Background: Oral fingolimod (FTY720) is a sphingosine 1-phosphate receptor modulator being evaluated in a phase 3 multiple sclerosis (MS) study program. **Objectives:** To report safety findings from two relapsing-remitting MS (RRMS) phase 3 studies. **Methods:** In two double-blind studies, RRMS patients were randomized to receive once-daily FTY720 (0.5 mg or 1.25 mg), weekly intramuscular (IM) interferon beta-1a (IFNβ-1a) 30 μg (TRANSFORMS [12 months]), or placebo (FREEDOMS [24 months]). **Results:** Of 1292 patients, 1153 (89%) completed TRANSFORMS, 1123 (87%) on the study drug. Discontinuations were lower with FTY720 0.5 mg (10%) versus 1.25 mg (15%) or IM IFNβ-1a (12%). Of 1272 patients, 1033 (81%) completed FREEDOMS, 945 (74%) on the study drug. Discontinuations were lower with FTY720 0.5 mg (19%) versus 1.25 mg (31%) or placebo (28%). In TRANSFORMS and FREEDOMS, headache, nasopharyngitis, and fatigue were reported in >10% of all participants (also upper respiratory tract infection in FREEDOMS). A transient, generally asymptomatic bradycardia (8–10 bpm) occurred after the first dose (FREEDOMS: 3.3% with FTY720 1.25 mg; 2.1% with 0.5 mg; 0.7% with placebo) (TRANSFORMS: 2.4% with FTY720 1.25 mg; 0.5% with 0.5 mg; 0% with IM IFNβ-1a), as did infrequent atrioventricular (AV) conduction blocks (<0.5% for 0.5 mg group). In some patients, minor increases in blood pressure (1–3 mmHg increase in mean blood pressure) were observed within 6 months and persisted on therapy. Asymptomatic liver enzyme elevations were observed. In the two trials, macular edema occurred in 13 FTY720 patients (11 on 1.25 mg; 2 on 0.5 mg). Serious infections occurred in 1.7%, 0.2%, and 1.4% in the FTY720 1.25 mg, 0.5 mg, and IM IFNβ-1a groups, respectively, in TRANSFORMS; and in 2.6% (1.25 mg), 1.6% (0.5 mg), and 1.9% (placebo), respectively, in FREEDOMS. Five deaths were reported in the two trials: two on placebo, and three (two fatal herpes infections) on FTY720 1.25 mg. Malignancy was more common with FTY720 in the 1-year TRANSFORMS study but more common in the placebo group in the 2-year FREEDOMS study. **Conclusions:** FTY720 is generally well tolerated but is associated with transient bradycardia, infrequent AV conduction block, macular edema, and elevations of liver transaminases. Collective data do not suggest an increased risk of overall infections or malignancies.

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Poster Presentations

Friday, June 4 (6:30 pm - 8:00 pm)


Keywords: disease-modifying treatment in MS