Poster #3570

Solriamfetol and Cognitive Function in Obstructive Sleep Apnea With Excessive Daytime Sleepiness and Impaired Cognition Stratified by Primary Airway Therapy Adherence: SHARP

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Key Question

- Does the impact of solriamfetol treatment on cognitive function and excessive daytime sleepiness (EDS) in obstructive sleep apnea (OSA) differ by positive airway pressure (PAP) therapy adherence?

Conclusions

- Solriamfetol treatment led to similar improvements in both objective and subjective cognition, as well as reductions in EDS in participants regardless of adherence to PAP therapy
- Solriamfetol demonstrated a favorable safety and tolerability profile in both adherence groups, with no serious adverse events or discontinuations due to treatment
- These results suggest that solriamfetol provides additional benefits to PAP therapy in patients with cognitive impairment related to OSA and EDS, and non-adherence to PAP therapy did not lead to clinically meaningful differences in therapeutic effects on cognition or daytime sleepiness

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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, Reunion–Research; Harmony, Idorsia –Speaker; Procter & Gamble, and Zevra.
R.K. 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.M.L. Eglit, C. Streicher and **H. Tabuteau** are current employees of Axsome Therapeutics.

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Introduction

- Many patients with excessive daytime sleepiness (EDS) associated with obstructive sleep apnea (OSA) experience cognitive impairment, including forgetfulness and difficulty concentrating, which can substantially interfere with daily function[1,2]
- While positive airway pressure (PAP) therapy can ameliorate some symptoms of EDS and reduce cognitive impairment, cognitive deficits may persist[2]; additionally, poor PAP adherence is common,[3,4] and studies have shown that non-adherence is associated with poor cognitive outcomes[5]
- Solriamfetol (Sunosi®) is a dopamine/norepinephrine reuptake inhibitor, with agonistic properties at TAAR1 and serotonin 1A receptors, approved to treat EDS associated with OSA (37.5–150 mg/day)[6,7]
- Data from prior studies have demonstrated that solriamfetol improves EDS in participants with OSA without impact to primary OSA therapy[8]
- In SHARP, a randomized, double-blind, placebo-controlled crossover study, solriamfetol improved cognition in participants with OSA and cognitive impairment; the safety profile suggests solriamfetol was well tolerated[9]
- **Objective**: This post hoc analysis of data from the SHARP trial stratified participants with cognitive impairment related to OSA and EDS by adherence to PAP therapy. Effects of solriamfetol on objective and subjective cognitive function, as well as EDS, were evaluated among PAP-adherent and non-adherent/non-PAP participants

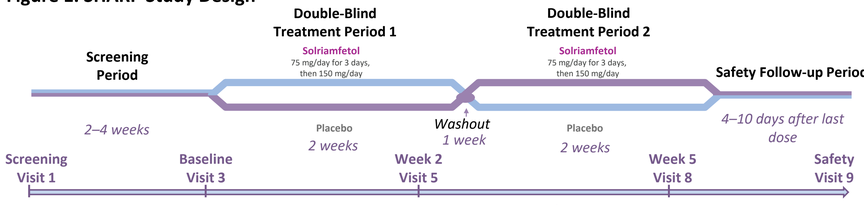
Methods & Study Design

- The SHARP Trial (NCT04789174) was a randomized, double-blind, placebo-controlled, 2-period crossover trial (**Fig. 1**)

PAP Adherence Criteria

- PAP adherence was defined as PAP usage for >4 hours per night on ≥70 % of nights (5 nights/week), assessed over the month prior to study enrolment
- The non-adherent or non-PAP group includes participants who did not meet the PAP adherence criteria or who did not report PAP use
- Participants were instructed to maintain their pre-enrolment PAP usage pattern throughout the study

Figure 1. SHARP Study Design



BC-CCI, British Columbia Cognitive Complaints Inventory; ESS, Epworth Sleepiness Scale; DSST RBANS, Digital Symbol Substitution Test Repeatable Battery for the Assessment of Neuropsychological Status; PGI-S, Patient Global Impression of Severity.

Key Findings

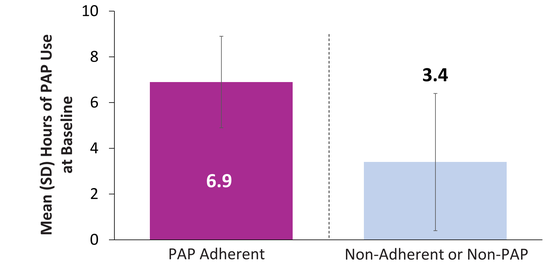
Table 1. Baseline Sociodemographic and Clinical Characteristics by PAP Adherence Status

	PAP Adherent (n=34)	Non-Adherent or Non-PAP (n=25)
Age, mean (SD), years	53.4 (9.0)	50.5 (12.6)
Sex (female), n (%)	9 (26)	12 (48)
Race, n (%)		
White	29 (85)	14 (56)
Black/African American	4 (12)	8 (32)
Asian	0	3 (12)
Unknown	1 (2.9)	0
Body mass index, mean (SD), kg/m²	32.8 (4.5)	31.5 (4.1)
DSST RBANS, age-corrected, mean (SD)	6.8 (1.1)	6.7 (1.0)
BC-CCI, mean (SD)	11.4 (2.6)	11.5 (2.4)
PGI-S score (cognitive function), mean (SD)	2.1 (0.7)	2.4 (0.7)
ESS score, mean (SD)	14.6 (2.5)	14.6 (3.1)

BC-CCI, British Columbia Cognitive Complaints Inventory; DSST RBANS, Digital Symbol Substitution Test Repeatable Battery for the Assessment of Neuropsychological Status; ESS, Epworth Sleepiness Scale; PAP, positive airway pressure; PGI-S, Patient Global Impression of Severity.

- Baseline characteristics were well-balanced between the PAP-adherent and non-adherent or non-PAP groups (**Table 1**)

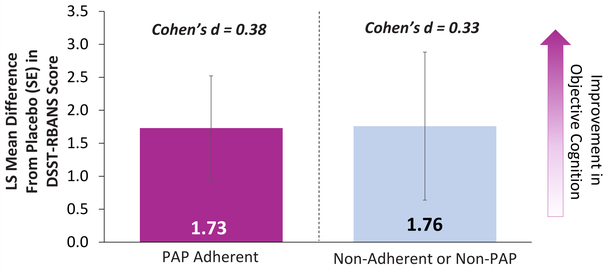
Figure 2. Baseline PAP Use by Adherence Group



PAP, positive airway pressure.

- PAP use was reported by 42 (71%) of participants, all 34 participants in the adherent group and 8 in non-adherent or non-PAP group; 17 participants in the non-adherent or non-PAP group did not use PAP therapy

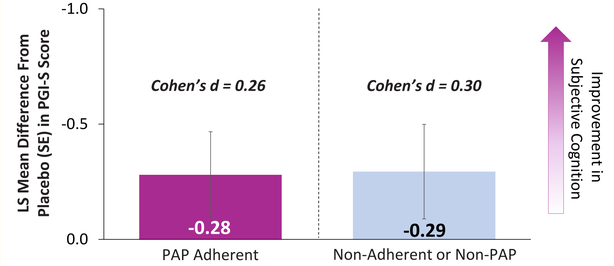
Figure 3. Impact of Solriamfetol on DSST-RBANS Score by PAP Adherence



DSST RBANS, Digital Symbol Substitution Test Repeatable Battery for the Assessment of Neuropsychological Status; LS, least squares.

- Solriamfetol treatment led to similar improvements in DSST RBANS scores (objective cognition) versus placebo across adherence groups (**Fig. 3**)

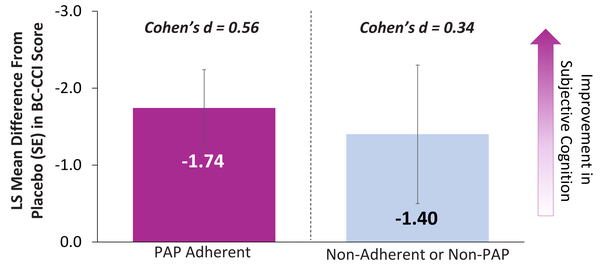
Figure 4. Impact of Solriamfetol on PGI-S Score by PAP Adherence



Note: The ordinate has been reversed so that upward is greater improvement with solriamfetol.
PGI-S, Patient Global Impression of Severity; LS, least squares.

- Solriamfetol led to similar reductions in PGI-S scores (overall subjective cognitive impairment) versus placebo across adherence groups (**Fig. 4**)

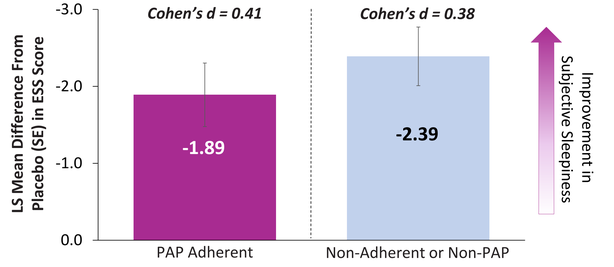
Figure 5. Change From Baseline in BC-CCI Score by PAP Adherence



Note: The ordinate has been reversed so that upward is greater improvement with solriamfetol.
BC-CCI, British Columbia Cognitive Complaints Inventory; LS, least squares.

- Solriamfetol treatment led to similar reductions in BC-CCI scores (subjective cognitive complaints) versus placebo across adherence groups (**Fig. 5**)
- A higher proportion of participants treated with solriamfetol reported 'none or minimal' cognitive complaints compared to placebo in both PAP-adherent (66% vs 50%) and non-adherent or non-PAP (75% vs 50%) groups

Figure 6. Change from Baseline in ESS Score by PAP Adherence



Note: The ordinate has been reversed so that upward is greater improvement with solriamfetol.
EDS, excessive daytime sleepiness; ESS, Epworth Sleepiness scale; LS, least squares.

- Solriamfetol treatment led to comparable reductions in ESS scores (subjective EDS) relative to placebo across adherence groups (**Fig. 6**)

Safety

- The number of participants reporting TEAEs was comparable across adherence groups for both participants treated with solriamfetol (adherent, 7/33; 21.2%; non-adherent or non-PAP, 4/25, 16.0%) and placebo (adherent, 2/34; 5.9%; non-adherent or non-PAP, 4/24; 16.7%)
- No serious TEAEs, TEAEs leading to treatment discontinuation, or TEAEs leading to study withdrawal were observed with solriamfetol treatment in either the PAP-adherent or non-adherent or non-PAP groups