Teriflunomide Reduced MS Relapse Rate by 31%

BY SHARON WORCESTER
FROM THE ANNUAL CONGRESS OF THE EUROPEAN COMMITTEE FOR TREATMENT AND RESEARCH IN MULTIPLE SCLEROSIS (ECTRIMS)

Teriflunomide, a novel oral disease-modifying drug, significantly reduced the annualized relapse rate and the risk of disability progression in relapsing multiple sclerosis by about 31% in a 2-year, phase III trial. The study of Teriflunomide in Reducing the Frequency of Relapses and placebo, said Dr. O’Connor of St. Michael’s Hospital, Toronto. He is the principal investigator for TEmSO.

“In my view, teriflunomide is a safe and effective new monotherapy, and it represents a potential first-line treatment for patients with relapsing MS,” he said during a press briefing on the TEMSO findings.

The safety profile of teriflunomide in this study was a particularly strong, positive point, he added. The overall adverse event rates were the same in the placebo and treatment groups, as were the rates of adverse events leading to permanent discontinuation of treatment. Patients in the teriflunomide group experienced more nausea, diarrhea, increases in alanine transaminase, and hair thinning than those in the placebo group, but these effects were mild and patients in both groups were generally very well tolerated, and no opportunistic infections occurred, he said.

TEMZO participants were adults aged 18-55 years with relapsing MS and a score of 5.5 or lower on the Expanded Disability Status Scale, and had experienced at least one relapse in the year prior to enrollment, or two relapses in the prior 2 years.

The availability of an oral agent for the treatment of this complex and progressively disabling disease is very good news for MS patients, Dr. Giancarlo Comi said during the press briefing.

“Of course it is central in the management of these patients to have available drugs to modify the disease course – we are literally entering a period where we can provide patients with much better support than ever before,” said Dr. Comi of Clinica Neurologica, Ospedale San Raffaele, Milan, Italy.

Indeed, other ongoing research is also demonstrating the safety and efficacy of teriflunomide, both as monotherapy and in combination with other treatments, said Dr. Mark Freedman of the Multiple Sclerosis Research Clinic at Ottawa (Canada) Hospital. Dr. Freedman and co-authors are investigators in the TEMSO trial.

For example, an open-label extension of a phase II trial of teriflunomide, which was also reported at the ECTRIMS congress, showed that teriflunomide was well tolerated during 8 years of continuous use following a 36-week double-blind portion of the study. Also, teriflunomide in combination with subcutaneous injection of interferon beta-1a has been shown to improve MRI outcomes in MS patients to a significantly greater extent than those who received placebo, Dr. Freedman said that the results from a second phase III study of teriflunomide are expected to be reported in 2012.

Major Finding: Compared with the placebo group, those in both the 7-mg and 14-mg teriflunomide groups experienced a statistically significant 31% reduction in the annualized relapse rate, which was the primary end point.

Data Source: A randomized, placebo-controlled phase III trial (TEMZO) involving 1,088 patients with relapsing MS.

Disclosures: Sanofi-Aventis sponsored the trial. Dr. O’Connor, Dr. Comi, and Dr. Freedman disclosed financial relationships with many companies that manufacture drugs for MS, including Sanofi-Aventis.

Accumulation of Disability in Patients with Multiple Sclerosis (TEMZO), which was sponsored by Sanofi-Aventis, randomized 1,088 patients to receive a single daily dose of 7 mg or 14 mg of teriflunomide or placebo.

The primary end point – the annualized relapse rate – was significantly lower in the 7-mg and 14-mg groups (0.370 and 0.369, respectively) than it was in placebo-treated patients (0.539). These rates represented a statistically significant reduction of 31% compared with placebo. Patients in the 14-mg group also experienced a significant 30% reduction in the risk of disability progression, Dr. Paul O’Connor reported at the congress.

Teriflunomide is the active metabolite of leflunomide, a synthetic, low-molecular-weight drug that was approved by the Food and Drug Administration in 2002 for the treatment of rheumatoid arthritis. The metabolite is a reversible inhibitor of the cytidine dehydro-orotate dehydrogenase (DHODH), which exerts anti-inflammatory, antiproliferative, and immunosuppressive effects, but the mechanisms by which it does so are not yet completely understood. Inhibition of pyrimidine biosynthesis (via suppression of DHODH) and interference with tyrosine kinase activity both contribute to the reduction of disease as determined by total lesion volume, for example, was reduced by 39% and 67% in the 7-mg and 14-mg dose groups, respectively, compared with placebo, said Dr. O’Connor of St. Michael’s Hospital, Toronto. He is the principal investigator for TEMSO.

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