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Autologous Stem cell Transplantation International Crohn's disease trial

Submission date	Recruitment status	[ ] Prospectively registered
21/05/2010	No longer recruiting	[ ] Protocol
Registration date	**Overall study status**	[ ] Statistical analysis plan
21/05/2010	Completed	[ ] Results
Last Edited	**Condition category**	[ ] Individual participant data
29/05/2015	Digestive System	[ ] Record updated in last year

Plain English summary of protocol

Background and study aims
Crohn's disease is a long-term condition that causes inflammation of the lining of the digestive system. Some patients fail to respond to the best clinical treatment in Crohn's disease and some only experience a temporary benefit, which is why the search for more effective treatments is continuing. Recently, an experimental treatment has been developed for severe Crohn's disease, called 'high dose immunoablation followed by autologous hematopoietic stem cell transplantation'. Hematopoietic blood stem cells are young, undifferentiated blood cells that can develop into differentiated ones, including lymphocytes, and over-reactive lymphocytes are thought to contribute to the development of Crohn's disease. This study involves removing your over-active lymphocytes (immunoablation) and replacing them using blood stem cells that had been taken (harvested) from your body earlier in the study. Conventional medication only temporarily suppresses the over-reactive lymphocytes.
At present, about 30 patients suffering from Crohn's disease have been treated with stem cell transplantation worldwide. The results from those studies suggest that the therapy may be effective, but it cannot be concluded yet whether this treatment is better than any best clinical practice. An international collaborative group of medical specialists has agreed that this issue can only be solved by conducting a scientifically sound clinical study in which institutions from all over the world participate. This study is a European collaboration and we aim to treat a total of 48 patients in the different countries that are taking part.

Who can participate?
Patients aged between 18 and 50 years with severe Crohn's disease who have not responded to immunosuppressant medication.

What does the study involve?
Participants will have a number of investigations before undergoing stem cell mobilisation. Stem cell mobilisation involves suppressing the bone marrow with a cytotoxic drug (cyclophosphamide) before stimulating it to release large numbers of stem cells into the circulation. These are collected through a tube inserted into a vein and stored until needed. The drug used for mobilisation is also effective against Crohn's disease, thus this phase results in a treatment by itself. Participants are then randomly allocated to undergo bone marrow abolition and stem cell re-infusion either immediately or with a delay of 1 year. Bone marrow abolition

involves high doses of cytotoxic drugs to destroy the initial bone marrow. Then the stem cells that were harvested earlier are transplanted (re-infused) into your blood, like a regular blood transfusion thereafter homing into the bone marrow. The re-infused stem cells give rise to a new generation of immune cells, replacing cells of the original 'sick' immune system. Patients are evaluated at intervals and the progress over the first year is compared. Patients are followed up for five years.

What are the possible benefits and risks of participating?
By comparing the progress of patients who undergo early stem cell transplantation with those who receive late stem cell transplantation, the study will allow the value of immunoablation and stem cell transplantation to be assessed, whilst offering this new procedure to all patients that enter the study. It is possible that the process of mobilisation may give some benefit. The study will allow some assessment of this effect and control for it when assessing transplantation. High dose immunoablation followed by autologous stem cell transplantation is an intensive treatment with risks of severe complications which on rare occasions have been fatal. These complications may require hospitalisation at any time and include: infections, bleeding, heart failure, respiratory insufficiency (breathing difficulties), kidney failure, lymphoma. Less severe, but more frequent (reversible) toxicities include: nausea, fever, alopecia (hair loss), infertility, arthralgia (joint pain), myalgia (muscle pain), menstrual disorders and hematuria (blood in the urine) due to irritation of the lining of the bladder. Of course, the treating physicians will do their utmost to prevent these from occurring and treat them as best as they can when serious complications do occur. The process of stem cell mobilisation can incur similar risks as the high dose immunoablation. There is also a high risk of developing septic complications (severe infections requiring hospitalisation or lengthening your stay in hospital) during the stem cell mobilisation phase of the study and therefore your health will be closely monitored throughout this period.

Where is the study run from?
Nottingham University Hospital (UK).

When is the study starting and how long is it expected to run for?
The study started in July 2007 and will run until March 2017. Recruitment has closed but follow-up is ongoing.

Who is funding the study?
Broad Medical Research Programme (BMRP) (USA).

Who is the main contact?
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Contact information

Type(s)
Scientific

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Clinical Trials Information System (CTIS)
2005-003337-40

Protocol serial number
7107

Study information

Scientific Title
A multicentre randomised interventional treatment trial of hematopoietic stem cell mobilisation followed by high dose immuno-ablation and autologous stem transplantation versus hematopoietic stem cell mobilisation only in Crohn's disease

Acronym
ASTIC

Study objectives
To evaluate the potential benefit of hematopoietic stem cell mobilisation followed by high dose immuno-ablation and autologous stem transplantation versus hematopoietic stem cell mobilisation only followed by best clinical practice.

On 05/08/2013, Belgium was added to the countries of recruitment and the overall trial end date was changed from 01/07/2010 to 01/03/2017. Recruitment has closed but follow-up is ongoing.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Warwickshire Local Research Ethics Committee, 13/02/2006, ref: 06/Q2803/3

Primary study design
Interventional

Study design
Multicentre randomised interventional treatment trial

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Topic: Oral and Gastrointestinal; Subtopic: Oral and Gastrointestinal (all Subtopics); Disease: Gastrointestinal

Interventions
Open label, randomised, multicentre study comparing early transplantation procedure with transplantation carried out to the same protocol but delayed by one year. The status of patients undergoing early HSCT will be evaluated after one year and compared to those about to undergo delayed HSCT.

Intervention Type
Procedure/Surgery

Primary outcome(s)
Proportion of patients in sustained disease remission at one year. Sustained disease remission, based upon ECCO consensus is defined as: A minimum of a 3 month period of Crohn's disease activity index (CDAI) less than 150 without steroids or immunosuppressive drugs and no mucosal erosion or ulceration at ileocolonoscopy and no definite evidence of small bowel Crohn's Disease on barium studies.

Key secondary outcome(s)
1. Proportion of patients in alternative sustained disease remission as measured by a minimum of 3 months with the alternative Harvey Bradshaw score less than or equal to 3, without steroids or immunosuppressive drugs* and no mucosal erosion or ulceration at ileocolonoscopy and no definite evidence of small bowel Crohn's Disease on barium studies
2. Weeks in symptomatic remission (Crohns Disease Activity Index [CDAI] less than or equal to 150) over one year
3. Weeks in alternative symptomatic remission (Harvey Bradshaw score less than or equal to 3) over one year
4. Mean change from baseline in CDAI at one year
5. Mean change from baseline in Harvey Bradshaw score at one year
6. Mean CDAI over months 3-12 after transplant date, regardless of treatment
7. Median Harvey Bradshaw score over months 3 - 12 after transplant date, regardless of treatment
8. Total steroid use over one year
9. Steroid use over months 3 - 12
10. Number of days in clinical remission (CDAI less than or equal to 150 and on prednisolone less than or equal to 10 mg/day)
11. Number of days in alternative clinical remission (Harvey Bradshaw score less than or equal to 3 and on prednisolone less than or equal to 10 mg/day)
12. Days in drug free remission (CDAI less than or equal to 150 and not on steroids or any immuno-suppressive drugs*)
13. Days in alternative drug free remission (Harvey Bradshaw score less than or equal to 3 and not on steroids or any immuno-suppressive drugs*)
14. Time to and days in sustained disease remission
15. C-reactive protein (CRP) at one year and average over months 3 - 12
16. Platelet count at one year and average over months 3 - 12
17. Change in Crohn's Disease Endoscopic Index of Severity (CDEIS) over 12 months, based on blinded videotape comparisons
18. Histology, based on blinded comparisons

Completion date
01/03/2017

Eligibility

Key inclusion criteria
Mandatory:
1. Aged between 18 and 50 years (patients aged 50 - 65 years can participate if specially approved by the Trial Steering Committee)
2. Confirmed diagnosis of active Crohn's Disease:
2.1. Diagnosis of Crohn's disease based on typical radiological appearances and/or typical histology
2.2. Active disease at the time of registration to the trial, defined as Crohn's Disease Activity Index (CDAI) greater than or equal to 250 at any time within 3 months prior to trial entry, and greater than two of the following:
2.2.1. Raised C-reactive protein (CRP)
2.2.2. Endoscopic evidence of active disease confirmed on histology
2.2.3. Clear evidence of active small bowel Crohn's disease on small bowel barium study
3. Unsatisfactory course despite three immunosuppressive agents (usually azathioprine, methotrexate and infliximab) in addition to corticosteroids. Patients should have relapsing disease (i.e. greater than or equal to 1 exacerbation/year) despite thiopurines, methotrexate and /or infliximab maintenance therapy or clear demonstration of intolerance/toxicity to these drugs.
4. Impaired function and quality of life, compared to population means, on at least one of the following:
4.1. Inflammatory Bowel Disease Questionnaire (IBDQ)
4.2. European Questionnaire of Life Quality (EuroQol-5D)
4.3. Impaired function on Karnofsky Index
5. Current problems unsuitable for surgery and patient at risk for developing short bowel syndrome
6. Informed consent

Discretionary:
7. Wherever possible, diseased tissue should be accessible endoscopically for objective histological study
8. Small bowel disease that is extensive but does not extend to duodenum or terminal ileum is an exception, which will allow participation without endoscopy of diseased areas. All patients will however undergo flexible sigmoidoscopy.
9. Smokers may enter the study provided they have received intensive counselling about smoking
10. Patients with an ileostomy or colostomy may enter the study. Clinical activity should be assessed using modified CDAI and Harvey Bradshaw scoring method

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 Years

Sex
All

Key exclusion criteria
1. Pregnancy or unwillingness to use adequate contraception during the study, if a woman of childbearing age
2. Concomitant severe disease:
2.1. Renal: creatinine clearance less than 40 ml/min (measured or estimated)
2.2. Cardiac: clinical evidence of refractory congestive heart failure; left ventricular ejection fraction less than 45% by multigated radionuclide angiography (MUGA) or cardiac echo; chronic atrial fibrillation necessitating oral anticoagulation; uncontrolled ventricular arrhythmia; pericardial effusion with hemodynamic consequences as evaluated by an experienced echo cardiographer
2.3. Psychiatric disorders including active drug or alcohol abuse
2.4. Concurrent neoplasms or myelodysplasia
2.5. Bone marrow insufficiency defined as leucocytopaenia less than 3.0 x 10^9/l, thrombocytopenia less than 50 x 10^9/l, anaemia less than 8 g/dl, CD4+ T lymphopenia less than 200 x 10^6/l
2.6. Uncontrolled hypertension, defined as resting systolic blood pressure greater than or equal to 140 ml and/or resting diastolic pressure greater than or equal to 90 ml mercury despite at least two anti-hypertensive agents
2.7. Uncontrolled acute or chronic infection with human immunodeficiency virus (HIV), Human T-lymphotropic virus (HTLV) - 1 or 2, hepatitis viruses or any other infection the investigator or Steering Committee consider a contraindication to participation
2.8. Other chronic disease causing significant organ failure, including established cirrhosis with evidence of impaired synthetic function on biochemical testing and known respiratory disease causing resting arterial oxygen tension less than 8 kpa or carbon dioxide tension greater than 6.7 kpa. Patients not known to have respiratory disease need not have blood gas measurements.
2.9. Crohn's Disease symptoms predominantly due to fibrotic stricturing and unlikely to respond to immune manipulation, in the opinion of any of the investigators or the steering committee
3. Infection or risk thereof:
3.1. Current abscess or significant active infection
3.2. Perianal sepsis is not an exclusion provided there is natural free drainage or a Seton suture (s) have been placed
3.3. History of tuberculosis or at current increased risk of tuberculosis
3.4. Mantoux test result or other investigations that the investigator or Steering Committee regard as evidence of active tuberculosis
3.5. Abnormal chest x ray (CXR) consistent with active infection or neoplasm
4. Significant malnutrition: body mass index (BMI) less than or equal to 18, serum albumin less than 20 g/l
5. Previous poor compliance
6. Concurrent enrolment in any other protocol using an investigational drug or hematopoietic growth factor up to four weeks before study entry
7. Lack of funding

Date of first enrolment
01/07/2007

Date of final enrolment
05/08/2013

Locations

Countries of recruitment
United Kingdom

England

Belgium

Canada

France

Italy

Spain

Switzerland

Study participating centre
Nottingham University Hospital
Nottingham
United Kingdom
NG7 2UH

Sponsor information

Organisation
European Group for Blood and Marrow Transplantation (EBMT) (UK)

Funder(s)

Funder type
Research organisation

Funder Name
Broad Medical Research Programme (BMRP) (USA)

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?
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes
Study website	Study website	11/11/2025	11/11/2025	No	Yes