A randomized, double-blind, placebo-controlled, multi-center study of the safety and efficacy of Dexpramipexole in subjects with amyotrophic lateral sclerosis.

Published: 17-03-2011
Last updated: 27-04-2024

Primary:The primary objective of the study is to evaluate the efficacy of oral administration of dexpramipexole 150 mg twice daily compared to placebo for 12 months in subjects with ALS.Secondary:The secondary objectives of the study are to evaluate...

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

Summary

ID

NL-OMON38301

Source
ToetsingOnline

Brief title
EMPOWER

Condition

- Neuromuscular disorders

Synonym
Amyotrophic Lateral Sclerosis, Lou Gehrig's disease

Research involving
Human

Sponsors and support

Primary sponsor: Biogen Idec Limited
Source(s) of monetary or material Support: the pharmaceutical industry.

Intervention

Keyword: ALS, Amyotrophic Lateral Sclerosis, Motor Neurone Disease

Outcome measures

Primary outcome

• ALSFRS-R through 12 months

• Time to Death through 12 months

Secondary outcome

•Time to death or respiratory insufficiency (DRI): respiratory insufficiency is defined as receipt of a tracheostomy or the use of non-invasive ventilation (NIV) for >=22 hours per day for >=10 consecutive days. If NIV is used to meet the criteria for respiratory insufficiency, no measured slow vital capacity (SVC) at any subsequent assessment may be >50%.

•Time to death

•Respiratory decline: time to reach <=50% of predicted upright slow vital capacity (SVC) or death

•Change in muscle strength measurements (MSM), as determined by the overall megascore for hand-held dynamometry (HHD), through 12 months

•Change in ALS-related health quality, as measured by change in the total score on the Amyotrophic Lateral Sclerosis Assessment Questionnaire-5-Item Form (ALSAQ 5)

Study description

Background summary

Currently, only 1 medicine, Rilutek® (riluzole, Sanofi Aventis, approved by the United States [US] Food and Drug Administration in 1995 and the European Medicines Agency in 1996), is available for the treatment of ALS. Considering the seriousness of the disease, the lack of robust efficacy of riluzole, and limited options for further treatment, there remains a pressing unmet medical need for effective and safe treatments for ALS.
In a 2-part Phase 2 study conducted by Knopp Neurosciences Inc. (KNS 760704-CL201 [CL201]), dexpramipexole appeared to be well tolerated at doses ranging from 25 mg to 150 mg twice daily. Study results also showed a dose-dependent trend in slowing the rate of functional decline, as measured by change in the ALS Functional Rating Scale-Revised (ALSFRS-R), and a trend toward reduction in mortality of the 150 mg twice daily group compared to the 25 mg twice daily group.
This Phase 3 study is designed to determine the safety and efficacy of dexpramipexole in subjects with ALS.

Study objective

Primary:
The primary objective of the study is to evaluate the efficacy of oral administration of dexpramipexole 150 mg twice daily compared to placebo for 12 months in subjects with ALS.
Secondary:
The secondary objectives of the study are to evaluate the safety and pharmacokinetic (PK) profiles of oral administration of 150 mg twice daily dexpramipexole.

Study design

Multi-center, multi-national, randomized, double-blind, placebo controlled study stratified by investigational site, onset site (bulbar onset or others), and riluzole usage.

Per Protocol Am2 version 3, dated 03Apr2012, a DNA optional sub-study has been added to the protocol design.
Optional collection of DNA samples for genotyping was added to collect data that may help our understanding of ALS as well as treatment effects and side effects.

Intervention

Subjects will be randomly assigned in a 1:1 ratio to 1 of 2 treatment groups: oral dexpramipexole 150 mg twice daily or matching placebo.

Study burden and risks

Number of visits:
- 2 weeks after start of taking medicine on Day 1
- once every 2 months up to Month 18 (at Months 2, 4, 6, 8, 10, 12, 14, 16, and 18 after Day 1). Once the last patient in the study receives 12 months of study treatment, all patients will stop study treatment as part of this study and have the option to enter the follow-up study, so the patients may not be asked to attend all visits through to Month 18.
- one month after the last dose of study medicine.
-At the alternating months (Months 1, 3, 5, 7, 9, 11, 13, 15, and 17 from Day 1), the study staff will conduct assessments by calling and/or visiting at home.

-Subjects who plan to participate in the open-label extension:
Subjects should complete their regularly scheduled visits and continue to take study medication in the month prior to the last subject (LS) completing the month 12 visit. In the month after the Last Subject completes the Month 12 Visit, each of these subjects should complete an EOS Visit.
For subjects who complete the Month 18 Visit in the month prior to the Last Subject completing the Month 12 Visit, this Month 18 Visit will serve as the EOS Visit.
- Subjects who do not plan to participate in the open-label extension:
If the Month 12 Visit is scheduled within 1 month prior to the Last Subject completing Month 12, this visit will also serve as the EOS Visit. Study treatment will be discontinued and an SF will be performed. All other subjects who do not plan to participate in the open-label extension study will complete an EOS Visit within 1 month prior to the Last Subject completing Month 12. Study treatment will be discontinued and an SF will be performed.
- Subjects who withdraw prematurely from the study will be asked to return to complete an Early Termination (ET) Visit within 1 month of their last study treatment and a Safety Follow-up (SF) Visit at 30 days after their last study treatment. If the ET visit and SF occur at the same time, the assessments required at both the ET and SF Visits should be performed.

The following tests will be conducted at some or all of the study visits
• Medical history and physical examination
• Blood pressure, heart rate, respiration rate, temperature, weight, and height
• Neurological examination, including ALS condition and symptoms
• Muscle strength test using a hand-held device.
• Blood and urine tests
• Pregnancy tests (if applicable)
• Blood tests to check the level of study medicine in the blood
• Electrocardiogram (ECG)
• Lung function tests

• Questions about difficulties the patient has had, how well the patient feels, and how well the patient is able to do his usual activities
• Questions about if you are taking the study medicine as instructed
• Questions about any other treatments the patient is taking
• Questions about if the patients have any new side effects

For subjects who consent to participate in the genetic part (DNA collection) of the study, an extra 1-time blood sample will be drawn.

Contacts

Public
Biogen Idec Limited

Innovation House, 70 Norden Road 70
Maidenhead SL6 4AY
GB
Scientific
Biogen Idec Limited

Innovation House, 70 Norden Road 70
Maidenhead SL6 4AY
GB

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

1. Ability to understand the purpose and risks of the study and provide signed and dated informed consent and authorization to use protected health information (PHI) in accordance

with national and local subject privacy regulations.
2. Subject is between 18 and 80 years of age (inclusive) on Day 1.
3. Subject is diagnosed with sporadic or familial ALS.
4. Subject had onset of first ALS symptoms <=24 months prior to Day 1.
5. Subject meets the possible, laboratory-supported probable, probable, or definite criteria for diagnosing ALS according to the World Federation of Neurology El Escorial criteria
6. Subject has an upright SVC >=65% of predicted value for age, height, and gender at screening.
7. Subject has not taken riluzole for at least 30 days prior to Day 1, or has been on a stable dose of riluzole for at least 60 days prior to Day 1. (Riluzole-naïve subjects are permitted in the study.)
8. Subject is medically able to undergo the study procedures and to adhere to the visit schedule at the time of study entry.
9. Subject is able to take oral treatment without crushing or breaking the tablets at the time of study entry as assessed by the site Investigator.
10. Subjects of childbearing potential must practice effective contraception during the study and be willing and able to continue contraception for 1 month (females) or 3 months (males) after their last dose of study treatment.

Exclusion criteria

1 Subject in whom causes of neuromuscular weakness other than ALS have not been excluded.
2. Subject with significant cognitive impairment, clinical dementia, or psychiatric illness
3. Subject with a diagnosis of other neurodegenerative diseases (e.g., Parkinson*s disease, Alzheimer*s disease, etc.)
4. Subject with a clinically significant history of unstable or severe cardiac, oncologic, hepatic, or renal disease, or other medically significant illness
5. Subject with a clinically significant pre-existing pulmonary disorder not attributed to ALS
6. Subject with a history of severe drug allergy or severe allergic disease (anaphylactic shock)
7. Subject with clinically significant ECG abnormalities at the Screening visit
8. Subject with clinically significant abnormal clinical laboratory values, as determined by the Investigator at the Screening visit
9. Subject with absolute neutrophil count (ANC) <1.96 x 103/µL at the Screening visit or any documented history of neutropenia
10. Subject with aspartate aminotransferase (AST) or alanine aminotransferase (ALT) value >3.0 times the upper limit of normal at the Screening visit
11. Subject with creatinine clearance <=50 mL/minute at the Screening visit
12. Pregnant women or women breastfeeding
13. Subject with a history of alcohol or drug abuse within 1 year of Day 1, as determined by Investigator
14. Subject unlikely to comply with study requirements
15. Subject who has been exposed to any other experimental agent
16. Subject with prior exposure to dexpramipexole

17. Subject taking pramipexole or other dopamine agonists

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):	14-06-2011
Enrollment:	49
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	n/a
Generic name:	Dexpramipexole

Ethics review

Approved WMO Date:	17-03-2011
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	24-05-2011

Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	07-07-2011
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	28-07-2011
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	04-08-2011
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	02-09-2011
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	20-10-2011
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	12-07-2012
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	03-08-2012
Application type:	Amendment
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	EUCTR2010-022818-19-NL
ClinicalTrials.gov	NCT01281189
CCMO	NL35564.041.11