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A pilot trial to test whether terazosin treatment lowers the levels of biomarkers of neurodegeneration (nerve cell damage) in the blood, spinal fluid, and urine of amyotrophic lateral sclerosis patients over 6 months

Submission date
02/11/2021

Recruitment status
No longer recruiting

Registration date
02/12/2021

Overall study status
Completed

Last Edited
10/03/2025

Condition category
Nervous System Diseases

[X] Prospectively registered
[X] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[_] Record updated in last year

Plain English summary of protocol

Background and study aims

Amyotrophic lateral sclerosis (ALS), also known as motor neuron disease (MND), is a neurodegenerative disease in which motor neurons deteriorate leading to progressive weakness. Treatment options are very limited. Laboratory evidence suggests that an enzyme called phosphoglycerate kinase 1 (PGK1) might help to protect motor neurons by increasing their energy availability. The drug terazosin is known to activate PGK1, and researchers at the University of Oxford and University of Edinburgh have shown that terazosin helps motor neuron survival in laboratory models of the disease. Terazosin is a drug that is routinely prescribed to patients either for high blood pressure or for symptoms arising from an enlarged prostate gland in men, where it acts through a different mechanism from PGK1 activation.

As motor neurons deteriorate in ALS, they release substances that can be measured in body fluids and give an indication of how active the disease is. These are called biomarkers. In this pilot study, we will test whether terazosin treatment significantly lowers the levels of biomarkers in the blood, spinal fluid and urine at intervals over the course of 6 months. We will also monitor clinical measurements of disease progression, such as the ALS Functional Rating Score and the spirometry ‘breathing’ test, which are carried out as part of your routine clinical appointments. If this study shows that terazosin alters biomarker levels, suggesting that it potentially slows the disease process in patients with ALS, it would then make a strong case for a larger-scale clinical trial.

Who can participate?

Adults over 18 years, diagnosed with ALS and first onset of symptoms between 9 - 24 months ago.

What does the study involve?
Participants will take up to 10mg oral terazosin daily for up to 6 months. There will be 3 face-to-face study visits (at baseline, 3 months and 6 months), involving the following procedures: ALSFRS-R questionnaire, spirometry test, blood samples, lumbar puncture, urine sample, blood pressure measurement.

What are the possible benefits and risks of participating?
There are potential risks associated with the blood sampling and lumbar puncture, plus the side effects of the drug (how much detail do you need?). No guaranteed direct benefit to participants, however, we hope that the results of this study will help to inform future research into treatments for ALS.

Where is the study run from?
University of Oxford (UK)

When is the study starting and how long is it expected to run for?
August 2021 to March 2025

Who is funding the study?
My Name’5 Doddie Foundation (UK)

Who is the main contact?
Prof. Kevin Talbot, kevin.talbot@ndcn.ox.ac.uk
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Contact information

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Scientific

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Additional identifiers

Clinical Trials Information System (CTIS)
2021-003345-38

Integrated Research Application System (IRAS)
301752

Central Portfolio Management System (CPMS)
51286

Protocol serial number
PID 15775

Study information

Scientific Title
Terazosin RepUrposing STudy in amyotrophic lateral sclerosis: a pilot study targeting PGK1 with terazosin in ALS patients

Acronym

TRUST

Study objectives
Terazosin treatment significantly affects key biomarkers of neurodegeneration in patients with amyotrophic lateral sclerosis (ALS)

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 21/12/2022, East Midlands – Leicester Central REC (Equinox House, City Link, Nottingham NG2 4LA, UK; +44 (0)207 104 8070; leicestercentral.rec@hra.nhs.uk),ref: 21/EM/0251

Primary study design
Interventional

Study design
Single-centre interventional open-label non-randomized non-controlled proof of concept study

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Amyotrophic lateral sclerosis

Interventions
Total duration of intervention and follow-up is 6 months. Participants will take up to 10mg oral terazosin daily for up to 6 months. There will be 3 face-to-face study visits (at baseline, 3 months and 6 months), involving the following procedures: ALSFRS-R questionnaire, spirometry test, blood samples, lumbar puncture, urine sample, blood pressure measurement.

Intervention Type
Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Terazosin

Primary outcome(s)
Plasma neurofilament light chain measured using ELISA assay at baseline and 6 months

Key secondary outcome(s)
1. CSF biomarkers measured using ELISA assay at baseline, 3 months and 6 months (neurofilament light chain, phosphorylated neurofilament heavy chain, chitotriosidase 1, chitinase 3-like protein 1, chitinase 3-like protein 2 and PGK1)
2. Plasma biomarkers measured using ELISA assay at baseline, 3 months and 6 months (neurofilament light chain and phosphorylated neurofilament heavy chain)
3. Urine biomarker measured using ELISA assay at baseline, 3 months and 6 months (Titin N-terminal fragment)

4. Functional status measured using the Revised ALS Functional Rating Scale (ALSFRS-R) score measured at baseline, 3 months and 6 months
5. Lung strength measured using Forced Vital Capacity (FVC) at baseline, 3 months and 6 months
6. Survival (data obtained by reviewing patient notes)
7. Adverse events related to IMP and proportion of patients that drop out due to adverse events (data collected from patients)

Completion date
31/03/2025

Eligibility

Key inclusion criteria
1. Participant is willing and able to give informed consent for participation in the study
2. Male or female, aged 18 years or above
3. Diagnosed with ALS (Gold Coast Criteria)
4. Symptom onset (first weakness) 9-24 months (inclusive) at enrolment
5. Taking riluzole at a stable dose for at least 4 weeks prior to enrolment, or will refrain from starting riluzole for the duration of the study, or have never taken riluzole
6. Able to swallow tablets safely
7. Willing to use highly effective contraception for the duration of trial treatment and for a duration of 80 days after the last dose

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 Years

Sex
All

Key exclusion criteria
1. Using non-invasive ventilation (NIV)
2. Pregnancy
3. Any other significant disease, disorder, or finding which may significantly increase the risk to the volunteer because of participation in the study, affect the ability of the volunteer to participate in the study or impair interpretation of the study data
4. Hypersensitivity to the IMP or any of its excipients (including lactose)
5. Taking terazosin or other alpha adrenergic blockers (doxazosin, prazosin, tamsulosin, silodosin, trazodone, tolazoline, phentolamine, phenoxybenzamine) at time of screening visit or within the 3 months prior to baseline visit
6. Ongoing use of sildenafil, tadalafil, or vardenafil
7. Taking anti-coagulant medication, e.g. warfarin or apixaban

8. Symptomatic postural hypotension or history of postural hypotension
9. Systemic hypotension (systolic BP ≤90mmHg or diastolic BP≤60mmHg)
10. History of micturition syncope
11. Contraindications to lumbar puncture
12. Taking part in a current CTIMP or have taken part in any CTIMP in the 3 months prior to recruitment

Date of first enrolment
03/08/2022

Date of final enrolment
31/05/2024

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
John Radcliffe Hospital
Oxford University Hospitals NHS Foundation Trust
Headley Way
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Sponsor information

Organisation
University of Oxford

ROR
https://ror.org/052gg0110

Funder(s)

Funder type
Charity

Funder Name

Results and Publications

Individual participant data (IPD) sharing plan

The data-sharing plans for the current study are unknown and will be made available at a later date

IPD sharing plan summary

Data sharing statement to be made available at a later date

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			28/06/2023	No	No
Protocol file	version 2.0	13/12/2021	16/09/2022	No	No