A Phase 2, Multicenter, Randomized, Double-Blind, Placebo-Controlled Study Evaluating Safety and Efficacy of CORT113176 (Dazucorilant) in Patients with Amyotrophic Lateral Sclerosis (DAZALS)

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This study has been transitioned to CTIS with ID 2024-514082-19-00 check the CTIS register for the current data. The aim of this phase 2 study is to investigate the safety and efficacy of dazucorilant in the target ALS patient population.

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

Summary

ID

NL-OMON53408

Source
ToetsingOnline

Brief title
DAZALS

Condition

- Neuromuscular disorders

Synonym
Disease of nerve cells that control muscles, Neurodegenerative syndrome

Research involving

Human

Sponsors and support

Primary sponsor: Corcept Therapeutics
Source(s) of monetary or material Support: Corcept Therapeutics Incorporated

Intervention

Keyword: Amyotrophic Lateral Sclerosis (ALS), Dazucorilant, Efficacy, Safety

Outcome measures

Primary outcome

Primary Efficacy Endpoint

• Change from Baseline to Week 24 in the ALS Functional Rating Scale-Revised

(ALSFRS-R) total

score.

Primary Safety Endpoint

• Incidence of AEs, SAEs, treatment-related AEs, AEs by severity, and deaths

due to AEs.

Secondary outcome

• Change from Baseline to Week 24 in muscle strength (assessed using hand-held

dynamometer).

• Change from Baseline to Week 24 in:

* Percent Slow Vital Capacity

* EQ-5D-5L.

• Time to death.

• Time to respiratory support >22 hours per day for 7 days.

• Time to death or time to respiratory support >22 hours per day for 7 days.

• Combined Assessment of Function and Survival (CAFS).

• Plasma samples for pharmacokinetic (PK) analysis will be obtained in a

dedicated PK substudy in a subset (~20%) of patients at the Week 3 visit. The

dazucorilant AUC and Cmax will be reported.

Study description

Background summary

Amyotrophic lateral sclerosis (ALS) is a rare and fatal condition with insufficient treatment options. It is characterized by progressive degeneration of motor neurons in both the brain and spinal cord and leads to progressive muscle weakness, relentless disability and, generally, death within 3-5 years of the onset of symptoms. There are limited pharmacological options in ALS and they are mainly aimed at symptomatic treatment. The only existing authorized drug for the treatment of ALS in the European Union is Riluzole.

Dazucorilant has been selected for development based on promising results in mouse models of ALS. Efficacy has been demonstrated in the Wobbler mouse, a widely recognized model of ALS. Administration of dazucorilant for 21 days improved many aspects of the disease in these mice, including reducing forelimb atrophy, overcoming impaired performance in the rotarod test, and inhibiting neurodegeneration and inflammation.
In the phase 1 studies with dazucorilant, no significant safety risks were found and the most common side effects of dazucorilant were gastrointestinal complaints, headache and back pain.

Study objective

This study has been transitioned to CTIS with ID 2024-514082-19-00 check the CTIS register for the current data.

The aim of this phase 2 study is to investigate the safety and efficacy of dazucorilant in the target ALS patient population.

Study design

This is a multicenter, parallel-arm, placebo-controlled randomized, double-blind study. Adults meeting all inclusion and exclusion criteria will be

randomized to one of three treatment arms in a 1:1:1 ratio. In the 24-week double-blind treatment period, patients will be randomized to receive 150 mg of CORT113176, 300 mg of CORT113176, or a corresponding placebo once daily for 24 weeks. Randomization will be stratified by prior use of ALS drugs riluzole and/or edaravone (yes/no) and region of disease onset (bulbar/other). Study visits will be once every three weeks. Visits in weeks 9, 15 and 21 during the treatment period are remote and by telephone.

Patients who participated in the double-blind treatment period (i.e., completed all visits) are eligible to participate in a 132-week open-label extension (OLE) study. Participation in the OLE study is voluntary and a new informed consent form must be signed. Patients that have chosen to participate in the OLE must be enrolled within 28 days of the week 24 visit of the double-blind period. Clinic visits will be at baseline and in OLE-week 4, 12, 20, 24, 36, 52, 84, 100 and 116. Phone visits will take place in weeks 8, 16 and 20. A follow-up telephone visit will take place after 4 weeks at the end of the OLE-treatment (OLE-week 136) to collect safety information.

Patients who complete the double-blind treatment period and who choose not to participate in the OLE study enter the follow-up period of 132 weeks. Patients are contacted by telephone 4, 12, 24, 48, 74, 96, 120 and 132 weeks post-treatment to collect safety information and long-term follow-up information.

If a patient participate to the randomised, double-blind study and the OLE part, the maximal study duration for a patient would be 168 weeks.

Intervention

Patients are randomized in a 1:1:1 ratio to receive CORT113176 150 mg, CORT113176 300 mg, or placebo once daily. All patients, regardless of the arm to which they were randomized, will take one dose (corresponding to 4 capsules/dose) per day. Study drug is administered orally once daily with food and 240 ml of water, at approximately the same time each day.

Study burden and risks

The study medication may have side effects. It cannot be excluded that side effects will be serious, long lasting or permanent. All options will be used to minimize any discomfort. These side effects were found in previous studies with dazucorilant:
• abdominal pain (in about three in ten volunteers)
• abdominal discomfort (in about four in ten volunteers)
• back pain (in about two in ten volunteers)
• constipation (in about one in ten volunteers)
• diarrhea (in about one in ten volunteers)

• indigestion, or digestive complaints (in about one in ten volunteers)
• headache (in about seven in ten volunteers)
• decrease in platelet count in less than one in ten volunteers) during the treatment period.
The study medication may also have side effects that we don't know yet.

Other disadvantages are possible negative consequences as a result of the measurements during the study. In addition, the participant is asked to invest time in the study, visit the hospital for study visits and undergo research procedures.

Participating in this study may have medical benefits, but it is not certain. By participating, the participant can help physicians better understand the safety of the study drug and how well it works for the treatment of ALS. This may be valuable in the future for new patients with ALS.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age

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

Inclusion criteria

1. Male and female patients >=18 years of age with ALS as defined by Gold Coast Criteria.
2. Patients with sporadic or familial ALS with a risk of ALS progression characterized by an ENCALS risk profile score >=-6 and <= -3.
3.Regulatory-authority-approved therapies for the treatment of ALS are permitted. If taking riluzole and/or edaravone, and/or sodium phenylbutryte and taurursodial, must have been on a stable dose of riluzole for >=30 days and/or edaravone for >=60 days and/or sodium phenylbutyrate and taurursodial maintenance dosage >=30 days prior to Screening.
4. Medically able to undergo the study procedures and to adhere to the visit schedule at the time of study entry, as determined by the Investigator.
5. Able to understand the purpose and risks of the study; willing and able to adhere to scheduled visits, treatment plans, laboratory tests, and other study evaluations and procedures.
6. Provide written informed consent for participation in the study.
7. Male patients and female patients of childbearing potential must agree to use a protocol-specified method of contraception from screening and during the study until 28 days after last dose of study drug.

Exclusion criteria

1. History of a clinically significant non-ALS neurologic disorder, including, but not limited to, muscular dystrophy, spinal stenosis, peripheral neuropathy, inherited neuropathies, Alzheimer*s disease, cervical spondylosis, Parkinson*s disease, Lewy body dementia, vascular dementia, Huntington*s disease, epilepsy, stroke, multiple sclerosis, multifocal motor neuropathy, diabetic neuropathy, brain tumor, or brain infection/abscess. 2. Inability to swallow capsules. 3. Blood platelet count <150,000/mm3. 4. Renal impairment indicated by eGFR <=30 mL/min/1.73m2. 5. Human immunodeficiency virus (HIV) or current chronic/active infection with hepatitis C virus or hepatitis B virus including patients with chronic or active hepatitis B as diagnosed by serologic tests. 6. Women who are pregnant, planning to become pregnant, or are breastfeeding. Women of childbearing potential who are unwilling or unable to use highly effective method of contraception from screening through the duration of treatment and up to 28 days after last dose of study drug. 7. Known liver impairment (Child-Pugh Class A, B, or C). 8. History of Class III/IV heart failure (per New York Heart Association). 9. At the time of Screening, any use of non-invasive ventilation (NIV), e.g., continuous positive airway pressure [CPAP], noninvasive bi-level positive airway pressure [NPPV] or noninvasive volume ventilation [NVV] for any portion of the day, or mechanical ventilation via tracheostomy, or on any form

of oxygen supplementation. 10. Any form of cancer within the 5 years before first dose in this study (with the exception of basal cell and/or squamous cell cancer of the skin that has been treated completely and is without evidence of local recurrence or metastasis). 11. History of any other clinically significant cardiovascular, renal, hepatic, endocrine, metabolic, respiratory, gastrointestinal (GI), bleeding, autoimmune, neurological, psychiatric disorder, or unstable medical condition (other than ALS), as judged by the Investigator. 12. History and/or symptoms of adrenal insufficiency. 13. Abnormal liver function defined as aspartate aminotransferase (AST) or alanine aminotransferase (ALT) >3 × upper limit of normal (ULN). 14. QTcF interval based on the mean of 2 ECGs of >450 ms, for men and >470 ms for women. 15. History of additional risk factors for torsades de pointes (e.g., heart failure, hypokalemia, family history of long-QT syndrome). 16. Positive nasopharyngeal PCR test for SARS-CoV-2 on Day -1 or within 8 weeks prior to Screening. 17. Ongoing use of any strong CYP3A4 inhibitor/inducer or any medication with a narrow therapeutic index that is predominantly metabolized by CYP2C8. 18. Taking, or have taken, any strong CYP3A inducer within 30 days (or 5 half-lives if longer) before Screening, or any strong CYP3A inhibitor within 14 days before Screening. 19. Current or anticipated need, in the opinion of the Investigator, of a diaphragm pacing system (DPS) during the study period. 20. Received any live or attenuated vaccine within 30 days, before the first dose of study drug. Exceptions may apply on a case-by-case basis, if considered not to interfere with the objectives of the study, as agreed by the PI and the Corcept Medical Monitor. 21. Currently using glucocorticoids or have a history of regular systemic glucocorticoid use at any dose within the last 12 months or 3 months for inhaled products before first dose of study drug. (Patients who have stopped glucocorticoid use should have an alternative option if their condition deteriorates during the study.) 22. Participation in a clinical trial for ALS involving small molecules within 30 days of the Screening, or treatment with another investigational drug (including through compassionate use programs), biological agent, or device within 30 days or 5 half-lives of study agent, whichever is longer. No prior treatment with small interfering RNA, stem cell therapy, or gene therapy is allowed at any time in the patient*s history. 23. Unstable or poorly controlled comorbid disease process of any organ system currently requiring active treatment or likely to require treatment adjustment during the study. 24. Previous exposure or treatment with glucocorticoid receptor modulators or antagonists. 25. History of hypersensitivity or severe reaction to the study drug*s excipients. 26. In the Investigator*s opinion, should not participate in the study or may not be capable of providing informed consent or following the study schedule. This includes, but is not limited to, presence of unstable psychiatric disease, cognitive impairment, dementia, or substance abuse within 2 years prior to Screening. 27. Is a family member of one of the Sponsor*s employees, the Investigator, or the site staff working directly on the study.

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):	15-11-2022
Enrollment:	15
Type:	Actual

Medical products/devices used

Registration:	No
Product type:	Medicine
Brand name:	niet van toepassing
Generic name:	Dazucorilant

Ethics review

Approved WMO Date:	07-06-2022
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	07-09-2022
Application type:	First submission

Review commission:	METC NedMec
Approved WMO Date:	05-02-2023
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	21-03-2023
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	26-05-2023
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	25-07-2023
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	03-05-2024
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	13-05-2024
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	18-06-2024
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	26-07-2024
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
EU-CTR	CTIS2024-514082-19-00
EudraCT	EUCTR2021-005611-31-NL
CCMO	NL80995.041.22