A Phase 2 Randomized, Double-Blind, Placebo-Controlled Study to Evaluate the Efficacy, Safety, Tolerability, and Pharmacokinetics of NBI-921352 as Adjunctive Therapy in Subjects with hSCN8A Developmental and Epileptic Encephalopathy Syndrome (SCN8A-DEE)

Published: 11-11-2021
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Main objective: To assess the efficacy of NBI-921352 as adjunctive therapy on the frequency of countable motor seizuresSecondary Objectives • To evaluate the efficacy of NBI-921352 using the Clinical and Parent/Caregiver Global Impression of Change...

Ethical review	Approved WMO
Status	Will not start
Health condition type	Encephalopathies
Study type	Interventional

Summary

ID

NL-OMON52008

Source
ToetsingOnline

Brief title
NBI-921352-DEE2012

Condition

- Encephalopathies

Synonym
Encephalopathy, Epilepsy

Research involving
Human

Sponsors and support

Primary sponsor: Neurocrine Biosciences, Inc.
Source(s) of monetary or material Support: pharmaceutical industry

Intervention

Keyword: Encephalopathy, Epilepsy

Outcome measures

Primary outcome

Percentage change from baseline in 28-day seizure frequency for countable motor seizures during the treatment period of the study.

Secondary outcome

• Treatment response of >= 50% decrease for countable motor seizures

• Treatment response of >= 25%, >= 75%, or 100% decrease in countable motor seizures

• Clinical Global Impression of Change (CGIC) at each study visit

• Parent/Caregiver Global Impression of Change (GIC) at each study visit

• Change from Baseline in Clinical Global Impression of Severity (CGIS)

• Change from Baseline in Parent/Caregiver Global Impression of Severity (GIS)"

Other secondary endpoints (maintenance period):

• Percentage Change from Baseline in 28-day Seizure Frequency for countable motor seizures

• Treatment response of >= 25%, >= 50%, >= 75%, or 100% decrease for countable

motor seizures

Study description

Background summary

This Phase 2 randomized, double-blind, placebo-controlled study is designed to evaluate the efficacy, safety, tolerability, and PK of NBI-921352 doses administered tid as adjunctive therapy in subjects with Developmental and Epileptic Encephalopathy Syndrome (SCN8A-DEE).

Study objective

Main objective:
To assess the efficacy of NBI-921352 as adjunctive therapy on the frequency of countable motor seizures

Secondary Objectives
• To evaluate the efficacy of NBI-921352 using the Clinical and Parent/Caregiver Global Impression of Change scales and the Clinical and Parent/Caregiver Global Impression of Severity scales.
• To characterize the pharmacokinetics of NBI-921352 and determine the effect of NBI-921352 on plasma levels of concomitant ASMs and evaluated metabolites.
• To evaluate the safety and tolerability of NBI-921352.

Study design

This is a Phase 2 randomized, double-blind, placebo-controlled study to evaluate the efficacy, safety, tolerability, and pharmacokinetics of NBI-921352 as adjunctive therapy in subjects with SCN8A-DEE. Approximately 52 male and female subjects will be randomized for study participation according to the study eligibility criteria. Subjects will be randomized 1:1 (NBI-921352:placebo).

Intervention

Subjects will be randomized 1:1 to NBI-921352 versus placebo. Both NBI-921352 and placebo will be administered orally. The starting dose of NBI-921352 will be based on the subject's weight at the screening visit. The dose will be titrated (increased) every week at each of the 2 lowest titration dose levels and every 2 weeks at each of highest titration dose levels. Subjects will continue to receive the highest tolerated dose during the maintenance period.

Study burden and risks

Subjects will participate in the study for the duration of 30 weeks. Subjects will need to come to the hospital more often than they normally would and undergo additional tests. These include physical and neurological examinations, ECGs, pregnancy tests, urine/blood/saliva tests, and questionnaires, including mental health assessments. Aside from these interventions, participation in this study involves blood draws (venipuncture) and in the course of 30 weeks (7-9 visits) 92-116 ml blood will be taken. Risks may include adverse effects of the study drug. Subjects may also feel discomfort during some of the tests.

Currently no therapies are indicated to treat SCN8A-DEE, and seizures in SCN8A-DEE patients are typically very resistant to existing antiseizure medications (ASMs). SCN8A-DEE patients are at risk for developmental delay, cognitive impairment, life-threatening status epilepticus, and SUDEP, and the lack of an effective therapy for these patients establishes a clear unmet medical need. The available NBI-921352 data suggest that targeting the VSD4 binding site enables the improved potency, selectivity, and favorable nonclinical safety profile of NBI-921352 relative to other sodium channel inhibitors.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (12-15 years)
Adolescents (16-17 years)
Adults (18-64 years)

Inclusion criteria

• Be a male or female 12 to 21 years of age, inclusive.
• Have a diagnosis of SCN8A-DEE supported by both clinical and genetic findings
• Have on average at least 1 countable motor seizure per week and not be seizure-free for more than 20 consecutive days.
• Being treated with at least 1 other ASM, but no more than 4 ASMs.
• Have failed to achieve seizure freedom with at least 2 ASMs.
• Must be using a nocturnal alerting system or practice consistent with standards of care at the time of screening and continue to use this for the duration of the study.
• Must have an adequate rescue medication regimen per the investigator's judgment in place at the time of screening and for the duration of the study.
• Have a body weight of at least 10 kg
• The subject's parent/caregiver is able to accurately identify seizure types, especially countable motor seizures and is able to complete seizure diary

Exclusion criteria

• Have previously been enrolled in this study and received blinded treatment.
• Have participated in an interventional clinical trial <30 days prior to screening.
• Have symptoms that would be more consistent with another epilepsy disorder such as Dravet syndrome (eg, fever-induced episodes of status epilepticus, frequent myoclonic seizures, worsening on sodium channel blockers, absence seizures with generalized spike-and-wave EEG as the sole seizure type).
• Are currently receiving cannabinoids or medical marijuana except Epidiolex/Epidyolex, unless approved by the Sponsor.
• Are currently taking systemic steroids (excluding inhaled medication for asthma treatments). If subject has received these medications in the past, must be off these medications for at least 3 months prior to the screening visit and these drugs may not be initiated during the duration of the study. Intermittent steroids to treat nonepilepsy related diseases (such as allergies or dermatological conditions) are not exclusionary.
• Have a history of moderate or severe head trauma or other neurological

disorders or systemic medical diseases that are, in the investigator's opinion, likely to affect nervous system functioning.
• Have a clinically significant medical condition or chronic disease that in the opinion of the investigator would preclude the subject from participating in and completing the study or that could confound interpretation of study outcome.
• Have clinically significant abnormal vital signs at the screening visit as determined by the investigator.
• Have one or more clinical laboratory test values outside the reference range, based on blood samples taken at the screening visit, that are of potential risk to the subject's safety
• Have, at the screening visit, an ECG finding of a corrected QT interval using Fridericia's formula (QTcF) >450 msec or presence of any significant cardiac abnormality.

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:	Will not start
Enrollment:	4
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	n/a
Generic name:	NBI-921352

Ethics review

Approved WMO Date:	11-11-2021
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	04-08-2022
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

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	EUCTR2020-003140-83-NL
ClinicalTrials.gov	NCT04873869
CCMO	NL79058.056.21

Study results

Summary results
Trial never started