In vivo measurement of lymphocyte kinetics during immune reconstitution after hematopoietic stem cell transplantation using [6,6-2H2]-glucose labeling

Published: 03-01-2012
Last updated: 28-04-2024

To get more insight into lymphocyte kinetics during immune reconstitution after hematopoietic stem cell transplantation

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Haematological disorders NEC
Study type	Observational invasive

Summary

ID

NL-OMON39524

Source
ToetsingOnline

Brief title
SILAS: Stable Isotope Labeling After Stemcelltransplantation

Condition

- Haematological disorders NEC

Synonym
Stemcell transplatation; immune reconstitution

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: Klinische Fellowship ZonMW

Intervention

Keyword: Hematopoietic stemcell transplantation, immune reconstitution, lymphocyte turnover

Outcome measures

Primary outcome

Lymphocyte subset production rates and life spans during immune recovery

following HSCT

Secondary outcome

Not applicable

Study description

Background summary

Hematopoietic stem cell transplantation (HSCT) often provides the best chance for a cure for many malignant and non-malignant diseases. Conditioning regimens are however intense and render the immune system and in particular the T lymphocyte compartment depleted for extended periods of time. This puts HSCT patients at an increased risk to develop opportunistic infections and about 10-20% of stem cell transplant recipients even die of infectious complications. Enhancing immune reconstitution following stem cell transplantation is therefore an area of intensive research.
Much of our understanding of immune reconstitution and in particular lymphocyte recovery following stem cell transplantation is based on irradiated mouse models and in humans on longitudinal descriptive studies of reappearing lymphocyte subsets in the blood. We will study lymphocyte recovery dynamics in patients who underwent HSCT by measuring lymphocyte production rates and life spans through in vivo stable-isotope labeling with [6,6-2H2]-glucose (deuterated glucose). A better understanding of lymphocyte recovery dynamics will offer new venues to develop approaches to enhance immune recovery following HSCT.

Study objective

To get more insight into lymphocyte kinetics during immune reconstitution after hematopoietic stem cell transplantation

Study design

All participants will be admitted to the AMC for a 24-hour infusion of [6,6-2H2]-glucose. Label decay will be followed for a period up to 6 months. The amount of label within sorted lymphocyte subsets of interest will be measured at predetermined intervals using gas chromatography mass spectrometry (GC/MS). With the help of mathematical models the production rates and life spans of these lymphocyte subsets can then be calculated.

Study burden and risks

- Benefit: Using in vivo deuterated glucose labeling we will study turnover rates of lymphocyte subsets (such as naïve, memory, effector CD4 and CD8 T cells, B cells and NK cells) following HSCT, to obtain a better understanding of adaptive immune recovery following HSCT. This is much needed to develop new approaches to shorten the time that HSCT patients are at increased risk to develop opportunistic infections (group benefit). There is no personal benefit for the participants.

- Burden: During [6,6-2H2]-glucose labeling (up-labeling phase): 24-hour admission to the AMC for continuous i.v. [6,6-2H2]-glucose administration; blood draw before labeling (one venapuncture; 56 ml); blood sampling through finger pricks every 4 hours starting after one hour of labeling. After labeling (down-labeling phase): blood sampling through venapunctures (56 ml per draw) at predetermined intervals after infusion up until 6 months after labeling. Total volume of blood drawn (including t=0): 9 x 56 ml of blood = 504 ml in 6 months.
- Risks: Deuterium is a naturally occurring, stable isotope that has been applied a.o. to study glucose and adipocyte metabolism and lymphocyte turnover in healthy adults, elderly individuals and HIV-infected patients. It has an excellent safety profile. Apart from occasional mild transient vertigo or dizziness during label infusion no side effects have been reported.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

• Patients who underwent autologous or allogeneic stem cell transplantation because of a hematological malignancy
• Complete remission before HSCT
• Age 18-65 years
• WHO performance score 0-2
• Outpatient clinic patients
Inclusion criteria - specific for autologous HSCT
• Indication for HSCT: relapsed non-Hodgkin*s lymphoma
• Remission-induction chemotherapy schedule including Rituximab
• Conditioning regimen: BEAM chemotherapy (BCNU (Carmustine), Ara-C (cytarabine), etoposide (VP16), Melphalan)
Inclusion criteria - specific for allogeneic HSCT
• Indication for HSCT: acute myeloid leukemia (AML)
• Type of transplant: non-mismatched sibling donor (n=5) and matched unrelated donor (MUD; n=5), non-T cell depleted peripheral blood derived stem cell transplant
• Conditioning regimen (myeloablative): cyclophosphamide and total body irradiation for sibling donors; cyclophosphamide, total body irradiation and anti-thymocyte globulin for unrelated donors
• No or minimal immune suppression (prednisone <= 10 mg/day, no cyclosporine, no mycophenolate mofetil)

• No active graft versus host disease

Exclusion criteria

• Acute graft-versus-host disease or infectious complications necessitating hospital admission;
• Active hematological malignancy;
• HIV, hepatitis B, hepatitis C infection
• Pre-treatment with immunomodulatory or lymphocyte depleting drugs such as lenalidomide, fludarabine or alemtuzumab
• AML relapse and/or previous autologous or allogeneic HSCT
• Significant renal, hepatic or cardiac dysfunction
• Diabetes mellitus type 1, DM type 2
• Alcohol and/or drug abuse
• Unwilling or not capable to use effective means of birthcontrol

Study design

Design

Study type:	Observational invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	27-08-2012
Enrollment:	25
Type:	Actual

Ethics review

Approved WMO Date:	03-01-2012
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	23-12-2013
Application type:	Amendment
Review commission:	METC Amsterdam UMC

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
CCMO	NL37582.018.11