Studie naar ontstekingsmechanismen in patiënten met fistels bij de ziekte van Crohn

No registrations found.

Ethical review	Not applicable
Status	Recruiting
Health condition type	-
Study type	Observational non invasive

Summary

ID

NL-OMON20469

Source
Nationaal Trial Register

Brief title
-

Health condition

Perianal fistula, Crohn's disease, lymphocyte trafficking, vedolizumab, perianale fistels, ziekte van Crohn.

Sponsors and support

Primary sponsor: Academic Medical Center (AMC), Amsterdam
Source(s) of monetary or material Support: Takeda

Intervention

Outcome measures

Primary outcome

To demonstrate key-players of lymphocyte trafficking in infiltrates and neoangiogenesis of fistula tracts in patients with Crohn’s disease and compare this with cryptoglandular fistula.

Secondary outcome

-

Study description

Background summary

Crohn’s disease is an inflammatory bowel disease in which focal or in some cases transmural inflammation is seen, which can involve any segment from the gastro-intestinal tract. This transmural inflammation disrupts intestinal mucosal integrity, favoring the development of abscesses and fistulas. The prevalence of CD is approximately 200-300 per 100.000 persons in both Europe and North America (1, 2).

Perianal fistulas are a common and difficult problem in CD patients, and affect approximately 20-25% of patients. Patients experience symptoms of anal pain, purulent discharge and incontinence, which result in high morbidity and impaired quality of life. Therapeutic options for fistulae are limited: medical options include antibiotics, immunosupressives (such as azathioprine and cyclosporine) and anti-TNF antibodies. Their clinical effect is often limited and despite medical treatment more than one third of patients suffers from recurring fistulae. The recent global consensus guidelines on fistulizing CD contain algorithms proposing a combined medical and surgical approach.

The pathogenesis of perianal fistula in CD is not well understood. The hypothesis of the ‘gut homing lymphocyte paradigm’ states that, in IBD, after pathogen invasion of the intestinal mucosa and initiation of an immunogenic response, priming of T-cells occur in the Peyer’s patches or mesenteric lymph nodes. The primed T-cells are released into the circulation, were specific adhesion molecules like mucosal addressin cell adhesion molecule-1 (MAdCAM-1) are required for the cells to home to the site of inflammation. Memory T-cells with gut-homing properties express the integrin α4β7 and the CC chemokine receptor CCR9. The binding between α4β7 and MAdCAM-1 is activated by CCL25, through ligation of CCR9 on the T-cell.

Vedolizumab (also called MLN0002, ENTYVIO; KYNTELES; Vedolizumab for Injection; or MLN0002 IV) is a humanized monoclonal antibody (mAb) that specifically binds to the human lymphocyte integrin α4β7. By binding to the α4β7 integrin, vedolizumab antagonizes its adherence to MAdCAM-1, impairing the migration of gut homing lymphocytes into the gastrointestinal mucosa. This way, vedolizumab acts as a gut-selective immunomodulator.

In the CD maintenance trial of Sandborn et al, closure of fistula in patients with draining fistulae at baseline was seen in significantly more patients treated with Vedolizumab 300mg iv Q8 at week 52 as compared to placebo treated patients (41,2% versus 11,1%, P=0.03). It is not known whether this was due to endoscopic remission of inflammation in the proctum. If MAdCAM-1 would be inappropriately expressed in the neoangiogenesis of the inflammatory

tissue of the fistula neoepithelium, a direct effect of vedolizumab on reducing inflammatory influx could explain the observed effect. Thus far, the expression of MAdCAM-1 as well as the presence α4β7-positive lymphocytes has not been studied in fistula tracts.

Our aim is to demonstrate key-players of lymphocyte trafficking in infiltrates and neoangiogenesis of fistula tracts in patients with Crohn’s disease. In addition, we also want to see if there is a difference seen in comparison with the infiltrate present in cryptoglandulair fistula tracts.

Study objective

Gut-homing lymphocytes play a role in the development and maintainence of perianal fistula in Crohn's disease patients.

Study design

1 single collection, no follow-up.

Intervention

- Flushing of sodium chloride 0,9% through the fistula tract, collection for flow cytometric analysis.

Contacts

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Eligibility criteria

Inclusion criteria

- Group 1: CD patients with perianal fistula, referred for surgical treatment including seton placement and/or advancement flap plasty.

* Diagnosis of CD, established by clinical and endoscopic evidence and corroborated by a histopathology report

* Age ≥ 18 years, either male or female

* Ability to give informed consent

- Group 2: Patients with cryptoglanudular perianal fistula, without CD, referred for surgical treatment

* Age ≥ 18 years, either male or female

* Ability to give informed consent

Exclusion criteria

- Inability to give informed consent

Study design

Design

Study type:	Observational non invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	N/A , unknown

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	06-07-2016

Enrollment:	30
Type:	Anticipated

Ethics review

Not applicable

Application type:	Not applicable

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	NL6799
NTR-old	NTR6985
Other	AMC : W16_136

Study results