New MS Agent Reduces Relapse Rate, Disability

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TORONTO — The investigational drug fingolimod at doses of 0.5 mg and 1.25 mg appears to be a safe and effective treatment for adults with multiple sclerosis, based on data from more than 1,000 patients.

In previous studies, fingolimod had "a clear cut effect on inflammatory outcomes" in relapsing-remitting multiple sclerosis patients, said Dr. Ludwig Kappos of University Hospital in Basel, Switzerland.

The current phase III study addressed whether the effects of fingolimod (FTY720) persisted over time, and whether a 0.5-mg dose is as effective as the previously studied 1.25-mg dose. The main outcome was relapse rate per year over a 2-year follow-up period.

The Food and Drug Administration is scheduled to review the safety and efficacy data for fingolimod this month.

The Fingolimod (FTY720) vs. Placebo in Relapsing-Remitting Multiple Sclerosis (FREEDOMS) study included 1,272 patients aged 18-55 years.

The average age of the patients was 37 years, and the average duration of MS was 8 years.

Patients with systemic or immune system disease were excluded, and 1,033 patients completed the study.

Patients were randomized to receive a daily dose of 1.25 mg fingolimod, 0.5 mg fingolimod, or a placebo.

The annualized relapse rate was reduced by 54% in patients who took 0.5 mg of fingolimod and by 60% in those who took 1.25 mg of fingolimod.

There was no significant difference in effectiveness between the doses, and both doses were significantly more effective than the placebo.

After 24 months, significantly more patients in either fingolimod group (70%-75%) were relapse free, compared with 46% of the placebo group.

In addition, both the 1.25-mg and 0.5-mg doses of fingolimod were associated with of 32% and 30%, reductions, respectively, in the risk of 3-month confirmed disability progression. Both reductions were significant, compared with placebo.

Similarly, both the 1.25-mg and 0.5-mg doses were associated with reductions in risk of 6-month confirmed disability progression of 40% and 37%, also significant compared with placebo.

Safety and tolerability data for the study population were presented separately in a poster by Dr. Paul O'Connor of St. Michael's Hospital, Toronto, and his colleagues.

In the safety analysis, the researchers evaluated all patients at baseline screening, week 2, and months 1, 2, 3, 6, 9, 12, 15, 18, 21, and 24.

Overall, the incidence of any adverse event was 94% in both of the fingolimod groups and 93% in the placebo group. The incidence of an adverse event that caused a patient to stop treatment was 14% in the 1.25-mg group, and 8% in both the 0.5-mg and placebo groups.

Serious adverse events were reported in 51 patients (12%) in the 1.25-mg group, 42 patients (10%) in the 0.5-mg group, and 56 patients (13%) in the

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Major Finding: The annualized relapse rate was reduced by 54% in multiple sclerosis patients who took 0.5 mg of fingolimod and by 60% in those who took 1.25 mg of fingolimod. After 24 months, around 70% of patients given fingolimod were relapse free, compared with 46% of the placebo group.

Data Source: A randomized, double-blind, placebo-controlled phase III study of 1,272 adults with MS.

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placebo group. Serious adverse events included cardiovascular disorders, neoplasms, nervous system disorders, macular edema, and abnormal liver function test results.

Sinus bradycardia, the most common ECG finding, occurred in 47 patients (11%) in the 1.25-mg group, 20 patients (5%) in the 0.5-mg group, and 6 patients (2%) in the placebo group.

In addition, first- and second-degree atrioventricular blocks were reported in 20 patients (5%) and 1 patient (0.2%), respectively, in the 0.5-mg group, compared with 37 patients (9%) and 4 patients (1%), respectively, in the 1.25-mg group.

Malignant neoplasms were reported in 4 patients in each of the fingolimod groups and in 10 patients in the placebo group.

All 11 cases of skin cancer reported in the study were successfully treated with excision.

Abnormal liver function tests were reported more than twice as frequently in the fingolimod 1.25-mg and 0.5-mg groups, compared with placebo (19%, 16%, and 5%, respectively).

But "liver enzyme elevations were asymptomatic and improved once therapy was discontinued; no patient developed liver failure," the investigators wrote.

In the 1.25-mg group, one case of ischemic stroke occurred during the study period, and a transient ischemic attack occurred 8 months after the discontinuation of treatment.

No clinically relevant pulmonary function changes were observed in any of the groups.

All seven reported cases of macular edema occurred in the group that took 1.25 mg of fingolimod, and all cases resolved after treatment was discontinued.

The overall incidence of infections was similar (69%-72%) for all three groups, and included herpesvirus infections, lower respiratory tract infections, and urinary tract infections.

The results support safety data from previous studies and suggest that most patients with MS tolerate oral fingolimod, the researchers said.

Also consistent with previous studies, "the overall safety profile of fingolimod 0.5 mg appears to be more favorable than that of the 1.25-mg dose," they added. ■