Can the steady-state hematopoiesis be improved post-ASCT by infusion of the autologous stem cell transplant directly in the bone marrow compartment?

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To improve the steady hematopoiesis post-ASCT by infusing the autologous transplant directly in the bone marrow compartment.(protocol page 6)

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Anaemias nonhaemolytic and marrow depression
Study type	Interventional

Summary

ID

NL-OMON31554

Source
ToetsingOnline

Brief title
Reinfusion of ASCT transplant in the bone marrow compartment.

Condition

- Anaemias nonhaemolytic and marrow depression

Synonym
Stem cell infusion and transplantation

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Groningen
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: Autologous stem cells, homing: bone marrow compartment.

Outcome measures

Primary outcome

- Duration of the granulocytopenia (<0.1 x 109/l, <0.5 x 109/l) and

thrombocytopenia (<10 x 109/l, 20 x 109/l) in days.

- Transfusion independence of thrombocyte transfusion and erythrocyte

transfusion in days.

- Graft failure. A graft failure is defined as a granulocyte count <0.5x109/l

six weeks following reinfusion autologous stem cell transplant.

- Pelvis infection.

- Judgement of bone marrow function 6-9 months after ASCT. This will take place

by in-vitro research of the bone marrow transplant and by performing an FLT-PET.

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Secondary outcome

N.a.

Study description

Background summary

Introduction and rationale
Autologous stem cell transplantation is a frequently applied treatment modality for patients with multiple myeloma (MM) and relapsing lymphoma. The autologous stem cell transplant is re-infused intravenously following high-dose chemotherapy. Post-ASCT a gradual normalization of peripheral blood cell counts occurs but normal peripheral blood cell counts of all three lineages is noticed in only 40% of the patients one year post-transplantation3. The consequences are that future chemotherapy application is limited in the case of relapsing

disease. In this situation the hematopoietic stem cell compartment demonstrates an increased susceptibility for the cytotoxic effects of chemotherapy resulting in prolonged periods of peripheral pancytopenia.
The observed impaired regenerative capacity of the stem cell compartment post-ASCT and the impaired cell function under conditions of stress (chemotherapy) might be attributed to: (1) an impaired hematopoietic stem cell (HSC) function and engraftment due to accumulated DNA damage of stem cells and micro-environment as result of chemotherapy exposure; (2) a limited number of hematopoietic stem cells lodge in the bone marrow compartment due to the lack of relevant homing receptors and trapping of the infused cells in lung, liver and spleen; (3) an impaired homing of cells that are part of the micro-environment which limits the regenerative capacity of the stem cell compartment.
These findings result in a *relative* shortage of HSC*s in the bone marrow compartment and as consequence a higher productive rate of remaining bone marrow cells for producing adequate peripheral blood cells counts. These findings are in line with preliminary results demonstrating that bone marrow progenitors 6-9 months post-ASCT have the phenotypic profile of granulocyte-macrophage progenitors (GMP) instead of common myeloid progenitors (CMP). Moreover post-ASCT patients demonstrate a higher proliferative activity of the bone marrow compartment at normal peripheral blood cell counts as tested in-vivo with FLT-PET scanning.

Recent findings in mice and human have demonstrated that engraftment and recovery of hematopoietic cells following ASCT can be improved by infusing the autologous stem cell transplant directly in the bone marrow compartment4-8. This approach has the advantage that the lodging of the HSC*s in the bone marrow is less dependent on the migratory/adhesion capacity of the cells. In addition the cells are directly located in their own micro-environment, and an concomitant regeneration of microenvironment and hematopoietic compartments take place.
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Study objective

To improve the steady hematopoiesis post-ASCT by infusing the autologous transplant directly in the bone marrow compartment.
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Study design

The study design is a pilot study. The feasibility of the autologous stem cell re-infusion will be explored in 15 patients diagnosed with lymphoma and MM.

Intervention

The admittance of the stem cell transplant immediately in the bone marrow compartment.

Study burden and risks

- Tingle the spina iliaca; a subcutaneous anaesthesia will be given in advance.
- If the transplant does not catch. If day-21 after transplant there is no granulocyte (<0.1 x 109/l) or thrombocyte (10x < 109/l) recovery if there is no other cause then a complete stem cell transplant (>5 x 106 CD34+ cells/kg) will be infused through the blood stream.
- Perform an FLT-PET.

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 (n=15) with an MM or a relapse lymphoma who are considered for an ASCT. The conditioning consists of high dose melphalan by the MM (200 mg/m2) or BEAM in patients with a relapse lymphoma.
- During the leucophereses procedure 10 x 106 CD34+ cells/kg have to be collected. The patient receives 5 x 106 CD34+ cells/kg.
- The spina iliaca anterior superior has to be approached easily.
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Exclusion criteria

- inadequate stem cell collection (<10x106 CD34+ cells/kg)
- previous radiotherapy on pelvis
- previous infections complications in the pelvis region
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Study design

Design

Study phase:	2
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	01-01-2009
Enrollment:	15
Type:	Actual

Medical products/devices used

Product type:	Medicine

Generic name:	Somatic cells autologous

Ethics review

Approved WMO Date:	29-07-2008
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	28-08-2008
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)

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
EudraCT	EUCTR2008-003537-25-NL
CCMO	NL20975.000.08