mnda motor neurone disease association

Research

TUDCA-ALS clinical trial

Information Sheet DB

TUDCA-ALS (Safety and efficacy of tauroursodeoxycholic acid (TUDCA) as add-on treatment in patients affected by amyotrophic lateral sclerosis (ALS)) is a clinical trial taking place in Italy, Germany, UK, France, Belgium, the Netherlands and Ireland. It will test a new potential therapy for ALS, the most common form of MND. The drug to be tested is called TUDCA.

This information sheet explains how TUDCA works and how it may be used to treat MND, the criteria that need to be met for a person to take part and what taking part in the trial will involve. A full, much more detailed explanation of the study will be provided by a trial doctor to everyone who takes part. This information sheet contains an outline of the study only.

Not everyone can participate in a trial. There are several rules, or criteria, that people with MND must meet to participate in this trial and some criteria that will exclude people from participating. A summary of the inclusion criteria is listed on pages 3-4.

To visit the TUDCA-ALS website, go to www.tudca.eu.

The content is split into the following sections:

Disclaimer: *Please note that information provided in this information sheet is based on a review of the currently available literature. This information sheet was written by the MND Association staff who are not clinicians and so any information provided in this sheet should not be considered a clinical advice. You should always discuss potential treatments with your clinician.*

This symbol is used to highlight **our other publications**. To find out how to access these, see *Further information* at the end of this sheet.

What do the words and abbreviations mean?

Biomarker:	Unique biological signature of a specific disease, or group of diseases.
Cerebrospinal fluid (CSF):	Cushioning fluid encasing the brain and spinal cord.
Tauroursodeoxycholic acid (TUDCA):	Substance found in small traces in the bile acid of humans.
Lumbar puncture:	Medical procedure in which a thin needle is introduced into the spine to collect cerebrospinal fluid.
Placebo:	An inactive compound ('dummy drug') randomly given to half of participants in most clinical trials.

1: Background

Amyotrophic Lateral Sclerosis (ALS) is the most common form of motor neurone disease (MND). Although ALS is not a disease of the liver and bile duct, there is evidence that increasing the levels of TUDCA can slow the rate of death of the motor neurone.

The purpose of this study is to test the safety and effectiveness of low doses of tauroursodeoxycholic acid in people with ALS and, in particular, to find out if it may slow down the progression of the disease.

What is Tauroursodeoxycholic acid and how does it work?

Tauroursodeoxycholic acid (TUDCA) is a substance naturally produced by the body and found in small trace amounts in the bile. TUDCA works by camouflaging a stress chemical that triggers a chemical cascade that results in the death of a distressed or damaged cell.

Has it been tested before?

TUDCA is currently licensed to be used as a treatment in certain diseases of the liver in the USA. However, there is a growing body of evidence to suggest that TUDCA might be a potential therapeutic drug for a number of neurodegenerative diseases including Alzheimer's Disease, Parkinson's Disease and Huntington's Disease.

A recent Phase 2 clinical trial looking at TUDCA over a 6-month period in 34 people with ALS showed that TUDCA is safe to administer for a short period of time and might be slowing down the progression of the disease.

Purpose of the trial

The TUDCA-ALS Phase 3 clinical trial will look at the safety and efficacy of taking TUDCA in combination with riluzole over a long period of time (18 months).

The trial will recruit 440 people recently diagnosed with ALS across 26 centres across Italy, Germany, UK, France, Belgium, the Netherlands and Ireland.

For further information about how clinical trials are conducted, see: Information sheet D – *Clinical trials.*

Aims of the trial

TUDCA-ALS aims to determine the effects TUDCA has on people with ALS and, in particular, if it has the potential to slow down the progression of the disease. To test this, the team will measure the effect of TUDCA on disease progression, survival, changes in breathing and quality of life. In addition, they will be carefully monitoring any side effects that people may experience when taking this drug.

As this is a placebo-controlled trial, it is important for people taking part to understand that only one half of the participants will be given the active drug (TUDCA), whereas the other half will receive an inactive agent (placebo). All participants will be randomly allocated to one of these groups.

As part of the work, the researchers will search for biomarkers (unique biological signatures of the disease), in the blood and cerebrospinal fluid (CSF). Finding biomarkers for ALS would allow us to show whether a drug is working, monitor the progression of the disease, and potentially lead to a speedier diagnosis.

For further information about biomarkers, see: Information Sheet G: *Biomarkers.*

2: Taking part in the trial

Where will the trial take place?

The following seven centres will be recruiting participants in the UK and Ireland:

Sheffield: Royal Hallamshire Hospital (the lead centre for the UK)
Preston: Preston Hospital
Liverpool: The Walton Centre
Plymouth: Derriford Hospital
Salford: Salford Royal Hospital
Stoke: Royal Stoke University Hospital
Dublin: Beaumont Hospital

How are people selected for the trial?

Not everyone can participate in a trial. There are several criteria that people with ALS must meet to participate in this trial (inclusion criteria) and some criteria that may exclude people from participating (exclusion criteria). Some important inclusion criteria are listed below (the full list is available at http://www.tudca.eu/take-part/).

In addition to these criteria, once the researchers have reached their target number of participants (the UK has a target of 70 participants), they will not be able to include any more.

Inclusion criteria (who can take part?)

To be eligible to take part in the initial stage of the clinical trial, participants need to meet the following criteria:

- Age between 18 and 80
- Recently diagnosed with ALS (with a disease duration of 18 months or less, starting from the time of first symptoms)
- No swallowing difficulties
- Stable on riluzole treatment

Exclusion criteria (who cannot take part?)

- People with other causes of neuromuscular weakness
- People with other neurodegenerative diseases
- People with significant cognitive impairment, clinical dementia or psychiatric illness
- Women of child-bearing age without contraception, who are pregnant or breast feeding
- People with severe cardiac and pulmonary disease
- People with an active peptic ulcer

What would I have to do if I took part?

The study is divided into three stages:

Stage 1

Once you have given your consent to take part in the study, you will be asked to undertake a detailed 'screening' evaluation to confirm that you meet all the eligibility criteria for the trial. This will include taking blood samples and, if you are happy, samples of your cerebrospinal fluid (CSF) to act as a baseline for the start of the study.

Stage 2

After three months you will be re-screened for eligibility to confirm that you are able to continue with the study. If you are taking riluzole, you will be monitored to ensure that you are stable whilst taking riluzole (the only current treatment that slows progression of ALS). If you are not currently taking riluzole, you will start taking riluzole at your enrolment into the study and be followed for three months to ensure that you are stable whilst taking riluzole.

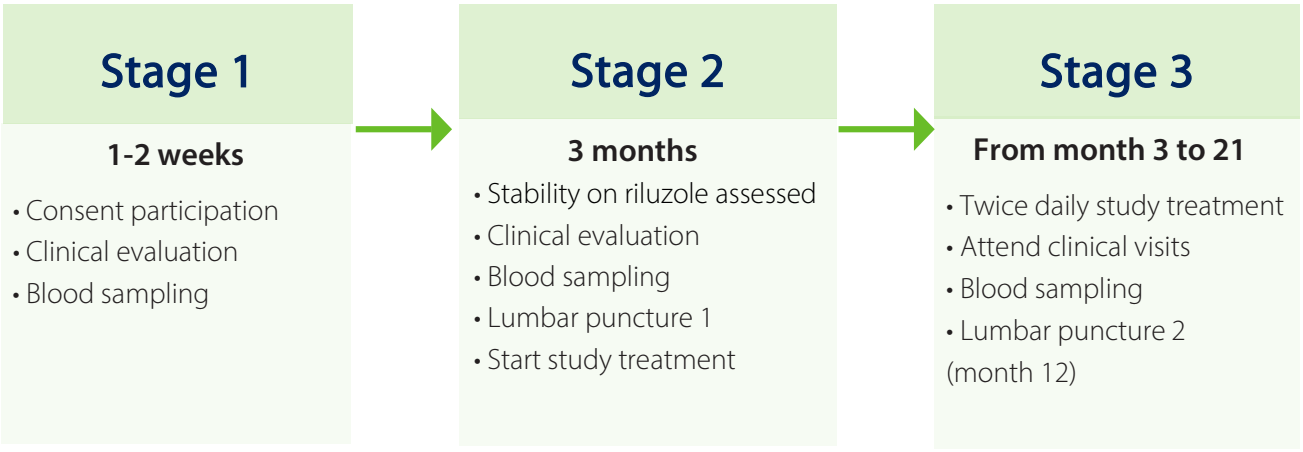
Stage 3

A computer system will randomly allocate you to one of the two trial groups; either to receive a placebo, or TUDCA. Neither you nor your study doctor will know which group you've been allocated to.

You will then begin to receive the treatment capsules (either TUDCA or placebo). You will take 4 capsules in the morning and night every day for 18 months.

Throughout the 18-month period you will be asked to visit the clinic every 3 months for routine checks of your symptoms and blood sampling. At some of these visits you will also be asked to complete assessments similar to those you underwent at your screening visit.

After the study is finished, you can continue taking riluzole which will be prescribed to you by your GP or neurologist. You will not be provided with the TUDCA treatment as the data of its safety over a long period of time and any beneficial effects will still be unknown until their analysis.



Why will a placebo be used?

It is important to note that half of the participants in the trial will not receive the TUDCA treatment. This 'control' group is essential if the trial is to demonstrate convincingly whether TUDCA provides benefits over the 'placebo' drug. Placebo is a 'dummy drug' that has no beneficial (or adverse) effects. A placebo looks, tastes, and smells the same as the active drug to ensure that everyone involved in the clinical trial "blinded" as to who is taking the active drug and who is taking placebo. This is called a double-blind study.

For further information about how clinical trials are conducted, see: Information sheet D – *Clinical trials*.

3: TUDCA treatment for people unable to take part in the trial

We are aware that a number of people living with ALS will not be eligible to take part due to the exclusion criteria such as having difficulties with swallowing or have been diagnosed with other conditions.

TUDCA is administered in 1g doses via the ingestion of 4 capsules that contain 250mg of TUDCA. Anyone taking part in the trial will be required to swallow 4 capsules twice a day (once in the morning and once in the evening). There is currently no data available to understand what will happen if the drug is administered via a feeding tube or

Percutaneous endoscopic gastrostomy (PEG).

Exclusion of people living with other conditions is to prevent a potential interaction of treatments, which might bias the real effect of TUDCA in combination with riluzole. Additionally, presence of symptoms due to other conditions might also bias the observed effect of the study treatment.

As TUDCA is still an experimental treatment, it is not currently available as an NHS treatment for ALS. However, if the trial does indicate that TUDCA provides benefits for people living with ALS then the TUDCA-ALS project team will look to apply for this to be registered as a treatment, providing they are able to provide enough evidence to satisfy the drug licensing authorities.

The MND Association understand that people with ALS need to hold the hope that research will find an answer to the disease. Please be aware that clinical trials are not treatments, but medical experiments that may or may not be successful.

The results of the trial are due in the **first half of 2023**.

What should I consider before taking part?

Location of the centres and travel should be taken into consideration by people who wish to participate. Support by a carer might be especially necessary due to the length of the study and the likely progression of the disease symptoms. Please make sure to carefully discuss your participation in the study with your carer before agreeing to take part.

4: I think I am eligible to take part, what next?

If you think that you are eligible to take part, please talk this through with your local MND neurologist. If they haven't heard of this research study, please show them a copy of this information sheet.

If they agree that you might be eligible to take part, they will be able to refer you to one of the participating centres. The centres in this clinical trial will be initially recruiting from their local area. Due to the complexity of the study, there may be a limit to the numbers of people that can be recruited at any one time.

5: How do I find out more?

Further information

You may find these information sheets from the MND Association helpful:

D – *Clinical trials*
G – *Biomarkers*

We also provide the following guides:

Living with motor neurone disease – our main guide to help you manage the impact of the disease

Caring and MND: support for you – comprehensive information for unpaid or family carers, who support someone living with MND

Caring and MND: quick guide – the summary version of our information for carers

You can download most of our publications from our website at

www.mndassociation.org/publications or order in print from the MND Connect helpline, who can provide further information and support.

MND Connect can also help locate external services and providers, and introduce you to our available services, including your local branch, group, Association visitor or regional care development adviser.

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MND Association website and online forum
Website: **www.mndassociation.org**
Online forum: **forum.mndassociation.org** or through the website

We welcome your views

Your feedback is important to us, as it helps improve our information for the benefit of people living with MND and those who care for them. If you would like to provide feedback on any of our information sheets, you can access an online form at: **www.surveymonkey.co.uk/r/infosheets_research**

You can request a paper version of the form or provide direct feedback by email: research@mndassociation.org.

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