Concurrent Improvement of Depressive and Anxiety Symptoms in Patients with Postpartum Depression Treated with the Oral Neuroactive Steroid Zuranolone

Introduction

— Postpartum depression (PPD) is one of the most common mood disorders complicating pregnancy and postpartum period.
— In the United States, estimates of new mothers experiencing PPD symptoms each year vary by state from 3% to 23%, with an average of 13.2%.
— PPD is associated with significant impairments in mother-infant bonding and maternal function, including breastfeeding and quality of interactions with the infant, which can have long-term sequelae on the child's health and development. 1-3
— Multiple environmental and biological risk factors have been proposed to play a role in the development of PPD. 4-6

Methods

- Women (N=315), ages 18-45, ≤6 months postpartum, diagnosed with PPD (defined as a major depressive episode in the 6th week postpartum and a baseline HAMD-17 ≥17), were administered study drug in an outpatient setting.
- Patients were randomized 1:1 to receive zuranolone 30 mg or placebo once daily for 14 days, with 4 weeks follow-up.
- The change from baseline (CFB) in HAMD-17 at Day 15 was the primary endpoint.
- Secondary endpoints included the CFB in the HAMD-17 at all other measured timepoints, the CFB in the Montgomery-Asberg Depression Rating Scale (MADRS), and the CFB in the Montgomery-Asberg Anxiety Rating Scale (MADRS-A).

Results

- The zuranolone and placebo arms included 76 and 74 patients, respectively, who were randomized and included in the efficacy analyses.
- Baseline demographic and patient characteristics were well balanced between the two treatment arms (Table S1).
- As previously presented, patients treated with zuranolone met the primary efficacy endpoint at Day 15 by achieving a significantly greater HAMD-17 total score CFB vs those who received placebo.
- Zuranolone was generally well tolerated, as previously described. 7-9
- One subject experienced a serious adverse event (SAE) in the zuranolone arm that resolved after dose reduction and remained on study treatment.
- There were no reports of loss of consciousness or syncope in either arm. 10

Conclusions

- Zuranolone treatment in patients with PPD has previously been shown to provide rapid (HAMD-17 total score by Day 3) and sustained (HAMD-17 total score of all measured timepoints through Day 45) improvement in depressive symptoms.
- Post hoc analyses showed that a higher proportion of zuranolone-treated patients achieved concurrent improvement in depression and anxiety symptoms compared to placebo at both Day 15 and Day 45 (p<0.0001) using the HAMD-17 and HAMA-A scale combination.
- Concurrent improvement was defined as using two scale combinations: a HAMD-17 total score ≤7 and a HAMA-A total score ≤10, or MADRS total score ≤32 and a HAMA-A total score ≤7.
- CFB in HAMD-17, HAMA-A, and MADRS total scores were evaluated using the least-squares mean from a mixed-effect model for repeated measures. Concurrent improvement rates were assessed using Fisher's exact test, while estimates for odds ratios (ORs) and 95% confidence intervals (CI) for ORs were derived using generalized estimating equations models for repeated measures, adjusting for baseline covariates.
- Secondary endpoints and post hoc analyses were not adjusted for multiplicity.