# A Phase III, Randomized, Double-Blind, Placebo-Controlled, Multicenter Trial to Evaluate the Safety and Efficacy of AMX0035 Versus Placebo for 48-week Treatment of Adult Patients with Amyotrophic Lateral Sclerosis (ALS)

Published: 06-07-2021
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This study has been transitioned to CTIS with ID 2023-508511-23-00 check the CTIS register for the current data. To assess safety and efficacy of AMX0035 for treatment of ALS.

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

## Summary

### ID

NL-OMON54389

**Source**
ToetsingOnline

**Brief title**
Phoenix

### Condition

- Neuromuscular disorders

**Synonym**
Disease of nerve cells that control muscles, Neurodegenerative syndrome

**Research involving**
Human

## Sponsors and support

**Primary sponsor:** Amylyx Pharmaceuticals Inc.
**Source(s) of monetary or material Support:** Amylyx Inc.

## Intervention

**Keyword:** AMX0035, Amyotrophic Lateral Sclerosis (ALS), Efficacy, Safety

## Outcome measures

### Primary outcome

1. To assess the impact of AMX0035 treatment compared to placebo on disease progression over 48 weeks based on change form baseline of ALSFRS-R and survival.

### Secondary outcome

1. To assess the impact of AMX0035 compared to placebo on Slow Vital Capacity (SVC) in adult patients with ALS over 48 weeks; 2. To assess patient quality of life (QOL; using the 40-item ALS assessment questionnaire [ALSAQ-40] patient-reported outcome [PRO]) during treatment with AMX0035 compared to placebo in adult patients with ALS over 48 weeks; 3. To assess AMX0035 compared to placebo on the time to any decline in King's and MiToS stages as derived from ALSFRS-R data over 48 weeks; 4. To assess the impact of AMX0035 compared to placebo on ventilation free survival (defined as death, tracheostomy for respiratory distress or permanent non-invasive ventilation [>22 hours per day for 7 consecutive days]) in adult patients with ALS over 48 weeks; 5. To assess AMX0035 compared to placebo on patient health status (using the EQ-5D descriptive system and the EQ visual analogue scale [EQ VAS] PRO during

treatment with AMX0035 over 48 weeks. Finally, a secondary objective of the trial is to assess the long-term overall survival of all-cause mortality beyond the 48 week Treatment Period of adult patients with ALS treated with AMX0035 or placebo until time of death or End of Study.

# Study description

### Background summary

ALS is a very serious and fatal condition characterized by progressive degeneration of the upper and lower motor neurons. There are limited pharmacological options in the treatment of ALS and they focus on symptom treatment. The only existing authorized medicine for treating ALS in the European Union is Riluzole.

In a randomized, Phase II, placebo-controlled trial, AMX0035 administered orally for 24 weeks as add-on treatment to Investigator selected standard of care showed statistical significant and clinically meaningful benefit on a validated functional outcome (ALS Functional Rating Scale-Revised [ALSFRS-R]), allowing participants to maintain their independence longer. Secondary endpoints measuring breathing and muscle strength showed effects in the same direction and with similar magnitude as the primary endpoint although not statistically significant. AMX0035 did not demonstrate significant safety concerns and the most notable drug-related adverse events were diarrhea and nausea.

### Study objective

This study has been transitioned to CTIS with ID 2023-508511-23-00 check the CTIS register for the current data.

To assess safety and efficacy of AMX0035 for treatment of ALS.

### Study design

This is a Phase III, randomized, double-blind, placebo-controlled trial. Adult patients with clinically definite or clinically probable ALS according to the revised El Escorial criteria, meeting all inclusion and exclusion criteria, will be randomly assigned in a 3:2 ratio to AMX0035 or matching placebo. Participants will first receive an oral dose of study drug once a day in the morning (AMX0035 or placebo; one sachet per day) for approximately 14-21 days.

For participants who tolerate the treatment, the dose will then be escalated (beginning the following day; e.g., Trial Day 15 to 22 or later) to twice a day oral dosing in the morning and evening (two sachets per day) for the remainder of a 48-week treatment duration. After the Baseline Visit (Day l), the enrolled participants will complete an outpatient clinic visit approximately every 12 weeks (+ 2 weeks) at Week 12, Week 24, Week 36, and Week 48/End of Trial. Because it is anticipated that the ongoing Coronavirus disease (COVID-19) pandemic will continue to affect many sites, alternatively the actual site visits may be conducted using telemedicine or as a home visit by a site nurse or staff per local practice and allowances. Other trial assessments will be performed at 4-week and 12-week intervals.

**Intervention**

Participants will be randomly assigned in a3:2 ratio to oral (or feeding tube) AMX0035 treatment (a fixed-dose combination of sodium phenylbutyrate [PB] and taurursodiol) or matching placebo. For the first 14 to 21 days of dosing, participants will take I sachet daily and if tolerated will increase to 2 sachets daily.

AMX0035 or matching placebo will be supplied by Amylyx to the site pharmacy as a carton box containing single use sachets. Each AMX0035 sachet contains active ingredients in a powder formulation with 3 g PB and 1 g taurursodiol. Study drug powder is mixed with water and taken orally (or via feeding tube).

**Study burden and risks**

The study drug may have side effects. It cannot be excluded that side effects can be serious, long lasting or may never go away. All efforts will be used to reduce any discomfort from participation in this study. The following side effects have been found in patients with ALS during previous studies using AMX0035 (occurs in 1 out of 10 people, or more):
- Diarrhea
- Constipation
- Nausea
- Weakness of the muscles
- Fall
- Headache
- Dizziness
- Viral infections of the upper respiratory tract

The most common side effects of AMX0035 found in patients with ALS during previous studies are diarrhea and nausea (approximately 1 out of 5 people). The study drug may also cause side effects that are unknown.

Other disadvantages can be possible adverse effects/discomforts of the tests and procedures applied in the study. In addition, the patient and caregiver have to invest time in participation in the study. The patient has to attend clinic visits for the required study visits, undergo testing procedures, and be available for phone or video calls.

Advantages: The patients current condition of ALS will be assessed carefully. The study drug may slow down ALS disease progression, but this is not certain. It may be that participation in this study does not provide any benefit for the patient's health. However, the patient will contribute to increase the knowledge about the treatment of ALS.

## Contacts

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**Scientific**
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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 or female, at least 18 years of age; 2. Diagnosis of ALS (clinically definite or clinically probable), made by a physician who is experienced with management of ALS, as defined by the World Federation of Neurology revised El Escorial criteria; 3. Time since onset of first symptom of ALS should be <24 months prior to randomization; Date of ALS symptom onset is defined as the onset of weakness (in the limbs, bulbar region, or trunk). Weakness in the bulbar region includes dysarthria and dysphagia; 4. If the participant is to be treated with riluzole and/or edaravone during the course of the trial, then treatment with riluzole and/or edaravone was, at the time of the Baseline Visit, previously started and maintained at a stable regimen for at least 14 days for riluzole and/or for a full treatment cycle for edaravone; 5. Capable of providing informed consen[ 6. Capable and willing to follow trial procedures including visits to the trial clinic remote visits, and survival status reporting requirements; 7. Women of childbearing potential (WOCBP; e.g., not post-menopausal for at least one year or surgically sterile*) must agree to use adequate birth control** for the duration of the trial and 3 months after the last dose of study drug; 8. Women must not be pregnant or planning to become pregnant for the duration of the trial and 3 months after last dose of study drug; 9. Men must agree to practice contraception for the duration of the trial and for at least 3 months after last dose of study drug; 10. Men must not plan to father a child or to provide sperm for donation for the duration of the trial and 3 months after the last dose of study drug;

## Exclusion criteria

1. Presence of tracheostomy or PAV; defined as >22 hours daily of mechanical ventilation for more than 1 week (7 days); 2. Slow Vital Capacity (SVC) less than 55%; 3. History of known allergy to phenylbutyrate or bile salts; 4. Abnormal liver function defined as bilirubin levels and/or aspartate aminotransferase (AST) and/or alanine aminotransferase (ALT) > 5 times the upper limit of the normal (obtained within 12 weeks from first dose); 5.5. Renal insufficiency as defined by estimated glomerular filtration rate (eGFR) <60 mL/min/1.73m2 (from a local laboratory within 12 weeks or central laboratory within 6 weeks from first dose at the Baseline Visit); 6. Pregnant women (confirmed by a pregnancy test within 7 days prior to first dose) or women currently breastfeeding; 7. Current severe biliary disease which may result in the Investigator medical judgement in biliary obstruction including for example active cholecystitis, primary biliary cirrhosis, sclerosing cholangitis, gallbladder cancer, gangrene ofthe gallbladder, abscess ofthe gallbladder; 8. History of Class III/IV heart failure (per New York Heart Association - NYHA); 9. Participant under severe salt restriction where the added salt intake due to treatment would put the participant at risk, in the

Investigator clinical judgment; 10. Presence of unstable psychiatric disease, cognitive impairment, dementia or substance abuse that would impair ability of the participant to provide informed consent, according to Investigator judgment; 11. Clinically significant unstable medical condition (other than ALS) (e.g., cardiovascular instability, systemic infection, untreated thyroid dysfunction, clinically significant laboratoy test or ECG abnormality) that would pose a risk to the participant if he/she were to participate in the trial, according to Investigator judgment; 12. Previous treatment for ALS with cellular therapies or gene therapies; 13. Currently enrolled on another trial involving use of an investigational therapy; (or within 5.5 plasma half-lives) prior to first dose at Baseline Visit; 14. 14. Previous treatment with sodium phenylbutyrate (PB) or taurursodiol within 30 days from first dose at Baseline Visit; 15. Implantation of Diaphragm Pacing System (DPS); 16. Currently or previously treated within the last 30 days (or 5 half-lives, whichever is longer) from first dose at the Baseline Visit or planned exposure during the treatment period to any prohibited medications listed in Section 6.7 of the protocol.

# Study design

## Design

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| Study phase: | 3 |
| Study type: | Interventional |
| Intervention model: | Parallel |
| Allocation: | Randomized controlled trial |
| Masking: | Double blinded (masking used) |
| Control: | Placebo |
| Primary purpose: | Treatment |

## Recruitment

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| Recruitment status: | Recruiting |
| Start date (anticipated): | 03-12-2021 |
| Enrollment: | 31 |
| Type: | Actual |

### Medical products/devices used

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| Product type: | Medicine |
| Brand name: | Not applicable |
| Generic name: | Phenylbutyrate and Taurursodiol |

## Ethics review

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| Approved WMO Date: | 06-07-2021 |
| Application type: | First submission |
| Review commission: | MEC-U: Medical Research Ethics Committees United (Nieuwegein) |
| Approved WMO Date: | 03-09-2021 |
| Application type: | First submission |
| Review commission: | MEC-U: Medical Research Ethics Committees United (Nieuwegein) |
| Approved WMO Date: | 24-11-2021 |
| Application type: | Amendment |
| Review commission: | MEC-U: Medical Research Ethics Committees United (Nieuwegein) |
| Approved WMO Date: | 30-11-2021 |
| Application type: | Amendment |
| Review commission: | MEC-U: Medical Research Ethics Committees United (Nieuwegein) |
| Approved WMO Date: | 10-03-2022 |
| Application type: | Amendment |
| Review commission: | MEC-U: Medical Research Ethics Committees United (Nieuwegein) |
| Approved WMO Date: | 16-03-2022 |
| Application type: | Amendment |
| Review commission: | MEC-U: Medical Research Ethics Committees United (Nieuwegein) |

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| Approved WMO Date: | 27-05-2022 |
| Application type: | Amendment |
| Review commission: | MEC-U: Medical Research Ethics Committees United (Nieuwegein) |
| Approved WMO Date: | 08-06-2022 |
| Application type: | Amendment |
| Review commission: | MEC-U: Medical Research Ethics Committees United (Nieuwegein) |
| Approved WMO Date: | 21-08-2022 |
| Application type: | Amendment |
| Review commission: | MEC-U: Medical Research Ethics Committees United (Nieuwegein) |
| Approved WMO Date: | 29-08-2022 |
| Application type: | Amendment |
| Review commission: | MEC-U: Medical Research Ethics Committees United (Nieuwegein) |
| Approved WMO Date: | 11-06-2023 |
| Application type: | Amendment |
| Review commission: | MEC-U: Medical Research Ethics Committees United (Nieuwegein) |
| Approved WMO Date: | 21-06-2023 |
| Application type: | Amendment |
| Review commission: | MEC-U: Medical Research Ethics Committees United (Nieuwegein) |
| Approved WMO Date: | 11-01-2024 |
| Application type: | Amendment |
| Review commission: | MEC-U: Medical Research Ethics Committees United (Nieuwegein) |
| Approved WMO Date: | 16-01-2024 |
| Application type: | Amendment |

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| Review commission: | MEC-U: Medical Research Ethics Committees United (Nieuwegein) |

# 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 | CTIS2023-508511-23-00 |
| EudraCT | EUCTR2021-000250-26-NL |
| ClinicalTrials.gov | NCT05021536 |
| CCMO | NL78255.100.21 |