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Does addition of subcutaneous interferon alpha 2b for 6 months only to the treatment of Behcet s disease significantly reduce the number of patients requiring immunosuppressive agents to control their disease over the following 3 years?

Submission date
21/09/2000

Recruitment status
No longer recruiting

Registration date
21/09/2000

Overall study status
Completed

Last Edited
02/10/2014

Condition category
Musculoskeletal Diseases

[X] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

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)

2004-004301-18

Protocol serial number
G0100196

Study information

Scientific Title
A prospective, randomised, parallel-group, single-masked clinical trial to assess the effect of the addition of subcutaneous interferon-alpha 2b for 6 months only in the treatment of Behcets disease, and whether it significantly reduces the number of patients requiring immunosuppressive agents to control their disease over the following 3 years

Study objectives
As of 03/06/2009 this record was extensively updated to include basic trial information, and details of the CMR sub-study. At this time, the anticipated start and end dates were also updated; the initial trial dates were as follows:
Initial anticipated start date: 01/09/1999
Initial anticipated end date: 01/09/2004
All updates can be found under the relevant field under the above update date.

Added 03/06/2009:
The addition of subcutaneous interferon alpha (IFN alpha) to standard treatment regimes in Behcet's disease (BD) significantly reduces the relapse rate of systemic disease and further loss of vision.

Treatment for the complications of BD currently relies heavily on long-term treatment with corticosteroids and other immunosuppressive agents. These drugs do not modify the natural history and therefore need to be given over long periods of time. In addition, they have serious systemic side effects and, apart from corticosteroids, are expensive. In this study, we therefore intend to address the question of whether IFN alpha has the unique ability to modify the disease course of BD.

Cardiovascular Magnetic Resonance (CMR) sub-study:
A sub-study to this trial is also being performed; all details of this sub-study will appear in the relevant fields under the sub-heading CMR study.

At recruitment all patients will be offered a baseline Cardiovascular Magnetic Resonance (CMR) study. This will assess endothelial dysfunction, total carotid artery wall volume (a measure of atheroma), left and right ventricular volumes, mass and function and also look for the presence of any myocardial fibrosis. Patients will be invited for follow-up scans at 6 months, 1, 2 and 3 years.

Added 28/07/09:
The primary sponsor and funding source were changed. The previous sponsor was
Medical Research Council (MRC) (UK)
20 Park Crescent
London
W1B 1AL
United Kingdom
+44 (0)20 7636 5422

+44 (0)20 7436 6179
clinical.trial@headoffice.mrc.ac.uk

Ethics approval required
Old ethics approval format

Ethics approval(s)
Added 03/06/2009:
Oxfordshire Research Ethics Committee (REC) A, 22/03/2005, ref: 05/Q1604/5

CMR Study:
Royal Brompton Hospital Ethics Committee, 28/11/2005

Primary study design
Interventional

Study design
Randomised controlled trial

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Ophthalmology, rheumatology and immunology

Interventions
Added 03/06/2009:
Weekly injections of subcutaneous pegylated-IFN alpha 2b (0.3 ug/kg) will be given to the test group for six months, in addition to the drug regimen that would normally be used to control disease activity. Because a large proportion of patients receiving IFN alpha are likely to experience transient flu-like symptoms, it is not feasible for patients in the test and control groups to be effectively masked. Therefore, the control group will be treated with conventional treatment alone, without placebo injections. IFN alpha treatment will be discontinued after 6 months, and the patients followed-up to 3 years, with formal review every 6 months.

The proposed trial is within four centres in London and to improve the balance and efficiency of the study, allocation will be based on the methods of minimisation maintaining balance by trial centre, history of systemic and /or ocular involvement and duration of disease at onset of trial (for less than 3 years/3 years or more). The nature of the treatment does not necessitate a 7 day per week 24-hour service. Remote randomisation will be provided by a well-established day-time (UK) randomisation service based in Manchester. The patient's details will be encrypted to comply with the UK Data Protection Act and emailed to the randomisation service. A reply will be sent giving a trial number and the allocation of medication. The time delay caused by such a procedure is not seen as a problem.

It is proposed to use standardised objective measures made by outcome assessors masked to treatment allocation. The outcome assessors would be forbidden to ask questions about treatment and side effects and the patients would be reminded prior to each assessment not to reveal anything regarding treatment or side effects to the assessor. Protocols for step-wise reduction in medication will be followed in both groups. The statistical analysis will be undertaken masked to treatment allocation.

Intervention Type
Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Interferon alpha 2b

Primary outcome(s)
Added 03/06/2009:
1. The percentage of patients in each group who have quiescent disease enabling their steroid dose to be reduced to 10 mg or less and their second-line agent withdrawn during the follow-up period will be calculated
2. The number of ocular and systemic disease relapses over time will be compared between the two groups. These will be classified as mild, moderate or severe using pre-determined criteria.

CMR study:
1. Endothelial-dependent brachial artery flow-mediated dilatation
2. Total carotid artery wall volume (left and right)
3. Left and right ventricular end diastolic volume (LVEDV and RVEDV)
4. Left and right ventricular end systolic volume (LVESV and RVESV)
5. Left and right ventricular ejection fraction (LVEF and RVEF)
6. Left and right ventricular mass (LVM and RVM)

Key secondary outcome(s)
Added 03/06/2009:
1. The number of new serious complications (vascular, neurological and ocular involvement) occurring over the follow-up period will be counted and compared to those in the group not given the IFN
2. The disease activity and chronic fatigue questionnaires will be scored and the scores added up and compared in the two groups as well as in each patient at the beginning and end of the study

Completion date
01/01/2012

Eligibility

Key inclusion criteria
Added 03/06/2009:
1. Patient is male or female greater than 18 years of age
2. Patient has a diagnosis of Behcet's disease (as defined by the International Study Group criteria for Behcet's disease)
3. Patient requires systemic treatment, either:
3.1. With or without steroids, plus/or
3.2. A second-line agent for treatment of systemic or ocular disease, e.g., azathioprine, cyclosporine, methrotrexate, cyclophosphamide, cellcept, infliximab, tacrolimus
4. Patient is willing and able to have weekly subcutaneous injections of interferon alpha 2b for 26 weeks
5. Female patients of child-bearing potential agree to use an adequate form of contraception if

randomised to receive interferon for 12 months
6. The patient has been on stable dose(s) of systemic medication for the past 4 weeks or patient will be able to maintain a stable dose of systemic medication 4 weeks before baseline visit in order to commence study
7. The patient anticipates being available for the duration of the study
8. The patient is prepared to be randomised to remain on their 'standard treatment' for the duration of the trial
9. Patients with ocular inflammation from Behcet's disease: it must possible to visualise the retina. The patient does not have major ocular media opacities such as large axial corneal scars, cataract and vitreous haemorrhage.
10. Patient is willing:
10.1. To attend for three monthly formal review for the first 6 months and then at 12, 18, 24 and 36 months for the clinical trial
10.2. More visits may be required for clinical needs
10.3. To the other aspects of follow-up, including access to their previous medical notes from the referring physician
11. Requiring systemic treatment with steroids and a second-line agent, or second-line agent(s) alone for either systemic or ocular disease
12. Able and willing to have weekly subcutaneous injections
13. Women may enrol only following counselling about the need for adequate contraception
14. Patients in whom the systemic medication has been changed within the last 4 weeks will be delayed entry to the trial until the drug dosages have been stable for 4 weeks or more

CMR study:
Patients with a contraindication to cardiovascular magnetic resonance will be suitable for enrolment in the trial but will not be invited for CMR scans. This includes patients with metallic implants and pacemakers, and patients with severe claustrophobia.

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 Years

Sex
All

Key exclusion criteria
Added 03/06/2009:
1. Has the patient had any previous treatment with interferon?
2. Patient's weight is less than 50 kg
3. Patient has hypersensitivity to the active substance/any excipients/any interferon preparation
4. Patient has relevant drug allergy or contraindications to use of any of the medications
5. If female - is the patient pregnant, planning to become pregnant and/or breastfeeding
6. Does the patient have any of the following conditions:

6.1. Autoimmune hepatitis
6.2. History of a severe psychiatric disorder (including severe depression that required referral to a psychiatrist)
6.3. Severe renal dysfunction
6.4. Severe hepatic dysfunction
6.5. Epilepsy and/or compromised central nervous system dysfunction
6.6. Pre-existing thyroid abnormalities for which thyroid function cannot be maintained in the normal range by medication
7. Does the patient has any history of severe pre-existing cardiac disease including unstable or uncontrolled cardiac disease within the last 6 months
8. Is there any reason that the patient's participation in the clinical trial is inadvisable, according to best clinical judgement (e.g. significant medical history)

Date of first enrolment
01/06/2006

Date of final enrolment
01/01/2012

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Department of Clinical Ophthalmology
London
United Kingdom
EC1V 9EL

Sponsor information

Organisation
Moorfields Eye Hospital NHS Foundation Trust (UK)

ROR
https://ror.org/03zaddr67

Funder(s)

Funder type
Charity

Funder Name
Current information as of 29/07/2009:

Funder Name
The Moulton Charitable Trust (UK)

Funder Name
Initial information at time of registration:

Funder Name
Medical Research Council (MRC) (UK) (ref: G0100196)

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

Funder Name
Funding was sought but not approved

Results and Publications

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	01/06/2015	Yes	No