

Assessing the effect of Triumeq in amyotrophic lateral sclerosis

Submission date 22/02/2021	Recruitment status No longer recruiting	<input checked="" type="checkbox"/> Prospectively registered <input checked="" type="checkbox"/> Protocol
Registration date 14/12/2021	Overall study status Stopped	<input type="checkbox"/> Statistical analysis plan <input type="checkbox"/> Results
Last Edited 15/09/2025	Condition category Nervous System Diseases	<input type="checkbox"/> Individual participant data <input type="checkbox"/> Record updated in last year

Plain English summary of protocol

Background and study aims

Amyotrophic lateral sclerosis (ALS) is a progressive motor neuron disease. Unfortunately, there are limited medications available for ALS. The only available treatment is riluzole, which tends to provide only minimal benefit. Therefore, there is a high need for further research using other medications, to help improve the options for treatment for this disease.

There has been laboratory research that suggests that a virus called an endogenous retrovirus may be the cause or trigger for ALS in some people. This virus may be of the same family (although quite different) to the virus that causes HIV (also called 'AIDS'). Researchers are intending to test if an anti-viral medication that is a very effective treatment for HIV, may also be effective for people who have ALS.

Triumeq, commonly prescribed for HIV treatment, is an antiviral medication that is a combination of three medications: dolutegravir 50 mg, abacavir 600 mg, and lamivudine 300 mg. Triumeq is approved by the Therapeutic Goods Administration (TGA) to treat HIV patients. However, it is not approved to treat ALS. Therefore, it is an experimental treatment for ALS. The aim of this study is to determine whether Triumeq is effective at delaying the progression of ALS, and whether it is safe and well-tolerated in patients with ALS. The Lighthouse study demonstrated Triumeq to be safe and well tolerated in people with ALS.

Who can participate?

Patients aged 18 years and over with ALS

What does the study involve?

The entire study will last for around 2 years. Participation is voluntary. Participation in this study will involve up to 10 visits (about 2 hours each) roughly every 3 months, and as many telephone calls as participants would like, to make sure they are comfortable with the research process. Participants will be assessed throughout the project using assessment scales to determine if it is suitable for them to continue the medication.

Participants will be randomly allocated to receive either Triumeq or a matching placebo (dummy drug) once daily in addition to standard care. The random allocation will be done using a computer maintained by the King's Clinical Trials Unit. Two thirds of research participants will receive active Triumeq and one third will receive matched placebo capsules. A placebo is a medication with no active ingredients and so has no medical benefit. It looks like the real thing,

but it is not. The study is a 'double-blind' study. This means that neither participants nor the study doctor will know which treatment they are receiving. However, in certain circumstances the study doctor can find out which treatment participants are receiving. This study has been designed to make sure the researchers interpret the results fairly without any bias and avoids study doctors or participants jumping to conclusions.

There are a number of procedures and reviews that will be carried out at different times over the 24 months:

1. Demographics
2. Review of medical history
3. Physical examination/vital signs
4. Neurological exam
5. Blood collection
6. Urine collection
7. Throat or nasal swab: the doctor/nurse/research coordinator will perform either a throat or nasal swab to check for COVID-19 infection
8. Spirometry (breathing) test
9. Questionnaire completion
10. ECG test

What are the possible benefits and risks of participating?

The researchers cannot guarantee or promise that participants will receive any benefits from this research; however, possible benefits may include some relief of ALS symptoms. The tests provided may help participants learn about their general health. This study may assist doctors and scientists to help people suffering from symptoms with ALS in the future.

Medical treatments often cause side effects. Participants may have none, some or all of the effects listed below, and they may be mild, moderate or severe. There may be side effects that the researchers do not expect or do not know about and that may be serious. Many side effects go away shortly after treatment ends. However, sometimes side effects can be serious, long-lasting or permanent. If a severe side effect or reaction occurs, the study doctor may need to stop the treatment.

The following side effects have been experienced by people taking Triumeq:

Common side effects (occur in 1 out of 10 people): fever, not feeling well, discouragement, nausea, rash, irritability, loss of interest and/or pleasure, trouble concentrating and/or sleeping.

Uncommon side effects (occur in 1 out of 100 people): neuropathy (tingling in fingers and toes), anxiety, difficulty moving, weight loss, itching and hair loss as well as high blood sugar.

Rare side effects (occur in 1 out of 10, 000 people): abnormal liver function tests, low blood pressure dizziness or light-headedness, fainting or lack of concentration or fatigue, acute inflammation of the pancreas, nausea, fever and a swollen and or tender abdomen and hepatitis, joint pain, abdominal pain and yellowing of the skin.

Where is the study run from?

King's College London (UK)

When is the study starting and how long is it expected to run for?

January 2020 to June 2025

Who is funding the study?

1. National Institute for Health Research (NIHR) (UK)
2. FightMND (Australia)
3. Motor Neurone Disease Research Institute of Australia (Australia)
4. Treatment Research Initiative to Cure ALS (TRICALS)

Who is the main contact?

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Shared inbox
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Contact information

Type(s)

Public

Contact name

Ms Sylvia Wilczynska

Contact details

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+44 (0)20 7848 0532
sylvia.1.wilczynska@kcl.ac.uk

Additional identifiers

Clinical Trials Information System (CTIS)

2020-005069-15

Integrated Research Application System (IRAS)

271218

ClinicalTrials.gov (NCT)

NCT05193994

Protocol serial number

IRAS 271218

Study information

Scientific Title

Randomized double-blind placebo-controlled Phase III trial of Triumeq in amyotrophic lateral sclerosis

Acronym

Lighthouse II

Study objectives

Activation of a human endogenous retrovirus is a key component of the pathogenesis of amyotrophic lateral sclerosis (ALS), and blocking its lifecycle with antiretroviral therapy will therefore provide an effective treatment.

Ethics approval required

Old ethics approval format

Ethics approval(s)

Approved 01/02/2022, London - Westminster Research Ethics Committee (Equinox House, City Link, Nottingham, NG2 4LA, UK; +44 (0)207 104 8066, +44 (0)207 104 8236, +44 (0)207 104 8283; westminster.rec@hra.nhs.uk), ref: 22/LO/0059

Study design

Double-blind (participant, investigators) 2:1 randomized placebo-controlled international multi-centre trial

Primary study design

Interventional

Study type(s)

Treatment

Health condition(s) or problem(s) studied

Amyotrophic Lateral Sclerosis (ALS)

Interventions

Lighthouse II is an international, phase III, multi-centre, parallel-group, placebo-controlled, blinded (participant, investigators, analyst) randomised controlled trial of Triumeq (abacavir 600 mg, lamivudine 300 mg and dolutegravir 50 mg) or matched placebo, once daily in addition to standard care, in a 2:1 treatment/placebo allocation ratio in participants with ALS, in order to determine the superiority of treatment versus placebo. If the trial is not terminated at a planned interim analysis, the trial will continue until 24 months after the last enrolled participant or a minimum of 212 events have occurred, whichever is first.

Intervention Type

Drug

Phase

Phase III

Drug/device/biological/vaccine name(s)

Abacavir, lamivudine, dolutegravir

Primary outcome(s)

Overall survival, defined as time to mortality from any cause. This will be recorded and reported on an ongoing basis from the participant randomisation. The primary outcome timepoint is at 24 months.

Key secondary outcome(s)

1. Combined assessment of survival and measures of daily functioning using the ALSFRS-R total score (CAFS) at baseline, 3, 6, 9, 12, 15, 18, 21 and 24 months

2. Daily functioning is measured by using the ALSFRS-R total score at baseline, 3, 6, 9, 12, 15, 18, 21 and 24 months
3. Respiratory function is measured by slow vital capacity (SVC) (% predicted of normal according to the GLI-2012 reference standard) at baseline, 3, 6, 9, 12, 15, 18, 21 and 24 months
4. Plasma creatinine levels are measured using safety blood test at baseline, 3, 6, 9, 12, 15, 18, 21 and 24 months
5. Clinical disease stage, defined as mean time spent in each stage of the King's Staging Scale and the ALS Milano-Torino staging systems (MITOS, derived from ALSFRS-R) at baseline, 3, 6, 9, 12, 15, 18, 21 and 24 months
6. Safety based on safety assessments including:
 - 6.1. Physical examinations at baseline, 3, 6, 9, 12, 15, 18, 21 and 24 months
 - 6.2. Clinical laboratory evaluations at baseline, 3, 6, 9, 12, 15, 18, 21 and 24 months
 - 6.3. Vital signs at baseline, 3, 6, 9, 12, 15, 18, 21 and 24 months
 - 6.4. Frequency of adverse events (AEs) or serious adverse events (SAEs) – ongoing from participant randomisation
7. Tolerability measured by medication discontinuation – ongoing from participant randomisation
8. Cognitive function measured by using Edinburgh Cognitive and Behavioural ALS Screen (ECAS) at baseline, 12 and 24 months
9. Quality of life, defined as total scores on the Visual Analogue Scale (single-item scale) and EQ-5D-5L questionnaire at baseline, 3, 6, 9, 12, 15, 18, 21 and 24 months
10. Laboratory parameters, e.g. urine P75ECD, plasma neurofilament light and heavy chain, HERVK expression and genotyping (UNC13a / C9orf72), measured by blood and urine tests at baseline, 3, 6, 9, 12, 15, 18, 21 and 24 months

Completion date

30/06/2025

Reason abandoned (if study stopped)

The study was stopped for futility based on an interim analysis of the trial data.

Eligibility

Key inclusion criteria

Current inclusion criteria as of 13/02/2024:

1. Age \geq 18 years at the time of screening
2. Diagnosis of ALS according to the Gold Coast Criteria
3. Capable of providing informed consent and complying with trial procedures
4. TRICALS risk profile > -6.0 and < -2.0
5. Those taking Riluzole must be on a stable dose for at least 30 days prior to the baseline visit or must have stopped taking Riluzole at least 30 days prior to the baseline visit
6. Women must not become pregnant (e.g., post-menopausal, surgically sterile, using highly effective birth control methods or not having potentially reproductive sex) for the duration of the study plus five days. Highly effective methods of birth control are those with a failure rate of $< 1\%$ per year when employed consistently and correctly, e.g. combined (oestrogen and progestogen containing) hormonal contraception or progestogen-only hormonal contraception
7. Women of childbearing potential must have a negative serum pregnancy test at screening and be non-lactating. Patients will be advised regarding appropriate contraception. A menstruation history will be taken at each visit. Women of childbearing potential are defined as females who are fertile, following menarche and until becoming post-menopausal unless permanently sterile. Permanent sterilisation methods include hysterectomy, bilateral salpingectomy and bilateral oophorectomy

8. For participants taking antacids (regularly or as required), the participant is willing and able to avoid taking antacids for at least 6 hours before and 2 hours after Triumeq
9. Participants taking taurursodiol supplements (TUDCA) can participate in this trial if the supplement does not contain sodium phenylbutyrate.
10. Participants taking taurursodiol supplements (TUDCA) that also contain sodium phenylbutyrate must be willing to stop supplementation 30 days prior to randomisation.

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5. Those taking Riluzole must be on a stable dose for at least 30 days prior to the baseline visit or must have stopped taking Riluzole at least 30 days prior to the baseline visit
6. Women must not become pregnant (e.g., post-menopausal, surgically sterile, using highly effective birth control methods or not having potentially reproductive sex) for the duration of the study. Highly effective methods of birth control are those with a failure rate of $< 1\%$ per year when employed consistently and correctly, e.g. combined (oestrogen and progestogen containing) hormonal contraception or progestogen-only hormonal contraception
7. Women of childbearing potential must have a negative serum pregnancy test at screening and baseline and be non-lactating. Women of childbearing potential are defined as females who have experienced menarche and are not surgically sterilised (e.g. hysterectomy or bilateral salpingectomy) or post-menopausal (defined as at least 1 year since last regular menstrual period)
8. For participants taking antacids (regularly or as required), participant is willing and able to avoid taking antacids for at least 2 hours before and 6 hours after Triumeq

Participant type(s)

Patient

Healthy volunteers allowed

No

Age group

Adult

Lower age limit

18 years

Sex

All

Total final enrolment

419

Key exclusion criteria

Current exclusion criteria as of 13/02/2024:

1. People who are HLA-B*5701 positive
2. Known hypersensitivity to dolutegravir, abacavir or lamivudine, or to any of the excipients
3. Safety Laboratory Criteria at screening:
 - 3.1. ALT \geq 5 times upper limit of normal (ULN)

- 3.2. AST \geq 3 times ULN
- 3.3. Bilirubin \geq 1.5 times ULN with clinical indicators of liver disease
- 3.4. Creatinine clearance $<$ 30 ml/min
- 3.5. Platelet concentration of $<$ 100 x10⁹ per l
- 3.6. Absolute neutrophil count of $<$ 1x10⁹ per l
- 3.7. Haemoglobin $<$ 100 g/l
- 3.8. Amylase \geq 2 times ULN
- 3.9. Lactate \geq 2 times ULN
4. Moderate to severe hepatic impairment, as defined by local clinical guidelines
5. Presence of HIV antibodies at screening
6. Presence of Hepatitis C antibodies at screening unless participants have had effective treatment for Hepatitis C
7. Presence of Hepatitis B core or surface antigen at screening
8. Participation in any other investigational drug trial or using investigational drug within 30 days prior to screening
9. Use of NIV \geq 22 h per day or having a tracheostomy
10. Edaravone dose within 30 days prior to screening. Edaravone is approved by the FDA and in Japan, but remains an investigational product in Europe and Australia
11. Clinically significant history of unstable or severe cardiac, oncological, psychiatric, hepatic, or renal disease or other medically significant illness
12. Taking medication contraindicated with Triumeq: dofetilide or fampridine (dalfampridine)
13. Taking Tofersen within 3 months prior to screening.

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 - 3.2. AST \geq 3 times ULN
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 - 3.5. Platelet concentration of $<$ 100 x10⁹ per l
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11. Clinically significant history of unstable or severe cardiac, oncological, psychiatric, hepatic, or renal disease or other medically significant illness
12. Taking medication contraindicated with Triumeq: dofetilide or fampridine (dalfampridine)

Date of first enrolment

31/01/2022

Date of final enrolment

29/09/2024

Locations

Countries of recruitment

United Kingdom

England

Australia

Ireland

Netherlands

New Zealand

Slovenia

Spain

Sweden

Study participating centre

King's College Hospital

King's College Hospital NHS Foundation Trust

Denmark Hill

London

United Kingdom

SE5 9RS

Study participating centre

Royal Hallamshire Hospital

Sheffield Teaching Hospitals NHS Foundation Trust

Glossop Road

Sheffield

United Kingdom

S10 2JF

Study participating centre

John Radcliffe Hospital

Oxford University Hospitals NHS Foundation Trust

Headley Way
Oxford
United Kingdom
OX3 9DU

Study participating centre

The Walton Centre

The Walton Centre NHS Foundation Trust
Liverpool
United Kingdom
L9 7LJ

Study participating centre

Royal Preston Hospital

Royal Preston NHS Trust
Sharoe Green Lane
Fulwood
Preston
United Kingdom
PR2 9HT

Study participating centre

University College London

National Hospital London MND Care Centre
Queen Square
London
United Kingdom
WC1N 3BG

Study participating centre

The Perron Institute

Ground Floor, RR Block
QEII Medical centre
8 Verdun Street
Nedlands
Nedlands
Australia
WA 6009

Study participating centre

MQ Health Neurology

MQ Health Neurology
Suite 204, Level 2, F10A Building
2 Technology Place
Sydney
Australia
NSW 2109

Study participating centre**Launceston General Hospital**

274-280 Charles St
Launceston
Australia
TAS 7250

Study participating centre**The University of Sydney - Brain and Mind Centre**

Room 434, Level 4, M02F
94 Mallett Street
Camperdown
Sydney
Australia
NSW 2050

Study participating centre**Flinders Medical Centre**

Flinders Drive
Bedford Park
South Australia
Australia
SA 5042

Study participating centre**Royal Brisbane and Women's Hospital**

Neurology Department
Level 7, Ned Hanlon Building, Butterfield Street
Herston
Brisbane
Australia
4029

Study participating centre

UMC Utrecht

Utrecht
Netherlands
3584 CX

Study participating centre

Beaumont Hospital

Dublin
Ireland
D09V2N0

Study participating centre

Karolinska University Hospital

Stockholm
Sweden
SE-171 76

Study participating centre

Calvary Health Care Bethlehem

476 Kooyong Rd, Caulfield
Melbourne
Australia
3162

Study participating centre

Christchurch Hospital

2 Riccarton Avenue, Christchurch Central City
Christchurch
New Zealand
4710

Study participating centre

Del Mar Hospital

Pg. Marítim de la Barceloneta, 25, 29, Ciutat Vella
Barcelona
Spain
08003

Study participating centre

Dunedin Hospital

201 Great King Street, Central Dunedin
Dunedin
New Zealand
9016

Study participating centre

Derriford Hospital

Derriford Road, Derriford
Plymouth
United Kingdom
PL6 8DH

Study participating centre

Royal Stoke University Hospital

Newcastle Road
Stoke-on-trent
United Kingdom
ST4 6QG

Study participating centre

St George's Hospital

Blackshaw Rd
London
United Kingdom
SW17 0QT

Study participating centre

UMC Ljubljana

Zaloška cesta 7
Ljubljana
Slovenia
1000

Study participating centre

Sunshine Coast Hospital

6 Doherty St, Birtinya
Queensland
Australia
4575

Study participating centre

Tauranga Hospital

829 Cameron Road, Tauranga South

Tauranga

New Zealand

3112

Study participating centre

The Ann Rowling Clinic/University of Edinburgh

Chancellor's Building, Edinburgh Bioquarter, 49 Little France Crescent

Edinburgh

United Kingdom

EH16 4SB

Study participating centre

Wellington Hospital

49 Riddiford Street, Newtown

Wellington

New Zealand

6021

Study participating centre

La Fe Hospital

Avinguda de Fernando Abril Martorell, 106, Quatre Carreres

Valencia

Spain

46026

Study participating centre

Navarra Hospital Complex

C. de Irunlarrea, 3

Pamplona

Spain

31008

Sponsor information

Organisation

King's College London

ROR

<https://ror.org/0220mzb33>

Organisation

Macquarie University

Organisation

Stichting TRICALS Foundation

Funder(s)**Funder type**

Government

Funder Name

Efficacy and Mechanism Evaluation Programme

Alternative Name(s)

NIHR Efficacy and Mechanism Evaluation Programme, Efficacy and Mechanism Evaluation (EME), EME

Funding Body Type

Government organisation

Funding Body Subtype

National government

Location

United Kingdom

Funder Name

FightMND

Alternative Name(s)

Fight MND

Funding Body Type

Government organisation

Funding Body Subtype

Trusts, charities, foundations (both public and private)

Location

Australia

Funder Name

Motor Neurone Disease Research Institute of Australia

Alternative Name(s)

MND Research Institute of Australia, MND Research Institute, MNDRIA

Funding Body Type

Private sector organisation

Funding Body Subtype

Other non-profit organizations

Location

Australia

Funder Name

Treatment Research Initiative to Cure ALS (TRICALS)

Results and Publications

Individual participant data (IPD) sharing plan

The datasets generated during and/or analysed during the current study will be stored in a repository.

IPD sharing plan summary

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol file	version 2.6	20/10/2021	26/01/2023	No	No
Protocol file	version 4.0	19/10/2023	23/02/2024	No	No
Study website	Study website	11/11/2025	11/11/2025	No	Yes