Treatment Satisfaction and Clinical Improvement After Switch to Fingolimod

DX29

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CONCLUSIONS

- **Patients reported significantly greater treatment satisfaction with regard to Global Satisfaction, Effectiveness, Side Effects, and Convenience after therapy change to fingolimod vs continued treatment with SoC DMT.**
  - **Satisfaction with Convenience was notably increased from baseline to month 6.**
- **There was physician-perceived clinical improvement at 6 months in the fingolimod 0.5-mg group but not in the SoC DMT group.**
- **AE patterns were similar to those observed in phase 3 trials, and AE rates were as expected given the study design.**
  - **A high proportion of patients in the SoC DMT group remained on their prerandomization DMT (ie, were not experiencing tolerability or safety problems), leading to a potential selection bias.**

INTRODUCTION

- Stopping or switching multiple sclerosis (MS) therapy is common in clinical practice and can improve outcomes[1-5]; however, data reporting patient satisfaction with therapy change are scarce.
- Treatment satisfaction is an important factor in therapy adherence and affects treatment outcomes.[6]
- 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 MS.*
  - In 3 phase 3 randomized, double-blind, controlled studies, fingolimod 0.5 mg has demonstrated efficacy in reducing the annualized relapse rate by 52% vs intramuscular (IM) interferon (IFN) β-1a ($P<0.001$)[7] and by 48%–54% vs placebo ($P<0.001$),[8,9] with a well-characterized safety profile.

OBJECTIVE

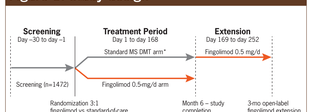
- To assess patient-reported outcomes and physician assessments of a change in therapy to fingolimod 0.5 mg once daily vs standard-of-care (SoC) disease-modifying therapy (DMT) in patients with relapsing forms of MS who are candidates for a therapy change from their previous DMT
  - Patient-reported treatment satisfaction and physician-reported clinical improvement are presented.

METHODS

Study Design

- The phase 4 study to Evaluate Patient Outcomes, Safety, and Tolerability of Fingolimod (EPOC; NCT01216072) was a randomized, open-label, active-comparator, multicenter study in the United States and Canada.
- Patients were randomized 3:1 to fingolimod or SoC DMT (remaining on their prerandomization DMT or changing to another DMT based on the investigator's judgment) for 6 months with no washout period between previous therapy and fingolimod treatment **(Figure 1)**.
- The protocol and informed consent form were reviewed and approved by an institutional review board or independent ethics committee at each study center, and each patient provided written informed consent.

Figure 1. Study design



DMT=disease-modifying therapy; IFN=interferon; IM=intramuscular; MS=multiple sclerosis; SC=subcutaneous.
**IFNβ-1b 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 SC 20 mg once daily.*

Patients

- Eligible patients were 18–65 years of age with relapsing forms of MS as defined by the 2005 revised McDonald criteria[10] and had an Expanded Disability Status Scale score of 0–5.5.
- Patients were required to be fingolimod-naive and 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 SC 20 mg once daily).
- Key exclusion criteria were significant cardiac history; macular edema; active infection; treatment with immunosuppressants, immunoglobulins, or monoclonal antibodies ≤6 months before screening; any 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.

Assessments

- The patient-reported Treatment Satisfaction Questionnaire for Medication (TSQM) consists of 14 items forming 4 specific scales (Global Satisfaction, Effectiveness, Convenience, and Side Effects).[6]
  - The primary endpoint was the change from baseline in the Global Satisfaction scale of the TSQM at month 6.
  - The change from baseline in the TSQM Effectiveness, Convenience, and Side Effects scales were secondary endpoints.
  - Scores were summed for each scale and transformed to scores ranging from 0–100 points, with higher scores indicating greater satisfaction.
- The physician-reported Clinical Global Impression–Improvement (CGI-I) scale was another secondary endpoint.
  - The CGI–I is scored from 1–7 (1 = very much improved, 4 = no change, 7 = very much worse).

Statistical Analysis

- Changes from baseline to month 6 on the TSQM scales were analyzed by an analysis of covariance model that included baseline score as a covariate and treatment group as a main effect.
- Least squares mean TSQM treatment differences and associated 95% CIs were based on the fitted linear model.
- CGI–I scores at month 6 were analyzed by analysis of variance with treatment group as the factor.
- Missing values were imputed by the last-observation-carried-forward method.

RESULTS

Patients

- 1053 patients were enrolled (United States, n=1032; Canada, n=21), and 943 (89.6%) completed the study.
- In the SoC DMT group, 219 (89%) patients remained on their prerandomization SoC DMT.
- Patient characteristics were balanced across treatment groups **(Table 1)**.

Treatment Satisfaction

- A greater increase from baseline on the Global Satisfaction scale was observed in the fingolimod 0.5-mg group than in the SoC DMT group, indicating that patients had greater treatment satisfaction with fingolimod 0.5 mg ($P<0.001$; **Figure 2A**).
- Patients reported greater satisfaction after 6 months' treatment with fingolimod 0.5 mg than with SoC DMT on the Effectiveness, Side Effects, and Convenience scales (all $P<0.001$; **Figure 2B**).
  - Satisfaction on the Convenience scale was markedly increased in the fingolimod 0.5-mg group but not the SoC DMT group.
- Baseline scores for each TSQM scale were similar in the 2 treatment groups **(Table 2)**.

Physician-Reported Improvement

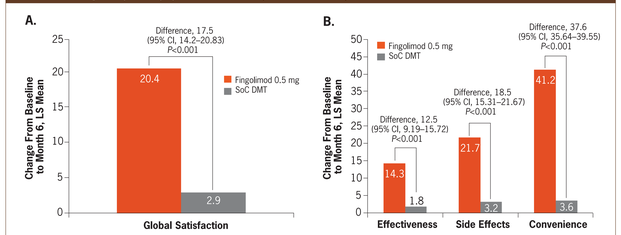
- At month 6, physicians reported some improvement in patients in the fingolimod 0.5-mg group but no change in the SoC DMT group (CGI–I scores, 3.2 vs 3.9, respectively; $P<0.0001$; **Figure 3**).

Table 1. Patient demographic and clinical characteristics

Characteristic*	Fingolimod 0.5 mg (n=790)	SoC DMT (n=263)
Women, n (%)	601 (76.1)	208 (79.1)
Age, y	46.0 (9.82)	45.1 (9.82)
Race, n (%)		
White	642 (81.3)	211 (80.2)
Black	113 (14.3)	43 (16.3)
Asian	3 (0.4)	0
Native American	4 (0.5)	1 (0.4)
Other	28 (3.5)	8 (3.0)
Time since first MS symptom, y	12.1 (8.38)	11.7 (8.44)
Relapses in past year, n	0.8 (1.20)	0.8 (1.32)
Relapses in past 2 years, n	1.4 (2.04)	1.4 (1.93)
EDSS score	2.4 (1.32)	2.4 (1.32)
DMT at screening, n (%)		
IFNβ-1b SC	125 (15.8)	46 (17.5)
IFNβ-1a IM	205 (25.9)	60 (22.8)
IFNβ-1a SC	196 (24.8)	65 (24.7)
Glatiramer acetate	263 (33.3)	92 (35.0)
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.
** Values are mean (SD) unless otherwise noted.*
† Natalizumab.

Figure 2. Change from baseline to month 6 (LOCF) on TSQM (A) Global Satisfaction (primary endpoint) and (B) Effectiveness, Side Effects, and Convenience subscales



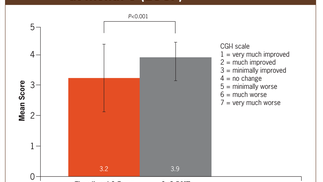
DMT=disease-modifying therapy; LOCF=last observation carried forward; LS=least squares; SoC=standard of care; TSQM=Treatment Satisfaction Questionnaire for Medication.

Table 2. Mean TSQM scores at baseline and month 6 (LOCF)

TSQM Scale	Fingolimod 0.5 mg	SoC DMT
Global Satisfaction	n=767	n=239
Baseline	60.0	58.2
Month 6	80.1	62.6
Effectiveness	n=773	n=243
Baseline	62.2	60.9
Month 6	76.3	63.4
Side Effects	n=762	n=239
Baseline	70.0	66.7
Month 6	91.0	72.1
Convenience	n=768	n=240
Baseline	54.8	55.1
Month 6	96.2	58.7

DMT=disease-modifying therapy; LOCF=last observation carried forward; SoC=standard of care; TSQM=Treatment Satisfaction Questionnaire for Medication.

Figure 3. Physician-rated mean CGI–I scores at month 6 (LOCF)



CGI–I=Clinical Global Impression–Improvement; DMT=disease-modifying therapy; LOCF=last observation carried forward; SoC=standard of care.
Error bars represent SD.

Safety

- Adverse events (AEs) occurred in 78.8% and 62.0% of patients with fingolimod 0.5 mg and SoC DMT, respectively **(Table 3)**.
- The most common AEs with fingolimod were headache (12.4%), fatigue (11.5%), upper respiratory tract infection (6.5%), dizziness (6.4%), and nausea (6.1%).
- There were no deaths in the study.

Table 3. Patients experiencing adverse events

AE, n (%)	Fingolimod 0.5 mg (n=783)	SoC DMT (n=245)
Any AE	617 (78.8)	152 (62.0)
Treatment-related AEs	342 (43.7)	29 (11.8)
AE leading to discontinuation	41 (5.2)	4 (1.6)
Serious AE	31 (4.0)	5 (2.0)
Deaths	0	0
Most common AEs with fingolimod (≥5%)		
Headache	97 (12.4)	8 (3.3)
Fatigue	90 (11.5)	14 (5.7)
Upper respiratory infection	51 (6.5)	9 (3.7)
Dizziness	50 (6.4)	7 (2.9)
Nausea	48 (6.1)	5 (2.0)
Nasopharyngitis	43 (5.5)	13 (5.3)
Hypertension	43 (5.5)	4 (1.6)
Diarrhea	41 (5.2)	4 (1.6)
Urinary tract infection	40 (5.1)	10 (4.1)
Lymphocyte count decreased	39 (5.0)	0
Back pain	39 (5.0)	7 (2.9)

AE=adverse event; DMT=disease-modifying therapy; SoC=standard of care.

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Disclosures

The study was supported by Novartis Pharmaceuticals Corporation. E. Fox has received consulting fees and/or research support from Bayer Pharmaceuticals, Biogen Idec, Eli Lilly & Company, EMD Serono, Genzyme, Neura, Novartis, Ono Pharmaceutical, Opexa Therapeutics, Pfizer, Roche Diagnostics, Sanofi-Aventis, and Teva Neuroscience. K. Edwards has received consulting fees and/or research support from Acorda Therapeutics, Actelion, Biogen Idec, Eli Lilly & Company, EMD USA, Genzyme, Janssen Pharmaceutica, Novartis, Sanofi-Aventis, and Serono Inc. J. G. Burch has nothing to disclose. E. Kim, L. Pestreich, K. McCague, and L. M. Barbato are employees and stockholders of Novartis Pharmaceuticals.

Acknowledgments

The authors thank Valerie P. Zediak, PhD, for medical writing support of this poster. Editorial support was provided by Complete Healthcare Communications, Inc., Chadds Ford, PA. Medical writing and editorial support was funded by Novartis Pharmaceuticals Corporation.

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