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Enclosure:

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Efficacy of brexpiprazole in combination with sertraline on individual symptoms of post-traumatic stress disorder in adults

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Introduction

- Symptoms of post-traumatic stress disorder (PTSD) are heterogenous and complex, can vary over time, and cause dysfunction and disability.[1-3] Symptom heterogeneity reflects the complex and varied ways in which different people react to different traumas.[4]
- Specific symptoms cause different degrees of burden,[2] and some symptoms (eg, sleep disturbance) can be particularly difficult to treat.[5]
- 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),[6] Trial 071 (NCT04124614; Phase 3),[7] and Trial 072 (NCT04174170; Phase 3).[8]
  - In flexible-dose Trials 061 and 071, there were greater improvements in PTSD symptoms with brexpiprazole + sertraline than sertraline + placebo.[6,7]
  - In fixed-dose Trial 072, no treatment difference was observed.[8]
  - Across the three trials, no new safety issues were identified.[9]
- Previous pooled analyses of brexpiprazole + sertraline have explored changes in overall PTSD symptoms,[10] and symptom clusters.[11]

Please also visit **poster 169** for CAPS-5 symptom cluster analyses

- The aim of this pooled post hoc analysis of flexible-dose Trials 061 and 071 was to evaluate changes in individual PTSD symptoms with brexpiprazole + sertraline versus sertraline + placebo.

Methods

Trial designs

Please also visit **poster 171** for additional detail on 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.
- 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.
- The CAPS-5 is a 30-item structured interview, in which 20 items assess PTSD symptom severity.[12] The 20 items are scored from 0 (absent) to 4 (extreme/incapacitating) (total score range 0-80).[12]

Post hoc analysis

- Data were pooled from Trials 061 and 071.
- Least squares (LS) mean changes from randomization (Week 1) to Week 10 in CAPS-5 individual item scores were 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), without adjustment for multiplicity.
- Data were analyzed regardless of symptom presence at baseline.

Results

- 434 patients had CAPS-5 data at randomization and post-randomization (brexpiprazole + sertraline, n=225; sertraline + placebo, n=209).
- Baseline characteristics are summarized in Table 1.
- CAPS-5 item scores at randomization (Week 1) are shown in Figure 1. The item with the highest mean score at randomization (Week 1) was "sleep disturbance".
- 19 of 20 CAPS-5 items showed numerically greater improvement at Week 10 with brexpiprazole + sertraline than sertraline + placebo (nominal $P<0.05$ for 11/20 items) (Figure 1).
- On CAPS-5 Total score, the LS mean change from randomization (Week 1) to Week 10 was –18.0 with brexpiprazole + sertraline, and –12.7 with sertraline + placebo ($P<0.0001$; data previously reported).[10]

Table 1: Baseline demographic and clinical characteristics (Trials 061 and 071 pooled)

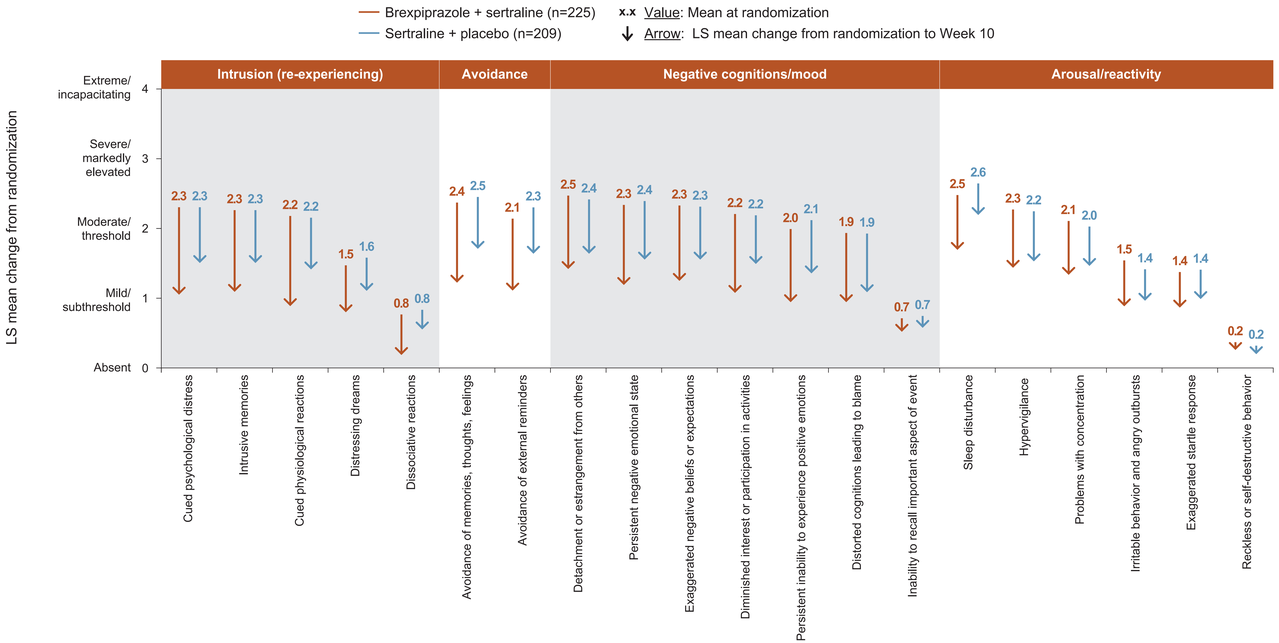
	Brexpiprazole + sertraline (n=225)	Sertraline + placebo (n=209)
Demographic characteristics		
Age, years	38.7 (12.0)	38.0 (12.1)
Female, n (%)	158 (70.2)	156 (74.6)
Male, n (%)	67 (29.8)	53 (25.4)
Weight, kg	86.1 (21.5)	85.6 (22.5)
BMI, kg/m^2	30.3 (6.8) [n=224]	30.0 (7.2)
Race, n (%)		
Black or African American	51 (22.7)	46 (22.0)
White	157 (69.8)	143 (68.4)
Other	17 (7.6)	20 (9.6)
Ethnicity, n (%)[a]		
Hispanic or Latino	29 (12.9)	29 (13.9)
Not Hispanic or Latino	193 (85.8)	178 (85.2)
Clinical characteristics		
CAPS-5 Total score at randomization (Week 1)	37.5 (9.0)	37.9 (8.7)
CGI-S score at randomization (Week 1)	4.5 (0.7) [n=226]	4.5 (0.8) [n=214]
Time since traumatic event, years	5.1 (3.4)	4.5 (3.2)
Time since onset of symptoms, years	5.1 (3.5) [n=224]	4.4 (3.2)
Previous pharmacotherapy, n (%)	80 (35.6)	71 (34.0)
Previous psychotherapy, n (%)	86 (38.2)	69 (33.0)

Efficacy sample; values are mean (SD) unless otherwise stated

[a]For a small number of patients in each pooled group, ethnicity was unknown/other

BMI=body mass index; CAPS-5=Clinician-Administered PTSD Scale for DSM-5; CGI-S=Clinical Global Impression – Severity of Illness; DSM-5=Diagnostic and Statistical Manual of Mental Disorders, fifth edition; PTSD=post-traumatic stress disorder; SD=standard deviation

Figure 1: Change from randomization (Week 1) to Week 10 in CAPS-5 item scores by symptom cluster (Trials 061 and 071 pooled)



Brexpiprazole + sertraline	–1.29	–1.20	–1.32	–0.69	–0.60	–1.16	–1.05	–1.07	–1.17	–1.12	–1.15	–1.07	–1.04	–0.22	–0.81	–0.88	–0.82	–0.70	–0.56	–0.04
Sertraline + placebo	–0.83	–0.78	–0.78	–0.51	–0.31	–0.76	–0.67	–0.79	–0.84	–0.78	–0.73	–0.79	–0.87	–0.18	–0.48	–0.75	–0.61	–0.50	–0.46	–0.06
Week 10 brexpiprazole + sertraline vs sertraline + placebo (nominal *P* value)	0.0004	0.0014	<0.0001	0.18	0.0025	0.0027	0.0066	0.058	0.011	0.011	0.0016	0.030	0.16	0.57	0.022	0.31	0.083	0.084	0.42	0.74

n-values are at Week 1 (randomization); items are sequenced by baseline score within each symptom cluster

CAPS-5=Clinician-Administered PTSD Scale for DSM-5; DSM-5=Diagnostic and Statistical Manual of Mental Disorders, fifth edition; LS=least squares; PTSD=post-traumatic stress disorder

Conclusions

In a pooled analysis of two flexible-dose trials in adults, brexpiprazole + sertraline was associated with numerically greater improvements in 19 of 20 individual PTSD symptoms versus sertraline + placebo.

Please also visit:
- **Poster 169** for CAPS-5 symptom cluster analyses
- **Poster 171** for an analysis of patient-reported outcomes

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Key contributors

Arash Javanbakht, Ahmad Abdrabboh, Ferhat Ardic and Cecilia Brain developed the concept for this analysis. Zhen Zhang analyzed the data. All authors were involved in data interpretation, and reviewed and approved the content for poster presentation.

Study registration number

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Disclosures

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