SUPPLEMENTAL MATERIAL

Impairment in Functioning and Quality of Life in Patients With Idiopathic Hypersomnia: The Real World Idiopathic Hypersomnia Outcomes Study (ARISE)

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ARISE Study Screener

Screener Welcome Message

Thank you for your interest in this research study. You will first be asked some questions to see if you are eligible for this study. If you are eligible, you will be asked to complete an online questionnaire. After that, you may be asked to call into an automated voice response system to answer a few additional questions.

Screener

1. What is your age? _____ years old **[IF <21 or >65, TERMINATE]**

2. What is your gender?
   a. Female
   b. Male
   c. Non-binary
   d. I prefer not to answer

3. Do you currently reside in the US?
   a. Yes
   b. No **[TERMINATE]**

4. What state do you currently reside in?
   a. **[PROGRAMMING NOTE: PROVIDE DROP-DOWN MENU OF ALL STATES]**

5. Are you a current employee of Jazz Pharmaceuticals or have an immediate family member who is a current Jazz Pharmaceuticals employee?
   a. Yes **[TERMINATE]**
   b. No

6. Which, if any, of the following conditions are you **currently diagnosed** with? (***Please do not select any condition where you had a prior diagnosis that is no longer current or has changed to a different diagnosis.) Please select all that apply.***
   a. Anxiety
   b. Bipolar disorder or any other psychotic disorders
   c. Circadian rhythm sleep disorders (e.g., jet lag, shift work sleep disorder)
   d. Fibromyalgia or chronic fatigue syndrome
   e. History of head injury that resulted in loss of consciousness in the past 5 years
   f. History of seizures
   g. Hypothyroidism (low thyroid levels)

h. Idiopathic hypersomnia (IH) **[MUST BE SELECTED TO CONTINUE]**
i. Insomnia
j. Kleine-Levin syndrome
k. Major depressive disorder
l. Multiple sclerosis
m. Narcolepsy **[TERMINATE]**
n. Obstructive sleep apnea (OSA) **[TERMINATE]**
o. Parasomnia disorder (e.g., sleep terrors/night terrors, sleepwalking, nightmares)
p. Parkinson's disease
q. Periodic limb movement disorder (PLMD)
r. Post-traumatic stress disorder (PTSD)
s. REM sleep behavior disorder (RBD) (i.e., acting out dreams during sleep)
t. Restless legs syndrome (RLS)
u. Stroke or transient ischemic attack (TIA)
v. Other disorder that may be associated with excessive daytime sleepiness or fatigue (please specify): _____
w. None **[EXCLUSIVE, TERMINATE]**

7. Approximately how many hours do you sleep in a typical night?
   a. **[PROGRAMMING NOTE: PROVIDE DROP-DOWN LIST OPTIONS OF 0-16]**

   [TERMINATE IF LESS THAN 7]

8. During the course of a typical day, approximately how many hours do you sleep? ***Please think about the total amount of time during the day that you spend napping.***
   a. Provide drop-down list options of 0 - 16

   [PROGRAMMING NOTE: IF Q7 + Q8 IS >24, SHOW ERROR NOTE STATING THAT THE NUMBER OF HOURS CANNOT BE GREATER THAN 24]

9. Do you have a **current diagnosis** of cataplexy (i.e., sudden, brief loss of muscle strength or control caused by strong emotions)?
   a. Yes **[TERMINATE]**
   b. No

10. How long ago have you been diagnosed with **idiopathic hypersomnia**?
    Less than 6 months ago **[TERMINATE]**
    a. 6 to 11 months
    b. 1 year
    c. 2 years

d. 3 years
e. 4 years
f. 5 years
g. 6 years
h. 7 years
i. 8 years
j. 9 years
k. 10 or more years

11. Please select which of the following tests or measures you have ever taken to diagnose your sleep disorder. ***Please select all that apply.***
    a. Multiple sleep latency test - MSLT (i.e., daytime nap study)
    b. Polysomnography - PSG (i.e., sleep study conducted in a sleep unit or lab)
    c. Wrist actigraphy (i.e., test with a band on your wrist) to measure nighttime sleep and daytime naps
    d. Sleep log
    e. I don't know/I can't recall **[EXCLUSIVE]**
    f. None **[EXCLUSIVE]**

12. From the list below, please select the condition for which you have a <u>current</u> diagnosis <u>and</u> your doctor has told you is the cause of your symptoms related to your sleep disorder. ***Please select the best response.***
    a. Hypersomnia associated with a psychiatric disorder
    b. Hypersomnia due to a medication or substance
    c. Hypersomnia not otherwise specified
    d. Idiopathic hypersomnia (IH) **[MUST BE SELECTED TO CONTINUE]**
    e. Insufficient sleep syndrome
    f. Kleine-Levin syndrome
    g. Narcolepsy Type 1 (with cataplexy or hypocretin deficiency)
    h. Narcolepsy Type 2 (without cataplexy or hypocretin deficiency)
    i. Narcolepsy (type not specified)
    j. Obstructive Sleep Apnea (OSA)
    k. None

13. Which of the following prescriptions are you <u>currently</u> taking to treat your **idiopathic hypersomnia**? ***Please select all that apply.***
    a. Amphetamine stimulants [Common brand names include Adderall, Adderall XR, Dexedrine, Dextrostat, Vyvanse, Desoxyn]
    b. Methylphenidate stimulants [Common brand names include Ritalin, Concerta, Daytrana, Focalin, Focalin XR, Metadate, Quillivant XR]
    c. Wake-promoting agents [Common brand names include Provigil (modafinil); Nuvigil (armodafinil)]
    d. Solriamfetol [Sunosi]

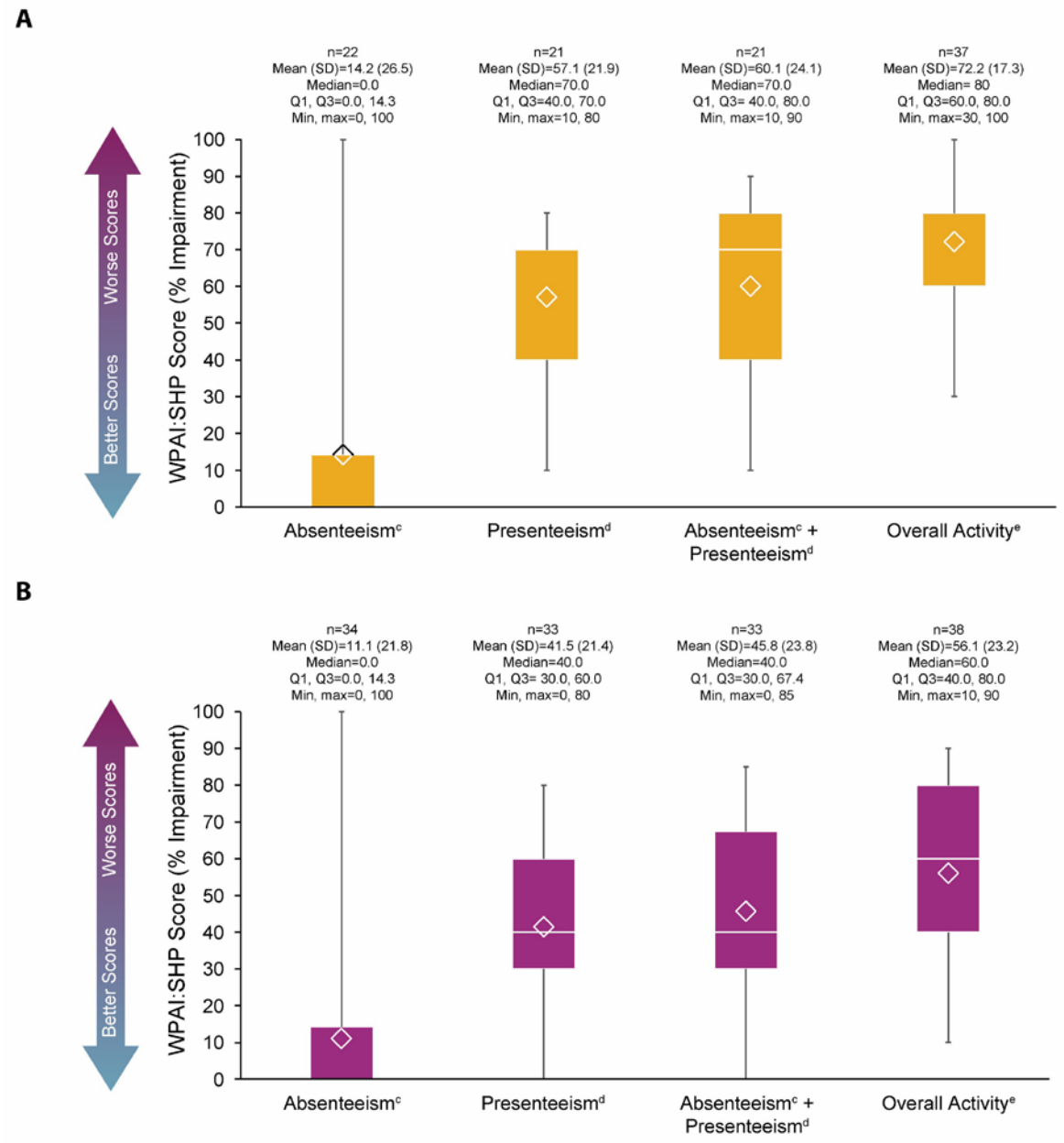
e. Histamine receptor agent [Wakix (pitolisant)]
f. Sodium oxybate [Xyrem]
g. Calcium, magnesium, potassium and sodium oxybates [Xywav]
h. SSRI antidepressant medications [Common brand names include Prozac, Zoloft, Paxil, Lexapro, Celexa, Luvox]
i. SNRI antidepressant medications [Common brand names include Effexor, Cymbalta, Savella, Fetzima, Pristiq]
j. Tricyclic antidepressant medications [Common brand names include Elavil (amitriptyline), Anafranil (clomipramine), Norpramin (desipramine), Tofranil (imipramine), Pamelor (nortriptyline), Vivacillo (protriptyline), Sinequan (doxepin)]
k. MAOI antidepressant medications [Common brand names include Eldepryl or Zelapar (selegiline)]
l. Other (please specify): _____
m. I am currently not on any prescription medications for my idiopathic hypersomnia **[EXCLUSIVE]**

14. Please enter your email to receive your honoraria once you have completed the study.
Your email will only be used to send you your honoraria at the end of the study and to invite you to participate in future research opportunities. Your information will not be sold or shared with the study sponsor or anyone outside of this project. All data from this study will be de-identified for analysis.
a. _____ email

[IF NOT QUALIFIED, SHOW TERMINATE MESSAGE AND CLOSE]
Unfortunately, you are not eligible to participate in this research study. Thank you for your interest in this study.

IF QUALIFIED, SHOW CALIFORNIA EXPERIMENTAL SUBJECT'S BILL OF RIGHTS FORM (FOR CA-BASED PATIENTS) OR INFORMED CONSENT FORM FOR NON-CA-BASED PATIENTS.

Supplemental Figure 1. WPAI:SHP scores[a] in participants with LST[b] (A) and participants without LST[b] (B)



The bottom and top edges of the box indicate the first and third quartiles, the line inside the box is the median, and the marker inside the box is the mean. The whiskers extending from the box indicate the minimum and maximum values.
LST, long sleep time; Max, maximum; Min, minimum; Q1, first quartile; Q3, third quartile; SD, standard deviation; WPAI:SHP, Work Productivity and Activity Impairment Questionnaire: Specific Health Problem.
[a]Items relating to absenteeism and work productivity were completed only by participants who were employed; the item relating to activity impairment was completed by all participants.
[b]Long sleep was defined as ≥11 hours of sleep in a 24-hour period (self-reported).
[c]Absenteeism was defined as percent work time missed due to idiopathic hypersomnia.
[d]Presenteeism was defined as percent impairment while working.
[e]Refers to overall daily activity, other than working.

Supplemental Table 1. Functioning and QoL Measures by Age Group, Wake-Promoting Agent Monotherapy, or Stimulant Monotherapy

	Age Group, years			WPA Monotherapy		Stimulant Monotherapy	
Assessment	**≥20 to <30**	**≥30 to <40**	**≥40**	**Yes**	**No[a]**	**Yes**	**No[a]**
FOSQ-10 total score[b], n	31	17	19	12	55	25	42
Mean (SD)	10.5 (2.7)	11.1 (3.3)	10.8 (2.6)	12.0 (3.5)	10.5 (2.6)	10.7 (2.3)	10.8 (3.0)
Median	10.2	11.3	11.2	11.3	10.7	10.7	11.0
Min, max	6.0, 16.2	5.0, 17.0	6.0, 15.2	6.2, 17.0	5.0, 15.7	6.0, 15.2	5.0, 17.0
Neuro-QoL Social Roles[c], n	34	21	20	12	63	29	46
Mean (SD)	40.7 (5.4)	43.0 (5.3)	40.9 (4.1)	43.6 (8.6)	41.0 (4.0)	41.0 (3.7)	41.7 (5.8)
Median	39.9	42.7	41.3	41.3	40.6	40.6	41.3
Min, max	29.5, 60.2	33.5, 60.2	32.7, 49.2	33.5, 60.2	29.5, 49.2	35.0, 49.2	29.5, 60.2
Neuro-Qol Stigma[d], n	34	21	20	12	63	29	46
Mean (SD)	57.2 (5.7)	56.2 (7.1)	58.5 (4.8)	55.7 (5.6)	57.6 (5.9)	56.6 (5.6)	57.7 (6.1)
Median	57.0	56.2	57.0	55.8	57.0	57.0	57.0
Min, max	39.2, 70.8	39.2, 67.5	49.3, 68.5	47.6, 64.0	39.2, 70.8	39.2, 65.7	39.2, 70.8
BC-CCI score[e], n	34	21	20	12	63	29	46
Mean (SD)	11.4 (4.5)	9.1 (5.1)	11.6 (4.9)	10.7 (2.8)	10.9 (5.1)	11.2 (5.0)	10.6 (4.7)
Median	12.0	8.0	13.0	10.0	12.0	12.0	11.0

	Age Group, years			WPA Monotherapy		Stimulant Monotherapy	
Assessment	**≥20 to <30**	**≥30 to <40**	**≥40**	**Yes**	**No[a]**	**Yes**	**No[a]**
Min, max	2.0, 18.0	2.0, 18.0	3.0, 18.0	8.0, 15.0	2.0, 18.0	2.0, 18.0	2.0, 18.0
PHQ-9 score[f], n	34	21	20	12	63	29	46
Mean (SD)	13.6 (5.1)	11.3 (5.2)	11.3 (5.9)	9.8 (5.0)	12.8 (5.4)	12.0 (4.8)	12.5 (5.8)
Median	13.5	10.0	11.5	8.0	12.0	12.0	12.5
Min, max	5.0, 26.0	2.0, 22.0	3.0, 25.0	5.0, 19.0	2.0, 26.0	3.0, 26.0	2.0, 25.0
WPAI:SHP[g]							
Absenteeism[h], n	25	17	14	9	47	22	34
Mean (SD)	14.8 (30.2)	8.5 (17.7)	12.5 (15.8)	12.8 (22.0)	12.2 (24.1)	13.9 (29.9)	11.3 (18.8)
Median	0.0	0.0	7.5	0.0	0.0	0.0	0.4
Min, max	0.0, 100.0	0.0, 66.7	0.0, 50.0	0.0, 66.7	0.0, 100.0	0.0, 100.0	0.0, 75.0
Presenteeism[i], n	23	17	14	9	45	20	34
Mean (SD)	50.9 (20.9)	38.2 (22.7)	53.6 (23.7)	42.2 (27.3)	48.7 (21.9)	46.0 (23.9)	48.5 (22.3)
Median	50.0	40.0	60.0	60.0	50.0	45.0	55.0
Min, max	0.0, 80.0	10.0, 80.0	10.0, 80.0	0.0, 70.0	10.0, 80.0	10.0, 80.0	0.0, 80.0
Absenteeism + presenteeism, n	23	17	14	9	45	20	34
Mean (SD)	54.8 (21.8)	41.7 (25.9)	57.5 (26.0)	46.5 (32.0)	52.4 (23.4)	48.3 (24.5)	53.2 (25.1)
Median	59.5	40.0	67.0	60.0	53.3	50.0	62.0

	Age Group, years			WPA Monotherapy		Stimulant Monotherapy	
Assessment	**≥20 to <30**	**≥30 to <40**	**≥40**	**Yes**	**No[a]**	**Yes**	**No[a]**
Min, max	0.0, 85.0	10.0, 90.0	10.0, 87.5	0.0, 90.0	10.0, 87.5	10.0, 87.5	0.0, 90.0
Overall activity[j], n	34	21	20	12	63	29	46
Mean (SD)	65.9 (23.1)	58.6 (22.9)	66.5 (18.7)	52.5 (29.6)	66.2 (19.7)	66.9 (18.5)	62.2 (23.8)
Median	70.0	60.0	65.0	55.0	70.0	70.0	70.0
Min, max	10.0, 100.0	10.0, 90.0	30.0, 100.0	10.0, 90.0	10.0, 100.0	30.0, 100.0	10.0, 100.0

BC-CCI, British Columbia Cognitive Complaints Inventory; FOSQ-10, Functional Outcomes of Sleep Questionnaire, short version; Max, maximum; Min, minimum; Neuro-QoL, Quality of Life in Neurological Disorders; PHQ-9, Patient Health Questionnaire 9; QoL, quality of life; SD, standard deviation; WPA, wake-promoting agent; WPAI:SHP, Work Productivity and Activity Impairment Questionnaire: Specific Health Problem.

[a]Participants in the "No" column included participants who took no medication, as well as those who took that type of medication along with 1 or more other medications for idiopathic hypersomnia.

[b]Range of scores is 5–20; lower scores indicate worse impairment.

[c]Ability to participate in social roles and activities. Raw scores were converted into T-scores (mean, 50; SD, 10) for comparison with the mean score from a general reference population, as published in the *Neuro-QoL User Manual*. Range of possible T-scores is 24.1–60.2; higher scores indicate better outcomes.[1]

[d]Perceptions of self and publicly enacted negativity, prejudice, and discrimination as a result of disease-related manifestations. Raw scores were converted into T-scores (mean, 50; SD, 10) for comparison with the mean score from a clinical reference population, as published in the *Neuro-QoL User Manual.* Range of possible T-scores is 39.2–81.5; higher scores indicate worse outcomes.[1]

[e]Scores range from 0 to 18 and are classified into the following groups: 0–4 = broadly normal cognition; 5–8 = mild cognitive complaints; 9–14 = moderate cognitive complaints; 15–18 = severe cognitive complaints.[2]

[f]Overall scores range from 0 to 27, with the following severity level ratings for depressive symptoms: 0–4 = minimal; 5–9 = mild; 10–14 = moderate; 15–19 = moderately severe; 20–27 = severe.[3]

[g]Higher scores represent greater impairment. Items relating to absenteeism and work productivity were completed only by participants who were employed; the item relating to activity impairment was completed by all participants.

[h]Absenteeism was defined as percent work time missed due to idiopathic hypersomnia.

[i]Presenteeism was defined as percent impairment while working.

[j]Refers to overall daily activity, other than working.

References

1. National Institute of Neurological Disorders and Stroke (NINDS). *User Manual for the Quality of Life in Neurological Disorders (Neuro-QoL) Measures, Version 2.0.* Bethesda, MD: National Institute of Neurological Disorders and Stroke; 2015.
2. Iverson GL, Lam RW. Rapid screening for perceived cognitive impairment in major depressive disorder. *Ann Clin Psychiatry.* 2013;25(2):135-140.
3. Kroenke K, Spitzer RL, Williams JB. The PHQ-9: validity of a brief depression severity measure. *J Gen Intern Med.* 2001;16(9):606-613.