A Phase 2a Open-label Study to Evaluate Prediction of Response to Golimumab Using a Transcriptomic Profile in Subjects with Moderately to Severely Active Ulcerative Colitis

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OBJECTIVES AND HYPOTHESIS Primary ObjectiveThe primary objective is to evaluate the accuracy of the length-109 probe set panel in predicting mucosal healing (ie, improvement in the endoscopic appearance of the mucosa) at Week 6, as measured by the...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Gastrointestinal ulceration and perforation
Study type	Interventional

Summary

ID

NL-OMON40782

Source
ToetsingOnline

Brief title
PROgECT

Condition

- Gastrointestinal ulceration and perforation

Synonym
inflammation of the colon

Research involving

Human

Sponsors and support

Primary sponsor: Janssen-Cilag
Source(s) of monetary or material Support: Industry; Janssen Research & Development

Intervention

Keyword: Golimumab, Prediction, Ulcerative Colitis

Outcome measures

Primary outcome

EFFICACY EVALUATIONS/ENDPOINTS

Efficacy evaluations will include:

* Mayo score and Partial Mayo score

* C-reactive protein (CRP)

* Fecal lactoferrin and fecal calprotectin

* Ulcerative Colitis Endoscopic Index of Severity (UCEIS)

Clinical Endpoints

Clinical endpoints include: mucosal healing, clinical response, and clinical

remission, all at Week 6 and at Week 30; change from baseline in the Mayo score

at Week 6 and at Week 30; change from baseline in the partial Mayo score, CRP concentration, fecal lactoferrin concentration, and fecal calprotectin concentration, all over time through Week 50; the association between the UCEIS score and Mayo endoscopy score at Week 0, Week 6, and at Week 30; the partial Mayo score response through Week 50; and the partial Mayo score remission through Week 50.

PHARMACOKINETIC EVALUATIONS

Venous blood samples for measuring serum golimumab concentrations will be collected from subjects at
Weeks 0, 6, 30, 50, and 58.

IMMUNOGENICITY EVALUATIONS

Venous blood samples for assessment of antibodies to golimumab will be collected from subjects at
Weeks 0, 6, 30, 50, and 58.

BIOMARKER EVALUATIONS

Biomarker evaluations will include:

* Mucosal biopsy RNA and histology samples

* Serum samples for biomarkers

* Whole blood total RNA

Primary Endpoint

The primary endpoint is the AUCROC of the length-109 probe set panel in predicting mucosal healing at Week 6.

Major Secondary Endpoints

The major secondary endpoints are:

* The AUCROC of the length-109 probe set panel in predicting clinical response at Week 6 and at Week 30.

* The AUCROC of the length-109 probe set panel in predicting clinical remission at Week 6 and at Week 30.

* The AUCROC of the length-109 probe set panel in predicting mucosal

healing at Week 30.

Other Endpoints

Other endpoints include: the AUCROC of subsets of the length-109 probe set

panel in predicting mucosal healing, clinical response and/or clinical

remission at Week 6 and/or at Week 30; the AUCROC of the length-109 probe set

panel or subset thereof in predicting partial Mayo response and/or partial Mayo

remission at Week 50; the AUCROC of molecular panel(s) identified from whole

blood gene expression profiles in predicting mucosal healing, clinical response

and/or clinical remission at Week 6 and/or at Week 30.

Secondary outcome

na

Study description

Background summary

SIMPONI® (golimumab) is a fully human monoclonal antibody with an immunoglobulin G
(IgG)1 heavy chain isotype (G1m[z] allotype) and a kappa light chain isotype. The molecular
weight of golimumab ranges from 149,802 to 151,064 daltons. Golimumab binds to human
tumor necrosis factor alpha (TNF*) with high affinity and specificity and neutralizes TNF*
bioactivity.
Since 2009, subcutaneously (SC) administered SIMPONI has received marketing approval in the
United States (US), Canada, the European Union (EU), and other countries

worldwide for the
indications of rheumatoid arthritis (RA), psoriatic arthritis, and ankylosing spondylitis.
SIMPONI has subsequently received marketing approval in the US for the treatment of
ulcerative colitis (UC).

Study objective

OBJECTIVES AND HYPOTHESIS Primary Objective

The primary objective is to evaluate the accuracy of the length-109 probe set panel in predicting mucosal healing (ie, improvement in the endoscopic appearance of the mucosa) at Week 6, as measured by the Area under a Receiver Operating Characteristic (ROC) curve (AUCROC).

Secondary Objectives

The secondary objectives are:

1. To evaluate the accuracy of the length-109 probe set panel in predicting clinical response at Week 6 and at Week 30 as measured by the AUCROC.

2. To evaluate the accuracy of the length-109 probe set panel in predicting clinical remission at Week 6 and at Week 30 as measured by the AUCROC.

3. To evaluate the accuracy of the length-109 probe set panel in predicting mucosal healing at Week 30 as measured by the AUCROC.

Overall safety will be assessed.

Study design

OVERVIEW OF STUDY DESIGN

This is a Phase 2a, open-label, multicenter study to evaluate the accuracy of the length-109 probe set panel in predicting response to golimumab treatment in subjects with moderately to severely active UC.

Intervention

DOSAGE AND ADMINISTRATION

All subjects enrolled in the study will receive the approved induction SC dose regimen of 200 mg at Week 0 followed by 100 mg at Week 2. At Week 6 and thereafter through Week 50, subjects will receive the SC maintenance dosage of

golimumab that has been approved for UC in the country in which the study is being conducted. In countries where there is no local labeling of golimumab in subjects with UC, a maintenance dosage of 100 mg every 4 weeks (q4w) will be used.

At Weeks 0 and 2, golimumab will be administered at the investigative site. Beginning at Week 6, subjects will have the option to self administer golimumab at home after being properly trained; the training must be documented. Training will occur at the investigative site under the supervision of a health care professional. A caregiver may also be trained to administer golimumab. Subjects who are not able or unwilling to self administer golimumab will return to the investigative site for each administration of golimumab.

Study burden and risks

The predictive panel (ie, the length-109 probe set panel or subsets thereof) developed in the
C0524T17 and C0524T18 studies has the potential to identify subjects with UC who may be
more likely to respond to golimumab treatment. Although the predictive panel was discovered in
the ACT1 infliximab study, it is being optimized for prediction of response to golimumab. This
study is being conducted to confirm and extend the prior findings, which will allow verification
of this predictive panel or subsets of this panel in subjects with UC.

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

Each potential subject must satisfy all of the following criteria to be enrolled in the study:
1. Subjects must be a man or woman 18 years or older, inlusive
2. Have a clinical diagnosis of UC at least 3 months prior to screening
3. Have a clinical daignosis of moderately to severely active ulcerative colitis (UC), defined as a baseline (Week 0) Mayo score of 6 to 12 (inclusive),
4. Must have a screening endoscopy with a > <= 2 endoscopy sub score of the Mayo score as
determined by a central reading of the video endoscopy
5. Prior or current medication for UC must be as per protocol (page 25-26)
6. Prior to the screening endoscopy or the earliest entry in the Mayo diary card (whichever of these 2 events comes first) the following conditions must be met:
- per protocol requirements for treatment with 6- mercaptopurine, azathioprine, or methotrexate;
- per protocol requirements for treatment with oral 5-aminosalicylate or oral corticosteroids;
- treatment must have been discontinued for at least 2 weeks for rectal corticosteroids, rectal 5-aminosalicylate compounds, parenteral corticosteroids, total parenteral nutrition, pentoxifylline, thalidomide or related agents, and antibiotics for the treatment of UC;
- treatment with 6-thioguanine, mercaptopurine and azathioprine must have been discontinued for at least 4 weeks
7. Must have had a colonoscopy as per the time frame described in the protocol for the following: extensive colitis for > <= 8 years; disease limited to the left side of the colon for > <= 10 years; participants > <= 45 years of age to assess for the presence of adenomatous polyps
Must meet the tuberculosis and hepatitis B virus screening criteria as defined in the protocol

Exclusion criteria

The presence of any of the following:
1. Have severe extensive colitis;
2. UC limited to the rectum only or to <20 cm of the colon;
3. a stoma;
4. a fistula (or history of a fistula);
5. symptomatic colonic or small bowel obstruction;
6. adenomatous colonic polyps (or history of adenomatous colonic polyps); or indeterminate colitis or clinical findings suggestive of Crohn's disease
7. History of extensive colonic resection (eg, less than 30 cm of colon remaining) or colonic mucosal dysplasia;
8. requires (or has required within the 2 months prior to screening) surgery for active gastrointestinal bleeding, peritonitis, intestinal obstruction, intra abdominal or pancreatic abscess requiring surgical drainage
9. Have received the following concomitant or previous medical therapies: biologic therapy targeted at tumor necrosis factor alpha (eg, infliximab, adalimumab, golimumab, etanercept, certolizumab); natalizumab within 12 months of first golimumab administration; agents that deplete B- or T-cells (eg, rituximab, alemtuzumab, or visilizumab) within 12 months of first golimumab administration, or continue to manifest depletion of Bor T-cells more than 12 months after completion of therapy with lymphocyte depleting agents; cyclosporine, tacrolimus, sirolimus, or mycophenolate mofetil within 8 weeks prior to first administration of golimumab; vedolizumab within 8 weeks prior to first golimumab administration; apheresis (ie, Adacolumn apheresis) within 2 weeks prior to first administration of golimumab; any investigational drug within 4 weeks prior to first administration of golimumab or within 5 half-lives of the investigational agent, whichever is longer; or oral corticosteroids at a dose of greater than 40 mg of prednisone or its equivalent per day
10. Have received, or are expected to receive, any live viral or bacterial vaccination within 8 weeks (or longer as indicated in the package insert of the relevant vaccine) prior to the first administration of golimumab or have had Bacille Calmette-Guerin (BCG) vaccination within 12 months of screening
11. History of, or currently active illness, considered to be clinically significant by the Investigator or any other illness that the Investigator considers should exclude the participant from the study or that could interfere with the interpretation of the study results.

Study design

Design

Study phase:	2
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	21-03-2014
Enrollment:	6
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	golimumab
Generic name:	Simponi
Registration:	Yes - NL intended use

Ethics review

Approved WMO

Date:	13-06-2014
Application type:	First submission
Review commission:	METC Amsterdam UMC

Approved WMO

Date:	24-09-2014
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
EudraCT	EUCTR2013-002042-36-NL
ClinicalTrials.gov	NCT01988961
CCMO	NL48339.029.14