Mesenchymal Stem Cells for the treatment of Crohn's Disease

No registrations found.

Ethical review	Positive opinion
Status	Recruitment stopped
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON22654

Source
NTR

Brief title
MSC and CD

Health condition

Crohn's Disease
de ziekte van Crohn

Sponsors and support

Primary sponsor: Leids Universitair Medisch Centrum
Source(s) of monetary or material Support: Maag Lever Darm Stichting (MLDS)

Intervention

Outcome measures

Primary outcome

1. Safety: rate of (serious) adverse events in the study population

2. Feasibility: determination of the number of expanded MSCs in relation to the amount of bone marrow collected, number of passages required and time to reach study target doses.

Secondary outcome

1. Induction of clinical response (reduction of CDAI > 70) or clinical remission (CDAI below 150) at six weeks.

2. Mucosal healing (videoendoscopy with biopsies) at six weeks.

3. Biological response (CRP reduction) at six weeks.

Study description

Background summary

Crohn's Disease (CD) is a severe disorder with significant morbidity and major impact on quality of life. Despite the availability of a range of medications there still remains a need for therapeutic alternatives because patients may not respond to existing therapeutic choices, they may become refractory to their medication, or they may develop treatment limiting toxicities.
In recent years it has become evident that bone marrow derived mesenchymal stem cells (MSCs) have potent immunomodulatory effects. MSCs are pluripotent cells that can differentiate into several mesenchymal tissues, including fibroblasts, osteoblasts, adipocytes and chondrocyte progenitors. MSCs have potent immunosuppressive effects on T and B cells in vitro and in animal models of chronic inflammation. Encouraging results have been obtained in patients with steroid resistant acute and severe Graft versus Host Disease (GvHD), including GvHD of the gut. We hypothesize that infusion of MSCs may similarly provide a novel treatment option in the treatment of patients with CD with less side effects than existing immunosuppressive therapies.

This open label, non randomized, non blinded, prospective, clinical phase Ib study, is designed to test the safety and feasibility of autologous MSC therapy in patients with refractory Crohn's Disease.
Ten patients, of at least 18 years of age and with moderate to severe Crohn's disease (CDAI > 220) refractory to state of the art treatment protocols (including infliximab), will be included. Bone marrow will be aspirated from the posterior iliac crest of all patients. The processing of the cells will take place at the GMP Stem Cell Laboratory Facility of the LUMC. Patients will receive two MSC infusions (2.0 x 10^6 MSCs per kilogram body weight, intravenously), 7 days apart.

Primary outcomes are defined as safety (rate of (serious) adverse events in the study population) and feasibility (determination of the number of expanded MSCs in relation to the

amount of bone marrow collected, number of passages required and time to reach study target doses).

Study objective

It is safe and feasible to administer autologous bone marrow derived MSCs for treatment of Crohn's Disease (CD).

Study design

N/A

Intervention

MSC infusion: two doses of 2.0 x 106 MSCs per kilogram body weight, intravenously, 7 days apart.

Contacts

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Eligibility criteria

Inclusion criteria

1. Men and women > 18 years of age.

2. Subject is willing to participate in the study and has signed the informed consent.

3. Subject must have had CD for at least 3 months from the time of initial diagnosis. The diagnosis of CD must have been confirmed by endoscopic and histologic evidence. If no previous confirmation of diagnosis is available or if previous diagnosis is not deemed conclusive, at time of screening endoscopy, histology should be performed to confirm diagnosis of CD.

4. Moderate to severe disease as defined by a CDAI score > 220, refractory to conventional medications and the affected ileocolonic site is endoscopically accessible.

5. At some time during the course of the subject's Crohn's disease (CD), subject must have received both steroids and immunosuppressive agents (for example, azathioprine, 6-mercaptopurine, methotrexate, or infliximab) which did not result in an adequate response to treatment.

6. Subjects included in the study might be receiving 5-aminosalicylic acid, azathioprine, 6-mercaptopurine, methotrexate, prednisone, or any similar drug at the time of enrolment and is allowed to have a history of infliximab treatment, provided the following conditions are fulfilled:

- The dose of 5-ASA must have been stable for at least 4 weeks prior to enrolment.

- The dose of steroids must have been stable for at least 4 weeks prior to enrolment.

- The dose of immunosuppressants (for example azathioprine, 6MP, or methotrexate) must have been stable for at least 8 weeks prior to enrolment and the subject on therapy for at least three months prior to enrolment.

- The last dose of infliximab is > 8 weeks prior to enrolment.

7. No need for immediate surgery (obstruction, abscess).

8. Patients must be able to adhere to the study visit schedule and protocol requirements.

9. If female and of child-bearing age, subject must be non-pregnant, non-breastfeeding, and use adequate contraception.

10. Patients must be able to give informed consent and the consent must be obtained prior to any study procedure.

Exclusion criteria

1. Patients with evidence of infection or abscesses.

2. Patients suffering from renal- or hepatic failure.

3. A psychiatric, addictive, or any disorder that compromises ability to give truly informed consent for participation in this study.

4. Use of any investigational drug within 1 month prior to screening or within 5 half-lives of the investigational agent, whichever is longer.

5. Change in concomitant medication:

- 5-ASA and steroids should be on a stable dose > 4 weeks;

- Immunosuppressants (e.g. azathioprine, 6MP or methotrexate) should be on a stable dose > 8 weeks,

- infliximab or other anti-TNF antibody therapy should not be administered < 8 weeks.

6. Serious infections (such as pneumonia or pyelonephritis) in the previous 3 months. Less serious infections (such as acute upper respiratory tract infection [colds] or simple urinary tract infection) need not be considered exclusions at the discretion of the investigator.

7. Documented HIV infection.

8. Active hepatitis B, hepatitis C or TB.

9. Subjects who currently have or who have had an opportunistic infection (e.g., herpes zoster [shingles], cytomegalovirus, Pneumocystis carinii, aspergillosis, histoplasmosis, or mycobacteria other than TB) within 6 months prior to screening.

10. Have current signs or symptoms of severe, progressive or uncontrolled renal, hepatic, hematologic, gastrointestinal, endocrine, cardiac, neurologic, or cerebral disease (including demyelinating diseases such as multiple sclerosis).

11. Malignancy within the past 5 years (except for squamous or basal cell carcinoma of the skin that has been treated with no evidence of recurrence).

12. History of lymphoproliferative disease including lymphoma, or signs and symptoms suggestive of possible lymphoproliferative disease, such as lymphadenopathy of unusual size or location (such as nodes in the posterior triangle of the neck, infra-clavicular, epitrochlear, or periaortic areas), or splenomegaly.

13. Known recent substance abuse (drug or alcohol).

14. Poor tolerability of venapuncture or lack of adequate venous access for required blood sampling during the study period.

Study design

Design

Study type:	Interventional
Intervention model:	Other
Masking:	Open (masking not used)
Control:	N/A , unknown

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	28-01-2008
Enrollment:	10
Type:	Actual

Ethics review

Positive opinion

Date:	26-06-2008
Application type:	First submission

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
NTR-new	NL1311
NTR-old	NTR1360
Other	: P07-001
ISRCTN	ISRCTN wordt niet meer aangevraagd

Study results

Summary results

Duijvestein M, van den Brink GR, Hommes DW. Stem cells as potential novel therapeutic strategy for inflammatory bowel disease. Journal of Crohn's and Colitis (2008) 2, 99¡V106