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Thymoglobulin to prevent chronic graft versus host disease in hematopoietic progenitor cell transplantation patients

Submission date
18/02/2010

Recruitment status
No longer recruiting

Registration date
23/02/2010

Overall study status
Completed

Last Edited
21/01/2020

Condition category
Injury, Occupational Diseases, Poisoning

[X] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] 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

ClinicalTrials.gov (NCT)
NCT01217723

Protocol serial number
MCT-99786; CBMTG 0801

Study information

Scientific Title
A randomised trial of thymoglobulin to prevent chronic graft versus host disease in patients undergoing haematopoietic progenitor cell transplantation (HPCT) from unrelated donors

Study objectives
The addition of thymoglobulin to the preparative regimen will result in a decrease in the proportion of patients with chronic graft versus host disease (cGVHD), resulting in improved quality of life but without an increase in mortality, disease relapse or death due to infection.

Ethics approval required
Old ethics approval format

Ethics approval(s)
McMaster University-Hamilton Health Sciences Research Ethics Board, 28/01/2010

Study design
Phase III multicentre randomised clinical trial

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Chronic graft versus host disease

Interventions
This is a randomised trial. Patients randomised to the thymoglobulin arm will receive thymoglobulin 0.5 mg/kg on Days -2 and -1 prior to HPCT, and then a dose of 2.0 mg/kg on Day 0 (for a total dose of 4.5 mg/kg [actual body weight]). Quality of life questionnaires will be administered at screening and again at 6, 12 and 24 months post-HPCT. Participants will be asked to complete a cGVHD Symptom Scale at 100 days post-HPCT and again at 6, 12 and 24 months post-HPCT (and also at the time of diagnosis of cGVHD). Participants will also be asked to complete questionnaires related to health care resource utilisation and personal costs at 6, 12 and 24 months post-HPCT as part of a health cost comparison between the two study arms.

The preparative regimen for the control arm will not include thymoglobulin. Participants will be asked to complete the same questionnaires as the participants in the thymoglobulin arm. In both arms, all treatment and follow-up will be according to standard institutional practice (except for the addition of the thymoglobulin to the preparative regimen in the thymoglobulin arm).

Intervention Type
Drug

Phase
Phase III

Drug/device/biological/vaccine name(s)
Thymoglobulin

Primary outcome(s)
Freedom of cGVHD at 12 months from transplantation defined as withdrawal of all systemic immunosuppressive agents without resumption up to 12 months after transplantation.

Key secondary outcome(s))
1. Time to engraftment: complete blood count (CBC) measured daily until engraftment of platelets and neutrophils
2. Incidence of acute GVHD: participants will be assessed daily while in hospital and then according to local institutional practice until month 24
3. Incidence of cGVHD according to NIH Consensus criteria: measured at 100 days, 6 months, 12 months and 24 months using the "Chronic GVHD Assessment Form"
4. Incidence of cGVHD according to Sullivan Criteria: measured at day 100, months 6, 12 and 24 using the "Chronic GVHD Assessment Form"
5. Time to non-relapse mortality: time dependent variable
6. Time to all-cause mortality: time dependent variable
7. Time to relapse of leukaemia: measured according to local institutional practice at time there are signs/symptoms of relapse
8. Incidence of graft rejection or failure: CBC measured daily until engraftment of platelets and neutrophils
9. Incidence of serious infection: participants are assessed for signs of infection according to local institutional practice
10. Incidence of cytomegalovirus (CMV) activation: screening CMV is to occur according to local institutional practice
11. Quality of life: questionnaires collected at screening, 6, 12 and 24 months
12. Cost effectiveness: questionnaires collected at screening, 6, 12 and 24 months
13. Incidence of specific organ grades (National Institutes of Health [NIH]) of cGVHD: measured at 100 days, 6 months, 12 months and 24 months post-HPCT
14. Number of months on immunosuppression up to 12 months post-transplant: measured at 100 days, 6, 12 and 24 months post-transplant using the "Chronic GVHD Assessment Form"
15. Proportion of patients needing immunosuppression at 24 months: measured at 24 months post-HPCT using the "Chronic GVHD Assessment Form"
16. Doses of immunosuppressive drugs at 12 months: measured (assessed) at 12 months using the "Chronic GVHD Assessment Form"
17. Immunosuppressive therapy at time of diagnosis of cGVHD, prior to treatment of cGVHD: measured (assessed) at time of diagnosis of cGVHD. "Chronic GVHD Assessment Form" is to be completed at this time.

Completion date
01/12/2015

Eligibility

Key inclusion criteria
1. The recipient is aged between 16 and 70 years, either sex
2. The recipient has an haematologic malignancy i.e. one of:
2.1. Acute leukaemia, myeloid, lymphoid, or biphenotypic, in 1st or 2nd remission or be in early relapse (no chemotherapy within three months and blasts less than 10% and with previous remission having been longer than 3 months)
2.2. Chronic myeloid leukaemia, in chronic or stable accelerated phase
2.3. Chronic lymphocytic leukaemia
2.4. Lymphoma

2.5. Myelodysplastic syndrome
2.6. Myeloproliferative disorder
3. The recipient will receive one of the specified preparative regimens
4. The recipient will receive either a bone marrow ("HPC, Marrow") or blood progenitor cell ("HPC, Apheresis") graft
5. The recipient has an unrelated donor who with high resolution typing is either fully MHC matched at HLA-A, B, C and DRB1 with the recipient or is 1-antigen or 1-allele mismatched at A, B, C or DRB1 loci
6. The recipient meets the transplant centre's criteria for unrelated donor allogeneic transplantation, either myeloablative or non-myeloablative (syn. RIC)
7. The recipient has good performance status (Karnofsky greater than or equal to 60%)
8. Recipient has given signed informed consent
9. For the questionnaire component only, be able to complete the questionnaires in English or with a validated translation

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Sex
All

Total final enrolment
203

Key exclusion criteria
1. The recipient is human immunodeficiency virus (HIV) antibody positive
2. The recipient has a hypersensitivity to rabbit proteins or thymoglobulin pharmaceutical excipients, glycine or mannitol
3. The recipient has an active infection (i.e. infection requiring oral or intravenous [IV] therapy)
4. The recipient (if female and of childbearing potential) is pregnant or breast-feeding at the time of enrolment
5. The recipient (if female and of childbearing potential) does not agree to use an adequage contraceptive method from the time of enrolment until a minimum of one year following transplant
6. The recipient (if male and fertile) does not agree to use an adequate contraceptive method from the time of enrolment until a minimum of one year following transplant
7. For the questionnaire component only, the recipient is unable to participate due to cognitive, linguistic or emotional difficulties (i.e. the recipient can participate in the main study but will be excluded from the questionnaire component)

Date of first enrolment
10/03/2010

Date of final enrolment
01/12/2015

Locations

Countries of recruitment
Canada

Study participating centre
1200 Main St. West
Hamilton
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Sponsor information

Organisation
McMaster University (Canada)

ROR
https://ror.org/02fa3aq29

Funder(s)

Funder type
Research organisation

Funder Name
Canadian Institutes of Health Research (CIHR) (Canada) - http://www.cihr-irsc.gc.ca (ref: MCT-99786)

Alternative Name(s)
Instituts de Recherche en Santé du Canada, The Canadian Institutes of Health Research (CIHR), Canadian Institutes of Health Research (CIHR), Canadian Institutes of Health Research | Ottawa ON, CIHR - Welcome to the Canadian Institutes of Health Research, CIHR, IRSC

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
Canada

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

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	01/02/2016		Yes	No
Results article	results	01/02/2020	21/01/2020	Yes	No