A Randomized, Placebo-Controlled, Double-blind, Single Ascending Dose, First in Human Phase 1 Study to Evaluate the Safety, Tolerability, and Pharmacokinetics of QRL-101 in Healthy Participants.

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Ethical review	Approved WMO
Status	Completed
Health condition type	Spinal cord and nerve root disorders
Study type	Interventional

Summary

ID

NL-OMON53647

Source
ToetsingOnline

Brief title
Single Ascending Dose Study of QRL-101 in Healthy Participants

Condition

- Spinal cord and nerve root disorders

Synonym
ALS, amyotrophic lateral sclerosis

Research involving

Human

Sponsors and support

Primary sponsor: QurAlis Corporation
Source(s) of monetary or material Support: Pharmaceutical industry

Intervention

Keyword: Healthy Participants, Pharmacokinetics, QRL-101, Safety

Outcome measures

Primary outcome

To determine the safety and tolerability of QRL-101 after a single oral dose in

Healthy Participants

Secondary outcome

To determine the pharmacokinetic (PK) profile of QRL-101 after a single oral

dose in Healthy Participants

Study description

Background summary

QRL-101 is a new compound that may potentially be used for the treatment of amyotrophic lateral sclerosis (ALS). ALS is a rare disease where nerve cells in the brain and spinal cord that are responsible for movement are getting damaged and die. This results in loss off coordination, muscle mass, muscle strength, speaking, swallowing, and eventually respiratory function. ALS gets worse over time and current treatments only bring about a small increase in lifespan. There is no cure. QRL-101 is being developed as a potential treatment for ALS as lab tests have shown that it can reduce the overactivation of cells. Increased overactivation in nerve cells in brain and spinal cord is known to be related to shortened lifespan in ALS patients.

Study objective

In this study we will investigate how safe the new compound QRL-101 is and how well it is tolerated when it is used by healthy subjects. A single dose of the

study compound will be given to each participant.

We will also investigate how quickly and to what extent QRL-101 is absorbed by, transported through, and eliminated from the body.

We compare the effects of QRL-101 with the effects of a placebo. A placebo is a compound without any active ingredient. Please note that when the term *study compound* is used in this document, we mean QRL-101, placebo, or both.

This is the first study where QRL-101 is given to humans. QRL-101 has already been extensively tested in the laboratory and on animals. QRL-101 will be tested at various dose levels. There are multiple groups with ascending dose levels, meaning the next group will receive a higher dose than the previous group.

Study design

The study will take a maximum of 40 days from the screening until the follow-up visit.
In total the volunteer will come to the research center 3 times:
- once for the screening.
- once for a stay in the research center of 4 days (3 nights).
- once for a follow-up visit on Day 10 (+/- 2 days).

Intervention

A single dose of QRL-101 or placebo is given on Day 1.

The volunteer will be given QRL-101 or placebo as oral capsules with 240 milliliters (mL) of (tap) water or as an oral liquid of the study compound in water (in total 240 mL). The study compound will be given after the volunteer has fasted (no eating or drinking, except water) for at least 2 hours. Fasting will continue until 1 hour after dosing. Drinking water is not allowed from 1 hour before dosing until 1 hour after dosing. If the study compound is given as a liquid, the volunteer will receive a mint strip (e.g., Listerine strip) before and after dosing to mask the taste of the study compound.

The table below shows an overview of the planned doses for each group where the study compound is given as capsules.

Group Dose*
1 1 mg QRL-101 or placebo
2 2 mg QRL-101 or placebo
3 6 mg QRL-101 or placebo
4 12 mg QRL-101 or placebo
5 24 mg QRL-101 or placebo

6 # mg QRL-101 or placebo
7 # mg QRL-101 or placebo
8 # mg QRL-101 or placebo
9 # mg QRL-101 or placebo

*The doses to be used from Group 6 onwards will be decided based on the results of the previous groups.

The table below shows the planned doses for each group where the study compound is given as a liquid.
Group Dose*
A1 6 mg QRL-101 or placebo
A2 # mg QRL-101 or placebo
A3 # mg QRL-101 or placebo
A4 # mg QRL-101 or placebo
A5 # mg QRL-101 or placebo
A6 # mg QRL-101 or placebo
A7 # mg QRL-101 or placebo
* The doses to be used from Group A2 onwards will be decided based on the results of the previous groups.

Study burden and risks

Blood draw
Drawing blood may be painful or cause some bruising. The use of the indwelling cannula (a tube in a vein in the arm) can sometimes lead to inflammation, swelling, hardening of the vein, blood clotting, and bleeding in the environment (bruising) of the puncture site. In some individuals, a blood draw can sometimes cause pallor, nausea, sweating, low heart rate, or drop in blood pressure with dizziness or fainting.

In total, we will take about 85 milliliters (mL) of blood from the volunteer from screening to follow-up. This amount does not cause any problems in adults. To compare: a blood donation involves 500 mL of blood being taken each time at once. If the investigator thinks it is necessary for the safety of a subject, extra samples might be taken for possible additional testing. If this happens, the total amount of blood drawn may be more than the amount indicated above.

Heart tracing
To make a heart tracing, electrodes (small, plastic patches) will be placed on the volunteers arms, chest and legs. Prolonged use of these electrodes can cause skin irritation (rash and itching).

Coronavirus test (only done when required per ICON policy)
Samples for the coronavirus test will be taken from the back of the volunteers nose and throat using swabs. Taking the samples only takes a few seconds, but can cause discomfort and can give an unpleasant feeling. Taking a sample from

the back of the volunteers throat may cause the volunteer to gag. When the sample is taken from the back of the volunteers nose, the volunteer may experience a stinging sensation and the volunteers eyes may become watery

Contacts

Public
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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. Age 18 to 70 years of age inclusive at the time of signing the informed consent.
2. Clinical chemistry laboratory values within acceptable range for the population, as per
investigator judgment.
3. Body mass index of 18 to 32 kg/m2 (inclusive).
4. Are male or female participants, including those of childbearing potential

a. Females of childbearing potential must use at least 1 highly effective method of contraception (see Table APP.3) during the trial and must have been using contraception for at least 28-days prior to the first dose of IMP and agree to use contraception during the study and after the study for at least 91 days; based on a rounding up of 5 predicted 5-hour half-lives in humans plus 90 days after the last dose of the study drug.
b. Men who are sexually active must agree to use a condom, if their partner is a woman of childbearing potential. They do not need to use any contraception if:
- they have had a vasectomy, and surgical success has been confirmed by medical assessment;
- their partner has had a bilateral tubal ligation; or
- their partner is not of childbearing potential.
Men must also refrain
i. from donating sperm, or
ii. from unprotected sex with a female partner who is a woman of childbearing potential (WOCBP) for 91 days; based on a rounding up of 5 predicted 5-hour half-lives in humans plus 90 days after the last dose of the study drug.
Contraceptive use by participants should be consistent with local regulations regarding the
methods of contraception for those participating in clinical studies.
Contraception requirements
and definition of nonchildbearing potential are detailed in HMA CTFG Contraception guidance.
5. Capable of giving signed informed consent, which includes compliance with the requirements and restrictions listed in the informed consent form (ICF) and in this protocol.

Exclusion criteria

1. QurAlis Corporation employees, Contract Research Organization employees, investigator or site personnel directly affiliated with this study and the immediate families of either of these. Immediate family is defined as a spouse, parent, child, or sibling, whether biological or legally adopted. 2. Currently enrolled in any other clinical trial involving a study drug or off-label use of a drug or device, or any other type of medical research judged not to be scientifically or medically compatible with this study. 3. Any participant in >4 studies a year and/or who has participated in a clinical trial within 1 month of expected dosing date. 4. Positive COVID-19 test, collected when required per site policy, at the Day -1 visit. 5. Answered *yes* to either Question 3, 4 or 5 on the *Suicidal Ideation* portion of the Columbia-Suicide Severity Rating Scale (C-SSRS) and the ideation occurred within the past month; or 6. Answered *yes* to any of the suicide-related behaviors on the *Suicidal Behavior* portion of C-SSRS and the behavior occurred within the past month
Further criteria apply

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	22-12-2022
Enrollment:	128
Type:	Actual

Ethics review

Approved WMO Date:	29-11-2022
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	15-12-2022
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	31-03-2023
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

Approved WMO

Date:	03-04-2023
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	20-06-2023
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	21-01-2024
Application type:	Amendment
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	EUCTR2022-002484-30-NL
CCMO	NL82817.056.22

Study results

Date completed:	27-12-2023
Results posted:	03-10-2024

First publication
19-09-2024