New Strategies Help Depressed Patients Become Symptom Free

Ed. Note: *The following is a press release from the National Institute Of Mental Health.*

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Results of the nation's largest depression study show that one in three depressed patients who previously did not achieve remission using an antidepressant became symptom-free with the help of an additional medication and one in four achieved remission after switching to a different antidepressant. The study, funded by the National Institutes of Health's National Institute of Mental Health (NIMH), shows that people whose depression is resistant to initial treatment can achieve remission - the virtual absence of symptoms - when treated with a second strategy that either augments or switches medications. This is the first study to examine the effectiveness of different treatment strategies for those who did not become symptom-free after initial medication.

John Rush, M.D., and Madhukar H. Trivedi, M.D., of the University of Texas Southwestern Medical Center (UTSWMC), and colleagues report on the first major results of the clinical trial, known as the STAR*D (Sequenced Treatment Alternatives to Relieve Depression) study, in two papers published in the March 23, 2006 issue of the *New England Journal of Medicine*.

"These findings provide important treatment options to mental health clinicians and the millions of Americans who struggle with treatment-resistant depression," said NIH Director Elias A. Zerhouni, M.D.

Patients who did not experience a remission of symptoms during the first level of the Star*D study - in which they initially took the antidepressant citalopram, a selective serotonin reuptake inhibitor (SSRI), for up to 14 weeks - were eligible to enter level 2 of the trial where they were offered additional treatment options designed to help them become symptom-free.

"If the first treatment attempt fails, patients should not give up," said NIMH's director Thomas Insel, M.D. "By remaining in treatment, and working closely with clinicians to tailor the most appropriate next steps, many patients may find the best single or combination treatment that will enable them to become symptom-free."

The 1,439 patients who were eligible and volunteered to enter level 2 were presented with seven different treatment options. Only very few participants said that all of the choices were equally acceptable and allowed themselves to be randomly assigned to any one of them. All the rest of the participants identified at least one of the treatments as being unacceptable, and chose to limit the treatments to which they would allow themselves to be randomly assigned. Fifty-one percent (727) of the patients chose options that included switching to a different medication and were randomly assigned to one of the three switch medications. Thirty-nine percent (565) chose options that included augmenting the citalopram they were already taking, and were randomly assigned to one of the two augmenting medications.

The 727 patients who received the switch medication treatments were randomized to take one of three medications currently available and used in practice - sertraline (an SSRI that targets the neurotransmitter serotonin), bupropion-SR (a non-SSRI antidepressant), or venlafaxine-XR (an agent that targets serotonin and norepinephrine, another neurotransmitter).

Rush and colleagues found that 25 percent of the patients who switched to a new medication became symptom-free within 14 weeks; this was similar within each of the three treatment groups. Additionally, no significant differences were found in the efficacy, safety or tolerability of the three medications to which patients were switched.

"Contrary to what previous research suggests, this study shows that all three medications the patients switched to, despite having different mechanisms of action, appear to be useful options for treating depression following failure on the first SSRI," said Rush. "The results provide patients and doctors with important information that intolerance or lack of efficacy with one SSRI seems not to predict the same with another."

The 565 patients who received the augment medication were randomized to take either bupropion-SR (a non-SSRI antidepressant) or buspirone (a medication that enhances the action of an SSRI) in addition to the SSRI citalopram that they were already taking in Level 1. Within 14 weeks of using either treatment, about one third of the patients who enrolled in the augmentation study became symptom-free, Trivedi and colleagues reported. Both combinations appeared similar in terms of remission; however, those who augmented citalopram with bupropion-SR experienced fewer symptoms, a greater degree of symptom relief and lower side effects compared to those who augmented with buspirone.

"Augmenting the first medication may be an effective way for people with depression to become symptom-free," said Trivedi. "Augmenting earlier in the course of treatment, or perhaps prescribing a combination of drugs to patients initially, may be more effective than using one treatment alone."

According to the researchers, the switch and augment treatments cannot be directly compared because of the way the trial was designed. The results, however, can be used to help guide treatment choices within each group; it also may be that different people respond better to one as opposed to another treatment.

"Further research may help customize the treatment to the individual patients," says Rush. Study participants who still did not achieve remission in level 2 had the option of completing up to two additional levels of treatment. Results from levels 3 and 4 of the STAR*D trial will be published later this year.

STAR*D is part of an overall NIMH effort to conduct practical clinical trials in "real world" settings that address public health issues important to those persons affected by major mental illnesses.

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For more information on STAR*D level 2, visit:

- Primary Results for Sequenced Treatment Alternatives to Relieve Depression (STAR*D) Study
- Questions and Answers about the NIMH Sequenced Treatment Alternatives to Relieve Depression (STAR*D) Study - Level 2 Results, Published in *New England Journal of Medicine*, March 23, 2006

For more information on STAR*D level 1, visit:

- Initial Results Help Clinicians Identify Patients With Treatment-Resistant Depression
- Questions and Answers about the NIMH Sequenced Treatment Alternatives to Relieve Depression (STAR*D) Study - Level 1 Results, Published in *American Journal of Psychiatry*, January 1, 2006

For general information on the STAR*D study, visit:

- Sequenced Treatment Alternatives to Relieve Depression at ClinicalTrials.gov
- Questions and Answers about the NIMH Sequenced Treatment Alternatives to Relieve Depression (STAR*D) Study - Background
- PATIENT GUIDE: New Strategies for Treating Depression

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