A randomised sequential trial of Lithium in amyotrophic lateral sclerosis

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To determine the effect of lithium treatment (plasma levels between 0,4-0,8 mEq/liter) versus placebo - in addition to riluzole 2dd 50 mg - on reaching a clinical endpoint in patients with ALS.

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

Summary

ID

NL-OMON31977

Source
ToetsingOnline

Brief title
Lithium trial in ALS

Condition

- Neuromuscular disorders

Synonym
amyotrophic lateral sclerosis (ALS), motor neuron disease

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Utrecht
Source(s) of monetary or material Support: Prinses Beatrix Fonds

Intervention

Keyword: ALS, lithium

Outcome measures

Primary outcome

The primary outcome measure is survival. Survival is defined as the time from inclusion to reaching a clinical endpoint. A clinical endpoint is reached when death, tracheostomy, permanent assisted ventilation (PAV) or non-invasive ventilation (NIV) for over 16 hours occurs. Permanent assisted ventilation is defined as intubation with artificial ventilation ultimately leading to tracheostomy or death

Secondary outcome

A secundary study parameter is the rate of decline in daily functioning and the occurrence of adverse effects and events.

Study description

Background summary

Amyotrophic lateral sclerosis (ALS) is a neurodegenerative disease with loss of motor neurons in the brain and spinal cord. The disease is characterized by progressive muscle weakness. The median survival is 3 years. To date, only one drug, i.e. riluzole, has proven to extend survival in patients with ALS, but only by approximately 3 to 6 months. A recent study on ALS-mice and a small cohort of patients (n=44) has shown a favourable effect of lithium on disease progression and survival.

Study objective

To determine the effect of lithium treatment (plasma levels between 0,4-0,8 mEq/liter) versus placebo - in addition to riluzole 2dd 50 mg - on reaching a clinical endpoint in patients with ALS.

Study design

Double-blind placebo controled trial with sequential analysis.

Intervention

One group is treated with lithiumcarbonate, the dosage depending on the plasma level (0,4-0,8mmol/l). The other group receives a placebo (at random dosage).

Study burden and risks

Patients who participate in the study should visit the outpatient clinic five times the first year, afterwards follow-up by telephone can take place. In the beginning frequent control of lithium plasma levels should be performed (approximately weekly). As soon as the patient is adequately established on the medication, the controls can be reduced untill two times a year (together with riluzol controls). Lithium can cause adverse effects and there is a risk for toxicity to occur. Considering the theoretical and clinical support for the hypothesis that lithium is effective in ALS we think it compensates for the risks. By means of profound planning of the study we aim at maximal risk reduction.

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. Definite, probable, or probable-laboratory supported ALS according to the revised El Escorial World Federation of Neurology criteria.
2.Intake of riluzole 2dd 50 mg
3. A disease duration (at inclusion) of more than 6 months and less than 36 months (disease onset is defined as the date of first symptoms excluding muscle cramps and fasciculations)
4. Vital capacity (VC%) >= 70 % of normal value
(slow expiration, best of a minimum of three and a maximum of five measurements, with a respiratory function validly assessable and spontaneous, non-assisted ventilation)
5. Age 18 - 85 years (inclusive)
6. Capable of thoroughly understanding the trial information given; has signed the informed consent.

Exclusion criteria

1. Tracheostomy, tracheostomal ventilation of any type, non-invasive ventilation more than 16 hours/ day, or supplemental oxygen during the last three months prior to inclusion.
2. Any medical condition or intoxication known to have an association with motor neuron dysfunction, which might confound or obscure the diagnosis of ALS.
3. Presence of any concomitant life-threatening disease or any disease or impairment likely to interfere with functional assessment.
4. Contra indications for lithium therapy*.
5. Interaction of lithium with other medication.
*Renal failure. Severe cardiac diseases. Brain damage. Addison disease. Hypothyroidism unresponsive to thyroid hormone suppletion. Precaution in patients with a (possibly) disturbed sodiumbalance like in extreme perspiration and sodium depleted diet.

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):	18-11-2008
Enrollment:	191
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	lithium carbonate
Generic name:	lithium carbonate
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	06-08-2008
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	16-09-2008
Application type:	First submission
Review commission:	METC NedMec

Approved WMO Date:	24-03-2009
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

ID: 20046
Source: Nationaal Trial Register
Title:

In other registers

Register	ID
EudraCT	EUCTR2008-002110-22-NL
CCMO	NL22827.041.08
OMON	NL-OMON20046