Request for Copy of Published Material

The materials provided in response to your request, unless otherwise stated, are the property of the copyright holder. Copyright and other intellectual property laws protect these materials. Reproduction or retransmission of the materials, in whole or in part, in any manner, without the prior written consent of the copyright holder, is a violation of copyright law. A single copy of the materials is provided to you pursuant to a license to do so that has been granted by the copyright holder to us. You may not redistribute or reproduce the materials in any forms without prior written consent of the copyright holder of the materials.

<u>Please note, this is an investigational product and is not approved by the US Food and Drug Administration (FDA).</u>

Enclosure:

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

Clinically Meaningful, Caregiver-Rated Improvements in ADHD Symptoms Following 6 Weeks of Centanafadine Treatment in Pediatric Patients With ADHD

Dorothee Oberdhan¹, Caroline L. Ward¹, Taisa Skubiak¹, Na Jin¹, Judy van Stralen²

Presenting on behalf of the authoring group: Mike Hogan¹

¹Otsuka Pharmaceutical Development & Commercialization, Inc., Rockville, MD, United States; ²Center for Pediatric Excellence, Ottawa, ON, Canada

Poster 140 Scan the QR code to receive a PDF of

INTRODUCTION

- Attention-deficit/hyperactivity disorder (ADHD) is one of the most common pediatric neurodevelopmental disorders, characterized by symptoms of inattention, hyperactivity, and impulsivity^{1,2}
- Two phase 3 trials evaluated the efficacy and safety of oncedaily, extended-release centanafadine (CTN)—a norepinephrine, dopamine, and serotonin reuptake inhibitor—for the treatment of ADHD in pediatric participants (children aged 6–12 years and adolescents aged 13–17 years)

OBJECTIVE

• To evaluate the clinically meaningful, caregiver-rated improvements in ADHD symptoms following 6 weeks of CTN treatment in pediatric participants with ADHD

METHODS

- **Studies:** Two phase 3, multicenter, randomized, double-blind, placebo-controlled trials conducted in the United States and Canada (children: NCT05428033; adolescents: NCT05257265)
- Eligible participants: Children (6–12 years; the trial is ongoing in younger participants [4–5 years, inclusive], which will be reported separately) or adolescents (13–17 years) 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 oncedaily extended-release high-dose CTN, low-dose CTN, or placebo for up to 6 weeks without titration
- Dosing:
- Children: Weight-based, with participants divided into the following 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, respectively, if they were randomized to high-dose CTN. Weight categories were combined for data analyses
- Adolescents: High-dose (328.8 mg) CTN, low-dose (164.4 mg) CTN, or placebo

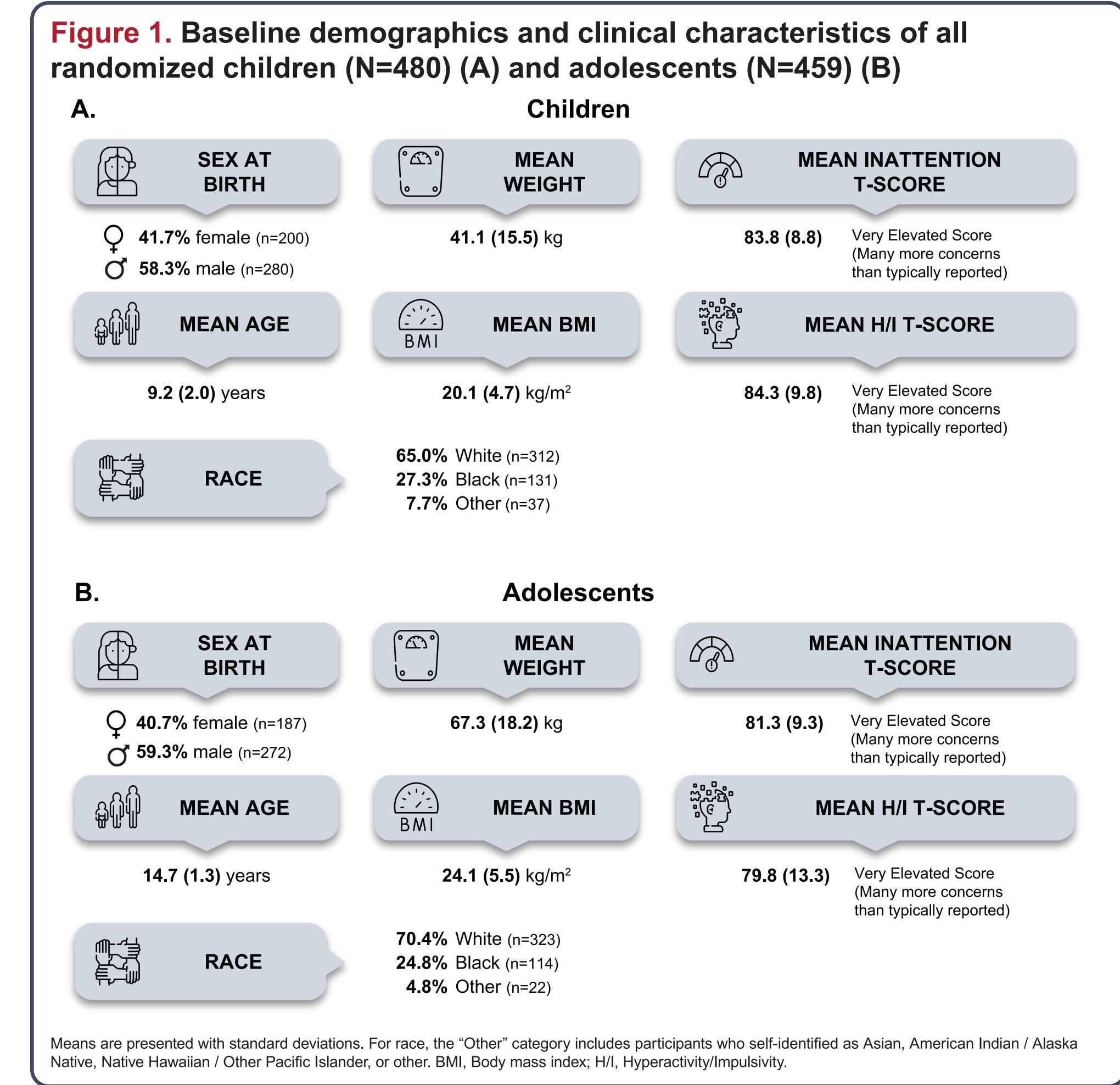
- Efficacy outcomes:
- Clinically meaningful within-patient change was analyzed for the key secondary endpoint, change from baseline in the Conners 3–Parent Short (PS) T-scores for Inattention (defined as ≥14-point improvement) and Hyperactivity/Impulsivity (defined as ≥13-point improvement), up to Week 6
- Clinically meaningful within-patient change thresholds were estimated using an anchor-based approach
- Analysis:
- Clinically meaningful within-patient change was analyzed via Cochran-Mantel-Haenszel tests on the last observation carried forward population
- The time from randomization to reaching the clinically meaningful within-patient change threshold of Conners 3–PS T-scores for the first time was analyzed via a log-rank test
- 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
- Other outcomes: Safety and tolerability

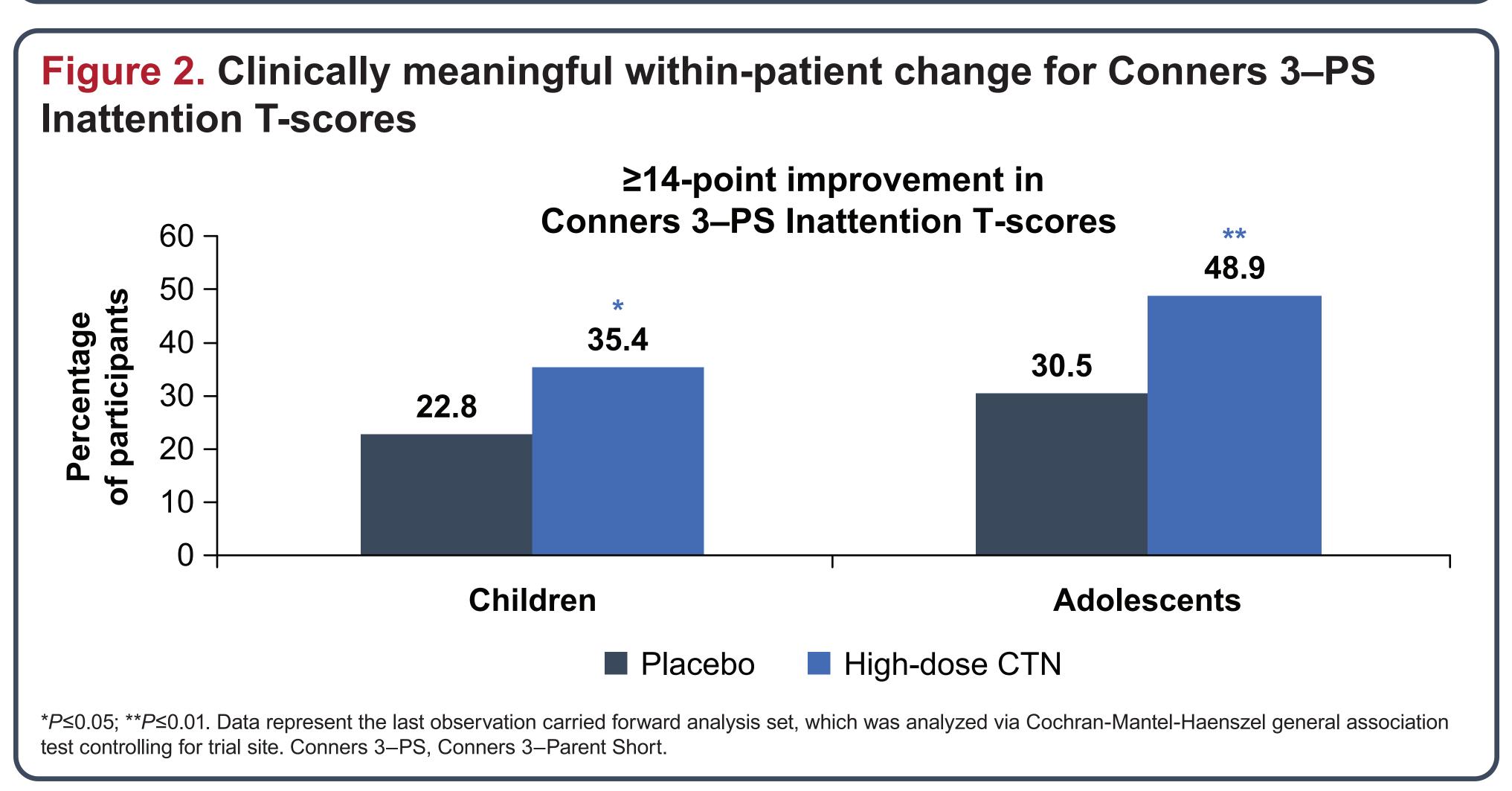
RESULTS

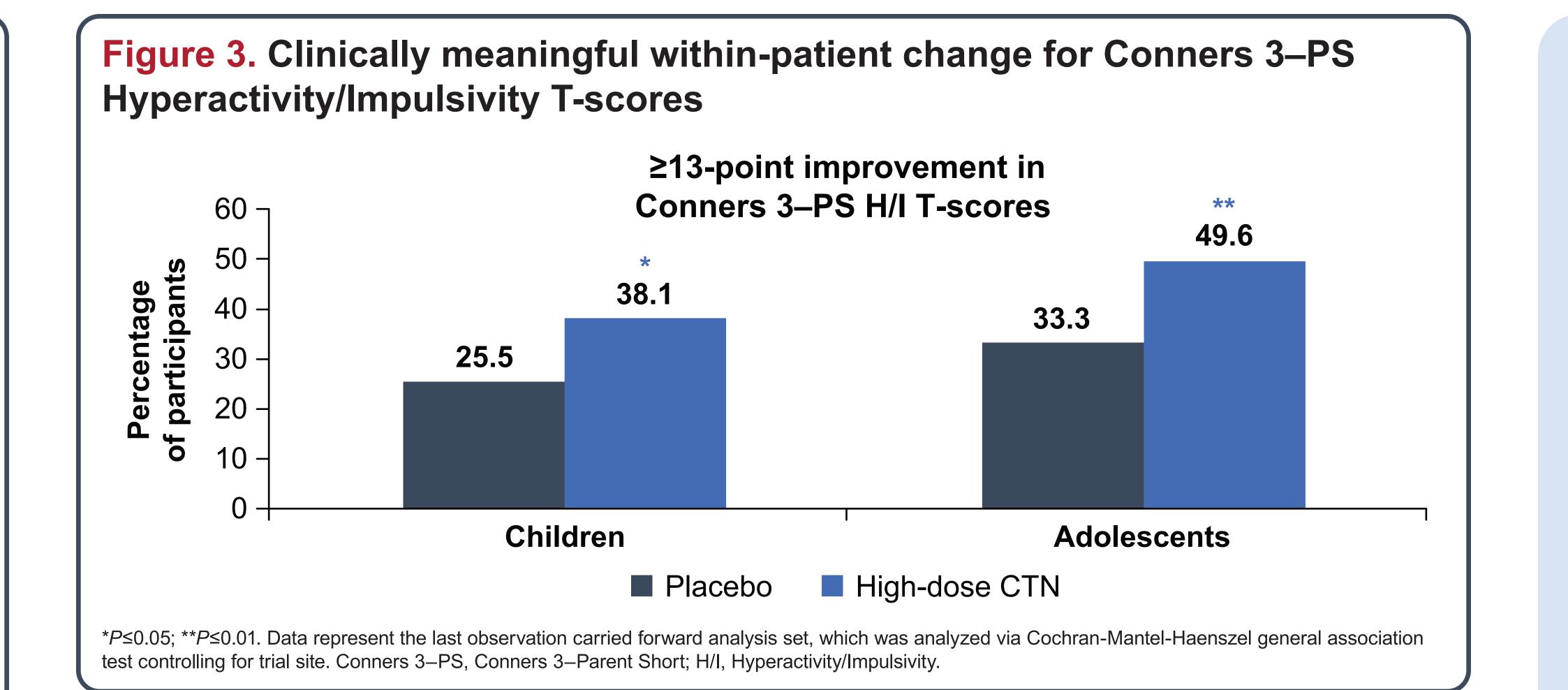
- Overall, 76.5% (367/480) of children (mean age 9.2 years, 58.3% male; Figure 1A) and 80.8% (371/459) of adolescents (mean age 14.7 years, 59.3% male; Figure 1B) completed their respective studies
- Up to Week 6, a numerically greater proportion of patients treated with high-dose CTN had a ≥14-point improvement in Conners 3–PS Inattention T-scores when compared to placebo (children: 35.4% vs 22.8%, P=0.0174; adolescents: 48.9% vs 30.5%, P=0.0013) (Figure 2)
- Up to Week 6, a numerically greater proportion of patients treated with high-dose CTN had a ≥13-point improvement in Conners 3– PS Hyperactivity/Impulsivity T-scores when compared to placebo (children: 38.1% vs 25.5%, P=0.0233; adolescents: 49.6% vs 33.3%, P=0.0066) (Figure 3)
- For both populations, the time from randomization to reaching the clinically meaningful within-patient change threshold of Conners 3–PS T-scores for the first time was significantly earlier in the high-dose CTN group compared with the placebo group for Inattention (children: P=0.0451; adolescents: P=0.0060) and Hyperactivity/Impulsivity (children: P=0.0067; adolescents: P=0.0029), demonstrating a rapid onset of separation from placebo (**Figure 4**)

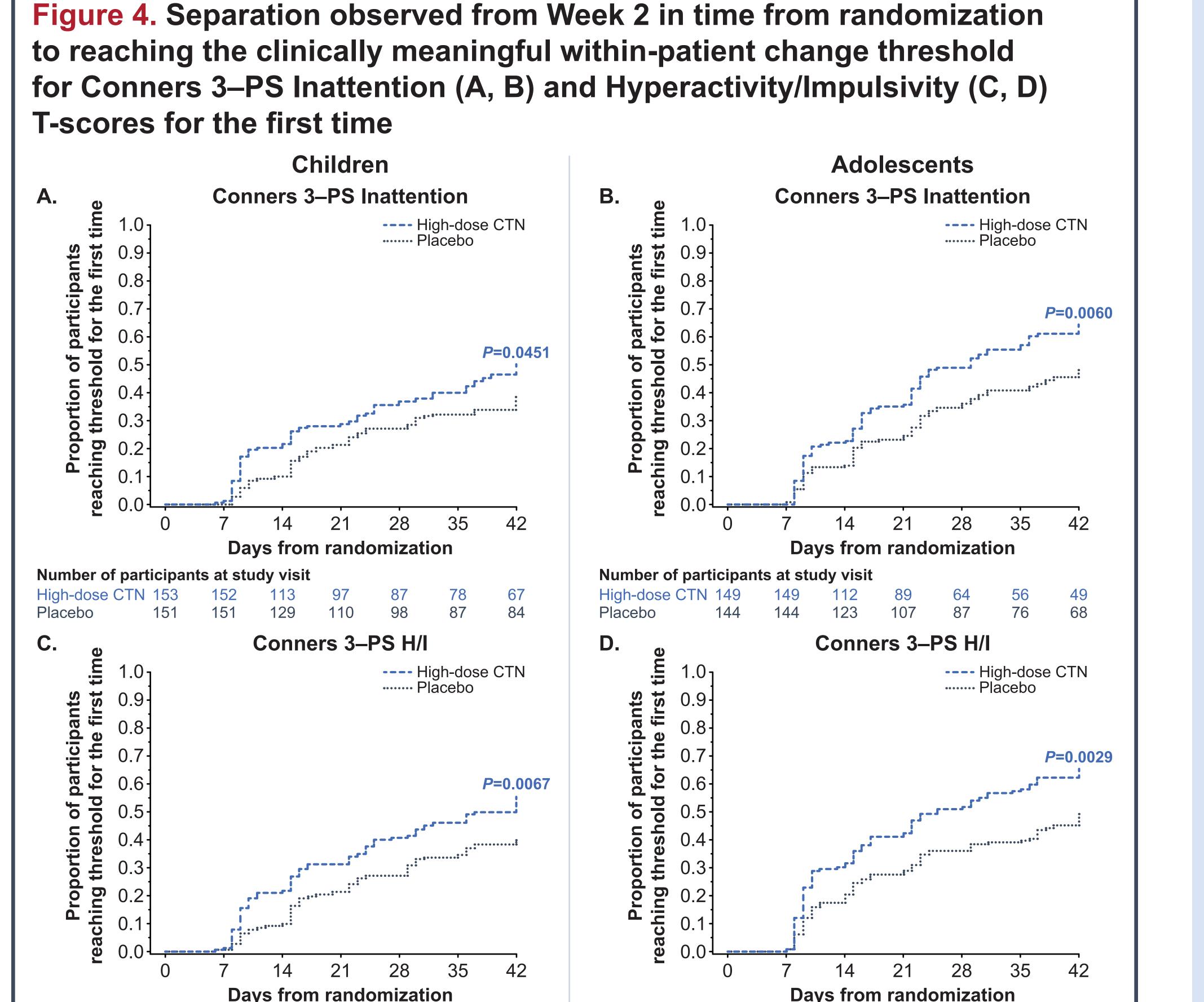
Safe

• 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%) for children, and decreased appetite (15.2%), nausea (9.9%), headache (6.0%), and rash (6.0%) for adolescents









Number of participants at study visit

CTN, centanafadine; Conners 3–PS, Conners 3–Parent Short; H/I, Hyperactivity/Impulsivity.

CONCLUSIONS

 Once-daily high-dose CTN was efficacious with a favorable safety profile and significant clinically meaningful within-patient change in ADHD symptoms as measured by the Conners 3–PS for children and adolescents

References

- 1. Drechsler R, et al. Neuropediatrics. 2020;51(5):315-35.
- 2. Sharma A, et al. *Ann Pharmacother*. 2014;48(2):209-25.

Acknowledgements

Medical writing and poster development support were provided by The Medicine Group, LLC (New Hope, PA, United States) in accordance with Good Publication Practice guidelines.

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.

Funding

The study and poster development support were sponsored by Otsuka Pharmaceutical Development & Commercialization, Inc., Princeton, NJ, United States.

Disclosures

DO, CLW, TS, and NJ are all full-time employees of Otsuka Pharmaceutical Development & Commercialization, Inc. JvS has received consulting fees from Janssen, Otsuka, Purdue, and Takeda. She has received advisory board fees, educational grants, and speaker fees from Janssen, Purdue, and Takeda. She owns Johnson & Johnson stock and has received research grants from Elvium and Takeda. She has received funding for multi-center trials as a primary investigator for Biohaven, Emalex, GW Research Ltd., Janssen, Nuvelution, Otsuka, and Teva.

Poster presented at Psych Congress 2025; September 17–21, 2025; San Diego, CA, USA.

Previously presented at the American Psychiatric Association (APA) 2025; May 17–21, 2025; Los Angeles, CA, USA.