Prospective Observational Study to Validate a Novel PRO Tool and Imaging Index Items in Stricturing Crohn*s Disease

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

Summary

ID

NL-OMON54147

Source
ToetsingOnline

Brief title
STARWP3

Condition

- Gastrointestinal inflammatory conditions

Synonym
Crohn's disease, inflammatory bowel disease

Research involving
Human

Sponsors and support

Primary sponsor: Alimentiv

Source(s) of monetary or material Support: Helmsley Charitable Trust

Intervention

Keyword: MRE, Patient Reported Outcome (PRO), Stricture Radiology Index (SRI), Stricturing Crohn's disease

Outcome measures

Primary outcome

Validation of the PRO

Responsiveness of SRI index

Secondary outcome

N/A

Study description

Background summary

The development of a stricture in patients with Crohn*s disease (CD) marks an important event that portends an increased risk of disease complications and surgery. Up to 11% of patients with CD present with a stricture at diagnosis, and in long-term follow up, up to one-third of patients will progress to a stricturing phenotype. The mechanisms by which fibrotic predominant strictures develop in CD are complex. An excessive repair response to transmural inflammation causes a reduction in luminal diameter that is dependent on both the pleiotropic actions of inflammatory mediators and the interplay of profibrotic genetic, cellular, and microbiota-related factors. A variety of endoscopic scoring indices are sensitive to mucosal changes in CD, but stricture assessment can be potentially challenging for several reasons. Of note, an endoscopy cannot visualize the transmural nature of stricturing disease, the luminal length of many strictures, penetrating complications in the peri-enteric mesentery, upstream bowel dilation and obstruction, or proximally located strictures and inflammation. In the case of multiple strictures, an inability to pass the endoscope through the first stricture will preclude assessment of all bowel segments. Cross-sectional imaging, particularly with computed tomography enterography (CTE) and magnetic resonance enterography (MRE), has therefore emerged as an accurate method for assessing stricturing CD and its obstructing and penetrating complications. Both modalities have demonstrated high sensitivity (> 85%) and specificity (> 90%)

for identifying CD strictures and provide useful adjunctive information that can alter clinical management in a substantial proportion of patients. Recent consensus recommendations from the CONSTRICT study group define criteria for a stricture on CTE or MRE as: luminal narrowing, wall thickening, and prestenotic dilation. However, this definition has not been formally validated. Health status as reported directly from the patient without interpretation of anyone else, commonly referred to as a patient-reported outcome (PRO), are an essential component for patient care. Although several PRO instruments have been developed in the inflammatory bowel disease (IBD) therapeutic area, there is currently no validated PRO measure for stricturing CD. Therefore, it is hypothesized that development of rigorous clinical definitions and outcome tools for stricturing CD will allow testing of antifibrotic therapies in patients with these complications.

Study objective

The objectives of this study are to:
1. Perform quantitative testing of a novel stricture patient-reported outcome (PRO) tool, including validation and assessment of responsiveness.
2. Assess responsiveness of the MRI-based stricture radiology index (SRI) items.

Study design

Approximately 165 patients with stricturing Crohn*s disease (CD) will be enrolled across multiple sites in North America and/or Europe to participate in a 24-week data collection study.

Subjects will undergo 2 imaging assessments during the study, a CTE or MRE scan at baseline and at 24 weeks (end of study [EOS]), performed as part of routine clinical SOC CTE or MRE or performed as a study CTE or MRE in the event that an SOC imaging assessment is not available, followed by best medical therapy. The baseline CTE or MRE must be completed within +/-4 weeks of consent. An SOC contrast-enhanced
abdominopelvic CT performed within ±4 weeks of informed consent may be collected as the baseline imaging assessment if a stricture meeting the eligibility criteria is captured.

Pseudonymized CTE or MRE scans will be assessed by expert central readers using the Mayo Clinic Biomedical Imaging Resource (BIR) workstation central reading platform for eligibility assessment.

Subjects will receive SOC medical therapies with proven efficacy for management of CD at the discretion of their treating physician as part of routine care.
The course of best medical therapy will typically depend on the therapies the subject is taking at the time of obstruction and the degree of inflammation in

the stricture as assessed on baseline CTE or MRE. If the baseline imaging is performed prior to consent, there must be no change to subject treatment for CD between the time of imaging assessment and informed consent.

For analysis, subjects will be classified into 1of 2 groups:
1. Subjects who receive standard medical therapy and endoscopic balloon dilation (EBD)
2. Subjects who receive standard medical therapy.

Subjects will complete electronic patient-reported outcome (ePRO) assessments throughout the study using their own electronic devices.
• From Weeks 1 to 4, subjects will complete the Patient CDAI (Crohn*s Disease Activity Index) Diary and STARPRO daily; the PGI-S (Patient Global Impression -Severity) will be completed at Screening/Baseline (day of informed consent) and on Day7 of every weekly period from Weeks 1 to 4.
• At Weeks 12 and 24 (EOS) only, subjects will complete the Patient CDAI Diary and STARPRO, once daily for 7 days; the PGI-S will be completed on Day 7 at Week 12 and Week 24 (EOS) only.
• The SIQ-CD (Symptoms and Impacts Questionnaire for CD) will be completed once daily for 7 days at Weeks 1, 12, and 24/EOS.
• In addition to the above schedule, from Weeks 12 to 24/EOS, subjects will complete a *Patient Daily Symptom Check-In* (one question, once daily) asking if their symptoms have changed. If symptoms have changed, patients will be required to complete the STARPRO and Patient CDAI Diary daily for 7 days; the PGI-S will also be completed on the 1stday of symptom change and once again on the 7th day following a change in symptoms.

Study burden and risks

The current observational study is considered to be of minimal risk to participating subjects. Subjects will be treated for their stricturing CD as per routine clinical care. Study-specific assessments are noninvasive (e.g., patient-reported data collection via questionnaires or at-home testing) or in line with routine clinical care. Three study blood samples will be collected and stored at baseline, week 12 (if in-person visit) and week 24 .
The direct benefit to subjects includes receiving standard of care (SOC) and medical follow-up for this condition in a tertiary care IBD-specialized center. There is the potential to benefit future patients with stricturing CD with successful validation of outcome measures. Regulatory-accepted outcome measures for assessment of stricturing CD may enable development and approval of effective drugs.

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

1. An established diagnosis of CD.
2. Documented symptomatic stricturing small bowel CD in reach of colonoscopy (i.e., a portion of the stricture is located within 15 cm of the ileocecal valve or ileocecal anastomosis).
3. Anastomotic or naïve small bowel CD stricture(s) at the time of the baseline imaging assessment (CTE, MRE, or CT)
4. Clinical symptoms consistent with obstruction within 1 month of the baseline imaging.

Exclusion criteria

1. Internal penetrating disease as shown by fistula, abscess, or inflammatory mass (phlegmon) at baseline or during follow-up. A blind-ending sinus is not excluded.

2. Gastrointestinal malignancies.
3. More than 2 distal ileal strictures at the time of baseline imaging assessment (where 2 strictures within 3 cm are considered the same stricture; a long segment with multiple areas of narrowing or multiple strictures that have inflammation between them is counted as 1 stricture).
4. A terminal ileal stricture in a subject with end ileostomy, where the stricture is confined within the subcutaneous tissues and does not extend intra-abdominally.
5. A diverting loop ileostomy proximal to the dominant stricture.
6. Total proctocolectomy with an ileoanal or Kock pouch.
7. Stricturoplasty in the distal ileum.
8. Contraindication to CTE or MRE or inability to undergo CTE or MRE (e.g., claustrophobia).
9. Change in treatment for CD between baseline imaging assessment (CTE, MRE or CT) and informed consent, if imaging assessment is performed within 4 weeks prior to consent.

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	11-05-2022
Enrollment:	15
Type:	Actual

Ethics review

Approved WMO

Date:	13-11-2021
Application type:	First submission

Review commission:	METC Amsterdam UMC
Approved WMO Date:	16-06-2022
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	29-11-2023
Application type:	Amendment
Review commission:	MEC Academisch Medisch Centrum (Amsterdam) Kamer G4-214 Postbus 22660 1100 DD Amsterdam 020 566 7389 mecamc@amsterdamumc.nl
Approved WMO Date:	25-11-2024
Application type:	Amendment
Review commission:	MEC Academisch Medisch Centrum (Amsterdam) Kamer G4-214 Postbus 22660 1100 DD Amsterdam 020 566 7389 mecamc@amsterdamumc.nl

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	NL76184.018.21