A PHASE 3, MULTI-CENTER, DOUBLE-BLIND, RANDOMIZED, PLACEBO-CONTROLLED TRIAL TO EVALUATE THE EFFICACY AND SAFETY OF RELDESEMTIV IN PATIENTS WITH AMYOTROPHIC LATERAL SCLEROSIS (ALS)

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Neuromuscular disorders
Study type	Interventional

Summary

ID

NL-OMON52262

Source
ToetsingOnline

Brief title
COURAGE-ALS

Condition

- Neuromuscular disorders

Synonym
ALS, Amyotrophic Lateral Sclerosis

Research involving

Human

Sponsors and support

Primary sponsor: Cytokinetics Inc
Source(s) of monetary or material Support: Cyotkinetics Inc

Intervention

Keyword: ALS, Amyotrophic Lateral Sclerosis, reldesemtiv

Outcome measures

Primary outcome

The primary study outcome is the change from baseline to Week 24 in ALSFRS-R

total score.

Secondary outcome

The secondary outcomes of study are:

• Combined assessment of change in ALSFRS-R total score, time to onset of

respiratory insufficiency, and survival time up to Week 24

• Change from baseline to Week 24 in the percent predicted FVC

• Change from baseline to Week 24 in the

ALSAQ-40 total score

• Change from baseline to Week 24 in handgrip strength (average of both hands).

Study description

Background summary

Reldesemtiv, a fast skeletal muscle troponin activator (FSTA), is being investigated as a potential therapy to slow the decline of skeletal muscle function in patients with ALS. This pivotal trial with reldesemtiv is being conducted in ALS patients and is designed to assess the effect of reldesemtiv on functional outcomes during treatment up to 48 weeks. The first trial with reldesemtiv in ALS patients (FORTITUDE-ALS [CY 5022]) after 12 weeks of dosing, showed that patients on all doses of reldesemtiv tended to decline less than patients on placebo for slow vital capacity (SVC) and ALS Functional Rating Scale-Revised (ALSFRS-R), with larger and clinically meaningful differences emerging over time. The results support progression in a further clinical trial with a longer dosing duration.

Study objective

The purpose of this study is to evaluate whether the new drug reldesemtiv is effective and safe in patients with ALS.
The primary objective is to assess the effect of reldesemtiv versus placebo on functional outcomes in ALS.

The secondary objectives are:
• To assess the effect of reldesemtiv versus placebo on combined functional and survival outcomes in ALS

• To assess the effect of reldesemtiv versus placebo on ventilatory function

• To assess the effect of reldesemtiv versus placebo on quality of life

• To assess the effect of reldesemtiv versus placebo on handgrip strength.

Study design

This is a Phase 3, double-blind, randomized, placebo-controlled trial of reldesemtiv in patients aged 18 to 80 with ALS.

The screening and qualification period for the trial will be no more than 14 days in duration. Approximately 555 eligible ALS patients will be randomized (2:1) to receive the following dose of reldesemtiv or placebo (stratified by riluzole use/non-use and edaravone use/non-use) for the first 24 weeks (double-blind, placebo-controlled period):
• 300 mg reldesemtiv twice a day for a 600 mg total daily dose (TDD)
• Placebo twice daily
At the end of the 24-week double-blind, placebo-controlled period, patients will transition to the active drug period, where all patients will receive the following dose of reldesemtiv for the next 24 weeks:
• 300 mg reldesemtiv twice a day for a 600 mg TDD for patients who were not down titrated during the 24 weeks of blinded dosing

• 150 mg reldesemtiv twice a day for a 300 mg TDD for patients who were down titrated for any reason during the 24 weeks of blinded dosing

Intervention

• 300 mg reldesemtiv twice a day for a 600 mg total daily dose (TDD)
• Placebo twice daily
At the end of the 24-week double-blind, placebo-controlled period, patients will transition to the active drug period, where all patients will receive the following dose of reldesemtiv for the next 24 weeks:
• 300 mg reldesemtiv twice a day for a 600 mg TDD for patients who were not down titrated during the 24 weeks of blinded dosing
• 150 mg reldesemtiv twice a day for a 300 mg TDD for patients who were down titrated for any reason during the 24 weeks of blinded dosing

Study burden and risks

physical examination 2x
weight, BMI 8x
neurological examination 3x
ecg 5x
blood and urine sampling 17x
lung function tests16x
muscle strength tests 8x
questionnaires 15x
when participating in potential PK sub study: 7 additional blood samples

Contacts

Public
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Scientific
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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

Males or Females between the ages of 18 and 80 years of age, inclusive

• Diagnosis of familial or sporadic ALS (defined as meeting the laboratory-supported probable, probable, or definite criteria for ALS according to the World Federation of Neurology El Escorial criteria published in 2000 [Brooks 2000]). Patients who meet the possible criteria are eligible if they have lower motor neuron findings; those who have purely upper motor neuron findings are ineligible.

• First symptom of ALS <= 24 months prior to screening. The qualifying first symptoms of ALS are limited to manifestations of weakness in extremity, bulbar, or respiratory muscles. Cramps, fasciculations, or fatigue should not be taken in isolation as a first symptom of ALS.
• ALSFRS-R total score <= 44 at screening. Patients with a total score of 45 or higher may be rescreened 60±7 days following the original screening date and be deemed eligible if their ALSFRS-R total score is <= 44 or if their score is 2 or more points less than at initial screening.
Such patients must continue to meet all other inclusion/exclusion criteria at the time of rescreening.
• Upright FVC >= 65.0% of predicted for age, height, sex and ethnicity at screening according to
Global Lung Initiative equation
• Able to perform reproducible pulmonary function tests defined as being able to perform FVC at screening with variability of the 2 highest raw values of less than 10% with a maximum of 5 trials permitted. Screening FVC results must be reviewed and approved by the central review process prior to randomization.
• Must be either on riluzole for >= 30 days prior to screening or have not taken it for at least 30 days
prior to screening
• Must have completed at least 2 cycles of edaravone at the time of screening

or have not received it for at least 30 days prior to screening
• Able to swallow whole tablets at the time of screening
. Clinical laboratory findings within the normal range, or if outside the normal range, not deemed clinically significant by the Investigator, except as specifically indicated as laboratory exclusion

Exclusion criteria

• eGFRCr and eGFRCysC < 45.0 mL/min/1.73 m2 at screening

• Urine protein/creatinine ratio > 1 mg/mg (113 mg/mmol) at screening

• Alanine aminotransferase (ALT) or aspartate aminotransferase (AST) >= 3-times the upper limit of normal (ULN)

• Total bilirubin (TBL), direct or indirect bilirubin above the ULN.

• Cognitive impairment, related to ALS or otherwise that impairs the patient*s ability to understand and/or comply with study procedures and provide informed consent

• Other medically significant neurological conditions that could interfere with the assessment of ALS
symptoms, signs or progression.

• Presence at screening of any medically significant cardiac, pulmonary, gastrointestinal, musculoskeletal, or psychiatric illness that might interfere with the patient*s ability to comply with study procedures or that might confound the interpretation of clinical safety or efficacy data

• Has a tracheostomy

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial

Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	19-01-2022
Enrollment:	10
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	nvt
Generic name:	reldesemtiv

Ethics review

Approved WMO Date:	01-09-2021
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	25-11-2021
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	10-06-2022
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	11-07-2022
Application type:	Amendment
Review commission:	METC NedMec

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	EUCTR2020-004040-29-NL
CCMO	NL77133.041.21