Randomized trial of oral teriflunomide for relapsing multiple sclerosis.

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Abstract
BACKGROUND: Teriflunomide is a new oral disease-modifying therapy for relapsing forms of multiple sclerosis.

METHODS: We concluded a randomized trial involving 1088 patients with multiple sclerosis, 18 to 55 years of age, with a score of 0 to 5.5 on the Expanded Disability Status Scale and at least one relapse in the previous year or at least two relapses in the previous 2 years. Patients were randomly assigned (in a 1:1:1 ratio) to placebo, 7 mg of teriflunomide, or 14 mg of teriflunomide once daily for 108 weeks. The primary end point was the annualized relapse rate, and the key secondary end point was confirmed progression of disability for at least 12 weeks.

RESULTS: Teriflunomide reduced the annualized relapse rate (0.54 for placebo vs. 0.37 for teriflunomide at either 7 or 14 mg), with relative risk reductions of 31.2% and 31.5%, respectively (P<0.001 for both comparisons with placebo). The proportion of patients with confirmed disability progression was 27.3% with placebo, 21.7% with teriflunomide at 7 mg (P=0.08), and 20.2% with teriflunomide at 14 mg (P=0.03). Both teriflunomide doses were superior to placebo on a range of end points measured by magnetic resonance imaging (MRI). Diarrhea, nausea, and hair thinning were more common with teriflunomide than with placebo. The
incidence of elevated alanine aminotransferase levels (≥1 times the upper limit of the normal range) was higher with teriflunomide at 7 mg and 14 mg (54.0% and 57.3%, respectively) than with placebo (35.9%); the incidence of levels that were at least 3 times the upper limit of the normal range was similar in the lower- and higher-dose teriflunomide groups and the placebo group (6.3%, 6.7%, and 6.7%, respectively). Serious infections were reported in 1.6%, 2.5%, and 2.2% of patients in the three groups, respectively. No deaths occurred.

**CONCLUSIONS:** Teriflunomide significantly reduced relapse rates, disability progression (at the higher dose), and MRI evidence of disease activity, as compared with placebo. (Funded by Sanofi-Aventis; TEMSO ClinicalTrials.gov number, NCT00134563.)

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