A Randomized, Double-blind, Placebo-Controlled Study to Evaluate the Efficacy, Safety, and Tolerability of TAK-861 for the Treatment of Narcolepsy With Cataplexy (Narcolepsy Type 1)

Published: 05-12-2022
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Primary: - To assess the effect of TAK-861 on excessive daytime sleepiness (EDS) as measured by sleep latency from the Maintenance of Wakefulness Test (MWT).Please refer to the Study protocol for detailed description on the secondary Objective of...

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

Summary

ID

NL-OMON53459

Source
ToetsingOnline

Brief title
TAK-861-2001

Condition

- Sleep disturbances (incl subtypes)

Synonym
narcolepsy with cataplexy / sleep disorders

Research involving
Human

Sponsors and support

Primary sponsor: Takeda
Source(s) of monetary or material Support: Takeda Development Center Americas;Inc

Intervention

Keyword: Cataplexy, Narcolepsy, 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.

- WCR at Week 8

- Occurrence of at least 1 treatment-emergent adverse event (TEAE).

Please refer to protocol section for a detailed Secondary study parameters.

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 type 1 (NT1).

Narcolepsy with cataplexy, or NT1, has been defined by International Classification of Sleep Disorders, 3rd Edition (ICSD-3) criteria as having low levels of orexin (OX) in the cerebrospinal fluid (CSF) (<=110 pg/mL, or less than one-third of normal levels), resulting from the nearly complete loss of OX-producing neurons. An orexin type-2 receptor (OX2R) agonist is thus the first approach to directly address the loss of OX peptide in the brain in as it may restore OX2R signaling at the postsynaptic receptors and may be more effective than current therapies in treating the entire NT1 pentad, especially EDS and cataplexy.

Please refer to the Introduction section, study background detailed in the study protocol.

Study objective

Primary:
- To assess the effect of TAK-861 on excessive daytime sleepiness (EDS) as measured by sleep latency from the Maintenance of Wakefulness Test (MWT).

Please refer to the Study protocol for detailed description on the secondary Objective of the study.

Study design

This is a randomized, double-blind, placebo-controlled, multicenter, 8-week parallel group study to evaluate the efficacy, safety, and tolerability of 4 oral dose regimens of TAK-861.

Please refer to the Study Design detailed in the Study protocol.

Intervention

Arm 1 - dose of 1mg app 3 hours apart
Arm 2 - dose of 4mg app 3h apart
Arm 3 - dose 2mg follow 5mg app 3h apart
Arm 4 dose 7mg daily
Arm 5 matching placebo

As study is blinded patients in Arm 1-4 also will receive placebo

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, 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

Public
Takeda

Hayden Avenue 95
Lexington MA 02421
US
Scientific
Takeda

Hayden Avenue 95
Lexington MA 02421
US

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

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 body mass index (BMI) within the range 18 to 40 kilogram per square meter [kg/m^2] (inclusive).
3. The participant has an International Classification of Sleep Disorders, 3rd Edition (ICSD-3) diagnosis of narcolepsy type 1 (NT1) by polysomnography (PSG)/Multiple Sleep Latency Test (MSLT), performed within the past 10 years.
4. The participant is positive for the human leukocyte antigen (HLA) genotype HLA-DQB1*06:02 or results from cerebrospinal fluid (CSF) testing indicate the participant's CSF orexin (OX)/hypocretin-1 concentration is <110 picograms per milliliter ([pg/mL] (or less than one-third of the mean values obtained in

normal participants within the same standardized assay).

Exclusion criteria

1. The participant has a current medical disorder, other than narcolepsy with cataplexy, associated with EDS.
2. The participant has medically significant hepatic or thyroid disease.
3. The participant has a history of cancer in the past 5 years (does not apply to participants with carcinoma in situ that has been resolved without further treatment or basal cell cancer)
4. The participant has clinically significant coronary artery disease, a history of myocardial infarction, clinically significant angina, clinically significant cardiac rhythm abnormality, or heart failure.
5. The participant has a clinically significant history of head injury or head trauma.
6. 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).
7. 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, intellectual disability, 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.
d. Current active major depressive episode (MDE) or who have had an active MDE in the past 6 months.
8. The participant has a history of cerebral ischemia, transient ischemicattack (<5 years ago), intracranial aneurysm, or arteriovenous malformation.
9. The participant has a positive test result for hepatitis B surface antigen, hepatitis C virus antibody, or human immunodeficiency virus(HIV) antibody/antigen.
10. The participant's renal creatinine clearance (Cockcroft-Gault Equation) is <=50 mL/minute.
11. The participant has alanine aminotransferase (ALT) or aspartate aminotransferase (AST) values >1.5 times the upper limit of normal (ULN).
12. The participant is considered by the investigator to be at imminent risk of suicide or injury to self, others, or property, or the participant has attempted suicide within the past year.

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:	Recruiting
Start date (anticipated):	17-04-2023
Enrollment:	4
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	-
Generic name:	-

Ethics review

Approved WMO Date:	05-12-2022
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:	14-08-2023
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	15-08-2023
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	23-08-2023
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	EUCTR2022-001654-38-NL

Register	ID
ClinicalTrials.gov	NCT05687903
CCMO	NL82933.100.22