

Effects of Solriamfetol on Cognition in Obstructive Sleep Apnea With Excessive Daytime Sleepiness and Impaired Cognition in the SHARP Clinical Trial

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Key Questions

- What are the effects of solriamfetol treatment on individual cognitive complaints related to concentration, memory and thinking skills as measured by the British Columbia Cognitive Complaints Inventory (BC-CCI)?
- What are the effects of solriamfetol treatment on individual functional items of the BC-CCI that assess social functioning, vocational functioning, and management of personal relationships?

Conclusions

- Consistent with previous reports showing improvement on objective cognitive measures, solriamfetol led to significant subjective improvements overall, and particularly in subjective cognitive domains that may be related to **memory, executive functioning, and processing speed**
- Solriamfetol has the potential to improve subjective cognitive functioning in participants with impaired cognition associated with OSA and EDS

References

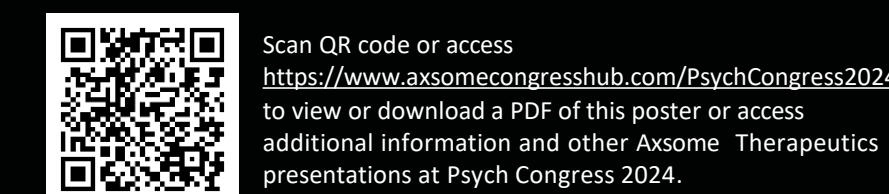
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Acknowledgments

This study was supported by Axsome Therapeutics, Inc. and Jazz Pharmaceuticals. The development of this presentation was supported by Axsome Therapeutics, Inc. Under the direction of the authors, Jacob Huffman, PhD, of Peloton Advantage, LLC, an OPEN Health company, provided medical writing and editorial support for this poster, which was funded by Axsome Therapeutics, Inc. The authors thank the participants who contributed data, personnel who collected data, and consultants who contributed to the design of the SHARP Study.

Disclosures

H.P.A. Van Dongen serves as a paid consultant to Jazz Pharmaceuticals.
E.B. Leary was employed by Jazz Pharmaceuticals during the time the study was conducted and is a current employee of Axsome Therapeutics.
C. Drake serves as a consultant to Axsome, Harmony, Takeda, Procter & Gamble, Agnimed, Zevra – Research, Harmony, Idorsia, Reunion – Speaker; Procter & Gamble, and Zevra.
R. Bogan serves as a consultant to Axsome Therapeutics, Avadel, Harmony, Jazz Pharmaceuticals, and Takeda and is on the speakers bureau for Axsome Therapeutics, Harmony, Idorsia, and Jazz Pharmaceuticals.
J. Jaeger is an employee of Cognition Metrics, LLC; Cognition Metrics received research support from Jazz Pharmaceuticals and Axsome Therapeutics.
G. Eglit and H. Tabuteau are current employees of Axsome Therapeutics.



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Introduction

- Excessive daytime sleepiness (EDS) is common in patients with obstructive sleep apnea (OSA), and can persist in up to 28% of patients despite use of primary airway therapy¹⁻³
- Patients with EDS associated with OSA can have deficits in several cognitive domains⁴⁻⁵
- Solriamfetol (Sunosi®) is a dopamine and norepinephrine reuptake inhibitor with agonistic properties at trace amine-associated receptor 1 (TAAR1) and serotonin 1A receptors⁶⁻⁷
- Solriamfetol is approved in the United States, Canada, and select European countries to treat EDS associated with OSA (37.5–150 mg)

SHARP Trial (NCT04789174)

- Objective:** to assess whether solriamfetol improves cognitive function in patients with EDS associated with OSA and extant impaired cognition
- This **post hoc analysis** evaluated the effects of solriamfetol on individual cognitive complaints and functional items on the **British Columbia Cognitive Complaints Inventory (BC-CCI)**

Methods & Study Design

Figure 1. SHARP Study Design

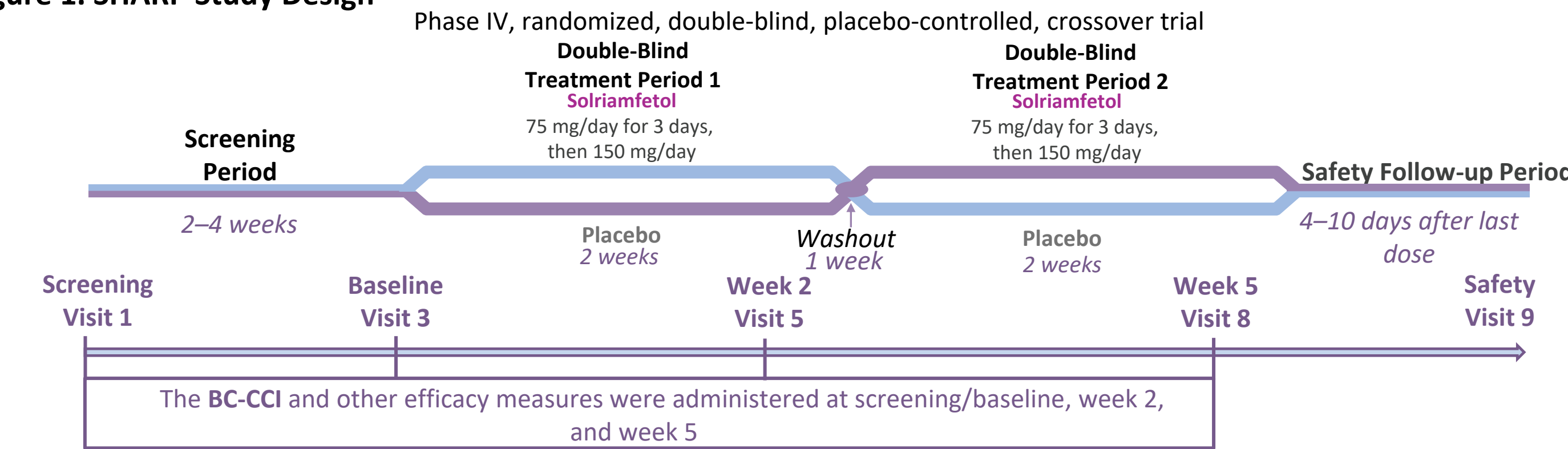
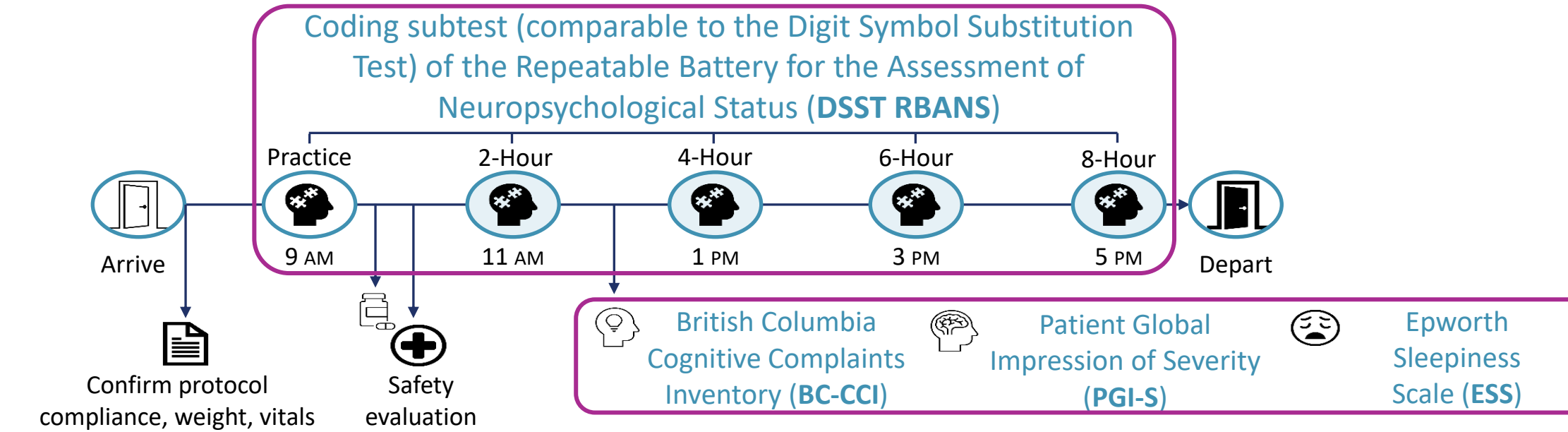


Figure 2. Clinical Visit Structure



Key Findings

Table 1. Baseline Demographics and Clinical Characteristics

- Of 173 participants screened, 59 were enrolled and had baseline data, 58 had data available for efficacy analyses, and 57 completed the study
- Baseline characteristics, including baseline total BC-CCI scores, were generally similar between groups – Baseline scores on individual BC-CCI items were generally similar between groups
- Among participants using positive airway pressure, average use was ≥6 hours per night

	Solriamfetol/ placebo (n=30)	Placebo/ solriamfetol (n=29)	Overall (N=59)
Age, mean (SD), years	52.5 (10.5)	51.9 (11.1)	52.2 (10.7)
Sex (female), n (%)	10 (33.3)	11 (37.9)	21 (35.6)
Race, n (%)			
White	24 (80.0)	19 (65.5)	43 (72.9)
Black/African American	4 (13.3)	8 (27.6)	12 (20.3)
Asian	1 (3.3)	2 (6.9)	3 (5.1)
Unknown	1 (3.3)	0	1 (1.7)
Body mass index, mean (SD), kg/m ²	32.8 (4.7)	31.6 (4.0)	32.2 (4.4)
Digit Symbol Substitution Test, age-corrected, mean (SD)	6.6 (1.3)	6.9 (0.8)	6.8 (1.1)
BC-CCI, mean (SD)	11.4 (2.5)	11.4 (2.5)	11.4 (2.5)
Patient Global Impression of Severity (cognitive function), mean (SD)	2.2 (0.8)	2.3 (0.7)	2.3 (0.7)
Epworth Sleepiness Scale total score, mean (SD)	14.8 (2.8)	14.3 (2.7)	14.6 (2.8)
Positive airway pressure use, n (%)	22 (73.3)	20 (69.0)	42 (71.2)
Adherent use (≥4 h/night for 70% of nights), n (%)	18 (60.0)	16 (55.2)	34 (57.6)
Hours of use (among all users), mean (SD)	6.0 (2.4)	6.6 (2.7)	6.3 (2.5)

Table 2. Baseline Scores on Individual BC-CCI Items

- Baseline scores on individual BC-CCI items were generally similar for participants randomized to solriamfetol/placebo versus placebo/solriamfetol

	Mean (SD)	Solriamfetol/ placebo (n=29)	Placebo/ solriamfetol (n=29)	Overall (N=58)
Cognitive complaint items	Forgetfulness/memory problems	1.93 (0.70)	2.00 (0.71)	1.97 (0.70)
	Poor concentration	2.10 (0.86)	2.21 (0.68)	2.16 (0.77)
	Trouble expressing thoughts	1.93 (0.80)	1.76 (0.74)	1.84 (0.77)
	Trouble finding the right word	1.97 (0.82)	1.79 (0.56)	1.88 (0.70)
	Slow thinking speed	1.93 (0.75)	1.93 (0.80)	1.93 (0.77)
	Trouble figuring things out	1.62 (0.73)	1.76 (0.64)	1.69 (0.68)
Functional items	Vocational functioning	1.97 (1.05)	1.83 (0.97)	1.90 (1.00)
	Family/friends functioning	1.52 (1.02)	1.72 (1.16)	1.62 (1.09)
	Social/recreational functioning	1.66 (1.11)	1.66 (1.04)	1.66 (1.07)

Figure 4. Primary Findings and Safety

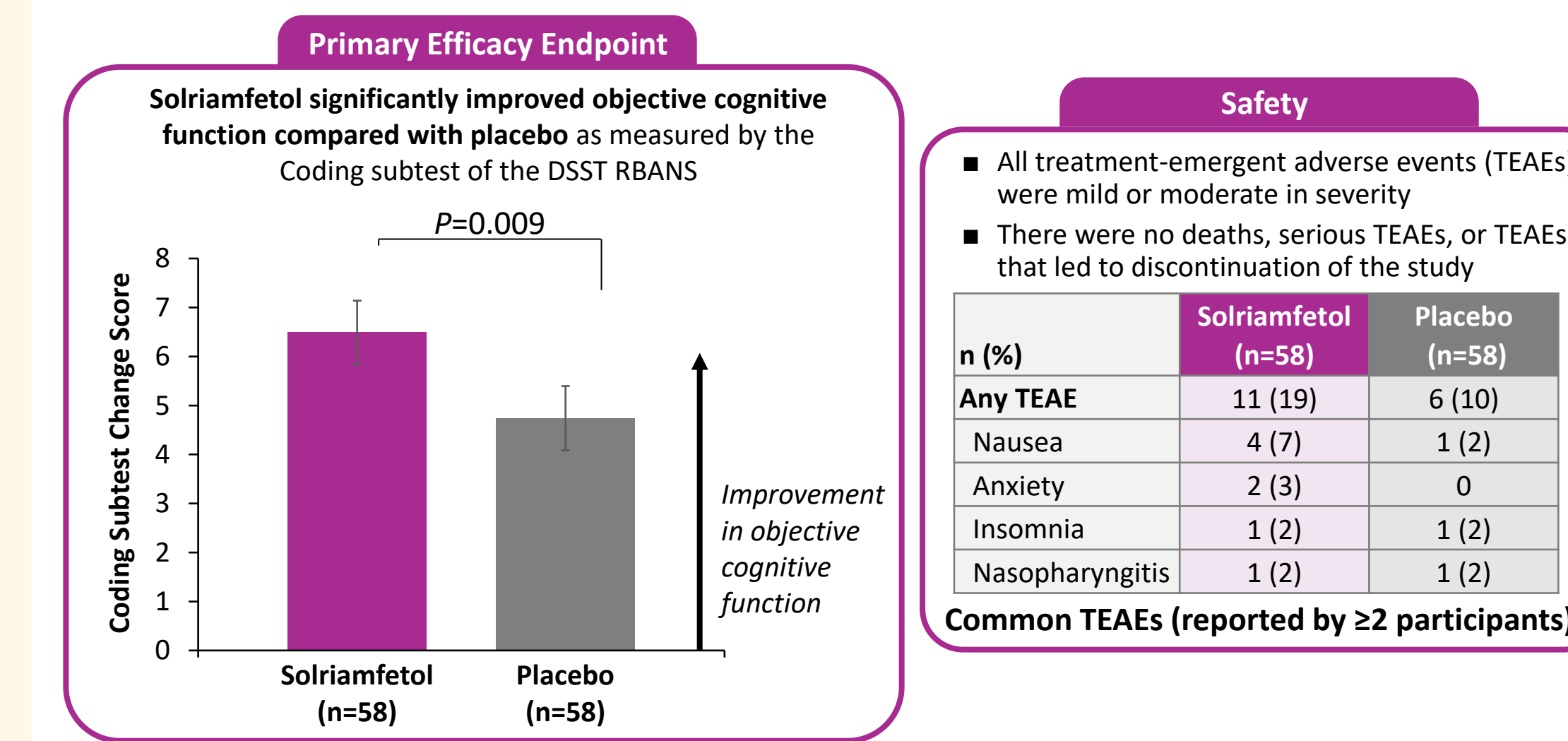


Figure 5. Overall Improvement in Subjective Cognitive Function

- Overall, BC-CCI scores showed greater reduction from baseline (ie, more improvement in subjective cognitive function) after solriamfetol treatment compared with placebo

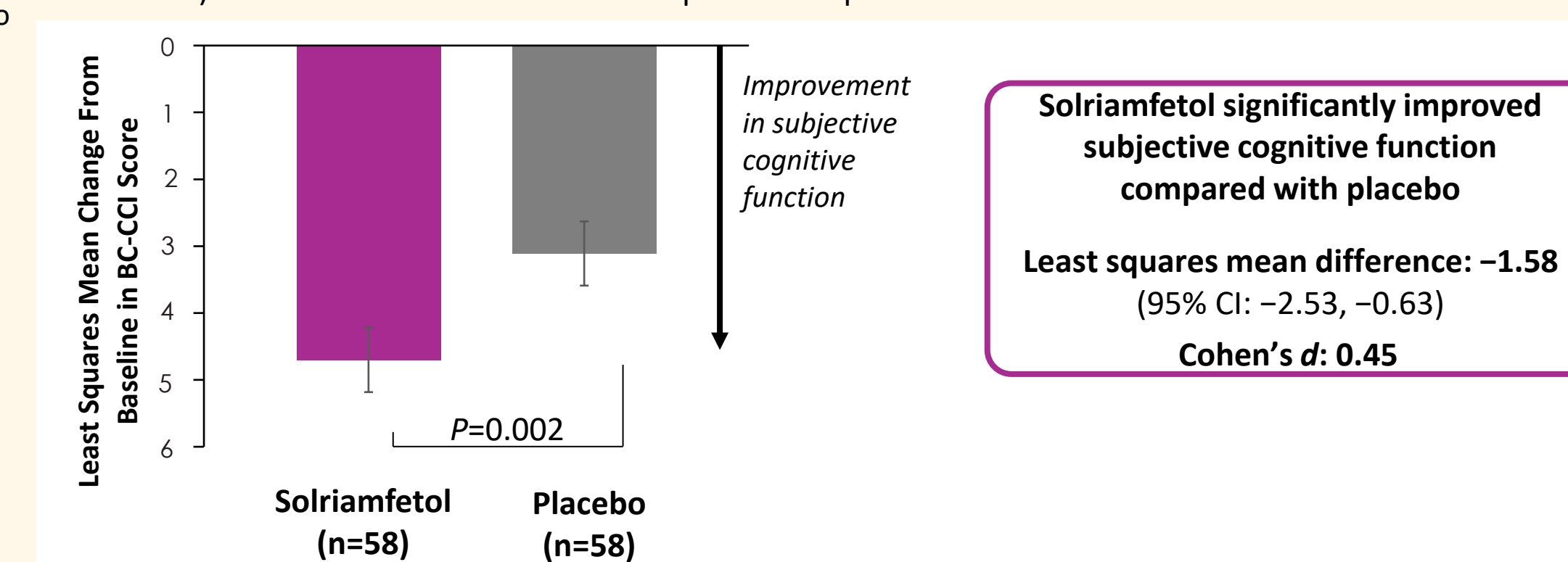


Figure 3. British Columbia Cognitive Complaints Inventory¹⁰ – Subjective Cognition

6 Cognitive Complaint Items

Participants were asked to rate their **problems with concentration, memory, and thinking skills** during the past 7 days. Questions included:

- Forgetfulness/memory problems
- Poor concentration
- Trouble expressing thoughts
- Trouble finding the right word
- Slow thinking speed
- Trouble figuring things out or solving problems

A 4-point scale (0–3) was used with higher scores indicating greater cognitive impairment:

- 0 = Not at all
- 1 = Some
- 2 = Quite a bit
- 3 = Very much

3 Functional Items

Participants were asked to answer questions about how the cognitive complaints impacted their ability to function in the last 7 days. Questions included:

- Symptoms made it difficult to do job
- Symptoms made it difficult to have good relationships with family and friends
- Symptoms made it difficult to enjoy social activities, recreational activities, or hobbies

Answer options included:

- False, Not at all true
- Slightly true
- Mainly true
- Very true

Classifications for Cognitive Complaints for the BC-CCI Total Scores

Calculated as the sum of the 6 cognitive complaint responses

- 0 to 4:** “broadly normal”
- 5 to 8:** “mild” cognitive complaints
- 9 to 14:** “moderate” cognitive complaints
- 15 to 18:** “severe” cognitive complaints

Figure 6. Cognitive Complaint Items

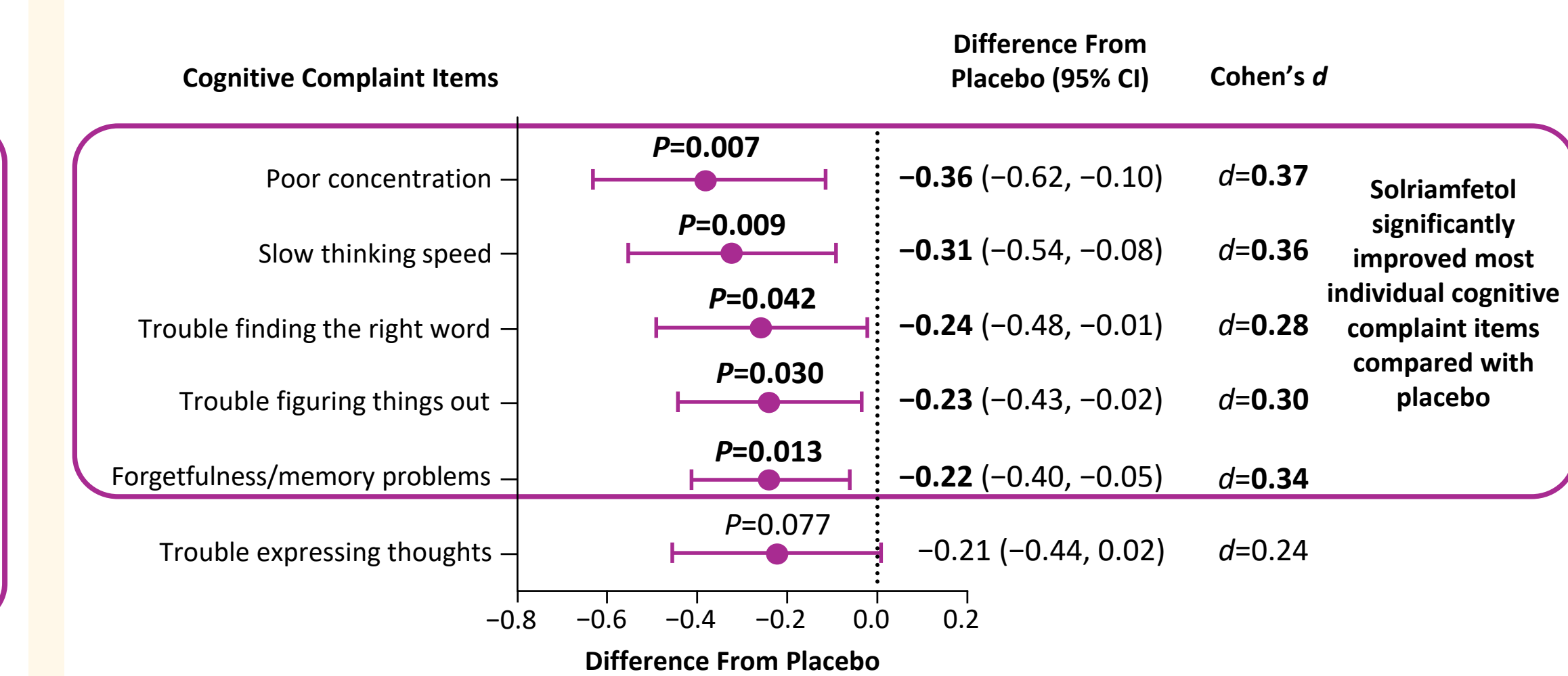


Figure 7. Functional Items

