Background: Oral fingolimod (FTY720), a sphingosine 1-phosphate receptor modulator, has shown efficacy on magnetic resonance imaging (MRI) data and relapse-related outcomes in a 6-month, placebo-controlled, phase 2 study and a 12-month, comparative, phase 3 study with intramuscular interferon beta-1a. **Objectives:** To report 24-month efficacy results from the FREEDOMS phase 3 trial of fingolimod once daily versus placebo in patients with relapsing-remitting MS (RRMS).

**Methods:** In this randomized, double-blind study, RRMS patients (18–55 years) with Expanded Disability Status Scale (EDSS) score of 0 to 5.5 and ≥1 relapse in the previous year (or ≥2 in the previous 2 years) were randomized to receive fingolimod (0.5 mg or 1.25 mg) or placebo. The 24-month primary efficacy end point was annualized relapse rate (ARR). The principal secondary end point was time-to-3-month-confirmed disability progression (1-point EDSS increase from baseline or 0.5-point increase if baseline EDSS was ≥5.5). Other clinical and MRI measures were included as secondary outcome measures.

**Results:** Of 1272 patients, 1033 (81%) completed the study; baseline demographics of the groups were similar. The ARR was reduced by 54% with fingolimod 0.5 mg (0.18 relapses/year) and 60% with fingolimod 1.25 mg (0.16) versus placebo (0.40; P < .001 for both comparisons). Fingolimod reduced the risk of 3-month confirmed disability progression, compared with placebo, over 24 months by 30% to 32% (0.5 mg and 1.25 mg, respectively; P = .02 for both comparisons). The reduction in risk of 6-month confirmed disability progression was 37% to 40% (1.25 mg; P ≤ .01 for both comparisons). At month 24, 70% to 75% of fingolimod-treated patients were free from relapses versus 60% of placebo-treated patients (P < .001 for both comparisons). Time-to-first relapse was delayed in the two fingolimod groups, as was the risk of relapse (the latter by 52% to 62% vs. placebo; P < .001 for both comparisons). Mean T2 lesion count was reduced by 74% with fingolimod compared with placebo.

**Conclusions:** Both oral fingolimod doses had beneficial effects on ARR, disability progression, and MRI outcomes compared with placebo in patients with RRMS.

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