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Centanafadine for Attention-Deficit/Hyperactivity Disorder in Adolescents: A Randomized Clinical Trial

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Abstract

Objective: This randomized, double-blind, placebo-controlled trial evaluated the efficacy, safety, and tolerability of centanafadine-a norepinephrine, dopamine, serotonin reuptake inhibitor-in the treatment of attention-deficit/hyperactivity disorder (ADHD) in adolescents.

Method: Adolescents (aged 13-17 years, inclusive) with a primary diagnosis of ADHD were randomized to once-daily centanafadine 164.4 mg, 328.8 mg, or placebo for 6 weeks. Dosing was not titrated. The primary endpoint was change from baseline in the ADHD Rating Scale, version 5 (ADHD-RS-5) symptoms total raw score at week 6. This trial is registered with ClinicalTrials.gov (NCT05257265).

Results: Of 459 participants (centanafadine 164.4 mg, n = 155; 328.8 mg, n = 155; placebo, n = 149), 451 received ≥1 dose of study drug and 371 (80.8%) completed the trial. At week 6, improvements in ADHD-RS-5 symptoms total raw score were significantly greater with centanafadine 328.8 mg than with placebo (-18.50 [0.93] vs -14.15 [0.93]; p = .0006); centanafadine 164.4 mg did not meet the primary endpoint. Centanafadine 328.8 mg showed separation from placebo at week 1, the first postbaseline timepoint, with the effect maintained throughout the study. Treatment-emergent adverse events (TEAEs) occurred in 48 of 153 (31.4%, 164.4 mg), 76 of 151 (50.3%, 328.8 mg), and 35 of 147 (23.8%, placebo) participants. The most common (≥5% any group) TEAEs were decreased appetite, nausea, headache, and rash. Most TEAEs were of mild or moderate severity; 3 events were severe: liver function test increase (n = 1, 164.4 mg); aggression (n = 1, 164.4 mg); and somnolence (n = 1, placebo).

Conclusion: Centanafadine 328.8 mg was efficacious for ADHD treatment in adolescents. Both doses were generally safe and well tolerated.

Plain language summary: Centanafadine is a drug under investigation for the treatment of attention-deficit/hyperactivity disorder (ADHD). This clinical trial tested how well centanafadine worked in treating symptoms of ADHD in adolescents (ages 13 to 17 years) when compared to placebo. A total of 459 adolescents participated in this clinical trial. Adolescents treated with higher-dose centanafadine (328.8 mg) had greater improvement in ADHD symptoms at 6 weeks compared to those treated with placebo or centafadine at lower dose (164.4 mg). Centanafadine was generally safe and generally well tolerated in adolescents.

Clinical trial registration information: A Trial of Centanafadine Efficacy and Safety in Adolescents With Attention-Deficit/Hyperactivity Disorder; https://clinicaltrials.gov/study/NCT05257265 DIVERSITY & INCLUSION STATEMENT: We worked to ensure sex and gender balance in the recruitment of human participants. We worked to ensure race, ethnic, and/or other types of diversity in the recruitment of human participants. We worked to ensure that the study questionnaires were prepared in an inclusive way. One or more of the authors of this paper self-identifies as a member of one or more historically underrepresented racial and/or ethnic groups in science. One or more of the authors of this paper self-identifies as a member of one or more historically underrepresented sexual and/or gender groups in science. One or more of the authors of this paper self-identifies as living with a disability. We actively worked to promote sex and gender balance in our author group. The author list of this paper includes contributors from the location and/or community where the research was conducted who participated in the data collection, design, analysis, and/or interpretation of the work.

Keywords: adolescent; attention-deficit/hyperactivity disorder; centanafadine; efficacy; safety.

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