

CVD May Be Linked to Depression in Lupus

BY MITCHEL L. ZOLER

PHILADELPHIA — Patients with lupus have a high prevalence of depression, which may be linked to the cardiovascular disease that's also highly prevalent in lupus patients.

Cardiovascular disease and cardiovascular risk “may precipitate development of depression in patients with lupus,” Laura Julian, Ph.D., said at the annual meeting of the American College of Rheumatology. It's also possible that depression in patients with systemic lupus erythematosus (SLE) exacerbates cardiovascular disease by making patients poorly compliant with treatment. “The relationship between cardiovascular disease and depression [in lupus patients] may be bidirectional,” she said.

Because of this apparent interrelationship, physicians who care for SLE patients should regularly screen them for depression and treat it when diagnosed. Physicians should also be diligent about screening for and treating cardiovascular disease risks in lupus patients, said Dr. Julian, a neuropsychologist at the University of California, San Francisco.

“Our working hypothesis is that accumulation of vascular disease in specific white-matter regions of the brain might precipitate development of depression. In lupus patients there is a very high risk of cardiovascular outcomes, so we think this is reasonable,” she said in an interview. This etiology has been called vascular depression.

Evidence supporting the occurrence of vascular depression in SLE patients came from following patients who were enrolled in the Lupus Outcomes Study, which enrolled patients with SLE at the University of California, San Francisco. Dr. Julian and her associates collect-



Laura Julian, Ph.D., says vascular disease in specific white-matter regions may cause the depression.

ed data from 725 lupus patients who were followed for more than 5 years. More than 90% of the patients were women, and average age at entry to the study was 51.

At entry and regularly during follow-up, the patients were assessed for depression by having them complete the CES-D (Center for Epidemiology Studies–Depression) scale, a commonly used, self-report, 20-question survey. People who scored 23 or higher on the CES-D were considered to have probable depression. In the series, 23% met this set of criteria at baseline.

During follow-up, about 12% of the SLE patients developed depression each year, but another 10% who had been previously identified with depression remitted. Dr. Julian said this pattern is typical for depression, which

generally occurs and remits over time.

Dr. Julian and her associates analyzed a variety of demographic and clinical variables to see which factors were linked with new-onset depression during the 5 years of follow-up. A multivariate analysis identified three measures that had a significant association: a socioeconomic status below the poverty level, which linked with a greater than threefold risk for incident depression; a history of myocardial infarction or stroke, linked with a twofold greater rate of new depression; and greater SLE disease activity, linked with a 12% higher rate of new depression.

Analyzing the data a different way, the researchers found that through the 5 years of follow-up, 25% of the SLE patients without a history of cardiovascular disease or poverty had an episode of new depression. Among those with either cardiovascular disease or poverty, the rate for a new depression episode was about 40%. And in patients with a history of both cardiovascular disease and poverty, 80% had an episode of incident depression during the study.

The CES-D could also be used to diagnose depression in a routine-practice setting, and it would be reasonable for physicians to screen patients with SLE for depression every few months, Dr. Julian said. So far, there is no evidence proving that conventional behavioral and medical treatments for depression are effective in SLE patients, but until this is evaluated in a study, it is reasonable to use these treatments on depressed SLE patients, she said.

Dr. Julian said that she had no financial disclosures. ■

📺 Watch a video interview with Dr. Julian at <http://www.youtube.com/watch?v=jm4KZ6KFoMM>.

Eplivanserin Beats Flurazepam On Next-Day Cognitive Effects

BY BRUCE JANCIN

ISTANBUL, TURKEY — The novel sleep aid eplivanserin proved to be well tolerated, with no effects on next-day cognitive or psychomotor performance, whether given alone or in combination with zolpidem in a randomized, double-blind, placebo- and benzodiazepine-controlled crossover trial.

Eplivanserin (Ciltyri) is an investigational agent, the furthest along in terms of development in a new drug class called the antagonists of serotonin two-A receptors, or ASTARs. Eplivanserin increases EEG slow-wave sleep, Dr. Christine Roy explained at the annual congress of the European College of Neuropsychopharmacology.

As an ASTAR, eplivanserin would be expected to avoid impairment of next-day functioning, unlike benzodiazepines, which exert their hypnotic effect by binding to GABA receptors, added Dr. Roy of Sanofi Aventis in Chilly-Mazarin, France.

She presented a study in which eplivanserin's effects upon cognitive and psychomotor performance were compared to those of flurazepam and placebo in 24 healthy subjects. In the first portion of the study, participants were randomized to a single bedtime 30-mg dose of flurazepam or placebo. The next morning they had to complete six psychometric tests. After a 21-day washout period,

subjects were switched to the other treatment arm and testing was repeated.

The morning after taking flurazepam, participants displayed significantly worse cognitive performance, significantly more sedation, and—somewhat surprisingly—significantly better psychomotor performance than after placebo.

In the second phase of the study, subjects took 5 mg of eplivanserin or placebo at bedtime on 21 consecutive nights, then took the six psychometric tests on the morning of day 22. That night they took 10 mg of immediate-release zolpidem (Ambien) with their eplivanserin or placebo, then once again underwent psychometric testing the following morning. Then the eplivanserin and placebo groups were crossed over, and the sequence was repeated.

After 21 nights of eplivanserin, the test results for next-day cognitive and psychomotor performance and sedation weren't significantly different from the following 21 nights of placebo. The same was true after taking eplivanserin plus zolpidem, compared with placebo plus zolpidem, Dr. Roy reported.

In September, the Food and Drug Administration responded to Sanofi Aventis' application for marketing approval for eplivanserin with a request for additional data on the drug's risk/benefit ratio.

Dr. Roy's randomized trial was sponsored by Sanofi Aventis. ■

Early Pain Reduction Flags Greater Duloxetine Efficacy

BY BRUCE JANCIN

ISTANBUL, TURKEY — Early marked reduction in pain in response to duloxetine proved to be the strongest predictor of significant long-term improvement in depressive symptoms in depressed subjects in the German PADRE study.

A 50% or greater improvement in self-gauged overall pain symptoms on a visual analog scale (VAS) after 4 weeks on the selective norepinephrine reuptake inhibitor was associated with a threefold greater likelihood of achieving at least a 50% decrease on the clinician-rated Inventory for Depressive Symptomatology (IDS) scale at 6 months, the primary study end point, Dr. Michael Linden said at the annual congress of the European College of Neuropsychopharmacology.

PADRE was a prospective observational study in which 4,517 adult outpatients with a depressive episode received treatment with duloxetine (Cymbalta) at 693 centers in Germany. Lilly Deutschland and Boehringer Ingelheim sponsored the study. The mean age of participants was 52 years, and 72% were women.

The mean baseline score on the clinician-rated IDS was 40 on the 0-84 scale. Eighty percent of subjects had moderate to severe painful symptoms at base-

line (VAS score of greater than 30 out of a possible 100). During the 6-month study, 26.5% of subjects dropped out.

The mean VAS pain score in the overall study population improved from 55 at baseline to 31 at 6 months. Forty-eight percent of patients reported at least a 50% reduction in pain on the VAS after 4 weeks of treatment, a clinically significant improvement. Nearly two-thirds of these early pain responders experienced remission of their depression by 6 months as defined by an Inventory for IDS score of 12 or less; this remission rate was twice that of patients who did not achieve at least a 50% decrease in pain at 4 weeks, noted Dr. Linden of Charité University Hospital, Berlin.

The secondary end point was the change over 6 months in the KUSTA, a 100-point German-language depression scale encompassing mood, activity, sleep, and tension/relaxation. The mean KUSTA improved from a baseline of 25 to 58 points at 6 months in those who did not show a significant pain response by 4 weeks, and by an additional 13.3 points in those who did.

Seventeen percent of PADRE participants reported one or more treatment-emergent adverse events, most commonly mild nausea and other GI side effects, hyperhidrosis, vertigo, and headache. There was no weight gain during the 6 months of therapy. ■