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 final maximum dose received.

— All BRX patients received 33 μg/kg/h for the first 4 hours, followed by 60 μg/kg/h for the next 20 hours. For the next 28 hours, BRX60 patients received 60 μg/kg/h and BRX90 patients received 90 μg/kg/h. All BRX patients were then dosed down to 60 μg/kg/h for 4 hours and 30μg/kg/h for 4 hours until the infusion was completed.

— 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 in HAMD-17 total score at Hour 60. The integrated dataset of three pivotal studies in PPD was used for these analyses.

— As previously presented, patients treated with BRX and BRX60 had the primary efficacy endpoint at Hour 60, by achieving significantly greater HAMD-17 total score CFRL vs placebo receiving p<0.001 for both.

— Significant differences vs placebo in HAMD-17 CFRL favoring BRX were observed by Hour 24 (BRX90: p=0.0012; BRX60: p=0.0013) and were sustained at all measured timepoints until Day 30.

— Significant differences vs placebo in HAMD-17 CFRL favoring BRX were observed at:
  • Hour 24: BRX90 (p=0.0010); BRX80 (p=0.0001).
  • Hour 60: BRX90 (p=0.0014); BRX80 (p=0.0001).
  • Hour 72: BRX90 (p=0.0007); BRX80 (p=0.0001).

— Significant differences vs placebo in HAMD-17 CFRL favoring BRX were observed at:
  • Hour 24: BRX90 (p=0.0010); BRX80 (p=0.0001).
  • Hour 60: BRX90 (p=0.0014); BRX80 (p=0.0001).
  • Hour 72: BRX90 (p=0.0007); BRX80 (p=0.0001).

— Significant differences vs placebo in HAMD-17 CFRL favoring BRX were sustained at all measured timepoints until Day 30 (BRX90: p=0.0404; BRX80: p=0.005).

Results

— The BRX Posed, BRX60, and placebo arms included 140, 102, 38, and 107 patients who were randomized and included in the efficacy analyses, respectively.10

— Baseline demographics and patient characteristics were well balanced between the treatment arms and have been described in detail previously.10-11

— BRX common TEAEs (≥5% of BRX and ≥2x placebo rate) included flushing/hot flush.

— Detailed adverse event rates including events of sedation/somnolence and loss of consciousness have been described in detail previously.10-11

— BRX caused sedation/somnolence requiring dose interruption/reduction in some patients (5% of BRX compared with 0% of placebo-treated patients). Some patients also had loss of altered state of consciousness (4% of BRX compared with 0% of placebo-treated patients). Time to recovery from loss/altered state of consciousness, after dose interruption, ranged from 15 to 60 minutes. All patients recovered with dose interruption, with no direct sequelae.

— The efficacy, tolerability, and efficacy of BRX in PPD were evaluated in three double-blind, placebo-controlled trials (RCTs). All patients were monitored throughout the entire 60-hour infusion in a monitored setting, with four weeks follow-up.

— Patients recovered with dose interruption, with no direct sequelae.

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

— As previously presented, patients treated with BRX and BRX60 had the primary efficacy endpoint at Hour 60, by achieving significantly greater HAMD-17 total score CFRL vs patients receiving placebo p<0.001 for both.

— Significant differences vs placebo in HAMD-17 CFRL favoring BRX were observed by Hour 24 (BRX90: p=0.0012; BRX60: p=0.0013) and were sustained at all measured timepoints until Day 30.

— Significant differences vs placebo in HAMD-17 CFRL favoring BRX were observed at:
  • Hour 24: BRX90 (p=0.0010); BRX80 (p=0.0001).
  • Hour 60: BRX90 (p=0.0014); BRX80 (p=0.0001).
  • Hour 72: BRX90 (p=0.0007); BRX80 (p=0.0001).

— Significant differences vs placebo in HAMD-17 CFRL favoring BRX were sustained at all measured timepoints until Day 30 (BRX90: p=0.0404; BRX80: p=0.0051).

Conclusions

— BRX treatment in women with PPD has previously been shown to provide rapid (Hour 24 for HAMD-17 total score and Beech-6 score) and sustained (HAMD-17 total score and Beech-6 score at all subsequent measured time points up to Day 30) compared with placebo.10-12

— In addition to its effects on core symptoms of depression, rapid improvements were also noted in a number of PPD-related symptoms (e.g., restlessness and psychomotor agitation) that are not typically measured in clinical trials, including symptoms of anxiety from the HAMD-17-A/S.

— As previously presented, patients treated with BRX and BRX60 had the primary efficacy endpoint at Hour 60, by achieving significantly greater HAMD-17 total score CFRL vs patients receiving placebo p<0.001 for both.

— Significant differences vs placebo in HAMD-17 CFRL favoring BRX were observed by Hour 24 (BRX90: p=0.0010; BRX80: p=0.0001).

— Significant differences vs placebo in HAMD-17 CFRL favoring BRX were observed at:
  • Hour 24: BRX90 (p=0.0010); BRX80 (p=0.0001).
  • Hour 60: BRX90 (p=0.0014); BRX80 (p=0.0001).
  • Hour 72: BRX90 (p=0.0007); BRX80 (p=0.0001).

— Significant differences vs placebo in HAMD-17 CFRL favoring BRX were sustained at all measured timepoints until Day 30 (BRX90: p=0.0404; BRX80: p=0.0051).

— Baseline mean HAMD-17-A/S scores were 10.0 in BRX-pooled, 9.0 in BRX60, and 9.8 in Placebo at Day 30.

— In BRX-pooled group, significant differences vs placebo in HAMD-17- A/S CFRL were observed at Hour 4 (p=0.0188), and all measured timepoints to Hour 24 (p<0.0001).

— The FS employed dosage is 60 μg/kg/h.