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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Learning Objectives

Upon completion of this activity, participants should be able to:

- Recognize that some individuals with obstructive sleep apnea (OSA) and excessive daytime sleepiness (EDS) have deficits in cognitive functioning
- Understand that solriamfetol treatment led to improvements in overall subjective cognitive function, as measured by the British Columbia Cognitive Complaints Inventory (BC-CCI)
- Know that item analysis of the BC-CCI indicated improvements in cognition in domains that may be related to memory, executive functioning, and processing speed

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

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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, Apnimed, Zevra – Research; Harmony, Idorsia – 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.
G. Eglit, C. Goulding, 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 therapy[1-3]
- Patients with EDS associated with OSA can have deficits in several cognitive domains[4-5]
- Solriamfetol (Sunosi®) is a dopamine and norepinephrine reuptake inhibitor with agonistic properties at trace amine–associated receptor 1 (TAAR1) and serotonin 1A receptors[6-7]
- Solriamfetol is approved in the United States, Canada, and select European countries to treat EDS associated with OSA (37.5–150 mg/day) and narcolepsy (75–150 mg/day)[7-9]

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

Phase IV, randomized, double-blind, placebo-controlled, crossover trial

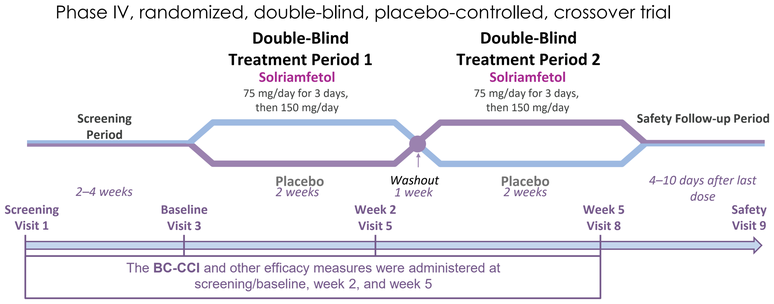


Figure 2. Clinical Visit Structure

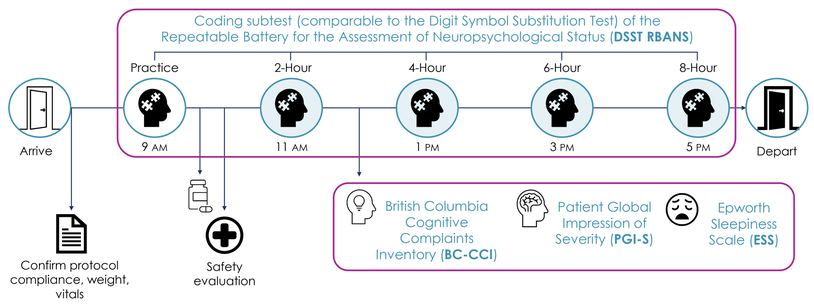


Figure 3. British Columbia Cognitive Complaints Inventory[10] – Subjective Cognition

6 Cognitive Complaint Items

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

1. Forgetfulness/memory problems
2. Poor concentration
3. Trouble expressing thoughts
4. Trouble finding the right word
5. Slow thinking speed
6. 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:

1. Symptoms made it difficult to do job
2. Symptoms made it difficult to have good relationships with family and friends
3. 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

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

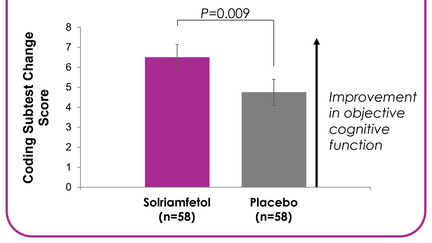
- Baseline scores on individual BC-CCI items were generally similar for participants randomized to solriamfetol/placebo versus placebo/solriamfetol

	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

Primary Efficacy Endpoint

Solriamfetol significantly improved objective cognitive function compared with placebo as measured by the Coding subtest of the DSST RBANS



Safety

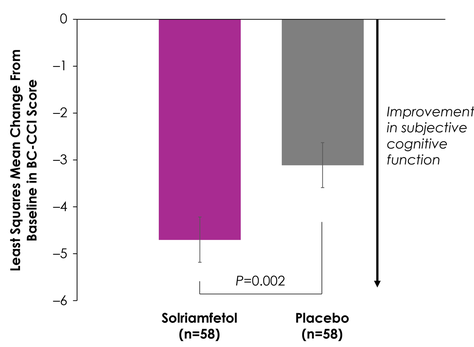
- All treatment-emergent adverse events (TEAEs) were mild or moderate in severity
- There were no deaths, serious TEAEs, or TEAEs that led to discontinuation of the study

n (%)	Solriamfetol (n=58)	Placebo (n=58)
Any TEAE	11 (19)	6 (10)
Nausea	4 (7)	1 (2)
Anxiety	2 (3)	0
Insomnia	1 (2)	1 (2)
Nasopharyngitis	1 (2)	1 (2)

Common TEAEs (reported by ≥2 participants)

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

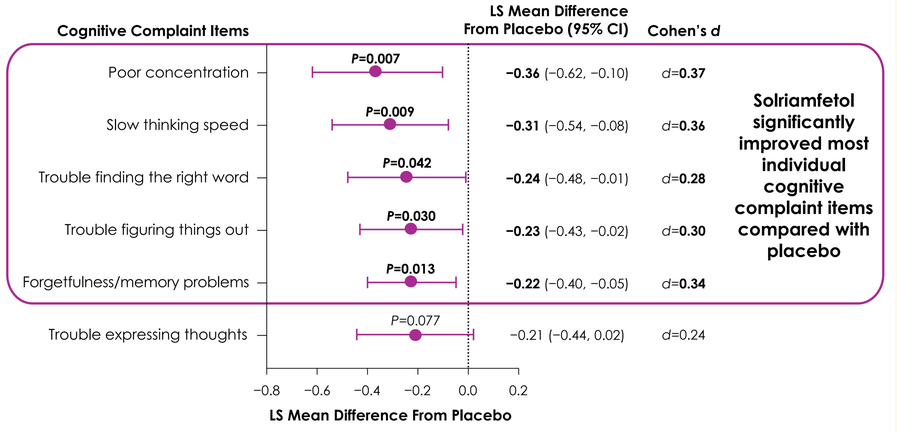


Solriamfetol significantly improved subjective cognitive function compared with placebo

Least squares mean difference: −1.58
(95% CI: −2.53, −0.63)

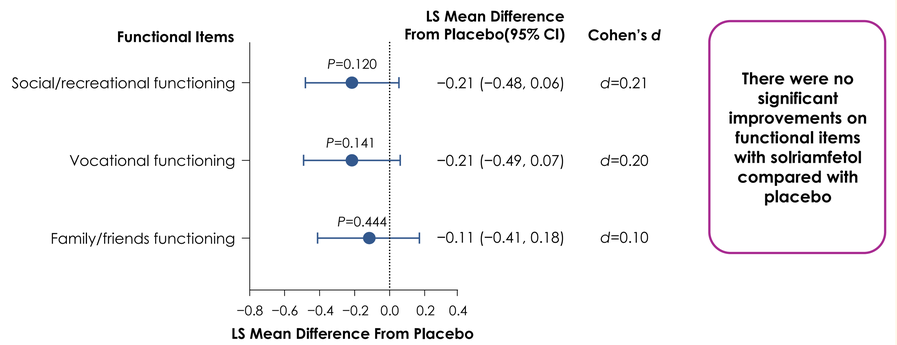
Cohen's *d*: 0.45

Figure 6. Cognitive Complaint Items



Solriamfetol significantly improved most individual cognitive complaint items compared with placebo

Figure 7. Functional Items



There were no significant improvements on functional items with solriamfetol compared with placebo