Efficacy and Tolerability of Tauroursodeoxycholic Acid in Amyotrophic Lateral Sclerosis (TUDCA-ALS)

This study is currently recruiting participants.
Verified by Istituto Nazionale Neurologico Carlo Besta, April 2009

First Received: April 7, 2009   Last Updated: June 8, 2010   History of Changes

Purpose

The preclinical rationale for tauroursodeoxycholic acid (TUDCA) use in treating patients with amyotrophic lateral sclerosis (ALS) stems from the demonstration of antioxidant, antiapoptotic and neuroprotective properties of TUDCA in the central nervous system (CNS), both in vitro and in vivo models.

This protocol is meant for assessing if the addition of TUDCA to the conventional therapy can improve the therapeutic outcome in patients affected by ALS.

Safety will be assessed for all subjects, for the entire duration of the study. 20 patients affected by ALS with site of onset in the limbs will be recruited.

All enrolled subjects will continue receiving riluzole and vitamin E at the same regimen as before entering the trial. Based on an appropriate random code, subjects will be divided into two groups of equal size treated, after a lead-in period of 3 months, by oral route with TUDCA at the dose 2 g daily for 1 year or with identical placebo by oral route at the same dosing schedule, under double-blind conditions.

Every concomitant and/or supportive therapy will be admitted.

Evaluation criteria:

Efficacy. Primary evaluation parameter will be the ALSFRS-R (2) according to the consensus conference on designing and implementing clinical trials in ALS (3). Primary endpoint will be the ALSFRS-R slope during the treatment period as compared to the lead-in period.

Efficacy. Secondary parameters will include FVC%, the SF-36 quality of life rating scale, Time to tracheotomy from starting of study medication dosing (if appropriate), Survival Time from starting of study medication dosing (if appropriate) and the number of patients showing an improvement ≥ 15% in ALSFRS-R slope as compared to...
the lead-in period (responders).

Safety. Incidence, severity and type of adverse events; changes in clinical laboratory findings.

<table>
<thead>
<tr>
<th>Condition</th>
<th>Intervention</th>
<th>Phase</th>
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</table>
| Amyotrophic Lateral Sclerosis | Drug: tauroursodeoxycholic acid (TUDCA)  
Drug: Placebo                      | Phase II |

Study Type: Interventional  
Study Design: Allocation: Randomized  
Control: Placebo Control  
Endpoint Classification: Safety/Efficacy Study  
Intervention Model: Single Group Assignment  
Masking: Double Blind (Subject, Caregiver, Investigator, Outcomes Assessor)  
Primary Purpose: Treatment

Official Title: A Randomized, Double-blind Multicenter Pilot Study vs. Placebo for the Evaluation of Efficacy and Tolerability of Tauroursodeoxycholic Acid Administered by Oral Route as Add on Treatment in Patients Affected by Amyotrophic Lateral Sclerosis

Resource links provided by NLM:

- Genetics Home Reference related topics: amyotrophic lateral sclerosis
- MedlinePlus related topics: Amyotrophic Lateral Sclerosis, Antioxidants
- Drug Information available for: Tauroursodeoxycholic acid, Ursodeoxycholic acid
- U.S. FDA Resources

Further study details as provided by Istituto Nazionale Neurologico Carlo Besta:

Primary Outcome Measures:

- Amyotrophic Lateral Sclerosis functional rating scale (ALSFRS)-R slope  
  [ Time Frame: 1 year ] [ Designated as safety issue: Yes ]

Secondary Outcome Measures:

- Forced vital capacity (FVC) % [ Time Frame: 1 year ] [ Designated as safety issue: Yes ]
- SF-36 quality of life rating scale [ Time Frame: 1 year ] [ Designated as safety issue: Yes ]
- Time to tracheostomy from starting of study medication dosing (if appropriate)  
  [ Time Frame: 1 year ] [ Designated as safety issue: Yes ]
- Survival time from starting of study medication dosing (if appropriate)  
  [ Time Frame: 1 year ] [ Designated as safety issue: Yes ]

Estimated Enrollment: 26
Study Start Date: June 2008
Estimated Study Completion Date: December 2010
Estimated Primary Completion Date: December 2009 (Final data collection date for primary outcome measure)

<table>
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<tr>
<th>Arms</th>
<th>Assigned Interventions</th>
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<tbody>
<tr>
<td>TUDCA: Experimental</td>
<td>Drug: tauroursodeoxycholic acid (TUDCA)</td>
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</table>
Oral route at the dose of 1 g b.i.d. (2 g daily) for 1 year

| Comparator | Drug: Placebo identical placebo by oral route at the same dosing schedule |

Eligibility

Ages Eligible for Study: 18 Years to 75 Years
Genders Eligible for Study: Both
Accepts Healthy Volunteers: No

Criteria

Inclusion Criteria:
- Caucasian male or female out-patients;
- aged 18 to 75 years inclusive;
- diagnosis of "probable" or "definite" amyotrophic lateral sclerosis according to the El Escorial revised criteria (1);
- first symptoms of ALS by no more than 1.5 years;
- in treatment with steady regimen of riluzole and vitamin E for a minimum of 3 months before study entry, and desiring its continuation;
- FVC ≥ 75% of predicted;
- no conditions known to be contraindications to the use of TUDCA;
- written informed consent.

Exclusion Criteria:
- subjects who underwent tracheostomy;
- subjects who underwent resection of gall bladder;
- subjects with signs of conduction blocks of motor nerves, sensory nerves or both on nerve conduction study;
- subjects with clinical signs of dementia;
- subjects with active peptic ulcer;
- subjects with active malignancy;
- female subjects who are pregnant or lactating
- subjects who have received an experimental drug or have participated in a clinical trial within 3 months prior to screening
- employees of the investigator or study centre with direct involvement in the proposed study or other studies under the direction of that investigator or study centre.

Contacts and Locations

Please refer to this study by its ClinicalTrials.gov identifier: NCT00877604

Contacts

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Locations

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Milan, Italy, 2013

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More Information

Publications:


Robertson J, Kriz J, Nguyen MD, Julien JP. Pathways to motor neuron degeneration in transgenic...


Responsible Party: Istituto Nazionale Neurologico Carlo Besta (Istituto Nazionale Neurologico Carlo Besta)

ClinicalTrials.gov Identifier: NCT00877604  History of Changes

Other Study ID Numbers: TUDCA200701, EudraCT No.: 2007-001592-10

Study First Received: April 7, 2009

Last Updated: June 8, 2010

Health Authority: Italy: National Monitoring Centre for Clinical Trials - Ministry of Health

Keywords provided by Istituto Nazionale Neurologico Carlo Besta:
- ALS
- Therapy
- Tauroursodeoxycholic acid
- TUDCA
- antioxidant
- antiapoptotic drug
- neuroprotective drug

Additional relevant MeSH terms:
- Amyotrophic Lateral Sclerosis
- Sclerosis
- Motor Neuron Disease
- Spinal Cord Diseases
- Central Nervous System Diseases
- Nervous System Diseases
- Neurodegenerative Diseases
- Neuromuscular Diseases
- Pathologic Processes
- Tauroursodeoxycholic acid
- Taurochenodeoxycholic Acid
- Neuroprotective Agents
- Cholagogues and Choleretics
- Gastrointestinal Agents
- Therapeutic Uses
- Pharmacologic Actions
- Antiviral Agents
- Anti-Infective Agents
- Protective Agents
- Physiological Effects of Drugs
- Central Nervous System Agents

ClinicalTrials.gov processed this record on August 04, 2010