MS Oral Options Warrant Cautious Optimism

BY SHERRY BOSCHERT

HONOLULU – Oral therapies for relapsing-remitting multiple sclerosis that are in development have neurologists feeling both excited and a bit apprehensive. “There are a whole slew of orals coming,” Dr. Manko Kita, director of the multiple sclerosis center at Virginia Mason Medical Center, Seattle.

She commodated a session on multiple sclerosis trials that included a report on a pooled analysis of safety data on the only approved oral therapy for multiple sclerosis, fingolimod (Gilenya). (See story on p. 10.) The session also included positive phase III clinical trial results for the experimental oral teriflunomide. Earlier in the meeting, separate investigators reported positive phase III clinical trial results for the experimental oral teriflunomide therapy teriflunomide. Earlier in the meeting, separate investigators reported positive phase III clinical trial results for the experimental oral teriflunomide therapy teriflunomide.

Another oral agent under study, BG-12 (dimethyl fumarate), received Fast Track designation from the Food and Drug Administration and is in phase III clinical trials. Cldadrine (Leustatin), which is currently marketed as a chemotherapy for certain leukemias and lymphomas, initially was rejected by the FDA when it was submitted for approval as an oral therapy for multiple sclerosis. Following resubmission by the manufacturer, the FDA in early 2011 sent a letter to the company acknowledging sufficient data on the drug’s efficacy in multiple sclerosis but requiring more data on safety and risk-benefit considerations before it could be approved. Dr. Kita’s commodator, Dr. Benjamin N. Greenberg, commented after the session that with the expected approvals of several oral agents over the next few years, “I’m getting concerned that there’s going to be a little bit of a free-for-all coming.” But he added, “It’s good to have options. We’re all thrilled.”

The only head-to-head comparison of an oral therapy against another active treatment for multiple sclerosis so far is a study of fingolimod vs. interferon, he noted. Direct comparisons of the various oral agents will be needed to help clinicians develop treatment strategies, said Dr. Greenberg, a neurologist at the University of Texas Southwestern Medical Center, Dallas.

Gilenya may have some superiority, compared with once-weekly interferon dosing, Dr. Kita said, but its potential adverse cardiovascular effects and “downstream consequences in terms of effects on different organ systems makes another oral daily alternative with less toxicity that much more appealing.”

Dr. Aaron Miller of Mount Sinai School of Medicine, New Jersey, and Dr. Jerry S. Wolinsky of the University of Texas, Houston, presented results of the Teriflunomide Multiple Sclerosis Oral (TEMSO) trial during the session. The multinational, double-blind study randomized 1,088 patients with relapsing-remitting multiple sclerosis to a single daily dose of 7 mg or 14 mg of teriflunomide or placebo for 2 years.

Both doses reduced the annualized relapse rate by approximately 31%, compared with placebo. The annualized relapse rate was 0.37 in each of the treatment groups and 0.54 in the placebo group. The risk of disability progression also was significantly reduced by 30% in the 14-mg group but was not significantly different in the 7-mg group, compared with placebo.

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Dr. MILLER

No Improvement in MS With Ginkgo biloba, Simvastatin

BY SHERRY BOSCHERT

FROM THE ANNUAL MEETING OF THE AMERICAN ACADEMY OF NEUROLOGY

HONOLULU – Ginkgo biloba and simvastatin were not helpful in patients with relapsing-remitting multiple sclerosis in separate randomized controlled trials.

Treatment with ginkgo at 120 mg twice a day for 12 weeks produced no significant, short-term improvements in cognitive function by only 21 patients. The addition of simvastatin (Zocor) to interferon therapy for multiple sclerosis in a separate study did not significantly reduce the annualized relapse rate after 1-3 years, investigators reported at the meeting.

In the first study, both the ginkgo and placebo groups had improved average scores on a battery of neuropsychological tests. There were no significant differences between groups in scores on the Paced Auditory Serial Addition Test, the California Verbal Learning Test II, the Controlled Oral Word Association Test, or the Stroop Color–Word Test, said Dr. Jesus Lovera of Louisiana State University, New Orleans.

The two groups also did not differ significantly in secondary outcomes (including perceived cognitive deficits, family reports of cognitive deficits, fatigue, or depression) or in rates of adverse events. In the ginkgo group, one patient had an MI and one developed a severe depressive episode requiring hospitalization, but these were not attributed to ginkgo.

While the study found no short-term cognitive benefits from ginkgo, it did not assess any potential long-term benefits, Dr. Lovera said. There were no approved treatments for impairment of cognition in people with multiple sclerosis, which affects 40%-50% of patients.

Dr. Per Soelberg Sørensen and his associates in a separate presentation on a study of 307 treatment-naive patients who were starting treatment with interferon-beta-1a (IFN-beta-1a, Avonex) for relapsing-remitting multiple sclerosis. They were randomized to add-on therapy with either placebo or 80 mg/day of simvastatin (40 mg/day in the first month) for 1-3 years. Patients were followed clinically every 3 months and brain MRIs were conducted at baseline and after 1 year of treatment. At least 90% of follow-up was completed by 136 patients in the simvastatin group and 132 in the placebo group.

In the study, the annualized documented relapse rate was 31% higher in the simvastatin group (0.19) compared with the placebo group (0.14), but the difference was not statistically significant, said Dr. Sørensen of the Danish Multiple Sclerosis Center in Righospitalet, Copenhagen. The annualized total rate of documented and undocumented relapses was 37% higher in the simvastatin group (0.44), compared with the placebo group (0.38). Patients who received simvastatin had more new or enlarging T2 lesions on MRI than did those who received placebo (3 vs. 2.5). These and other measures were not statistically significant differences between groups, but suggested a trend toward more disease activity in the simvastatin group compared with placebo.

Dr. lovera and two of his associates disclosed financial relationships with EMD Serono, Teva Pharmaceuticals, Biogen Idec, and/or Pfizer. The ginkgo and placebo were provided by Dr. Willmar Schwabe GmbH, Karlsruhe, Germany. The U.S. Department of Veterans Affairs funded his study.

Dr. Sørensen and two of his associates disclosed financial relationships with Biogen Idec, Merck Serono, Teva Neurosciences, Genmab, Novartis, Bayer Schering, and/or Sanofi-Aventis. The study was funded by Biogen Idec.