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Long-Term Effects of Solriamfetol on Quality of Life in Participants With Excessive Daytime Sleepiness Associated With Narcolepsy or Obstructive Sleep Apnea

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Background

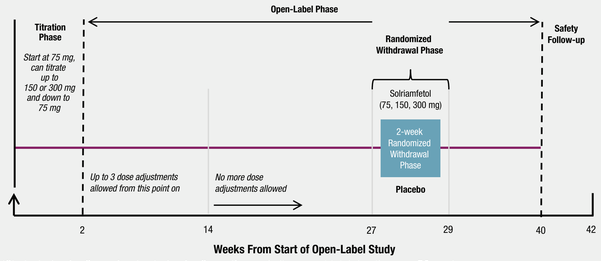
- Excessive daytime sleepiness (EDS) is a prominent symptom of narcolepsy and obstructive sleep apnea (OSA) with many adverse consequences, including reductions in functioning and daily activities, poor quality of life, and increased risk of workplace and driving accidents[1-3]
- Solriamfetol (JZP-110) is a dopamine and norepinephrine reuptake inhibitor[4] approved by the US Food & Drug Administration (Sunosi™) to improve wakefulness in adults with EDS associated with narcolepsy or OSA. The approved dose range of solriamfetol in the US is 75 to 150 mg once daily for patients with narcolepsy and 37.5 to 150 mg once daily for patients with OSA[5]
- In two 12-week phase 3 studies, solriamfetol demonstrated robust wake-promoting effects,[6,7] along with improvements in functioning, work productivity, and health-related quality of life (HRQoL) in participants with EDS associated with narcolepsy or OSA[8,9]
- Long-term maintenance of efficacy in reducing EDS has been demonstrated with open-label solriamfetol treatment (up to 52 weeks) in participants with narcolepsy or OSA[10]

Objective

- To evaluate whether reductions in EDS observed during long-term treatment with solriamfetol were accompanied by improvements in functional status, work productivity, and HRQoL in participants with narcolepsy or OSA

Methods

Figure 1. Study Design[a]



[a]Study design for Group A only; design for Group B was similar except total duration was 52 weeks.

- Participants with narcolepsy or OSA who had previously completed clinical trials of solriamfetol were eligible[6,7,11-13]
- Due to differences in time between prior study completion and enrollment in the long-term study, there were 2 groups
  - Group A: enrolled in the long-term study immediately after completion of 12-week phase 3 studies
  - Group B: historically completed phase 2 studies or the 6-week phase 3 study and were subsequently enrolled in the long-term study
- Open-label solriamfetol treatment was initiated at 75 mg, and was titrated to 75, 150, or 300 mg during a 2-week titration phase, which was followed by an open-label maintenance phase (75 mg, 150 mg, or 300 mg), with total study duration of 40 weeks for Group A and 52 weeks for Group B (not shown)
- Impact of EDS on functional status, work/activity impairment related to narcolepsy or OSA, and general HRQoL was assessed with the Functional Outcomes of Sleep Questionnaire short version (FOSQ-10), Work Productivity Activity Impairment Questionnaire: Specific Health Problem (WPAI:SHP; specified as narcolepsy or OSA), and 36-Item Short Form Health Survey Version 2 (SF-36v2), respectively; safety and tolerability were evaluated throughout the study
- Analyses were performed using the safety population, defined as participants who received at least 1 dose of solriamfetol
- No formal statistical testing (including missing data imputation) was performed for open-label analyses; summary statistics are reported for the overall study population and the narcolepsy/OSA subgroups, showing data for the combined solriamfetol dose groups; subgroup analyses were conducted by indication (narcolepsy or OSA)

Results

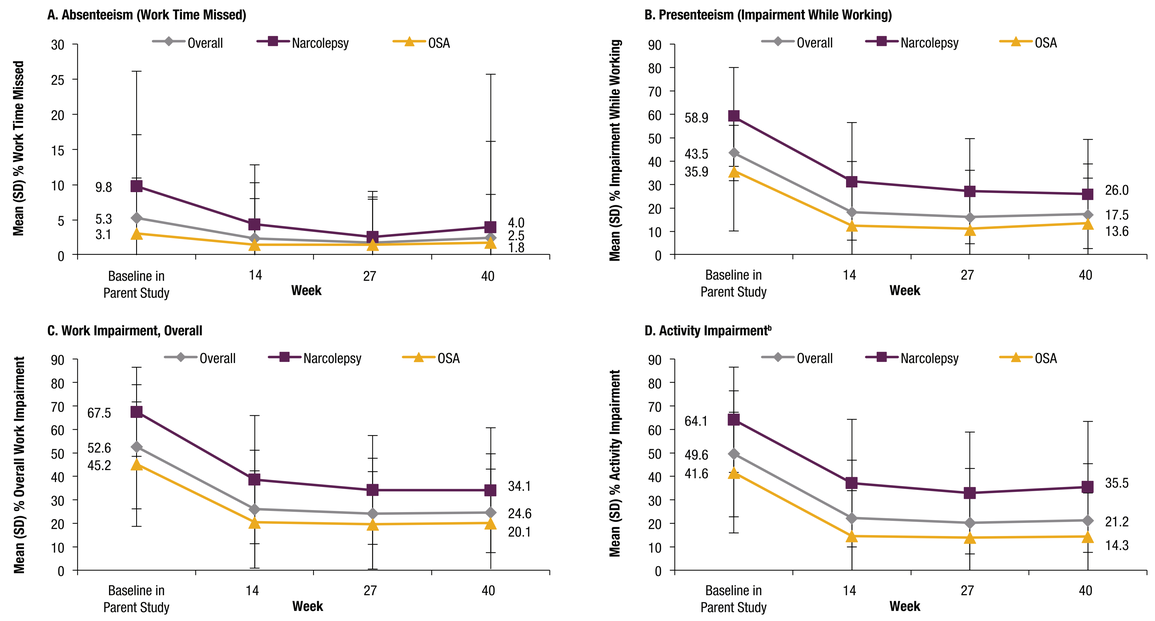
Table 1. Demographic Characteristics of the Safety Population

Variable	Overall (N=643)	Narcolepsy (n=226)	OSA (n=417)
Age, years, mean (SD)	49.3 (14.2)	38.7 (13.5)	55.1 (10.7)
Male, n (%)	337 (52.4)	80 (35.4)	257 (61.6)
Race, n (%) White	506 (78.7)	181 (80.1)	325 (77.9)
BMI, kg/m^2, mean (SD)	31.7 (5.9)	28.3 (5.8)	33.5 (5.1)

BMI, body mass index; OSA, obstructive sleep apnea; SD, standard deviation.

- Participants with OSA were, on average, older, predominately male, and had a higher BMI compared with participants with narcolepsy
- A total of 458 (71.2%) participants (narcolepsy, 66.4%; OSA, 73.9%) completed the study; of the 185 (28.8%) who discontinued, the most frequently reported reasons for discontinuation were AEs (narcolepsy, 10.2%; OSA, 9.1%) and lack of efficacy (narcolepsy, 17.3%; OSA, 3.6%)

Figure 2. Improvements in EDS-Related Work/Activity Impairments on the WPAI:SHP Were Maintained for the Study Duration (Group A)[a]



[a]Group B showed similar results. [b]Regular daily activities, other than work at a job. Note: A negative change from baseline indicates improvement. EDS, excessive daytime sleepiness; OSA, obstructive sleep apnea; SD, standard deviation; WPAI:SHP, Work Productivity Activity Impairment Questionnaire: Specific Health Problem.

- Only about 50% of participants were employed, which is consistent with data for populations with narcolepsy[16] or OSA[17] and suggests these conditions are a substantial burden
- At baseline, rates of absenteeism were low, and higher among participants with narcolepsy vs OSA; both groups reported high rates of presenteeism, mean overall work impairment, and activity impairment
- Solriamfetol reduced presenteeism, overall work impairment, and activity impairment by a minimum of 25% from baseline of the parent study, and these improvements were sustained for the duration of treatment

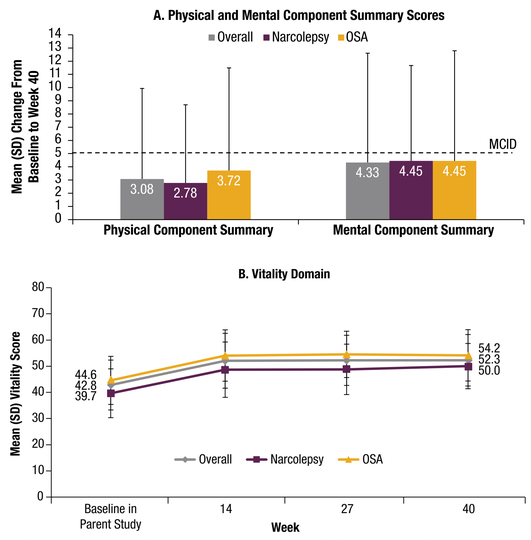
Table 2. Clinical Characteristics of the Safety Population (Group A)

Variable	Overall (N=643)	Narcolepsy (n=226)	OSA (n=417)
Baseline FOSQ-10, mean (SD)[a]	n=518	n=185	n=333
	13.1 (3.2)	11.6 (3.0)	13.9 (3.0)
Baseline WPAI, mean % (SD)[a]			
Work time missed	n=332	n=111	n=221
	5.3 (11.8)	9.8 (16.3)	3.1 (7.9)
Overall work impairment	n=324	n=107	n=217
	52.6 (26.5)	67.5 (19.0)	45.2 (26.5)
Impairment while working	n=326	n=108	n=218
	43.5 (26.6)	58.9 (21.1)	35.9 (25.7)
Activity impairment	n=516	n=184	n=332
	49.6 (26.8)	64.1 (22.4)	41.6 (25.7)
Baseline SF-36, mean (SD)[a]	n=519	n=186	n=333
Physical component score	46.2 (8.5)	46.2 (8.7)	46.1 (8.4)
Mental component score	48.6 (9.2)	45.4 (9.5)	50.4 (8.5)
Role physical	42.8 (10.6)	39.5 (11.3)	44.7 (9.6)
General health	49.1 (9.3)	48.7 (9.6)	49.4 (9.2)
Vitality	42.8 (9.5)	39.7 (9.3)	44.6 (9.2)
Physical functioning	48.4 (8.1)	49.4 (8.0)	47.9 (8.1)
Bodily pain	49.2 (9.7)	50.3 (10.2)	48.5 (9.3)
Role emotional	48.8 (9.8)	47.4 (10.4)	49.5 (9.4)
Mental health	51.2 (7.9)	49.5 (8.7)	52.1 (7.3)
Social functioning	46.1 (10.4)	41.6 (11.5)	48.6 (8.9)

[a]Baseline in the parent study. FOSQ-10, Functional Outcomes of Sleep Questionnaire short version; OSA, obstructive sleep apnea; SD, standard deviation; SF-36, Short Form Health Survey; WPAI, Work Productivity Activity Impairment.

- In general, participants with narcolepsy had greater impairments in functional status and work productivity/activity compared with participants with OSA
- In matched controls without narcolepsy, normative rates of absenteeism, presenteeism, overall work impairment, and activity impairment have been estimated to be 7.3%, 21.7%, 24.8%, and 33.8%, respectively[16]; in matched controls without OSA, normative rates have been estimated to be 3.9%, 14.8%, 16.9%, and 19.9%, respectively[17]

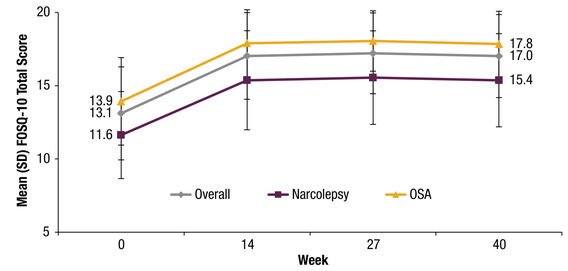
Figure 3. Improvements in General HRQoL Change Scores on the SF-36 Were Maintained for the Study Duration (Group A)[a]



[a]Group B showed similar results. Dashed horizontal line represents the MCID for a change in SF-36v2 score.[18] Note: A positive change from baseline indicates improvement. MCID, minimal clinically important difference; OSA, obstructive sleep apnea; SD, standard deviation; SF-36, Short Form Health Survey Version 2.

- Solriamfetol improved both the physical component summary and mental component summary scores, and these improvements were maintained for the duration of treatment
- For both narcolepsy and OSA participants, the vitality domain had the largest magnitude of change; however, there was high variability between participants on all domain scores (data not shown), suggesting the SF-36 has limited sensitivity to detect change in these populations

Figure 4. Improvements in EDS-Related Impairments in Functional Status on the FOSQ-10 Were Maintained for the Study Duration (Group A)[a]



[a]Group B showed similar results. Note: A positive change from baseline indicates improvement. EDS, excessive daytime sleepiness; FOSQ-10, Functional Outcomes of Sleep Questionnaire short version; SD, standard deviation.

- Baseline FOSQ-10 total scores for both indications were lower than normal values (normal=total score between 17.9 and 20),[14] suggesting difficulties with productivity, activity level, vigilance, social outcomes, and relationships due to EDS
- Improvement in FOSQ-10 total scores from baseline of the parent study exceeded the minimal important difference (minimal important difference range of 1.74 to 2.00 for narcolepsy and 1.64 to 2.06 for OSA)[15] and was sustained for the duration of solriamfetol treatment

Table 3. Treatment-Emergent Adverse Events (TEAEs) Across the Entire Study

TEAE	Number (%) of Participants in Combined Solriamfetol Groups: Overall (N=643)	Narcolepsy (n=226)	OSA (n=417)
At least one TEAE	482 (75.0)	169 (74.8)	313 (75.1)
Serious TEAE	27 (4.2)	6 (2.7)	21 (5.0)
TEAEs leading to discontinuation	59 (9.2)	23 (10.2)	36 (8.6)
Death	1 (0.2)[a]	0	1 (0.2)
Most common TEAEs[b]			
Headache	71 (11.0)	31 (13.7)	40 (9.6)
Nausea	57 (8.9)	26 (11.5)	31 (7.4)
Insomnia	51 (7.9)	16 (7.1)	35 (8.4)
Nasopharyngitis	54 (8.4)	19 (8.4)	35 (8.4)
Dry mouth	47 (7.3)	14 (6.2)	33 (7.9)
Anxiety	46 (7.2)	21 (9.3)	25 (6.0)
Decreased appetite	32 (5.0)	18 (8.0)	14 (3.4)
Upper respiratory tract infection	32 (5.0)	10 (4.4)	22 (5.3)

[a]Due to sepsis; [b]≥5% in combined solriamfetol groups for any indication. OSA, obstructive sleep apnea.

- Serious TEAEs were reported in 27 (4.2%) participants: 21 with OSA (5.0%) and 6 with narcolepsy (2.7%)
  - Five participants, 4 with OSA and 1 with narcolepsy, had an SAE that was considered related to study drug by the investigator
- There was 1 death due to sepsis
  - A 70-year old immunosuppressed male with OSA on solriamfetol 300 mg, who had a history of diabetes mellitus, rheumatoid arthritis, pulmonary fibrosis, coronary artery disease, and bipolar disorder
  - The death was considered unrelated to study drug by the investigator

Conclusions

- In participants with narcolepsy or OSA, long-term treatment with solriamfetol is associated with clinically meaningful, sustained improvements in functional status, work productivity, and HRQoL measures for up to 52 weeks
- The safety profile was consistent with prior placebo-controlled studies of solriamfetol

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