Comparison of treatment retention and satisfaction with fingolimod, interferons and glatiramer acetate in PREFER*MS*

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Introduction

- At least 4 injectable disease-modifying therapies (iDMTs) are approved for relapsing forms of multiple sclerosis (RMS): glatiramer acetate (GA), intramuscular (IM) interferon (IFN) β-1a, and subcutaneous (SC) IFNβ-1a and IFNβ-1b.
- Suboptimal adherence to iDMTs is common among patients with RMS and reduces therapeutic effectiveness.[1,2]
- Fingolimod 0.5 mg is a once-daily oral therapy approved for the treatment of RMS.[3]
- PREFER*MS* was the first large, randomized, prospective study to demonstrate higher therapy retention with oral fingolimod 0.5 mg/day than with iDMTs in patients with RMS.[4]

Objective

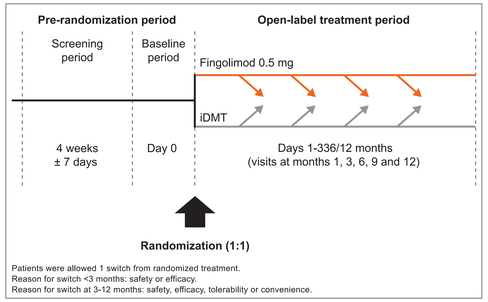
- To compare treatment retention and satisfaction with fingolimod versus specific iDMTs in patients with RMS.

Methods

Study design

- PREFER*MS* was a 12-month, phase 4, open-label, active-controlled, randomized, multicenter study conducted at 117 sites across the United States.
- The primary endpoint was patient retention on randomized treatment over 12 months.
- Enrolled patients were treatment naïve or had previously received only 1 class of iDMT (IFNβ or GA).
- Patients were randomized (1:1) to fingolimod or a pre-selected iDMT (IFNβ-1a IM, IFNβ-1a SC or GA) and followed up quarterly for 12 months.
- A single on-study treatment switch was allowed after 3 months, or earlier for efficacy or safety reasons (**Figure 1**).

Figure 1. PREFER*MS* study design



Patients were allowed 1 switch from randomized treatment.
Reason for switch <3 months: safety or efficacy.
Reason for switch at 3-12 months: safety, efficacy, tolerability or convenience.

Analyses

- *Post hoc* analyses compared treatment retention and satisfaction with fingolimod versus IFNβ-1a IM, IFNβ-1a SC, any IFNβ and GA.
- Retention was analyzed over 12 months as the proportion of patients completing the study on randomized treatment.
  - Between-group differences in retention were calculated by normal approximation using continuity correction.
- Treatment satisfaction was based on pooled responses of 'somewhat satisfied', 'very satisfied' and 'extremely satisfied' on the Medication Satisfaction Questionnaire;[3] analyses were performed at the end of randomized treatment (EoRT) and at the end of study (EoS).
  - At EoRT, patients had received only randomized treatment.
  - At EoS, some patients had received only randomized treatment, and some had received both randomized treatment and a treatment switch.
- Comparisons were made using the Cochran–Mantel–Haenszel test, adjusted for treatment and treatment naïvety.
- PREFER*MS* was not powered for subgroup analyses, which were for hypothesis generation only.
- No adjustment was made for multiple comparisons.

Results

- Of 875 patients randomized, 861 (98.4%) were included in the full analysis set (IFNβ-1a IM, n=76; IFNβ-1a SC, n=90; all IFNβs, n=197; GA, n=231; fingolimod, n=433). Baseline characteristics were similar in the fingolimod and iDMT treatment groups (**Table 1**).

Treatment retention

- A significantly greater proportion of patients completed the study on randomized treatment in the fingolimod group than in the iDMT group overall and in the individual iDMT groups (**Figure 2**).
- The most common reason for discontinuation of any IFNβ was influenza-like symptoms, and for GA it was injection site reaction (**Table 2**).

Treatment satisfaction

- A greater proportion of patients expressed satisfaction with fingolimod than with an iDMT at the last assessment on randomized treatment (**Figure 3**).
- There were no significant differences in patient satisfaction between treatment groups at the EoS (**Figure 3**).
  - This may reflect the large proportion of patients initially randomized to iDMTs who switched to fingolimod.

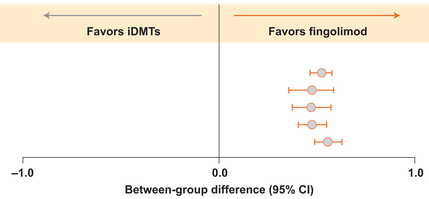
Table 1. PREFER*MS* patient demographics and baseline characteristics

Characteristic	Fingolimod (n=433)	IFNβ-1a IM (n=76)	p-value	IFNβ-1a SC (n=90)	p-value	Any IFNβ (n=197)	p-value	GA (n=231)	p-value
Age, years	41.6 (10.86)	40.9 (10.46)	0.5967	41.2 (11.05)	0.7436	41.1 (10.48)	0.6124	42.2 (10.31)	0.4492
Sex, n (%)									
Male	125 (28.9)	21 (27.6)	0.8260	21 (23.3)	0.2868	46 (23.4)	0.1488	61 (26.4)	0.5011
Female	308 (71.1)	55 (72.4)		69 (76.7)		151 (76.6)		170 (73.6)	
Race, n (%)									
Caucasian	354 (81.8)	63 (82.9)	ND	69 (76.7)	ND	159 (80.7)	ND	188 (81.4)	ND
Black	67 (15.5)	10 (13.2)		19 (21.2)		33 (16.8)		36 (15.6)	
Asian	1 (0.2)	0 (0.0)		0 (0.0)		0 (0.0)		1 (0.4)	
Native American	1 (0.2)	0 (0.0)		0 (0.0)		0 (0.0)		1 (0.4)	
Pacific Islander	0 (0.0)	1 (1.3)		1 (1.1)		2 (1.0)		0 (0.0)	
Other	10 (2.3)	2 (2.6)		1 (1.1)		3 (1.5)		5 (2.2)	
Height, cm	168.5 (9.02)	168.5 (9.03)	0.9647	167.3 (9.48)	0.2755	167.7 (9.07)	0.3578	167.4 (10.50)	0.1918
Weight, kg	82.87 (20.07)	81.99 (20.38)	0.7249	82.97 (22.15)	0.9680	82.28 (21.75)	0.7388	84.74 (23.06)	0.2780
BMI, kg/m²	29.17 (6.68)	28.83 (6.74)	0.6867	29.59 (7.41)	0.5907	29.17 (7.15)	0.9998	30.24 (7.89)	0.0657
Duration of MS since diagnosis, years	4.43 (6.67)	4.50 (6.50)	0.9275	3.32 (5.26)	0.1386	3.67 (5.68)	0.1661	4.70 (6.17)	0.6110
Duration of MS since first symptoms, years	7.30 (8.21)	7.73 (7.90)	0.6746	6.16 (7.11)	0.2191	6.81 (7.43)	0.4727	7.51 (7.86)	0.7490
Number of relapses in the past year	0.6 (0.95)	0.5 (0.79)	0.3623	0.8 (1.33)	0.1808	0.6 (1.06)	0.9111	0.5 (0.85)	0.4972
Number of relapses in the past 2 years	0.9 (1.51)	0.8 (1.13)	0.5494	1.2 (1.85)	0.1386	0.9 (1.50)	0.7691	0.9 (1.34)	0.9335
EDSS score	2.36 (1.56)	2.42 (1.50)	ND	2.43 (1.47)	ND	2.52 (1.48)	ND	2.37 (1.53)	ND
T2 lesion volume, cm³	7.65 (11.60)	8.96 (12.40)	ND	7.90 (12.15)	ND	7.55 (11.53)	ND	7.35 (8.88)	ND
Normalized brain volume, cm³	1521.42 (83.91)	1523.16 (77.49)	ND	1514.46 (76.43)	ND	1524.85 (79.17)	ND	1499.49 (97.82)	ND
Number of Gd⁺ lesions	1.08 (3.75)	0.96 (2.00)	ND	1.57 (4.98)	ND	1.11 (3.64)	ND	0.63 (2.38)	ND

Data are mean (SD) unless stated otherwise.
Comparisons between fingolimod and iDMT groups were made using the χ^2 test (excluding missing values) for categorical variables and a 2-sample t-test for continuous variables.
BMI, body mass index; EDSS, Expanded Disability Status Scale; MS, multiple sclerosis; ND, not determined.

Figure 2. Retention rates and between-treatment-group differences in retention rates in PREFER*MS*

Treatment group	Percentage retained (n/N)	Between-group difference vs fingolimod, %	p-value
Fingolimod	**81.3 (352/433)**	**–**	**–**
Any iDMT	**29.2 (125/428)**	**52.1**	**<0.0001**
IFNβ-1a IM	34.2 (26/76)	47.1	<0.0001
IFNβ-1a SC	34.4 (31/90)	46.9	<0.0001
Any IFNβ	33.5 (66/197)	47.8	<0.0001
GA	25.5 (59/231)	55.8	<0.0001



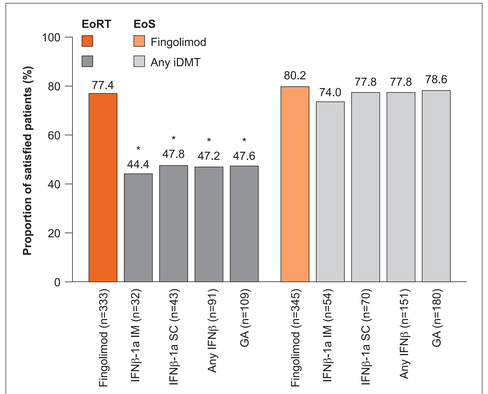
Comparisons were made using the Cochran–Mantel–Haenszel test, adjusted for treatment and treatment naïvety.
Between-group differences were calculated by normal approximation using continuity correction.

Table 2. Primary reasons for discontinuing randomized treatment

Reason	Fingolimod (n=433)	IFNβ-1a IM (n=76)	IFNβ-1a SC (n=90)	Any IFNβ (n=197)	GA (n=231)
Injection-site reaction	–	1 (1.3)	8 (8.9)	12 (6.1)	49 (21.2)
Frequency of injections	–	–	3 (3.3)	3 (1.5)	26 (11.3)
Inconvenient administration	–	3 (3.9)	7 (7.8)	14 (7.1)	19 (8.2)
Relapse	5 (1.2)	2 (2.6)	3 (3.3)	7 (3.6)	7 (3.0)
Needle phobia	–	5 (6.6)	1 (1.1)	7 (3.6)	6 (2.6)
Presence of disease activity on MRI	–	–	1 (1.1)	1 (0.5)	5 (2.2)
Influenza-like symptoms	–	18 (23.7)	11 (12.2)	32 (16.2)	2 (0.9)
Lipoatrophy	–	–	–	–	1 (0.4)
Depression	1 (0.2)	–	3 (3.3)	3 (1.5)	1 (0.4)
Hepatic side effects	7 (1.6)	–	2 (2.2)	3 (1.5)	–
Spasticity	–	1 (1.3)	–	1 (0.5)	–
Infection	–	–	–	–	–
Macular edema	1 (0.2)	–	–	–	–
Bradycardia	–	–	–	–	–
Presence of neutralizing antibodies	–	–	–	–	–
Other	13 (3.0)	11 (14.5)	13 (14.4)	29 (14.7)	29 (12.6)

Data are n (%).
MRI, magnetic resonance imaging.

Figure 3. Treatment satisfaction in patients randomized to fingolimod or iDMTs at EoRT and at EoS



*p<0.0001.
Fingolimod (N=433), IFNβ-1a IM (N=76), IFNβ-1a SC (N=90), any IFNβ (N=197), GA (N=231).
Between-group comparisons were conducted for individual iDMTs versus fingolimod, and were based on treatment group at randomization, not treatment after switching.
Data at EoRT (time on randomized treatment) and the EoS (time on randomized and switched treatments) show the treatment effect in randomized groups before and after any treatment switches, respectively; EoRT and EoS were the same visit for patients who did not switch from randomized treatment.
Treatment satisfaction was the sum of the proportions of patients stating 'somewhat satisfied', 'very satisfied' or 'extremely satisfied' on the Medication Satisfaction Questionnaire.
Comparisons were made using the Cochran–Mantel–Haenszel test, adjusted for treatment and treatment naïvety.

Conclusions

- In PREFER*MS*, treatment retention was higher with fingolimod than with any iDMT.
- Trends towards greater treatment satisfaction and improved tolerability were observed with fingolimod compared with iDMTs.
  - Treatment satisfaction was similar for all individual iDMTs.

References

1. Devonshire V et al. *Eur J Neurol.* 2011;18:69-77.
2. Patti F. *Patient Prefer Adherence* 2010;4:1-9.
3. Novartis Pharmaceuticals Corporation. Prescribing information. Gilenya®. 2016. Available from: https://www.pharma.us.novartis.com/product/pi/pdf/gilenya.pdf (Accessed 8 February 2017).
4. Cree B *et al. Neurology* 2016;86(Suppl. 16):P3.115.

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Disclosures

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