MARCH 2009 A Supplement To VOL 14 — NO 3 — SUPPL 4

CNS SPECTRUMS®

THE INTERNATIONAL JOURNAL OF NEUROPSYCHIATRIC MEDICINE

EXPERT PANEL SUPPLEMENT

PHARMACOLOGIC AND THERAPEUTIC STRATEGIES IN TREATMENT-RESISTANT DEPRESSION

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ABSTRACT

Treatment-resistant depression (TRD) is defined as the failure of an episode of major depression to respond fully to the adequate administration of a treatment that is known to be effective. TRD comprises many different clinical scenarios, including bipolar and unipolar depression, and known adequate treatments include psychotherapeutic and pharmacotherapeutic regimens. Studies have shown that ~50% of patients with major depressive disorder (MDD) receiving antidepressants experienced a clinical response (≥50% reduction in symptoms). When first-line antidepressant strategies fail to bring about response or remission of an episode of depression, clinicians may reevaluate the patient's diagnosis, ensure that any or all comorbidities have been diagnosed properly, and assess treatment adherence. It is common for clinicians to resort to second-, third-, and sometimes fourth-line treatment strategies to reach full remission of a depressive episode. These strategies may entail a within-class antidepressant switch, an out-of-class switch, or augmenting the first-line antidepressant. The major rationale for augmentation is that it builds upon whatever gains have been made with the first treatment trial. An adjunctive treatment may also target selected symptoms, such as a benzodiazepine or buspirone for anxiety symptoms, or modafinil for fatigue or lethargy. Augmentation of antidepressants with an atypical antipsychotic is a common polypharmacy strategy in the treatment of MDD. Some atypical antipsychotics possess affinity for the 5-HT_{1D} or 5-HT_{1A} receptor, both of which are of interest to treating depressive symptoms. There is an urgent need to continue to expand the repertoire of treatments available for MDD, including TRD. The long-term efficacy and safety data for atypical augmentation strategies must still be established, and these strategies must be compared to other augmentation or switching strategies.

This activity is jointly sponsored by the Mount Sinai School of Medicine and MBL Communications, Inc.

https://doi.org/10.1017/S1092852900003497 Published online by Cambridge University Press

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Credit Designation

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Statement of Need and Purpose

Although numerous clinical trials have demonstrated the clinical efficacy and safety of antidepressant drugs, their overall efficacy in MDD is, at best, modest. Studies have shown that ~50% of patients with MDD receiving antidepressants experienced a clinical response (≥50% reduction in symptoms). It is common for clinicians to resort to second-, third-, and sometimes fourth-line treatment strategies to reach full remission of a depressive episode.There are extensive data on switching or augmenting antidepressants for treatment-resistant episodes of depression. A careful evaluation of each patient's history, combined with the results of controlled clinical studies, can lead to improved outcomes and safety in clinical practice.

Target Audience

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

Learning Objectives

- Define treatment-resistant depression (TRD) and how it relates to therapy, treatment response, and a spectrum of severity so that patients are accurately diagnosed with TRD.
- Assess the validity and accuracy of a patient's current diagnosis and treatment strategy before enacting a second- or third-line switch or augmentation strategy.
- List the relative advantages and disadvantages of polypharmacy—combination and augmentation—strategies for TRD treatment.

Faculty Disclosures

John P. O'Reardon, MD, associate professor of psychiatry at the University of Pennsylvania, is a consultant to Bristol-Myers Squibb and Eli Lilly; and receives grant/research support from CenRx BioPharma, Cyberonics, and Medtronic.

Michael E. Thase, MD, professor of psychiatry at the University of Pennsylvania, has served as a consultant to AstraZeneca, Bristol-Myers Squibb, Cephalon, Cyberonics, Eli Lilly, Forest, GlaxoSmithKline, Janssen, MedAvante, Neuronetics, Novartis, Organon, Sepracor, Shire, Supernus, and Wyeth; is on the speaker's bureau of AstraZeneca, Bristol-Myers Squibb, Cyberonics, Eli Lilly, GlaxoSmithKline, sanofi-aventis, Schering Plough, and Wyeth; and has received grant/research funding from Eli Lilly and Sepracor.

For the past or future 12 months (date disclosed: 2/13/2009), **George I. Papakostas, MD**, associate professor of psychiatry at Harvard Medical School, has served as a consultant/advisor to Eli Lilly, GlaxoSmithKline, Otsuka, Pierre Fabre Medicament, and Shire; has served on the speaker board for Bristol-Myers Squibb; has received research support from Bristol-Myers Squibb, Pamlab, Pfizer, Precision Human Biolaboratories, and the National Institute of Mental Health; and has received honoraria from Astra Zeneca, Bristol-Myers Squibb, Eli Lilly, GlaxoSmithKline, Jannsen-Cilag, Lundbeck, Otsuka, Pamlab, Pfizer, Pierre Fabre Medicament, and Servier. Dr. Papakostas discusses off-label investigational use of olanzapine, risperidone, ziprasidone, and quetiapine as adjunctive therapy for major depressive disorder.

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

Sanjay J. Mathew, MD, has served as an advisor/consultant to AstraZeneca and Jazz.

Acknowledgment of Commercial Support

Funding for this activity has been provided by an educational grant from Eli Lilly and Company.

Activity Review Information

The activity content has been peer-reviewed by Sanjay J. Mathew, MD, Assistant Professor of Psychiatry at Mount Sinai School of Medicine. Review Date: February 19, 2009.

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 15 and 16. 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
Termination date: March 31, 2011

The estimated time to complete this activity is 2 hours.

https://doi.org/10.1017/S1092852900003497 Published online by Cambridge University Press

CNS Spectrums (ISSN 1092-8529) is published monthly by MBL Communications, Inc., 333 Hudson Street, 7th Floor, New York, NY 10013.

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https://doi.org/10.1017/S1092852900003497 Published online by Cambridge University Press