To Reveal Root of Incomplete SSRI Response, Ask

BY ROBERT FINN
San Francisco Bureau

SAN FRANCISCO — The goal of antidepressant treatment should be remission, but most clinical trials use a 50% response in 50% of patients as the criterion for effectiveness. Only about 20%-30% of patients achieve complete remission, and this suggests that additional treatment will be necessary, Jeffrey M. Levine, M.D., said at the annual meeting of the American College of Physicians.

But before changing a patient’s selective serotonin reuptake inhibitor (SSRI) prescription because of an incomplete response, physicians should consider a series of questions, said Dr. Levine of the Albert Einstein College of Medicine, New York. First, determine whether the patient is taking the medication. Studies indicate that about 50% of SSRI prescriptions are filled only once. In addition, find out whether the patient is using alcohol or illicit drugs.

Next, use this as an opportunity to re-review relevant medical history. Has the patient had recent thyroid function and HIV tests? Is he or she taking any other medications, such as glucocorticoids, β-blockers, or fluoroquinolones that could affect depression treatment? Has the patient been evaluated for sleep apnea?

It may be productive to employ the systematic approach suggested by the mnemonic GUTTENs for possible causes of altered mental state, said Dr. Levine.

G: grand mal
U: unipolar
T: toxic, traumatic, encephalopathy
T: metabolic
E: endocrine/metabolic, neurological, neoplastic, systemic/ autoimmune
N: ask about domestic violence, ongoing safety issues, or threats to the patient.

If a patient is being abused or threatened by a partner, your antidepressants are not going to work for [him or her] better,” Dr. Levine said.

Consider whether the patient may have something to gain from depression. “If a patient has a comp case or a disability case going at this moment, it may be irrelevant or it may be very relevant.” Dr. Levine said.

It may just not be the time they’re going to get better.”

Consider the possibility that the patient may have something to gain from depression. “It may just not be the time they’re going to get better.”

If the physician answers all of those questions to his or her satisfaction, and the patient still has an incomplete SSRI response, physicians should consider a series of questions, said Dr. Levine.

First, consider whether the patient may have something to gain from aggression. “If a patient has a comp case or a disability case going at this moment, it may be irrelevant or it may be very relevant.”

Dr. Levine disclosed serving on the speakers’ bureaus for Pfizer Inc.

Pilot Study: Drug Combo Spurred Speedier Antidepressant Effects

BY DAMIAN MCNAMARA
Miami Bureau

BOCA RATON, Fla. — A comparison of escitalopram and bupropion might produce early remission in as many as one-third of patients with unipolar depression, according to a pilot study presented at a meeting of the New Clinical Drug Evaluation Unit sponsored by the National Institute of Mental Health.

However, the faster onset of action and increased remission rate observed with this combination compared with monotherapy come at a cost of increased adverse events.

“In my mind, the adverse events were manageable in most patients,” said Jonathan W. Stewart, M.D., a researcher with the department of psychiatry at the University of Miami, Miami. Delays are inherent in a sequential mono-therapy approach to antidepressant treatment. Mechanistic delays include the time it takes for biochemical effects to occur. Dosing delays occur as physicians wait for a patient to get better before increasing the dose. In addition, there are programmatic delays because “we wait to see if the first one does not work before we start the second drug,” he said.

Dr. Stewart assessed 29 outpatients with major depressive disorder. The mean age was 38 years, and the patients were moderately depressed at study entry. Exclusion criteria included a history of severe depression, substance abuse, bipolar disorder, or current use of other psychoactive drugs.

“We decided to mix escitalopram (Lexapro) with bupropion (Wellbutrin). This combination may address a mechanistic delay inherent in” treatment with selective serotonin reuptake inhibitors, Dr. Stew-

art said. He added that the use of two effective antidepressants might overcome programmatic delays.

There was a rapid dose escalation during the first 15 days, after which dosages were stabilized to day 56. Almost half of the patients, 49%, followed the protocol dosing, and 54% were on the maximum dosages at study completion at 8 weeks.

At 2 weeks, 10 of 29 patients (34%) met remission criteria—defined as a Hamilton Rating Scale for Depression (HAM-D) score of less than 8. “So we’re getting a third of the patients better at 2 weeks,” he noted. The mean score at week 2 was 11.

By comparison, there is a 6% remission rate with monotherapy at 2 weeks, according to Dr. Stewart’s own unpublished data for more than 500 patients. A total of 18 patients (62%) met remission criteria, and the mean HAM-D score was 6. Dr. Stewart said that the remission rate with monotherapy in his own unpublished data is 38%.

A total of 6 patients withdrew from the study, four because of adverse events. The most common adverse events were sleep related (reported by 5% of participants), including daytime sedation and insomnia. A total of 38% reported gastrointestinal effects, including abdominal pain and constipation, and 24% reported sexual effects, including decreased libido and anorgasmia. Patients also reported word-finding difficulty, headaches, dizziness, hives, sweating, increased blood pressure, and dizziness.

Despite the early onset of action of an escitalopram-bupropion combination, efficacy beyond 2 weeks looks similar to other combinations, Dr. Stewart said.