Allogeneic bone marrow derived mesenchymal stromal cells for the treatment of refractory proctitis in Ulcerative Colitis

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To assess the safety of endoscopic injected allogeneic bone marrow derived mesenchymal stromal cells (BMMSCs) in refractory proctitis.

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

Summary

ID

NL-OMON48876

Source
ToetsingOnline

Brief title
BMMSC proctitis

Condition

- Gastrointestinal inflammatory conditions

Synonym
Ulcerative Colitis

Research involving
Human

Sponsors and support

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

Intervention

Keyword: Inflammatory bowel disease, Mesenchymal stromal cells (MSC), Ulcerative Colitis

Outcome measures

Primary outcome

The safety, tolerability and feasibility of endoscopic injected MSCs in the

distal colon of patients with refractory proctitis after 6 weeks.

Secondary outcome

At 2, 6 and 24 weeks

1. To assess changes in the Mayo Score (appendix C) before and after BMMSC

treatment; as an indication of efficacy.

At 2, 6, 12 and 24 weeks

2. To assess changes in patient-reported outcome measures (PROMs) using the

mHealth index (appendix D) [71].

3. To summarize the changes in serum c-reactive protein (CRP) and fecal

calprotectin.

At 6 and 24 weeks

4. To compare histologic disease activity before and after local BMMSC

treatment using the Geboes score (appendix E).

5. To evaluate the effects of this intervention on immunological parameters and

local MSC persistence.

At 6, 12, 24 weeks

6. To evaluate the effect of local treatment with allogeneic BMMSCs on the quality of life using the Short Form Health Survey (SF-36) (appendix F) and the short Inflammatory Bowel Disease Questionnaire (sIBDQ) (appendix G).

Study description

Background summary

Patients with inflammatory bowel disease can present with proctitis, inflammation limited to the rectum. Although most of the patients with proctitis respond to conventional local 5-aminosalicylicacid (5-ASA) or corticosteroid treatment, a subset does not. For this group the next treatment option is a systemic immunosuppressive drug with considerable side-effects. Therefore, new local therapies for proctitis are needed.

Study objective

To assess the safety of endoscopic injected allogeneic bone marrow derived mesenchymal stromal cells (BMMSCs) in refractory proctitis.

Study design

Fourteen patients will receive allogeneic BMMSCs. BMMSCs will be injected during endoscopy in 4 to 8 places in the inflamed rectum (number of injections depending on the length of inflammation). Seven patients will be treated with 5x106 MSCs/ spot and seven patients with 10x106 MSCs/ spot.

Intervention

Endoscopically injected BMMSCs in the rectum.

Study burden and risks

In a recent review no side effects are associated with MSC therapy. However based on in vitro data potential risks of this study include: i) the suppression of immune responses resulting in an increased rate of infections. It should be noted that the current immunosuppressive treatment strategies for

ulcerative colitis are associated with higher immune suppression risks; ii) tumorigenicity and ectopic tissue formation. To evaluate these potential risks, patients will be followed for 1 year following MSC treatment. For more detailed information regarding safety refer to the enclosed IB.

Refractory UP is a clinical problem, with limited effective treatments and severe impairment of patient*s quality of life. The potent immunomodulatory effects and contribution to tissue repair of MSCs, together with the preliminary results of our latest study with allogeneic BMMSC in perianal fistulizing CD and our recent animal study, suggest that local injection of these cells could be a promising option for treatment of refractory UP. The local injection of allogeneic BMMSCs could avoid in these patients surgery to create a stoma or longstanding use of systemic medication, which can both lead to a significantly impaired quality of life. In light of the above, we believe that the risks of the proposed procedure are minor.

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

a) Men and women >= 18 years of age;
b) Patient must have ulcerative colitis confirmed by endoscopic and histologic evidence;
c) Inflammation must be limited to the rectum (up to 15 cm beyond the anal verge), confirmed by endoscopy maximum 3 months before baseline (slight inflammation in other parts of the colon is accepted with a maximum Mayo Score of 1);
d) Moderate to severe proctitis indicated by a Mayo Score of 2 or 3;
e) Proctitis must be refractory to conventional medical therapy. Which means that at some time during the course of the disease, patient must have received rectal 5-ASA therapy and rectal corticosteroid therapy for at least 4 weeks which did not result in an adequate response to treatment;
f) If treated with rectal therapy, therapy must be stopped two weeks before endoscopic implantation of MSCs and only restarted after 6 weeks;
g) If treated with oral 5-ASA therapy, dose must be stable for 4 weeks prior to study entry and remain on same dose during the first 6 weeks after MSC treatment;
h) If treated with oral corticosteroids, dose must be stable for 2 weeks prior to study entry and remain on same dose during the first 6 weeks after MSC treatment;
i) If treated with 6-mercaptopurine, methotrexate, azathioprine, vedolizumab or anti-TNF therapy patients must have been on medication for 3 months and a stable dose for 2 months prior to study entry and remain on same dose during the first 6 weeks after MSC treatment;
j) If female and of child-bearing age, patient must be non-pregnant, non-breastfeeding, and use adequate contraception;
k) Patient is willing to participate in the study and has signed the informed consent. Consent must be obtained prior to any study procedure.

Exclusion criteria

a) Patients suffering from renal- or hepatic failure;
b) Use of any investigational drug within 1 month prior to screening or within 5 half-lives of the investigational agent, whichever is longer;
c) Positive stool culture for enteric pathogens (salmonella, shigella, and campylobacter), positive C. difficile toxin, or positive stool ova and parasite exam;
d) All active infections requiring treatment;
e) Patients who had tuberculosis or an opportunistic infection (e.g., herpes zoster [shingles], cytomegalovirus, Pneumocystis carinii, aspergillosis, histoplasmosis) within 6 months prior to screening;
f) 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);
g) Any dysplasia in the colon in the past 5 years, except for a successfully removed sporadic adenoma;
h) Very severe proctitis; expected to result in hospitalization/ surgery within 3 months;

i) Previous treatment with allogeneic MSCs;
j) Any other condition which in the opinion of the investigator would make the patient unsuitable for enrollment, or could interfere with the patient participating in and completing the study;
k) Patient is unwilling or unable to comply with the study procedures.

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	09-08-2018
Enrollment:	14
Type:	Actual

Medical products/devices used

Product type:	Medicine
Generic name:	Somatic cels allogenic

Ethics review

Approved WMO

Date:	12-12-2017
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)

Approved WMO

Date:	27-03-2018
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	12-04-2019
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	14-05-2019
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	24-06-2019
Application type:	Amendment
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

ID: 21802
Source: NTR
Title:

In other registers

Register	ID
EudraCT	EUCTR2017-003524-75-NL
CCMO	NL63157.000.17
OMON	NL-OMON21802