

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

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

Ethische beoordeling	Niet van toepassing
Status	Werving gestart
Type aandoening	-
Onderzoekstype	Observationeel onderzoek, zonder invasieve metingen

Samenvatting

ID

NL-OMON20469

Bron

NTR

Verkorte titel

-

Aandoening

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

Ondersteuning

Primaire sponsor: Academic Medical Center (AMC), Amsterdam

Overige ondersteuning: Takeda

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

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.

Toelichting onderzoek

Achtergrond van het onderzoek

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, immunosuppressives (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, where 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 $\alpha 4\beta 7$ and the CC chemokine receptor CCR9. The binding between $\alpha 4\beta 7$ 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 $\alpha 4\beta 7$. By binding to the $\alpha 4\beta 7$ 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 neoeepithelium, 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 $\alpha 4\beta 7$ -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 cryptoglandular fistula tracts.

Doel van het onderzoek

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

Onderzoeksopzet

1 single collection, no follow-up.

Onderzoeksproduct en/of interventie

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

Contactpersonen

Publiek

Department of Gastroenterology & Hepatology
Academic Medical Center
P.O. Box 22700
Cyriel Y. Ponsioen
Amsterdam 1100 DD
The Netherlands

Wetenschappelijk

Department of Gastroenterology & Hepatology
Academic Medical Center
P.O. Box 22700
Cyriel Y. Ponsioen
Amsterdam 1100 DD
The Netherlands

Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

- 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 $\geq$ 18 years, either male or female

* Ability to give informed consent

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

* Age $\geq$ 18 years, either male or female

* Ability to give informed consent

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

- Inability to give informed consent

Onderzoeksopzet

Opzet

Type:	Observationeel onderzoek, zonder invasieve metingen
Onderzoeksmodel:	Anders
Toewijzing:	Niet-gerandomiseerd
Blinding:	Open / niet geblindeerd
Controle:	N.v.t. / onbekend

Deelname

Nederland	
Status:	Werving gestart
(Verwachte) startdatum:	06-07-2016
Aantal proefpersonen:	30
Type:	Verwachte startdatum

Ethische beoordeling

Niet van toepassing	
Soort:	Niet van toepassing

Registraties

Opgevolgd door onderstaande (mogelijk meer actuele) registratie

Geen registraties gevonden.

Andere (mogelijk minder actuele) registraties in dit register

Geen registraties gevonden.

In overige registers

Register	ID
NTR-new	NL6799
NTR-old	NTR6985
Ander register	AMC : W16_136

Resultaten