Patient-Reported Outcomes After Fingolimod Switch: Early Consistent Benefit

DX07

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CONCLUSIONS

- **In this post hoc analysis of the EPOC study, patients with relapsing forms of MS reported improved satisfaction, fatigue, and depression 3 months after switching from standard-of-care DMT to fingolimod 0.5 mg.**
  - **In addition, physicians rated improvement as greater with fingolimod vs standard-of-care DMT at month 3.**
- **Treatment differences appeared consistent across subgroups defined by age, sex, prior treatment, duration of prior treatment, EDSS score, and time since first symptoms.**
- **These data suggest a benefit as early as 3 months after switching to fingolimod across a variety of PROs and physician impression of improvement.**

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]
- In the Trial Assessing Injectable Interferon vs Fingolimod Oral in Relapsing-Remitting MS (TRANSFORMS), fingolimod significantly improved the annualized relapse rate (ARR) vs intramuscular interferon (IFN) β-1a (0.16 vs 0.33; 52% reduction; *P*<0.001).[1]
- In the Fingolimod Research Evaluating Effects of Daily Oral Therapy in Multiple Sclerosis (FREEDOMS) and FREEDOMS II studies, fingolimod significantly improved the ARR vs placebo (FREEDOMS: 0.18 vs 0.40, 55% reduction, *P*<0.001; FREEDOMS II: 0.21 vs 0.40, 48% reduction, *P*<0.001)[2,3] as well as magnetic resonance imaging (MRI) outcomes.
  - Significant effects of fingolimod 0.5 mg in delaying the first confirmed relapse were apparent as early as day 82 of treatment in FREEDOMS and day 64 in FREEDOMS II (both *P*<0.05). Fingolimod also significantly reduced the proportion of patients with MRI activity at month 6 vs placebo (*P*<0.001 in both studies) and significantly reduced brain volume loss (–35% [*P*=0.006] and –39% [*P*=0.012], respectively) by month 6. See poster DX17[4] for details.
- Although not widely used in MS research, patient-reported outcomes (PROs) are useful in assessing patient perspectives on treatment efficacy.[5]
- The objective of the phase 4 study to Evaluate Patient Outcomes, Safety, and Tolerability of Fingolimod (EPOC; NCT01216072) was to assess PROs and physician assessments of a change in therapy to fingolimod 0.5 mg once daily vs standard-of-care disease-modifying therapy (DMT) in patients with relapsing forms of MS who are candidates for a therapy change from their previous DMT.
  - This post hoc analysis analyzed early PROs 3 months after switching to fingolimod in the overall study population and patient subgroups.

METHODS

Study Design

- Patients were randomly assigned 3:1 to open-label fingolimod or standard-of-care DMT (remained on prerandomization DMT or switched DMTs based on investigator's judgement) for 6 months with no washout period.
- Full study methods are presented in posters DX29 and DX20.[6,7]

Assessments

Patient-reported outcomes

- PRO instruments were administered during the screening visit and at months 3 and 6.
- The Treatment Satisfaction Questionnaire for Medication (TSQM) comprises 14 items forming 4 scales: Global Satisfaction, Effectiveness, Convenience, and Side Effects.[8]
  - Scores were summed for each scale and transformed to scores ranging from 0–100 points, with higher scores indicating greater satisfaction.
- The Fatigue Severity Scale (FSS) is a 9-item instrument, with items rated from 1 (less fatigue) to 7 (more fatigue) and a total score calculated as an average of the individual item scores.[9]
- The Beck Depression Inventory (BDI)–II comprises 21 questions scored from 0–3 and summed, for a total score of 0–63; a higher score indicates more severe depression.[10]

Physician-rated assessment

- At months 3 and 6, investigators administered the Clinical Global Impression of Improvement (CGI-I), a 7-point scale (1 = very much improved; 7 = very much worse) that provides a global evaluation of patient clinical change over time.

[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.*

Statistical Analysis

- This post hoc analysis reports outcomes assessed at month 3; results were analyzed using descriptive statistics.
- Outcomes were assessed for the overall population and by age (≤40 vs >40 years), sex, prior DMT type (IFNβ vs glatiramer acetate [GA]), duration of prior DMT (≤3.7 vs >3.7 years), baseline Expanded Disability Status Scale (EDSS) score (<2.5 vs ≥2.5), and time since first MS symptoms (≤10.8 vs >10.8 years); cutoff points reflect median values.

RESULTS

Patients

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

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

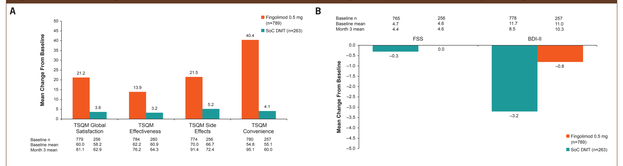
Characteristic	Fingolimod 0.5 mg (n=790)	SoC DMT (n=263)
Age, y*	46.0 (9.8)	45.1 (9.8)
Women, n (%)	601 (76.1)	208 (79.1)
Race, n (%)		
White	642 (81.3)	211 (80.2)
Black	113 (14.3)	43 (16.3)
Native American	4 (0.5)	1 (0.4)
Asian	3 (0.4)	0
Other	28 (3.5)	8 (3.0)
Duration of MS symptoms, y*	12.1 (8.4)	11.7 (8.4)
Number of relapses*		
Past year	0.8 (1.2)	0.8 (1.3)
Past 2 years	1.4 (2.0)	1.4 (1.9)
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.
**Data are mean (SD).*

Patient-Reported Outcomes at Month 3

- For the TSQM Global Satisfaction subscale, mean improvement from baseline was greater with fingolimod vs standard-of-care DMT at month 3 **(Figure 1A)**.
  - Scores for the Effectiveness, Side Effects, and Convenience subscales showed the same pattern.
- Improvements from baseline in FSS and BDI-II scores were greater with fingolimod vs standard-of-care DMT **(Figure 1B)**.
- Mean ± SD CGI-I scores at month 3 were 3.4±1.0 with fingolimod vs 3.9±0.7 with standard-of-care DMT.

Figure 1. Mean change from baseline in PROs at month 3 for (A) TSQM and (B) FSS and BDI-II (full-analysis set, LOCF)

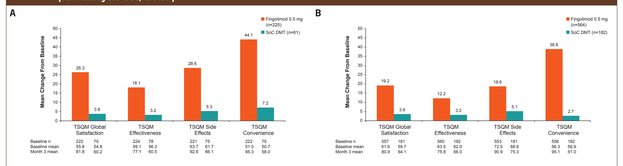


BDI-II=Beck Depression Inventory–II; DMT=disease-modifying therapy; FSS=Fatigue Severity Scale; LOCF=last observation carried forward; PRO=patient-reported outcome; SoC=standard of care; TSQM=Treatment Satisfaction Questionnaire for Medication.

Subgroup Analysis at Month 3

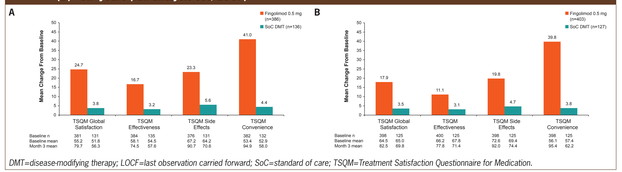
- In the subgroup analyses, improvement in TSQM Global Satisfaction, Effectiveness, and Side Effects scores with fingolimod appeared to be greater in patients aged ≤40 vs >40 years **(Figure 2)**, with a prior treatment duration of ≤3.7 vs >3.7 years **(Figure 3)**, and with time since first symptoms of ≤10.8 vs >10.8 years **(Figure 4)**.
- With both fingolimod and standard-of-care DMT, there appeared to be less improvement in TSQM Side Effects scores in patients with prior GA therapy vs prior IFNβ therapy; however, patients with prior GA therapy had higher baseline scores for this scale **(Figure 5)**.
- TSQM scores did not differ substantially by sex or EDSS score.
- FSS and BDI-II scores did not differ substantially by age, sex, prior treatment, time on prior therapy, EDSS score, or time since first symptoms.
- Mean CGI-I scores did not differ substantially by age, sex, prior treatment, time on prior therapy, EDSS score, or time since first symptoms.

Figure 2. Mean change from baseline in TSQM scores at month 3 for patients aged (A) ≤40 and (B) >40 years (full-analysis set, LOCF)



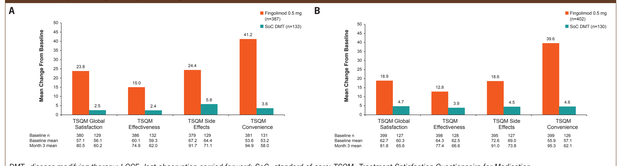
DMT=disease-modifying therapy; LOCF=last observation carried forward; SoC=standard of care; TSQM=Treatment Satisfaction Questionnaire for Medication.

Figure 3. Mean change from baseline in TSQM scores at month 3 by prior treatment durations of (A) ≤3.7 and (B) >3.7 years (full-analysis set, LOCF)



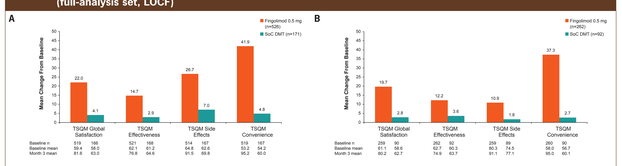
DMT=disease-modifying therapy; LOCF=last observation carried forward; SoC=standard of care; TSQM=Treatment Satisfaction Questionnaire for Medication.

Figure 4. Mean change from baseline in TSQM scores at 3 months with time since first symptoms of (A) ≤10.8 and (B) >10.8 years (full-analysis set, LOCF)



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

Figure 5. Mean change from baseline in TSQM scores at 3 months with (A) IFNβ and (B) GA as prior treatment (full-analysis set, LOCF)



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

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Disclosures

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