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European trial of Minocycline IN Amyotrophic Lateral Sclerosis

Submission date	Recruitment status	[X] Prospectively registered
26/02/2007	Stopped	[ ] Protocol
Registration date	**Overall study status**	[ ] Statistical analysis plan
03/05/2007	Stopped	[ ] Results
Last Edited	**Condition category**	[ ] Individual participant data
29/07/2009	Nervous System Diseases	[ ] Record updated in last year

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

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Additional identifiers

Clinical Trials Information System (CTIS)
2006-003992-11

Protocol serial number
G0501266

Study information

Scientific Title

Acronym
EMINALS

Study objectives
Please note that as of 26/09/2007 this trial was stopped.

The principal hypothesis is that minocycline will prove to be a clinically useful, cost-effective and safe disease-modifying (neuroprotective) treatment in Amyotrophic Lateral Sclerosis (ALS) by decreasing the rate of progression (reflected by improved survival at 18 months) and the rate of deterioration of function and Quality of Life (QL).

In order to test the hypothesis that minocycline modifies Central Nervous System (CNS) cytokine production and/or pro-apoptotic pathways and that the changes observed can be related to CNS minocycline concentrations and drug response, we will collect blood and CerebroSpinal Fluid (CSF) samples from a sample of 200 patients (Institute of Psychiatry/ King's College London and Paris).

We also wish to test the hypothesis that genetic variations in genes coding for cytokines (e.g. MCP-1) and drug efflux pump proteins influence response to minocycline therapy. We will therefore collect blood for DNA extraction from all patients in the trial.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Not provided at time of registration

Study design
Multi-centre international double-blind randomized, parallel group stratified controlled trial

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Amyotrophic lateral sclerosis (ALS)/motor neuron disease (MND)

Interventions
1000 patients (500 in each arm) will be recruited over twelve months.

All patients will be stabilised on riluzole 100 mg daily and be randomised to either of the following study groups:
1. 200 mg minocycline daily as capsules containing 50 mg base of minocycline, four to be taken in the morning, with subject upright, for 18 months
2. Matching placebo, 18 months

This trial is sponsored jointly by King's College London (UK) and Assistance Publique Hopitaux de Paris (France).

Intervention Type
Drug

Phase
Not Specified

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

Primary outcome(s)
Survival (death alone) at 18 months. For the event rate, death alone will be used and ascertained through death certificates to achieve complete data for date.

Key secondary outcome(s))
1. ALS Functional Rating Scale, revised version (ALSFRS-R)
2. EuroQol EQ-5D
3. Client Service Receipt Inventory (CSRI), which will be specifically adapted for this study
4. Safety will be assessed through adverse event reports according to GCP standards required by the European Directive, and by haematological and biochemical analyses
5. Blood (1000 patients) and CSF (200 patients) will be collected for biomarkers of drug action and for pharmacokinetic and pharmacogenomic studies

Completion date
31/03/2010

Reason abandoned (if study stopped)
During the set up phase, new information emerged (a similar negative finding trial in the US) that meant the investigators have had to re-think the study completely and in essence, the study as it was registered cannot happen.

Eligibility

Key inclusion criteria
1. Possible, probable (clinically or laboratory) or definite ALS according to the revised version of the El Escorial World Federation of Neurology criteria (The Airlie House Statement: http://www.wfnals.org/). The onset form (bulbar or limb) and disease type (familial or sporadic) will be recorded; source documents will include a full report of an electromyogram (EMG) reported by an experienced neurophysiologist as compatible with ALS
2. Disease duration more than 6 months (required by the El Escorial Criteria as the minimum time required to determine that there has been progression) and less than 5 years (inclusive); disease onset defined as date of first muscle weakness
3. Vital Capacity (VC) greater than or equal to 40 % of predicted
4. Age: greater than or equal to 18 years (inclusive)
5. Sex: male or female. In the case of a female with childbearing potential, the patient must use adequate contraceptive measures and must not be pregnant or breast-feeding

6. Continuously treated with riluzole for at least 3 months and stabilised at 100 mg/day (50 mg twice a day) without significant adverse drug reactions
7. Capable of understanding the information given and giving fully informed consent

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Not Specified

Lower age limit
18 years

Sex
Not Specified

Key exclusion criteria
1. Previous participation in another clinical study within the preceding 12 weeks
2. Tracheostomy, assisted ventilation of any type during the preceding three months
3. Existing gastrostomy
4. Any medical condition known to have an association with motor neuron dysfunction which might confound or obscure the diagnosis of ALS
5. Presence of any concomitant life-threatening disease or any disease or impairment likely to interfere with functional assessment
6. Confirmed hepatic insufficiency or abnormal liver function (aspartate aminotransferase [AST] and/or alanine aminotransferase [ALT] greater than 1.5 the upper limit of the normal range)
7. Renal insufficiency (serum creatinine greater than 200 µmol/L [2.26 mg/dL])
8. Evidence of major psychiatric disorder or clinically evident dementia precluding evaluation of symptoms
9. Known hypersensitivity to any component of the study drugs or to drugs in this class
10. Likely to be unco-operative or to fail to comply with the trial requirements or to be inaccessible in the event of an emergency
11. Unable or unwilling to use an effective method of contraception if a woman of childbearing age

We have chosen inclusion criteria that are permissive (i.e., sensitive) without sacrificing specificity. The El Escorial Criteria of the World Federation of Neurology (The Airlie House Statement: http://www.wfnals.org/) are internationally accepted research diagnostic criteria with high specificity and sensitivity.

Date of first enrolment
01/09/2007

Date of final enrolment
31/03/2010

Locations

Countries of recruitment
United Kingdom

England

France

Study participating centre
MRC Centre for Neurodegeneration Research
London
United Kingdom
SE5 8AF

Sponsor information

Organisation
King's College London (UK)

ROR
https://ror.org/0220mzb33

Funder(s)

Funder type
Research council

Funder Name
Medical Research Council (MRC) (UK)

Alternative Name(s)
Medical Research Council (United Kingdom), UK Medical Research Council, Medical Research Committee and Advisory Council, MRC

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration