



Once-nightly sodium oxybate (FT218) improved symptoms in people with narcolepsy: a plain language summary of publication

Clete A Kushida, Michael J Thorpy, Julie Flygare, Asim Roy, Jordan Dubow & David Seiden

To cite this article: Clete A Kushida, Michael J Thorpy, Julie Flygare, Asim Roy, Jordan Dubow & David Seiden (2022) Once-nightly sodium oxybate (FT218) improved symptoms in people with narcolepsy: a plain language summary of publication, *Future Neurology*, 17:3, FNL60, DOI: [10.2217/fnl-2022-0005](https://doi.org/10.2217/fnl-2022-0005)

To link to this article: <https://doi.org/10.2217/fnl-2022-0005>



© 2022 The Authors



Published online: 14 Jul 2022.



Submit your article to this journal [↗](#)



Article views: 6474



View related articles [↗](#)



View Crossmark data [↗](#)

Plain Language Summary of Publication

Once-nightly sodium oxybate (FT218) improved symptoms in people with narcolepsy: a plain language summary of publication

Clete A Kushida¹, Michael J Thorpy², Julie Flygare³, Asim Roy⁴, Jordan Dubow⁵ & David Seiden⁵¹Stanford University School of Medicine, Redwood City, CA, USA; ²Department of Neurology, Montefiore Medical Center, New York, NY, USA;³Patient Author, Project Sleep, Los Angeles, CA, USA; ⁴Ohio Sleep Medicine and Neuroscience Institute, Dublin, OH, USA; ⁵Avadel Pharmaceuticals, Chesterfield, MO, USA

First draft submitted: 30 March 2022; Accepted for publication: 10 June 2022; Published online: 14 July 2022

Summary

What is this summary about?

This is a plain language summary of an article originally published in the journal *Sleep*. Once-nightly **sodium oxybate (ON-SXB)** for short; also known as FT218) is a potential treatment for excessive daytime sleepiness (EDS for short) and sudden muscle weakness known as **cataplexy**. The US Food and Drug Administration (FDA) is deciding whether to approve **ON-SXB** to be prescribed to adults with **narcolepsy**. The REST-ON clinical study looked at whether **ON-SXB** was better than a substitute that had no medicine in it (called a **placebo**) at treating **narcolepsy** symptoms.

How to say (double click to play sound)...

Sodium oxybate: SOH-dee-um AAK-see-bayt**Narcolepsy:** NAAR-kuh-lep-see**Cataplexy:** KAT-uh-plek-see

What were the results?

The results of this study showed that people who took **ON-SXB** were able to stay awake longer during the day, felt less sleepy in the daytime, had less **cataplexy**, and were more improved overall than people who took **placebo**. Common side effects with **ON-SXB** were nausea, vomiting, dizziness, bedwetting, and headache.

What do the results mean?

If approved by the FDA, people with **narcolepsy** may have the option to choose a form of **sodium oxybate** that they only have to take once at bedtime. They could avoid taking a second middle-of-the-night dose.

Who is this article for?

People with **narcolepsy**, their families, and their caregivers. Healthcare professionals may be interested to learn more, especially because people with narcolepsy may not always be diagnosed quickly.

Who sponsored this study?

Avadel Pharmaceuticals supported this work.

What is narcolepsy?



Narcolepsy is a disease that affects about 1 in 2000 people.

People with **narcolepsy** experience periods of extreme sleepiness during the day. Some also experience **cataplexy**. **Cataplexy** is a sudden muscle weakness. It is usually triggered by an emotion like laughter or surprise.

People who have **cataplexy** have **narcolepsy** type 1 (NT1 for short). People without **cataplexy** have **narcolepsy** type 2 (NT2 for short).

People with either type of **narcolepsy** may experience trouble sleeping at night, and have paralysis or hallucinations when falling asleep or upon awakening.

Narcolepsy can make it difficult for people to work or study and it can affect family relationships.



Why was the study carried out?

Doctors have used **sodium oxybate** to treat **narcolepsy** for over 20 years. People who take **sodium oxybate** need to take 2 doses every night. They take the first dose at bedtime and the second dose 2.5 to 4 hours later. Some people may find it hard to wake up in the middle of the night to take the second dose.



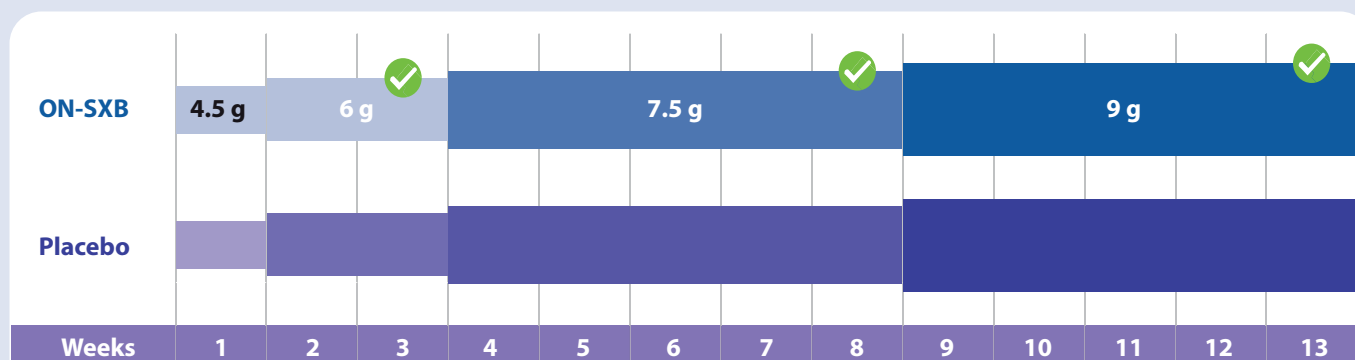
Once-nightly **sodium oxybate** (**ON-SXB** for short; also known as FT218) is a new form of **sodium oxybate** under review at the US Food and Drug Administration (FDA for short) that people with **narcolepsy** take once each night at bedtime. They do not need to wake up in the middle of the night to take a second dose.



The **REST-ON** clinical study looked at whether **ON-SXB** was better than **placebo** at treating **narcolepsy** symptoms.

How was the study carried out?

The timing of study treatment doses and tests for narcolepsy symptoms during REST-ON:



✓ Tests to see if **narcolepsy** symptoms improved were done at weeks 3, 8 and 13. Side effects could be reported at any time.

- REST-ON was a 13-week clinical study. Neither the participants in the study nor the people running the study knew whether they were taking **ON-SXB** or a substitute that had no medicine in it (called a **placebo**). This is known as a double-blind study. The study tested whether **narcolepsy** symptoms improved more with **ON-SXB** than with **placebo**.
- In REST-ON, about half of the participants took **ON-SXB**. The other half took **placebo**.
- People took
 - **ON-SXB** 4.5 g or **placebo** on week 1
 - **ON-SXB** 6 g or **placebo** on weeks 2 and 3
 - **ON-SXB** 7.5 g or **placebo** for weeks 4–8
 - **ON-SXB** 9 g or **placebo** for weeks 9–13
- They took the medicine at bedtime every night.

The REST-ON study used 3 main measures to see whether **ON-SXB** improved people's narcolepsy symptoms

1

Improvement on a test used to assess daytime sleepiness, called the **Maintenance of Wakefulness test**.

This test was done in a clinic after an overnight visit. It measured the average number of minutes they could stay awake when sitting quietly for half an hour. People took this test five times during the test day.

2

Clinical Global Impression of Improvement of "much" or "very much" improved.

A study doctor decided if the person seemed better, the same, or worse than they did at the start of the study.

- 1 — Very much improved
- 2 — Much improved
- 3 — Minimally improved
- 4 — No change
- 5 — Minimally worse
- 6 — Much worse
- 7 — Very much worse

3

Fewer weekly cataplexy episodes.

People in the study wrote down the number of cataplexy episodes they had each day in a sleep diary. This was only tested in people who had cataplexy episodes.

4

The researchers also looked at other measures such as a test called the **Epworth Sleepiness Scale (ESS)** for short). People rated how likely they were to doze off when doing 8 real-life situations (for example, watching television), on a scale from 0 ("never") to 3 ("high").

These tests were taken and scores were given at baseline, which is at the start of the study before they took any medication, and on weeks 3, 8, and 13.

5

The study also looked at side effects that were likely caused by **ON-SXB**. People reported any side effects they had during the study. The person's doctor decided if the side effect was caused by **ON-SXB**.

The Epworth Sleepiness Scale asks people to rate how likely they are to doze off in certain situations. Examples of these situations from the ESS are below:

- Sitting and reading
- Watching television
- Sitting inactive in a public place
- As a passenger in a car for 1 hour
- Lying down to rest in the afternoon
- Sitting and talking to someone
- Sitting quietly after lunch
- In a car, stopped for a few minutes in traffic

The scale for each question goes from 0 ("never") to 3 ("high"). A score of 24 means the person is extremely sleepy. A score between 0 and 10 is considered to be the normal range. People who do not have excessive daytime sleepiness typically would rate themselves in this range.

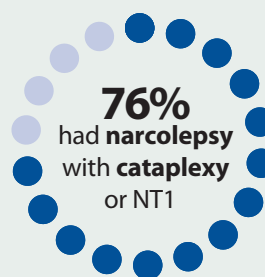
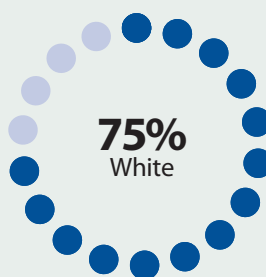
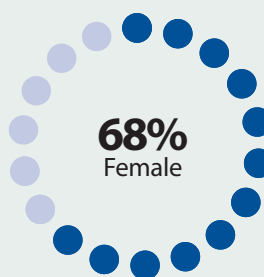
Who took part in the study?

212 people

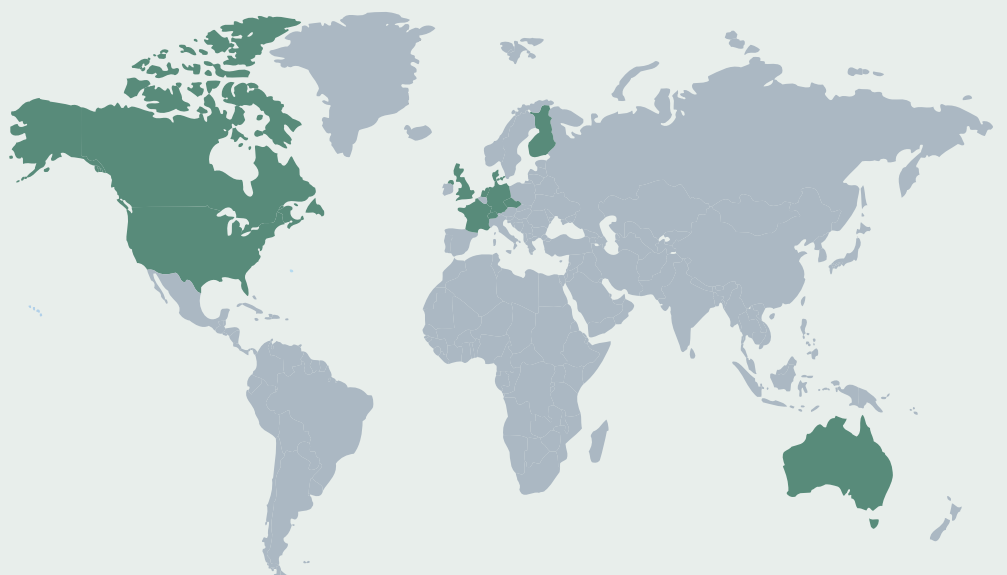
Took part in REST-ON and took at least 1 dose of drug

16–72 years

The average age was 31 years old



About half of the people lived in the USA. The rest lived in Australia, Canada, Czech Republic, Denmark, Finland, France, Germany, the Netherlands, Switzerland or the UK.

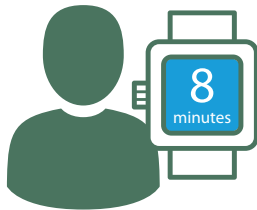


What were the overall results of the study?

1

Participants who took **ON-SXB** did better on the Maintenance of Wakefulness test and stayed awake longer at all 3 **ON-SXB** doses than those who took a **placebo**.

At week 3 with the 6 gram **ON-SXB** dose:

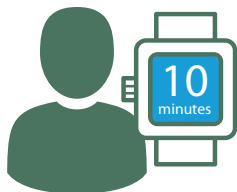


Participants who took **ON-SXB** were able to stay awake on average 8 minutes longer.



Participants who took a **placebo** were able to stay awake about 3 minutes longer.

At week 8 with the 7.5 gram **ON-SXB** dose:

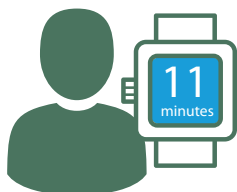


Participants who took **ON-SXB** were able to stay awake on average almost 10 minutes longer.



Participants who took a **placebo** were able to stay awake about 3 minutes longer.

At the end of the study (week 13), participants who took 9 grams of **ON-SXB** improved more than those who took a **placebo**:



Participants who took **ON-SXB** were able to stay awake on average almost 11 minutes longer.



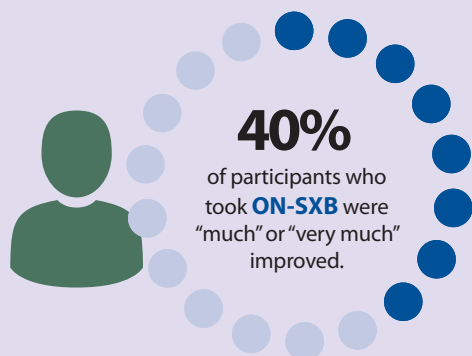
Participants who took a **placebo** were able to stay awake almost 5 minutes longer.

These results were highly statistically significant. This means that it is unlikely that they were due to chance. It is quite likely that these results are due to **ON-SXB**.

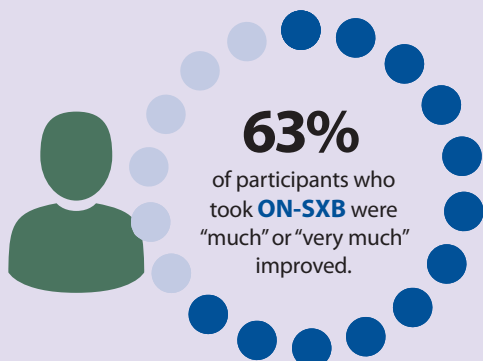
2

More participants who took **ON-SXB** were considered to be “much” or “very much” improved at all 3 doses compared to those who took **placebo**.

At week 3 with 6 grams of **ON-SXB**:



At week 8 with 7.5 grams of **ON-SXB**:



At the end of the study (week 13) with 9 grams of **ON-SXB**:



These results were highly statistically significant. This means that it is unlikely that they were due to chance. It is quite likely that these results are due to **ON-SXB**.

3

Participants who took **ON-SXB** had fewer **cataplexy** episodes at all 3 doses than those who took **placebo**.

At week 3 with the 6 gram **ON-SXB**:

Participants who took **ON-SXB** had about 7 fewer **cataplexy** episodes per week



Participants who took **placebo** had about 3 fewer **cataplexy** episodes per week



At week 8 with 7.5 grams of **ON-SXB**:

Participants who took **ON-SXB** had about 10 fewer **cataplexy** episodes per week



Participants who took **placebo** had about 4 fewer **cataplexy** episodes per week



At the end of the study (week 13) with 9 grams of **ON-SXB**:

Participants who took **ON-SXB** had about 12 fewer **cataplexy** episodes per week



Participants who took **placebo** had about 5 fewer **cataplexy** episodes per week

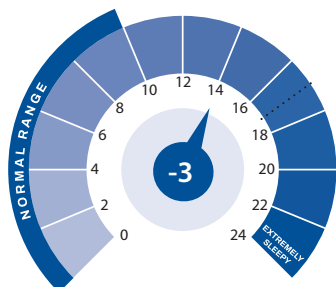


These results were highly statistically significant. This means that it is unlikely that they were due to chance. It is quite likely that these results are due to **ON-SXB**.

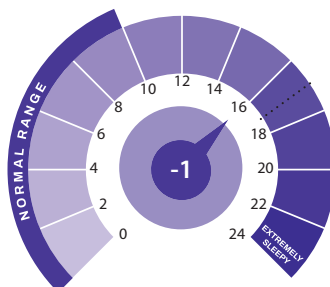
4

At weeks 3, 8, and 13, participants who took **ON-SXB** rated themselves as less sleepy on the Epworth Sleepiness Scale than those who took **placebo**.

At week 3 with 6 grams of **ON-SXB**:

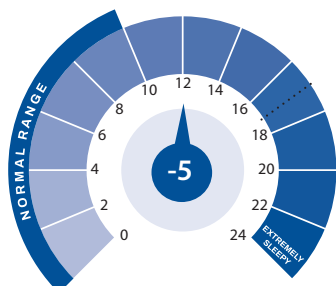


Participants who took **ON-SXB** had scores that were lower by about 3 points

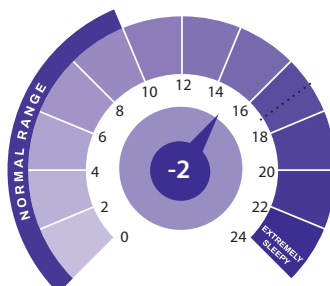


Participants who took **placebo** had scores that were lower by about 1 point

At week 8 with 7.5 grams of **ON-SXB**:

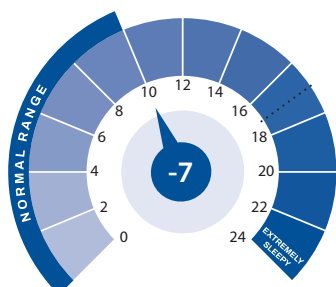


Participants who took **ON-SXB** had scores that were lower by about 5 points

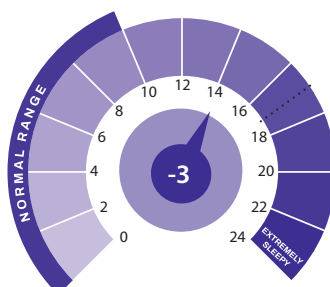


Participants who took **placebo** had scores that were lower by about 2 points

At the end of the study (week 13) with 9 grams of **ON-SXB**:



Participants who took **ON-SXB** had scores that were lower by almost 7 points



Participants who took **placebo** had scores that were lower by almost 3 points

The average score with **ON-SXB** at the end of the study was 10.4 points out of 24 points and was 14.9 points out of 24 points for people who took **placebo**.

These results were highly statistically significant. This means that it is unlikely that they were due to chance. It is quite likely that these results are due to **ON-SXB**.

What were the most common side effects?

5

The most common side effects that doctors thought were due to **ON-SXB** were:



Dizziness



Nausea and vomiting



Headache



Bedwetting

Side effects happened more often when **ON-SXB** was first started and when the dose increased. The side effects tended to happen less often if a person continued to take their **ON-SXB** dose.

Side effects with **ON-SXB** in REST-ON:

Side effect	Vomiting	Nausea	Weight loss	Loss of appetite	Dizziness	Sleepiness	Headache	Bedwetting	Anxiety	Sleepwalking
Placebo	2% (2 of 105)	3% (3 of 105)	None (0 of 105)	None (0 of 105)	None (0 of 105)	1% (1 of 105)	6% (6 of 105)	None (0 of 105)	1% (1 of 105)	None (0 of 105)
ON-SXB 4.5 g	3% (3 of 107)	6% (6 of 107)	1% (1 of 107)	4% (4 of 107)	6% (6 of 107)	None (0 of 107)	7% (7 of 107)	2% (2 of 107)	3% (3 of 107)	1% (1 of 107)
ON-SXB 6 g	3% (3 of 97)	8% (8 of 97)	None (0 of 97)	4% (4 of 97)	4% (4 of 97)	1% (1 of 97)	5% (5 of 97)	4% (4 of 97)	None (0 of 97)	2% (2 of 97)
ON-SXB 7.5 g	6% (5 of 88)	7% (6 of 88)	None (0 of 88)	3% (3 of 88)	6% (5 of 88)	2% (2 of 88)	6% (5 of 88)	9% (8 of 88)	3% (3 of 88)	None (0 of 88)
ON-SXB 9 g	5% (4 of 77)	1% (1 of 77)	4% (3 of 77)	3% (2 of 77)	5% (4 of 77)	4% (3 of 77)	None (0 of 77)	9% (7 of 77)	1% (1 of 77)	None (0 of 77)

What do the results of this study mean?

- The REST-ON study results show that **ON-SXB** works to treat **narcolepsy** symptoms in some people and that people could usually tolerate the medicine.
- On average, people who took 6 g, 7.5 g, or 9 g of **ON-SXB** were able to stay awake longer during the day, were **less sleepy, felt better overall**, and **had fewer cataplexy episodes than people who took a placebo**.
- If approved by the FDA, people with **narcolepsy** may have the option to choose an SXB drug that they only have to take once at bedtime. **They could avoid taking a second middle-of-the-night dose.**
- **People should talk to their doctors or healthcare providers about the best narcolepsy medicine for them.**



Where can readers find more information on this study?

The original article is called “Once-nightly **sodium oxybate** (FT218) demonstrated improvement of symptoms in a phase 3 randomized clinical trial in patients with **narcolepsy**” and was published in *Sleep* in 2022. This paper is free to access. You can access the paper using the links below:

- <https://pubmed.ncbi.nlm.nih.gov/34358324/>
- <https://academic.oup.com/sleep/article/45/6/zsab200/6343406>

You can read more about the REST-ON study at the following website:

- Enter the trial number NCT02720744 into the “Other terms” search field at www.clinicaltrials.gov

The Epworth Sleepiness Scale is available here:

- <https://epworthsleepinessscale.com/about-the-ess/>

You can find additional information about the Epworth Sleepiness Scale here:

- <https://sleep.hms.harvard.edu/education-training/public-education/sleep-and-health-education-program/sleep-health-education-90>

You can find more information about **narcolepsy** at these websites:

- www.ninds.nih.gov
- <https://project-sleep.com>
- www.narcolepsydisrupts.com
- <https://narcolepsynetwork.org>

Acknowledgments

The authors thank the people who took part in the REST-ON study and their families. People who participate in clinical studies play a key role in advancing science and medicine and we would like to acknowledge the people who participated in this study.

Financial & competing interests disclosure

CA Kushida (Department of Psychiatry and Behavioral Sciences, Stanford University Medical Center, Redwood City, CA, USA) has received payment for consulting or serving on advisory boards for Avadel Pharmaceuticals, XW Pharma, and Jazz Pharmaceuticals. MJ Thorpy (Department of Neurology, Montefiore Medical Center, New York, NY, USA) has received payment for speaking, consulting, or serving on advisory boards for Axsome Therapeutics, Balance Therapeutics, Eisai, Avadel Pharmaceuticals, Harmony Biosciences, Jazz Pharmaceuticals, NLS Pharmaceuticals, Suven Life Sciences Ltd., and Takeda Pharmaceutical Co. J Flygare (Project Sleep) has received payment for consulting for Avadel Pharmaceuticals and Jazz Pharmaceuticals, and for presenting to employees and at a focus group meeting of payer representatives for Takeda Pharmaceuticals Co. A Roy (Ohio Sleep Medicine and Neuroscience Institute, Dublin, OH, USA) has received grant/research support for Jazz Pharmaceuticals, Suven, Inspire, Nyxoah, LivaNova, and Avadel Pharmaceuticals and has received payment for speaking, consulting, or serving on advisory boards for Jazz Pharmaceuticals, Suven, Inspire, and Avadel Pharmaceuticals. J Dubow is a former employee of Avadel Pharmaceuticals and has received payment for consulting to Avadel. D Seiden is an employee of Avadel Pharmaceuticals.

Medical writing support was provided by Jennifer Fetting, PhD, of The Curry Rockefeller Group, LLC (Tarrytown, NY, USA). Avadel funded the medical writing support and journal publishing costs of this plain language summary of the publication and reviewed the final draft for scientific accuracy and readability.