Vibrance-3: Study Design and Methods for a Phase 2, Randomized, Placebo-Controlled, Parallel-Group Study Evaluating the Safety and Efficacy of ALKS 2680 in Patients With Idiopathic Hypersomnia

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INTRODUCTION

- Idiopathic hypersomnia (IH) is a central disorder of hypersomnolence characterized by excessive daytime sleepiness (EDS), with sleep inertia, long/unrefreshing naps, and prolonged nighttime sleep[1]
- Orexin acts as a key regulator of wakefulness via activation of multiple downstream wake-promoting pathways[2]
- Targeting the orexin system may address EDS across hypersomnolence disorders with orexin deficiency (narcolepsy type 1 [NT1]) and without orexin deficiency (eg, narcolepsy type 2 [NT2], IH)[3]
- Unlike NT1, IH is not characterized by a loss of orexin-producing neurons or low endogenous central nervous system orexin levels
- ALKS 2680 is a highly potent, oral, and selective orexin 2 receptor agonist being developed as a once-daily treatment for narcolepsy and IH
- In a phase 1b study in patients with IH, single doses of ALKS 2680 at 5, 12, and 25 mg demonstrated statistically significant, clinically meaningful improvements in mean sleep latency, improved self-reported alertness on the Karolinska Sleepiness Scale, and were generally well tolerated[4,5]
- The results of the phase 1b study demonstrated that ALKS 2680 may have clinical benefits for patients with IH and helped inform dose selection for the Vibrance-3 phase 2 study
  - ALKS 2680 is also being evaluated in patients with NT1 and NT2 in the phase 2 Vibrance-1 (NCT06358950) and Vibrance-2 (NCT06555783) studies, respectively

OBJECTIVE

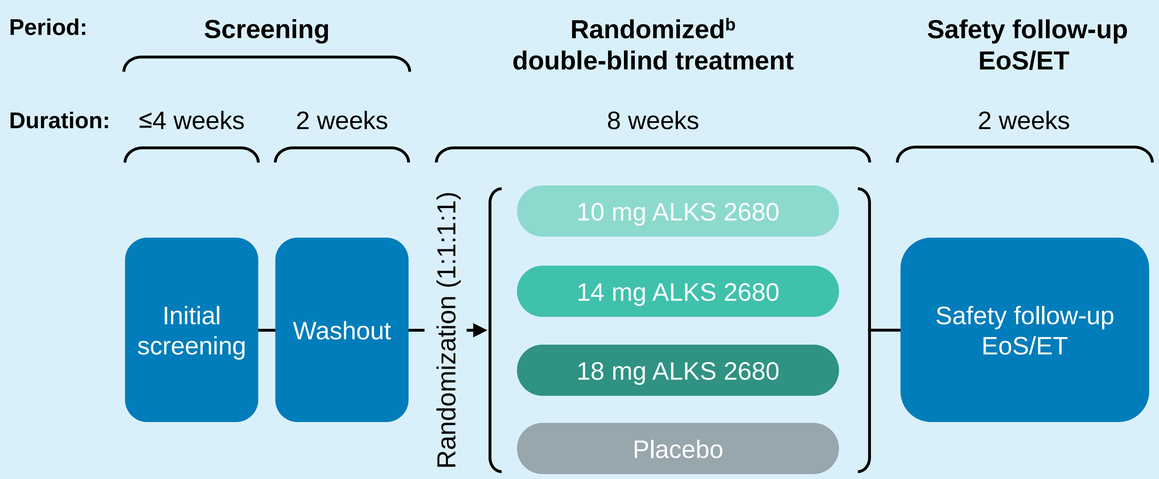
- The Vibrance-3 study (ClinicalTrials.gov identifier: NCT06843590)[6] aims to assess the safety and efficacy of once-daily ALKS 2680 compared with placebo through 8 weeks of treatment in adults with IH

METHODS

STUDY DESIGN

- Vibrance-3 is a phase 2, randomized, double-blind, placebo-controlled, parallel-group, dose-range–finding study (**Figure 1**)[6]
- Following a 2-week washout period from current standard of care, patients will be randomized 1:1:1:1 to receive placebo or ALKS 2680 once daily at doses of 10, 14, or 18 mg for 8 weeks
- Patients who complete Vibrance-3 may be eligible to roll over into a separate open-label, long-term extension study (NCT06767683)

FIGURE 1: Vibrance-3 Study Design[a]



[a]The study is being conducted in the USA, Australia, and Europe. [b]Randomization will stratify by region (USA and rest of world) and by the duration of nighttime sleep (<9 hours, 9-11 hours, and >11 hours).
EoS = end of study; ET = early termination.

STUDY POPULATION

- Planned enrollment is approximately 96 patients with IH
- Key inclusion and exclusion criteria are described in **Figure 2**

FIGURE 2: Key Inclusion and Exclusion Criteria

Inclusion Criteria[6,a]

- Adults ≤70 years of age[6]
- BMI ≥18 and ≤40 kg/m^2
- Meets the diagnostic criteria of IH according to ICSD-3-TR guidelines[6,7]
- Has residual excessive daytime sleepiness (ESS score >12 at the end of the screening period)
- Able to discontinue any medications prescribed for the management of IH symptoms, as well as any medications that may impact sleep or wake, for the duration of the study

Exclusion Criteria[6,a]

- Presence of other significant comorbid medical conditions, including other sleep, cardiovascular, and psychiatric disorders

[a]Additional criteria apply. Eligibility will be determined on an individual basis by the study investigator.
BMI = body mass index; ESS = Epworth Sleepiness Scale; ICSD-3-TR = *International Classification of Sleep Disorders, Third Edition, Text Revision*; IH = idiopathic hypersomnia.

STUDY ENDPOINTS

- Primary, secondary, and exploratory endpoints are summarized in **Figure 3**

FIGURE 3: Study Endpoints

Primary Endpoint

- Change in ESS from baseline to Week 8[6]

Secondary Endpoints

- Change in IHSS from baseline to Week 8[6]
- Safety and tolerability parameters including TEAEs, clinical laboratory assessments, vital signs, ECG, and C-SSRS

Exploratory Endpoints

- Clinician- and patient-reported outcomes, including:
  - MWT
  - CGI-S
  - KSS
  - PGI-S
- Change in sleep stages as measured by EEG

CGI-S = Clinical Global Impression of Severity; C-SSRS = Columbia-Suicide Severity Rating Scale; ECG = electrocardiogram; EEG = electroencephalogram; ESS = Epworth Sleepiness Scale; IHSS = Idiopathic Hypersomnia Severity Scale; KSS = Karolinska Sleepiness Scale; MWT = Maintenance of Wakefulness Test; PGI-S = Patient Global Impression of Severity; TEAE = treatment-emergent adverse event.

SUMMARY

- Vibrance-3 is evaluating once-daily ALKS 2680 over 8 weeks in patients with IH
- To learn about participation or patient referrals for Vibrance-3, please visit vibrancestudies.com or ClinicalTrials.gov/study/NCT06843590

Visit vibrancestudies.com

Visit Vibrance-3 at ClinicalTrials.gov

References

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Disclosures

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