Depression: Addressing Partial Response After First-Line Antidepressant Treatment

Michael E. Thase, MD; Maurizio Fava, MD; Andrew A. Nierenberg, MD

Major depressive disorder (MDD) remains a leading cause of disability worldwide (Table 1). Despite the range of available first-line treatments for MDD, many patients do not achieve full remission with initial antidepressant therapy and continue to experience depressive symptoms. Clinicians must be prepared to assess and treat these residual symptoms to reduce patients’ risk of relapse. The online CME series “Depression: Addressing Partial Response After First-Line Antidepressant Treatment” (visit psychiatrist.com and enter keyword “wellness”) features 3 activities that provide assessment tools and treatment strategies to help clinicians monitor and treat partial response and residual symptoms in their patients with MDD. Following a summary of these activities, Drs Thase, Fava, and Nierenberg review the results and feedback from participants who completed one or more of the activities in this series and discuss areas for future education.

SUMMARY OF ACTIVITIES

Dr Thase’s activity “Residual Symptoms and the Risk of Relapse in Major Depression” states that a considerable proportion of patients will not achieve asymptomatic remission after initial MDD treatment and that residual symptoms increase the risk of relapse. Clinicians should regularly assess patients’ symptoms and treatment response using scales such as the 9-item Patient Health Questionnaire, Quick Inventory of Depressive Symptomatology–Self-Report, or Beck Depression Inventory. For patients with inadequate response, clinicians should address barriers, such as inadequate dosage or patient nonadherence, and decide whether augmenting therapy or switching medications is warranted.

In his activity “Assessing Response to Treatment and Recognizing Residual Depression Symptoms,” Dr Fava recommends that clinicians use both categorical and dimensional approaches to assess treatment response. A categorical approach assesses the overall degree of change that a patient experiences during treatment (eg, partial response), while a dimensional approach uses measurement-based assessment tools to determine the degree of change in symptoms. While rating scales can measure symptoms over time, no single scale is ideal for measuring every symptom. A combination of patient-rated and clinician-rated scales is best. Clinicians must consider whether patients who have what appear to be residual symptoms actually have comorbidities or treatment-emergent side effects. For
patients experiencing true residual symptoms, clinicians must decide whether more time on the current treatment is needed or if the patient would benefit from switching or augmenting options.

Strategies for improving partial response, which are given in Dr Nierenberg’s activity “Strategies for Achieving Full Remission When First-Line Antidepressants Are Not Enough,” include starting focused psychotherapy (such as cognitive-behavioral therapy or interpersonal therapy), switching antidepressants (within or outside of the same class), or augmenting current treatment with another antidepressant, lithium, thyroid hormone, or an atypical antipsychotic. Adjunctive agents can be used to target specific symptoms, such as fatigue or insomnia. As with other treatment decisions, clinicians should consider cost, tolerability, adherence, and patient preference.

**SUMMARY OF SERIES OUTCOMES**

Drs Thase, Fava, and Nierenberg discussed the educational outcomes for the activity series, including participants’ satisfaction with the online activities as well as the results from posttest questions that are designed to measure knowledge, competence, and performance. The objectives for this series were for clinicians to assess patients for residual depressive symptoms and adjust treatment for patients who respond to treatment but do not reach full symptom remission. A follow-up e-mail, sent to participants 2 months after they complete an online activity, asked clinicians if they have implemented the clinical strategies and what barriers they encountered. Participants mentioned barriers such as a lack of staff/resources and a need for more information.

**Dr Thase:** The majority of activity participants were office-based psychiatrists. Satisfaction ratings for the series were above average, at 4.2 out of 5.

Each activity has a posttest question. Comparing the answers to the questions between a control group and the activity completers revealed that 2 of the 3 activities produced statistically significant improvement in knowledge and competence (\(P = .0002\) and \(P = .02\)). For the other activity, 75% of the control group answered correctly, leaving little room for improvement; however, a greater percentage of activity completers (83%) answered correctly. The clinical strategies for this series were to assess patients’ residual symptoms with a measurement-based tool and to switch, combine, or augment medications for patients who do not fully respond to treatment. Participants were asked how often they currently used and planned to use these strategies. Comparing the current and planned use for each strategy revealed a nominal change (Figure 1).

**Dr Nierenberg:** It looks like there was a ceiling effect.

**Dr Thase:** Yes. The people who responded were already doing quite well, but there was a small increase in planned use.

**FUTURE EDUCATIONAL NEEDS**

**Dr Thase:** What topics could we target in follow-up activities to support further change in physicians’ practices concerning the use of measurement-based care to address residual symptoms of depression?

**Dr Nierenberg:** I would imagine we should try to help physicians look at their workflow to find out what about these activities helps and what makes it a challenge to implement the clinical strategies. For example, links to measurement tools are provided in the activities, which should help readers, but a lack of staff may impede implementation of

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**Table 1. Leading Causes of Burden of Disease (DALYs) in Countries by Income, 2004**

<table>
<thead>
<tr>
<th>Rank</th>
<th>World</th>
<th>Low-Income Countries</th>
<th>Middle-Income Countries</th>
<th>High-Income Countries</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Lower respiratory infections</td>
<td>Lower respiratory infections</td>
<td>Unipolar depressive disorders</td>
<td>Unipolar depressive disorders</td>
</tr>
<tr>
<td>2</td>
<td>Diarrheal diseases</td>
<td>Diarrheal diseases</td>
<td>Ischemic heart disease</td>
<td>Ischemic heart disease</td>
</tr>
<tr>
<td>3</td>
<td>Unipolar depressive disorders</td>
<td>HIV/AIDS</td>
<td>Cerebrovascular disease</td>
<td>Cerebrovascular disease</td>
</tr>
<tr>
<td>4</td>
<td>Ischemic heart disease</td>
<td>Malaria</td>
<td>Road traffic accidents</td>
<td>Alzheimer and other dementias</td>
</tr>
<tr>
<td>5</td>
<td>HIV/AIDS</td>
<td>Prematurity and low birth weight</td>
<td>Lower respiratory infections</td>
<td>Alcohol use disorders</td>
</tr>
<tr>
<td>6</td>
<td>Cerebrovascular disease</td>
<td>Neonatal infections and other</td>
<td>COPD</td>
<td>Hearing loss, adult onset</td>
</tr>
<tr>
<td>7</td>
<td>Prematurity and low birth weight</td>
<td>Birth asphyxia and birth trauma</td>
<td>HIV/AIDS</td>
<td>COPD</td>
</tr>
<tr>
<td>8</td>
<td>Birth asphyxia and birth trauma</td>
<td>Unipolar depressive disorders</td>
<td>Alcohol use disorders</td>
<td>Diabetes mellitus</td>
</tr>
</tbody>
</table>

Data from the World Health Organization.\(^1\)  
Abbreviations: AIDS = acquired immunodeficiency syndrome, COPD = chronic obstructive pulmonary disease, DALY = disability-adjusted life year, HIV = human immunodeficiency virus infection.
measurement-based care. A question for future activities is whether the use of tools can save time overall.

Dr Thase: Concerning residual symptoms and incomplete remission, we could explore topics related to cognition, which may be targeted by new agents like vortioxetine. Vortioxetine significantly improved measures of cognition compared with placebo in an 8-week study (P < .0001). This agent could be an option when switching medication.

Dr Fava: Anecdotally, I have been using vortioxetine for augmentation at a low dose of 5 mg/d. In my experience, it seems to address residual symptoms such as lack of motivation and impaired cognition. However, it has not been studied as an adjunctive agent yet.

Dr Thase: Adjunctive agents, such as aripiprazole and the investigational drug brexipiprazole, may resolve residual symptoms in patients with MDD. Another antidepressant agent recently approved by the US Food and Drug Administration for MDD is the serotonin-norepinephrine reuptake inhibitor levomilnacipran, which could be explored among subsets of depressed patients, such as those with fatigue, anergia, or functional impairments.

Comorbid conditions are another area we could focus on in the future to help physicians resolve depression. Of the approximately 30% of our patients who meet remission criteria, whom we consider treatment successes, the majority have at least 1 residual symptom (median = 3), so they are statistically less likely to remain remitted over time. Incomplete remission remains an important unmet need.

Drug names: aripiprazole (Abilify), levomilnacipran (Fetzima), vortioxetine (BrintelliX).

Disclosure of off-label usage: Dr Thase has determined that, to the best of his knowledge, no investigational information about pharmaceutical agents that is outside US Food and Drug Administration–approved labeling has been presented in this activity.

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References


