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

Submission date	Recruitment status	[ ] Prospectively registered
18/02/2008	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)
NCT00530348

Clinical Trials Information System (CTIS)
2007-001161-14

Protocol serial number

CAMMS323; ACTRN12608000435381

Study information

Scientific Title
A phase 3 randomised, rater-blinded study comparing two annual cycles of intravenous alemtuzumab to three-times weekly subcutaneous interferon beta-1a (Rebif®) in treatment-naïve patients with relapsing-remitting multiple sclerosis

Acronym
CARE-MS I

Study objectives
Current hypothesis as of 22/06/2009:
The purpose of this study is to establish the efficacy and safety 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 not previously received treatment to suppress MS, except steroids. Patients will have monthly laboratory 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 alemtuzumab or Rebif® at a 2:1 ratio (i.e., 2 given 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 neurologic 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 alemtuzumab as a treatment for relapsing-remitting multiple sclerosis (MS), in comparison with Rebif® (interferon beta-1a). The study will enrol patients who have not previously received treatment to suppress MS, except steroids. 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 alemtuzumab or Rebif® at a 2:1 ratio (i.e., 2 given 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 neurologic 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)

Nottingham Research Ethics Committee (UK), 09/11/2007, ref: 07/H0408/118.
All other centres will seek ethics approval before recruiting patients.

Primary study design
Interventional

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

Study type(s)
Treatment

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

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

Details of Lead Principal Investigator for UK sites:
Dr Alasdair Coles
Addenbrooke's Hospital
Box 165
Hill's Road
Cambridge, CB2 2QQ
United Kingdom

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
01/03/2011

Eligibility

Key inclusion criteria
Amended as of 22/06/2009:
Point 6 below has been removed from the inclusion criteria.

Initial information at time of registration:
1. Males and females, aged 18 - 50 years
2. Diagnosis of multiple sclerosis (MS) and cranial magnetic resonance imaging (MRI) scan demonstrating white matter lesions attributable to MS within 5 years
3. Onset of MS symptoms within 5 years of screening
4. Expanded Disability Status Scale (EDSS) score 0.0 to 3.0
5. Greater than or equal to 2 MS attacks within 24 months, with greater than or equal to 1 attack within 12 months
6. 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. Received prior therapy for MS other than corticosteroids
2. Exposure to immunosuppressive or immunomodulatory agents other than systemic corticosteroid treatment
3. Received treatment with a monoclonal antibody for any reason
4. Previous treatment with any investigational drug (i.e. medication that is not approved at any dose for any indication)
5. Has 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
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
07/09/2007

Date of final enrolment
02/09/2009

Locations

Countries of recruitment
United Kingdom

England

Argentina

Australia

Brazil

Canada

Croatia

Czech Republic

France

Germany

Mexico

Poland

Russian Federation

Serbia

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