Avanir, Biogen, Novartis, Questcor, Genzyme, and Teva; has served as a speaker or a member of a speakers bureau for Allergan, Acorda, Avanir, Biogen, Novartis, Questcor, Genzyme, and Teva; has received research support from Allergan, Acorda, Avanir, Biogen, Novartis, Questcor, Genzyme, and Teva; and has received income in an amount equal to or greater than $250 from Allergan, Acorda, Avanir, Biogen, Novartis, Questcor, Genzyme, and Teva. S. Li has served as a consultant to Novartis, TechData, and Celgene. N. Agashivala, R. Hashmonay, P. Chin, and E. Kim are employees and stockholders of Novartis Pharmaceuticals Corporation.

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