A Phase 3, Open-Label Extension Study of Tirasemtiv for Patients with Amyotrophic Lateral Sclerosis (ALS) who Completed VITALITY-ALS (CY 4031)

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The primary objective is to assess the long-term safety and tolerability of tirasemtiv, inpatients with ALS

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

Summary

ID

NL-OMON45447

Source
ToetsingOnline

Brief title
CY 4033

Condition

- Neuromuscular disorders

Synonym
ALS, Amyotrophic Lateral Sclerosism

Research involving
Human

Sponsors and support

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

Intervention

Keyword: ALS, Amyotrophic, CK-2017357, Lateral Sclerosis, Tirasemtiv

Outcome measures

Primary outcome

The primary objective is to assess the long-term safety and tolerability of

tirasemtiv, in patients

with ALS.

Secondary outcome

The secondary objectives are:

* To compare the clinical course of patients who completed treatment with

tirasemtiv in

CY 4031 with those who completed treatment with placebo in CY 4031 during

continued treatment of both groups with tirasemtiv during CY 4033

* To compare the clinical course of patients who completed treatment with

tirasemtiv in

CY 4031 during that study with their clinical course during continued treatment

with

tirasemtiv during CY 4033

* To compare the clinical course of patients who completed treatment with

placebo in

CY 4031 during that study with their clinical course during treatment with

tirasemtiv

during CY 4033

Study description

Background summary

CY 4033 is an open-label extension study with the selective fast skeletal muscle troponin activator, tirasemtiv, in patients with ALS who finished double-blind study drug and completed participation (through Week 56) in the CY 4031 study (VITALITY-ALS).

Study objective

The primary objective is to assess the long-term safety and tolerability of tirasemtiv, in patients with ALS

Study design

Following enrollment, patients will begin dosing of tirasemtiv 125 mg twice daily (250 mg/day) for a period of 4 weeks and will titrate to their tolerated dose, the maximum dose being 250 mg twice daily (500 mg/day). The Principal Investigator, or designee with prescriptive authority in their local jurisdiction, may decide to up-titrate, maintain dose, or down-titrate the patient to the previously tolerated dose of tirasemtiv. Patient clinic visits will occur at Day 1, Week 4, Week 8, Week 12, Week 24, Week 36, Week 48, and every 12 weeks thereafter. Patients will be contacted by phone to assess their tolerability at Week 2, Week 6, and Week 10. If a patient decides to discontinue tirasemtiv, the patient will come into the clinic for the Tirasemtiv Discontinuation Visit and the 28 Day Safety Follow-up Visit if the patient is able; otherwise the patient will be contacted by phone for these visits.

Intervention

Following enrollment, patients will begin dosing of tirasemtiv 125 mg twice daily (250 mg/day) for a period of 4 weeks and will titrate to their tolerated dose, the maximum dose being 250 mg twice daily (500 mg/day). The Principal Investigator, or designee with prescriptive authority in their local jurisdiction, may decide to up-titrate, maintain dose, or down-titrate the

patient to the previously tolerated dose of tirasemtiv.

Study burden and risks

Ernstige bijwerkingen (SAE's) tijdens de dubbelblinde behandeling kwamen vaker voor bij tirasemtiv dan bij placebo (9,0% vs. 5,4%). De meest voorkomende ernstige bijwerking was respiratoire insufficiëntie, die was opgetreden bij één patiënt op tirasemtiv en drie patiënten op placebo, terwijl verwarde toestand en delirium waren opgetreden bij twee patiënten op tirasemtiv en geen van de patiënten op placebo. Van de patiënten die ten minste één dosis van het dubbelblinde studiemiddel kregen, trokken meer patiënten op tirasemtiv zich terug uit het onderzoek na randomisatie dan patienten op placebo (respectievelijk 97 versus 26 patiënten). Bijwerkingen (AE's) die vaker bij tirasemtiv voorkwamen dan bij placebo (> 10% verschil) waren duizeligheid (50,8% versus 19,7%), vermoeidheid (33,2% vs. 14,2%) en misselijkheid (21,9% vs. 7,8%).
Patiënten op tirasemtiv verloren meer gewicht dan de patiënten op placebo (verandering vanaf baseline tot week 12: -1,70 kg vs. -0,79 kg; p = 0,006). Gewichtsverlies was significant groter bij patiënten met gastrointestinale bijwerkingen (bijvoorbeeld misselijkheid en verminderde eetlust) bij beide behandelingen. Echter, dergelijke bijwerkingen kwamen vaker bij tirasemtiv dan bij placebo (43,5% versus 25,8%).

pag. 16 van Protocol 1.0 13Jul2016

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. Able to comprehend and willing to sign an Informed Consent Form (ICF). If verbal consent is given, a Legal Designee of the patient must sign the ICF form;2. Completed participation on study drug and the Follow-Up Visit in the CY 4031 study;3. Male patients, who have not had a vasectomy AND confirmed zero sperm count, must agree for the duration of their participation in the study to either:;a. Use a condom during sexual intercourse with female partners who are of childbearing potential (i.e., following menarche until post-menopausal if not anatomically and physiologically incapable of becoming pregnant) AND to have female partners use a highly effective means of contraception (see below):;OR;b. Abstain from sexual intercourse during participation in the study. ;4. Female patients who are not post-menopausal (* 1 year) or sterilized, must:;a. Not be breastfeeding;b. Have a negative pregnancy test;c. Have no intention to become pregnant during participation in the study,;AND;d. Practice sexual abstinence, defined as refraining from intercourse during the duration of the study OR if male partners are not vasectomized with a confirmed zero sperm count, require use of a condom AND use of a highly effective contraceptive measure, for the duration of the study such as:;* Combined (estrogen and progestogen containing) oral, intravaginal, or transdermal hormonal contraception associated with inhibition of ovulation;* Progestogen-only oral, injectable, or implantable hormonal contraception associated with inhibition of ovulation;* Intrauterine device (IUD);* Intrauterine hormone-releasing system (IUS);* Bilateral tubal occlusion

Exclusion criteria

1. Has a diaphragm pacing system (DPS) at study entry or anticipate DPS placement during the course of the study;2. Has taken any investigational study drug (other than tirasemtiv) prior to dosing, within 30 days or five half-lives of the prior agent, whichever is greater;3. Use of tizanidine and theophylline-containing medications during study participation;4. Participation or planning to participate in another clinical trial involving stem cell therapy for the treatment of ALS or another investigational drug

Study design

Design

Study phase:	3
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	06-07-2017
Enrollment:	1
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Tirasemtiv
Generic name:	Not known yet

Ethics review

Approved WMO Date:	14-03-2017
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	07-06-2017
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)

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	EUCTR2016-002629-13-NL
CCMO	NL59871.041.17