A Randomized, Double-blind, Placebo-Controlled Study to Evaluate the Efficacy, Safety, and Tolerability of TAK-861 for the Treatment of Narcolepsy Without Cataplexy (Narcolepsy Type 2)

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Primary:- To assess the effect of TAK-861 on EDS as measured by sleep latency from the MWT.Secondary:- To assess the effect of TAK-861 on EDS as measured by the Epworth Sleepiness Scale (ESS) total score. - To evaluate the safety and tolerability of...

Ethical review	Approved WMO
Status	Pending
Health condition type	Sleep disturbances (incl subtypes)
Study type	Interventional

Summary

ID

NL-OMON53780

Source
ToetsingOnline

Brief title
TAK-861-2002

Condition

- Sleep disturbances (incl subtypes)

Synonym
Narcolepsy type 2, sleeping disorder

Research involving
Human

Sponsors and support

Primary sponsor: Takeda Development Center Americas, Inc.
Source(s) of monetary or material Support: The sponsor as completed in section B7.

Intervention

Keyword: Narcolepsy type 2, Phase 2, TAK-861

Outcome measures

Primary outcome

Change from baseline to Week 8 in mean sleep latency from the MWT.

Secondary outcome

- Change from baseline to Week 8 in ESS total score.

- Occurrence of at least 1 TEAE.

For additional / exploratory endpoints please refer to the study protocol.

Study description

Background summary

This study is designed to evaluate the efficacy, safety, and tolerability of multiple oral doses of TAK-861 in participants with narcolepsy without cataplexy (narcolepsy type 2 [NT2]).

Narcolepsy without cataplexy, or NT2, has been defined in the International Classification of Sleep Disorders, 3rd Edition (ICSD-3) criteria as having EDS with mean sleep latency of <=8 minutes and 2 or more sleep onset REM periods (SOREMPs) on Multiple Sleep Latency Test (MSLT) (or with 1 SOREMP on preceding polysomnography (PSG) replacing 1 SOREMP on MSLT). Patients with NT2 do not have cataplexy, and cerebrospinal fluid (CSF) levels of orexin (OX) are greater than 110 pg/mL, or greater than one-third of the normal average. The presumed pathophysiology of NT2 is unclear. However, as many as 30% of patients with narcolepsy without cataplexy are found to have CSF OX levels that are lower than normal.

TAK-861 is a selective agonist of OX2R that has demonstrated wake-promoting effects even in the absence of OX deficiency. Nonclinical pharmacology studies showed wake-promoting effects of TAK-861 in a murine narcolepsy model and also in mice and nonhuman primates with no known OX deficiency. In TAK-861-1002, single doses of TAK 861 40 mg and 15 mg demonstrated a significant improvement in the objective and subjective measures of wakefulness assessed in an acute sleep delayed paradigm model in healthy adults. The available nonclinical information and emerging clinical safety, tolerability, and PK profiles of single and multiple doses of TAK-861 in healthy participants in the TAK-861-1001 study support this study.

Study objective

Primary:
- To assess the effect of TAK-861 on EDS as measured by sleep latency from the MWT.

Secondary:
- To assess the effect of TAK-861 on EDS as measured by the Epworth Sleepiness Scale (ESS) total score.
- To evaluate the safety and tolerability of TAK-861.

Please refer to the study protocol for additional / exploratory objectives.

Study design

This is a randomized, double-blind, placebo-controlled, multicenter, 8-week parallel group study to evaluate the efficacy, safety, and tolerability of 2 oral dose regimens of TAK-861.

Approximately 60 (male and female) participants with NT2, who satisfy the inclusion and exclusion criteria, will be randomized such that a participant has an equal chance of being assigned to any 1 of 3 arms: 2 TAK-861 dose regimens or matching placebo. Randomization will be stratified by region. Starting on the morning of Day 1, the study drug will be administered at approximately the same time each day for 8 weeks.

Participants who have provided informed consent will complete a screening period of up to 45 days (see protocol body, Section 6.8.1 for different washout periods) to washout any NT2 medication (if applicable). Participants will be asked to complete an eDiary, starting from the initial screening visit, no later than Day -16.

Participants will remain confined overnight at the study site during the following times:
- Days -2 to 1 (1 mandatory overnight at Day -2; 1 optional overnight at Day

-1).
- Days 27 to 28 (1 overnight).
- Days 55 to 56 (1 overnight).

After the Week 8 visit, participants will have the option to participate in a long-term extension (LTE) study under a separate protocol (assuming protocol is open for enrollment). Participants who enroll in the LTE study will not have follow-up visits captured under this study protocol.

For participants who do not participate in the LTE study, every effort should be deployed to have them complete a first follow-up visit approximately 7 days after the final study drug intake and a second follow-up visit (home healthcare visit) approximately 28 days after the final study drug intake. For participants who early terminate the study, every effort should be deployed to have them complete an early termination visit as soon as possible and a follow-up visit (in-clinic visit or home healthcare visit if available) approximately 28 days after the last dose of study drug. Participants not participating in the LTE study can restart their discontinued medications after the first follow-up visit or early termination visit.

Intervention

The following treatments will be administered orally:
• TAK-861 Dose Regimen 1: 2 mg twice daily approximately 3 hours apart
• TAK-861 Dose Regimen 2: 7 mg once daily (QD) or 2 mg followed by 5 mg approximately 3 hours apart
• Matching placebo

Dose Regimen 2 (7 mg total daily dose) will be administered as either 7 mg QD or 2 mg followed by 5 mg; the decision will be made before randomization of the first participant.

Study treatment will be administered at approximately 8 am and 11 am. (Participants assigned to a QD dose regimen will receive placebo for the second dose.) Study treatment will be administered for 8 weeks.

Study burden and risks

Section E describes the burden and risks of participation as well as the (possible) benefit.

Review of available nonclinical and clinical data, including the nonserious, mild TEAEs reported in ongoing Study TAK-861-1001 and TAK-861-1002, supports a favorable benefit-risk ratio for this study with TAK 861. Refer to the latest version of the TAK-861 IB for the overall benefit/risk assessment and the most current information regarding drug metabolism, PK, efficacy, and safety of TAK

861.

Please refer to protocol section 2.3 for a detailed benefit/risk assessment.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

1. The participant is aged 18 to 70 years, inclusive, at the time of signing the informed consent form (ICF).
2. The participant has an International Classification of Sleep Disorders, 3rd edition (ICSD-3) diagnosis of NT2 by preceding polysomnography (PSG)/ multiple sleep latency test (MSLT), performed within the past 5 years.

Note: If there is a potential participant with NT2 for whom a diagnostic nocturnal polysomnography (nPSG)/MSLT was performed more than 5 years ago or is

not available, the site may repeat the diagnostic PSG/MSLT.

Exclusion criteria

1. The participant has a current medical disorder, other than narcolepsy without cataplexy, associated with EDS.
2. The participant has history of epilepsy, seizure, or convulsion, or has a family history of inherited disorders associated with seizure (except for a single febrile seizure in childhood).
3. The participant has one or more of the following psychiatric disorders:
a. Any current unstable psychiatric disorder.
b. Current or history of manic or hypomanic episode, schizophrenia or any other psychotic disorder, including schizoaffective disorder, major depression with psychotic features, bipolar depression with psychotic features, obsessive compulsive disorder, mental retardation, organic mental disorders, or mental disorders due to a general medical condition as defined in the Diagnostic and Statistical Manual of Mental Disorders, 5th Edition (DSM-5).
c. Current diagnosis or history of substance use disorder as defined in the DSM-5. Note: If the history of substance use disorder is more than 12 months before baseline, the participant may be allowed to enroll in the study after consultation with the sponsor or designee. (Participant must also have negative urine drug screen at the screening and Day -2 visit.)
d. Current active major depressive episode (MDE) or who have had an active MDE in the past 6 months.
4. The participant has a history of cerebral ischemia, transient ischemic attack (<5 years ago), intracranial aneurysm, or arteriovenous malformation.
5. The participant had major surgery or donated or lost 1 unit of blood (approximately 500 mL) within 4 weeks before the screening visit.

Study design

Design

Study phase:	2
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-05-2023
Enrollment:	2
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	Not yet available
Generic name:	Not yet available

Ethics review

Approved WMO Date:	12-12-2022
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	21-03-2023
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	05-05-2023
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	09-08-2023
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	14-08-2023

Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	24-08-2023
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
EudraCT	EUCTR2022-002966-34-NL
ClinicalTrials.gov	NCT05687916
CCMO	NL82934.100.22