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Enclosure:

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

Impact of Intrinsic Factors on the Efficacy of Centanafadine in an Adult Population with Attention-Deficit/Hyperactivity Disorder

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Poster 145

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INTRODUCTION

- Attention-deficit/hyperactivity disorder (ADHD) is a chronic and prevalent neurodevelopmental disorder in adults, characterized by symptoms of inattention, hyperactivity, and impulsivity—all of which can affect overall quality of life (QoL) for patients and their families[1]
- ADHD is associated with significant humanistic and economic burden on the patient and society, especially in adults, even after remission of some symptoms[2-5]
- Centanafadine (CTN)—a norepinephrine, dopamine, serotonin reuptake inhibitor (NDSRI)—was studied in two phase 3 trials for the treatment of ADHD in adults aged 18–55 years[6]
- The two phase 3 trials were the first large-scale studies to demonstrate the efficacy profiles of CTN in adults with ADHD, meeting the primary (change from baseline in Adult ADHD Investigator Symptom Rating Scale [AISRS] total score), and key secondary endpoint (change from baseline in Clinical Global Impression of Severity for ADHD (CGI-S-ADHD), at Week 6[6]

OBJECTIVE

- This pooled analysis evaluated the impact of intrinsic factors on the efficacy of CTN in adults with ADHD

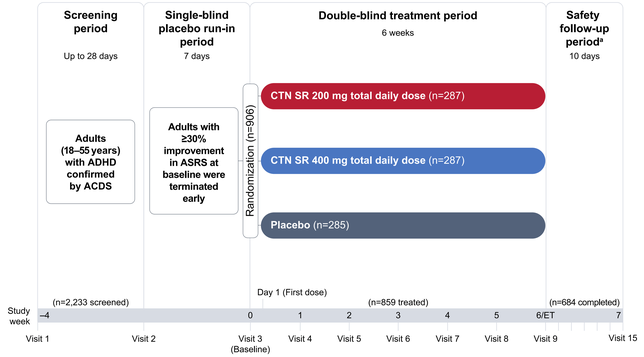
METHODS

- **Study:** Two identically designed phase 3, multicenter, randomized, double-blind, placebo-controlled trials conducted in the US (NCT03605680 and NCT03605836) (**Figure 1**)
- **Eligible patients:** Adults (18–55 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 Adult ADHD Clinical Diagnostic Scale (ACDS)
- **Treatment:** Patients were randomized (1:1:1) to receive CTN 200 mg, CTN 400 mg, or placebo for up to 6 weeks
- **Primary & key secondary efficacy endpoints:** Change from baseline in the AISRS total score and CGI-S-ADHD at Week 6
- **Analysis:** Mixed-effect model for repeated measures, with trial site, treatment group, visit, and treatment group-by-visit interaction as factors and baseline-by-visit interaction as a covariate; used "unstructured" covariance matrix
  - Endpoints were not controlled for multiplicity, and all *P*-values are therefore descriptive

RESULTS

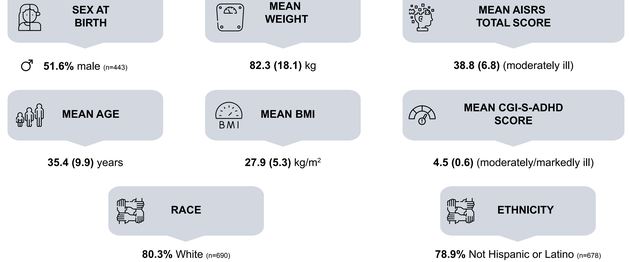
- A total of 859 adults were analyzed for efficacy and 684 (75.5%) completed the study; 51.6% were male at birth 80.3% (n=690) White, and 19.8% (n=170) Hispanic or Latino (**Figure 2**)
- Across the pooled adult population, the male and female, White, and non-Hispanic or Latino subgroups treated with CTN 200 and 400 mg demonstrated improvement in the core symptoms of ADHD per AISRS total score versus placebo at Week 6 (**Figure 3**)
- Improvements in symptom severity per the CGI-S were observed in the male, White, and not Hispanic/Latino subgroups treated with CTN versus placebo (**Figure 4**)
- Overall, there were no significant treatment-by-subgroup interactions at the 0.05 level, indicating a similar effect across all subgroups
- The treatment effect for CTN was similar between males and females but was lower for adults who were Hispanic or Latino compared to those who were not Hispanic or Latino based on the changes from baseline in AISRS total score and CGI-S score at Week 6
- Due to small sample sizes, no clinically meaningful conclusions regarding the treatment effect size can be made for the Asian, American Indian or Alaska Native, Native Hawaiian or other Pacific Islander, and 'other' populations

Figure 1. Study design



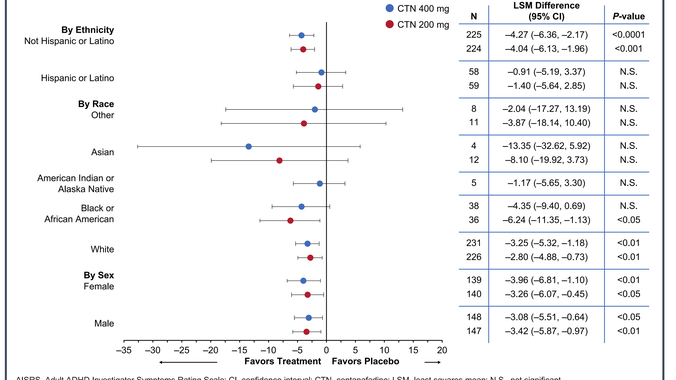
[a]All patients were required to participate in the 7-day follow-up period, with follow-up telephone calls at Days 1, 3, and 5 after the last dose of trial treatment, and in-clinic follow-up visits at Days 2 and 7 after the last dose of trial treatment. Patients who terminated early, decided to not enroll, or were not eligible to enroll in the open label trial were required to participate in an additional follow-up telephone call 10 days after the last dose of trial treatment. ACDS, Adult ADHD Clinical Diagnostic Scale; ADHD, attention-deficit/hyperactivity disorder; ASRS, Adult ADHD Self Report Scale; CTN SR, centanafadine sustained release; ET, end of treatment.

Figure 2. Baseline demographics and clinical characteristics of the pooled population (N=859)



Means are presented with standard deviations. AISRS, Adult ADHD Investigator Symptoms Rating Scale; BMI, body mass index; CGI-S-ADHD, Clinical Global Impression-Severity for ADHD.

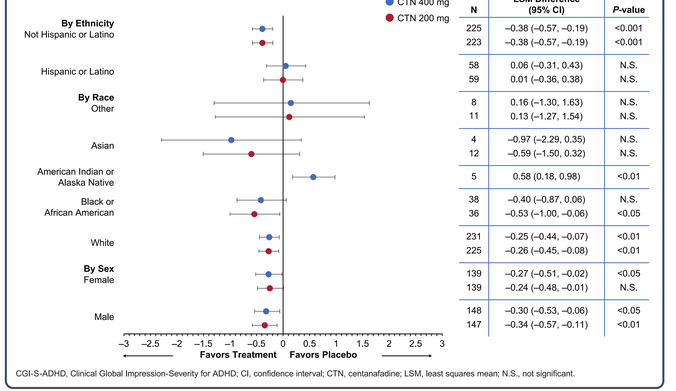
Figure 3. LSM change from baseline in AISRS total score by sex, race, and ethnicity at Week 6



	N	LSM Difference (95% CI)	*P*-value
By Ethnicity			
Not Hispanic or Latino	225	−4.27 (−6.36, −2.17)	<0.0001
	224	−4.04 (−6.13, −1.96)	<0.001
Hispanic or Latino	58	−0.91 (−5.19, 3.37)	N.S.
	59	−1.40 (−5.64, 2.85)	N.S.
By Race			
Other	8	−2.04 (−17.27, 13.19)	N.S.
	11	−3.87 (−18.14, 10.40)	N.S.
Asian	4	−13.35 (−32.62, 5.92)	N.S.
	12	−8.10 (−19.92, 3.73)	N.S.
American Indian or Alaska Native	5	−1.17 (−5.65, 3.30)	N.S.
Black or African American	38	−4.35 (−9.40, 0.69)	N.S.
	36	−6.24 (−11.35, −1.13)	<0.05
White	231	−3.25 (−5.32, −1.18)	<0.01
	226	−2.80 (−4.88, −0.73)	<0.01
By Sex			
Female	139	−3.96 (−6.81, −1.10)	<0.01
	140	−3.26 (−6.07, −0.45)	<0.05
Male	148	−3.08 (−5.51, −0.64)	<0.05
	147	−3.42 (−5.87, −0.97)	<0.01

AISRS, Adult ADHD Investigator Symptoms Rating Scale; CI, confidence interval; CTN, centanafadine; LSM, least squares mean; N.S., not significant.

Figure 4. LSM change from baseline in CGI-S-ADHD score by sex, race, and ethnicity at Week 6



	N	LSM Difference (95% CI)	*P*-value
By Ethnicity			
Not Hispanic or Latino	225	−0.38 (−0.57, −0.19)	<0.001
	223	−0.38 (−0.57, −0.19)	<0.001
Hispanic or Latino	58	0.06 (−0.31, 0.43)	N.S.
	59	0.01 (−0.36, 0.38)	N.S.
By Race			
Other	8	0.16 (−1.30, 1.63)	N.S.
	11	0.13 (−1.27, 1.54)	N.S.
Asian	4	−0.97 (−2.29, 0.35)	N.S.
	12	−0.59 (−1.50, 0.32)	N.S.
American Indian or Alaska Native	5	0.58 (0.18, 0.98)	<0.01
Black or African American	38	−0.40 (−0.87, 0.06)	N.S.
	36	−0.53 (−1.00, −0.06)	<0.05
White	231	−0.25 (−0.44, −0.07)	<0.01
	225	−0.26 (−0.45, −0.08)	<0.01
By Sex			
Female	139	−0.27 (−0.51, −0.02)	<0.05
	139	−0.24 (−0.48, −0.01)	N.S.
Male	148	−0.30 (−0.53, −0.06)	<0.05
	147	−0.34 (−0.57, −0.11)	<0.01

CGI-S-ADHD, Clinical Global Impression-Severity for ADHD; CI, confidence interval; CTN, centanafadine; LSM, least squares mean; N.S., not significant.

CONCLUSIONS

- CTN treatment demonstrated improvement in core ADHD symptoms and symptom severity versus placebo irrespective of sex, race, ethnicity in adults with ADHD

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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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