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Enclosure:

POSTER: Krystal J, Abdarabboh A, Ardic F et al. Presented at Psych Congress, September 17-19, 2025, San Diego, CA

Effect of brexpiprazole in combination with sertraline on post-traumatic stress disorder symptom clusters: intrusion, avoidance, negative cognitions/mood and arousal/reactivity



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Introduction

Methods

Trial designs

period, with a follow-up.

- Trial 072: 365 of 553 (66.0%)

scoring is described in Box 1.

Post hoc analysis

to Week 1).

The primary efficacy endpoint of each trial

was the change in Clinician-Administered

from randomization (Week 1) to Week 10.

Change from randomization (Week 1) to

PTSD Scale for DSM-5 (CAPS-5) Total score

Week 10 in CAPS-5 symptom cluster scores

was also assessed. CAPS-5 symptom cluster

Efficacy data were included for all treated

patients who had a randomization (Week

evaluation. In Trials 071 and 072, patients

were also required to satisfy enrichment

criteria (CAPS-5 Total score ≥27 at

1) and ≥1 post-randomization CAPS-5 Total

randomization [Week 1] and <50% change

in CAPS-5 Total score from baseline [Day 0]

- Symptoms of post-traumatic stress disorder (PTSD) can be characterized into four clusters:1,2
- Intrusion (re-experiencing the trauma) - Avoidance of associations with the trauma
- Negative alterations in cognitions
- Amplified arousal and reactivity
- Across each cluster, symptoms are associated with a high burden and impaired functioning.3,4

Investigators, trial staff, and patients were

blinded to treatment allocation, the timing of

randomization, and the timing of final efficacy

assessments. Thus, the trials appeared as a

continuous, 12-week, double-blind treatment

- The efficacy and safety of brexpiprazole in combination with sertraline in PTSD have been 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 Trials 061 and 071, brexpiprazole + sertraline was associated with greater improvements (P<0.05) in PTSD symptoms than sertraline + placebo.^{5,6} In Trial 072, no treatment difference was observed.7 Across the three trials, no new safety issues were identified.8
- Building on overall efficacy on PTSD symptoms, the aim of this pooled post hoc analysis was to evaluate the efficacy of brexpiprazole in combination with sertraline on the four symptom clusters of PTSD.

Box 1: CAPS-5 symptom clusters^{9,10}

CAPS-5 symptom cluster severity scores are calculated by summing the individual item severity scores for symptoms contained in a given DSM-5 cluster (criterion B, C, D, or E)

Intrusion (re-experiencing) (criterion B) Negative cognitions/mood (criterion D)

Number of randomly assigned patients who

- 2. B2 Distressing dreams completed each trial:
- 3. B3 Dissociative reactions - Trial 061: 231 of 321 (72.0%) 4. B4 - Cued psychological distress
- Trial 071: 250 of 416 (60.1%) 5. B5 - Cued physiological reactions
 - Score range: 0-20

Avoidance (criterion C)

6. C1 - Avoidance of memories,

1. B1 – Intrusive memories

- thoughts, feelings

7. C2 - Avoidance of external remind

- Score range: 0-8

Arousal/reactivity (criterion E)

15. E1 – Irritable behavior and angry outbursts

Score range: 0-28

16. E2 - Reckless or self-destructive behavior

8. D1 – Inability to recall important aspect of event

9. D2 - Exaggerated negative beliefs or expectations

13. D6 – Detachment or estrangement from others

12. D5 - Diminished interest or participation in activities

14. D7 - Persistent inability to experience positive emotions

10. D3 - Distorted cognitions leading to blame

11. D4 - Persistent negative emotional state

- 17. E3 Hypervigilance 18. E4 – Exaggerated startle response
- 19. E5 Problems with concentration
- 20. E6 Sleep disturbance
- Score range: 0-24

Response options: 0=absent; 1=mild/subthreshold; 2=moderate/threshold; 3=severe/markedly elevated; 4=extreme/incapacitating

CAPS-5=Clinician Administered PTSD Scale for DSM-5:

DSM-5=Diagnostic and Statistical Manual of Mental Disorders, fifth edition; PTSD=post-traumatic stress disorder

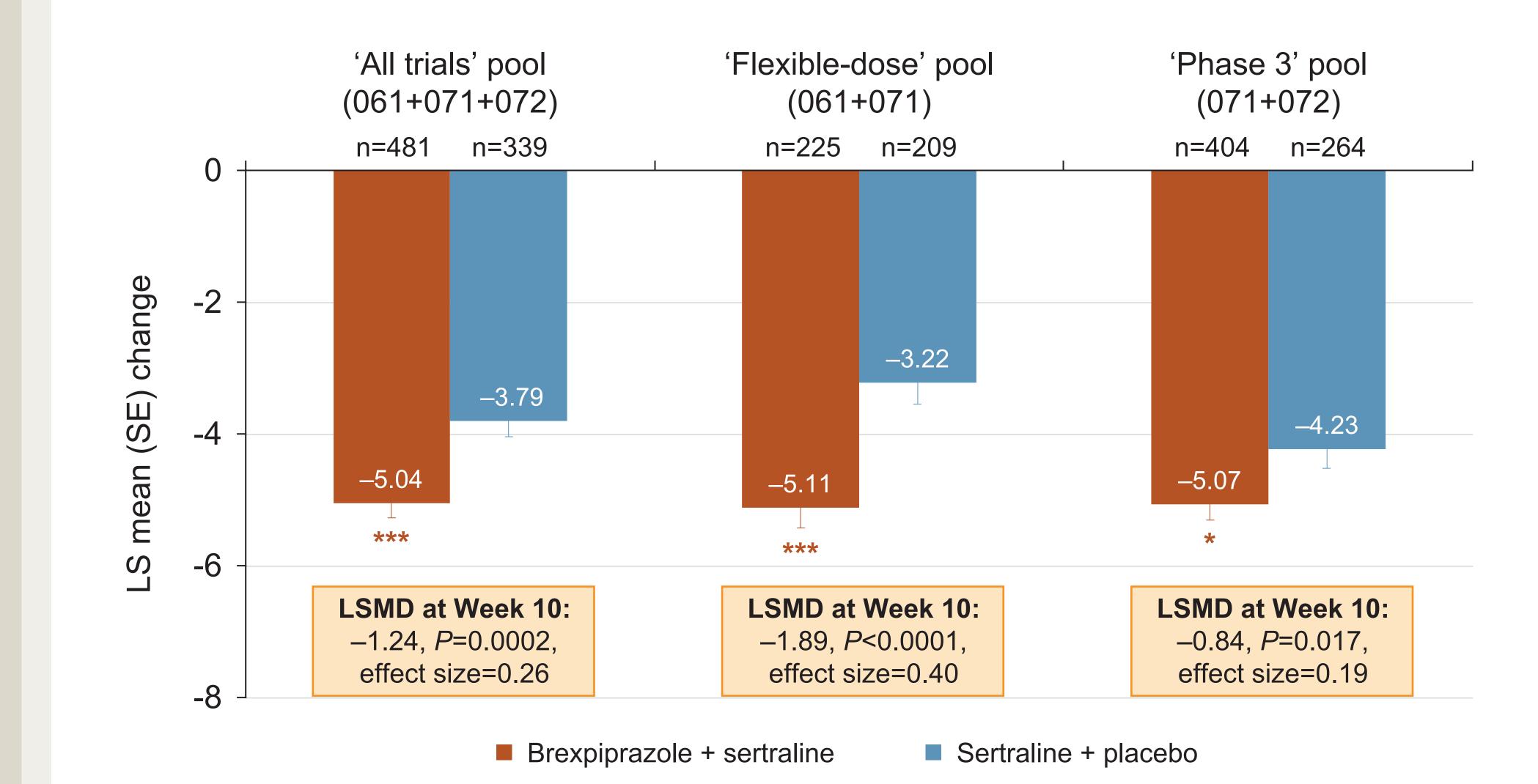
Box 2: Pooling scenarios included in this analysis

 Three pooling scenarios were explored, whereby data were pooled for the total dataset, based on flexibility of brexpiprazole dosing, or based on trial phase (Box 2). 		'All trials' pool	'Flexible-dose' pool	'Phase 3' pool
 In each pool, the least squares (LS) mean change from randomization (Week 1) to Week 10 in CAPS-5 symptom cluster scores were compared between brexpiprazole + sertraline and sertraline + placebo using a mixed model for repeated measures (MMRM). Effect size was calculated based on MMRM. 	Trial 061 (Phase 2; flexible-dose)			
	Trial 071 (Phase 3; flexible-dose)			
	Trial 072 (Phase 3; fixed-dose)			

Results

*P<0.05, ***P<0.001 versus sertraline + placebo; MMRM, efficacy sample

Figure 1: Change from randomization (Week 1) to Week 10 in CAPS-5 symptom cluster score - intrusion (re-experiencing)



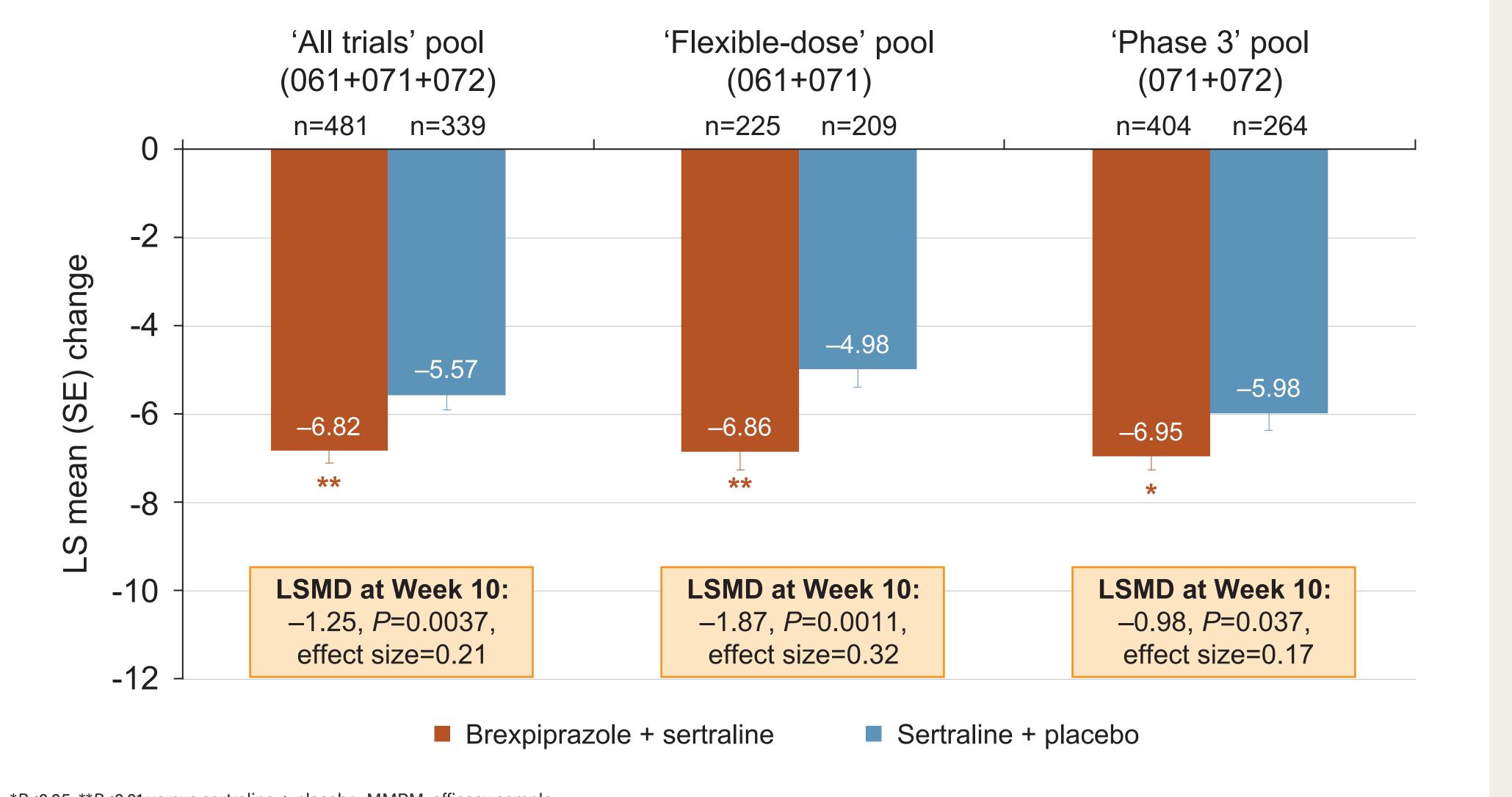


Mean (SD) CAPS-5 intrusion (re-experiencing) score at randomization (Week 1): 'All trials' pool: brexpiprazole + sertraline, 9.3 (3.4); sertraline + placebo, 9.4 (3.5)

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

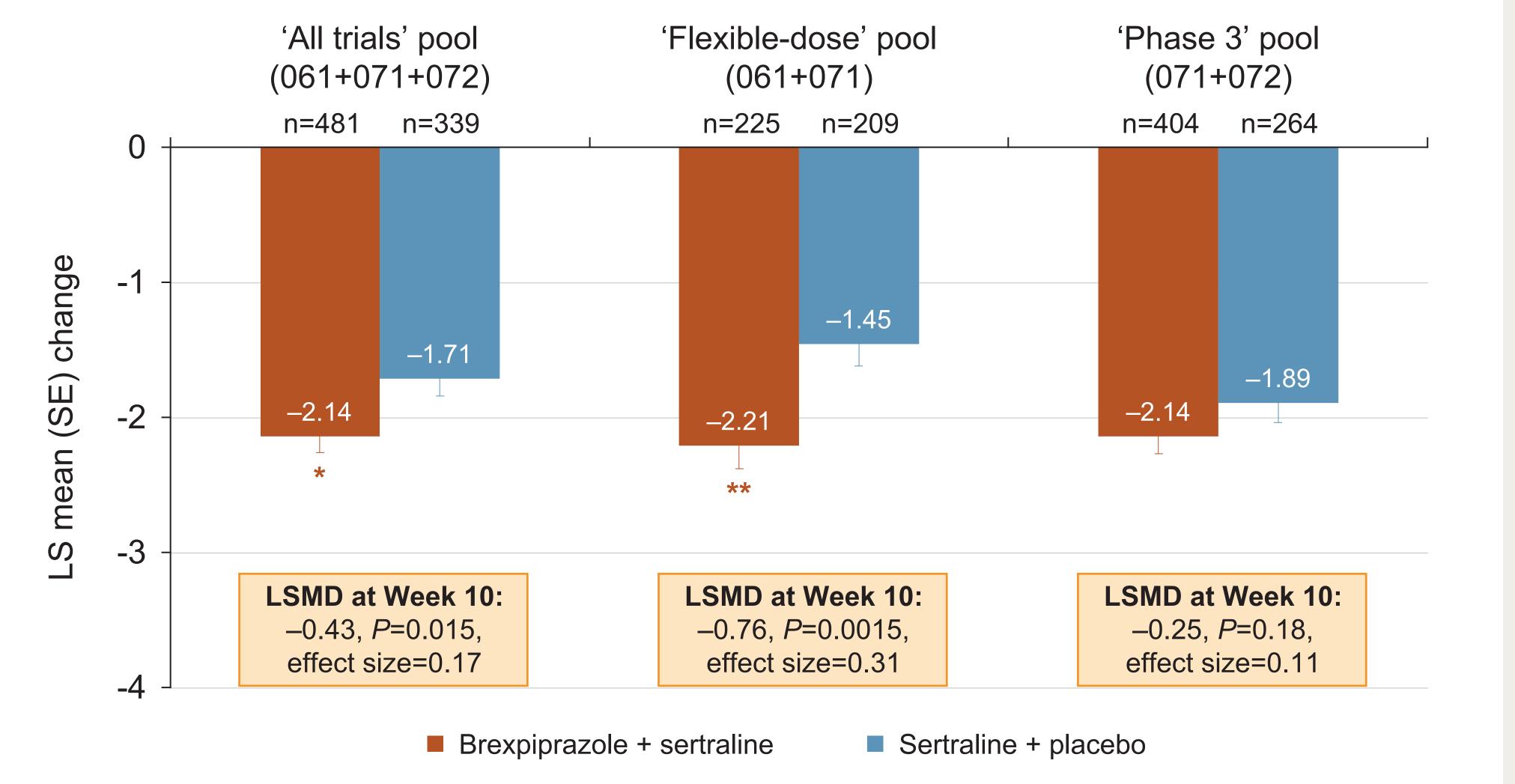
'Flexible-dose' pool: brexpiprazole + sertraline, 9.0 (3.4); sertraline + placebo, 9.1 (3.5); 'Phase 3' pool: brexpiprazole + sertraline, 9.5 (3.4); sertraline + placebo, 9.6 (3.4)

LSMD=least squares mean difference; MMRM=mixed model for repeated measures; PTSD=post-traumatic stress disorder; SD=standard deviation; SE=standard error



*P<0.05, **P<0.01 versus sertraline + placebo; MMRM, efficacy sample Mean (SD) CAPS-5 negative cognitions/mood score at randomization (Week 1): 'All trials' pool: brexpiprazole + sertraline, 14.1 (4.1); sertraline + placebo, 14.2 (4.3); 'Flexible-dose' pool: brexpiprazole + sertraline, 14.0 (4.4); sertraline + placebo, 14.1 (4.5); 'Phase 3' pool: brexpiprazole + sertraline, 14.3 (3.8); sertraline + placebo, 14.5 (3.9) CAPS-5=Clinician-Administered PTSD Scale for DSM-5; 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; PTSD=post-traumatic stress disorder; SD=standard deviation; SE=standard error

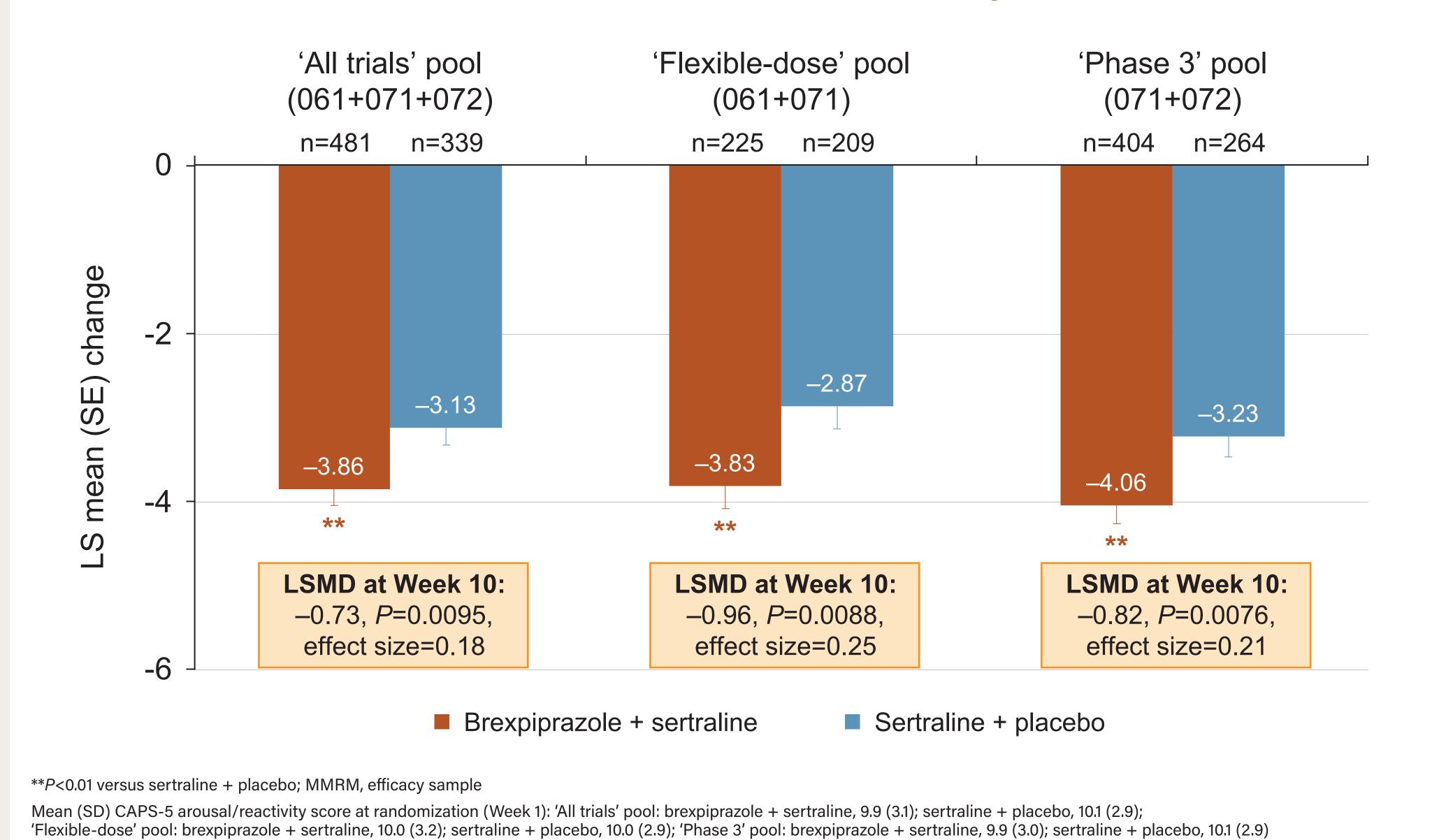
Figure 2: Change from randomization (Week 1) to Week 10 in CAPS-5 symptom cluster score - avoidance



*P<0.05, **P<0.01 versus sertraline + placebo; MMRM, efficacy sample

'Flexible-dose' pool: brexpiprazole + sertraline, 4.5 (1.6); sertraline + placebo, 4.8 (1.7); 'Phase 3' pool: brexpiprazole + sertraline, 4.7 (1.6); sertraline + placebo, 4.8 (1.6) CAPS-5=Clinician-Administered PTSD Scale for DSM-5; 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; PTSD=post-traumatic stress disorder; SD=standard deviation; SE=standard error

Figure 4: Change from randomization (Week 1) to Week 10 in CAPS-5 symptom cluster score - arousal/reactivity



CAPS-5=Clinician-Administered PTSD Scale for DSM-5; 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; PTSD=post-traumatic stress disorder; SD=standard deviation; SE=standard error

Conclusions

trials' pool), 434 patients ('Flexible-dose' pool), and 668 patients ('Phase 3' pool). Demographic and clinical characteristics,

Data were analyzed for 820 patients ('All

including CAPS-5 symptom cluster scores (Figures 1-4), were similar between treatment groups.

 Change from randomization (Week 1) to Week 10 in CAPS-5 symptom cluster scores is presented in Figures 1-4.

In pooled analyses of adult trials, brexpiprazole + sertraline was associated with greater improvements in the four PTSD symptom clusters than sertraline + placebo.

Please also visit:

- **Poster 170** for CAPS-5 individual item analyses
- Poster 171 for an analysis of patient-reported outcomes

Previously presented at NEI Congress, November 7-10, 2024, Colorado Springs, CO, USA.

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Key contributors

- Ahmad Abdrabboh, Ferhat Ardic, Csilla Csoboth, Nanco Hefting, and Brian Pflug developed the concept for this analysis. Zhen Zhang and Huan Jiang 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, NCT04174170.

Disclosures

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