Reduction in Insomnia Symptoms in Patients with Postpartum Depression (PPD) Treated With the Neuroactive Steroid Brexanolone Injection

Methods

- The primary endpoint in all studies was the least-squares mean (LSM) change from baseline (CBF) in mean HAMD-17 total score at Hour 60.
- LSM HAMD-17 CFB was analyzed using a mixed effects model for repeated measures.
- Secondary endpoints included HAMD-17 total score at all other time points.

Results

- Patients received a 60-hour continuous infusion of placebo or BRX in a monitored setting, with four weeks follow-up.
- The primary endpoint in all studies was the least-squares mean (LSM) change from baseline (CFB) in mean HAMD-17 total score at Hour 60.
- LSM HAMD-17 CFB was analyzed using a mixed effects model for repeated measures.
- Secondary endpoints included HAMD-17 total score at all other time points.

Conclusions

- BRX treatment in women with PPD has previously been shown to provide rapid (Hour 24 for HAMD-17 total score and Bech-6 score) and sustained improvement in depressive symptoms (HAMD-17 total score and Bech-6 score at all subsequent measured time points up to Day 30) compared with placebo.

In addition to its effects on core depressive symptoms in this trial, these post hoc analyses showed that BRX treatment also resulted in significantly greater improvement compared to placebo in reported symptoms of insomnia from the HAMD-17-ins.

Introduction

- Postpartum depression (PPD) is one of the most common medical complications during and after pregnancy.1,2
- In the United States, estimates have mothers who identify with PPD to range between 15% to 24%, with an average of 13.2%.3
- PPD is associated with significant impairments in mothers', infants' bonding and maternal function,1,4 resulting in potential long-term developmental consequences and caring for the child,1,2 with implications for the child's health and development.1,2,5

Altered sleep states are both a risk factor and a symptom of PPD.6,7

- Reduced sleep quality may be predictive of increased depressive symptomology.6,7
- Brexanolone injection (BRX),8 a neuroactive steroid and GABAA receptor positive allosteric modulator with a pharmacological profile distinct from benzodiazepines,9 is approved by the FDA for the treatment of PPD in adults.10

The safety, tolerability, and efficacy of BRX in PPD were evaluated in three double-blind, randomized, placebo-controlled trials (RCTs; NCT02934204 and NCT02934205).11,12

- A single 60-hour infusion of BRX titrated to a maximum dose of 90 μg/kg/h resulted in statistically and clinically significant improvements in depressive symptoms compared with placebo at the primary endpoint (Hour 60), assessed by change from baseline in the 17-item Hamilton Rating Scale for Depression total score (HAMD-17; p<0.0001).12
- In addition, CFB using the predefined Bech-6 subscale of HAMD-17 favored BRX90 compared with placebo at Hour 60 (p=0.0035; p=0.0003; p<0.0001; **p=0.0035; ***p=0.0053).11,12
- Post hoc analyses from an integrated dataset of the pivotal BRX RCTs assessed an effect on insomnia symptoms using the 17-item Hamilton Rating Scale for Depression (HAMD-17) insomnia subscale (HAMD-17-ins).12

Conclusions

- BRX treatment in women with PPD has previously been shown to provide rapid (Hour 24 for HAMD-17 total score and Bech-6 score) and sustained improvement in depressive symptoms (HAMD-17 total score and Bech-6 score at all subsequent measured time points up to Day 30) compared with placebo.

The FDA-approved dosage is 90 μg/kg/h.