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A study to explore the safety and acceptability of a treatment called ILB in patients with Amyotrophic Lateral Sclerosis

Submission date
22/07/2019

Recruitment status
No longer recruiting

Registration date
05/11/2019

Overall study status
Completed

Last Edited
23/07/2024

Condition category
Nervous System Diseases

[_] Prospectively registered
[X] Protocol
[X] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
Amyotrophic Lateral Sclerosis (ALS) belongs to a wider group of disorders known as motor neuron diseases and mainly involves the nerve cells (neurons) in the body. Neurons receive and send messages from the body to the brain and back to the body and are responsible for controlling voluntary muscle movement. Voluntary muscles produce movements like chewing, walking and talking. ALS is caused by gradual deterioration (degeneration) and death of motor neurons. In ALS, the motor neurons degenerate or die, and stop sending messages to the muscles. Unable to function, the muscles gradually weaken and waste away. Eventually the brain loses its ability to initiate and control voluntary movement.
The disease is progressive, meaning the symptoms get worse over time and most people with ALS die from respiratory failure, usually within 3 to 5 years from when the symptoms first appear. Currently there is no cure for ALS and no effective treatment to halt or reverse the progression of the disease (National Institute of Neurological Disorders and Stroke, Fact Sheet) https://www.ninds.nih.gov/Disorders/Patient-Caregiver-Education/Fact-Sheets/Amyotrophic-Lateral-Sclerosis-ALS-Fact-Sheet.
The aim of this study is to explore the safety and acceptability of a type of low molecular weight Dextran Sulfate called ILB.
ILB has been developed by a small Swedish industry company called TikoMed. TikoMed along with colleagues at the University of Birmingham have tested this drug in a number of pre-clinical (animal studies) and in 79 humans (69 healthy volunteers and 10 patients with diabetes). Results of these studies indicate there may be some beneficial effects to using ILB in a number of diseases including ALS. This will be the first study in this patient group.

Who can participate?
Patients with a diagnosis of ALS that meet the eligibility criteria

What does the study involve?
Patients will be closely monitored for any side-effects; for changes in ALS symptoms and on their quality of life during and after the study. At the end of the study we will know if ILB is safe and if it is acceptable to ALS patients.

What are the possible benefits and risks of participating?
There may be no immediate clinical benefit from taking part , and you may or may not feel better from participating in this study. At best we would hope to reduce the rate of disease progression but unfortunately this drug will not offer a cure for the disease. However, the study has been designed to help us gain a better understanding of this drug and may result in changes in the future treatment and follow-up of patients with ALS.
The possible disadvantages and risks of taking part in this study are:
- Possible side-effects from taking the drug
- The drug may not be effective and delay you starting standard treatment
- Attending multiple treatments and follow-up appointments

Where is the study run from?
University Hospitals Birmingham NHS Foundation Trust, UK

When is the study starting and how long is it expected to run for?
March 2019 to April 2021 (updated 18/03/2020, previously: February 2020)

Who is funding the study?
TikoMed, Sweden

Who is the main contact?
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Contact information

Type(s)
Scientific

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Additional identifiers

Clinical Trials Information System (CTIS)
2018-000668-28

Integrated Research Application System (IRAS)
242984

ClinicalTrials.gov (NCT)
NCT03705390

Protocol serial number
RG-17-250; CPMS 39097, IRAS 242984

Study information

Scientific Title
A Phase II pilot safety and tolerability study of ILB in patients with Motor Neurone Disease (MND) /Amyotrophic Lateral Sclerosis (ALS)

Acronym
ALS

Study objectives
The primary aim of the trial is to determine the safety and tolerability of ILB administered subcutaneously weekly in ALS patients. The secondary aim is to describe the effect of ILB administered subcutaneously weekly:
- upon the severity of symptoms associated with ALS present at entry into the study
- upon development of new symptoms associated with ALS during the study
- upon patients' quality of life during the study
To assess changes in biomarkers, including urinary p75ECD and plasma NfL patients

Ethics approval required
Old ethics approval format

Ethics approval(s)

Approved 08/08/2018, South Central – Oxford B Research Ethics Committee (Whitefriars, Level 3, Block B, Lewin's Mead, Bristol, BS1 2NT; +44 (0)20 7104 8049; nrescommittee.southcentral-oxfordb@nhs.net),
ref: 18/SC/0368

Study design
Non-randomised; Interventional; Design type: Treatment, Drug

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Amyotrophic lateral sclerosis (ALS), also known as motor neurone disease (MND)

Interventions
Our research will answer an important question: will ILB be safe and acceptable for patients with ALS. We will do this by measuring the number and severity of unanticipated experiences or reactions (both serious and non-serious) that occur when patients are treated with ILB, these events will be graded, recorded and closely monitored. Similarly we also hope to be able to assess how acceptable the treatment is to ALS patients. In addition to the safety and tolerability assessments we would hope to be able to describe the effect of ILB on patients ALS symptoms, and on their quality of life.

We don’t know if ILB will have any effect on the patients in this study or ALS patients generally but the information gained from this study will help researchers develop future studies in this disease area.

The study can be broken down into 5 key stages:

Stage 1 Screening tests
Stage 2 The start of treatment, within 14 days of the screening tests
Stage 3 Weekly hospital visits for 24 weeks for safety checks and study injections
Stage 4 End of treatment visit at week 12 with additional tests for safety checks
Stage 5 Follow up – includes visits to hospital at 16, 20 and 24 weeks for safety checks

Intervention Type
Other

Phase
Phase II

Primary outcome(s)
1. Safety - measured by the incidence of serious adverse events (SAEs) and adverse events (AEs) using CTCAE v4.0. Events will be summarised by grade, relatedness, admitting event (for SAEs); expectedness and sequelae
2. Tolerability - measured by the incidence of intolerable adverse events reported for the duration of the trial and up to 30 days after the last treatment visit.. An intolerable adverse

event will satisfy all of the following criteria:
2.1. Associated with a serious adverse event or a drug discontinuation of greater than three weeks
2.2. Grade 3, 4 or 5 in severity according to CTCAE version 4
2.3. In the opinion of the Investigator is i) definitely related or ii) probably related or iii) possibly related to the study drug treatment
3. Adverse events which are considered unrelated or probably not related will not be classed as intolerable events, reported throughout the trial and up to 30 days after the last treatment visit
4. Quantity of study drug administered is measured through: total drug administered, number of administrations, number and length of interruptions and number of discontinuations and will be reported at each treatment administration visit

Key secondary outcome(s))
1. Revised ALS Functional Rating Scale (ALSFRS-R) This is a functional rating scale, including assessments of communication, mobility, feeding, dressing and respiration will be completed at every visit (screening, wk 1-10, follow up wk1, 16, 20, 24)
2. ALS Assessment Questionnaire (ALSAQ-40) This patient-reported outcome measures the subjective well-being of patients. It is broader than ALSFRS-R and adds assessment of emotional reactions will be completed at every visit (screening, wk 1-10, follow up wk1, 16, 20, 24)
3. Urinary p75ECD; this is a biological fluid-based biomarker of ALS disease progression measured at wk1, wk 5, wk 12, wk 24
4. NfL in plasma; this is a bloodbased biomarker for neurodegeneration measured at wk1, wk 5, wk 12

Completion date
30/04/2021

Eligibility

Key inclusion criteria
1. Patients > = 18 years and who have provided written informed consent to participate in the study
2. Prior to trial entry patients will have a definite diagnosis of ALS according to El Escorial Criteria. All patients will demonstrate either:
2.1 Presence of UMN (increased tone, brisk reflexes) as well as LMN (weakness, wasting and fasciculation) signs in the bulbar region and at least two of the other spinal regions (cervical, thoracic or lumbosacral) OR
2.2 Presence of UMN and LMN signs in all three spinal regions (cervical, thoracic or lumbosacral)
3. Electrophysiological tests (Electromyography (EMG) / Nerve Conduction Study (NCS)) that supports the diagnosis of Motor Neurone Disease (MND)
4. Forced Vital Capacity (FVC) > = 50% of predicted value for gender, height and age at screening and a mean Sniff Nasal Inspiratory Pressure (SNIP) > = 50% of predicted value for age
5. Adequate haematological function (Hb> = 10g/dl), absolute neutrophil count > = 1.5x109/L and a platelet count > = 60 x109/L
6. International Normalised Ratio (INR) < = 1.5, aPTT 30 – 40 seconds, PT 11-13.5 seconds
7. Patient willing and able to comply with scheduled visits, treatment plan and other study procedures.
8. Patients taking Riluzole must have discontinued treatment > = 28 days prior to study entry (and following consent to take part in the study)

9. Women Of Child Bearing Potential (WOCBP) who agree to use highly effective means of contraception (as defined in the Heads of Medicines Agencies_Clinical Trials Facilitation Group (HMA_CTFG) guideline for the entirety of the study

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Total final enrolment
11

Key exclusion criteria
1. Patients classified as either probable or possible ALS according to El Escorial Criteria
2. Subjects in whom other causes of neuromuscular weakness have not been excluded.
3. Assisted ventilation of any type within 3 months before the screening visit or at screening
4. Patients requiring Radiologically Inserted Gastrostomy (RIG) or Percutaneous Endoscopic Gastroscopy (PEG) feeding
5. Involvement in any other interventional study involving use of another IMP or biological product within 3 months of screening
6. Any use of antioxidants, edaravone, tirasemtiv or CK-2127107 within 1 month before the screening visit.
7. Any botulinum toxin use within 3 months before the screening visit
8. Any form of stem cell or gene therapy for the treatment of amyotrophic lateral sclerosis (ALS)
9. Neuroimaging of brain and cervical spine with Magnetic Resonance Imaging (MRI) indicating compressive myelopathy as an alternate diagnosis
10. Laboratory examinations including Acetylcholine receptor (AChR) antibodies and Muscle Specific Kinase (MuSK) antibodies to exclude Bulbar onset Myasthenia gravis from Bulbar onset Motor Neurone disease as an alternate diagnosis and Antinuclear Antibodies (ANA), Anti-neutrophil cytoplasmic antibodies (ANCA), Extractable Nuclear Antigen (ENA) antibodies, Creatine Kinase (CK), electrophoresis and immunoglobulin indicating an alternate diagnosis for muscle disease like Myositis
11. Abnormal liver function defined as AST and/or ALT > 3 times upper limit of normal
12. Any head trauma, intracranial or spinal surgery within 3 months of trial entry
13. Patients who have had recurrent falls will be excluded to reduce the risk of intracerebral haemorrhage with this Investigational Medicinal Product (IMP)
14. Current use of an anticoagulant e.g Warfarin, Aspirin, Clopidogrel, any novel anticoagulants (NOAC)s or low molecular weight heparin
15. Uncontrolled hypertension
16. Current or previous history of heparin-induced thrombocytopenia
17. Active peptic ulcer disease

18. Known hypersensitivity to sulphur
19. Severe liver insufficiency
20. Patients with evidence of major psychiatric illness, significant cognitive impairment or clinically evident dementia that may interfere with the patient`s ability to comply with study procedures.
21. Pulmonary illness (e.g asthma or Chronic Obstructive Pulmonary Disease (COPD) requiring regular treatment
22. Patient judged to be actively suicidal by the Investigator during 3 months before the screening visit
23. Subjects with a diagnosis of another neurodegenerative disease (e.g. Parkinson`s disease, Altzheimers disease and Frontotemporal dementia)

Date of first enrolment
11/03/2019

Date of final enrolment
27/03/2020

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
University Hospitals Birmingham NHS Foundation Trust
Mindelsohn Way
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Sponsor information

Organisation
University of Birmingham

ROR
https://ror.org/03angcq70

Funder(s)

Funder type

Industry

Funder Name
TIKOMED AB

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are not expected to be made available.

IPD sharing plan summary
Not expected to be made available

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		11/07/2024	15/07/2024	Yes	No
Basic results	version 1.0	19/06/2024	20/06/2024	No	No
HRA research summary			28/06/2023	No	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes
Protocol file	version 8.0	25/11/2020	08/07/2024	No	No
Statistical Analysis Plan	version 1.0	14/06/2018	08/07/2024	No	No
Statistical Analysis Plan	version 2.0	11/09/2020	23/07/2024	No	No