Distribution of Endoscopic and Histologic Healing in Ulcerative Colitis

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To determine the anatomic distribution of endoscopic and histologic improvement in patients with pancolonic ulcerative colitis (UC) after 16 to 24 weeks of treatment with a biologic or tofacitinib therapy.

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

Summary

ID

NL-OMON55788

Source
ToetsingOnline

Brief title
RP1804

Condition

- Gastrointestinal inflammatory conditions

Synonym
inflammatory bowel disease, Ulcerative colitis

Research involving
Human

Sponsors and support

Primary sponsor: Alimentiv Inc.
Source(s) of monetary or material Support: Alimentiv Inc.

Intervention

Keyword: endoscopy, histology, pancolitis, Ulcerative colitis

Outcome measures

Primary outcome

• To determine the anatomic distribution of endoscopic improvement in UC patients with pancolitis treated with biologic or tofacitinib therapies.
Improvement will be defined as any decrease of outcome scores form baseline to post-treatment assessment.
o Measured by central reading of the Mayo Clinic Score (MCS) endoscopic subscore, Ulcerative Colitis Endoscopic Index of Severity (UCEIS), and visual analog scale (VAS), before and after biologic or tofacitinib induction therapy in at minimum 4 colonic segments (transverse colon, descending colon, sigmoid colon, rectum)

• To determine the anatomic distribution of histologic improvement in UC patients with pancolitis treated with biologic or tofacitinib therapies.
Improvement will be defined as any decrease of outcome scores from baseline to post-treatment assessment.
o Measured by central reading of the Robarts Histopathology Index (RHI), Nancy Histological Index (NHI), and Geboes Score (GS), before and after biologic or tofacitinib induction therapy in at minimum 4 colonic segments (transverse colon, descending colon, sigmoid colon, rectum)

Secondary outcome

• Proportion of patients achieving endoscopic remission in all colonic segments

except the distal colon, defined as: 1) endoscopic Mayo Clinic Score (MCS) = 0; 2) endoscopic MCS = 0 of 1; or 3) Ulcerative Colitis Endoscopic Index of Severity UCEIS <= 3

• Proportion of patients achieving endoscopic response in all colonic segments except the distal colon, defined as an improvement in endoscopic MCS >= 1-point compared to baseline

• Proportion of patients achieving histologic remission, defined as: 1) Robarts Histopathology Index (RHI) <= 3 with the lamina propria neutrophils and neutrophils in epithelium scores being 0; 2) Geboes Score (GS) = 0; of 3) Nancy Histological Index (NHI) <= 1

• Proportion of patients achieving histologic improvement, defined as: 1) 50% reduction in baseline RHI; or 2) >= 1-point reduction in NHI

• To determine if there is a correlation between the distribution and extent of endoscopic and histologic changes with changes in levels of fecal calprotectin in UC patients with pancolitis.

Study description

Background summary

Ulcerative colitis (UC) is a chronic inflammatory disease affecting the colon, with an annual incidence of 0 to 19.2 cases per 100,000 persons and a

prevalence of 37.5 to 248.6 cases per 100,000 persons in North America.
Over the last decade, the treatment of moderate to severe UC has improved with the introduction systemic Biological agents and oral small molecules (JAK-inhibitors), and treatment targets in UC have shifted. Where the gold standard was to achieve clinical remission currently, achieving endoscopic remission seems to be the most reliable factor associated with improved clinical outcomes. Histologic healing has also been determined as an important endpoint, as even among UC Patients in endoscopic remission approximately 30% will have persistent histologic activity.
Assessment of endoscopic and histologic healing in UC clinical trials is typically performed by flexible sigmoidoscopy, where additional biopsies can be taken. Currently, biopsy assessment parallels endoscopic scoring methods in UC, but does not account for the distribution in which endoscopic and histologic healing occurs in response to treatment. This presents a unique hurdle in drug development: as patients with residual distal inflammation can be categorized as non-responders even if large segments of the colon have demonstrated endoscopic and/or histologic improvement, since the endoscopic score will default to the worst affected part.
In addition to this, it is unclear whether a patchy distribution of healing is observed with systemic biologic agents or oral JAK inhibitor therapies. Understanding the pattern and directionality of histologic and endoscopic healing in UC treated with biologicals is critical for determining where to biopsy in UC clinical trials and for optimizing efficient drug development strategies.

Study objective

To determine the anatomic distribution of endoscopic and histologic improvement in patients with pancolonic ulcerative colitis (UC) after 16 to 24 weeks of treatment with a biologic or tofacitinib therapy.

Study design

A prospective observational cohort study enrolling a convenience sample of 50 patients with UC starting on standard of care (SOC) biologic or oral JAK inhibitor therapies with proven efficacy in UC (infliximab, adalimumab, golimumab, vedolizumab, or tofacitinib). Eligible patients with pancolonic UC extending to at least the ascending colon will undergo video-recorded colonoscopy prior to starting therapy, with biopsies taken from at minimum 4 colonic segments (transverse colon, descending colon, sigmoid colon, rectum). After 16 to 24 weeks of therapy, patients will undergo repeat colonoscopy and biopsies will be taken from the same areas to assess for endoscopic and histologic healing. All endoscopic and histologic outcomes will be evaluated by blinded central reviewers.

Study burden and risks

A colonoscopy with biopsies can cause complications such as bleeding, peritonitis or a perforation in the bowel wall. These complications are rare, however the taking of additional biopsies can slightly increase the risk of these occurring.

Contacts

Public
Alimentiv Inc.

100 Dundas Street Suite 200
London N6A 5B6
CA
Scientific
Alimentiv Inc.

100 Dundas Street Suite 200
London N6A 5B6
CA

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

1. Male or nonpregnant, nonlactating females (18 to 75 years old)
2. Confirmed diagnosis of UC (established by conventional clinical, endoscopic, and histologic diagnostic criteria)
3. Initiating therapy with infliximab, adalimumab, golimumab, vedolizumab, or tofacitinib
4. Clinically active disease (defined as a MCS >= 6 with rectal bleeding subscore (RBS) >= 1)

5. Endoscopically demonstrated pancolitis involving at minimum 4 colonic segments (transverse colon, descending colon, sigmoid colon and rectum), (defined by an MCS endoscopic subscore >= 1 in each colonic segment)
6. Provide written informed consent

Exclusion criteria

1. Patients who have failed 2 or more biologic therapies OR who have failed tofacitinib and 1 or more biologic therapies
2. Patients treated concurrently with rectal corticosteroids or rectal aminosalicylates (enemas or suppositories)
3. Patients with incomplete colonoscopy not reaching the cecum
4. Patients with inadequate or inappropriately collected biopsy specimens at baseline
5. Pregnant or lactating women

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	30-01-2020
Enrollment:	10
Type:	Actual

Ethics review

Approved WMO

Date:	13-06-2019
Application type:	First submission

Review commission:	METC Amsterdam UMC
Approved WMO Date:	23-06-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC

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	NL68564.018.19