Minocycline in Alzheimer’s Disease Efficacy Trial: The MADE Trial

https://www.neurodegenerationresearch.eu/survey/minocycline-in-alzheimers-disease-efficacy-trial-the-made-trial-2/

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Country

United Kingdom

Title of project or programme

Minocycline in Alzheimer's Disease Efficacy Trial: The MADE Trial

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MRC

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Start date of award

01/06/2013

Total duration of award in years

5.0

The project/programme is most relevant to:

Alzheimer's disease & other dementias

Keywords
Research Abstract

Research design: Multi-centre randomised double-blind placebo-controlled semi-factorial (2×1) design phase II clinical trial to test efficacy and tolerability of 400mg and 200mg minocycline in disease modification of Alzheimer’s disease (AD). Study population: 480 patients with very mild AD recruited from Memory Services within 9 academically-linked NHS Trusts and a wider network of Memory Services identified by DeNDRoN in England. Inclusion criteria (i) Diagnosis

of NINCDS-ADRDA possible or probable AD, (ii) Standardised Mini-Mental State Examination score >23, (iii) Consent to participate or agreeing to participate if capacity to give informed consent lost, (iv) Renal and hepatic function within normal limits, (v) If taking AD medication (memantine or cholinesterase inhibitor) on stable dose for at least 8 weeks. Exclusion criteria (i) Known allergy to tetracycline antibiotics, (ii) Serious or unstable medical condition that would represent contraindication to taking trial medication. Planned interventions: Participants will be randomised to 24 months daily treatment with 400mg minocycline, 200mg minocycline or matched placebo. Proposed outcome measures: Simple clinically relevant measures of cognition and function that are already used in much routine practise and which have been shown to have excellent psychometric properties and high sensitivity to change in earlier AD trials. Cognition will be assessed with the Standardised Mini-Mental State Examination (sMMSE) and function with the Bristol Activities of Daily Living Scale (BADLS). Assessment and follow-up: The sMMSE and BADLS will be administered within Memory Services at Baseline, 12 and 24 months. Proposed sample size: We aim to randomise 480 participants. Even in mild AD, patient attrition is inevitable in a long term treatment trial and we estimate that by 2 years, about 15% of patients will have died, a further 5% will be in institutional care and 20% will have been withdrawn from trial treatment. Outcome assessments will be sought for all surviving participants, irrespective of compliance and 2-year assessments should be available on at least 60% of participants (i.e. at least 300) which would provide 90% power at $p<0.05$ to detect a 0.4 SD effect size reduction in the primary outcome measures, the decline in sMMSE and BADLS for minocycline compared to placebo. The 12 month placebo decline on the sMMSE seen in the AD2000 trial was about 6 points (SD 5.0), and thus a 0.4 SD effect size is equivalent to 2 sMMSE points, or a reduction of a third in the rate of decline over 2 years, which is considered to be the minimum clinically important difference. Statistical power will be enhanced by use of repeated measures regression analyses including data at all time points thus minimising the impact of participant attrition. With 100 patients allocated 400mg minocycline and 100 patients allocated 200mg minocycline assessed at 2 years, we will have 80% power at $p<0.05$ to detect a 0.4 SD effect size treatment effect of 400mg compared to 200mg. Statistical analysis: Repeated measures regression techniques will be used to compare decline rates. Project timetables: During a 24-month recruiting phase we will need to recruit 2 participants per centre per month to meet targets if we are reliant on just the 9 primary recruiting sites.

Lay Summary
Further information available at:

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Investments > €500k

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Alzheimer's disease & other dementias

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