Novel Melatonergic Antidepressant Piques Interest

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VIENNA — "Agomelatine" was the word on everyones lips at the annual congress of the European College of Neuropsychopharmacology.

The buzz surrounding the first melatonergic antidepressant rose in reaction to the presentation at the congress of favorable results of a large randomized trial demonstrating sustained efficacy and no safety issues during 6 months of therapy, along with the first study showing efficacy in generalized anxiety disorder (GAD).

The expectation is that Servier, a French pharmaceutical company, will gain European marketing approval next year for agomelatine (Valdoxan) for treating major depression. Novartis, which has rights to develop and market it in the United States, has not yet applied to the Food and Drug Administration for marketing approval.

"[It] will provide an opportunity to give a new type of antidepressant to people who haven't responded or who can't tolerate other antidepressants," Dr. David Nutt, ECNP president and professor of psychopharmacology and head of the department of community-based medicine at the University of Bristol (England), said in an interview.

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DR. MÖLLER

In addition, it should be less likely than selective serotonin reuptake inhibitors (SSRIs) and selective serotonin-norepinephrine reuptake inhibitors (SNRIs) to cause problems with sleep or sexual function, he said.

Dr. Hans-Jürgen Möller, who has been involved in agomelatine research, summarized the trials experience as showing efficacy comparable to that of SSRIs and SNRIs, but with a superior safety profile.

"This looks like it will be the antidepressant drug with the best tolerability yet," said Dr. Möller, professor and chairman of the department of psychiatry at Ludwig-Maximilians-University, Munich.

Dr. Guy Goodwin presented interim 6-month results of a planned 1-year randomized double-blind placebo-controlled multicenter trial of agomelatine for prevention of depressive relapses. The study involved 492 outpatients with major depressive disorder and a mean baseline Hamilton Depression Rating Scale (HAM-D) score of 27 (10-13, mild depression; 14-17, mild to moderate; > 17 moderate to severe). They were placed by their psychiatrist or primary care physician on 25-50 mg/day of open-label agomelatine for 8-10 weeks. After that, the 339 responders defined by a HAM-D of 10 or less were randomized to double-blind agomelatine or placebo. Only 15% in the agomelatine group required 50 mg/day.

After 24 weeks of double-blind therapy, 22% of patients in the agomelatine arm had relapsed, compared with 47% of those on placebo: a 54% reduction in risk of relapse as defined by a HAM-D of 16 or more or a suicide attempt. Comparable benefit was seen in the most severely depressed subgroup. There were few relapses in the first 6-8 weeks after the abrupt switch to placebo, and an absence of withdrawal symptoms, said Dr. Goodwin, professor of psychiatry at University of Oxford (England).

Dr. Dan J. Stein reported on 121 nondepressed patients with general anxiety disorder randomized to 12 weeks of agomelatine at 25-50 mg/day or placebo. The remission rate as defined by a Hamilton Anxiety Rating Scale total score of 7 or less was 45% in the agomelatine group and 22% with placebo, said Dr. Stein, professor and chair of the department of psychiatry at University of Cape Town (South Africa).

Agomelatine is a melatonergic agonist at the MT1 and MT2 receptors and an antagonist at the 5-HT2c receptor. It has been shown to reset desynchronized circadian rhythms. At a satellite symposium sponsored by Servier, Dr. Raymond W. Lam said agomelatine has been shown in human studies to improve sleep quantity and architecture, normalizing the temporal distribution of restorative slow wave sleep. Dr. Lam is professor of psychiatry and head of the division of clinical neuroscience at the University of British Columbia, Vancouver.

Dr. Nutt, Dr. Möller, Dr. Goodwin, Dr. Stein, and Dr. Lam are consultants to Servier and other drug companies. ■