Anxiety Symptom Response in Patients with Postpartum Depression Treated with the Neuroactive Steroid Brexanolone Injection

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Introduction

- Postpartum depression (PPD) is one of the most common medical complications during and after pregnancy.
- Anxiety is a prominent symptom of PPD and has been associated with several severe diseases.
- Brexanolone injection (BRX), a neuroactive steroid GABA, receptor positive allosteric modulator with a pharmacological profile distinct from benzodiazepines, was included in the FDA for the treatment of PPD in adults.
- The safety, tolerability, and efficacy of BRX in PPD were evaluated in three double-blind randomized placebo-controlled trials (RCTs) where patients treated with BRX90 met the primary efficacy endpoint at Hour 60, by achieving significantly greater HAMD-17 total score change from baseline (p<0.0001).1,2
- Post hoc analyses from an integrated dataset of the three pivotal BRX RCTs assessed the effect on anxiety symptoms using the HAMD-17 anxiety/somatization subscale (A/S).

Conclusions

- BRX treatment in women with PPD has previously been shown to provide rapid (Hour 24 for HAMD-17 total score and Beck-D scale) and sustained improvement in depressive symptoms (HAMD-17 total score and Beck-D scale) from baseline to Day 30.2,10
- In addition to its effects on core symptoms of depression in this trial, these post hoc analyses showed that BRX treatment also resulted in significantly greater improvement in rated anxiety symptoms at all measured time points (up to Day 30) compared with placebo.2,12

Methods

- The integrated dataset of three pivotal studies in PPD was used for these analyses, with the pooled dataset referring to all patients receiving BRX in the first 24 hours regardless of the maximum dose received.
- Women (N=247) ages 18-45, within 7 days postpartum, with PPD (defined as a major depression episode with onset in the 3rd trimester or post partum) and a qualifying HAMD-17 total score (Studies A and B: HAMD-17≥22; Study C: HAMD-17≥17) were enrolled.
- BRX injection was given as a 60-hour continuous infusion of placebo or BRX in a monitored setting, with four weeks follow-up.

Results

- Baseline demographics and patient characteristics were well balanced between the treatment arms and have been described in detail previously.1,2
- As previously presented, patients treated with BRX90 met the primary efficacy endpoint at Hour 60, by achieving significantly greater HAMD-17 total score reduction vs patients receiving placebo (p<0.0001).1,2
- Significantly greater improvements were achieved in the HAMD-17, A/S score (±SEM) at all measured timepoints until Day 30 (p<0.0012).2,12
- The safety, tolerability, and efficacy of BRX in PPD were evaluated in three double-blind randomized placebo-controlled trials (RCTs) where patients treated with BRX90 met the primary efficacy endpoint at Hour 60, by achieving significantly greater HAMD-17 total score change from baseline (p<0.0001).1,2
- Post hoc analyses from an integrated dataset of the three pivotal BRX RCTs assessed the effect on anxiety symptoms using the HAMD-17 anxiety/somatization subscale (A/S).
- No significant differences were noted in the BRX90 group compared with placebo at Hour 24 (p=0.0173) and Day 30 (p=0.0213).
- Mean baseline Beck-D total score (±SEM) in the BRX90 group was 15.3±2.5 vs 15.7±2.8 in the placebo group (p=0.0394).
- Significant differences vs placebo in HAMD-17 A/S and Beck-D scores were observed at Hour 24 (p=0.0056 and p=0.0012) and were sustained at all measured timepoints until Day 30 (p<0.0490).

SUPPORT & DISCLOSURES

- Brexanolone (BRX), developed jointly by Sage Therapeutics and Baxalta, Inc., is being commercialized in the U.S. by Sage Therapeutics.
- Dr. Espinosa will be an unrestricted consultant to Baxalta/Sage Therapeutics for the next 12 months.
- Dr. Hinkle will be an unrestricted consultant to Baxalta/Sage Therapeutics for the next 12 months.
- Dr. Hinkle has no relationship with Sage Therapeutics/Sage.
- Dr. Ebert has no relationship with Sage Therapeutics/Sage.
- Dr. Kreuer has no relationship with Sage Therapeutics/Sage.
- Dr. Supe has no relationship.
- Dr. Kim has no relationship.
- Dr. Delgadillo has no relationship.
- Dr. Rabinow has no relationship.

SAFETY

- BRX common TEAEs (≥5% of BRX and ≥2 placebo rate) included dizziness and/or somnolence, dry mouth, loss of consciousness and flushing/hot flush.1,2
- Detailed adverse event rates including events of exudation/salivation and loss of consciousness have been described in detail previously.1,2
- BRX caused exudation/salivation requiring dose interruption/reduction in some patients (≤5% of BRX90 and ≤0.5% of placebo patients).1,2,15
- Some patients also had loss of state of consciousness (4% of BRX90 and ≤0.5% of placebo patients).1,2,15
- Time to recovery from loss of state of consciousness, and all adverse events, ranged from 3 to 80 minutes. All patients recovered with dose interruption.1,2,15

REFERENCES


- Haddad L, et al. —-The safety, tolerability, and efficacy of BRX in PPD were evaluated in three double-blind randomized placebo-controlled trials (RCTs) where patients treated with BRX90 met the primary efficacy endpoint at Hour 60, by achieving significantly greater HAMD-17 total score reduction vs patients receiving placebo (p<0.0001).1,2

- Martinez Botella G, et al. —-Follow-Up Period, Days 3-30. As previously presented, patients treated with BRX90 met the primary efficacy endpoint at Hour 60, by achieving significantly greater HAMD-17 total score change from baseline (p<0.0001).1,2

- Bech-6 subscale of HAMD-17 favored BRX90 compared with placebo (p<0.0001).1,2

- HAMD-17-A/S and Beck-D score at all subsequent follow-up visits. BRX90 compared with placebo.

- Treatment emergent adverse events (TEAEs) were assessed throughout the study. Post hoc analyses included the CFI in the HAMD-17 anxiety/somatization subscale (HAMD-17-A/S), which includes six items from HAMD-17: anxiety (phobic), anxiety (somatic), somatic symptoms (gastrointestinal), hypochondriasis, and insight) and HAMD-17-A/S responses (≥5% reduction from baseline score).

- Response assessments were analyzed using a generalized estimating equation approach.

- Secondary endpoints and post hoc analyses were not adjusted for multiplicity.