Impact of Seltorexant on Cognitive Performance of Adults with Major Depressive Disorder with Insomnia Symptoms

WHY

- Many individuals with major depressive disorder (MDD) experience inadequate response to standard antidepressant therapies and have residual symptoms, such as insomnia symptoms (IS), and/or subsequent deficits in cognitive function.
  - Further, sleep disturbance is associated with poor performance on cognitive tests for executive functioning, and cognitive deficits may be an important contributor to short- and long-term functional outcome in MDD.
- Seltorexant is being developed as adjunctive treatment to standard antidepressants for MDDIS.
- To investigate the impact of seltorexant on cognitive functioning, the cognitive performance of adults with MDDIS with an inadequate response to current standard antidepressant therapy was evaluated using a novel iPad-administered cognitive test battery in a global, phase 3, randomized trial (NCT04513912) of seltorexant vs quetiapine extended release (XR).

HOW

- Participants with MDDIS received either seltorexant (20 mg; n=366) or flexibly dosed quetiapine XR (150/300 mg; n=390) administered adjunctively to their current SSRI/SNRI regimen to which they had been only partially responsive.
- Cognition was evaluated at baseline, Week 10, and Week 26 using the novel iPad-administered ReVeRe.D cognitive test battery.
- Changes from baseline at Week 10 and 26 on ReVeRe.D cognitive tests were explored in the safety analysis set.

Presented by A. Wegener at 22nd Annual Scientific Meeting of The International Society for CNS Clinical Trials and Methodology (ISCTM); Washington, DC; February 18-20, 2026. A. Wegener is a research fellow at Johnson & Johnson.

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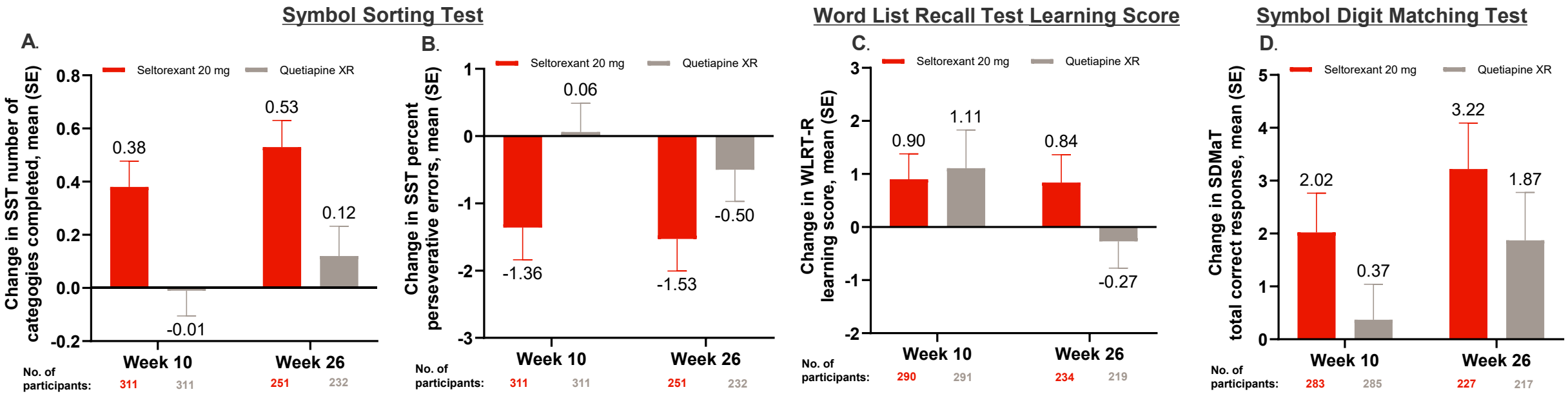
Change from baseline at Weeks 10 and 26 in ReVeRe.D cognitive tests



WHAT

- Significant differences between groups in favor of seltorexant were evident in the cognitive domain of executive function (**A, B**).
- Modest effects on verbal learning (**C**) and processing speed (**D**) trended toward favoring seltorexant.
- The minimal effects on other tests suggest the trends toward improvement were not due to other nonspecific factors (i.e., practice effects).
- These findings can inform the design of future studies and analyses aimed at evaluating how treatment interventions influence cognitive performance in individuals with MDDIS.

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