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Comparison of Alemtuzumab and Rebif® Efficacy in Multiple Sclerosis, Study Two

Submission date	Recruitment status	[ ] Prospectively registered
23/06/2008	No longer recruiting	[ ] Protocol
Registration date	**Overall study status**	[ ] Statistical analysis plan
11/03/2009	Completed	[X] Results
Last Edited	**Condition category**	[ ] Individual participant data
20/03/2020	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

ClinicalTrials.gov (NCT)
NCT00548405

Protocol serial number
CAMMS324 A2; NTR1469; ACTRN12608000426381

Study information

Scientific Title
A phase 3 randomised, rater- and dose-blinded study comparing two annual cycles of intravenous low- and high-dose alemtuzumab to three-times weekly subcutaneous interferon beta-1a (Rebif®) in patients with relapsing-remitting multiple sclerosis who have relapsed on therapy

Acronym
CARE-MS II

Study objectives
Amended hypothesis as of 24/06/2009:
The purpose of this study is to establish the efficacy and safety of two different doses of alemtuzumab as a treatment for relapsing-remitting multiple sclerosis (MS), in comparison with Rebif® (interferon beta-1a). The study will enrol patients who have received an adequate trial of disease-modifying therapies but continued to relapse while being treated, and who meet a minimum severity of disease as measured by magnetic resonance imaging (MRI). Patients will have monthly laboratory tests and comprehensive testing every 3 months. Every patient will receive active treatment; there is no placebo. The 24 mg alemtuzumab dose is closed to enrolment so newly enrolled patients will be randomly assigned to treatment with either 12 mg alemtuzumab or Rebif® at a 2:1 ratio (i.e., 2 given 12 mg alemtuzumab for every 1 given Rebif®). Alemtuzumab will be administered in two annual cycles, once at the beginning of the study and again 1 year later. Rebif® will be self-injected 3 times per week for 2 years. All patients will be required to return to their study site every 3 months for neurological assessment. In addition, safety-related laboratory tests will be performed at least monthly. Participation in this study will end 2 years after the start of treatment for each patient. Additionally, all patients who receive alemtuzumab will be followed in an extension study for safety and efficacy assessments. Patients who receive Rebif® and complete 2 years on study may be eligible to receive alemtuzumab in an extension study.

Initial information at time of registration:
The purpose of this study is to establish the efficacy and safety of two different doses of alemtuzumab as a treatment for relapsing-remitting multiple sclerosis (MS), in comparison with Rebif® (interferon beta-1a). The study will enrol patients who have received an adequate trial of disease-modifying therapies but continued to relapse while being treated, and who meet a minimum severity of disease as measured by magnetic resonance imaging (MRI). Patients will have monthly blood tests and comprehensive testing every 3 months. Every patient will receive active treatment; there is no placebo. Patients who qualify will be randomly assigned to treatment with either low-dose alemtuzumab, high-dose alemtuzumab, or Rebif® at a 2:2:1 ratio (i.e., there is a 4-in-5 chance patients will be assigned to receive alemtuzumab treatment and a 1-in-5 chance patients will be assigned to receive Rebif® treatment). Alemtuzumab will be administered in two annual cycles, once at the beginning of the study and again 1 year later. Rebif® will be self-injected 3 times per week for 2 years. All patients will be required to return to their study site every 3 months for neurological assessment. In addition, a safety-related blood test will be performed at least monthly. Participation in this study will end 2 years after the start of treatment for each patient. Additionally, all patients who receive alemtuzumab will be followed in an extension study for safety for at least 3 years after their last dose of alemtuzumab. Patients who receive Rebif® and complete 2 years on study may be eligible to receive alemtuzumab in an extension study.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Warwickshire Local Research Ethics Committee (UK), 24/12/2007, ref: 07/H1211/153. All other centres will seek ethics approval before recruiting patients.

Study design
Randomised parallel-assignment single-blind (outcome assessor) multi-centre trial

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Multiple sclerosis

Interventions
Experimental Intervention 1: alemtuzumab: 12 mg per day administered through IV, once a day for 5 consecutive days at Month 0 and 12 mg per day administered through IV, once a day for 3 consecutive days at Month 12

Experimental Intervention 2: alemtuzumab: 24 mg per day administered through IV, once a day for 5 consecutive days at Month 0 and 24 mg per day administered through IV, once a day for 3 consecutive days at Month 12 (please note that as of 24/06/2009 the 24 mg alemtuzumab dose is closed to enrolment).

Active Comparator: interferon beta-1a (Rebif®): 44 mcg administered 3-times weekly by SC injections for 2 years

Details of Lead Principal Investigator for the UK sites:
Dr Alasdair Coles
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Intervention Type
Drug

Phase
Phase III

Drug/device/biological/vaccine name(s)
Alemtuzumab, interferon beta-1a (Rebif®)

Primary outcome(s)

1. Time to Sustained Accumulation of Disability (SAD) (Time frame: 2 years)
2. Relapse Rate (Time frame: 2 years)

Key secondary outcome(s))
1. Proportion of patients who are relapse free at Year 2 (Time frame: 2 years)
2. Change from baseline in EDSS (Time frame: 2 years)
3. Acquisition of disability as measured by change from baseline in Multiple Sclerosis Functional Composite (MSFC) (Time frame: 2 years)
4. Percent change from baseline in MRI-T2 hyperintense lesion volume at Year 2 (Time frame: 2 years)

Completion date
01/04/2012

Eligibility

Key inclusion criteria
Amended as of 24/06/2009:
Point 7 has been removed from the below inclusion criteria.

Initial information at time of registration:
1. Males and females, aged 18 - 55 years old
2. Diagnosis of MS and MRI scan demonstrating white matter lesions attributable to MS
3. Onset of MS symptoms within 10 years of screening
4. Expanded Disability Status Scale (EDSS) score 0.0 to 5.0
5. Greater than or equal to 2 MS attacks within 24 months, with greater than or equal to 1 attack within 12 months
6. Greater than or equal to 1 MS attack (relapse) during treatment with a beta interferon therapy or glatiramer acetate after being on that therapy for at least 6 months within 10 years
7. Neurologically stable for the 30 days prior to the date the Informed Consent Form is signed

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Key exclusion criteria
1. Previous treatment with alemtuzumab
2. Previous treatment with any investigational drug (i.e. medication that is not approved at any

dose for any indication)
3. Treatment with natalizumab, methotrexate, azathioprine or cyclosporine in the past 6 months
4. Previous treatment with mitoxantrone, cyclophosphamide, cladribine, rituximab, or any other immunosuppressive, or cytotoxic therapy (other than steroid treatment)
5. Any progressive form of MS
6. Any disability acquired from trauma or another illness that could interfere with evaluation of disability due to MS
7. Major systemic disease that cannot be treated or adequately controlled by therapy
8. Active infection, or high risk for infection
9. Autoimmune disorder (other than MS)
10. Impaired hepatic or renal function
11. History of malignancy, except basal skin cell carcinoma
12. Medical, psychiatric, cognitive, or other conditions that compromise the patient's ability to understand the patient information, to give informed consent, to comply with the trial protocol, or to complete the study
13. Known bleeding disorder
14. Of childbearing potential with a positive serum pregnancy test, pregnant, or lactating
15. Current participation in another clinical study or previous participation in CAMMS323 (registered with ISRCTN21534255)
16. Previous hypersensitivity reaction to any immunoglobulin product
17. Known allergy or intolerance to interferon beta, human albumin, or mannitol
18. Intolerance of pulsed corticosteroids, especially a history of steroid psychosis
19. Inability to self-administer subcutaneous (SC) injections or receive SC injections from caregiver
20. Inability to undergo MRI with gadolinium administration
21. Unwilling to use a reliable and acceptable contraceptive method throughout the study period (fertile patients only)

Date of first enrolment
20/10/2007

Date of final enrolment
02/09/2009

Locations

Countries of recruitment
United Kingdom

England

Argentina

Australia

Austria

Belgium

Brazil

Canada

Croatia

Czech Republic

Denmark

France

Germany

Israel

Italy

Mexico

Netherlands

Poland

Russian Federation

Serbia

Spain

Sweden

Ukraine

United States of America

Study participating centre
Genzyme Therapeutics
Oxford
United Kingdom
OX4 2SU

Sponsor information

Organisation
Genzyme Corporation (USA)

ROR
https://ror.org/027vj4x92

Funder(s)

Funder type
Industry

Funder Name
Genzyme

Alternative Name(s)
Genzyme Corporation

Funding Body Type
Private sector organisation

Funding Body Subtype
For-profit companies (industry)

Location
United States of America

Funder Name
Bayer Schering

Alternative Name(s)

Funding Body Type
Private sector organisation

Funding Body Subtype
For-profit companies (industry)

Location
Germany

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	24/11/2012		Yes	No
Basic results				No	No