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Enclosure:

 POSTER: Davis L, Abdrabboh A, Ardic F et al. Presented at NEI Congress, November 6-9, 2025, Colorado Springs, CO, USA

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
- Across the three trials, no new safety issues were identified.8
- Previous analyses of brexpiprazole + sertraline have predominantly focused on clinician-reported
- 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 mode 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

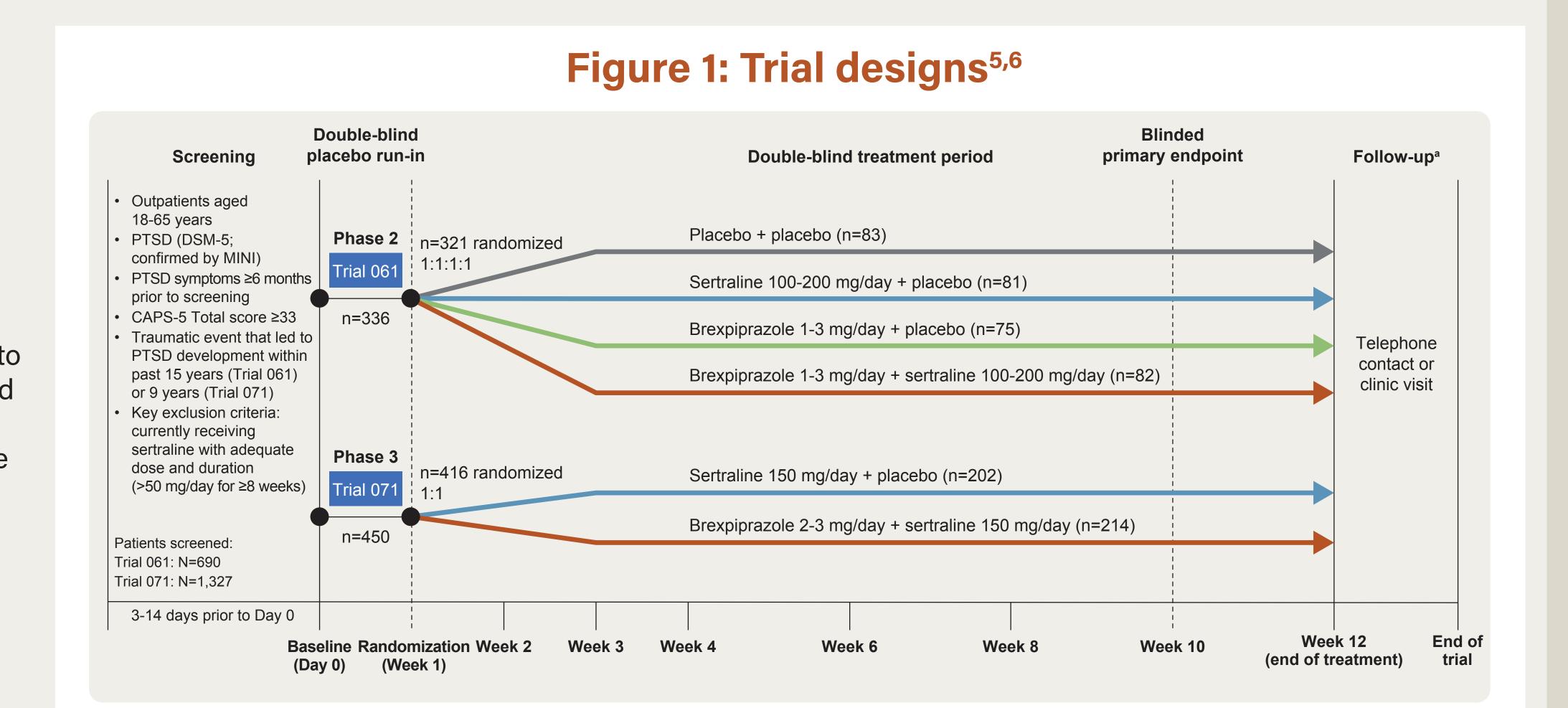
- The **B-IPF** is a patient-reported questionnaire that measures PTSD-specific psychosocial functioning across 7 items
- 1. Trouble with spouse or partner 5. Trouble with work
- 6. Trouble with education 2. Trouble with children
- 7. Trouble with daily activity 3. Trouble with family
- 4. Trouble with friendship

Item response options:

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

Total score of 0 (least impairment) to 100 eatest 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;



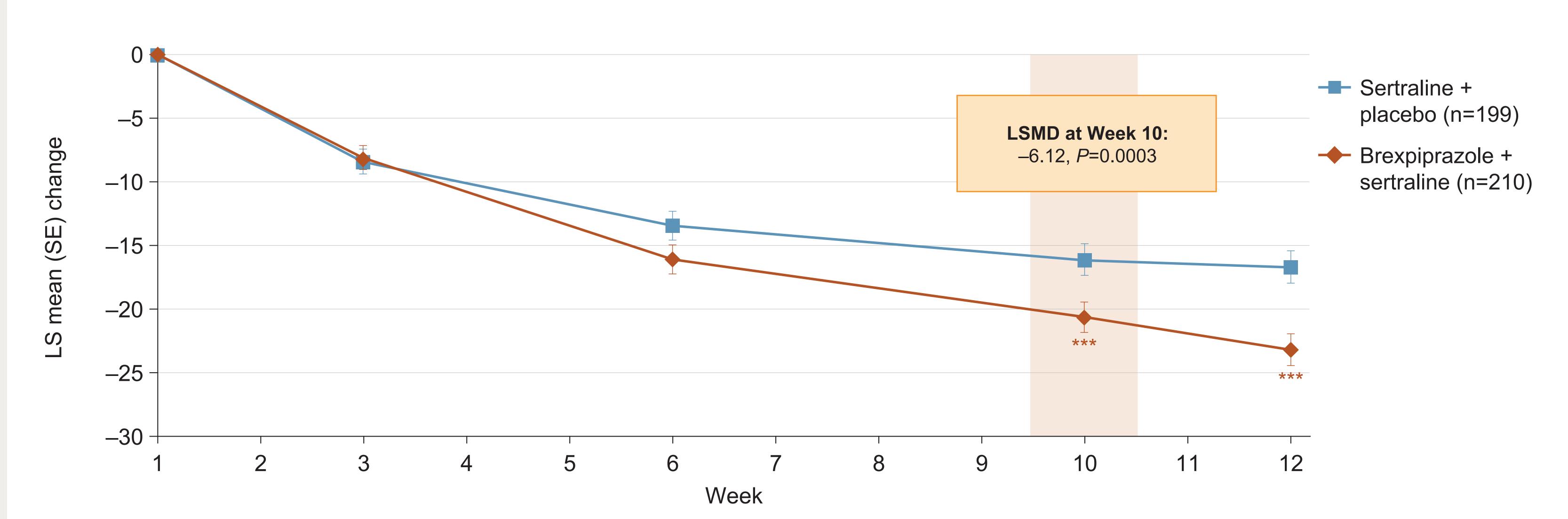
^aTrial 061: 14 (+2) days; Trial 071: 21 (+2) days

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)

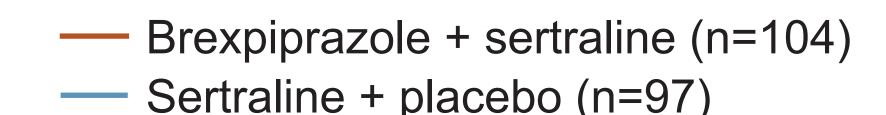


***P<0.001 versus sertraline + placebo; MMRM

Mean (SD) PCL-5 Total score at randomization (Week 1): sertraline + placebo, 46.5 (14.7); brexpiprazole + sertraline, 46.4 (13.6)

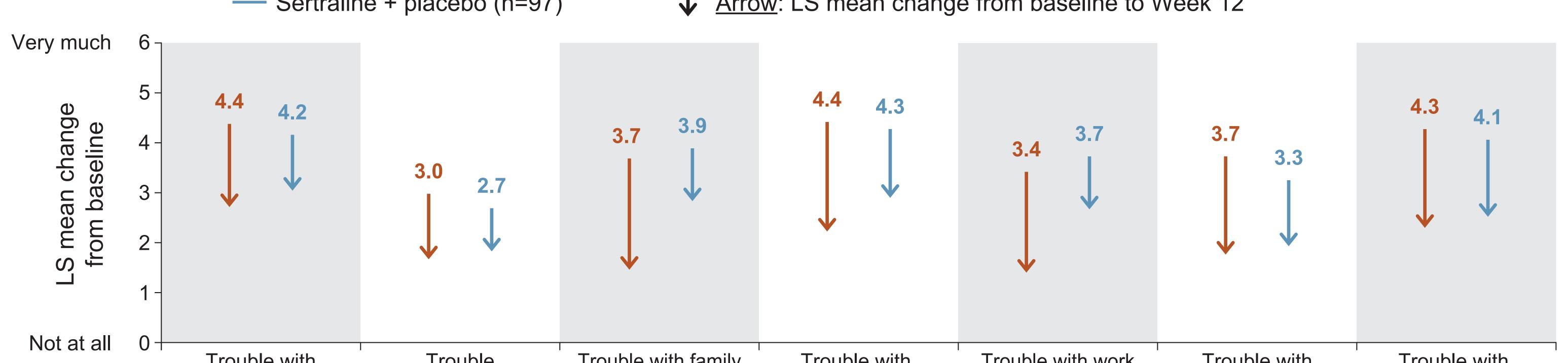
DSM-5=Diagnostic and Statistical Manual of Mental Disorders, fifth edition; LS=least squares; LSMD=least squares; PCL-5=PTSD Checklist for DSM-5; PTSD=post-traumatic stress disorder; SD=standard deviation; SE=standard error

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



x.x Value: Mean at baseline

Arrow: LS mean change from baseline to Week 12



Not at all 0-	Trouble with	Trouble	Trouble with family	Trouble with	Trouble with work	Trouble with	Trouble with	
	spouse or partner	with children		friendship		education	daily activity	
rexpiprazole + 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 +	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.

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 the following poster: Efficacy of rexpiprazole in combination with sertraline on individual symptoms of post-traumatic stress disorder

Previously presented at Psych Congress, September 17-21, 2025, San Diego, CA, USA.

1. Mann et al. Posttraumatic Stress Disorder. Treasure Island, Floric StatPearls Publishing, 2024.

- 2. Jellestad et al. J Psychiatr Res 2021; 136: 14-22.
- 3. Weldring et al. Health Serv Insights 2013; 6: 61-68. 4. Romero et al. Value Health 2022; 25 (7): 1090-1098.
- 5. Hobart et al. J Clin Psychiatry 2025; 86 (1): 24m15577.
- 6. Davis et al. JAMA Psychiatry 2025; 82 (3): 218-227. 7. Hobart et al. J Clin Psychopharmacol 2025. In press. 8. Behl et al. Poster presented at American Society of Clinical
- Psychopharmacology (ASCP) Annual Meeting, May 28-31, 2024 Miami Beach, Florida, USA. Poster #W12. 9. Behl et al. Poster presented at American Society of Clinical
- Psychopharmacology (ASCP) Annual Meeting, May 28-31, 2024 Miami Beach, Florida, USA. Poster #T7. 10. Davis et al. Poster presented at Psych Congress, October 29 November 2, 2024; Boston, Massachusetts, USA. Poster #104.
- 11. Krystal et al. Poster presented at NEI Congress, November 2-10, 2024; Colorado Springs, Colorado, USA. 12. Weathers et al. The PTSD checklist for DSM-5 (PCL-5). [Assessment] **Disclosures**
- 2013. Available at https://www.ptsd.va.gov/professional/assessmen adult-sr/ptsd-checklist.asp. Accessed 8 August 2025. 13. Marx et al. The Brief Inventory of Psychosocial Functioning (B-IPF)
- [Assessment] 2019. Available at https://ptsd.va.gov/PTSD/profe assessment/functioning-other/ipf_psychosocial_function.asp. Accessed 8 August 2025.

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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

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