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EXPERT ROUNDTABLE SUPPLEMENT

AUGMENTATION STRATEGIES IN THE TREATMENT OF MAJOR DEPRESSIVE DISORDER

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ABSTRACT

Under optimal circumstances, patients respond to treatments for major depression only 60% to 70% of the time. Therefore, there is a critical need for effective treatment strategies that augment available depression treatment. Currently, such strategies augment primary antidepressants with agents that increase the likelihood of treatment response. Augmentation agents include thyroid hormones, which are used to augment tricyclic antidepressants (TCAs); lithium, which also improves response to TCAs; and second-generation antipsychotics (SGAs), which are used to augment selective serotonin reuptake inhibitors and serotonin norepinephrine reuptake inhibitors. Other, less common, strategies include augmentation with stimulants, folate, and buspirone. Unfortunately, studies of augmentation efficacy are often limited or equivocal. Studies may overestimate the magnitude of effect, as augmentation may be attempted while patients still experience an initial response. Prescribers must be sure treatment strategies are not undermined by safety or tolerability concerns. Lithium, in particular, is not well tolerated by patients, and SGAs pose the risk of tardive dyskinesia, metabolic syndrome, and extrapyramidal symptoms. Clinicians must weigh these issues against a relatively limited base of knowledge.

In this Expert Roundtable Supplement, Michael E. Thase, MD, discusses the history of augmentation strategies for depression. J. Craig Nelson, MD, reviews recent findings on augmentation with thyroid hormone, lithium, buspirone, and modafinil. George I. Papakostas, MD, reviews the efficacy of augmentation with SGAs. Finally, Michael J. Gitlin, MD, provides an overview of safety and tolerability issues.

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Accreditation Statement

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This activity has been peer reviewed and approved by Eric Hollander, MD, Chair and Professor of Psychiatry at the Mount Sinai School of Medicine. Review Date: November 9, 2007.

Statement of Need and Purpose

Major depressive disorder (MDD) is the fourth largest contributor to the worldwide burden of disease and is expected to be second only to ischemic heart disease by the year 2020. Over 60% of suicide deaths in the United States are directly attributable to MDD, and >300,000 people successfully commit suicide in the US annually. Despite its prevalence, 50% of MDD cases go undetected, undiagnosed, and untreated. The impairment of depression can lead to decreased productivity, alcohol and substance abuse, and an increased risk of suicide. Treatment resistant depression (TRD) is frequently defined as depressive illness that does not fully remit after a single initial treatment failure. Patients who only achieve partial response or continue to experience residual symptoms are likely to show reduced functioning and an increased risk of relapse. Up to 50% of patients do not show a full response to their first antidepressant treatment. This has led to a re-emergence of interest in treatment augmentation research. There is a higher frequency of suicide in patients with TRD as opposed to those with treatment responsive MDD. Although the results of several open-label trials suggest a potential role of second-generation antipsychotics (SGAs) in TRD, there has been a paucity of double-blind, placebo-controlled studies confirming whether this treatment strategy is truly effective. New data continue to emerge and it is important to determine how these findings apply to each of the SGAs. It is also important to report on the safety, tolerability, and efficacy of augmenting with SGAs versus other augmentation or switching strategies for TRD.

Target Audience

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

Learning Objectives

- Recognize the efficacy, safety, and tolerability of augmenting pharmacologic treatment of major depressive disorder (MDD) with atypical antipsychotics.
- Discuss the challenges of limited response to MDD treatment and its impact on the course of illness.

Faculty Disclosures

Michael E. Thase, MD, is a consultant to AstraZeneca, Bristol-Myers Squibb, Cephalon, Cyberonics, Eli Lilly, GlaxoSmithKline, Janssen, MedAvante, Neuronetics, Novartis, Organon, Sepracor, Shire, Supernus, and Wyeth; is on the speaker's bureaus of AstraZeneca, Bristol-Myers Squibb, Cyberonics, Eli Lilly, GlaxoSmithKline, Organon, sanofi-aventis, and Wyeth; has equity in MedAvant; and receives book royalties from American Psychiatric Publishing, Guilford Publications, and Herald House. Dr. Thase discloses that he will discuss investigational uses of older pharmacologic agents for the treatment of major depressive disorder (MDD).

J. Craig Nelson, MD, is a consultant to and/or on the advisory boards of Abbott, Biovail, Bristol-Myers Squibb, Corcept, Eli Lilly, Forest, GlaxoSmithKline, Novartis, Orexigen, Organon, and Pfizer. Dr. Nelson discloses that he will discuss unapproved/investigational uses of pharmacologic agents for the treatment of MDD.

George I. Papakostas, MD, has served as a consultant to Aphios, Bristol-Myers Squibb, GlaxoSmithKline, Evotec, Inflabloc, Jazz, PAMLAB, Pfizer, and Wyeth; has received honoraria from Bristol-Myers Squibb, Evotec, GlaxoSmithKline, Inflabloc, Jazz, Lundbeck, PAMLAB, Pfizer, Titan, and Wyeth; and has received research support from Bristol-Myers Squibb, PAMLAB, and Pfizer. Dr. Papakostas discloses that he will discuss unapproved/investigational uses of aripiprazole, buspirone, olanzapine, pindolol, quetiapine, risperidone, triiodothyronine, and ziprasidone for the treatment of MDD.

Michael J. Gitlin, MD, has received honoraria from AstraZeneca, Bristol-Myers Squibb, Cephalon, Eli Lilly, GlaxoSmithKline, Pfizer, and Takeda. Dr. Gitlin discloses that he will discuss unapproved/investigational use of aripiprazole, clozapine, olanzapine, quetiapine, risperidone, and ziprasidone for the treatment of MDD.

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Peer Reviewers

David L. Ginsberg, MD, receives honoraria from AstraZeneca and GlaxoSmithKline.

Eric Hollander, MD, reports no affiliation with or financial interest in any organization that may pose a conflict of interest.

To Receive Credit for this Activity

Read this expert roundtable supplement, reflect on the information presented, and complete the CME posttest and evaluation on pages 18 and 19. To obtain credit, you should score 70% or better. Early submission of this posttest is encouraged. Please submit this posttest by December 1, 2009 to be eligible for credit.

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