A Phase 3 Randomized, Open-Label Study to Assess the Efficacy, Safety,and Pharmacokinetics of Golimumab Treatment, a Human anti-TNFα Monoclonal Antibody, Administered Subcutaneously in Pediatric Participants with Moderately to Severely Active Ulcerative Colitis

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Primary Objectives* To evaluate the efficacy of golimumab in inducing clinical remission as assessed by the Mayo score,in pediatric participants with moderately to severely active ulcerative colitis (UC).* To evaluate the safety profile of golimumab...

Ethical review	Approved WMO
Status	Pending
Health condition type	Gastrointestinal inflammatory conditions
Study type	Interventional

Summary

ID

NL-OMON52852

Source
ToetsingOnline

Brief title
PURSUIT 2

Condition

- Gastrointestinal inflammatory conditions

Synonym
Chronic inflammation of the colon, UC

Research involving
Human

Sponsors and support

Primary sponsor: Janssen-Cilag
Source(s) of monetary or material Support: Janssen-Cilag

Intervention

Keyword: children, colitis ulcerosa, golimumab, humane monoclonal antibody

Outcome measures

Primary outcome

Primary Objectives

* To evaluate the efficacy of golimumab in inducing clinical remission as

assessed by the Mayo score,

in pediatric participants with moderately to severely active ulcerative colitis

(UC).

* To evaluate the safety profile of golimumab, in pediatric participants with

moderately to severely

active UC.

Secondary outcome

Secondary Objectives

* To evaluate the efficacy of golimumab in inducing clinical response as

assessed by the Mayo Score

and clinical remission as measured by the Pediatric Ulcerative Colitis Activity

Index Score (PUCAI)

Score.

* To evaluate the efficacy of golimumab on endoscopic healing.

* To evaluate the efficacy of golimumab during the long-term phase.

* To evaluate the effect of golimumab on additional efficacy and quality of

life measures

* To evaluate the PK and exposure response of golimumab during short- and

long-term phases.

Additional Objective (Usability Assessment Substudy)

* To evaluate the potential for at home use of golimumab in the participant

population >=45kg during

the Usability Assessment Substudy.

Study description

Background summary

Golimumab was studied in a Phase 3 program of adults with moderately to severely active UC.
This program demonstrated that golimumab is an effective anti-TNFα therapy in adults and was
generally well-tolerated, with a safety profile consistent with that observed for golimumab in
other indications. Studies C0524T17 and C0524T18 were the basis for the approval of
golimumab in adults with moderately to severely active UC in both the US (15 May 2013) and
the EU (19 September 2013).
Golimumab has the potential to offer pediatric participants with moderately to severely active
UC a safe and effective therapy with a convenient SC injection option given every 4 weeks
(q4w).

Study objective

Primary Objectives
* To evaluate the efficacy of golimumab in inducing clinical remission as assessed by the Mayo score,
in pediatric participants with moderately to severely active ulcerative colitis (UC).
* To evaluate the safety profile of golimumab, in pediatric participants with moderately to severely
active UC.
Secondary Objectives
* To evaluate the efficacy of golimumab in inducing clinical response as assessed by the Mayo Score
and clinical remission as measured by the Pediatric Ulcerative Colitis Activity Index Score (PUCAI)
Score.
* To evaluate the efficacy of golimumab on endoscopic healing.
* To evaluate the efficacy of golimumab during the long-term phase.
* To evaluate the effect of golimumab on additional efficacy and quality of life measures
* To evaluate the PK and exposure response of golimumab during short- and long-term phases.
Additional Objective (Usability Assessment Substudy)
* To evaluate the potential for at home use of golimumab in the participant population >=45kg during
the Usability Assessment Substudy.

Study design

This is a multicenter, randomized, open-label golimumab study in pediatric participants aged 2 to 17
years with moderately to severely active UC, defined as a baseline Mayo score of 6 through 12, inclusive,
with an endoscopy subscore of >=2.
In this study, the remission rate of golimumab in pediatric participants will be formally compared with a
historical placebo remission rate derived from a meta-analysis of adult Phase 3 UC studies of golimumab
and other products approved in this indication utilizing similar populations and endpoints.
This study will also include a reference infliximab arm for the purpose of determining assay sensitivity
only if the success criteria are not met (versus historical placebo). No formal comparisons between
golimumab and infliximab will be performed.
Endoscopies performed for this study are to be performed using study software and submitted for central
review. Scoring for disease activity based on endoscopic appearance is to be performed both by the local

endoscopist and the central reviewer. All decisions to initiate (Week 0) or continue therapy (Week 6) will
be based on local reads. Analyses of the primary and major secondary endpoints will be based on locally
read endoscopy measures. Analyses of these endpoints will also be performed using the centrally read
endoscopy measures.
This 54-week study will consist of a 6-week short-term phase and a 48-week long-term phase followed by
a study extension (for eligible golimumab-treated participants).
Beginning at Week 58, participants who are eligible to continue receiving golimumab in the study
extension will be offered the option for self-administration (at least 12 years old and body weight >=45 kg)
or caregiver-administration (any age but body weight >=45 kg). This is optional; if a pediatric participant
or caregiver elects against self- or caregiver-administration, the health care professional will continue to
administer injections in this study.
An internal Data Monitoring Committee (consisting of Sponsor members [a gastroenterologist, a clinician
and a statistician at a minimum] outside of the study team), will be established to monitor safety data (for
both golimumab and infliximab treatments arms) on an ongoing basis until all participants reach the
Week 54 visit or terminate the study prior to the Week 54 visit.

Intervention

Golimumab
During the short-term phase, pediatric participants will receive dose regimens of subcutaneous (SC)
golimumab at Week 0 and Week 2 based on body weight as shown in Table I below. Participants must
weigh >=10 kg and be >70 cm tall. This is the lower range of weight and height that the pre-filled pen
(PFP-V) has been validated for to deliver SC golimumab. This limit accommodates >97% of all 2-year
old girls based on published growth charts (www.cdc.gov/growthcharts). Participants' golimumab doses
for all administrations through Week 10 (inclusive) will be based on the participants' weight and height at
Week 0 or, if not available, the most recent height and weight from screening. The same weight and
height should be used through Week 10. Golimumab doses from Week 14 through Week 54 will be based
on the participants' weight and height obtained with that week*s visit or the

height and weight measured at
the previous site visit. In the study extension, golimumab doses will be based on the participants' most
current weight and height or the last recorded height and weight.
At Week 6, all participants will be evaluated for clinical response;
participants in clinical response will
continue receiving open-label golimumab during the long-term phase.
Participants not in clinical response (as evaluated by the Mayo score) at Week 6 may have study agent
discontinued (and complete a safety follow-up at least 16 weeks after the last administration of
golimumab) OR may continue receiving golimumab for up to 2 additional doses at Weeks 6 and 10 as
specified in Table I at the discretion of the Investigator. At Week 14, these participants who received the
2 additional doses will need to demonstrate a partial Mayo response to continue on in the study;
participants in partial Mayo response will continue receiving open-label golimumab (q4w) during the
long-term phase (Table I). Participants who received the 2 additional doses and are not partial Mayo
responders at Week 14 will have study intervention discontinued and should complete a final safety
follow-up at least 16 weeks following the last administration of study intervention.

Infliximab
All participants in the infliximab treatment arm will be administered
infliximab 5 mg/kg at Weeks 0 and
2. Starting at Week 6, infliximab administrations of 5 mg/kg will continue q8w through Week 46 for
those participants in clinical response at Week 6. Infliximab doses for all administrations through Week 8
(inclusive) will be based on the participants' weight at Week 0 or, if not available, the most recent weight
from screening. The same weight should be used through Week 8. Infliximab doses from Week 14
through Week 46 will be based on the participants' weight obtained with that week*s visit or the weight
measured at the previous site visit.
For those participants not in clinical response at Week 6 (as defined by the Mayo score), or participants
who were in response at Week 6 but have a clinical flare in their UC (defined in Section 6.5.3) an
additional step-wise dose escalation approach may be taken at the investigators discretion. The first step is
a dose increase at Week 6 to 10 mg/kg [capped at 1 gm] q8w or 5 mg/kg at Weeks

6 and 8, and 10 mg/kg
(capped at 1 gm) at Week 14 and q8w thereafter, respectively). At Week 14, if the participant has
demonstrated a partial Mayo response, they will continue to receive infliximab 10mg/kg q8w.
Additionally, if the participant has not achieved a partial Mayo response by Week 14, starting at the
Week 14 visit, the investigators can also shorten the interval between doses to q4w.
At Week 22, those participants who had received an escalation in their infliximab dosing to 10 mg/kg
q4w will need to demonstrate a partial Mayo response to continue in the study. Participants in partial
Mayo response will continue receiving open-label infliximab 10 mg/kg q4w through Week 46.
Participants who have not achieved a partial Mayo response at Week 22 will have study intervention
discontinued and should complete a final safety follow-up at least 8 weeks following the last
administration of infliximab.
Participants who dose-escalate in response to a UC flare after Week 6 will be reassessed after two
administrations at the new higher dose. Participants in partial Mayo response will continue receiving
open-label infliximab through Week 46 at the new higher dose. Participants who have not achieved a
partial Mayo response will have study intervention discontinued and should complete a final safety visit
at least 8 weeks following the last administration of infliximab.
Finally, while dose escalation should be based on clinical criteria as described above, investigators at their
discretion may utilize infliximab serum levels to assist their decision making. This approach was chosen
as it most closely mimics clinical practice in treatment of pediatric UC, allowing investigators some
flexibility in dosing to treat their patients. After the Week 54 evaluations, participants receiving
infliximab will be transitioned off the study to standard medical care.

Study burden and risks

The expected therapeutic effect justifies the burden and risks for the participants.

Contacts

Public
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Scientific
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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (12-15 years)
Adolescents (16-17 years)
Children (2-11 years)

Inclusion criteria

-Must either be currently receiving treatment with, or have a history of having failed to respond to, or have a medical contraindication to at least 1 of the following therapies: oral or intravenous corticosteroids, 6- mercaptopurine, methotrexate or azathioprine OR must either have or have had a history of corticosteroid dependency (that is an inability to successfully taper corticosteroids without a return of the symptoms of ulcerative colitis [UC]) OR required more than 3 courses of corticosteroids in the past year
- Moderately to severely active UC (as defined by baseline Mayo score of 6 through 12 [endoscopy {sigmoidoscopy or colonoscopy} sub score assigned by local endoscopist], inclusive), including a (sigmoidoscopy or colonoscopy) sub score greater than or equal to (>=2)

- If receiving parenteral or enteral nutrition, must have been on a stable regimen for at least 2 weeks prior to the first administration of study intervention at Week 0
- No history of latent or active tuberculosis prior to screening
- Acceptable evidence of immunity to measles, mumps, rubella, and varicella

Exclusion criteria

- History of liver or renal insufficiency; significant cardiac, vascular, pulmonary, gastrointestinal, endocrine, neurologic, hematologic, rheumatologic, psychiatric (including suicidality), or metabolic disturbances
- History of malignancy or macrophage activation syndrome (MAS) or hemophagocytic lymphohistiocytosis (HLH)
- Have UC limited to the rectum only or to <20 percent (%) of the colon
- Presence of a stoma
- Presence or history of a fistula
- Contraindications to the use of golimumab or infliximab or anti-tumor necrosis factor (TNF-alpha) therapy per local prescribing information

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	02-01-2019
Enrollment:	4
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	Golimumab
Generic name:	Simponi
Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	infliximab
Generic name:	Remicade
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	27-09-2018
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	20-09-2019
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	08-01-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	24-02-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	07-04-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	06-05-2020
Application type:	Amendment

Review commission:	METC Amsterdam UMC
Approved WMO Date:	01-07-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	02-07-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	26-06-2021
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	26-08-2021
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	13-09-2021
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	23-09-2021
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	04-12-2021
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	01-02-2022
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	30-06-2022
Application type:	Amendment

Review commission:	METC Amsterdam UMC
Approved WMO Date:	08-08-2022
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	25-11-2022
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	19-12-2022
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
EudraCT	EUCTR2017-004496-31-NL
ClinicalTrials.gov	NCT03596645
CCMO	NL67053.018.18