Summary of the Phase 4 SHARP Study on the Effect of the Wake-Promoting Agent Solriamfetol on Cognitive Function in Obstructive Sleep Apnea With Excessive Daytime Sleepiness and Cognitive Impairment

Key Takeaway

- In the phase 4 SHARP study, solriamfetol significantly improved objective and subjective measures of cognitive function in patients with impaired cognitive function associated with obstructive sleep apnea and excessive daytime sleepiness

Background

Excessive daytime sleepiness (EDS) is the most common daytime symptom of obstructive sleep apnea (OSA) and occurs as a result of intermittent hypoxia and fragmented sleep. Up to 68% of patients with OSA and EDS show deficits in cognitive function, including memory, attention, and executive function, which can be burdensome.[1] Cognitive impairment can persist even with positive airway pressure (PAP) treatment.[2] Although wake-promoting agents are available, it is not known whether these agents can also improve cognitive function. **The recently published SHARP study assessed whether solriamfetol, a dopamine and norepinephrine reuptake inhibitor approved for EDS associated with OSA, improves cognitive function in participants with impaired cognition associated with OSA and EDS.**[3] SHARP is the first study to evaluate the effects of solriamfetol on cognitive functioning in this population. You can read the manuscript in full here.

Materials and Methods

Study design

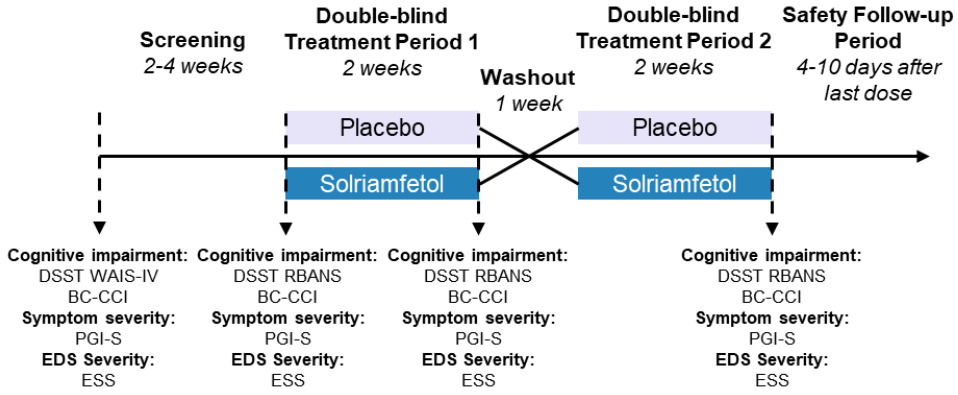
SHARP (NCT04789174) was a phase 4, randomized, double-blind, placebo-controlled, crossover trial. The study was conducted from May 2021 to September 2022 at 28 sites in North America (US, Canada) and Europe (United Kingdom, Netherlands, Spain, Italy).

Participants

Males and females 18 to 65 years old diagnosed with OSA per the *International Classification of Sleep Disorders*, 3rd Edition (ICSD-3) criteria, and EDS (defined as an Epworth Sleepiness Scale [ESS] score >10) participated in the study. Impaired cognitive function was defined as an age-corrected scaled score ≤8 at screening on the Digit Symbol Substitution Test (DSST), a subtest in the Wechsler Adult Intelligence Scale, 4th Edition (DSST WAIS-IV), and a score ≥9 on the British Columbia Cognitive Complaints Inventory (BC-CCI). To complete the WAIS-IV, participants must match numbers to symbols based on a key within 120 seconds. The BC-CCI is a validated 6-item questionnaire that assesses self-reported problems with concentration, memory, expressing thoughts, word finding, thinking, and problem solving. Participants were randomized 1:1 to treatment with oral solriamfetol or placebo each morning for 2 weeks, after which participants underwent a 1-week washout period and crossed over to receive the opposite treatment for 2 additional weeks.

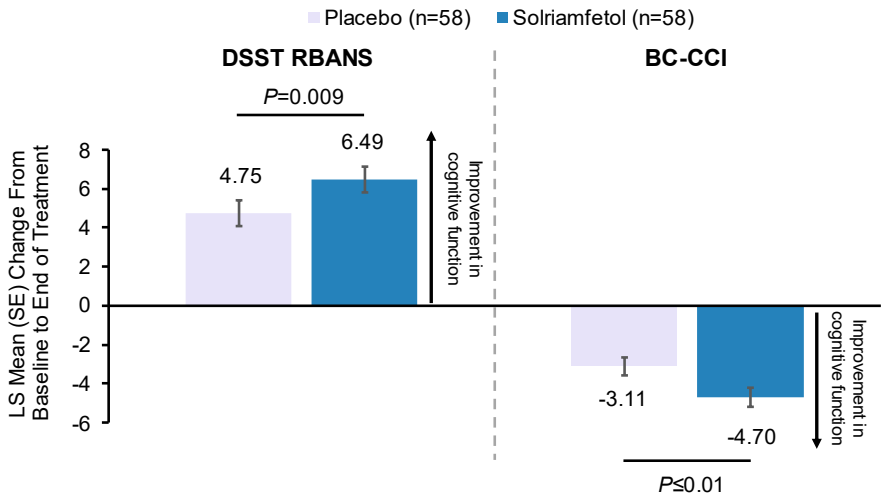
Assessments

Participants completed the Coding subtest, comparable with the DSST, of the Repeatable Battery for the Assessment of Neuropsychological Status (DSST RBANS) at 2, 4, 6, and 8 hours post-dose wherein participants were asked to match symbols to numbers within 90 seconds as an objective measure of cognition. Subjective cognition was assessed with the BC-CCI.



Results

Of 59 patients enrolled, mean age was 52.2 years; 36% were female, 73% were White, and 71% were PAP users. **Participants taking solriamfetol showed significantly greater improvement in DSST RBANS score compared with placebo, both when averaged across time points (primary endpoint) and at the individual post-dose assessments**. Subjective cognitive function was also significantly improved with solriamfetol as measured by the BC-CCI (decrease of –4.7 compared with –3.1 with placebo). In addition, significant improvements were seen in symptom severity (as measured by Patient Global Impression of Severity [PGI-S]) and EDS severity (as measured by ESS) with solriamfetol. The tolerability of solriamfetol in this study was consistent with its known safety profile; the most common treatment-emergent adverse events were nausea and anxiety.



Conclusions

Solriamfetol significantly improved objective and subjective measures of cognitive function and reduced perceived severity and sleepiness. These improvements were maintained over an 8-hour day. Thus, the results of the SHARP study support solriamfetol as a potential treatment to improve cognitive function in patients with cognitive impairment associated with OSA and EDS.

References

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2. Werli KS, Otuyama LJ, Bertolucci PH, et al. Neurocognitive function in patients with residual excessive sleepiness from obstructive sleep apnea: a prospective, controlled study. *Sleep Med.* 2016;26:6-11.
3. Van Dongen HPA, Leary EB, Drake C, et al. Results of the SHARP study: a randomized, placebo-controlled, double-blind, repeated-measures, crossover, phase IV clinical trial of the effect of the wake-promoting agent solriamfetol on cognitive function in OSA with excessive daytime sleepiness and cognitive impairment [published online ahead of print November 9, 2024]. *Chest.* doi: 10.1016/j.chest.2024.10.050.