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A Pilot Randomised controlled trial of Methotrexate for Chronic Inflammatory Demyelinating Polyradiculoneuropathy

Submission date	Recruitment status	[X] Prospectively registered
05/08/2005	No longer recruiting	[_] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
01/09/2005	Completed	[X] Results
Last Edited	**Condition category**	[_] Individual participant data
16/09/2009	Nervous System Diseases	

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
RMC1

Study information

Scientific Title

Acronym
RMC Trial

Study objectives
Null hypothesis - Because existing treatments are inadequate we will undertake a randomised controlled double blind parallel group study of methotrexate in chronic inflammatory demyelinating polyradiculoneuropathy (CIDP). Our null hypothesis is that addition of the weekly oral methotrexate to existing corticosteroid or intravenous immunoglobulin (IVIg) treatment does not reduce the dose of these agents needed to maintain participants in as good a clinical state as possible. The alternative hypothesis is that oral methotrexate does reduce the amount of these agents needed. The prognosis of CIDP is variable and currently unpredictable. Preliminary observational studies suggest that methotrexate may be moderately effective but is unlikely to be so dramatically effective as to make a placebo-controlled trial unnecessary.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Not provided at time of registration

Study design
Randomised placebo controlled trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Not specified

Study type(s)
Treatment

Participant information sheet

Health condition(s) or problem(s) studied
Inflammatory Demyelinating Polyradiculoneuropathy

Interventions
Participants will be randomised to receive oral methotrexate or placebo tablets 7.5 mg weekly for 4 weeks, 10 mg weekly for 4 weeks and then 15 mg weekly for 32 weeks. Both groups will receive folic acid supplements 5 mg twice a week to reduce the risk of side effects from methotrexate. After 16 weeks corticosteroids or IVIg will be reduced, subject to satisfactory

progress, at a rate of 20% of the baseline dose every 4 weeks. Such a reduction is done informally in practice by most experts in any case so that the reduction in corticosteroids or IVIg is not a big departure from usual practice. We are doing it in this trial because patients on corticosteroids or IVIg in optimal doses may not experience much improvement in impairment or disability and yet would benefit from reduction or withdrawal of corticosteroids or IVIg. Corticosteroids have well known side effects including obesity, hypertension, diabetes and osteoporosis. IVIg commonly causes headache and flu-like symptoms and requires attendance at hospital for several hours for intravenous infusions. It also has rare serious side effects and is expensive. Reduction in the dose of either treatment would reduce the side effects and costs.

Intervention Type
Drug

Phase
Not Specified

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

Primary outcome measure
Percentage change in mean weekly dose of corticosteroid or IVIg during weeks 3740 compared with weeks 14.

Secondary outcome measures
1. Overall, and average rate of, change of a 12point overall neuropathy disability score at grade 16 and 40 weeks compared with baseline
2. Overall, and average rate of, change in the Amsterdam Linear Disability Scale after 16 and 40 weeks
3. Overall, and average rate of, change in MRC sum score, expanded to include first dorsal interosseus and extensor hallucis longus, after 16 and 40 weeks
4. Serious adverse events (defined as those which are fatal, life-threatening, or require or prolong hospital admission) which are possibly or probably related to treatment

Overall study start date
01/11/2005

Completion date
31/10/2007

Eligibility

Key inclusion criteria
1. Diagnosis of CIDP by a consultant neurologist with a special interest in peripheral neuropathy
2. Chronically progressive, stepwise, or recurrent symmetric proximal and distal weakness with or without sensory dysfunction of all extremities, developing over at least 2 months
3. Absent or reduced tendon reflexes in all extremities
4. Ongoing treatment with at least one of IVIg (equivalent to at least 0.4 g/kg every 4 weeks) or corticosteroid (equivalent to at least prednisolone 5 mg daily). The dose must have been stable (within 25%) for at least 12 weeks.
5. Duration not less than 6 months

6. At least moderate disability and weakness in arms or legs according to defined criteria at baseline OR following reduction of steroid or IVIg dose at some time during the past year
7. Fulfillment of one of two sets of defined neurophysiological criteria at baseline or within the past 3 years

Participant type(s)
Patient

Age group
Adult

Sex
Both

Target number of participants
62

Key exclusion criteria
1. Age <18 years
2. Breast-feeding, pregnancy, planned pregnancy or unwillingness to practice contraception
3. Severe concurrent medical conditions which would prevent treatment or assessment, including significant haematological, renal, liver function or chest radiograph abnormalities
4. Alternative cause of peripheral neuropathy, such as drug or toxin, hereditary neuropathy or concomitant diseases such as human immunodeficiency virus (HIV) infection, Lyme disease, chronic active hepatitis, systemic lupus erythematosus, IgM paraprotein with anti-MAG antibodies, vasculitis, hematological and non-hematological malignancies. Diabetes mellitus will not be an exclusion criterion.
5. Presence of sphincter disturbance
6. Multifocal motor neuropathy (fulfilling defined criteria)
7. Atypical CIDP with pure sensory, persistent unifocal impairment or significant central nervous system (CNS) involvement
8. Immunomodulatory treatment other than IVIg or corticosteroids during the previous 12 weeks

Date of first enrolment
01/11/2005

Date of final enrolment
31/10/2007

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Department of Clinical Neuroscience
London

United Kingdom
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Sponsor information

Organisation
King's College London and Guy's and St Thomas' NHS Foundation Trust (Co-Sponsors) (UK)

Sponsor details
Guy's Campus
St Thomas Street
London
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SE19RT

Sponsor type
Not defined

ROR
https://ror.org/00j161312

Funder(s)

Funder type
University/education

Funder Name
King's College London (UK)

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	01/02/2009		Yes	No