and improved adherence among the top treatment benefits. Barriers to LAI use commonly cited by patients/caregivers included side effects and lack of effect on negative symptoms, while common barriers cited by HCPs included patient access/cost and limited knowledge around best prescribing practices. Treatment comparisons and/or switching were more commonly mentioned among patients/caregivers (51%) than HCPs (30%), suggesting a greater interest in optimizing treatment among patients. Patients/caregivers often compared individual LAIs with oral antipsychotics (OAs) or different LAIs, whereas it was more typical for HCPs to compare LAIs with OAs than to distinguish between different LAIs.

Conclusions. Based on social media posts, patients/caregivers and HCPs had different primary treatment goals/concerns and generally used different lexicons, which may affect communication. Overall, HCPs were more positive and less negative toward LAIs than patients/caregivers. Top benefits noted (relapse and adherence) were similar between groups, while top treatment barriers differed. These differences highlight the need to improve communication between patients/caregivers and HCPs in order to increase treatment satisfaction and potentially improve treatment outcomes.

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EMPOWERing the Next-Generation: A Phase 2 Program to Evaluate Emraclidine, a Selective M4 Positive Allosteric Modulator (PAM), for the Treatment of Schizophrenia

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Background. Emraclidine is a novel, highly selective positive allosteric modulator of M4 muscarinic acetylcholine receptors currently in development for the treatment of schizophrenia and Alzheimer's disease psychosis. By selectively activating M4 receptors, emraclidine may reduce excess dopamine signaling in the striatum, potentially leading to a reduction in psychotic symptoms. Unlike current antipsychotics, emraclidine does not interfere with signaling at dopamine, serotonin, or histamine receptors, which can lead to adverse events. A previous phase 1b study supports further investigation of emraclidine. The phase 2 EMPOWER program will fully evaluate the efficacy, safety, tolerability, and dose-range of once-daily (QD) emraclidine in schizophrenia.

Methods. EMPOWER-1 and EMPOWER-2 are two adequately powered, multicenter, randomized, double-blind, placebo-controlled, parallel group, 6-week inpatient studies of emraclidine monotherapy (10 mg QD, 15 mg QD, 30 mg QD). The trials are enrolling adult participants with schizophrenia who are experiencing an acute exacerbation of psychosis. Eligible participants will have a Positive and Negative Syndrome Scale (PANSS) Total Score between ≥85 and ≤120 and a Clinical Global Impression – Severity (CGI-S) score ≥4 at baseline. Both de novo participants and those who complete EMPOWER-1 or EMPOWER-2 will be eligible to participate in EMPOWER-3, a 52-week open label extension trial to evaluate the long-term safety and tolerability of emraclidine in adult participants with stable schizophrenia.

Results. Detailed study designs for the EMPOWER program will be presented. Primary outcome measure for EMPOWER 1 and 2 is change from baseline in PANSS total score at week 6. Other outcome measures include change from baseline in CGI-S score at week 6. Data from EMPOWER-3 will contribute to the overall evaluation of safety and tolerability of emraclidine in adult participants with schizophrenia.

Conclusions. The development of emraclidine is promising, as it selectively activates M4, a novel target that has been implicated in reducing psychotic symptoms while potentially avoiding many of the side effects currently associated with antipsychotics. The EMPOWER program aims to establish the efficacy, safety, tolerability, and appropriate dose-range of emraclidine in the treatment of schizophrenia.

Funding. Cerevel Therapeutics

Use of the Modified Functional Status Questionnaire to Assess Functioning in Patients with Parkinson's Disease Psychosis Treated with Pimavanserin

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Introduction. Patient-reported outcomes (PROs) are increasingly collected in clinical trials and real-world studies as they provide valuable information on the impact of a treatment from the patient's perspective. Studies in Parkinson's disease psychosis (PDP) have focused on hallucination and delusions, however individuals with PDP also face functional limitations associated with worsening psychosis. Assessing activities of daily living (ADLs) and functioning of PDP patients can help inform PDP treatment. The International Parkinson and Movement Disorder Society has recommended the use of the Functional Status Questionnaire (FSQ) which has been infrequently utilized. Prior results were reported from a Phase 4 open-label study examining the impact of pimavanserin on ADLs and

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functioning in patients with PDP which utilized a modified version of the FSQ (mFSQ) as the primary outcome measure. In this analysis, we provide additional data on the patient-reported mFSQ within specific domains and correlation to the Schwab & England ADL scale.
Methods. Eligible patients entered a 16-week single-arm, open-label study of once-daily oral pimvanserin (34mg). The 6 domain FSQ was modified to assess 5 domains by removing the work/performance domain since this was not applicable to the patients in this study. The mean change from baseline to week 16 was evaluated in mFSQ domains (Basic ADL, Intermediate ADL, Psychological Function, Quality of Interaction, Social Activity). In addition, correlation between Schwab & England ADL scale and observed mFSQ value across post-Baseline visits were evaluated.
Results. A total of 29 patients were enrolled in the study, mean age (70.2 years), 62% males. The MMRM LSM (SE) for mSFQ from baseline to Week 16 were the following within each domain: Basic ADL (n=22), 8.1 (2.41), p=0.0031; Intermediate ADL (n=21), 7.0 (3.00), p=0.0286; Psychological Function (n=22), 13.3 (1.94), p <.0001; Quality of Interaction (n=22), 12.3(2.07), p <.0001; and Social Activity (n=18), 25.8 (7.52), p=0.0026. All mFSQ domains were showing improvement at 16 weeks from baseline; however, the largest change was seen in Social Activity. The correlation of mFSQ and the Schwab & England ADL scales resulted in a correlation coefficient of r=0.6 (p <.0001) for patient total score and r=0.5 (p<.0001) for caregiver total score. There was a consistent trend among both scales which was demonstrating improvement among patients and caregivers.
Conclusions. This was the first open-label clinical trial to utilize the mFSQ in patients with PDP. In this small, proof-of-concept study, treatment with pimavanserin was associated with improvement across all mFSQ domains; most improvement was seen in social activity. Additionally, the mFSQ was significantly correlated with the Schwab & England ADL, thus this appears to be a promising scale deserving of further evaluation and use in clinical studies as well as in the clinic to complement other assessments.
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Phase 2A Efficacy, Safety, and Tolerability Study of PH80 Nasal Spray for Acute Management of Menopausal Vasomotor Symptoms (Hot Flashes) in Women

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Introduction. Vasomotor symptoms (hot flashes) are the most common symptom of menopause, affecting about 75% of menopausal women and about 40% of perimenopausal women. PH80, an investigational neuroactive nasal spray, is hypothesized to be a potential treatment for moderate to severe hot flashes due to menopause given that it rapidly activates olfactory to limbic-hypothalamic neural circuits that control autonomic activity, including body temperature and sweating. The primary objective of this Phase 2A clinical study was to explore the efficacy, safety, and tolerability of intranasal administration of PH80 for the acute management of hot flashes due to menopause.
Methods. The study was a randomized, double-blind, placebo-controlled, exploratory Phase 2A clinical study. PH80 nasal spray containing epoxyestrenolone 0.8 µg per 50 µL was self-administered intranasally; two sprays in each nostril (total dose = 3.2 µg) up to four times daily as needed for 4 consecutive weeks. One additional dose was allowed at night if subjects were awakened by hot flashes. During the study period, subjects recorded the number and severity of hot flashes, disruption in function, and sweating related to hot flashes. Patient global impression of change (PGI-C) and clinician global impression of severity (CGI-S) were also assessed.
Results. At baseline, subjects reported a daily mean of 7.7 hot flashes in the PH80 group (n = 18) and 8.0 in the placebo group (n = 18). After 1 week of treatment, the number of hot flashes dropped to 2.8 for PH80 and 6.4 for placebo (P <.001), and after 4 weeks of treatment, the number of hot flashes dropped to 1.5 for PH80 and 5.1 for placebo (P <.001). Treatment with PH80 significantly reduced the severity, disruption in function, and sweating associated with hot flashes during the treatment period as compared with subjects in the placebo group. There was a significant improvement in PGI-C for PH80 vs placebo at endpoint (P = .015) and a strong trend for improvement on CGI-S (P = .053). PH80 was well-tolerated with no serious adverse events (AEs); the AE profiles of PH80 and placebo were comparable. All 36 subjects completed 4 weeks of treatment and with no study discontinuations due to AEs.
Conclusions. The rapid onset, significant reduction in symptoms, and improved function induced by intranasal PH80 in menopausal women with hot flashes compared with placebo, observed as early as the end of week 1 of treatment, provide a strong signal for continued development of PH80 for the acute treatment of hot flashes due to menopause. The safety data further suggest that, if approved, PH80 will provide a substantial safety benefit over all currently available agents.
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