

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

Submission date 23/06/2008	Recruitment status No longer recruiting	<input type="checkbox"/> Prospectively registered
		<input type="checkbox"/> Protocol
Registration date 11/03/2009	Overall study status Completed	<input type="checkbox"/> Statistical analysis plan
		<input checked="" type="checkbox"/> Results
Last Edited 20/03/2020	Condition category Nervous System Diseases	<input type="checkbox"/> 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

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number
NCT00548405

Secondary identifying numbers

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

Secondary study design

Randomised parallel trial

Study setting(s)

Hospital

Study type(s)

Treatment

Participant information sheet

Not available in web format, please email to request a patient information sheet:
ukmedinfo@genzyme.com

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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Hill's Road
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United Kingdom

Intervention Type

Drug

Phase

Phase III

Drug/device/biological/vaccine name(s)

Alemtuzumab, interferon beta-1a (Rebif®)

Primary outcome measure

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

Secondary outcome measures

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)

Overall study start date

20/10/2007

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

Age group

Adult

Lower age limit

18 Years

Sex

Both

Target number of participants

700 (previously 1200 prior to 24/06/2009)

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

Argentina

Australia

Austria

Belgium

Brazil

Canada

Croatia

Czech Republic

Denmark

England

France

Germany

Israel

Italy

Mexico

Netherlands

Poland

Russian Federation

Serbia

Spain

Sweden

Ukraine

United Kingdom

United States of America

Study participating centre

Genzyme Therapeutics

Oxford

United Kingdom

OX4 2SU

Sponsor information

Organisation

Genzyme Corporation (USA)

Sponsor details

500 Kendall Street

Cambridge

Massachusetts

United States of America

02142

Sponsor type

Industry

Website

<http://www.genzyme.co.uk>

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

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?
Basic results				No	No
Results article	results	24/11/2012		Yes	No