Patient- and physician-reported outcomes after therapy switch from interferon or glatiramer acetate to fingolimod

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CONCLUSIONS

- **This head-to-head, randomized, open-label study showed switching to fingolimod from IFN or GA significantly improved global treatment satisfaction, particularly related to efficacy and convenience, compared with remaining on an individual IFN or GA.**
  - **The pattern of improvement was similar across measures after switching from any of the IFNs.**
- **The improvements in treatment satisfaction associated with a switch to fingolimod corresponded with significantly greater improvement in physician assessments of clinical improvement; benefits were also observed for depression and fatigue, although not all comparisons with continued SoC therapy reached statistical significance.**
- **These analyses indicate that patients and physicians perceive benefits of a therapy switch from IFNs or GA to fingolimod.**

INTRODUCTION

- Fingolimod is a once-daily, oral sphingosine 1-phosphate receptor modulator approved in the United States and European Union for the treatment of relapsing multiple sclerosis (MS).[1,2a]
- The phase 4 Evaluate Patient Outcomes, Tolerability, and Safety of Fingolimod (EPOC) trial (Clinical Trials identifier: NCT01216072) investigated patient-reported outcomes (PROs) and physician assessments following a change in therapy to fingolimod 0.5 mg once daily for 6 months vs remaining on standard-of-care (SoC) disease-modifying therapy (DMT).
- These exploratory post hoc analyses evaluated categorical data for PROs related to treatment satisfaction, depression, and fatigue and physician impressions of overall improvement.

OBJECTIVE

- To evaluate changes in patient- and physician-reported outcomes in subgroups of patients with immediate history of interferon (IFN) or glatiramer acetate (GA) treatment who were randomized to either switch to fingolimod or remain on their previous treatment

METHODS

Study Design and Patients

- EPOC was an open-label, randomized, multicenter study conducted in the United States and Canada in patients aged 18–65 years with relapsing forms of MS (2005 revised McDonald criteria[3]) and Expanded Disability Status Scale (EDSS) score of 0–5.5.
- Patients were randomized 3:1 to receive once-daily fingolimod 0.5 mg or SoC DMT (intramuscular [IM] IFNβ-1a 30 µg once weekly, subcutaneous [SC] IFNβ-1a 22 or 44 µg 3 times weekly, SC IFNβ-1b 0.25 mg every other day, or SC GA 20 mg once daily) for 6 months with no washout period.
- Eligible patients were fingolimod-naive, treated continuously for ≥6 months with an approved DMT, and considered candidates for a change in therapy.
  - Therapy change eligibility was decided by the treating physician (US patients) or required an inadequate response or poor tolerance to ≥1 MS therapy (Canadian patients).
- Key exclusion criteria were significant cardiac history; macular edema; active infection; treatment with immunosuppressants, immunoglobulins, or monoclonal antibodies for 6 months before screening; exposure to live or live-attenuated vaccines 1 month before screening; treatment with cladribine, cyclophosphamide or mitoxantrone at any time; or current treatment with class Ia or class III antiarrhythmic drugs.

Post Hoc Analyses

- 2 post hoc analyses (1 in patients previously treated with IFNβ and 1 in patients previously treated with GA) evaluated changes from baseline to 6 months (last observation carried forward) for the following instruments:
  - Treatment Satisfaction Questionnaire for Medication (TSQM); scaled from 0–100, with higher scores indicating greater satisfaction[4]
    - The TSQM domain of Global Satisfaction was the primary endpoint of this analysis. Scores were also calculated for the subscales of Effectiveness, Convenience, and Side Effects.
  - Beck Depression Inventory-II (BDI-II); scaled from 0–63, with higher scores indicating more severe depression[5]
  - Fatigue Severity Scale (FSS); scaled from 1–7, with higher scores indicating more severe fatigue[6]
  - Physician-assessed Clinical Global Impression of Improvement (CGI-I); scaled from 1–7 (1 = very much improved, 7 = very much worse)
- Analysis of covariance model with baseline scores as a covariate and treatment group as a main effect was used to assess outcomes. The least squares (LS) means, LS mean difference of the treatment groups, based on the fitted linear model, are reported. Missing data were imputed using the last-observation-carried-forward method. The same method was used in the primary analysis.

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

RESULTS

- At randomization
  - 205 patients switched to fingolimod 0.5 mg from IM IFNβ–1a, 196 from SC IFNβ-1a, and 125 from SC IFNβ-1b; 48, 58, and 39 patients remained on IM IFNβ-1a and SC IFNβ-1a and -1b, respectively.
  - 262 switched to fingolimod from GA, and 74 remained on GA.
- Patient demographics and characteristics were generally balanced across groups (**Table 1**).

Table 1. Patient demographics and baseline clinical characteristics

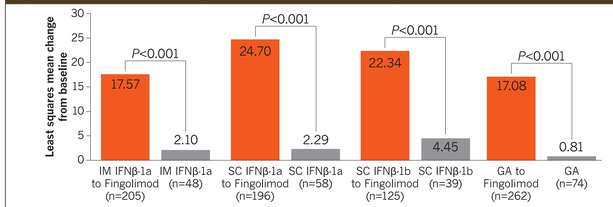
	IM IFNβ-1a to fingolimod 0.5 mg QD (n=205)	IM IFNβ-1a 30 µg QW (n=48)	SC IFNβ-1a to fingolimod 0.5 mg QD (n=196)	SC IFNβ-1a 22 or 44 µg TIW (n=58)	SC IFNβ-1b to fingolimod 0.5 mg QD (n=125)	SC IFNβ-1b 0.25 mg QOD (n=39)	GA to fingolimod 0.5 mg QD (n=262)	GA 20 mg QD (n=74)
Mean (SD) age, y	46.6 (9.90)	45.1 (10.48)	45.0 (10.39)	45.9 (10.25)	46.3 (10.20)	47.5 (8.97)	46.3 (9.14)	44.4 (9.97)
Women, n (%)	160 (78.0)	38 (79.2)	137 (69.9)	44 (75.9)	94 (75.2)	33 (84.6)	208 (79.4)	61 (82.4)
Race, n (%)								
White	165 (80.5)	36 (75.0)	160 (81.6)	44 (75.9)	94 (75.2)	31 (79.5)	222 (84.7)	64 (86.5)
Black	35 (17.1)	10 (20.8)	29 (14.8)	14 (24.1)	24 (19.2)	6 (15.4)	24 (9.2)	9 (12.2)
Asian	0	0	0	0	1 (0.8)	0	2 (0.8)	0
Native American	0	1 (2.1)	2 (1.0)	0	0	0	2 (0.8)	0
Other	5 (2.4)	1 (2.1)	5 (2.6)	0	6 (4.8)	2 (5.1)	12 (4.6)	1 (1.4)
Mean (SD) duration of MS symptoms, y	12.0 (7.90)	11.5 (7.87)	11.1 (7.89)	11.4 (8.04)	12.2 (8.64)	12.3 (6.78)	13.1 (8.91)	12.2 (9.36)
Mean (SD) number of relapses								
Previous 1 y	0.74 (5.54)	0.48 (1.66)	0.76 (6.30)	0.88 (3.64)	0.74 (3.90)	0.62 (1.84)	0.75 (5.53)	0.84 (3.12)
Previous 2 y	1.20 (7.78)	0.88 (2.72)	1.29 (8.54)	1.45 (5.05)	1.34 (5.50)	1.05 (2.83)	1.42 (9.60)	1.43 (5.81)
Mean (SD) EDSS score	2.5 (1.26)	2.4 (1.27)	2.4 (1.35)	2.3 (1.38)	2.4 (1.37)	2.5 (1.39)	2.5 (1.33)	2.4 (1.35)

EDSS=Expanded Disability Status Scale; GA=glatiramer acetate; IFN=interferon; IM=intramuscular; MS=multiple sclerosis; QD=once daily; QOD=every other day; QW=once weekly; SC=subcutaneous; SD=standard deviation; TIW=3 times weekly.

TSQM Scores

- Changes from baseline to 6 months in TSQM Global Satisfaction scores significantly favored switching to fingolimod vs remaining on IFNs or GA (all *P*<0.001, **Figure 1**).

Figure 1. Least squares mean changes from baseline to 6 months in TSQM Global Satisfaction scores*



GA=glatiramer acetate; IFN=interferon; IM=intramuscular; SC=subcutaneous; TSQM=Treatment Satisfaction Questionnaire for Medication.
*Full-analysis set, last observation carried forward.

- Changes from baseline to 6 months in TSQM scores for Effectiveness, Side Effects, and Convenience subscales significantly favored switching to fingolimod vs remaining on IFNs (all *P*<0.001, **Table 2**).
- Significant benefits were also observed in TSQM subscale scores for Effectiveness and Convenience in patients switching to fingolimod from GA (both *P*<0.001 vs remaining on GA); a nonsignificant trend favoring switching was observed for the Side Effects subscale (**Table 2**).

Table 2. Least squares mean changes from baseline to 6 months in TSQM subscales: Effectiveness, Side Effects, and Convenience*

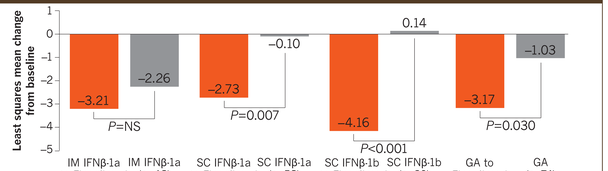
	IM IFNβ-1a to fingolimod 0.5 mg QD (n=205)	IM IFNβ-1a 30 µg QW (n=48)	SC IFNβ-1a to fingolimod 0.5 mg QD (n=196)	SC IFNβ-1a 22 or 44 µg TIW (n=58)	SC IFNβ-1b to fingolimod 0.5 mg QD (n=125)	SC IFNβ-1b 0.25 mg QOD (n=39)	GA to fingolimod 0.5 mg QD (n=262)	GA 20 mg QD (n=74)
Effectiveness	13.31†	1.37	15.07†	1.62	17.59†	0.68	12.16†	0.62
Side Effects	30.62†	6.56	27.83†	−0.42	21.50†	−1.24	9.25†	4.47
Convenience	43.83†	5.70	42.36†	1.66	41.57†	1.31	38.01†	3.11

GA=glatiramer acetate; IFN=interferon; IM=intramuscular; QD=once daily; QOD=every other day; QW=once weekly; SC=subcutaneous; TIW=3 times weekly; TSQM=Treatment Satisfaction Questionnaire for Medication.
*Full-analysis set, last observation carried forward.
†P<0.001 vs remaining on individual comparator.
‡P<0.111 vs remaining on individual comparator.

BDI-II and FSS Scores

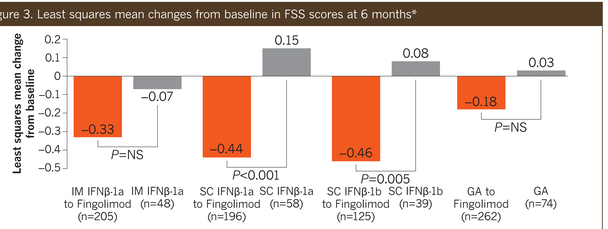
- Changes from baseline to 6 months in BDI-II and FSS scores favored switching to fingolimod vs remaining on IFNs or GA, although not all differences reached statistical significance (**Figures 2, 3**).

Figure 2. Least squares mean changes from baseline in BDI-II scores at 6 months*



BDI-II=Beck Depression Inventory II; GA=glatiramer acetate; IFN=interferon; IM=intramuscular; NS=not significant; SC=subcutaneous.
*Full-analysis set, last observation carried forward.

Figure 3. Least squares mean changes from baseline in FSS scores at 6 months*

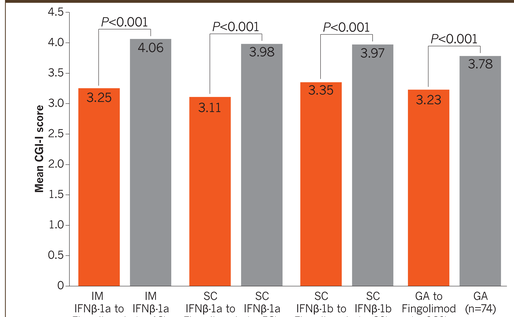


FSS=Fatigue Severity Scale; GA=glatiramer acetate; IFN=interferon; IM=intramuscular; NS=not significant; SC=subcutaneous.
*Full-analysis set, last observation carried forward.

CGI-I Scores

- Physician-assessed CGI-I scores at 6 months showed significantly greater improvement for patients who switched to fingolimod vs those remaining on IFNs or GA (all *P*<0.001, **Figure 4**).

Figure 4. Mean CGI-I score after completion of 6 months of treatment*



CGI=Clinical Global Impression of Improvement; GA=glatiramer acetate; IFN=interferon; IM=intramuscular; SC=subcutaneous.
*Full-analysis set, last observation carried forward.

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