Escitalopram Bests Duloxetine For Severe Major Depression

BY BRUCE JANCIN
Denver Bureau

Chicago — Severely depressed patients who fail to respond to 2 weeks of escitalopram at 10 mg/day typically do better with uptitration to 20 mg/day for 8 weeks than with a switch to 8 weeks of duloxetine at 60 mg/day, according to a multicenter double-blind randomized clinical trial.

The advantage of escitalopram (Lexapro) over duloxetine (Cymbalta) in terms of reduction in Montgomery-Asberg Depression Rating Scale (MADRS) scores was evident at week 1, Dr. Gregory M. Asnis said at the American Psychiatric Association's Institute on Psychiatric Services.

"Prior to switching nonresponders to escitalopram to another antidepressant, clinicians should consider increasing the dose to 20 mg/day—perhaps another 8 weeks," said Dr. Asnis, professor of psychiatry and behavioral sciences at Montefiore Medical Center, New York.

From a mean baseline MADRS score of 34.7, the escitalopram group showed a greater than 20-point average drop during 8 weeks of double-blind therapy.

The study involved 571 adults with severe major depressive disorder as defined by a baseline MADRS of 30 or more. They had a mean 11.6-year history of major depression, with an 11-month duration of their current episode. They were placed on escitalopram at 10 mg/day for 2 weeks. Of those who completed this 2-week single-blind lead-in phase, 90% were judged nonresponders, meaning they experienced less than a 50% improvement in MADRS scores. Then, 474 nonresponders were randomized double-blind to 8 weeks of treatment with escitalopram at 20 mg/day or duloxetine at 60 mg/day.

The primary study end point—time to premature treatment discontinuation—was closely similar in the two groups. The premature discontinuation rate was 20.5% in the escitalopram arm and 21.2% with duloxetine, indicating treatment equivalence from a safety and tolerability standpoint.

However, from a mean baseline MADRS score of 34.7, the escitalopram group showed a greater than 20-point average drop during 8 weeks of double-blind therapy—significantly greater than the reduction with duloxetine.

Moreover, more than half of the escitalopram group achieved remission as defined by a MADRS total score of 10 or less, significantly greater than the 40% rate with duloxetine.

These findings are in line with the results of previous studies indicating escitalopram is at least as effective as is duloxetine for the acute treatment of major depressive disorder, Dr. Asnis said. He cited a 194-patient, double-blind, 24-week Scottish study (Curr. Med. Res. Opin. 2007;23:1605-14) and a 278-patient, double-blind, 8-week U.S. trial (Clin. Drug Investig. 2007;27:481-92). In both studies significantly more patients dropped out of the duloxetine arm because of side effects, unlike in the trial presented by Dr. Asnis, where 5.7% in the escitalopram arm and 5.3% in the duloxetine arm withdrew because of adverse events.

The rates and types of side effects were generally similar in the two treatment groups in the trial presented by Dr. Asnis. Dry mouth was more common with duloxetine (10.2% vs. 5.7%), as were constipation (8.6% vs. 4.4%) and insomnia (8.6% vs. 3.9%).

The trial was supported by Forest Laboratories. Dr. Asnis disclosed that he serves as a consultant to Forest, Jazz Pharmaceuticals, and Sanofi-Aventis. ■

Paroxetine Tied to Sperm DNA Fragmentation

BY KERRI WACHTER
Senior Writer

Use of paroxetine (Paxil) appears to put healthy men at greater risk of sperm DNA fragmentation, according to data from a small study.

In a study of 35 healthy male volunteers, SSRI treatment was significantly correlated with increased DNA fragmentation (odds ratio 11.12, $P = 0.0003$) on multivariate logistic regression, after correcting for age and body mass index.

"Healthy volunteers demonstrated a dramatic increase in DNA fragmentation within just a few weeks of paroxetine treatment, without an apparent impact on standard semen parameters. This negative impact on sperm DNA fragmentation may affect reproductive outcomes, even with [intracytoplasmic sperm injection]," study investigator Dr. Cigdem Tanrikut said in an interview.

"Certainly, one should query male patients about SSRI use. However, based on these preliminary findings, it would be premature to suggest a patient come off of SSRIs altogether or change to an alternate therapy given the lack of data regarding other newer antidepressants," said Dr. Tanrikut, Director of Male Reproductive Medicine at Massachusetts General Hospital's Fertility Center in Boston.

Men in the study ranged in age from 18 to 65 years. Intake assessment included physical exam, semen analysis, and the Brief Sexual Function Inventory (BSFI). Repeat semen analysis was obtained before SSRI initiation.

Paroxetine was given for 5 weeks: 10 mg daily during week 1; 20 mg daily during week 2; 30 mg daily during weeks 3-4; and 20 mg daily during week 5. Semen analysis was performed at weeks 2 and 4. One month after cessation of the SSRI, a final semen analysis was then performed. The BSFI was completed at week 4 and at the final semen collection.

The unadjusted odds ratio of having abnormal DNA fragmentation while on paroxetine was 9.33. In addition, BSFI revealed significant sexual dysfunction on paroxetine as compared with baseline. Up to 35% of men noted significant changes in erectile function, and up to 47% of subjects reported ejaculatory difficulties while on paroxetine. At least partial recovery of sexual function was noted within 1 month after stopping treatment.

The study was supported by the Frederick J. and Theresa Dow Wallace Fund of the New York Community Trust and Brady Urology Foundation. ■

Cognitive and Prolonged Exposure Therapies Beat SSRI for Early PTSD

BY MICHELE G. SULLIVAN
Mid-Atlantic Bureau

Barcelona — When given within a month of the precipitating event, cognitive therapy and prolonged exposure therapy are equally effective at decreasing the incidence of posttraumatic stress disorder—and both strategies are significantly more effective than treatment with escitalopram, study results showed.

The drug was no better than placebo or no treatment at all, a finding that disappointed Dr. Arieh Y. Shalev. "I'm saddened by it," he said at the annual congress of the European College of Neuropsychopharmacology. "We wanted this to have a positive effect, because we thought, in the case of mass trauma, it would be very good to have a compound that could be distributed soon after the event."

Dr. Shalev, director and founder of the Center for Traumatic Stress at Hadassah University Hospital, Jerusalem, presented the results of a randomized controlled trial of early intervention for posttraumatic stress disorder (PTSD). The potential study group consisted of 5,285 survivors of a traumatic event, who were all identified by emergency room records. All the subjects were contacted by telephone within a few days of discharge.

Most of the traumatic events (75%) involved a motor vehicle accident, 14% were work related, and 4% were terrorist events.

Researchers invited 1,470 survivors who expressed some PTSD symptoms to a clinical assessment. Almost half (49%) declined this invitation right away, Dr. Shalev said, indicating an enormous cultural barrier to seeking PTSD treatment.

Of those who were assessed, 398 had qualifying symptoms; 298 of those subjects were randomized into the trial, with treatment beginning within 20 days of the traumatic event. Treatment arms included 12 weekly sessions of cognitive therapy, 12 weekly sessions of prolonged exposure, 12 weeks of blinded treatment with placebo or 20 mg of the SSRI escitalopram (Lexapro), or 12 weeks on a waiting list. The group on the waiting list received only weekly telephone calls to check on their well-being and respond to emergencies.

All groups showed significantly reduced rates of PTSD. Cognitive therapy and prolonged exposure had the lowest incidence of PTSD (18% and 21%, respectively). Although escitalopram reduced the incidence of PTSD to 61%, it was not any more effective than placebo or being placed on the waiting list; the incidence of PTSD was reduced to 59% with placebo and to 57% for those on the waiting list. ■

Obesity in Black Women May Signal Depression

Chicago — The odds of comorbid depression are 41% greater in obese than in nonobese African American women, according to a large national study.

Based upon this finding, obese African American women should routinely be screened for depression during office visits, Stephanie Sturgis said at the annual American Psychiatric Association's Institute on Psychiatric Services.

The study involved 9,343 randomly selected African American women from 36 states. They participated in the Centers for Disease Control and Prevention's 2006 Behavioral Risk Factor Surveillance System survey and completed the Patient Health Questionnaire–8 Anxiety and Depression Screen.

More than 40% of the women had a body mass index of 30 kg/m^2 or greater, and more than 13% were depressed, as defined by a score of 10 or more on their summed responses to the depression screen. That probably underestimates the true prevalence of depression nationally because institutionalized women were excluded, said Ms. Sturgis, a public health analyst at the CDC.

In obese African American women, the adjusted odds of depression were significantly increased in those with a college degree, who were 2.75-fold more likely to be depressed than were those with less education.

Depression also was significantly more common in obese African American women who were moderate drinkers than in either obese heavy drinkers or nondrinkers. After adjustment for potential confounders, the moderate drinkers were 2.1-fold more likely to be depressed. In other studies, heavy drinking is associated with depression. Ms. Sturgis said the reason for the increased prevalence of depression in the current study is unclear.

—Bruce Jancin