Improved Quality of Life After Therapy Change to Fingolimod

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CONCLUSION

- **Therapy change to fingolimod 0.5 mg was associated with greater improvements in physical and mental HRQoL, fatigue symptoms, and depression symptoms compared with continued treatment with SoC DMT.**

INTRODUCTION

- Quality of life (QoL), encompassing physical and mental functioning, is an important aspect of living with multiple sclerosis (MS) and may be improved by disease-modifying therapy (DMT).[1]
- 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.[a]
  - In 3 phase 3 randomized, double-blind, controlled studies, fingolimod 0.5 mg has demonstrated efficacy in reducing the annualized relapse rate vs intramuscular (IM) interferon (IFN) β-1a (52% reduction; $P<0.001$)[2] and placebo (54% and 48% reduction; both $P<0.001$),[3,4] with a well-characterized safety profile.
- Few data are available regarding the impact of fingolimod on QoL.
  - An exploratory analysis of a phase 2 study demonstrated that patients treated with fingolimod had improved health-related QoL (HRQoL) and reduced symptoms of depression compared with those receiving placebo after 6 months of treatment.[5]
  - Post hoc analysis of Trial Assessing Injectable Interferon vs Fingolimod Oral in Relapsing-Remitting Multiple Sclerosis (TRANSFORMS) data showed that, after 1 year of fingolimod treatment, patients experienced significantly less deterioration in their ability to perform daily activities compared with patients treated with IFNβ-1a IM.[6]

OBJECTIVE

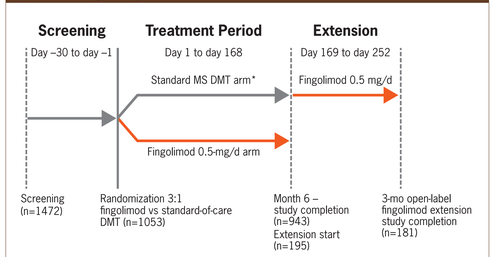
- To assess patient-reported outcomes (PROs) of a change in therapy to fingolimod 0.5 mg once daily vs standard-of-care (SoC) DMT in patients with relapsing forms of MS who are candidates for a therapy change from their previous DMT
  - Secondary PRO endpoints, including activities of daily living, fatigue, depressive symptoms, and HRQoL, are presented.

METHODS

Study Design

- The study to Evaluate Patient Outcomes, Safety, and Tolerability of Fingolimod (EPOC; NCT01216072) was a phase 4, 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)**.

Figure 1. Study design



DMT=disease-modifying therapy; IFN=interferon; MS=multiple sclerosis.
**IFNβ-1b 0.25 mg SC every other day, IFNβ-1a 30 µg IM once weekly, IFNβ-1a 22 or 44 µg SC 3 times weekly, or glatiramer acetate 20 mg SC once daily.*

- 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.

Patients

- Eligible patients were 18–65 years of age with relapsing forms of MS as defined by the 2005 revised McDonald criteria[7] and had an Expanded Disability Status Scale 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 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 primary endpoint was the change from baseline in treatment satisfaction (for results, see **Poster DX29**).[8]
- Secondary endpoints included the change from baseline on the following PROs:
  - Patient-Reported Indices for Multiple Sclerosis (PRIMUS)–Activities to assess activities of daily living[9]
    - Range possible scores, 0–30
    - Higher scores represent worse ability to perform activities of daily living
  - Fatigue Severity Scale (FSS) to assess fatigue[10]
    - Range possible scores, 1–7
    - Higher scores represent worse fatigue
  - Beck Depression Inventory (BDI)–II to assess depressive symptoms[11]
    - Range possible scores, 0–63
    - Higher scores represent worse symptoms
  - Short Form Health Survey v2 standard (SF-36) to assess HRQoL[12]
    - Range of possible scores, 0–100
    - Lower scores represent worse HRQoL

Statistical Analysis

- Changes from baseline in PRO 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 PRO treatment differences and associated 95% CIs were based on the fitted linear model.
- 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.
- Patient characteristics were balanced across treatment groups **(Table 1)**.

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)
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=disease-modifying therapy; EDSS=Expanded Disability Status Scale; MS=multiple sclerosis; SoC=standard of care.
**Values are mean (SD) unless otherwise noted.*

Patient-Reported Outcomes

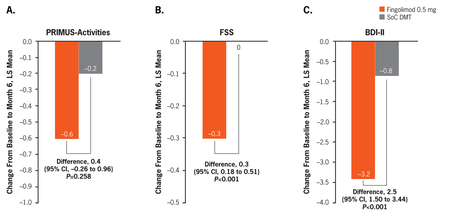
- Mean scores on PRIMUS-Activities, FSS, and BDI-II decreased (representing improvement in functioning/symptoms) from baseline to month 6 in the fingolimod 0.5-mg group **(Table 2)**.
  - Significantly greater treatment differences were observed on the FSS and BDI-II instruments with fingolimod 0.5 mg than with SoC DMT (both $P<0.001$), indicating that fingolimod treatment was associated with greater improvement in fatigue and depression symptoms **(Figure 2)**.

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

	Fingolimod 0.5 mg	SoC DMT
PRIMUS-Activities		
Patients, n	734	234
Baseline	5.2	5.2
Month 6	4.7	5.0
FSS		
Patients, n	750	239
Baseline	4.7	4.6
Month 6	4.3	4.6
BDI-II		
Patients, n	768	240
Baseline	11.7	11.0
Month 6	8.4	10.4

BDI-II=Beck Depression Inventory–II; DMT=disease-modifying therapy; FSS=Fatigue Severity Scale; LOCF=last observation carried forward; PRIMUS=Patient-Reported Indices for Multiple Sclerosis; PRO=patient-reported outcome; SoC=standard of care.
**Higher scores indicate worse functioning, fatigue, or depression.*

Figure 2. (A) Activities of daily living, (B) fatigue, and (C) depressive symptom score* changes from baseline to month 6 (LOCF)



BDI-II=Beck Depression Inventory–II; DMT=disease-modifying therapy; FSS=Fatigue Severity Scale; LOCF=last observation carried forward; LS=least squares; PRIMUS=Patient-Reported Indices for Multiple Sclerosis; SoC=standard of care.
**Higher scores indicate worse functioning, fatigue, or depressive symptoms.*

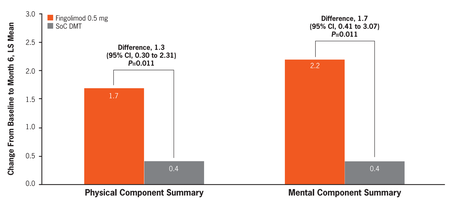
- Mean SF-36 scores were increased (representing improvement in HRQoL) for both physical and mental component summary measures in the fingolimod 0.5-mg group **(Table 3)**.
  - Significantly greater treatment differences were observed on both summary measures, indicating that fingolimod treatment was associated with greater improvement in physical and mental aspects of HRQoL than was SoC DMT **(Figure 3)**.

Table 3. Mean SF-36* summary scores at baseline and month 6 (LOCF)

	Fingolimod 0.5 mg	SoC DMT
Physical component summary		
Patients, n	724	222
Baseline	41.7	41.8
Month 6	43.4	42.3
Mental component summary		
Patients, n	724	222
Baseline	46.2	47.0
Month 6	48.4	47.1

DMT=disease-modifying therapy; LOCF=last observation carried forward; SF-36=Short Form Health Survey v2 standard; SoC=standard of care.
**Lower scores indicate worse quality of life.*

Figure 3. SF-36* summary score changes from baseline to month 6 (LOCF)



DMT=disease-modifying therapy; LOCF=last observation carried forward; LS=least squares; SF-36=Short Form Health Survey v2 standard; SoC=standard of care.
**Lower scores indicate worse quality of life.*

**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.*

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Disclosures

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