Autologous stem cell transplantation for the treatment of refractory Crohn*s disease: mechanisms of succes

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Ethical review	Approved WMO
Status	Recruiting
Health condition type	Gastrointestinal inflammatory conditions
Study type	Observational invasive

Summary

ID

NL-OMON39547

Source
ToetsingOnline

Brief title
Mechanisms of succes of ASCT for Crohn's disease

Condition

- Gastrointestinal inflammatory conditions

Synonym
granulomatous enteritis, Inflammatory bowel disease

Research involving
Human

Sponsors and support

Primary sponsor: Sint Antonius Ziekenhuis
Source(s) of monetary or material Support: Veni (ZonMw;NWO) Femke van Wijk;assistant professor/begeleider en AGIKO (ZonMW;NWO) Eveline Delemarre;uitvoerend

onderzoeker

Intervention

Keyword: Crohn's disease, Stem cell tranplantation

Outcome measures

Primary outcome

To investigate on the cost effectivity and the immunological mechanisms

involved in immune reconstitution and engraftment after ASCT in Crohn's disease

patients. To gain insight in the effect of ASCT on the microbiome

Secondary outcome

Not applicable

Study description

Background summary

Crohn' disease is a complex disorder of the gastrointeinal tract that affects over 35.000 patients in the Netherlands. Although available therapies are in general effective, a small subgroup of patients is refractory to treatment and are no candidates for surgery because of the risk of short bowel syndrome. ASCT is a *last resort* for these CD patients who are refractory to any type of therapy. Autologous SCT has been shown to induce dramatic and long-term improvements in a range of autoimmune disorders in patients undergoing this treatement for hematological malignancies. Also in Crohn's disease several series have been published reporting succesful remission induction after ASCT. The largest series has been reported bij Oyama et. al. in which twelve patients with active Crohn's disease were treated with ASCT. After one and a half year of follow up only one relapse was observed.
Although the underlying mechanisms remain largely unknown, immune reconstitution after profound depletion appears to favor the development of tolerance over pathogenic immunity. The first aim of the present study is to increase our understanding of the pathophysiology underlying the beneficial effect of autologous ASCT. We will investigate the immunological mechanisms involved in the (re)induction of immune tolerance in the setting of autologous ASCT. In addition by comparison of microbiome pre- and post transplantation we aim to gain insight in the role of microbiota in the pathogenesis of acitve

Crohn*s disease in patients with refractoryCrohn*s disease.

Study objective

The aim of the present study is to increase our understanding of the cost effectivity and the pathophysiology underlying the beneficial effect of autologous SCT. We will investigate the immunological mechanisms involved in the (re)induction of immune tolerance in the setting of autologous SCT. In addition by comparison of microbiome pre- and post transplantation we aim to gain insight in the role of microbiota in the pathogenesis of acitve Crohn*s disease in patients with refractory Crohn*s disease.

Study design

Biomaterial (serum, DNA, feces, tissue) will be collected from patients undergoing autologous stem cell transplantation for the treatment of Crohn's disease.This is an open label, non-randomized, non-blinded, prospective study. Patients will be recruited from the outpatient IBD clinics of the UMCU. Many patients will be referrals from other centers. The ASCT will take place in the st. Antonius Hospital. The expected recruitment is five patients per year.

Study burden and risks

The study related procedures for obtaining biomaterials (blood, fecal samples, tissue samples during colonoscopy) involve no risk or burden except the coloscopy with biopsy (risk of complicatiens is 0,3-1 per 1000)

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

1) Age between 18 and 65 years
2) Confirmed diagnosis of active Crohn*s Disease:
3) Active disease at the time of registration to the trial
4) Unsatisfactory course despite 3 immunosuppressive agents (usually azathioprine, methotrexate and infliximab or adalimumab) in addition to corticosteroids. Patients should have relapsing disease (i.e. >1 exacerbation/year) despite thiopurines, methotrexate and/or infliximab/adalimumab maintenance therapy or clear demonstration of intolerance / toxicity to these drugs.
4) Current problems unsuitable for surgery or patient is at risk for developing short bowel syndrome.

Exclusion criteria

1) Pregnancy or unwillingness to use adequate contraception during the treatement, if a woman of childbearing age
2) Concomitant severe disease
a) renal: creatinine clearance < 40 ml/min (measured or estimated)
b) cardiac: clinical evidence of refractory congestive heart failure
c) psychiatric disorders including active drug or alcohol abuse
d) concurrent or recent history of malignant disease (excl. non-melanoma skin cancer)
e) uncontrolled hypertension, defined as resting systolic blood pressure >= 140 and/or resting diastolic pressure >= 90 despite at least 2 anti-hypertensive agents.
f) uncontrolled acute or chronic infection with HIV, HTLV-1 or 2, hepatitis viruses or any other infection the investigators consider a contraindication to participation.
g) other chronic disease causing significant organ failure, including established cirrhosis with evidence of impaired synthetic function on biochemical testing and known severe respiratory disease.

h) Crohn*s Disease symptoms predominantly due to fibrotic stricturing and unlikely to respond to immune manipulation.
3) Infection or risk thereof
a) History of tuberculosis or at current increased risk of tuberculosis
b) Mantoux test result or other investigations that the investigator as evidence of active tuberculosis.
c) Abnormal chest x ray (CXR) consistent with active infection or neoplasm.
4) Previous poor compliance
5) Concurrent enrolment in any other protocol using an investigational drug or hematopoietic growth factor up to four weeks before study entry.

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	24-06-2014
Enrollment:	15
Type:	Actual

Ethics review

Approved WMO

Date:	25-11-2013
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

Approved WMO

Date:	27-01-2015
Application type:	Amendment

Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

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	NL42003.100.13