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Enclosure:

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Patient-reported symptom severity and functioning with brexpiprazole in combination with sertraline in adults with post-traumatic stress disorder

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Introduction

- Post-traumatic stress disorder (PTSD) is a prevalent psychiatric condition that is associated with impaired psychosocial and occupational functioning.[1,2]
- While clinician-reported measures reflect the clinician's perspective, patient-reported outcomes (PROs) reflect the patient's view.[3,4]
- The efficacy and safety of brexpiprazole in combination with sertraline was evaluated in three trials in the United States: Trial 061 (ClinicalTrials.gov identifier: NCT03033069; Phase 2),[5] Trial 071 (NCT04124614; Phase 3),[6] and Trial 072 (NCT04174170; Phase 3).[7]
  - In flexible-dose Trials 061 and 071, there were greater improvements in PTSD symptoms with brexpiprazole + sertraline than sertraline + placebo.[5,6]
  - In fixed-dose Trial 072, no treatment differences were observed.[7]
  - Across the three trials, no new safety issues were identified.[8]
- Previous analyses of brexpiprazole + sertraline have predominantly focused on clinician-reported measures.[9-11]
- This analysis evaluated PRO data from flexible-dose Trials 061 and 071: PTSD symptom severity using the PTSD Checklist for DSM-5 (PCL-5), and social, physical, emotional, and occupational functioning using the Brief Inventory of Psychosocial Function (B-IPF).

Methods

Trial designs

- Trials 061 and 071 enrolled adult outpatients with PTSD in the United States.
- The trials included a 1-week placebo run-in period followed by an 11-week randomized, double-blind treatment period with brexpiprazole + sertraline and sertraline + placebo treatment arms (Figure 1).
- The primary efficacy endpoint of each trial was the change in Clinician-Administered PTSD Scale for DSM-5 (CAPS-5) Total score from randomization (Week 1) to Week 10.
- In both trials, PCL-5 was also assessed ('other' efficacy endpoint).
- In Trial 071 only, B-IPF was a key secondary endpoint.
- The PCL-5 and B-IPF are described in Box 1.

Analysis

PCL-5 (Trials 061 and 071 pooled)

- Data were pooled from Trials 061 and 071, and least squares (LS) mean change from randomization (Week 1) to Week 10 in PCL-5 Total score was compared between brexpiprazole (1-3 mg/day) + sertraline (100-200 mg/day) and sertraline (100-200 mg/day) + placebo using a mixed model for repeated measures (MMRM).

B-IPF (Trial 071)

- For Trial 071, LS mean change from baseline (Day 0) to Week 12 in B-IPF Total (data previously reported)[6] and item scores were compared between brexpiprazole (2-3 mg/day) + sertraline (150 mg/day) and sertraline (150 mg/day) + placebo using MMRM, without adjustment for multiplicity.

Box 1: PCL-5 and B-IPF[12,13]

The **PCL-5** is a patient-reported questionnaire that assesses PTSD symptom severity in accordance with DSM-5 criteria, across 20 items

Item response options:

0=not at all; 1=a little bit; 2=moderately; 3=quite a bit; 4=extremely

Total score of 0 (least impairment) to 80 (greatest impairment), calculated by summing the scores for each of the 20 items

The **B-IPF** is a patient-reported questionnaire that measures PTSD-specific psychosocial functioning across 7 items

1. Trouble with spouse or partner
2. Trouble with children
3. Trouble with family
4. Trouble with friendship
5. Trouble with work
6. Trouble with education
7. Trouble with daily activity

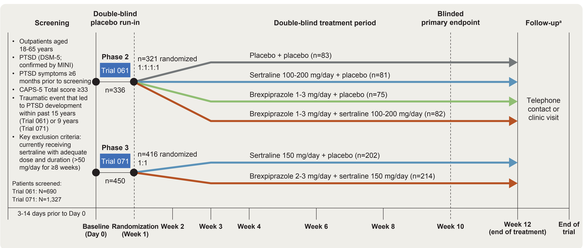
Item response options:

0=not at all; 1-5=somewhat; 6=Very much

Total score of 0 (least impairment) to 100 (greatest impairment), calculated by summing the scored items (possible range 0-42), and transformed to 0-100

DSM-5=Diagnostic and Statistical Manual of Mental Disorders, fifth edition; B-IPF=Brief Inventory of Psychosocial Function; PCL-5=PTSD Checklist for DSM-5; PTSD=post-traumatic stress disorder

Figure 1: Trial designs[5,6]



*Trial 061: 14 (±2) days; Trial 071: 21 (±2) days

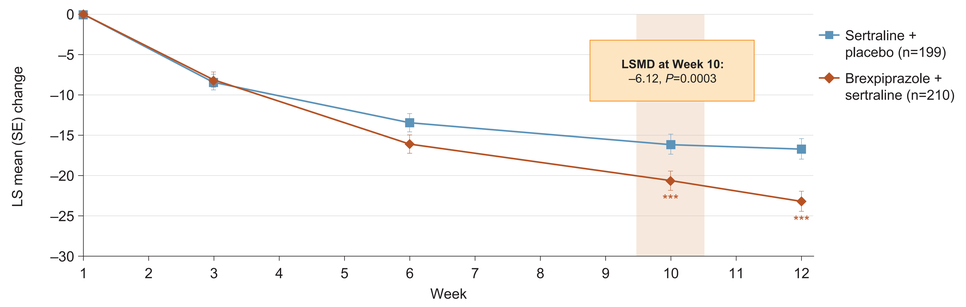
Trial 061 titration: brexpiprazole (flexible-dose): Week 1, 0.5 mg/day; Week 2, 1 mg/day; Week 3, 2 mg/day; Weeks 4-12, 1, 2 or 3 mg/day; brexpiprazole target dose 1-3 mg/day; sertraline (flexible-dose): Week 1, 50 mg/day; Week 2, 100 mg/day; Week 3, 150 mg/day; Weeks 4-12, 100, 150 or 200 mg/day; sertraline target dose 100-200 mg/day

Trial 071 titration: brexpiprazole (flexible-dose): Week 1, 0.5 mg/day; Week 2, 1 mg/day; Week 3, 2 mg/day; Weeks 4-12, 2 or 3 mg/day; sertraline (fixed-dose): Week 1, 50 mg/day; Week 2, 100 mg/day; Weeks 3-12, 150 mg/day

CAPS-5=Clinician-Administered PTSD Scale for DSM-5; DSM-5=Diagnostic and Statistical Manual of Mental Disorders, fifth edition; MINI=Mini International Neuropsychiatric Interview; PTSD=post-traumatic stress disorder

Results

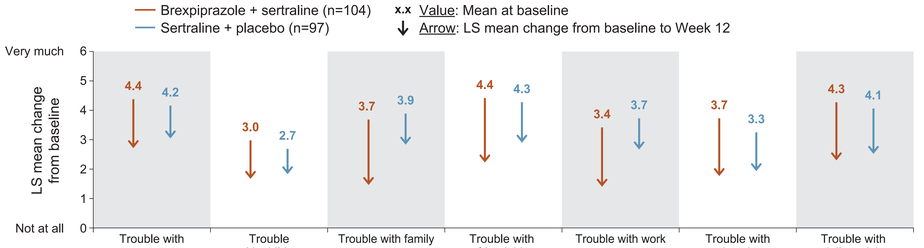
Figure 2: Change from randomization (Week 1) in PCL-5 Total score (Trials 061 and 071 pooled)



***P<0.001 versus sertraline + placebo; MMRM

Mean (SD) PCL-5 Total score at randomization (Week 1): sertraline + placebo, 46.5 (14.7); brexpiprazole + sertraline, 46.4 (13.6)
DSM-5=Diagnostic and Statistical Manual of Mental Disorders, fifth edition; LS=least squares; LSMD=least squares mean difference; MMRM=mixed model for repeated measures; PCL-5=PTSD Checklist for DSM-5; PTSD=post-traumatic stress disorder; SD=standard deviation; SE=standard error

Figure 3: Change from baseline (Day 0) to Week 12 in B-IPF item scores (Trial 071)



	Trouble with spouse or partner	Trouble with children	Trouble with family	Trouble with friendship	Trouble with work	Trouble with education	Trouble with daily activity
Brexpiprazole + sertraline	−1.72	−1.34	−2.25	−2.20	−2.03	−1.99	−1.98
Sertraline + placebo	−1.12	−0.88	−1.05	−1.37	−1.05	−1.32	−1.55
Week 12 brexpiprazole + sertraline vs sertraline + placebo (nominal *P* value)	0.12	0.24	0.0002	0.0083	0.0083	0.16	0.14

n-values are at baseline (Day 0)
B-IPF=Brief Inventory of Psychosocial Function; LS=least squares

PCL-5 (Trials 061 and 071 pooled)

- 409 patients were analyzed (brexpiprazole + sertraline, n=210; sertraline + placebo, n=199).
- Change from randomization (Week 1) to Week 10 in PCL-5 Total score is presented in Figure 2.

Please also visit **poster 170** for additional baseline characteristics data

B-IPF (Trial 071)

- 201 patients were analyzed (brexpiprazole + sertraline, n=104; sertraline + placebo, n=97).
- LS mean change from baseline (Day 0) to Week 12 in B-IPF Total score was −33.8 with brexpiprazole + sertraline, and −21.8 with sertraline + placebo (*P*=0.002; data previously reported).[6]
- Change from baseline (Day 0) to Week 12 in B-IPF item scores is presented in Figure 3.

Conclusions

Based on PRO measures from flexible-dose trials in adults, brexpiprazole + sertraline was associated with improvements in PTSD symptom severity (Trials 061 and 071 pooled) and with numerically greater improvements in functioning (Trial 071) versus sertraline + placebo.

Please also visit:
- **Poster 169** for CAPS-5 symptom cluster analyses
- **Poster 170** for CAPS-5 individual item analyses

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Key contributors

Lori L. Davis, Ahmad Abdrabboh, Ferhat Ardic, and Cecilia Brain developed the concept for this analysis. Huan Jiang and Hui Zeng analyzed the data. All authors were involved in data interpretation, and reviewed and approved the content for poster presentation.

Study registration number

ClinicalTrials.gov identifier: NCT03033069, NCT04124614.

Disclosures

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