Causes and consequences of disrupted bone marrow function following autologous stem cell transplantation, a pilot study

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Plasma cell neoplasms
Study type	Observational non invasive

Summary

ID

NL-OMON42488

Source
ToetsingOnline

Brief title
BM-003/53260

Condition

- Plasma cell neoplasms

Synonym
lymphoma, myeloma

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, bone marrow, disrupted, function

Outcome measures

Primary outcome

To obtain information regarding the increased vulnerability of HSPC for chemotherapy, in vitro culture assays will be performed in the absence and presence of cytostatic agents, in the presence and absence of mesenchymal cells (MSC*s). The response of these cells will further be analyzed regarding the induction of stress response (p53) and DNA damage response by performing gene profiling and western blotting. In addition, the genetic and epigenetic background of these cells will be analyzed and correlated with the obtained results by performing targeted sequencing and Chip-seq. For these assays at least 105 cells are required per experiment.

Secondary outcome

not applicable

Study description

Background summary

Autologous stem cell transplantation (ASCT) is an important treatment modality for patients with lymphoma and myeloma. In lymphoma patients it is mostly applied in relapsing disease following induction chemotherapy while in myeloma patients it is part of the upfront treatment in chemotherapy sensitive disease. In general, patients demonstrate a fast hematological recovery following high dose chemotherapy and reinfusion of autologous stem cells. However, in 10%-15% of the patients the recovery has a slower course, in particular regarding the platelets. In addition, it has been shown that despite normal peripheral blood

cell counts following ASCT, the hematopoietic compartment is in general affected by the applied transplantation procedure. This is reflected by an increased susceptibility to chemotherapy resulting in prolonged pancytopenia in 10%-20% of the patients. In addition, an increased incidence of myelodysplasia and acute myeloid leukemia has been demonstrated 3-6 years following ASCT, in general with an unfavorable prognosis. Apparently the hematopoietic compartment is more susceptible to stress response and more prone to malignant transformation, with the two processes likely interconnected with each other. Whether these aberrations are only linked to the hematopoietic compartment or also extend to the surrounding microenvironment is unresolved so far. In the present protocol we will study hematopoietic stem and progenitor cells (HSPC) in conjunction with the surrounding mesenchymal stem cells (MSC) focused on (a) mechanisms that contribute to the increased vulnerability of HSPC for chemotherapy and (b) defining molecular markers that contribute to the increased incidence of malignant transformation.

Study objective

The present study will be focused on defining the mechanisms that contribute to the increased vulnerability of HSPC for chemotherapy. In particular DNA damage response, ROS production and protective mechanism against stress response (NFR2) will be studied at RNA and protein level. In addition, the protective role of MSCs will be analyzed in these processes. To define molecular defects that contribute to these interactions, DNA will be collected from myeloid and T cells. The DNA will be studied by targeting sequencing for the most prevalent mutations that have been demonstrated in AML/MDS.

Study design

Bone marrow cells (20 ml) will be collected from patients at least 1 year following an ASCT and will be analyzed for a number of in vitro parameters.

Study burden and risks

The bone marrow aspiration is according to standard procedure. It causes a short pain when the local anasthetic is administered and short pain when the bone marrow sample is collected.

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 diagnosed with lymphoma or myeloma that have been treated with ASCT.
-At least 1 year following ASCT
-Age >18 years

Exclusion criteria

-Age <18 years
-Signs of active disease related to lymphoma or myeloma
-Pregnancy

Study design

Design

Study type: Observational non invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	05-11-2015
Enrollment:	30
Type:	Actual

Ethics review

Approved WMO

Date:	01-09-2015
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

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	NL53260.042.15