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EXPERT PANEL SUPPLEMENT

EFFICACY, SAFETY, AND TOLERABILITY CONSIDERATIONS IN THE NOVEL TREATMENT OF MAJOR DEPRESSIVE DISORDER

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ABSTRACT

Although studies have shown that current medications do offer benefit over placebo for major depressive disorder (MDD) treatment, there exist various barriers to the implementation of a treatment plan for both clinicians and patients. Once a treatment course is determined, patients may hold a negative perception of pharmacologic treatment of MDD, have limited access to additional care, or cease taking medication due to a poor relationship with their clinician. In addition, clinicians must ensure that the correct diagnosis of MDD is made at presentation, despite a potentially differing profile among patients, and that if patients do not respond to treatment, augmentation with other medications is evaluated. Lastly, researchers are investigating novel treatments for MDD, which may allow for more precise treatment of the disorder.

In this Expert Panel Supplement, Andrew Nierenberg, MD, reviews MDD treatment barriers including the heterogeneity of MDD, societal factors, the clinician-patient relationship, and treatment adherence; Sidney Kennedy, MD, FRCPC, discusses the efficacy, safety, and tolerability of current MDD treatments in the context of societal, patient, and methodological variables; R. Bruce Lydiard, PhD, MD, describes novel treatments for MDD, including augmentation strategies; and Mark Hyman Rapaport, MD, reviews the development of MDD treatment beyond the traditional monoamine models of the disorder.

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Statement of Need and Purpose

Major depressive disorder (MDD) is a chronic condition, especially in cases that do not respond easily to treatment. Despite the availability of different classes of drugs for the treatment of MDD, there are a number of clinically significant unmet needs, such as a high prevalence of drug resistance, partial response, subsyndromal symptomatology, recurrence, and relapse. Treatment resistant depression (TRD) is frequently defined as depressive illness that does not fully remit after a single initial treatment failure. Up to 50% of patients in primary care settings do not show a full response to their first antidepressant treatment. The likelihood of successful treatment of MDD decreases with an increasing number of unsuccessful treatment attempts. There is a higher frequency of suicide in patients with TRD as opposed to those with treatment responsive MDD.

The strengths and limitations of selective serotonin reuptake inhibitors and selective norepinephrine reuptake inhibitors have been realized, as many patients do not respond well to initial antidepressant treatment or achieve remission. This has led to a re-emergence of interest in treatment augmentation research. It is apparent that mood regulation involves multiple neurotransmitter systems, and this widens the potential for chemical manipulation and, thus, treatment options. The advent of atypical antipsychotics has had a major impact in schizophrenia and may offer clinical advantages in mood regulation beyond bipolar disorder. Clinicians need to be made aware of recent medical advances related to depression in order to improve their treatment capabilities. Patients who only achieve partial response or continue to experience residual symptoms are likely to show reduced functioning and an increased risk of relapse.

Target Audience

This activity is designed to meet the educational needs of psychiatrists.

Learning Objectives

At the completion of this activity, participants should be better able to:

- Estimate barriers to treatment response for patients with major depression to limit a chronic course of illness
- Evaluate the role of novel treatments for patients with MDD who do not achieve full remission
- Explain the efficacy, safety, and tolerability of novel treatment options available for major depression

Faculty Affiliations and Disclosures

Andrew Nierenberg, MD, is co-director of the Bipolar Clinic and Research Program and associate director of the Depression Clinical and Research Program at Massachusetts General Hospital, and professor of psychiatry at Harvard Medical School in Boston. Dr. Nierenberg is a consultant to or serves on the advisory boards of Abbott, Appliance Computing, Inc. (MindSite), AstraZeneca, Basilea, Brain Cells, Bristol-Myers Squibb, Eli Lilly, Genaissance, GlaxoSmithKline, Innapharma, Jazz, Merck, the National Institute of Mental Health (NIMH), Novartis, Ortho-McNeil/Janssen, Pfizer, PGx Health, Schering-Plough, Sepracor, Shire, Somerset, Takeda, and Targacept; is on the speaker's bureaus of Bristol-Myers Squibb, Cyberonics, Forest, Eli Lilly, GlaxoSmithKline, Massachusetts General Hospital Psychiatry Academy, and Wyeth; receives research support from Bristol-Myers Squibb, Cederroth, Cyberonics, Forest, Eli Lilly, GlaxoSmithKline, Lichtwer Pharma, NARSAD, NIMH, Ortho-McNeil/Janssen, Pamlab, Pfizer, the Stanley Foundation, and Wyeth; receives honoraria from Massachusetts General Hospital Psychiatry Academy; and owns stock in Appliance Computing, Inc. (MindSite).

Sidney Kennedy, MD, FRCPC, is professor of psychiatry at the University of Toronto, and is psychiatrist-in-chief at the University Health Network in Toronto. Dr. Kennedy is a consultant to and on the advisory boards of Advanced Neuromodulation Systems (ANS), AstraZeneca, Biovail, Eli Lilly, Lundbeck, Pfizer, Servier, and Wyeth; is on the speaker's bureau of ANS, AstraZeneca, Biovail, Boehringer-Ingelheim, Eli Lilly, Lundbeck, Servier, and Wyeth; and receives research support from ANS, AstraZeneca, the Canadian Institutes of Health Research, Eli Lilly, GlaxoSmithKline, Lundbeck, NARSAD, the Ontario Mental Health Foundation, the Ontario Problem Gambling Research Society, and the Stanley Foundation.

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R. Bruce Lydiard, PhD, MD, is a professor in the Department of Psychiatry and Behavioral Sciences at the Medical University of South Carolina in Charleston. Dr. Lydiard is a consultant to Eli Lilly and Takeda; and has received research support from AstraZeneca, Bristol-Myers Squibb, Eli Lilly, Forest, Pfizer, sanofi-aventis, UCB Pharma, and Wyeth. He discusses unapproved/investigational uses of quetiapine.

Mark Hyman Rapaport, MD, is chairman and professor of psychiatry and behavioral neurosciences, and the Poiler Endowed Chair in Schizophrenia and Related Disorders at Cedars-Sinai Medical Center and vice chairman and professor in residence in the Department of Psychiatry and Biobehavioral Sciences at the David Geffen School of Medicine at UCLA. Dr. Rapaport is consultant to Astellas, Brain Cells, Cyberonics, Dainippon-Sumitomo, the National Institute of Mental Health, and Wyeth; and receives research support from AstraZeneca, the National Center for Complementary and Alternative Medicine, the National Institute of Mental Health, Pfizer and Solvay. He discusses unapproved/investigational uses of celecoxib, MK-801.

CME Course Director **James C.-Y. Chou, MD**, is associate professor of psychiatry at Mount Sinai School of Medicine. Dr. Chou has received honoraria from AstraZeneca, Bristol-Myers Squibb, Eli Lilly, GlaxoSmithKline, Janssen, and Pfizer.

Sanjay J. Mathew, MD, is associate professor of psychiatry at Mount Sinai School of Medicine. Dr. Mathew has served as an advisor/consultant to AstraZeneca and Jazz.

Activity Review Information

The activity content has been peer-reviewed by Sanjay J. Mathew, MD.

Review Date: February 5, 2009.

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To Receive Credit for this Activity

Read this Expert Panel Supplement, reflect on the information presented, and complete the CME posttest and evaluation on pages 19 and 20. To obtain credit, you should score 70% or better. Early submission of this posttest is encouraged. Please submit this posttest by March 1, 2011 to be eligible for credit.

Release date: March 1, 2009
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The estimated time to complete this activity is 2 hours.

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