CONCLUSIONS

- Among patients who had discontinued previous DMTs before study entry, those who were treated with fingolimod had greater improvements in ARR than those who received placebo or IFNβ-1a IM.
- The greatest improvements in ARR with fingolimod compared with placebo and IFNβ-1a IM were seen in patients who were treatment-naïve, which may have important implications for treatment selection early in MS.

INTRODUCTION

- Increased relapse frequency early in the course of MS is associated with prolonged disability, and higher annualized relapse rates (ARRs) correlate with poorer outcomes.
- In phase 3 clinical trials, fingolimod significantly reduced relapses in patients with relapsing-remitting multiple sclerosis (RRMS) compared with placebo in FREEDOMS and FREEDOMS II, and with interferon (IFN)β-1a IM in TRANSFORMS.
- Pooled data from FREEDOMS, FREEDOMS II, and TRANSFORMS provided a larger study population than was available from the individual studies for post hoc analyses of the efficacy of fingolimod in patients with suboptimal response to previous disease modifying therapies (DMTs).

METHODS

Study designs and participants

- The pooled analyses included patients who had been randomized to receive oral fingolimod 0.5 mg or placebo once daily for 2 years in FREEDOMS and FREEDOMS II, or to receive oral fingolimod 0.5 mg once daily or IFNβ-1a IM 44 mg once weekly for 1 year in TRANSFORMS.

RESULTS

Study population

- In total, 2415 patients were included in the pooled analyses: 1212 in the fingolimod 0.5 mg group, 773 in the placebo group and 431 in the IFNβ-1a IM group. Table 1 presents patient disposition and study drug exposure. Results for the different study populations are presented in poster DX68.

Baseline demographics and disease characteristics were similar across treatment groups (Table 2).

Annualized relapse rates

- Perspective of treatment status at baseline (i.e. treatment-naïve or previously treated), and of the type of previous DMT, ARRs were significantly lower in patients treated with fingolimod 0.5 mg than in those who received placebo or IFNβ-1a IM (Figure 1).

- In patients who were IFNβ-naive at baseline, fingolimod significantly reduced ARR relative to placebo (59%; p<0.001) and to IFNβ-1a IM (42%; p=0.001). ARR reductions of 49% versus both placebo and IFNβ-1a IM (p<0.001) were observed in patients who had previously received IFNβ-1a IM.

- Similar results were observed for fingolimod-treated patients who had previously received GA: relative to placebo and to IFNβ-1a IM, fingolimod reduced ARR by 47% (p<0.001) and 43% (p<0.001), respectively. In GA-naïve patients, ARR was reduced by 58% (p<0.001) and 45% (p<0.001), respectively.

- Fingolimod therapy led to significant relative reductions in ARRs among patients who had discontinued their previous DMT owing to an unsatisfactory therapeutic response (94% vs. p<0.001) versus placebo; 53% (p<0.001) versus IFNβ-1a IM, and among those who had discontinued owing to an AE (17% (p=0.002) and 36% (p=0.059), respectively).

- Patients were aged 18–55 years, had been diagnosed with RRMS in accordance with the 2005 revised McDonald criteria, had one or more confirmed relapses in the previous year or two or more in the previous 2 years, and had a score of 0.5–0.8 on the Expanded Disability Status Scale (EDSS). Patients with prior optic neuritis were included.

- Baseline demographics and disease characteristics were similar across treatment groups (Table 2). Results for the different study populations are presented in poster DX68.

- Analyses were performed on the intention-to-treat populations pooled from all three trials.

- ARRs were obtained using a negative binomial regression model with study, treatment group, and treatment-by-subgroup as explanatory variables.

- 95% CIs are presented and p values indicate the statistical significance of treatment differences; p values were hypothesis generated only and no adjustments were made for multiple comparisons.

- Relapse outcomes in patients with multiple sclerosis treated with fingolimod by previous treatment with disease-modifying therapies

- Reasons for discontinuation of previous treatment (unsatisfactory therapeutic effect versus reasons other than AE) were considered to be a priori.

- Baseline demographics and patient characteristics (randomized population)

- Time since diagnosis, years
- Number of relapses within past year
- Number of Gd-enhancing lesions on baseline MRI

- Treatment history
- Treatment-naïve, n (%) 345 (44.6) 190 (44.0) 155 (38.7)
- Previous MS treatment, n (%) 282 (35.4) 75 (16.6) 207 (51.3)
- Previous IFNβ treatment, n (%) 241 (30.5) 117 (26.2) 124 (30.9)
- Previous GA treatment, n (%) 143 (18.5) 152 (34.6) 190 (47.8)

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