Assessing the Unmet Clinical Need and Opportunity for Digital Therapeutic Intervention in Schizophrenia: Perspective From People With Schizophrenia

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Abstract

Introduction. Recent research has highlighted the increasing ubiquity of smartphone ownership as well as the feasibility of digital interventions within schizophrenia. Digital therapeutics, a subset of digital interventions, have established standards for efficacy and safety and are subject to regulatory oversight as Software as a Medical Device. Here, we present data from a survey that assessed the opportunity and expectations that people with schizophrenia have for a digital therapeutic designed to be delivered on top of antipsychotic pharmacotherapy.
Methods. Seventy-five people with schizophrenia completed a 10-item survey. Participants were between 22 and 55 years of age, reported no hospitalizations or medication changes within the past 3 months, and were currently seeing a psychiatrist. For each question, participants were asked to rank responses to provide a clear understanding of their preferences.
Results. Patients with schizophrenia reported the survey items that most impacted their daily life were: difficulty meeting new people (17%) and difficulty setting goals/completing activities in daily life and not being productive in their free time (both at 13%). The greatest unmet treatment needs reported by people with schizophrenia were: improving social skills (19%); reducing distress related to disease (19%); and being more productive in their free time (13%). In terms of expectations for what a digital therapeutic would include, the items reported as most important were: sharing progress with providers (13%); teaching ways to deal with symptoms (13%); and helping to set and achieve goals (12%).
Conclusion. Many of the top unmet needs that people with schizophrenia identified can be uniquely targeted by a digital therapeutic that augments their ongoing standard of care.
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Rapid Antidepressant Effects and MADRS Item Improvements With AXS-05 (DEXTROMETHORPHAN-BUPROPION), an Oral NMDA Receptor Antagonist in Major Depressive Disorder: Results From Two Randomized Double-Blind, Controlled Trials

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Abstract

Background. AXS-05 (dextromethorphan-bupropion) is a novel, oral, investigational, NMDA receptor antagonist with multimodal activity being developed for MDD. The dextromethorphan component of AXS-05 is an NMDA receptor antagonist and a sigma-1 receptor agonist. The bupropion component of AXS-05 serves primarily to increase the bioavailability of dextromethorphan.
Methods. AXS-05 was evaluated in two double-blind, randomized, controlled, 6-week trials. The GEMINI trial (N=327) was placebo-controlled and the ASCEND trial (N=80) used bupropion as the control. Here we focus on efficacy in the first 2 weeks of treatment and present a pooled analysis of the individual items of the MADRS for AXS-05 as compared to control.
Results. In GEMINI, starting at Week 1, AXS 05 was superior ($p < 0.05$) to placebo on: mean MADRS improvement (7.3 vs. 4.9), MADRS response (15% vs. 7%), CGI-I (22% vs. 13%), CGI-S (0.7 vs. 0.4) and Q-LES-Q-SF (9.0% vs. 5.8%). At Week 2, AXS-05 was also statistically superior to placebo on MADRS remission (17% vs.8%) and on the SDS (6.8 vs. 4.5).

In ASCEND, from Week 2, AXS-05 was superior ($p< 0.05$) to bupropion on: mean MADRS improvement (12.5vs. 7.8), MADRS remission (26% vs. 3%), and CGI-S (1.41 vs. 0.9).

At Week 1, treatment with AXS-05 resulted in greater improvements ($p< 0.05$) in reported sadness, inner tension, inability to feel, pessimistic thoughts, and suicidal thoughts, as compared to control. At Week 6, AXS-05 demonstrated significant improvements over control on seven of the ten MADRS items.

In the GEMINI trial, the most commonly reported adverse events were dizziness, nausea, headache, diarrhea, somnolence, and dry mouth.
Conclusions. Treatment with AXS-05 resulted in rapid and broad antidepressant efficacy.
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