Transcript Details

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Seltorexant vs Quetiapine XR in MDD With Insomnia: A 26-Week Phase 3 Comparison

Announcer:
Welcome to DataPulse from Psych Congress 2025 on ReachMD. This activity titled Seltorexant Versus Quetiapine Extended Release in Major Depressive Disorder With Insomnia: A 26-Week Phase 3 Comparison is provided by Total CME.

Dr. Thase:
Hello from Psych Congress 2025 here in San Diego. I'm Dr. Michael Thase, and today I'll be discussing results from a 26-week, phase 3 trial comparing adjunctive seltorexant with quetiapine extended release in adults with major depressive disorder and insomnia symptoms.

This is a really relevant trial, because we have lots of choices for adjunctive therapy for our patients who don't remit with standard antidepressant treatment. Many of them involve atypical antipsychotics, and quetiapine XR is one such of those medications that has FDA approval for this. However, newer-generation antipsychotics have baggage, including weight gain and somnolence in the case of quetiapine as side effects. And so the idea of treating a patient with persistent insomnia despite antidepressant treatment with something that's not a newer-generation antipsychotic has important clinical implications for our patients.

So the study I'm reporting on today is a large study, half randomized to treatment with seltorexant, half randomized to treatment with quetiapine in the doses indicated for adjunctive therapy of major depressive disorder. They continued to take their antidepressants in this trial.

And the trial is unique in the sense that it's not just an acute phase trial, but it then continues for a full half a year to evaluate patients' improvements. Importantly, in terms of patients getting better, the 2 conditions were equal. So the seltorexant arm's patients did as well as the patients randomly assigned to receive quetiapine.

There were, however, important differences in tolerability and in discontinuation rates. So, for example, the proportion of patients who reported excessive daytime sleepiness or somnolence was 6.3% for seltorexant and 24.1% for quetiapine. Likewise, 5.7% of patients dropped out due to intolerable adverse events in seltorexant compared to 11.3% randomized to quetiapine. I think there's also a difference in weight gain, so that about 0.5 kg—or 1 lb more or less—in the seltorexant group compared to 2.1 kg on average in the quetiapine group.

So what we see here is a good case of having a therapeutic equivalence in terms of benefit, but significant differences in terms of tolerability. This is one piece in the puzzle of how to improve our adjunctive therapies, suggesting that a selective orexin-2 antagonist could handle improving symptoms and tolerability without the same side effect burden as a second-generation antipsychotic medication.

From the Psych Congress 2025, I'm Dr. Michael Thase and thank you for listening.

Announcer:
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