A Phase 2, multicenter, randomized, double blind, placebo controlled study to evaluate the efficacy and safety of SAR443820 in adult participants with amyotrophic lateral sclerosis, followed by an open label extension

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Primary, Part A: - To assess the effect of SAR443820 compared to placebo in reducing ALS progression as measured by the Amyotrophic Lateral Sclerosis Functional Rating Scale Revised (ALSFRS-R)Primary, Part B: - To assess the long-term effects of...

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

Summary

ID

NL-OMON53447

Source
ToetsingOnline

Brief title
ACT16970 Himalaya

Condition

- Neuromuscular disorders

Synonym
Amyotrophic Lateral Sclerosis, Lou Gehrig's Disease

Research involving

Human

Sponsors and support

Primary sponsor: Sanofi BV
Source(s) of monetary or material Support: Sanofi BV

Intervention

Keyword: ALS, Amyotrophic Lateral Sclerosis, Lou Gehrig's Disease

Outcome measures

Primary outcome

Part A: Change from baseline in the ALSFRS-R total score from screening to Week

24

Part B: Combined assessment of the function and survival (CAFS) score at Week

52

Secondary outcome

Part A:

- Combined assessment of the function and survival (CAFS) score at Week 24

- Change from baseline in slow vital capacity (SVC) to Week 24

- Muscle strength measured by handheld dynamometry (HHD) over 24 weeks

- Change from baseline in Amyotrophic Lateral Sclerosis Assessment

Questionnaire (ALSAQ-5) to Week 24

- Change from baseline in serum neurofilament light chain (NfL) to Week 24

- Incidence of adverse events (AE), serious adverse events (SAE),

treatment-emergent adverse events (TEAE), potentially clinically significant

abnormalities (PCSA) in laboratory tests, electrocardiogram (ECG), and vital

signs over 24 weeks

- Plasma concentration of SAR443820

Part B:

- Combined assessment of the function and survival (CAFS) score at Week 76 and Week 104

- Change from baseline in the ALSFRS-R total score to Week 52, Week 76, and Week 104

- Time from baseline to the occurrence of either death or permanent assisted ventilation (>22 hours daily for >7 consecutive days), whichever comes first, before Week 52, Week 76, and Week 104

- Time from baseline to the occurrence of death before Week 52, Week 76, and Week 104

- Change from baseline in slow vital capacity (SVC) to Week 52, Week 76, and Week 104

- Change from baseline in Amyotrophic Lateral Sclerosis Assessment Questionnaire (ALSAQ-5) to Week 52, Week 76, and Week 104

- Change from baseline in serum neurofilament light chain (NfL) to Week 52

- Incidence of adverse events (AE), serious adverse events (SAE), treatment-emergent adverse events (TEAE), potentially clinically significant abnormalities (PCSA) in laboratory tests, electrocardiogram (ECG), and vital signs during Part B

- Plasma concentration of SAR443820

Study description

Background summary

ALS is a fatal neurodegenerative disorder characterized by progressive loss of motor neurons in the cortex, brain stem, and spinal cord. Relentless and progressive muscle atrophy and weakness are hallmarks of ALS. Most patients with ALS die from respiratory failure within 3 to 5 years after disease onset. The 2 Food and Drug Administration (FDA)-approved ALS treatments demonstrate only a moderate effect either on survival (riluzole) or functional decline (edaravone). There is a significant unmet medical need for treating individuals with ALS. SAR443820 has demonstrated strong RIPK1 inhibition with high potency in vitro in various cell types.

Study objective

Primary, Part A:
- To assess the effect of SAR443820 compared to placebo in reducing ALS progression as measured by the Amyotrophic Lateral Sclerosis Functional Rating Scale Revised (ALSFRS-R)

Primary, Part B:
- To assess the long-term effects of SAR443820 on function and survival

Secondary, both Part A and Part B (long-term):
- To assess the effect of SAR443820 compared to placebo on a combined assessment of function and survival, respiratory function, muscle strength, and quality of life (QoL)
- To assess the pharmacodynamic (PD) effect of SAR443820 compared to placebo on a key disease biomarker
- To assess the safety and tolerability of SAR443820 compared to placebo
- To assess the pharmacokinetics (PK) of SAR443820

Study design

Phase 2, randomized, double-blind, placebo-controlled study followed by an open-label extension period.

Intervention

Participants will be randomized in a 2:1 ratio to the SAR443820 treatment arm or matching placebo arm as listed below:
• Treatment arm: SAR443820, 20 mg, BID
• Placebo arm: Placebo, BID

Study burden and risks

Risks related to blood sampling and side effects of the study drug.

Contacts

Public
Sanofi BV

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

• Male or female, 18-80 years of age (inclusive)
• Diagnosis of possible, clinically probable ALS, clinically probable laboratory-supported ALS, or clinically definite ALS according to the revised version of the El Escorial World Federation of Neurology criteria
• Time since onset of first symptom of ALS <=2 years.
• Slow Vital Capacity (SVC) >=60% of the predicted value.

• Be able to swallow the study tablets at the screening visit.
• Either not currently receiving riluzole or on a stable dose of riluzole for at least 4 weeks before the screening visit. Participants receiving riluzole are expected to remain on the same dose throughout the duration of the study.
• Either not currently receiving edaravone or on the approved standard schedule of edaravone treatment. Participants receiving edaravone must have completed at least 1 cycle of treatment before the screening visit and are expected to continue edaravone treatment throughout the duration of the study.
• Weight : Participants with a body weight no less than 45 kg and body mass index no less than 18 kg/m2.
• Female participants with childbearing potential are eligible to participate if they are not pregnant or breastfeeding and agree to use adequate contraceptive method during study intervention period and for at least 32 days after the last dose of study drug.
• Male participants must agree to use highly effective contraceptive method during the study period and for at least 92 days following their last dose of the study drug. Male participants must not donate sperms for the duration of study and 92 days after last dose of study drug.

Exclusion criteria

• A history of seizure (History of febrile seizure during childhood is allowed).
• Having central IV lines, such as a peripherally inserted central catheter (PICC) or midline or port-a-cath lines.
• With significant cognitive impairment, psychiatric disease, other neurodegenerative disorder (eg, Parkinson disease or AD), substance abuse, or any other condition that would make the participants unsuitable for participating in the study or could interfere with assessment or completing the study in the opinion of the Investigator.
• History of recent serious infection (eg, pneumonia, septicemia) within 4 weeks of the screening visit; infection requiring hospitalization or treatment with IV antibiotics, antivirals, or antifungals within 4 weeks of screening; or chronic bacterial infection (such as tuberculosis) deemed unacceptable as per the Investigator's judgment.
• With active herpes zoster infection within 2 months prior to the screening visit.
• A documented history of attempted suicide within 6 months prior to the screening visit, present with suicidal ideation of category 4 or 5 on the Columbia Suicide Severity Rating Scale (C-SSRS), or in the Investigator's judgment are at risk for a suicide attempt.
• History of unstable or severe cardiac, pulmonary, oncological, hepatic, or renal disease or another medically significant illness other than ALS precluding their safe participation in this study.
• Participants who are pregnant or are currently breastfeeding.
• A known history of allergy to any ingredients of SAR443820.

Prior/concomitant therapy :
• Currently or previously treated with any strong or moderate CYP3A4 inhibitors or strong CYP3A4 inducers listed in Appendix 10 of the protocol within the specified washout period before the screening visit.
• Received a live vaccine within 14 days before the screening visit.
• Participants with concurrent participation in any other interventional clinical study or who have received treatment with another investigational drug within 4 weeks or 5 half-lives of the investigational agent before the screening visit, whichever is longer.
• Participants who have received stem cell or gene therapy for ALS at any time in the past.
• Alanine aminotransferase (ALT) or aspartate aminotransferase (AST) >3.0 × upper limit of normal (ULN)
• Bilirubin >1.5 × ULN unless the participant has documented Gilbert syndrome (isolated bilirubin >1.5 × ULN is acceptable if bilirubin is fractionated and direct bilirubin is <35%)
• Serum albumin <3.5 g/dL
• Estimated glomerular filtration rate <60 mL/min/1.73 m2 (Modification of Diet in Renal Disease [MDRD])

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:	Recruitment stopped
Start date (anticipated):	13-04-2022
Enrollment:	6
Type:	Actual

Ethics review

Approved WMO Date:	21-12-2021
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	10-03-2022
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	23-05-2022
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	08-07-2022
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	29-10-2022
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	21-04-2023
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	26-04-2023
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	26-05-2023
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	31-05-2023

Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	02-06-2023
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	08-06-2023
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	07-12-2023
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	21-12-2023
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	27-12-2023
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	23-01-2024
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	13-03-2024
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	EUCTR2021-004156-4-NL
CCMO	NL79644.041.21
Other	U1111-1263-5766