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ADIS SUMMARY OF RESEARCH

# Adis Summary of Research: Effect of FT218, a Once-Nightly Sodium Oxybate Formulation, on Disrupted Nighttime Sleep in Patients with Narcolepsy: Results from the Randomized Phase III REST-ON Trial

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**Abstract**
Sodium oxybate is used to treat disrupted nighttime sleep due to narcolepsy, but patients need to awaken 2.5–4.0 h after their bedtime dose to take a second dose each night. FT218 is a once-nightly sodium oxybate (ON-SXB) extended-release formulation that avoids the need to wake up for a second dose. This Adis Summary of Research reports the effects of ON-SXB compared with placebo on nighttime sleep disruption in the phase III REST-ON trial. Patients with narcolepsy who received ON-SXB had improved perception of their sleep, including those patients also taking stimulants or wake-promoting agents.

This Adis Summary of Research summarizes the effects of FT218, a once-nightly sodium oxybate (ON-SXB) extended-release formulation, compared with placebo on nighttime sleep disruption in the phase III REST-ON trial [1].

## Background

- Narcolepsy is a chronic sleep disorder and disturbed or disrupted nighttime sleep is common in these patients.
- There are two main types of narcolepsy: with (type 1; NT1) or without (type 2; NT2) cataplexy (sudden loss of voluntary muscle control while awake).
- Sodium oxybate (SXB) is used to treat disrupted nighttime sleep due to narcolepsy, but has a short half-life requiring a second dose 2.5–4 h after the first dose each night.
- The extended release of ON-SXB avoids the need to wake up for a second dose.

**Study Objective**

The phase III randomized, double-blind REST-ON trial (NCT02720744) assessed the efficacy and safety of ON-SXB in people with narcolepsy. This article reported the impact of ON-SXB on nighttime sleep disruption in the REST-ON trial.

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## Study Design

### Study Interventions

Patients received ON-SXB with the dosage increasing at predefined intervals from 4.5 g, to 6 g, 7.5 g, and finally 9 g once nightly ($n = 111$) or placebo once nightly ($n = 111$) [Fig. 1].

### Study Endpoints

Change from baseline in: frequency of sleep stage transitions, nocturnal arousals (NAs), and patient-reported quality of sleep and refreshing nature of sleep.

### Patient Eligibility

Eligible patients were aged ≥ 16 years and diagnosed with narcolepsy (NT1 or NT2). Non-eligible patients were those previously treated with SXB (except use of SXB ≤ 4.5 g for ≤ 2 weeks and ≥ 1 year before study entry) or diagnosed with sleep apnea (apnea-hypoxis index ≥ 15) or any other sleep disorder known to cause excessive daytime sleepiness.

## Results

Patients receiving ON-SXB had improved nighttime symptoms on sleep (polysomnography) study (Table 1) and improved perception of their sleep (Table 2), compared with patients receiving placebo.

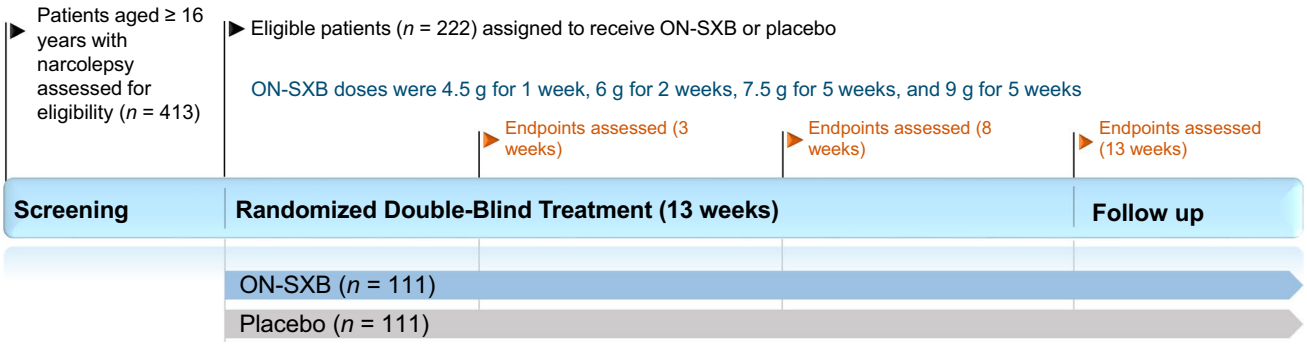


**Fig. 1** Trial design of the phase III REST-ON trial [1]. *ON-SXB* FT218 once-nightly sodium oxybate formulation

**Table 1** Efficacy of ON-SXB ($n$ = 97) and placebo ($n$ = 93) on sleep study secondary endpoints [1]

| | Assessment time | ON-SXB | PL |
|---|---|---|---|
| No. of sleep stage shifts | Week 3 | −9.7** | +1.3 |
| | Week 8 | −15.0** | +2.7 |
| | Week 13 | −20.5** | +2.1 |
| No. of nocturnal awakenings | Week 3 | −31.3* | −20.0 |
| | Week 8 | −39.3** | −19.8 |
| | Week 13 | −39.4** | −15.7 |

Change from baseline on polysomnography (least squares means) in modified intent-to-treat population

*ON-SXB* FT218 once-nightly sodium oxybate formulation, *PL* placebo

*$p < 0.05$, **$p < 0.001$ vs PL

**Table 2** Efficacy of ON-SXB ($n$ = 97) and placebo ($n$ = 93) on patient-reported outcomes (visual analog scale) [1]

| | Assessment time | ON-SXB | PL |
|---|---|---|---|
| Sleep quality | Week 3 | +11.9** | +5.0 |
| | Week 8 | +18.8** | +9.0 |
| | Week 13 | +21.4** | +11.0 |
| Refreshing nature of sleep | Week 3 | +13.0** | +6.7 |
| | Week 8 | +20.6** | +9.3 |
| | Week 13 | +23.8** | +12.4 |

Change from baseline (least squares means) in modified intent-to-treat population

*ON-SXB* FT218 once-nightly sodium oxybate formulation, *PL* placebo

**$p < 0.001$ vs PL

## Other Comments

- Results are for secondary endpoints, some of which were identified after study initiation (post hoc).
- ON-SXB reduced time in initial light sleep (N1) and rapid eye movement (REM) stages, and increased time spent in deep sleep (N3). It also increased delta wave power (a marker of deep sleep) and reduced the time to first REM sleep episode (REM latency) compared with placebo.
- Sleep measures improved with ON-SXB in patients who were or were not receiving stimulants, compared with those receiving placebo.

**Study Conclusion**

ON-SXB, a once-nightly formulation of SXB, improved the nighttime symptoms of narcolepsy, and improved patient perception of their sleep, including in those taking concomitant stimulants and/or wake-promoting agents.

## Declarations

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**Ethics approval, Consent to participate, Consent to publish, Availability of data and material, Code availability** Not applicable.

## Reference

1. Roth T, Dauvilliers Y, Thorpy MJ, et al. Effect of FT218, a once-nightly sodium oxybate formulation, on disrupted nighttime sleep in patients with narcolepsy: results from the randomized phase III REST-ON trial. CNS Drugs. 2022;36(4):377–87.