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# Assessment of bone marrow-derived Cellular Therapy in progressive Multiple Sclerosis (ACTiMuS)

**Submission date**
07/09/2012

**Recruitment status**
No longer recruiting

**Registration date**
11/09/2012

**Overall study status**
Completed

**Last Edited**
11/01/2019

**Condition category**
Nervous System Diseases

[X] Prospectively registered
[X] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[_] Record updated in last year

## Plain English summary of protocol

Background and study aims
Current treatments for multiple sclerosis (MS) are inadequate; the disease often progresses so that patients become disabled and current treatments can only reduce symptoms. New treatments to stop the disease process or promote repair are urgently required. The purpose of this study is to test the safety of bone marrow stem cell infusion in patients with MS. We want to find out what effects it has on you and your disability.

Who can participate?
This study will examine the effects of bone marrow stem cell infusion in 80 people who are known to have progressive MS.

What does the study involve?
Participants will first be assessed to determine their general fitness and degree of disability. This will involve attending the neurology department in Frenchay Hospital in Bristol for a clinical examination, blood test, chest X-ray and heart rhythm recording, all performed at the same visit. Participants will also be asked to complete a questionnaire regarding their level of disability. The blood test will include screening for some viruses, including HIV. We also request that a sample of blood is stored in case this is required for future comparison. Participants will attend Frenchay Hospital for an electrical (neurophysiological) test, an MRI scan of the brain and spinal cord, and a specialised eye scan known as optical coherence tomography (OCT). We will endeavour to co-ordinate appointments to minimise hospital appointments but we cannot always guarantee that tests will be performed on the same day. An MRI scan takes about 45 minutes and will involve an injection of gadolinium. The OCT examination involves application of eye drops which will wear off over a few hours but which will preclude driving home from the examination. Neurophysiological tests will record the speed of electrical signalling in a number of different pathways. They may cause some transient discomfort during stimulation of the muscles.

A blood collection will be performed on two occasions one year apart. This is identical to the procedure undertaken by a blood donor and involves collection of about 500 ml of blood. Bone marrow will be collected in Avon Haematology Unit under a general anaesthetic which lasts less

than one hour. The marrow is drawn from the pelvic bone using one needle puncture on the right and one on the left. In total, about 500-750 ml (about one pint) of marrow will be aspirated. A single core of marrow will also be removed. Local anaesthetic is left in the needle tracts to minimize discomfort on waking. Marrow donors usually experience some bruising or aching after the procedure, but this is generally well controlled with pain-relievers taken by mouth. About 20% of people need to stay in hospital overnight. Following the procedure, the marrow is cleaned to remove bits of bone and fat. The same day, the participant will receive an infusion into a peripheral vein of either blood or marrow, but will not be able to determine which. If blood is infused, the marrow sample will be frozen, then thawed and infused into the participant one year later. Those who receive marrow during the first infusion will receive blood one year later. About half of the participants will receive blood on the first infusion and half will receive marrow. Which they receive will be determined randomly and only the staff at NHS Blood and Transplant will know which infusion participants received on a given date.

The infusions will last under two hours, and the participant will be closely monitored by nursing staff with regular observations including temperature, pulse and blood pressure recording. Both infusions will be done in the Avon Haematology Unit. Participants will have the option of remaining in hospital overnight following bone marrow harvest, although this will probably not be necessary. Before participants leave the Haematology Unit, we will do a blood test to check that participants are not anaemic and we will probably suggest that participants take iron tablets for a few weeks.

You will be asked to donate a core of marrow along with a small sample of marrow fluid and peripheral blood (20 ml or four teaspoons) for laboratory research. Participants may enter the clinical study and withhold consent for donation of a research sample  this will not have any impact on their clinical care.

Participants may contact the research team directly if they experience any problems following the bone marrow harvest. Routinely, participants will be contacted by telephone at three days and 14 days after the procedure. They will be formally re-assessed in the out-patient clinic at six weeks, six and 12 months following each infusion. This will follow the same pattern as the entry assessment, although the chest X-ray should not need to be repeated unless clinically indicated, and the electrical studies, MRI and OCT assessments will be performed at the 12-month visits only. Participants will also be asked to complete two questionnaires at each time point and submit a written statement regarding their experience of the procedure at any point.

You will be expected to attend for all the appointments and investigations as detailed above, to donate marrow on two occasions one year apart and to have a short operation to collect bone marrow. You will receive one infusion of blood and one of marrow but you will not be told which you receive at the time. You may request this information only when the study is finished or if there is a clinical reason why you or your doctors need to know. You can continue to take your usual medications and you may be asked to take iron tablets for a short while. We would be very grateful if you would also complete two questionnaires on a total of seven occasions over two and a half years. We will ask you not to be involved in other research projects for the duration of this study.

What are the possible benefits and risks of participating?
Taking part in this study may or may not make your health better. While doctors hope the procedure will be useful for people with MS, there is no proof of this yet. We do know that the information from this study will help doctors learn more about bone marrow cell transfusion as a treatment for MS. This information could help future patients with MS.
You may have side effects while in the study. Everyone taking part in the study will be watched

carefully for any side effects. As this study involves a new treatment procedure, there might be side effects that we cannot predict. Side effects may be mild or very serious. Your health care team may give you medicines to help lessen side effects. In some cases, side effects can be serious, long lasting, or may never go away. There is also a small risk of death.

Likely risks and side effects which may be related to the procedure include a mild degree of lethargy and anaemia following bone marrow harvest and blood donation, mild nausea following a general anaesthetic, and some discomfort or bruising at the sites of marrow aspiration. Rare but serious side effects include infection of the transfused cells, clots forming in the vessels of the lungs or legs,
a dampening effect on the immune system which could lead to an increased susceptibility to infection, and death. If you suffer from any new symptom during the study, you should discuss this with the medical team.

We do not know the effects of this procedure on an unborn baby; therefore you should not take part in this study if you are pregnant, breast-feeding or you intend to become pregnant or father a child during the study. Women who might become pregnant will be asked to have a pregnancy test (urine or blood) before taking part. Women who could become pregnant must agree to use a reliable form of contraception during the course of this study. Any woman who finds that she has become pregnant while taking part in the study should tell her research doctor immediately. Arrangements will be made to monitor the health of both herself and her unborn baby. Should your partner become pregnant, it would be desirable for her to agree to medical supervision during the pregnancy and for the baby after it is born. The partner will be invited to sign a consent form to allow medical supervision.

If we discover an abnormality during screening before marrow collection, you will be informed and the treatment options discussed. Such a finding may have insurance implications.

Where is the study run from?
MS and Stem Cell Laboratories, University of Bristol, Frenchay Hospital, Bristol, UK.

When is the study starting and how long is it expected to run for?
Recruitment will start in autumn 2012 and participants will be recruited for approximately two and a half years.

Who is funding the study?
The Silverman Family Foundation, the MS Trust, the Medical Research Council (UK) and the Rosetrees Foundation.

Who is the main contact?
Professor Neil Scolding
n.j.scolding@bristol.ac.uk

# Contact information

### Type(s)
Scientific

### Contact name
Prof Neil Scolding

### Contact details
University of Bristol
Institute of Clinical Neurosciences
Frenchay Hospital
Bristol
United Kingdom
BS16 1JB

# Additional identifiers

### EudraCT/CTIS number

### IRAS number

### ClinicalTrials.gov number
NCT01815632

### Secondary identifying numbers
ACTiMuS v1 07/09/12

# Study information

### Scientific Title
Assessment of bone marrow-derived Cellular Therapy in progressive Multiple Sclerosis (ACTiMuS)

### Acronym
ACTiMuS

### Study objectives
We hypothesise that intravenously-delivered autologous bone marrow cellular therapy (BMCT) in chronic multiple sclerosis (MS) offers significant benefit. We hypothesize also that the mechanisms are multiple, and include immunomodulation and reparative and/or neuroprotective effects within the CNS; and are offered by one or more bone marrow (BM) stem cell sub-populations, jointly contributing to the therapeutic impact. Exploring and understanding these mechanisms, and the biology of the cells responsible, will allow the development of more effective reparative cell therapy in MS.
On this underlying hypothesis, we propose a phase 2 controlled trial in parallel with a significant body of translational and back-translational laboratory research, directed towards these questions:
1. Is autologous BM cell therapy truly beneficial in chronic MS as our small, uncontrolled phase 1 trial suggested?
2. Do BM mesenchymal stem cells from patients with MS differ in range or extent of reparative and neuroprotective properties from control individuals cells?
3. What therapeutic properties do BM stem cell sub-populations other than mesenchymal stem cells possess, and do these differ between MS patients and controls?
4. Can BM stem cell sub-populations be isolated from peripheral blood samples from MS patients following treatment, and for how long?

### Ethics approval required

Old ethics approval format

## Ethics approval(s)
NRES Committee West Midlands, 01/09/2014, ref: 14/WM/1083

## Study design
Prospective randomised double-blind placebo-controlled modified cross-over single centre study

## Primary study design
Interventional

## Secondary study design
Randomised controlled trial

## Study setting(s)
Hospital

## Study type(s)
Treatment

## Participant information sheet
Not available in web format, please use the contact details to request a patient information sheet

## Health condition(s) or problem(s) studied
Progressive multiple sclerosis

## Interventions
Randomisation to early transfusion of autologous marrow and late (12 months) autologous blood infusion or early autologous blood infusion with late (12 months) autologous marrow infusion

## Intervention Type
Other

## Phase
Not Applicable

## Primary outcome measure
Global evoked potential (GEP)

## Secondary outcome measures
1. EDSS and MSFC and MSIS-29
2. Brain and spinal cord magnetic resonance imaging (MRI) with and without gadolinium-enhancement
3. Optical coherence tomography (OCT)

## Overall study start date
03/12/2012

### Completion date
02/12/2017

# Eligibility

### Key inclusion criteria
1. Subject of either sex, 18 to 60 years (inclusive)
2. Diagnosis of clinically-definite MS as defined by the McDonald criteria
3. MS disease severity EDSS 4  6
4. Disease duration >5 years
5. Disease progression (not attributable to relapse) in the year prior to entry
6. Signed, written informed consent
7. Willing and able to comply with study visits according to protocol for the full study period

### Participant type(s)
Patient

### Age group
Adult

### Lower age limit
18 Years

### Upper age limit
60 Years

### Sex
Both

### Target number of participants
80; 60 with secondary progressive MS and 20 with primary progressive MS

### Key exclusion criteria
1. Pregnancy, breastfeeding or lactation
2. History of autologous/allogeneic bone marrow transplantation or peripheral blood stem cell transplant
3. Bone marrow insufficiency
4. History of lymphoproliferative disease or previous total lymphoid irradiation
5. Immune deficiency
6. History of current or recent (<5 years) malignancy
7. Chronic or frequent drug-resistant bacterial infections or presence of active infection requiring antimicrobial treatment
8. Frequent and/or serious viral infection
9. Systemic or invasive fungal disease within 2 years of entry to study
10. Significant renal, hepatic, cardiac or respiratory dysfunction
11. Contraindication to anaesthesia
12. Bleeding or clotting diathesis
13. Current or recent (within preceding 12 months) immunomodulatory therapy other than corticosteroid therapy
14. Treatment with corticosteroids within the preceding 3 months

15. Significant relapse within preceding 6 months
16. Predominantly relapsing-remitting disease over preceding 12 months
17. Radiation exposure in the past year other than chest / dental x-rays
18. Previous claustrophobia
19. Presence of implanted metal or other contraindication to MRI
20. Participation in another experimental study or treatment within previous 24 months

### Date of first enrolment
03/12/2012

### Date of final enrolment
02/12/2017

## Locations

### Countries of recruitment
England

United Kingdom

### Study participating centre
**University of Bristol**
Bristol
United Kingdom
BS16 1JB

## Sponsor information

### Organisation
North Bristol NHS Trust (UK)

### Sponsor details
Research & Innovation Office
Floor 3 Learning & Research
Southmead Hospital
Westbury on Trym
Bristol
England
United Kingdom
BS10 5NB

### Sponsor type
Hospital/treatment centre

### Website

http://www.nbt.nhs.uk/

**ROR**
https://ror.org/036x6gt55

# Funder(s)

**Funder type**
Charity

**Funder Name**
The Silverman Family Foundation (USA)

**Funder Name**
Multiple Sclerosis Trust

**Alternative Name(s)**
MS, MS Trust

**Funding Body Type**
Private sector organisation

**Funding Body Subtype**
Other non-profit organizations

**Location**
United Kingdom

**Funder Name**
Medical Research Council

**Alternative Name(s)**
Medical Research Council (United Kingdom), UK Medical Research Council, MRC

**Funding Body Type**
Government organisation

**Funding Body Subtype**
National government

**Location**
United Kingdom

**Funder Name**
Rosetrees Foundation (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? |
|---|---|---|---|---|---|
| Protocol article | protocol | 14/10/2015 | | Yes | No |
| HRA research summary | | | 28/06/2023 | No | No |