Immunological characteristics in UC patients that predict response on Vedolizumab

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Determine if there are immunological or patient characteristics in UC patients that predict the endoscopic response on Vedolizumab treatment.

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

Summary

ID

NL-OMON44411

Source
ToetsingOnline

Brief title
Characteristics in UC patients that predict the respons on Vedolizumab

Condition

- Gastrointestinal inflammatory conditions
- Autoimmune disorders

Synonym
inflammatory bowel disease, Ulcerative colitis

Research involving
Human

Sponsors and support

Primary sponsor: Rijnstate Ziekenhuis
Source(s) of monetary or material Support: Rijnstate ziekenhuis

Intervention

Keyword: Immunology, Ulcerative colitis, Vedolizumab

Outcome measures

Primary outcome

The description of the different mucosal T-cells, serological markers and

histological features at first presentation and at week 16 in UC patients.

Secondary outcome

Investigate if there are clinical and immunological differences between

patients with a better endoscopic response on Vedolizumab at week 16.

Study description

Background summary

Inflammatory Bowel Diseases (IBD) is a heterogeneous group of diseases regarding clinical presentation and treatment response. Incidence is increasing and disease burden is high due to the young age at onset and the chronic nature of the disease. Pathogenesis is complex and multifactorial based on interactions between genetic and environmental factors, gut microbiota and the immune system, leading to intestinal inflammation.

Alterations in T-cell subsets and homing of lymphocytes to gut mucosa were shown to play an important role in the pathogenesis of IBD1, causing inflammation primarily in the intestine but also in extra-intestinal tissues. The therapeutic arsenal is directed to suppress this immune mediated inflammatory reaction.
We previously reported different T-cell maturation profiles in the ileum/colon mucosa of newly diagnosed IBD patients which consist of mainly naïve T cells (Tn cells) and central memory T cells (Tcm cells) versus mainly effector memory T cells (Tem cells). Higher frequencies of Tn cells in patients with Crohn*s Disease (CD) were associated with a more extended and penetrating disease, reflecting a more aggressive initial presentation.2 Furthermore we recently identified several serum markers associated with disease activity and disease course (s-TNF R1, s-TNFR2, sIL2R, MMP1) in newly diagnosed Crohn*s disease patients.3

Migration of Tn * and Tcm cells to the gut is thought to be facilitated by tertiary lymphoid organs (TLOs) containing high endothelial venules (HEVs). The migration of T cells through HEVs is guided by different vascular addressins, such as MAdCAM-1 and peripheral lymph node addressin (PNAd). Differences in HEVs density and TLOs between newly diagnosed IBD patient with active disease has been recently described.4 Increased density of colonic extrafollicular HEVs in the early phase of disease was associated with more Tn- and Tcm cells in the inflamed gut mucosa, which could be responsible for maintaining a continuous inflammatory process. In patients with a lower density of HEVs (HEVlow) there is increased infiltration of effector memory T cells in the gut mucosa. Tem cells are known to express adhesion markers such as gut-homing markers *4*7 and CCR9. Targeting T-cell migration to the inflamed gut in IBD patients is gaining more and more interest.

Vedolizumab is a humanised IgG1 monoclonal antibody to *4*7 integrin approved for the treatment of Ulcerative colitis (UC) and CD5. Our aim is to investigate if there are immunological characteristics in UC patients that predict the response on Vedolizumab treatment. Our hypothesis is that HEVlow patients with more influx of *4*7+ Tem lymphocytes benefit more from Vedolizumab (anti- *4*7) treatment compared to HEVhigh patients. We will evaluate clinical en endoscopic activity in both UC groups on Vedolizumab.

Study objective

Determine if there are immunological or patient characteristics in UC patients that predict the endoscopic response on Vedolizumab treatment.

Study design

The study will be a prospectively observational pilot study that will be performed at the Departments of Gastro-enterology and Hepatology, Microbiology and Immunology and Pathology of the Rijnstate Hospital in Arnhem.

Study burden and risks

Sigmoidscopy with biopsies is a standard examination in patients with suspicion of exacerbation. Collection of biopsies during the endoscopy, ie without interventions like polypectomy, is a safe procedure (bleeding, perforation <0,001). In the regular clinical practice, different endoscopists take a variable number of biopsies (4-10) from sites of interest. The intervention in this study comprises taking 4 additional biopsies on top of the regular histological biopsies for immunological examination.
We take a venous bloodsample during a regular labcontrol.
At the week 16 during sigmoidscopy and blood checks the same additional samples will be taken as at baseline.
The burden and risks for patients are minimalized and comparable to the risk

related to the regular care procedures

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

- UC patients with an exacerbation under 5-ASA and/or thiopurines. An exacerbation is defined as clinical symptoms of diarrhoea, rectal blood loss, abdominal pain or weight loss who need sigmoidscopy to confirm endoscopic exacerbation.
- UC patients with moderate to severe disease activity (<= mayo 2 or mayo 3).
- Patients must be able and willing to provide written informed consent.
- Patients above the age of 18, both men and women.

Exclusion criteria

- UC patients under IFX treatment or after colectomy.
- UC patients under treatment with steroids.
- If the gastro-enterologist prefers to start Infliximab instead of Vedolizumab.
- Patients diagnosed with another immune suppressive disease (e.g. HIV).
- Patients who underwent splenectomy in the past.
- Patients diagnosed with any other autoimmune diseases (e.g. Diabetes Mellitus type I, rheumatoid arthritis, celiac disease, psoriasis, systemic lupus erythematosus).
- Patients diagnosed with cancer including hematologic malignancies (e.g. (non-)Hodgkin lymphoma , leukemia), solid tumors and carcinoma in situ, within 5 years before screening with the following caveats:
o Local basal or squamous cell carcinoma of the skin that has been excised and is considered cured is not exclusionary.
o Chronic myelogenous leukemia, hairy cell leukemia, melanoma, renal cell carcinoma, or Kaposi sarcoma are exclusionary irrespective of the duration of time before screening.
o Cervical smear indicating the presence of adenocarcinoma I situ (AIS), high-grade squamous intraepithelial lesions (HSIL), or cervical intraepithelial neoplasia (CIN) of grade>1, is exclusionary, irrespective of the duration of time before screening.

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	25-01-2018
Enrollment:	20
Type:	Actual

Ethics review

Approved WMO Date:	27-12-2017
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

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	NL63633.091.17