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Oveporexton for Narcolepsy Type 1

A Research Summary based on Dauvilliers Y et al. | 10.1056/NEJMoa2405847 | Published on May 15, 2025

WHY WAS THE TRIAL DONE?

Patients with narcolepsy type 1 have excessive daytime sleepiness caused by the loss of hypothalamic orexin-producing neurons. Oveporexton (TAK-861) is a highly selective oral orexin receptor 2–selective agonist that crosses the blood–brain barrier and has been shown to improve wakefulness in sleep-deprived healthy adults. Data on oveporexton in narcolepsy are needed.

HOW WAS THE TRIAL CONDUCTED?

Adults 18 to 70 years of age with narcolepsy type 1 were assigned to receive once- or twice-daily oveporexton or matching placebo for 8 weeks. The primary end point was the mean change from baseline to week 8 in average sleep latency, as assessed with the Maintenance of Wakefulness Test, a measure of a person's ability to stay awake under sleep-inducing conditions (range, 0 to 40 minutes; normal, ≥20).

TRIAL DESIGN

- Phase 2
- Double-blind
- Randomized
- Placebo-controlled
- Location: Australia, Europe, Japan, and the United States

RESULTS

The mean change from baseline in average sleep latency was significantly greater with each dose of oveporexton than with placebo. Adverse events were more common with oveporexton than with placebo. The most common adverse events with oveporexton were insomnia and increased urinary urgency and frequency; insomnia usually resolved within 1 week.

LIMITATIONS AND REMAINING QUESTIONS

- Although the oveporexton and placebo tablets were indistinguishable, functional unblinding was possible owing to differences in efficacy and side effects.
- These results need confirmation. A phase 3 trial has begun, and a long-term extension study is ongoing.

CONCLUSIONS

In adults with narcolepsy type 1, total daily oveporexton doses of up to 7 mg resulted in significant improvements in wakefulness over a period of 8 weeks.

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