A Novel Investigational Treatment for Hypersomnia: Where We Are and Where We Need to Go

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ZEVRA THERAPEUTICS

Zevra Is Committed to Rare Diseases

Zevra's Approach

Zevra is a patient-centric organization dedicated to developing transformational therapies for rare diseases with limited or no treatment options.

Our Mission Employ creative, outside-the-box strategies to overcome drug development and regulatory challenges and bring life-changing therapeutics to people with rare diseases.

Our Vision To give every promising rare disease therapy candidate a fighting chance to reach patients and improve their quality of life.

Zevra's Work in Idiopathic Hypersomnia

- Zevra announced top-line data from its placebo-controlled, double-blind Phase 2 clinical trial evaluating the safety and tolerability of KP1077 (serdexmethylphenidate, or SDX) in patients with idiopathic hypersomnia (IH).
  - These results will be presented at SLEEP 2024.
- The results from the completed Phase 2 trial provide key information for the design of a potentially pivotal Phase 3 trial of KP1077 in patients with IH.

Zevra Therapeutics, Inc. Corporate website. Available at: www.zevra.com
Zevra Therapeutics, Inc. News Release, March 26, 2024. Available at: https://investors.zevra.com/news-releases/news-release-details/zevra-therapeutics-announces-top-line-data-phase-2-clinical

PWIH Experience Multiple Symptoms With Excessive Daytime Sleepiness (EDS) Being Universal

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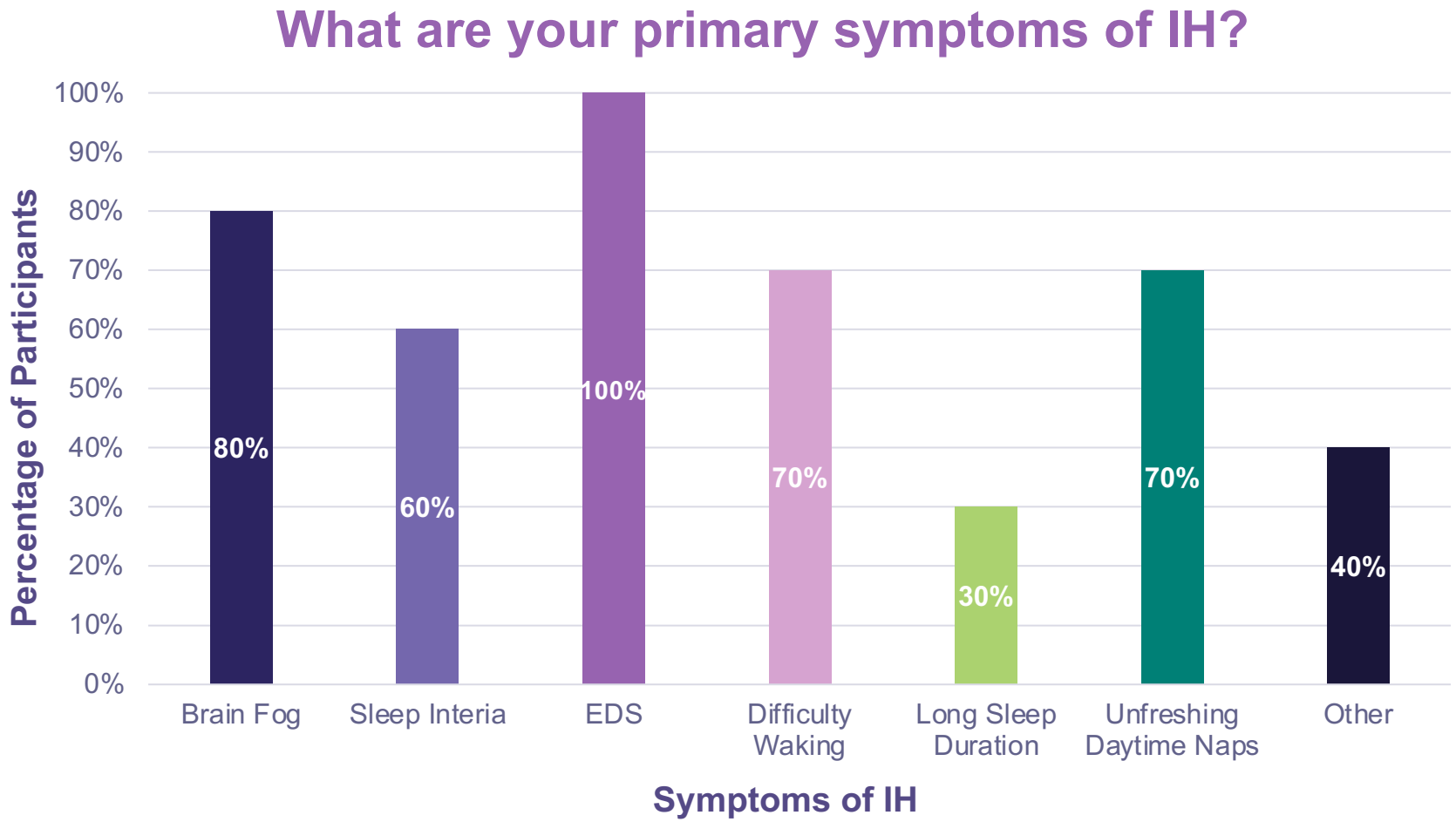
Responses from 10 persons with idiopathic hypersomnia (PWIH) in an advisory board survey

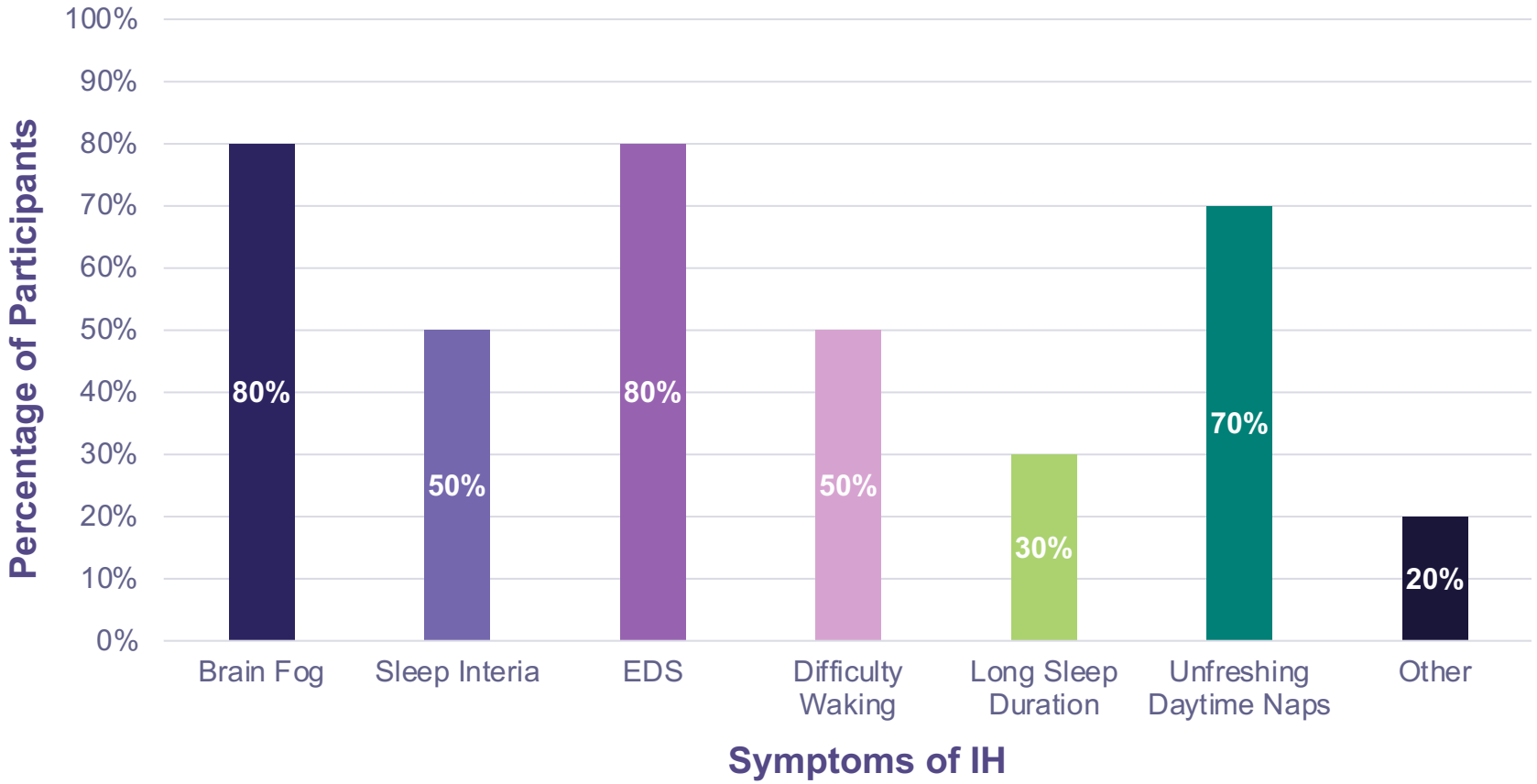


*Other includes cognitive dysfunction, short-term memory, and concentration issues

Primary Symptoms of IH Remain Despite Current Treatments

Responses from 10 persons with idiopathic hypersomnia in an advisory board survey

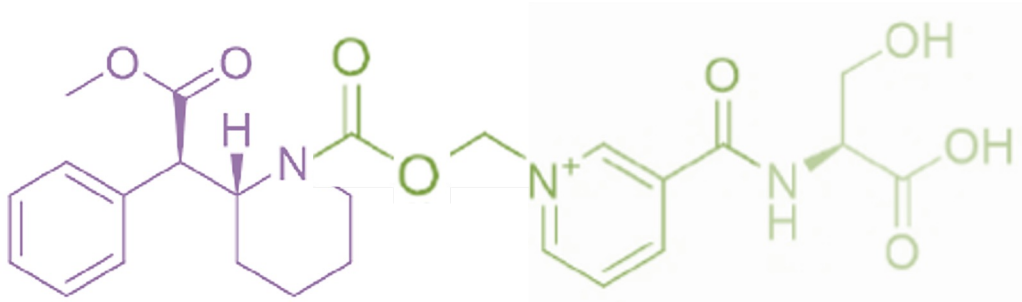
Despite treatment, please select the symptoms which are still most prominent.



Review of Zevra's Investigational Treatment for IH

Serdexmethylphenidate (SDX), a Pro-Drug of d-Methylphenidate

Serdexmethylphenidate (SDX) is a Pro-Drug of d-Methylphenidate

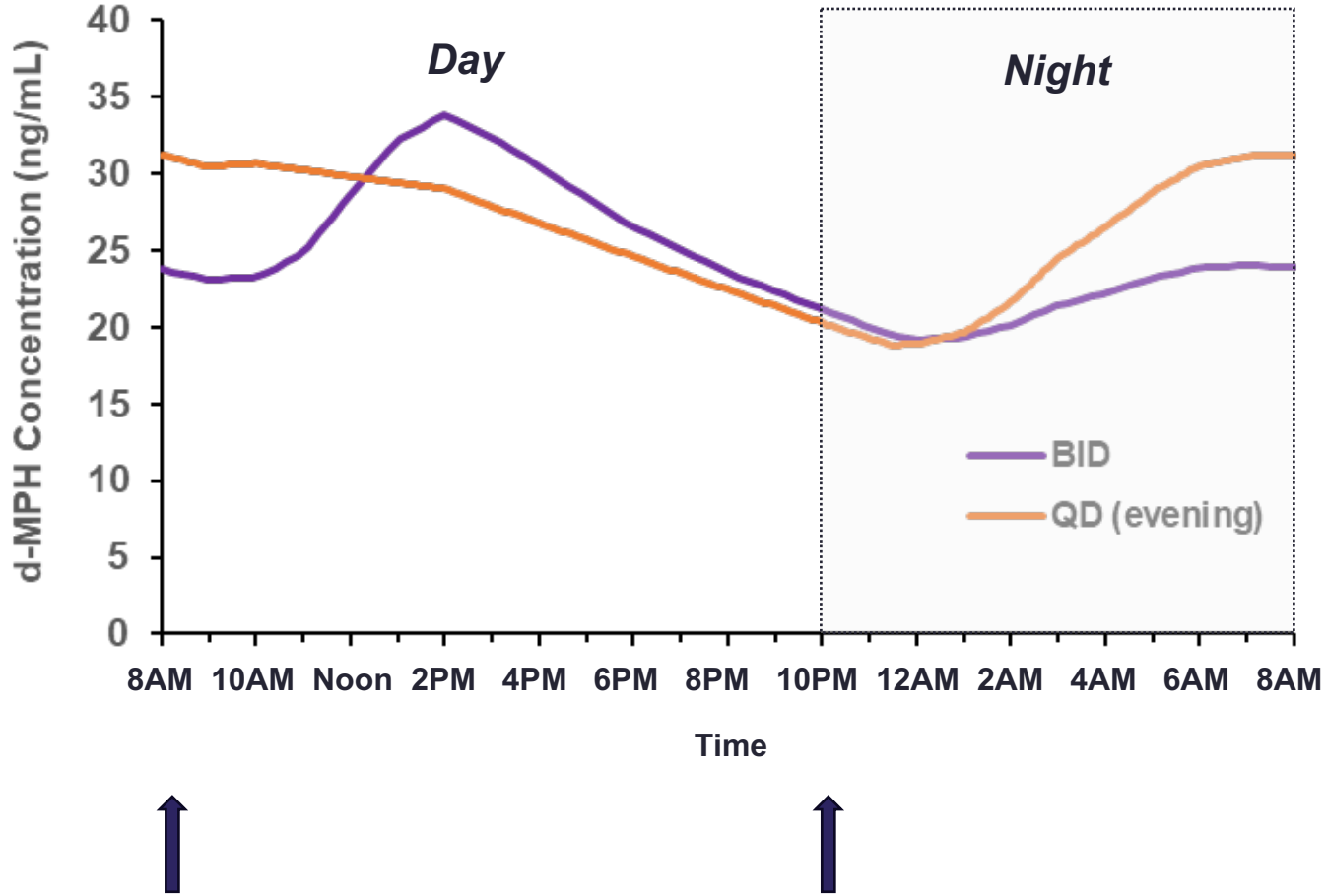


Active Drug: d-methylphenidate

Ligand: Carboxymethylene linker + niacin + L-serine

ClinicalTrials.gov Identifier NCT05668754. Available at: https://clinicaltrials.gov/study/NCT05668754?intr=serdexmethylphenidate&rank=2

Predicted d-MPH Plasma Levels in Individuals at Steady-State Dosing



BID: Morning Dose + Evening Dose

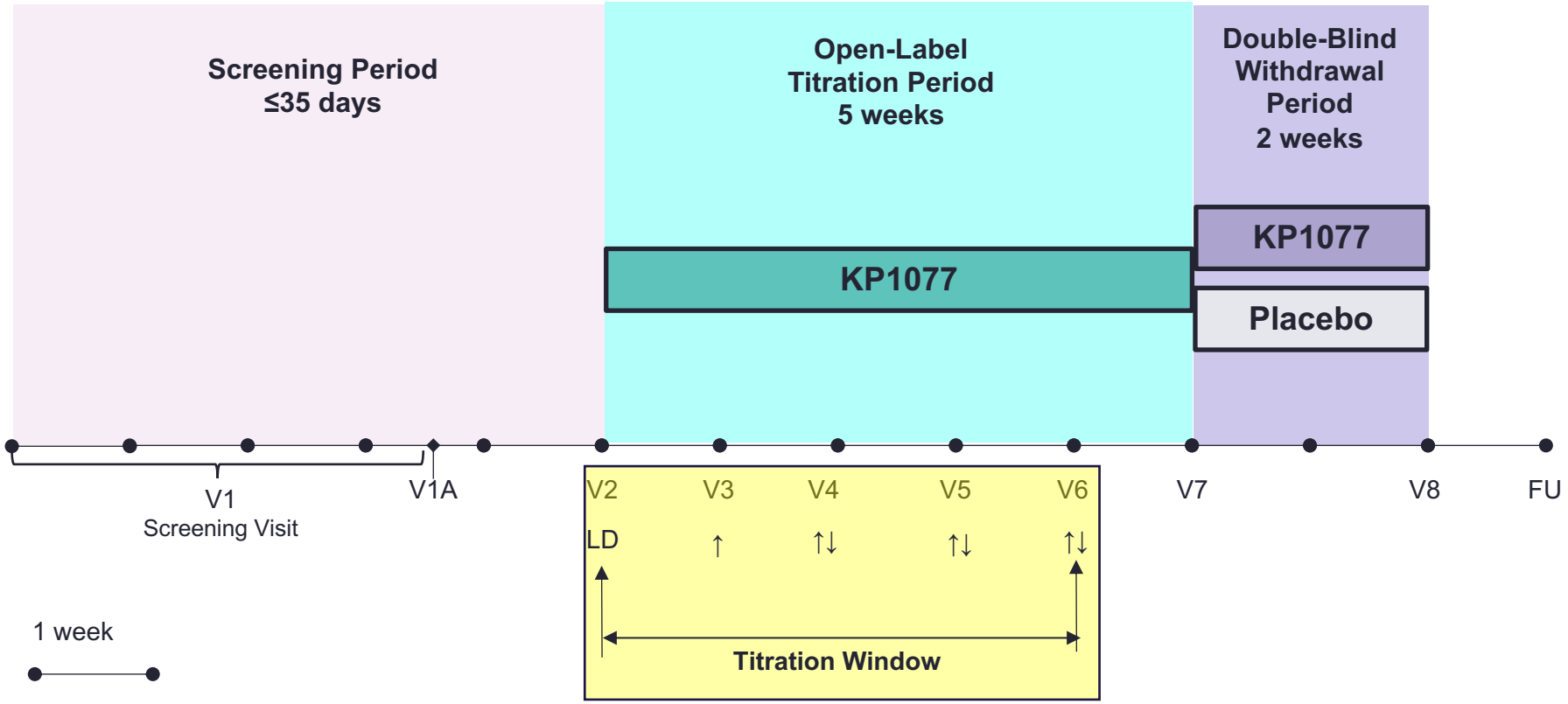
QD: Evening Dose

BID = Twice per day
(half daily dose 2x/day)
(1x at night (bedtime)/ 1x in morning)

QD = Once per day
(daily dose at night)
(1 x at night/bedtime)

ClinicalTrials.gov Identifier NCT05668754. Available at: https://clinicaltrials.gov/study/NCT05668754?intr=serdexmethylphenidate&rank=2

KP1077 Phase 2 Trial Design in People With IH



V = Visit; FU = Follow-Up Phone Call; LD = Low Dose (Starting Dose)

- Eligible participants with IH were titrated to an optimal dose of KP1077 in the 5-week open-label titration period
- After the titration period, patients were randomly assigned to placebo or continued KP1077 (optimized dose) during the 2-week double-blind withdrawal period

See Poster Board 271 at the Sleep 2024 Conference, on June 3, 2024, for more information about the Phase 2 trial results
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Most Adverse Events (AEs) Observed With KP1077 Were Mild and Resolved Quickly

Insomnia was the most frequent AE

- Most frequent AEs (>5%): insomnia (24%), headache (9%), anxiety (6%), nausea (6%), and decreased appetite (6%)
- Approximately same incidence and similar types of AEs in each dosing regimen
- Insomnia:
  - Most insomnia AEs in 1st week of treatment at lowest dose
  - Not related to dose or dosing regimen
  - Often transient not leading to discontinuation
  - Often not preventing titration to higher doses

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Many of the Reported Symptoms of IH Were Evaluated in the Phase 2 Trial

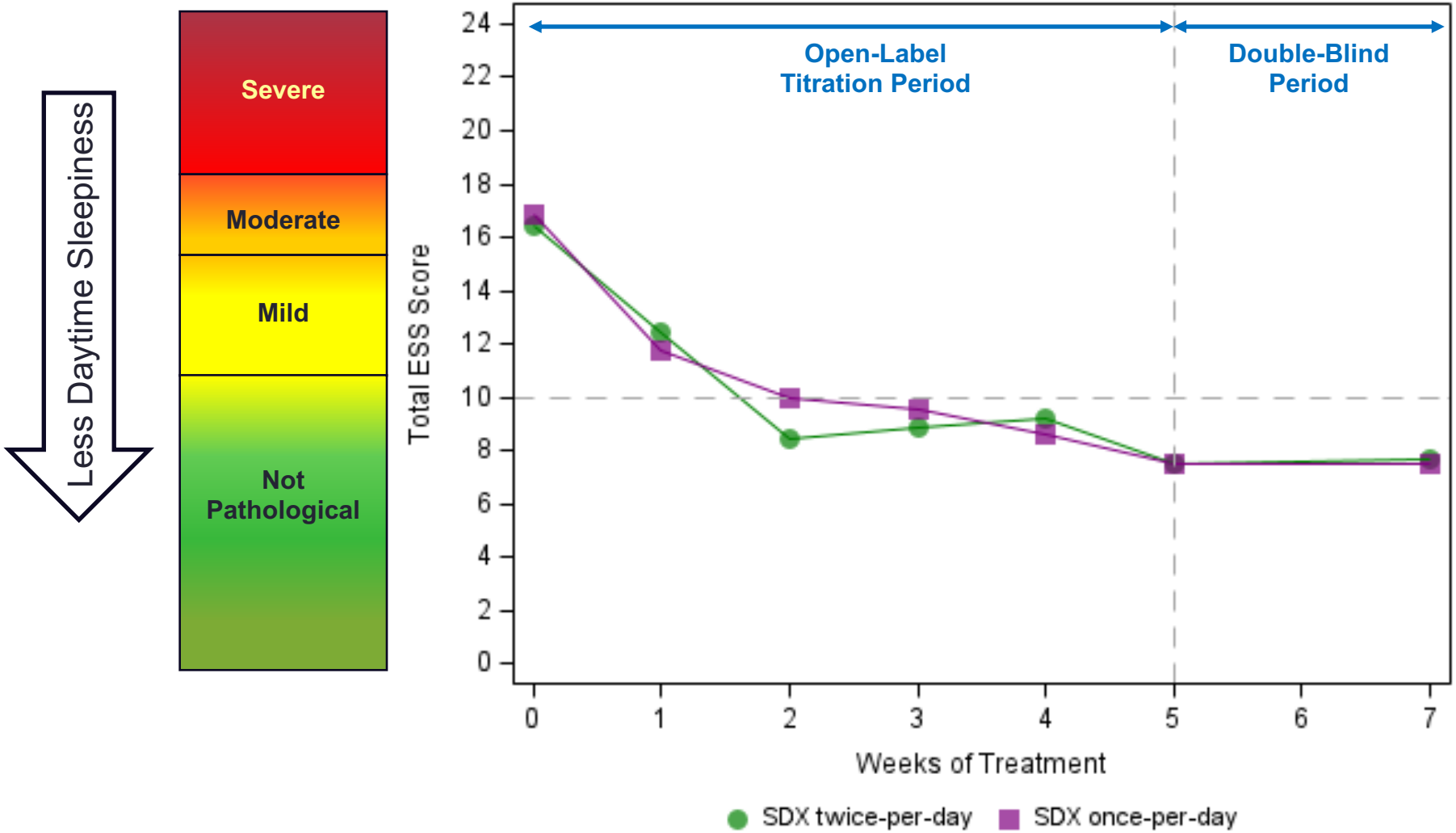
Primary and secondary endpoints were patient-reported evaluations

- Excessive daytime sleepiness (EDS) as measured by the Epworth Sleepiness Scale (ESS)
- Sleep inertia as measured by the Sleep Inertia Visual Analog Scale (SIVAS)
- Severity of IH symptoms and impaired function as measured by the IH Severity Scale (IHSS)
- Brain fog as measured by the Brain Fog Scale (BFS)

ClinicalTrials.gov Identifier NCT05668754. Available at: https://clinicaltrials.gov/study/NCT05668754?intr=serdexmethylphenidate&rank=2

Phase 2 Trial Results Showed a Reduction in Daytime Sleepiness

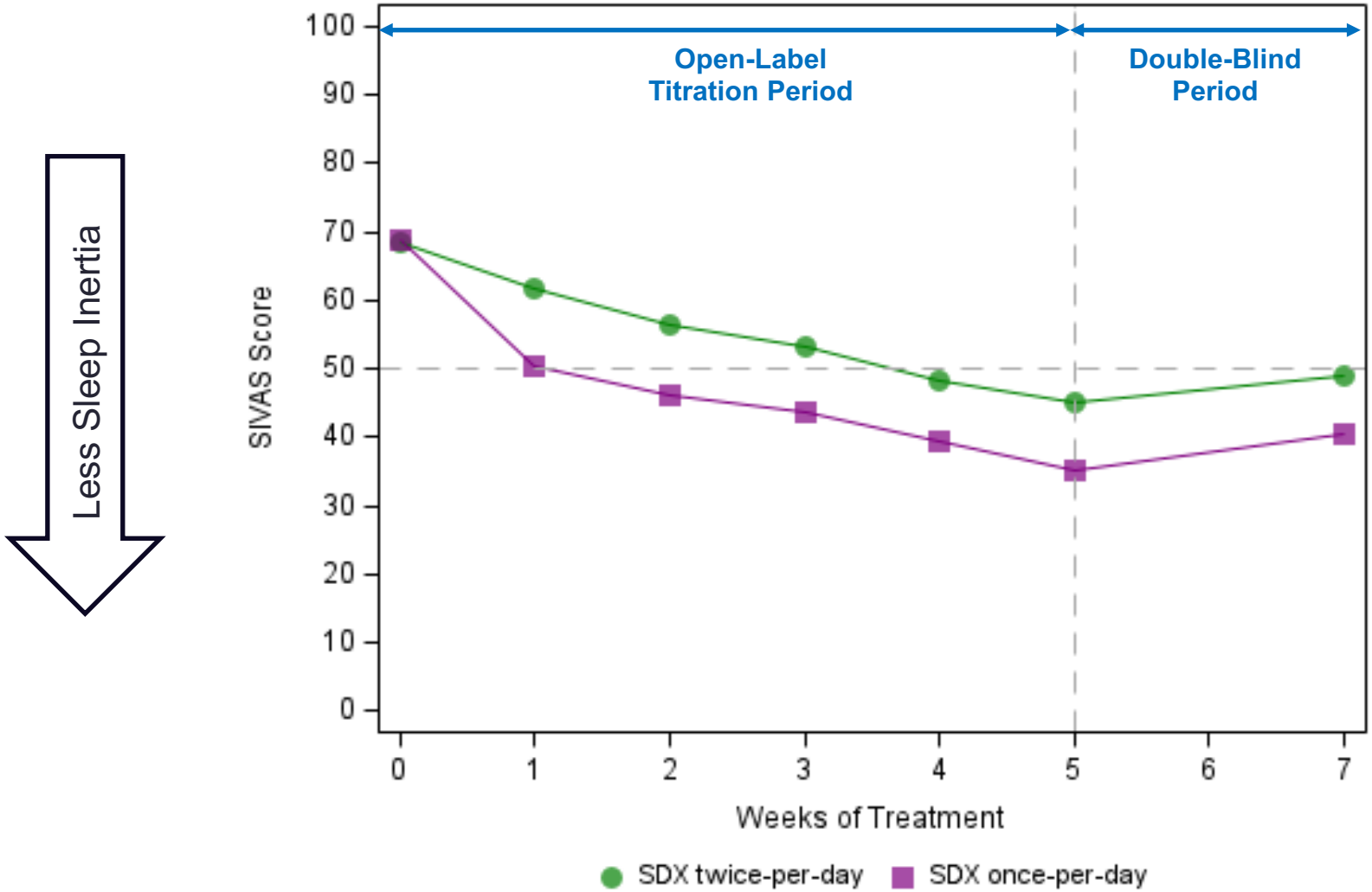
Study participants reported less daytime sleepiness throughout the 7-week trial



ClinicalTrials.gov Identifier NCT05668754. Available at: https://clinicaltrials.gov/study/NCT05668754?intr=serdexmethylphenidate&rank=2

Phase 2 Trial Results Showed a Reduction in Sleep Inertia

Study participants reported that it was easier to wake up in the morning



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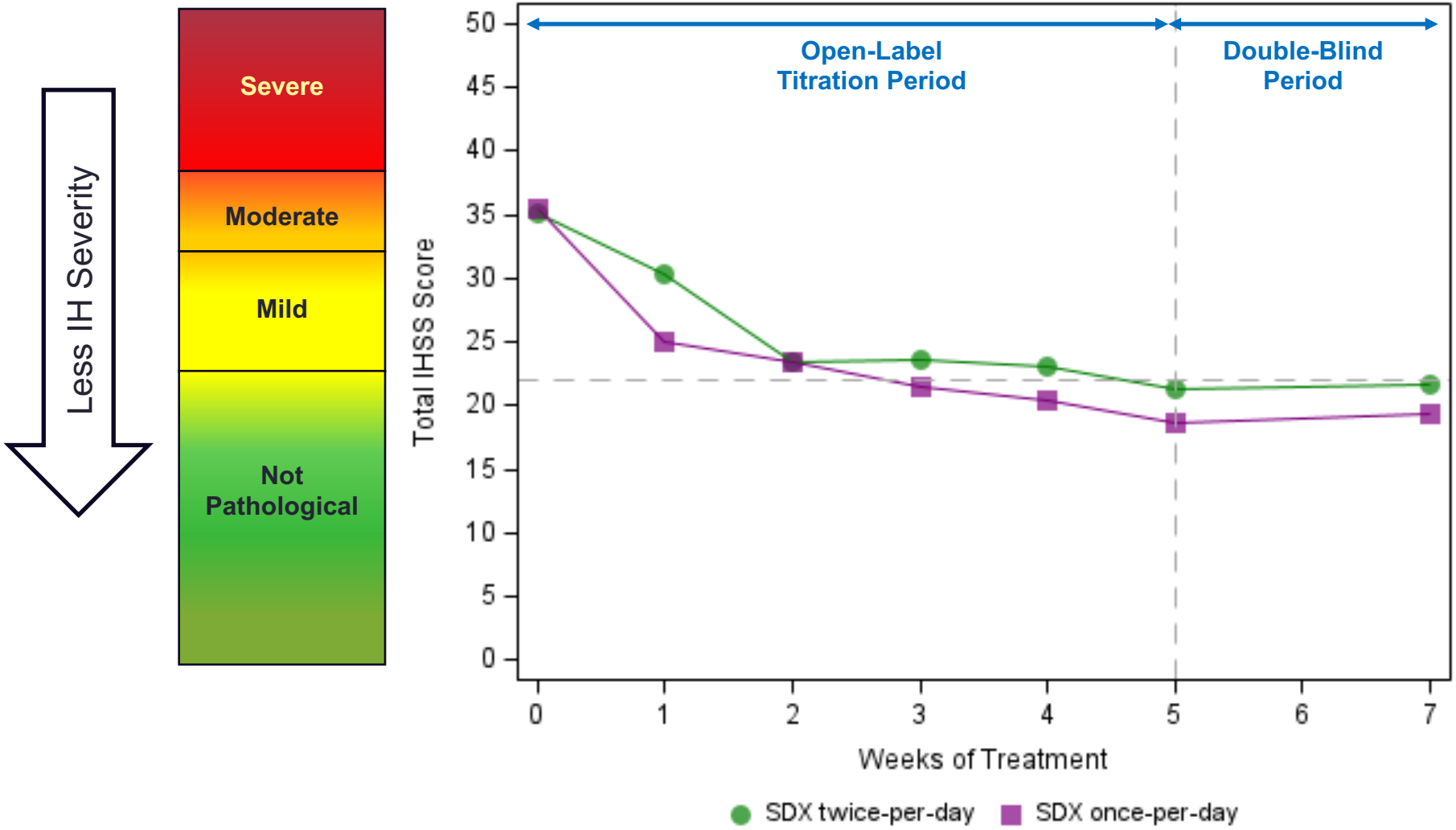
The Idiopathic Hypersomnia Severity Scale Measure Both IH symptoms and Impaired Function

The IHSS is a patient-reported questionnaire

- The IHSS measures severity of both nighttime and daytime IH symptoms
- The IHSS measures impaired daytime functioning
- Patients rate a severity and frequency on 17 question using a 4-or-5 point scale for each question
- The total score ranges from 0 to 50
    - A score of 22 or below is typical for people without any sleep disorder
    - Higher scores on the IHSS indicate more severe symptoms of IH

ClinicalTrials.gov Identifier NCT05668754. Available at: https://clinicaltrials.gov/study/NCT05668754?intr=serdexmethylphenidate&rank=2

Phase 2 Trial Results Showed a Reduction in the Severity of IH Symptoms and Impaired Function



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Brain Fog Scale

Please check which describes your mental state while experiencing "Brain Fog" during the last week. Check one for each item.

	Strongly Agree (4)	Agree (3)	Neutral (2)	Disagree (1)	Strongly Disagree (0)
1. Forgetful	☐	☐	☐	☐	☐
2. Difficulty thinking	☐	☐	☐	☐	☐
3. Difficulty focusing	☐	☐	☐	☐	☐
4. Cloudy	☐	☐	☐	☐	☐
5. Difficulty finding the right words/ communicating	☐	☐	☐	☐	☐
6. Mental fatigue	☐	☐	☐	☐	☐
7. Slow	☐	☐	☐	☐	☐
8. Mind went blank	☐	☐	☐	☐	☐
9. Spacey	☐	☐	☐	☐	☐
10. Difficulty processing what others say	☐	☐	☐	☐	☐
11. Exhausted	☐	☐	☐	☐	☐
12. Easily distracted	☐	☐	☐	☐	☐
13. Difficulty processing words read	☐	☐	☐	☐	☐
14. Confused	☐	☐	☐	☐	☐
15. Annoyed	☐	☐	☐	☐	☐
16. Sleepy	☐	☐	☐	☐	☐
17. Lost	☐	☐	☐	☐	☐
18. Detached	☐	☐	☐	☐	☐
19. Thoughts moving too quickly	☐	☐	☐	☐	☐

Exploratory Scale: Not validated in IH

Total Score:

- Range: 0-76
- Higher score = more symptoms/more severe symptoms
- Neutral = 38

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Phase 2 Trial Results Showed a Reduction in Brain Fog Symptoms

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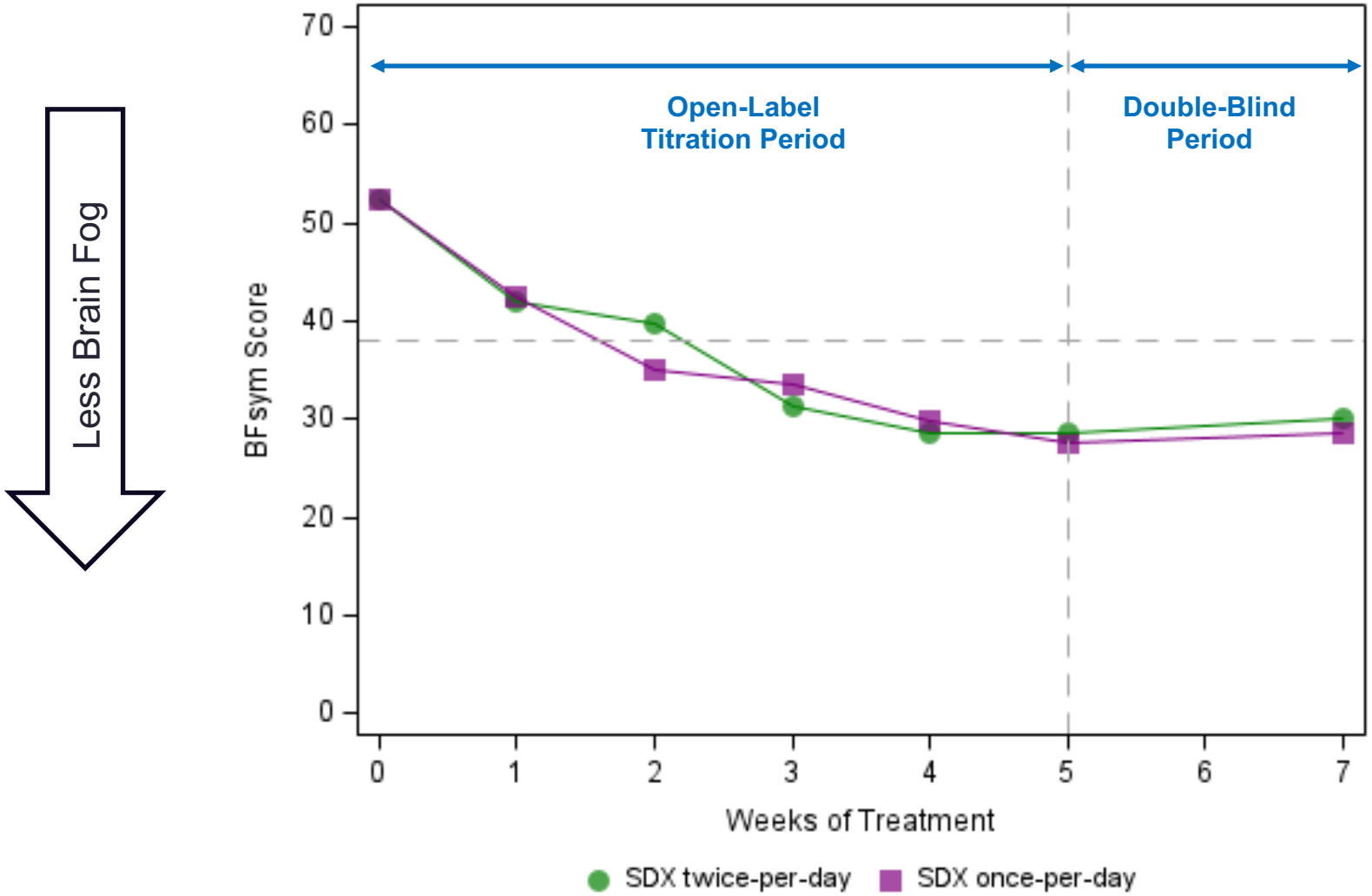
Captures patient-reported answers to 19 questions, rating the symptoms of brain fog



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Conclusions from the Phase 2 Trial

- KP1077 was well tolerated in people with IH, after either once-per-day or twice-per-day dosing
- Meaningful improvements in daytime sleepiness, sleep inertia, and brain fog were reported by the trial participants for both dosing regimens
- Results provided valuable information for the design of a potential Phase 3 trial needed for approval by FDA

- See **Poster Board 271** at the Sleep 2024 Conference, on June 3, 2024, for more information about the Phase 2 trial results

Zevra Therapeutics thanks the participants and investigators who made the Phase 2 trial possible

FDA, US Food and Drug Administration
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Questions and Answers

Thank you!

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