A prospective multicenter study to characterize magnetic resonance enterography assays for assessment of fibrosis in patients with Crohn's disease

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

Summary

ID

NL-OMON40715

Source
ToetsingOnline

Brief title
GA29423

Condition

- Gastrointestinal inflammatory conditions

Synonym
Crohn's disease, regional enteritis

Research involving
Human

Sponsors and support

Primary sponsor: Roche Nederland B.V.

Source(s) of monetary or material Support: F. Hoffmann La Roche Ltd.

Intervention

Keyword: Crohn's disease, enterography, fibrosis, magnetic resonance

Outcome measures

Primary outcome

The primary outcome measure is *gain of enhancement'' of affected intestinal segment(s) on MRE and histopathology of the corresponding segment(s), surgically resected, as the reference standard.

Secondary outcome

The technical outcome measures for this study are as follows:

* Measuring MRE image quality, as specified in the imaging review charter

* Measuring compliance with the MRE technical protocol for patient preparation and scanning, as specified in the imaging review charter

The secondary outcome measure is the MT ratio of affected intestinal segment(s) on MRE.

Safety Outcome Measures

The safety outcome measures for this study are as follows:

* Incidence, nature, and severity of adverse events (assessed and graded according to the grading criteria in Sections 5.3.3 and 5.3.4)

The exploratory outcome measures for this study are as follows:

* Serum, plasma, PAXgene blood RNA, and tissue biomarkers for inflammation and fibrosis

* MRE evaluation of wall thickness, edema, ulceration, pattern and time of

enhancement of the affected segment(s), and global and per-segment Magnetic

Resonance Index of Activity (MaRIA) scores (Rimola et al. 2009)

* Apparent diffusion coefficient of affected intestinal segment(s) on MRE

(Tielbeek et al. 2013)

Study description

Background summary

For patients who will have surgery for their Crohn's disease, generally scans are performed before the operation in order to assess the disease. This study is intended to find out whether magnetic resonance enterografie (MRE) may be used as an imaging method to assess the status of intestinal wall fibrosis in patients with Crohn's disease. MRE is a special type of magnetic resonance imaging (MRI) with which images of the colon and surrounding tissues are made, using radio waves and a strong magnetic field. This method does not use ionizing radiation.
Detection of fibrosis is necessary for an accurate / comprehensive evaluation of patients with CD, as the presence of fibrosis can affect the determination of whether the patient has to undergo medical or surgical treatment. Up to now only a few studies have been performed on the possible promising role of MRE in detecting fibrosis and detection of narrowing complications of CD. More information about previously conducted clinical studies on the potential of MRE in CD is described on pages 13 and 14 of the Protocol (Protocol GA29423, Version1).

Study objective

The overall aim of this study is to assess the feasibility of implementing MRE for use in evaluating fibrosis in patients with Crohn*s Disease (CD) in a multicenter setting.
The primary objective for this study is to evaluate *gain of enhancement* as an MRE-fibrosis metric using histopathology from surgically resected intestinal segments as the reference standard.
The technical objective for this study is to evaluate the feasibility of utilizing a standardized CD MRE-fibrosis protocol in a multicenter setting to obtain high quality MRE-fibrosis data.
The secondary objective for this study is to evaluate magnetization transfer (MT) contrast as an MRE fibrosis metric.

Exploratory Objectives
The exploratory objectives for this study are as follows:
*To evaluate diffusion-weighted imaging as an MRE-fibrosis metric
*To evaluate candidate serum and tissue biomarkers for bowel wall fibrosis in CD
*To explore new serum, plasma, and tissue biomarkers for bowel wall inflammation and fibrosis in CD

Study design

This is a prospective, multicenter imaging study conducted at six study sites in Europe. Approximately 60 patients (approximately 5 -15 patients per site) with a known diagnosis of CD who will be undergoing elective bowel surgery for management of their CD will be enrolled in the study. Eligible patients will have their CD well characterized clinically with respect to disease duration, disease phenotype (fistulizing, fibrostenosing, luminal, or mixed), disease location, concomitant medications for CD (including current and prior biologics use), past surgical history for CD, and smoking status. At screening, a blood chemistry profile will be completed to estimate glomerular filtration rate (GFR). Enrolled patients will undergo an MRE scan with IV and oral contrast during the study. If the surgical resection involves the colon, the MRE scan will be performed with colonic contrast as well. In addition to being able to define the fibrotic burden, the MRE will help guide the surgical resection.
The MRE scan must be performed no more than 8 weeks (preferably within 4 weeks or less) prior to the patient*s surgery.
Patients will be contacted by telephone within 48 hours after the MRE scan to monitor for any additional adverse events associated with the MRE.
Serum, plasma, and PAXgene blood RNA samples for biomarker assessments will be obtained during the MRE study visit (prior to the MRE scan) and after surgery.
Representative samples and specimen pictures, will be obtained from the surgically resected tissue of the most stenosed region and/or lesions of interest including fistulas, ulcers, and fissures. These samples will be analyzed at the central histopathology center at the University Hospitals Leuven and at Genentech. All MRE scans will be electronically submitted to Genentech, where quality checking will be performed before the scans are forwarded to the central MRE reading center at the Hospital Clinic de Barcelona.There is no therapeutic intervention in this study; the planned elective surgery for CD is being performed as standard of care for the patient. Patients should continue on their prescribed medications at the same doses from the time of the MRE until surgery.
Patients will be considered to have completed the study if they complete all study assessments; study completion will occur 24-72 hours after surgery.
Patients who do not complete the MRE or undergo surgery within 8 weeks after MRE will be discontinued from the study. Patients discontinuing early from the study may be replaced as determined by Genentech to achieve a target of approximately 60 patients.

Study burden and risks

This non-experimental study looks at the results of regular medical care and research, the patient will not be exposed to additional potential risks.
In this study, patients will undergo an MRE scan before the scheduled surgery takes place (no more than 8 weeks before surgery). Since this technique uses strong magnets, people with pacemakers, artificial heart valve, very large tattoos or a metal plate, pin, or other non-compatible medical implants or other metal objects in their bodies (including bullets, shrapnel, or dental implants) are not eligible for this procedure.
Pregnant patients are not eligible to participate in this study, if applicable, a pregnancy test will be done per patient.
There are risks associated with the use of gadolinium-containing contrast medium used for MRE scans. Patients with renal impairment are at higher risk. The most serious side effect of gadolinium is nephrogenic systemic fibrosis / nephrogenic fibrosing dermopathy (NSF / NFD), a scarring condition that can lead to kidney failure. NSF / NFD is very rare and is mainly observed in patients with impaired renal function. Because of this risk, blood of the patients will be tested prior to the MRE scan in order to determine the patients renal function. If the blood tests show that renal function is impaired, the patient cannot participate in this study.
During the MRE scan patients may experience claustrophobia (fear of being stuck in an enclosed space).
During this study, several small amounts of blood will be collected from a vein of the patients for laboratory testing for safety and for research into biomarkers (proteins). Bloodcollection can cause pain at the site where the needle is inserted, and there is a small risk of bruising and / or infection at the puncture site. Some people get dizzy, get an upset stomach or faint when their blood is collected.

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

Patients must meet the following criteria for study entry:
*Signed Informed Consent Form
*Age 18 years of age or above
*Able to comply with the study protocol, in the investigator*s judgment
*Undergoing elective surgery for resection of medically refractory CD and/or presumed fibrostenotic or perforating disease
*Doses of CD medications must be stable from the time after MRE scan until surgery is performed.
*Estimated GFR within local institutional cut-off limits for the safe use of MRE and IV contrast agents

Exclusion criteria

Patients who meet any of the following criteria will be excluded from study entry:
*Pregnant or lactating, or intending to become pregnant during the study
*Women who are not postmenopausal (at least 12 months of non-therapy-induced amenorrhea) or surgically sterile must have a negative urine pregnancy test result before the MRE scan. Pregnancy tests at screening or before surgery should be performed as per institutional standard of care for patients undergoing elective surgery.
*Require emergency surgery for peritonitis or bowel obstruction
*Inability to comply with study protocol
*Poor peripheral venous access
*Contraindications to magnetic resonance imaging (MRI), including non MRI compatible medical or dental implants, other ferromagnetic metal objects in the body, severe claustrophobia, very large tattoos, inability to lie still in a supine position for up to 40 minutes, or inability to meet local imaging site MRI eligibility requirements based on safety screening assessments

*Significant uncontrolled disease, such as cardiac, pulmonary, renal, hepatic, endocrine, neurological, gastrointestinal, or hematologic disorders, that would contraindicate MRE scan or surgery
*History of severe allergic, anaphylactic, or other hypersensitivity reactions to gadolinium-based contrast agents

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):	23-02-2015
Enrollment:	10
Type:	Actual

Ethics review

Approved WMO

Date:	24-12-2014
Application type:	First submission
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	NL49959.018.14