Schizophrenia. Addressing these gaps is critical to improving the management of patients.
Funding. Medscape Education, Cerevel Therapeutics

52-Week Open-Label Safety and Tolerability Trial of Centanafadine Sustained Release in Adults With Attention Deficit Hyperactivity Disorder (ADHD)

Osman Turkoglu, MD, Taisa Skubiak and Jessica McDonough, MD

Otsuka Pharmaceutical Development & Commercialization, Inc., Princeton, NJ

Introduction. Centanafadine (CTN) is a potential first-in-class norepinephrine/dopamine/serotonin triple reuptake inhibitor (NDSRI) in development for ADHD. In 2 pivotal adult ADHD trials, CTN sustained-release (SR) 200 mg/d and 400 mg/d, administered twice daily (BID), significantly reduced Adult ADHD Investigator Symptom Rating Scale (AISRS) total score vs placebo, with favorable safety and tolerability. Long-term effects of CTN SR 400 mg/d in adult ADHD are reported here.
Methods. Adults meeting *DSM-5* criteria for ADHD who completed a pivotal trial or enrolled de novo were eligible for the 52-week, phase 3, open-label trial. Uncontrolled comorbid psychiatric disorder, undifferentiated diagnosis of ADHD, prohibited medicines, or positive alcohol or drug screen were exclusionary. All patients (pts) received CTN SR BID, titrated to 400 mg/d by day 8, and fixed thereafter. Safety was primarily assessed by adverse events (AEs); laboratory results, physical examinations, vital signs, ECG, Study Medication Withdrawal Questionnaire (SMWQ), and Columbia-Suicide Severity Rating Scale (C-SSRS) were also assessed. Efficacy was assessed by AISRS, Clinical Global Impression-Severity (CGI-S) and ADHD Impact Module-Adult (AIM-A). Analyses were based on observed results using descriptive statistics. Baseline was relative to the first CTN dose in the open-label trial.
Results. Of 662 pts enrolled (mean [SD] age 36.7 [10.1] years; 51.1% female; 82.9% White), 653 received CTN SR; 345 pts completed the trial. Common discontinuation reasons were pt withdrawal (119; 18%), AEs (81; 12.2%), and lost to follow-up (41; 6.2%); 22 (3.4%) pts discontinued for lack of efficacy. Treatment-emergent AEs (TEAEs) occurred in 401 pts (61.4%); 16 (2.5%) had severe TEAEs. Common TEAEs were insomnia (8.0%), nausea (7.7%), diarrhea, and headache (7.0% each). Serious TEAEs occurred in 12 pts (1.8%); none were CTN related. AEs of special interest (n=18; 2.8%) included rash (n=5; 1 severe), papule, rash erythematous, rash maculopapular, rash papular, and urticaria (n=1 each); 3 discontinued. Abuse potential–related AEs occurred in 31 pts (4.7%). No deaths occurred. SMWQ scores were low throughout. Suicidal ideation/behavior occurred in 13 pts (2.0%) per C-SSRS. There were no trends in laboratory, vital sign, or ECG changes. Baseline mean (SD) AISRS Total, Inattentive, and Hyperactive-Impulsive scores were 34.4 [10.3], 19.2 [5.6], and 15.2 [6.0], respectively; mean (SD) changes at week 52 were −20.4 (11.9), −11.2 (6.6), and −9.2 (6.2). Baseline mean (SD) CGI-S score was 4.2 (0.9); mean (SD) change at week 52 was −1.5 (1.1). Baseline mean (SD) AIM-A score was 6.5 (1.8); mean change at week 52 was 1.23 (2.0).
Conclusions. Safety, tolerability, and exploratory efficacy results from this trial demonstrate that CTN SR 400 mg is a safe and effective long-term treatment for ADHD in adults.
Study Registration: NCT03605849
Previous presentation: APA Annual Meeting, May 20–24, 2023, San Francisco, CA
Funding. Otsuka

A Review and Comparison of FDA-Approved Transcranial Magnetic Stimulation (TMS) Protocols for Depression

Paula Gomes, MD, Ayyub Imtiaz, MD, Menachem Groden, MD and Muhammad Zaidi, MD

Saint Elizabeths Hospital, Department of Behavioral Health, Washington, DC

Introduction. Transcranial Magnetic Stimulation (TMS) is a Food and Drug Administration (FDA) approved treatment that induces neuronal activity in the left dorsolateral prefrontal cortex. TMS was initially developed to treat major depression after studies of patients with depression revealed hypometabolism in this brain region. Since it was first FDA approved in 2008, several types of TMS have been developed and its clinical indications expanded. Given the dearth of literature guiding clinicians in understanding different forms of TMS and their protocols, this poster will review the common and unique aspects of several forms of TMS in an effort to aid clinicians in appropriately utilizing this safe and effective neuromodulatory treatment.
Methods. Specific keywords were used to conduct a thorough but nonsystematic review of multiple databases, including PubMed, Google Scholar, and PsychInfo. Articles describing protocols rather than direct comparisons were selected. The outcomes regarding protocol guidelines, advantages, disadvantages, safety, and side effects were included in the review.
Results. The FDA approved types of TMS include repetitive TMS (rTMS), deep TMS (dTMS), intermittent theta burst stimulation (iTBS), and accelerated TMS (aTMS). While rTMS is limited to cortical tissue, other forms of TMS reach subcortical neurons with aTMS using functional magnetic resonance imaging (fMRI) to specifically locate the target area. dTMS was approved in 2013 and its session time is half that of rTMS. Subsequently developed TMS types have even shorter sessions; iTBS sessions are only 3 minutes and aTMS is 9 minutes per session. Most TMS protocols require 8-9 weeks for full treatment, but aTMS only needs 5 days. All TMS protocols stimulate at 120% of resting motor thresholds except for aTMS which adjusts based on the patient using fMRI results. Efficacy is mostly similar with rTMS, dTMS, and iTBS

https://doi.org/10.1017/S1092852924001755 Published online by Cambridge University Press