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.

Enclosure:

POSTER: Strawn JR, Hebert C, Childress AC, et al. Presented at: Psych Congress 2026, September 15-19, 2026; New Orleans, LA, USA.

Executive Function and Behavioral Regulation in Adults With ADHD and Comorbid Anxiety Disorders Treated With Centanafadine: Results From a Phase 3b Trial

Jeffrey R. Strawn[1], Corey Hebert[2], Ann C. Childress[3], Gregory Mattingly[4], Andrew J. Cutler[5], Zhen Zhang[6], Sheila Therriault[6], Elizabeth Brunner[7], Caroline L. Ward[6]

[1]Department of Psychiatry and Behavioral Neuroscience, University of Cincinnati College of Medicine, Cincinnati, OH, United States; [2]Department of Pediatrics, LSU Health Sciences Center, New Orleans, LA, United States; [3]Center for Psychiatry and Behavioral Medicine, Inc., Las Vegas, NV, United States; [4]Washington University School of Medicine, Midwest Research Group, St. Louis, MO, United States; [5]SUNY Upstate Medical University, Lakewood Ranch, FL, United States; [6]Otsuka Pharmaceutical Development & Commercialization, Inc., Princeton, NJ, United States; [7]Previously of Otsuka Pharmaceutical Development & Commercialization, Inc., Princeton, NJ, United States

Scan for Full Poster

Introduction

- Adults with attention-deficit/hyperactivity disorder (ADHD) and comorbid anxiety disorders may experience substantial executive dysfunction and behavioral dysregulation, contributing to functional impairment beyond the core symptoms of inattention, hyperactivity, and impulsivity[1-5]
- However, the effects of pharmacologic treatment on patient-reported executive functioning and behavioral regulation in daily life are less well characterized[4,6]
- Centanafadine, a norepinephrine-dopamine-serotonin reuptake inhibitor (NDSRI) and central nervous system stimulant, was recently approved for the treatment of ADHD in children, adolescents, and adults[7]

Objective

- This phase 3b trial evaluated the effect of centanafadine on executive function and behavioral regulation in adults with ADHD and comorbid anxiety disorders

Methods

- **Study:** A phase 3b, multicenter, randomized, double-blind, 8-week, placebo-controlled trial conducted in the US (NCT06973577)
- **Participants:** Adults (18–65 years) with ADHD (of any presentation) and diagnosed anxiety disorders (generalized and/or social), according to *Diagnostic and Statistical Manual of Mental Disorders*, 5th edition, Text Revision, (*DSM-5-TR*) criteria
- **Treatment:** Patients were randomized (1:1) to receive once-daily centanafadine extended-release 328.8 mg or placebo for up to 8 weeks
- **Secondary efficacy endpoints:** Change from baseline to Week 8 in the Behavior Rating Inventory of Executive Function-Adult Version (BRIEF-A) T-scores, including the Global Executive Composite and its component indices, the Behavioral Regulation Index and Metacognition Index
  - BRIEF-A is a 75-item self-report questionnaire assessing executive functioning and problems with self-regulation in daily life[8]
    - Behavioral Regulation Index reflects the ability to regulate behavior and emotions, including impulse control, cognitive shifting, emotional modulation, and self-monitoring
    - Metacognition Index reflects the ability to manage and guide task-oriented behaviors, including task initiation, working memory, planning/organizing, performance monitoring, and organization of materials
    - Global Executive Composite provides an overall summary of executive functioning derived from the Behavioral Regulation and Metacognition Indices
  - Items are rated from 1 (never) to 3 (often) based on experiences during the previous month; raw scores are converted to T-scores, with higher T-scores indicating worse executive function[8]
- Analysis: Efficacy endpoints were analyzed using a mixed-effect model for repeated measures, with trial site, treatment group, visit, and treatment group-by-visit interaction as fixed effects and baseline-by-visit interaction as a covariate; used "unstructured" covariance matrix
  - No adjustment was made for multiplicity; therefore, *P*-values are nominal and should be interpreted descriptively

Results

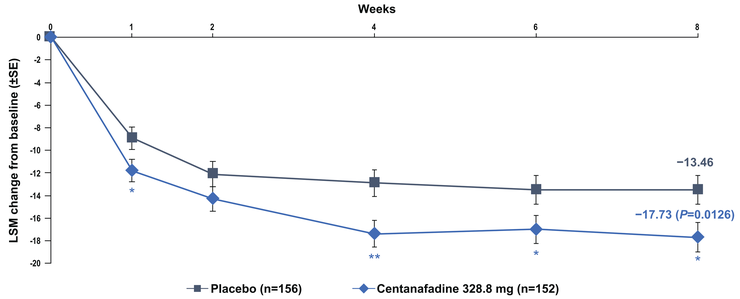
- A total of 315 adults (mean age 38 years, 64% female) were randomized to centanafadine (n=157) or placebo (n=158), with 241 (76.5%) completing the trial
- At baseline, mean ± standard deviation BRIEF-A T-scores were 77.4 ± 10.4 for the Global Executive Composite, 70.0 ± 11.5 for the Behavioral Regulation Index, and 79.5 ± 10.1 for the Metacognition Index, indicating severe executive functioning difficulties and impact on daily life (**Figure 1**)
- By Week 8, centanafadine was associated with greater improvement versus placebo on the overall Global Executive Composite, with a treatment difference of –4.3 (95% CI, –7.61 to –0.92) (**Figure 2**)
- On the Behavioral Regulation Index, similar improvement from baseline was seen, with a treatment difference of –4.1 (95% CI, –7.09 to –1.05) at Week 8 (**Figure 3**)
- Improvement was also observed on the Metacognition Index, with a treatment difference of –4.0 (95% CI, –7.34 to –0.64) versus placebo at Week 8 (**Figure 4**)
- Improvements were observed across domains within the Behavioral Regulation and Metacognition indices, including Inhibit, Shift, Self-Monitor, Initiate, Working Memory, Plan/Organize, and Organization of Materials; domains with less baseline impairment generally showed smaller improvements (**Figure 5**)

Figure 1. Baseline demographics and clinical characteristics

SEX AT BIRTH	MEAN WEIGHT	MEAN AGE	ANXIETY TYPE	RACE	MEAN BRIEF-A GEC	MEAN BRIEF-A BRI	MEAN BRIEF-A MI
64.4% female (n=203) **35.6%** male (n=112)	**80.4 (17.5)** kg	**38.1 (11.3)** years	**94.0%** GAD (n=296) **14.6%** SAD (n=46)	**0.6%** American Indian/Alaskan Native (n=2) **5.7%** Asian (n=18) **17.1%** Black or African American (n=54) **9.2%** Other (n=29) **67.0%** White (n=211)	**77.4 (10.4)** (severe)	**70.0 (11.5)** (moderate)	**79.5 (10.1)** (severe)

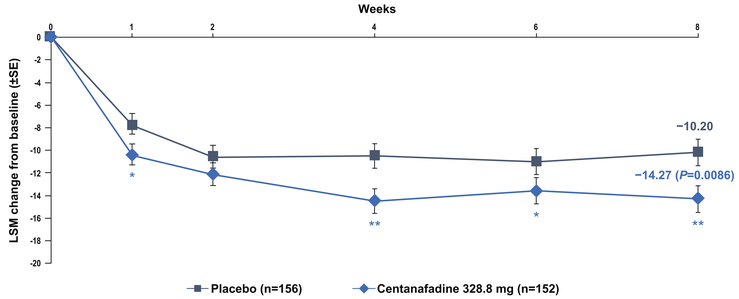
Baseline demographics and clinical characteristics are reported for the randomized population (N=315). Means are presented with standard deviations.
BRI, Behavioral Regulation Index; BRIEF-A, Behavior Rating Inventory of Executive Function-Adult Version; GAD, generalized anxiety disorder; GEC, Global Executive Composite; MI, Metacognition Index; SAD, social anxiety disorder.

Figure 2. Change from baseline in the BRIEF-A Global Executive Composite across 8 weeks



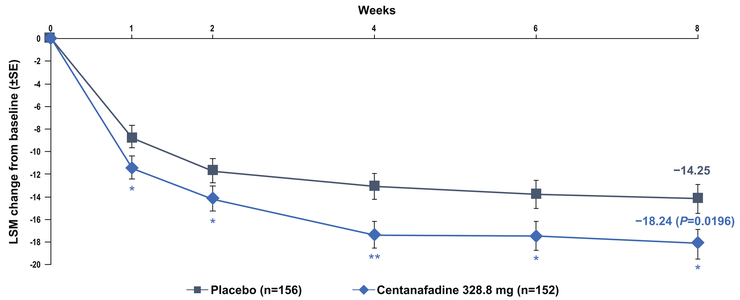
Efficacy analyses were conducted in the full analysis set (N=308).
*P<0.05, **P<0.01.
BRIEF-A, Behavior Rating Inventory of Executive Function-Adult Version; LSM, least squares mean; SE, standard error.

Figure 3. Change from baseline in the BRIEF-A Behavioral Regulation Index across 8 weeks



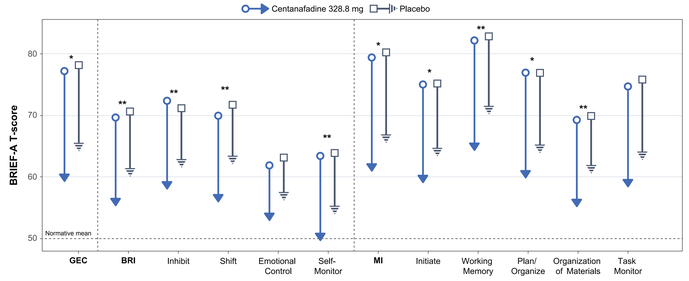
Efficacy analyses were conducted in the full analysis set (N=308).
*P<0.05, **P<0.01.
BRIEF-A, Behavior Rating Inventory of Executive Function-Adult Version; LSM, least squares mean; SE, standard error.

Figure 4. Change from baseline in the BRIEF-A Metacognition Index across 8 weeks



Efficacy analyses were conducted in the full analysis set (N=308).
*P<0.05, **P<0.01.
BRIEF-A, Behavior Rating Inventory of Executive Function-Adult Version; LSM, least squares mean; SE, standard error.

Figure 5. Change from baseline in the BRIEF-A line-items



Efficacy analyses were conducted in the full analysis set (N=308).
Open circle/square = baseline mean; arrow tip = baseline mean + least squares mean change from baseline.
BRIEF-A ranges: 50 typical to normal, <60 within expected range, 60–64 mildly elevated, 65–69 clinically elevated, ≥70 highly elevated.
*P<0.05, **P<0.01.
BRIEF-A, Behavior Rating Inventory of Executive Function-Adult Version; BRI, Behavioral Regulation Index; GEC, Global Executive Composite; MI, Metacognition Index.

Conclusions

- **In adults with ADHD and comorbid anxiety, centanafadine was associated with greater patient-reported improvements versus placebo across behavioral regulation, metacognitive functioning, and overall executive function and self-regulation assessed by the BRIEF-A**
- **These findings suggest that centanafadine may also improve ADHD-associated features beyond core symptoms, including difficulties with executive function, behavioral regulation, and self-regulation**

References

1. American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders*. 5th ed. Text Revision. American Psychiatric Association; 2022.
2. Song P, et al. *J Glob Health*. 2021;11:04009.
3. Adamis D, et al. *Ir J Med Sci*. 2024;193(5):2433-41.
4. Fu X, et al. *Front Psychiatry*. 2025;16:1597559.
5. Choi WS, et al. *PloS One*. 17(11), e0277175.
6. Katzman MA, et al. *BMC Psychiatry*. 2017;17(1):302.
7. SIMTRIYO® (centanafadine) extended-release capsules [prescribing information]. Princeton, NJ: Otsuka America Pharmaceutical, Inc.; 2026.
8. Roth RM, Gioia GA. Behavior rating inventory of executive function-adult version. Lutz (FL): Psychological Assessment Resources; 2005.

Acknowledgements

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

Disclosures

CH has been an advisory board member for GSK, Ironshore (Collegium), Otsuka, Rhodes, Supernus, and Teva; and has been on a speaker bureau for GSK, Ironshore (Collegium), Otsuka, Rhodes, and Supernus. **ACC** has been a consultant for Aardvark, Alora, Arbor, Attentiv, Aytu, Corium, Ironshore, Lumos, Neos, Neurocentria, Noven, Otsuka, Purdue, Rhodes, Sky, Sunovion, Supernus, Tris, and Zevra Therapeutics Inc.; has participated on speakers' bureaus for Collegium (Ironshore), Supernus, Takeda, and Tris; has received research support from Aardvark, Adlon, Akili, Allergan, Arbor, Emalex, IntraCellular, Collegium (Ironshore), Lumos, Neos, Otsuka, Purdue, Rhodes, Servier, Sunovion, Supernus, Suven, Syndeio, Takeda, Tris, and Zevra; has received writing support from Arbor, Collegium (Ironshore), Neos, Purdue, Rhodes, Sunovion, Takeda, and Tris; and has participated on advisory boards for Adlon, Akili, Arbor, Cingulate, Corium, Collegium (Ironshore), Otsuka, Purdue, Sunovion, Supernus, and Tris. **JRS** has received research support from the National Institutes of Health, PCORI Abbvie, and Definium; has received material support from Myriad Genetics; has consulted for AbbVie, Alkermes, Collegium, Definium, Newleos, Otsuka, Supernus, Sensorium, Vistagen, and Genomind; has served on the speaker's bureau for Abbvie, Collegium, Supernus, and Myriad Genetics; receives royalties from Springer Publishing and Cambridge University Press; receives honoraria from the Neuroscience Education Institute; serves as an author for UpToDate; and serves a member of a data safety monitoring board for Eli Lilly. **GM** serves as a speaker for Alkermes, Allergan Ironshore, Janssen, Lundbeck, Otsuka, Sunovion, and Takeda; serves as a consultant for Akili, Alkermes, Allergan, Axsome, Ironshore, Intra-Cellular, Ironshore, Janssen, Lundbeck, Otsuka, Neos, Purdue, Rhodes, Sage, Sunovion, Takeda, and Teva; and is a researcher for Akili, Alkermes, Allergan, Axsome, Boehringer, Janssen, Lundbeck, Medgenics, NLS-1 Pharma AG, Otsuka, Reckitt Benckiser, Roche, Sage, Sunovion, Supernus, Takeda, and Teva. **AJC** has been a consultant or advisory board member for AbbVie, Acadia, Actinogen, Alfasigma, Alkermes, Anavex Life Sciences, Arrivo BioVentures, Autobahn, Axsome, Aytu, Bristol Myers Squibb, Collegium, Definium, 4M, Helus, Incannex Healthcare, J&J Innovative Medicine, Jazz, Knight, Kye, Kuvatns Therapeutics, LivaNova, Lundbeck, Luye, MapLight, Mentavi, Neumora, Neurocrine Biosciences, Noven, Otsuka, Sensorium, Sirtsei, Supernus, Teva, Thynk, Transneural, Tris, Vanda, and Vistagen; has been on a speaker bureau for AbbVie, Alfasigma, Alkermes, Axsome, Aytu, Bristol Myers Squibb, Collegium, J&J Innovative Medicine, Knight, Kye, Lundbeck, Luye, Neurocrine, Noven, Otsuka, Supernus, Teva, Tris, and Vanda; was on a data safety monitoring board for Compass Pathways; and has stock options/equity in EMA Wellness, Evolution Research Group, 4M, Jupiter Neuroscience, Sensorium, and Transneural. **ZZ**, **ST**, and **CLW** are all full-time employees of Otsuka Pharmaceutical Development & Commercialization, Inc. **EB** was a former employee of Otsuka Pharmaceutical Development & Commercialization, Inc.