A multicentre prospective longitudinal observational study to evaluate biomarkers and mechanistic principles in moderate to severe ulcerative colitis (UC) patients treated with different targeted therapies.

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The development of targeted drugs has led to an improvement in disease control, but the long-term outcomes of the disease for the individual patient are still not optimal due to the fact that these therapies do not work at all in some patients or...

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

Summary

ID

NL-OMON52173

Source
ToetsingOnline

Brief title
ImmUniverse UC

Condition

- Gastrointestinal inflammatory conditions

Synonym
bowel inflammation, immune disease

Research involving

Human

Sponsors and support

Primary sponsor: Innovative Medecines Initiative (IMI) (EURICE)
Source(s) of monetary or material Support: GlaxoSmithKline,Innovative Medicines Initiative (IMI) EU,Pfizer,Sanofi-aventis

Intervention

Keyword: Biological therapy, Biomarkers, Intestinal inflammatory disease, Ulcerative colitis

Outcome measures

Primary outcome

• Remission defined as a total Mayo score of 2 or less with a Mayo endoscopy

score of 0 or 1 (without friability) and a bleeding score of 0 at week 14.

• Clinical response at week 14 defined as total Mayo score of 2 or less with

Mayo endoscopy score of 0 or 1 (without brittleness) and bleeding score of 0

The clinical response is divided into four subcategories:

• "Superresponder":

Meets clinical response criteria at week 14

• Responder:

Mayo score: 50% reduction / >= 3 improvement from baseline, but does not meet

the criteria for remission;

endoscopic Mayo: Does not meet the criteria for clinical response, but shows a

reduction in Mayo ES

• Partial Responder:

Mayo score: reduction to 30%, endoscopic Mayo: no formal improvement from Mayo ES but slight improvement in general physician assessment.

• Non Responder:

Reduction of less than 30% and no improvement in overall assessment at endoscopy

Secondary outcome

• diepe klinische remissie (Mayo-score 0-1 met SF <=1 en RB = 0)

• mucosale genezing (Mayo ES = 0; Nancy histologie-index: ulceratie: 0, neutrofielen: 0, chronisch infiltraat: 0 of 1).

• symptomatische remissie beoordeeld aan de hand van door de patiënt gerapporteerde uitkomst PRO 2 (SF 0-1 en RB 0)

• ziekteprogressie (flares)

• complicaties tot week 52:

o ziekenhuisopnames vanwege UC

o intensivering van de behandeling inclusief introductie van toxische langdurige therapieën (d.w.z. systemische glucocorticoïden)

o nieuwe stenose

o nieuwe fistel

o nieuwe ontwikkeling van PSC

o infecties

o darmchirurgie

Patiënten worden geclassificeerd in primaire en secundaire goed, laag en niet-reagerend (met meting van antilichaam titers tegen geneesmiddelen en geneesmiddelniveaus, indien beschikbaar); registratie met behulp van deze definities en de duur van de respons volgt (om langdurige - super responser's te identificeren als een relevante subgroep).

Study description

Background summary

There are so-called targeted therapies for the treatment of ulcerative colitis (UC). These are biologicals, or biological medicines with small molecules in their base. Biological medicines are antibodies directed against inflammatory substances or cells. The small molecules work on the inside of the cells in the body and ensure that the signal in the cell is not passed on to the cell nucleus, thus reducing inflammation in the intestine.

The research includes a collection of biomaterials. On the basis of the biomaterial, the course of ulcerative colitis under treatment with a biological medicine is followed for a maximum of 2 years. The study therefore has no

influence on the normal standard disease treatment.

The study collects medical data and periodically biomaterials (tissue, blood and feces) for analysis at the molecular level. These medical data and biomaterials are collected simultaneously from several participating hospitals and subsequently analysed jointly. Subsequently, there is an in-depth study to better understand the disease mechanisms and the changes during therapy at the cellular level, in order to allow more targeted therapy choices and adaptation for the individual patient.

This research is carried out in the Netherlands by the Amsterdam University Medical Center (Amsterdam UMC), location AMC in Amsterdam as a participating center. The study is being conducted in collaboration with the University Hospital in Leuven, Belgium, the Regional University Hospital in Nancy, France and is led by the University Medical Center Schleswig-Holstein (UKSH), on the campus in Kiel, Germany.

Study objective

The development of targeted drugs has led to an improvement in disease control, but the long-term outcomes of the disease for the individual patient are still not optimal due to the fact that these therapies do not work at all in some patients or that the effect over time. time is wasted. At present, the expected response to a particular drug and the further course of the disease are unfortunately hardly predictable for the individual patient. The aim of this research is to better understand disease mechanisms and changes during therapy at the molecular level, in order to allow more targeted therapy choices and adaptation for the individual patient. For this, new so-called biomarkers must be found. In the future, the response to a biological medicine can be better predicted at an early stage. In this way, the most suitable medicine for the individual can be selected before the start of the therapy and we can recognize a serious course and / or complication at an early stage of the disease.

Study design

The therapy with one or more of the biologicals concerns the groups: anti-TNF, anti-IL12 / 23, anti-integrin and JAK inhibitors (e.g. Adalimumab, infliximab, ustekinumab, vedolizumab and tofacitinib). The times at which outcomes are measured and biomaterial is collected are based on the times of routine checks during therapy with the biological drug.

Follow-up starts before the start of the first treatment with the drug (week 0 or screening), and then takes place during planned follow-up checks (at weeks 2, 6, 14, 26, 52, 78 and week 104). The time points may vary slightly depending on your individual treatment plan determined by the treating physician. Should one or more therapy changes be required during your treatment, the observation

plan for this new targeted drug will start over from the beginning (again from weeks 0, 2, 6, etc. until the maximum study duration of 104 weeks is reached). This variable observation plan enables the course of ulcerative colitis to be viewed with different treatment schedules of targeted drugs. The observation period of disease treatment activity is at least 1 to 2 years.

The collection of the biomaterial (tissue, blood and faeces) takes place during the above time points. The biopsies are taken during the endoscopy at week 0 and week 14. During each hospital visit, or (follow-up) check-up, blood is taken for analyzes (including metabolome testing, DNA testing and pharmacokinetics).

While previous studies looked at single molecular data types (-Omics layers) and samples (e.g. biopsies or blood), this project specifically aims to compare local and circulating individual features or signatures of the same individual over time and to obtain the complete range of disease activity. It is hypothesized that this orthogonal approach increases the ability to detect meaningful mechanisms and filter out predictive marker sets. The result of the integrated analysis will be the guiding principle for new molecular tests for patient stratification and treatment monitoring, that is, choosing the right therapeutic escalation at the right time.

Study burden and risks

In this study, targeted therapies are administered to patients with ulcerative colitis as part of standard care.

An important inclusion criterion is the prescription of targeted therapy. The choice of medications (all of which are approved for first-line use) is by the treating physician. All procedures are in accordance with standards of care.

Patients participating in this study can benefit from close clinical follow-up according to clinical guidelines. A direct benefit to the individual patient participating in this study is not expected. Results of this study may lead to a benefit for the group of patients suffering from the same disease.

Baseline and follow-up visits include clinical evaluation, assessment of disease activity and patient reported outcome, as well as biopsy procedures, blood and stool samples. Blood samples will usually be taken at time points when indicated in the clinical routine. The extra amount of blood taken during this trial is a maximum of 45 ml per visit. Therefore, patients with baseline hemoglobin <10 g / dl will not be enrolled.

There is no research-specific endoscopic procedure. All mucosal biopsies are taken at clinically indicated endoscopies. Any biopsy is associated with the risk of bleeding from where the sample was taken or a tear in the colon or rectal wall (perforation). Additional biopsies for research purposes may

therefore theoretically lead to a slightly increased risk and an extension of the endoscopic procedure (approximately 5 minutes).

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

Prescription of a targeted therapy, choice is by treating physician:
- Anti-TNF and, or Anti-IL 12/23 and, or Anti-integrin and, or JAK-inhibitors.

1. Male and female patients >= 18 years of age (at the time of signing the Informed Consent)
2. Signed written Informed Consent
3. Established diagnosis of ulcerative colitis with a minimum disease duration of 3 months

4. Moderate to severe active UC, defined by Mayo Score >= 6 including endoscopy score of >= 2
5. Indication to start any biological or small molecule agent (anti-TNF, anti-IL12/23, anti-integrin and JAK-inhibitors)
6. In case of treatment with corticosteroid: stabile dose for at least 3 weeks prior to baseline, dosage <= 20 mg prednisone
7. Indication for colonoscopy for the assessment of disease activity as for standards of care and current guidelines
8. Able to comply with the study procedures

Exclusion criteria

1. Diagnosis of indeterminate colitis, microscopic colitis, ischaemic colitis, infectious colitis, radiation colitis
2. Absolute contraindications to colonoscopy procedures, complication during previous endoscopy
3. Bleeding disorders
4. Indication for surgery for UC
5. Legal incapacity
6. Rectal topical therapy (enemas or suppositories) <= 2 weeks prior to baseline
7. Treatment with > 20 mg prednisone within 3 weeks prior to baseline
8. anaemia (haemoglobin < 10 g/dl) at baseline
9. Pregnant or breastfeeding women
10. Any circumstances which could contradict a study participation and lead the Investigator to assess the patient as unsuitable for study participation for any other reason

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	04-01-2022

Enrollment:	45
Type:	Actual

Ethics review

Approved WMO Date:	19-05-2021
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	16-05-2022
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
Other	00023031
CCMO	NL76502.018.21