Patient-Reported Outcomes After Fingolimod Switch: Results by Prior Therapy

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CONCLUSIONS

- **PROs are important to complement the efficacy and safety data determined in pivotal trials, completing a drug's benefit/risk profile.**
- **In this post hoc analysis of the EPOC study, patients with relapsing forms of MS reported improved satisfaction, activity limitation, quality of life, fatigue, and depression 6 months after switching from injectable SoC DMT to fingolimod 0.5 mg.**
  - In addition, physicians rated improvement as greater with fingolimod vs SoC DMT.
- **Improvements with fingolimod vs SoC DMT generally occurred in patients with previous IFNβ therapy and patients with previous GA therapy.**
- **EPOC demonstrates a consistent PRO benefit across multiple standardized tools in patients switching to fingolimod, irrespective of prior injectable DMT.**

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 12-month Trial Assessing Injectable Interferon vs Fingolimod Oral in Relapsing-Remitting Multiple Sclerosis (TRANSFORMS), fingolimod 0.5 mg significantly reduced the annualized relapse rate (ARR) vs intramuscular (IM) interferon (IFN) β-1a (0.16 vs 0.33, respectively; 52% reduction; $P<0.001$).[1]
- In a 1-year randomized extension of TRANSFORMS, patients switching from IFNβ-1a IM to fingolimod 0.5 mg had a relative reduction in ARR of 30% vs the core study ($P=0.049$).[2]
- Clinical trials have not assessed certain patient-reported outcomes (PROs) after the switch to fingolimod.
- 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 (SoC) disease-modifying therapy (DMT) in patients with relapsing forms of MS who are candidates for a therapy change from their previous DMT.
  - This was a post hoc analysis of PRO results at month 6 stratified by prior DMT.

METHODS

Study Design

- EPOC was a 6-month, randomized, open-label, multicenter study conducted 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 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 (2005 revised McDonald criteria[3]) and 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 [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.

Assessments

- PROs at screening and months 3 and 6
  - The Treatment Satisfaction Questionnaire for Medication (TSQM) Global Satisfaction, Effectiveness, Convenience, and Side Effects scales[4]
  - The Fatigue Severity Scale (FSS)[5]
  - The Beck Depression Inventory (BDI)–II[6]
- PROs at screening and month 6
  - The Patient-Reported Indices for Multiple Sclerosis (PRIMUS)–Activities scale, an assessment of activities of daily living[7]
  - The Short Form Health Survey (SF)–36 v2 standard mental and physical health summary scores
- Physician-rated assessment
  - At months 3 and 6, investigators completed the Clinical Global Impression of Improvement (CGI-I), a global evaluation of patient clinical change over time.

Statistical Analysis

- This post hoc analysis uses scores at month 6 (last observation carried forward [LOCF]) to assess outcomes stratified by prior DMT (IFNβ vs GA); results were analyzed using descriptive statistics.

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**.
  - At the screening visit, 697 patients (66.2%) were taking IFNβ, and 355 (33.7%) were taking GA.

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.
**All data are mean (SD) unless otherwise indicated.*

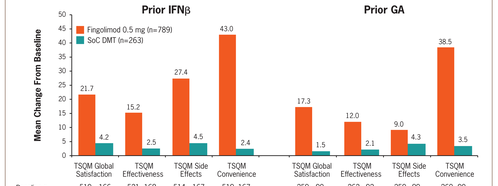
PROs

- Mean TSQM scores and mean change from baseline to month 6 (LOCF) are shown in **Figure 1**; data show a consistent benefit of fingolimod vs SoC DMT, irrespective of prior DMT.
- For the SF-36 physical and mental component summary measures, improvements from baseline at month 6 (LOCF) were also greater with fingolimod vs SoC DMT, irrespective of prior DMT **(Figure 2)**.
- PRIMUS-Activities scores were improved with fingolimod and SoC DMT at month 6 (LOCF); improvements were greater with fingolimod vs SoC DMT in patients with prior IFNβ therapy but not prior GA therapy **(Figure 3)**.
- FSS scores were improved with fingolimod but not with SoC DMT at month 6 (LOCF) irrespective of prior treatment **(Figure 4)**.
- At month 6 (LOCF), mean ± SD change from baseline in BDI-II total score with fingolimod vs SoC DMT was consistent in patients with prior IFNβ therapy (–3.3±7.2 vs –0.7±6.0, respectively) and prior GA therapy (–3.3±8.2 vs –0.3±7.9).

Physician Impression of Improvement

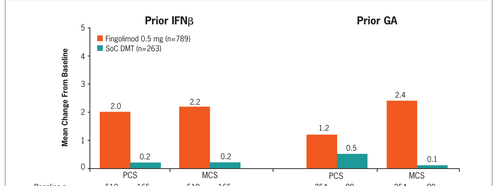
- Mean ± SD CGI-I scores with fingolimod vs SoC DMT at month 6 (LOCF) were 3.2±1.1 vs 3.9±0.6, respectively, for patients switching from IFNβ and 3.2±1.2 vs 3.8±0.7 for patients switching from GA.

Figure 1. Mean change from baseline in TSQM scores at month 6 (full-analysis set, LOCF)



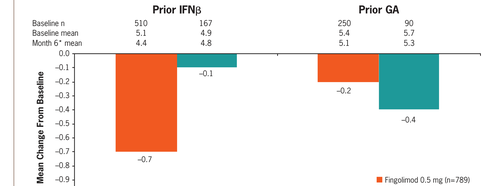
DMT=disease-modifying therapy; GA=glatiramer acetate; IFN=interferon; LOCF=last observation carried forward; SoC=standard of care; TSQM=Treatment Satisfaction Questionnaire for Medication.
**LOCF.*

Figure 2. Mean change from baseline in SF-36 summary scores at month 6 (full-analysis set, LOCF)



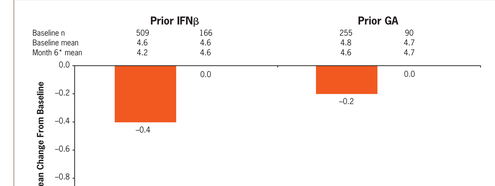
DMT=disease-modifying therapy; GA=glatiramer acetate; IFN=interferon; LOCF=last observation carried forward; MCS=Mental Component Summary; PCS=Physical Component Summary; SF-36=Short Form Health Survey-36; SoC=standard of care.
**LOCF.*

Figure 3. Mean change from baseline in PRIMUS-Activities scores at month 6 (full-analysis set, LOCF)



DMT=disease-modifying therapy; GA=glatiramer acetate; IFN=interferon; LOCF=last observation carried forward; PRIMUS=Patient-Reported Indices for Multiple Sclerosis; SoC=standard of care.
**LOCF.*

Figure 4. Mean change from baseline in FSS scores at month 6 (full-analysis set, LOCF)



DMT=disease-modifying therapy; FSS=Fatigue Severity Scale; GA=glatiramer acetate; IFN=interferon; LOCF=last observation carried forward; SoC=standard of care.
**LOCF.*

[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.*

References

1. Cohen JA, et al. *N Engl J Med*. 2010;362:402-415.
2. Khatri B, et al. *Lancet Neurol*. 2011;10:520-529.
3. Polman CH, et al. *Ann Neurol*. 2005;58:840-846.
4. Atkinson MJ, et al. *Health Qual Life Outcomes*. 2004;2:12.
5. Krupp LB, et al. *Arch Neurol*. 1989;46:1121-1123.
6. Beck AT, et al. *J Pers Assess*. 1996;67:588-597.
7. Doward LC, et al. *Mult Scler*. 2009;15:1092-1102.

Disclosures

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