St. John's Wort Equals Paroxetine in Study

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EXETER, ENGLAND — A proprietary formulation of St. John's wort was equivalent in efficacy to paroxetine for moderate to severe depression in a prospective, randomized, multicenter study, Stephan Klement, M.D., reported at a symposium on alternative and complementary therapies sponsored by the universities of Exeter and Plymouth.

A group of 101 German patients whose Hamilton Rating Scale for Depression (HAM-D) scores exceeded 22 points were randomized to receive standardized hypericum extract WS 5570 (Dr. Willmar Schwabe Pharmaceuticals, Karlsruhe, Germany) in an initial daily dose of 900 mg/day, or paroxetine (Paxil) in an initial dose of 20 mg/day.

Patients whose initial response was insufficient could increase the dose of hypericum extract to 1,800 mg/day or of paroxetine to 40 mg/day. Response was considered to be a reduction of 50% or greater on the HAM-D, and remission was defined as a HAM-D end point total score below 10, said Dr. Klement of Schwabe Pharmaceuticals.

In a preplanned interim analysis at 6 weeks, response rates were 60% in the hypericum group and 63% in the paroxetine group, while remission rates were 46.6% with hypericum and 42.9% with paroxetine. The rates in the two groups were comparable, he said in a poster session.

Adverse events when calculated as incidence densities were 0.039/day of exposure for hypericum and 0.056/day of exposure for paroxetine. This represents a 43.6% advantage for hypericum based on ratio.

These findings differ from those seen in another randomized trial that compared a different extract of St. John's wort (LI 160, Lichtwer Pharma, Berlin) with sertraline and placebo. In that study, performed in the United States by the Hypericum Depression Trial Study Group, neither sertraline nor the hypericum extract was significantly different from placebo in a group of 340 patients with major depression (JAMA 2002;287:1807-14).

"The major differences between the two trials can be attributed to different patient populations and the missing assay sensitivity in the [JAMA] trial," Dr. Klement told FAMILY PRACTICE NEWS.

Patients in the American trials were recruited from tertiary care clinics, and patients who had not responded to adequate trials of two antidepressant trials were included. The depressive episode had already persisted for more than 2 years in roughly one-third of patients, and for between 6 months and 2 years in a further third. This suggests that many of the patients were chronically depressed and some may have been treatment resistant, Dr. Klement said.

In the German study, patients were limited to only one previous adequate antidepressant therapy trial, "probably limiting the number of treatment-resistant patients," he said. The mean duration of the current depressive episode was significantly shorter in the German trial, suggesting that fewer patients were chronically depressed, and patients had sought care spontaneously in primary or secondary care settings.

The major drawback of the American study was its lack of assay sensitivity, Dr. Klement said. "Sertraline, a proven synthetic antidepressant, served as a positive control to check the sensitivity of the study. Neither St. John's wort extract nor sertraline differed significantly from placebo in the primary target criteria, which were reduction of the Hamilton depression total score and the number of patients showing complete remission."

The trial therefore did not have the assay sensitivity to document an antidepressant drug effect and thus does not appear to be useful for estimating the therapeutic potential of either St. John's wort or sertraline, he said, adding that in the German study, "no placebo group was included as it would have been unethical to give placebo to patients suffering from severe depression." ■

Expert Commentary

FAMILY PRACTICE NEWS asked David Spiegel, M.D., to comment on the new hypericum trial.

Dr. Spiegel, the Jack, Lulu, and Sam Willson Professor in the School of Medicine and associate chair of psychiatry and behavioral sciences, Stanford (Calif.) University, had this to say:

"This is an interesting study, well conducted but with the obvious drawbacks that it has no placebo control group. Also, it is always harder to prove statistically the absence of a difference (between hypericum and paroxetine) than the presence of a difference.

"The author is right that the JAMA study suffered because placebo patients actually did slightly better than those randomized to either hypericum or sertraline. Unfortunately, they used rather low doses of sertraline (50 or 100 mg) when one can prescribe up to 200 mg. Thus, neither treated group did especially well. They might have been treatment resistant, as the author suggests.

"This new study does provide suggestive, but not definitive, evidence that hypericum works as well for mild to moderate depression as paroxetine, but it does not rule out the possibility that this group of patients had transient depressive symptoms that are really responding to a placebo effect or the passage of time."