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Minocycline in Alzheimer's disease

Submission date	Recruitment status	[_] Prospectively registered
24/07/2013	No longer recruiting	[_] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
24/07/2013	Completed	[X] Results
Last Edited	**Condition category**	[_] Individual participant data
19/11/2019	Nervous System Diseases	

Plain English summary of protocol

Background and study aims
Alzheimers disease (a mental disorder) is a major public health issue and there is a clear need to discover and develop treatments that can stop or at least delay disease progression. Unfortunately, although we have drug treatments that can reasonably improve some of the symptoms of Alzheimer's disease, we do not yet have treatments that can slow down or stop deterioration. Minocycline is an antibiotic drug that has also been shown to slow down deterioration in some research using animal models. This makes it the most promising drug for treatment that is not currently in trials and it is cheap and well tolerated. This study will find out the effects of two years of minocycline treatment on deterioration in mental processes and activities of daily living in patients with early Alzheimer's disease assessed and managed within NHS Memory Services. If minocycline can be shown to be working well, this would rapidly pave the way for further studies and ultimately the availability of a low cost and safe treatment for this common and devastating condition.

Who can participate?
Any patient aged 50 or over, diagnosed with Alzheimer's disease, can participate in this study.

What does the study involve?
Participants will be randomly allocated to one of three groups: daily treatment with 400 mg minocycline, 200 mg minocycline or a dummy drug (placebo). They will undergo this treatment for two years.

What are the possible benefits and risks of participating?
It is possible that minocycline may slow the rate of progression of disease or reduce symptoms of Alzheimers disease, but this cannot be guaranteed. Participation will provide useful information about the disease and minocycline. It is possible that patients may experience side effects from taking the study drug. These side effects may include nausea, diarrhoea and dizziness. Rarely the drug can cause increased sensitivity to sunlight and, very rarely, joint pain. In addition, there is always a risk of unknown side effects occurring.

Where is the study run from?
The study is run across 20 sites in England and Scotland.

When is study starting and how long is it expected to run for?
The study started in June 2013 and will run until 2018.

Who is funding the study?
The study is funded by the National Institute of Health Research (NIHR), UK.

Who is the main contact?
Dr Olga Zubko
olga.zubko@kcl.ac.uk

Contact information

Type(s)
Scientific

Contact name
Dr Olga Zubko

Contact details
16 De Crespigny Park
London
United Kingdom
SE5 8AF
-
olga.zubko@kcl.ac.uk

Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
14866; 11/47/01

Study information

Scientific Title
The MADE Trial: Minocycline in Alzheimer's Disease Efficacy trial

Acronym
MADE

Study objectives
The MADE Trial will examine the effects of two years of minocycline treatment on deterioration in cognitive function and activities of daily living in patients with early Alzheimer's disease

assessed and managed within NHS Memory Services. If minocycline can be shown to have efficacy in the trial, this would rapidly pave the way for effectiveness trials and ultimately availability of a low cost and safe treatment for this common and devastating condition.

Ethics approval required
Old ethics approval format

Ethics approval(s)
London South REC, ref: 13//EE/0063

Study design
Randomised; Interventional; Design type: Treatment

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Not specified

Study type(s)
Treatment

Participant information sheet
Not available in web format, please use the contact details below to request a patient information sheet

Health condition(s) or problem(s) studied
Topic: Dementias and Neurodegenerative Diseases Research Network; Subtopic: Dementia; Disease: Alzheimer's Disease

Interventions
Drug Treatment. Participants will be allocated to one of three treatment arms:
1. Minocycline 400mg/day
2. Minocycline 200mg/day
3. Placebo
They will take the allocated treatment orally for a period of two years.

Intervention Type
Drug

Phase
Not Specified

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

Primary outcome measure

To determine whether minocycline is superior to placebo; Timepoint(s): Baseline and 2 years
1. Cognition will be measured using sMMSE
2. Functional ability will be measured using Bristol Activities of Daily Living Scale (BADLS)

Secondary outcome measures
Not provided at time of registration

Overall study start date
01/06/2013

Completion date
31/05/2018

Eligibility

Key inclusion criteria
1. Diagnosis by National Institute on Aging (NIA)/ Alzheimer's Association (AA) criteria of possible or probable Alzheimer's Disease (McKhann et al 2011)
2. Standardized Mini-Mental State Examination (SMMSE) score >23 with no upper limit
3. Consenting to participate
Target Gender: Male & Female; Upper Age Limit 100 no age limit or unit specified ; Lower Age Limit 45 no age limit or unit specified

Participant type(s)
Patient

Age group
Senior

Sex
Both

Target number of participants
Planned Sample Size: 480; UK Sample Size: 480

Total final enrolment
544

Key exclusion criteria
1. Known allergy to tetracycline antibiotics
2. Diagnosis of mild cognitive impairment
3. Female of childbearing potential. Patients must be surgically sterile (hysterectomy, bilateral salpingectomy/oophorectomy) for at least 6 months minimum or have undergone bilateral tubal occlusion/ligation at least 6 months prior or have been post-menopausal for at least 1 year.
4. Pregnancy and lactation.
5. Known chronic kidney disease stages 3-5
6. Lacks capacity to give informed consent
7. Abnormal serum chemistry laboratory value at Screening deemed to be clinically relevant by the investigator. Patients with creatinine clearance < 50 mL/min at Screening, according to the Cockcroft and Gault equation must be excluded.

8. Systemic Lupus Erythromatosis
9. Severe liver disease
10. Participation in another Clinical Trial of an Investigational Medicinal Product (IMP) in the previous 28 days
Contraindications, warnings and special precautions to minocycline use are not described further in the protocol and the investigator should refer to the Summary of Product Characteristics http://emc.medicines.org.uk/.

Date of first enrolment
01/06/2013

Date of final enrolment
31/05/2018

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
16 De Crespigny Park
London
United Kingdom
SE5 8AF

Sponsor information

Organisation
King's College London (UK)

Sponsor details
James Clerk Maxwell Building
57 Waterloo Road
London
England
United Kingdom
SE1 8WA

Sponsor type
University/education

ROR
https://ror.org/0220mzb33

Funder(s)

Funder type
Government

Funder Name
Medical Research Council

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

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Funder Name
Efficacy and Mechanism Evaluation Programme; Grant Codes: 11/47/01

Alternative Name(s)
NIHR Efficacy and Mechanism Evaluation Programme, EME

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Publication and dissemination plan
Not provided at time of registration

Intention to publish date

Individual participant data (IPD) sharing plan

IPD sharing plan summary

Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	01/02/2020	19/11/2019	Yes	No