Time to Response Varies

Depression *from page 1*

little bit closer to it," he said at the meeting, which also was sponsored by the University of Texas Southwestern Medical Center at Dallas and the University of New Mexico.

Since the trial's goal was remission, the first phase lasted 12-14 weeks during which time patients were treated with citalopram (Celexa), said Dr. A. John Rush, principal investigator of STAR*D and distinguished professor of psychiatry at the University of Texas Southwestern Medical Center at Dallas. Because remission is a higher standard, it takes longer to achieve than response to medication, the usual measure in shorter drug efficacy trials.

The STAR*D started in October 1999 and ends in September 2006 at 18 primary care settings and 23 psychiatric care settings. It enrolled 4,041 patients. The investigators reported that 28% of the 2,876 patients who could be evaluated after phase 1 achieved remission with citalopram.

More than a quarter of patients in both settings achieved remission as measured by the 17-item Hamilton Rating Scale for Depression (HAMD-17), and nearly half self-reported a response to medication (Am. J. Psychiatry 2006; 163:28-40).

"Primary care and specialist care, when treating similar patients with similar conditions, get similar results," Dr. Rush said.

He noted that two-thirds of people who responded on citalopram and half of those who remitted did so within the first 6 weeks.

Consequently, had the medication been switched or augmented by using a second drug at that point, a third of people who ultimately responded and half of those who remitted would not have had a long-enough trial.

"If we said augment after 6 weeks, that would have been a big mistake. They would be getting augmentation they did not need," Dr. Rush said, urging clinicians to increase doses and wait 8-10 weeks before making a treatment change in patients who do not get better.

"Some patients take longer to show benefits," he said. "I was impressed that we can see really nothing at 4 weeks and have a remission by 10 weeks."

Results will be reported later this year for 1,475 patients who moved to a follow-up phase after remitting on citalopram. An additional 1,127 patients left the study after the first phase.

The 1,439 who stayed for phase 2 included 583 patients who switched to bupropion (Wellbutrin-SR), sertraline (Zoloft), or venlafaxine (Effexor-XR), and 430 patients who augmented citalopram with bupropion or buspirone. Cognitive therapy also was used in 156 patients on an augmentation regimen as well as in 104 patients who were switched.

'You hang in for two steps and you have more than a 50% chance ... of getting rid of your depression.'

DR. RUSH

Remission rates and time to remission were similar for patients who switched medications, regardless of the antidepressant to which they were randomized.

About one-quarter self-reported remission and 17.6%-24.8% achieved remission based on the HAMD-17.

The patients who chose augmentation did a little better (32.9%-39% remitted according to their HAMD-17 scores), but outcomes were similar for the two augmenting medications.

All told, 30.6% of patients who switched or augmented achieved remission in phase 2. The cumulative remission rate for patients in the first and second phases of STAR*D was 53% (N. Engl. J. Med. 2006;354:1231-42).

"You hang in for two steps and you have more than a 50% chance of not just getting better but of getting rid of your depression," Dr. Rush said.

Just 377 patients who had not improved attempted a third step. Less than 20% of 235 patients achieved remission after switching to mirtazapine or nortriptyline. Yet to be announced are results for patients who augmented with lithium or T_3 thyroid hormone and for those patients who attempted a fourth step.

"They are significantly ill, and only modest numbers reached remission," Dr. Rush said of the patients in the third and fourth phases. For these patients, he said, "Innovative treatment methods are needed to increase remission sooner."

After Dr. Rush concluded his summary of STAR*D, Dr. James H. Kocsis offered an additional view. "The more treatment it takes you to get there, the worse your prognosis in the long run," said Dr. Kocsis of Cornell University, New York.

Dr. Kocsis also questioned whether the trial design gave patients too many choices. In his practice, after a patient fails two or three medications, he said, "I have an informed expert opinion about what I think they ought to do next. I don't just ask, 'What do you want?' and give them what they want. I educate them. I inform them."

He also called for a distinction between patients who switch medications because they cannot tolerate a drug and those who switch because of lack of response. "A person who switches for intolerance is not really treatment resistant," he said. "They haven't received the treatment."

Despite regrets about questions not addressed by STAR*D, Dr. Kocsis called the study elegant and complex, and praised the investigators for attaining "a lot of important and useful results."

Various manufacturers of antidepressants provided free medications for this trial. ■

Use a Rating Scale To Assess Progress

Don't ask depressed patients whether they feel any better since starting on an antidepressant, Dr. Rush advised clinicians at the meeting.

"If you ask a patient who is depressed for a global judgment, you are begging for a problem. They are not going to be accurate. They cannot be precise," he said, nonetheless touting self-reports as important in assessing symptoms and side effects during the course of therapy.

To find out how the patient is feeling, he recommended using a rating scale based on patient answers to specific questions. For example, "Did it take more than 2 hours to go to sleep? You can answer that yes or no."

The STAR*D trial used the Quick Inventory of Depressive Symptomatology (QIDS), available for download at www.ids-qids.org. "The QIDS-SR [self-report] total scores are highly comparable to a clinician rating using the same scale (the QIDS-C), though patients overall may score themselves a point higher than clinicians," Dr. Rush said.

"The patients will tell you they are no better and give you a QIDS with a 40% improvement at the same time," he added.

Dr. Gelenberg echoed those sentiments. "The patient is the last to know [he or she is] better. … The significant other and the formal rating scales are a much more sensitive indicator," he said, adding that using remission as a goal is important because the patients have a different point of view than that of the the clinician.

"Patients want to feel like themselves," he said. "We define remission as absence of symptoms and the patients define it as something more positive. They want to be well. These are not mutually exclusive. They complement each other."

Home-Based Skills Therapy for Autism Better Than Preschool

BY DIANA MAHONEY
New England Bureau

MONTREAL — Home-based intensive skills therapy for autism appears to be a more effective early intervention than integration into mainstream preschool classrooms, according to preliminary findings of a small pilot study reported at the 5th International Meeting for Autism Research.

In an effort to evaluate the success of community-based early intervention services for preschool children with autism, Amanda Morgan, a PhD candidate in the department of psychology at the University of New Brunswick in Fredericton, Canada, and her colleagues compared the 12-month outcomes of two groups of children diagnosed with an autism spectrum disorder. The mean age of the children at the start of the study was 33 months, ranging from 24 to 43 months.

One group, consisting of six children, received a minimum of 20 hours per week of one-on-one home-based interventions based on the applied behavior analysis (ABA) therapy model, whereas the second group of four children attended integrated preschool classrooms with teacher's assistants.

ABA therapy teaches by breaking down an objective into small steps, encouraging the mastery of one step at a time, and rewarding correct responses.

ABA is a highly structured, skills-based therapy that teaches by breaking an objective down into multiple small steps, encouraging the mastery of one step at a time, and rewarding correct responses. Integrating autistic children into regular classrooms is, by comparison, a less structured approach.

"The [thinking is] that by integrating children with autism into typical classrooms, they will benefit by learning to model 'typical' social behaviors, although studies are showing that this is not necessarily the case," commented Ms. Morgan in a poster presentation.

All of the children in the study underwent standardized testing at baseline and at 12 months thereafter. Such evaluation included the Child Development Index (CDI), the Childhood Autism Rating Scale, the Vineland Adaptive Behavior Scales: Survey Form, and the Psychoeducational Profile–Revised (PEP-R). At baseline, the mean scores on all the tests were similar in both groups. After 12 months, "mean improvement scores across the PEP-R, CDI, and Vineland measures were 15.9 months for the ABA group, compared with 5.5 months for the preschool groups," Ms. Morgan reported.

Although the statistically significant findings add substance to the growing body of literature demonstrating the efficacy of intensive skills-based therapies over classroom integration, "the results cannot be generalized to all school-based efforts, because some may incorporate elements of [ABA or other skills-based] approaches that would close the gap," said Ms. Morgan. "We need more information before making definitive statements."

In particular, a larger study population and a more controlled comparison of the important features of both types of interventions would be useful, she said.

Ms. Morgan reported no conflict of interest with respect to her presentation. ■