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Enclosure:

- POSTER: Ward CL, Oberdhan D, Jin N, et al. Presented at Psych Congress, September 17-21, 2025; San Diego, CA, USA.

Efficacy of Centanafadine on Conners 3 Content Scales in Children With Attention-Deficit/Hyperactivity Disorder

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Poster 143

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INTRODUCTION

- Attention-deficit/hyperactivity disorder (ADHD) is one of the most common pediatric neurodevelopmental disorders, characterized by symptoms of inattention, hyperactivity, and impulsivity—all of which can affect overall quality of life for patients and their families[1,2]
- Individuals with ADHD can also have impairments in executive functioning or high-level cognitive processes that include inhibition, switching between tasks, working memory, planning, monitoring, and verbal and design fluency[3]
- The Conners 3–Parent Short (PS) Content Scales measure some aspects of executive functioning as well as inattention, hyperactivity, and impulsivity[4]
- A phase 3 trial of children aged 6–12 years evaluated the efficacy and safety of once-daily, extended-release centanafadine (CTN), a norepinephrine, dopamine, serotonin reuptake inhibitor, for the treatment of ADHD

OBJECTIVE

- To evaluate the treatment impact of CTN on inattention, hyperactivity/impulsivity, and executive functioning in children with ADHD

METHODS

- **Study:** A phase 3, multicenter, randomized, double-blind, placebo-controlled trial conducted in the United States and Canada (NCT05428033)
- **Eligible participants:** Children (6–12 years of age) with a primary diagnosis of ADHD (of any presentation) according to *Diagnostic and Statistical Manual of Mental Disorders*, 5th edition (DSM-5) criteria, as confirmed by the Mini International Neuropsychiatric Interview for Children and Adolescents (MINI-KID)
- **Treatment:** Participants were randomized (1:1:1) to receive once-daily extended-release high-dose CTN, low-dose CTN, or placebo for 6 weeks without titration
  - CTN dosing was weight-based, with participants divided into four categories (<20, ≥20–<35, 35–50, or >50 kg) and receiving 41.1, 82.2, 123.3, or 164.4 mg, respectively, if they were randomized to low-dose CTN, or 82.2, 164.4, 246.6, or 328.8 mg if they were randomized to high-dose CTN. Weight categories were combined for the data analyses
- **Efficacy outcomes:** Change from baseline in the Conners 3–PS for the Inattention, Hyperactivity/Impulsivity, and Executive Functioning Content Scale T-scores at Week 6
- **Analysis:** Outcomes were analyzed using a mixed-effect model for repeated measures
  - Values presented are least squares mean change from baseline (standard error)
  - Low-dose CTN did not meet the primary endpoint; thus, low-dose CTN has been excluded from this presentation of secondary and/or exploratory endpoints and presented *P*-values were not controlled for multiplicity
  - All data reported here were collected via a parent/caregiver
- **Other outcomes:** Safety and tolerability

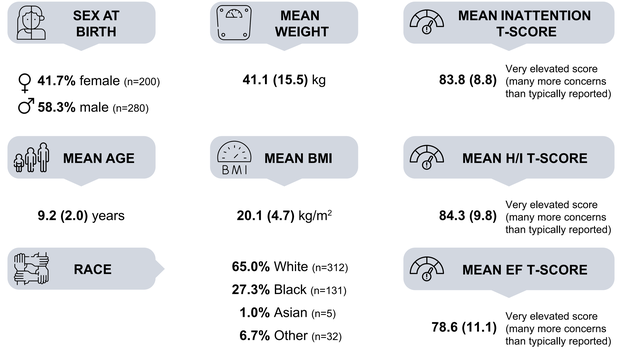
RESULTS

- Overall, 480 children were enrolled and randomized, and 76.5% (367/480) completed the study (mean age 9.2 years, 58.3% male) (**Figure 1**)
- Significant improvements from baseline in the Inattention Content Scale T-scores were reported by caregivers for high-dose CTN versus placebo (−11.9 [1.1] *vs* −6.4 [1.1], *P*=0.0002) (**Figure 2**)
- Improvements from baseline in the Hyperactivity/Impulsivity Content Scale T-scores were reported by caregivers for high-dose CTN versus placebo (−11.5 [1.1] *vs* −6.9 [1.1], *P*=0.0022) (**Figure 3**)
- Similarly, improvements in Executive Functioning Content Scale T-Scores were observed for high-dose CTN versus placebo (−11.3 [1.1] *vs* −6.8 [1.1], *P*=0.0026) (**Figure 4**)

Safety

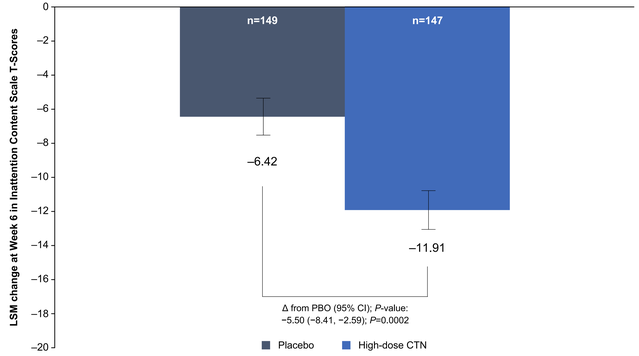
- Most treatment-emergent adverse events were mild to moderate, with the most common (≥5% in the high-dose CTN group and greater than placebo) being decreased appetite (7.6%) and rash (5.7%)

Figure 1. Baseline demographics and clinical characteristics of all randomized children (N=480)



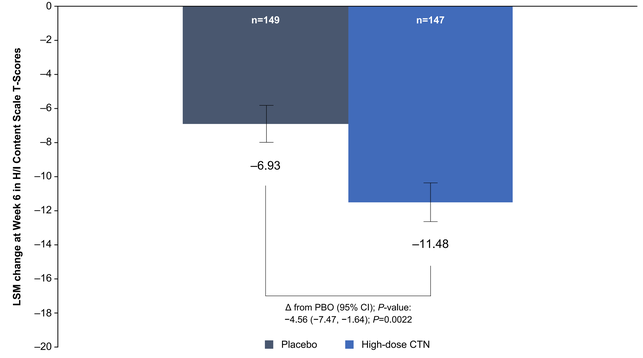
Means are presented with standard deviations. For race, the "Other" category includes participants who self-identified as American Indian / Alaskan Native, Native Hawaiian / Other Pacific Islander, or "other." BMI, body mass index; EF, Executive Functioning; H/I, Hyperactivity/Impulsivity.

Figure 2. LSM change at Week 6 in Conners 3–PS Inattention Content Scale T-scores



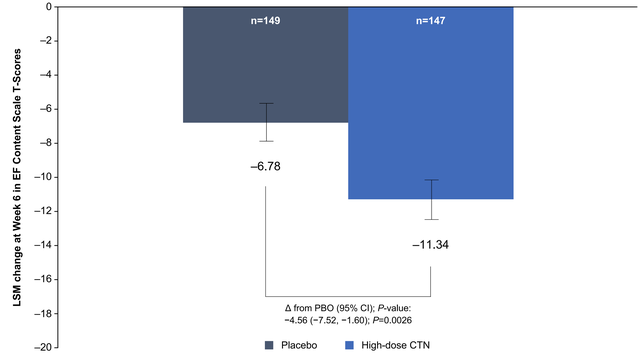
LSM change is derived from a mixed-effect model for repeated measures. Error bars are standard error of the means. CI, confidence interval; CTN, centanafadine; LSM, least squares mean; PBO, placebo.

Figure 3. LSM change at Week 6 in Conners 3–PS Hyperactivity/Impulsivity Content Scale T-scores



LSM change is derived from a mixed-effect model for repeated measures. Error bars are standard error of the means. CI, confidence interval; CTN, centanafadine; H/I, Hyperactivity/Impulsivity; LSM, least squares mean; PBO, placebo.

Figure 4. LSM change at Week 6 in Conners 3–PS Executive Functioning Content Scale T-scores



LSM change is derived from a mixed-effect model for repeated measures. Error bars are standard error of the means. CI, confidence interval; CTN, centanafadine; EF, Executive Functioning; LSM, least squares mean; PBO, placebo.

CONCLUSIONS

- Based on caregiver assessment, high-dose CTN showed an early and sustained impact on improving core inattention, hyperactivity/impulsivity, and executive functioning symptoms of ADHD in children when compared to placebo
- Once-daily extended-release high-dose CTN was efficacious, and had a favorable safety profile in the treatment of ADHD in children

References

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At Otsuka, we hold a deep respect for the value of every mind. We will not rest until mental illnesses and brain diseases are approached with the same priority and urgency as our physical health and recognized as chronic diseases that warrant early, equitable, and accessible intervention for patients and caregivers everywhere.

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