Combining Iclepertin (BI 425809) With Computerized Cognitive Training in Patients With Schizophrenia: Baseline Data From an Ongoing Phase II Trial

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Abstract

Introduction. There are currently no approved pharmacotherapies to treat cognitive impairment associated with schizophrenia (CIAS). Iclepertin (BI 425809) is a novel glycine transporter-1 inhibitor under development for treatment of CIAS. A previous study demonstrated pro-cognitive effects of iclepertin in patients with schizophrenia; however, concurrent cognitive stimulation could in theory enhance any pro-cognitive pharmacological effects on neuroplasticity. We present preliminary demographics and baseline data from a trial exploring the efficacy of iclepertin together with at-home computerized cognitive training (CCT).

Methods. This is an ongoing Phase II, double-blind, placebo-controlled, parallel-group trial in patients with schizophrenia on stable antipsychotic therapy across ~58 centers in 6 countries. Patients aged 18–50 years, compliant with CCT during the run-in period (completing ≥2 hours/week for 2 weeks), were randomized (1:1) to receive once-daily iclepertin 10 mg or placebo together with CCT for 12 weeks. Thereafter, minimum compliance for at-home CCT is 1 hour/week, with a target of ~30 hours across 3–5 sessions totaling 2.5 hours/week. Patients have been stratified to balance potential effects of age (18–40; 41–50 years). Primary endpoint is change from baseline (CfB) in neurocognitive composite T-score of the MATRICS Consensus Cognitive Battery (MCCB) at Week 12. Secondary endpoints include CfB in the Schizophrenia Cognition Rating Scale (SCoRS) total score, MCCB overall composite T-score, and Positive and Negative Syndrome Scale (PANSS) total scores. Novel exploratory endpoints include the Virtual Reality Functional Capacity Assessment Tool to assess daily functioning and the Balloon Effort Task to assess motivation in cognitive performance.

Results. Of the planned sample of 200 randomized patients, the overall treated population currently includes 183: 67% (n=122) are male; mean (standard deviation [SD]) age and time since first diagnosis are 38.2 (7.9) years and 13.5 (8.5) years. Overall, 49% (n=89) are White and 43% (n=79) are Black or African American; 80% (n=147) are from North America, 15% (n=28) from Europe, and 4% (n=8) from Australia/New Zealand. Mean (SD) baseline MCCB neurocognitive composite and overall T-scores (n=178) are 33.7 (11.9) and 32.5 (12.6). Mean (SD) baseline SCoRS total score (n=167) is 35.2 (8.7). Mean (SD) baseline PANSS total and negative symptom scale scores (n=183) are 64.7 (14.6) and 17.3 (5.4). Median (Q1, Q3) CCT compliance over the on-treatment period for patients who have completed or discontinued early is 2.00 (1.21, 2.51) hours/week.

Conclusion. This trial is, to our knowledge, the largest of its kind combining daily pharmacotherapy for CIAS with at-home CCT. It will indicate whether iclepertin together with concurrent cognitive stimulation provides enhanced cognitive benefit, and whether any improvements in neurocognition can translate into improved measures of daily functioning in patients.

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Comorbidities and Presenting Symptoms in a Real-World Population With Obstructive Sleep Apnea

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Abstract

Background. Obstructive sleep apnea (OSA) is a highly prevalent sleep disorder that is often associated with numerous medical and psychiatric comorbidities. Patients with OSA experience a variety of symptoms that can be burdensome and affect their quality of life and satisfaction with care. Excessive daytime sleepiness (EDS) is a common symptom of OSA, and can persist despite primary airway therapy (e.g., positive airway pressure [PAP]). This analysis aimed to characterize common comorbidities, as well as symptoms present at OSA diagnosis and their burden in a real-world population of participants with OSA.

Methods. US residents (≥18 years of age, self-reported clinician diagnosis of OSA [from 1/1/2015 to 3/31/2020]) completed a survey in Evidation Health's Achievement app that assessed self-reported sleepiness (Epworth Sleepiness Scale [ESS]), self-reported PAP usage, self-reported physician-diagnosed comorbidities, and information on their symptoms at time of OSA diagnosis. Self-reported PAP use was categorized as nonuse (no PAP use), nonadherent (<4 h/night or <5 d/wk), intermediate (4–6 h/night, ≥5 d/wk), or highly adherent (≥6 h/night, ≥5 d/wk). EDS was defined as ESS score >10. All data were summarized descriptively.

Results. In total, 2289 participants completed the survey (50.3% female; 82.5% White; mean ± standard deviation [SD] age, 44.8 ± 11.1 years; mean ± SD age at OSA diagnosis, 40.7 ± 11.4 years; mean ± SD body mass index, 35.4 ± 8.7 kg/m^2); 42.5% had EDS. Among the total population, 30.6% were PAP non-users, 6.7% were nonadherent, 9.8% were intermediate adherent, and 52.9% were highly adherent. Across the study population, the most

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common self-reported physician-diagnosed comorbidities were anxiety (44%) and depression (42%) followed by hypertension (39%), dyslipidemia (26%), and asthma (21%). Among the symptoms participants reported having had at the time of OSA diagnosis, the most common were EDS (79%), fatigue (79%), snoring (75%), and awakening with a dry mouth or sore throat (63%). Concentration/Memory problems (48%) and mood changes (46%) were also common. In the overall population, the symptoms present at the time of OSA diagnosis that were most likely to be highly burdensome were fatigue (53%), EDS (46%), snoring (35%), difficulty concentrating/memory issues (31%), and mood changes (25%).

Conclusions. These real-world survey data identify anxiety and depression as the most frequently reported comorbidities in a population of participants with OSA, each affecting over 40% of participants. In addition to classic OSA symptoms (e.g., EDS, fatigue, snoring, and awakening with dry mouth/sore throat), concentration/memory problems and mood changes were also common at the time of OSA diagnosis and were among the presenting symptoms most frequently reported as highly burdensome, along with fatigue, EDS, and snoring.

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Excessive Daytime Sleepiness in a Real-World Study of Participants With OSA With or Without Comorbid Depression

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Abstract

Background. Obstructive sleep apnea (OSA) is a sleep disorder that is highly comorbid with psychiatric disorders, including depression and anxiety. Excessive daytime sleepiness (EDS) is common in psychiatric disorders and OSA. In participants with OSA, EDS can persist despite use of positive airway pressure (PAP) therapy. This analysis of real-world data aimed to describe EDS and its relationship with PAP use in participants with and without depression.

Methods. US residents (≥18 years of age, self-reported physician diagnosis of OSA [from 1/1/2015 to 3/31/2020]) completed a survey in Evidation Health's Achievement app assessing subjective levels of sleepiness (Epworth Sleepiness Scale [ESS]) and self-reported PAP usage, categorized as nonuse (no PAP use), nonadherent (<4 h/night or <5 d/wk), intermediate (4-6 h/night, ≥5 d/wk), or highly adherent (≥6 h/night, ≥5 d/wk). ESS score >10 defined EDS. A linear model assessed relationships between PAP use and ESS score. *P*-values are uncontrolled for multiplicity (nominal).

Results. In total, 2289 participants (EDS, n=972; no EDS, n=1317) completed the survey (50.3% female; 82.5% White; mean±standard deviation [SD] age, 44.8 ± 11.1 years). Anxiety and depression were the most common comorbidities and were more common in participants with EDS (49% and 49%, respectively) than those without EDS (41% and 37%, respectively). Overall, EDS was more common among participants with comorbid depression (49%) than those without (38%), even among highly adherent PAP users (46% vs 30%, respectively). In a linear model (PAP users only), an additional 1 h/night of PAP use was associated with lower ESS scores in the subgroup of participants without depression (n=928; estimate [SE], −0.42 [0.09]; $P<0.05$), but not in the subgroup with depression (n=661; estimate [SE], −0.15 [0.10]; $P>0.05$). In a sensitivity analysis that excluded participants using medications that cause sleepiness, PAP use was associated with lower ESS scores regardless of depression status; however, EDS remained more common in participants with comorbid depression (46%) than in those without (36%).

Conclusions. In this real-world population of participants with OSA, those with EDS were more likely to have comorbid anxiety or depression. EDS was more common in participants with comorbid depression than those without, even with highly adherent PAP use. PAP use was associated with lower ESS scores in participants without comorbid depression, but not in those with comorbid depression; the use of medications that cause sleepiness may contribute to but does not fully explain this phenomenon.

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Genetic Behavioral Trait Assessment Paired With Personalized Recommendations and Coaching to Support Mental Health and Wellness

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Abstract

Background. Genetics, environment, and lifestyle each contribute to human behaviors. We have developed a direct-to-consumer genetic assay (Mental Health Map) that allows users to explore their genetic behavioral predispositions and potential interventions that may positively influence mental health and wellness. Based on preliminary consumer feedback suggesting increased desire to take action on their mental health and wellness, we initiated a pilot study to assess several measures of mental health and self-care in individuals both before and after reviewing their Mental Health Map.

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