A Phase 2/3, Randomized, Double-blind, Placebo- and Active-controlled, Parallel-group, Multicenter Protocol to Evaluate the Efficacy and Safety of Guselkumab in Participants with Moderately to Severely Active Crohn's Disease

Published: 30-04-2018
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This study has been transitioned to CTIS with ID 2023-504736-18-00 check the CTIS register for the current data. Primary Objectives (Phase 2 and Phase 3):- To evaluate the clinical efficacy of guselkumab in participants with Crohn*s disease- To...

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

Summary

ID

NL-OMON52566

Source
ToetsingOnline

Brief title
GALAXI

Condition

- Gastrointestinal inflammatory conditions

Synonym
Crohn's disease, Inflammatory bowel disease (IBD)

Research involving

Human

Sponsors and support

Primary sponsor: Janssen-Cilag
Source(s) of monetary or material Support: de sponsor van het onderzoek.

Intervention

Keyword: crohn's disease, guselkumab, phase 2/3 study, placebo controlled study

Outcome measures

Primary outcome

Primary End Point:

Phase 2: Change from baseline in the Crohn's Disease Activity Index (CDAI)

Score at Week 12.

Phase 3:

- Clinical remission at Week 12 (defined as CDAI score <150)

- Endoscopic response at Week 12

Secondary outcome

Secondary End Point:

Phase 2:

- Clinical remission at Week 12 (defined as CDAI score <150)

- Clinical response at Week 12 (defined as >=100-point reduction from baseline

in CDAI score or CDAI score <150)

- PRO-2 remission at Week 12 (defined based on average daily stool frequency

(SF) and average daily abdominal pain (AP) score)

- Clinical-biomarker response at Week 12 (clinical response based on CDAI score and reduction from baseline in CRP or fecal calprotectin)

- Endoscopic response at Week 12 (measured by the Simple Endoscopic Score for Crohn's Disease (SES-CD). The SES-CD is based on the evaluation of 4 endoscopic components across 5 ileocolonic segments, with a total score ranging from 0 to 56.)

Phase 3:

- Clinical remission at Week 48 (defined as CDAI < 150)

- Durable clinical remission at Week 48 (defined as CDAI<150 for the majority of visits between Week 12 and Week 48.)

- Corticosteroid-free clinical remission at Week 48 (defined as CDAI score <150 at Week 48 and not receiving corticosteroids at Week 48)

- PRO-2 remission at Week 12 and 48 (based on average daily stool frequency (SF) and average daily abdominal pain (AP) score)

- Endoscopic response at Week 48 (measured by the Simple Endoscopic Score for Crohn's Disease (SES-CD))

· Fatigue response at Week 12 (based on the PROMIS Fatigue Short Form 7a)

- Endoscopic remission at Week 12 and Week 48

Study description

Background summary

Currently, there are 3 classes of biologic agents approved for the treatment of moderately to severely active Crohn*s disease: tumor necrosis factor (TNF)

antagonist therapies (infliximab, adalimumab, certolizumab), integrin inhibitors (natalizumab and vedolizumab), and IL-12/23 inhibitors (ustekinumab). Although the introduction of biologic agents has significantly improved the clinical management of patients with moderately to severely active Crohn*s disease, a sizable proportion of the target patient population is non-responsive or will lose response over time. A review of the available data for approved biologic agents highlighted the unmet need in achieving and maintaining long-term remission, especially among patients who have previously failed biologic treatments. Therefore, there remains a high unmet need for new treatment options in Crohn*s disease that are safe and effective, especially new therapies that can provide improved long-term efficacy (ie, sustained remission) over currently available therapies.

Genetic and animal model studies have explored the contribution of IL-12 and IL-23 in driving the pathophysiology of Crohn*s disease. The results indicate that IL-23 plays a predominant role in inflammatory bowel disease (IBD) and emerging evidence suggests that blocking IL-23 alone may be a more effective strategy than blocking both IL-12 and IL-23. Clinical studies have successfully demonstrated that blockade of both IL-12 and IL-23 is effective in treating Crohn*s disease, leading to the approval of ustekinumab (STELARA) most recently. However, it has yet been determined whether targeting both IL-12/23 compared with specifically targeting of IL-23 alone, is a more effective treatment strategy clinically. Hence, the purpose of this protocol is to evaluate the efficacy and safety of guselkumab, a monoclonal antibody to IL-23, compared with placebo and compared an approved treatment for CD, ustekinumab (a monoclonal antibody to IL-12/23), in participants with Crohn*s disease.

Study objective

This study has been transitioned to CTIS with ID 2023-504736-18-00 check the CTIS register for the current data.

Primary Objectives (Phase 2 and Phase 3):
- To evaluate the clinical efficacy of guselkumab in participants with Crohn*s disease
- To evaluate the safety of guselkumab

Secondary Objectives:

Phase 2:
- To evaluate the dose-response of guselkumab to inform dose selection for the Phase 3 portion of this protocol
- To evaluate the efficacy of guselkumab on endoscopic improvement
- To evaluate the pharmacokinetics (PK), immunogenicity, and pharmacodynamics (PD) of guselkumab therapy

Phase 3:

- To evaluate the efficacy of guselkumab on endoscopic improvement
- To evaluate the impact of guselkumab on HRQOL
- To evaluate the PK, immunogenicity, and PD of guselkumab therapy

Study design

This is a Phase 2/3, Randomized, Double-blind, Placebo- and Active-controlled, Parallel-group, Multicenter Protocol. This protocol consists of 3 separate studies: a 48-week Phase 2 dose-ranging study (GALAXI 1) and two 48-week Phase 3 confirmatory studies (GALAXI 2 and GALAXI 3). In Phase 2, safety and efficacy of guselkumab dose regimens will be evaluated to support the selection of induction and maintenance dose regimens for confirmatory evaluation in Phase 3. Participants who complete the 48-week Phase 2 or Phase 3 studies may be eligible to enter the long-term extension (LTE). Approximately 1340 participants will be enrolled into this protocol globally. Throughout the 3 studies, efficacy, pharmacokinetic, biomarkers, and safety will be assessed. An external Independent Data Monitoring Committee (DMC), with defined roles and responsibilities as governed by a DMC charter, will assess the safety of participants enrolled under this protocol. After each review of safety data, they will make recommendations to the sponsor about the continuation of the protocol.

Intervention

Phase 2 treatment groups:

Phase 2 (GALAXI 1): Group 1 (Guselkumab):
Participants will receive guselkumab (Dose 1) by intravenous infusion, followed by guselkumab (Dose 2) by subcutaneous (SC) injection. Participants who are eligible and willing to continue guselkumab may enter the Long-Term Extension (LTE) phase and continue to receive guselkumab.

Phase 2 (GALAXI 1): Group 2 (Guselkumab):
Participants will receive guselkumab (Dose 3) by intravenous (IV) infusion, followed by guselkumab (Dose 2) by subcutaneous (SC) injection. Participants who are eligible and willing to continue guselkumab may enter the LTE phase and continue to receive guselkumab.

Phase 2 (GALAXI 1): Group 3 (Guselkumab):
Participants will receive guselkumab (Dose 4) by intravenous (IV) infusion, followed by guselkumab (Dose 5) by subcutaneous (SC) injection. Participants who are eligible and willing to continue guselkumab may enter the LTE phase and continue to receive guselkumab.

Phase 2 (GALAXI 1): Group 4 (Ustekinumab):
Participants will receive ustekinumab by intravenous (IV) infusion, followed by

subcutaneous (SC) injection. Participants who are eligible and willing to continue ustekinumab may enter the LTE and continue to receive ustekinumab.

Phase 2 (GALAXI 1): Group 5 (Placebo/Ustekinumab):
Participants will receive placebo administered by intravenous (IV) infusion. At Week 12, non-responders will receive active treatment (Ustekinumab) administered by intravenous (IV) infusion followed by subcutaneous (SC) injection. Participants who are eligible and willing to continue placebo/ustekinumab may enter the LTE and continue to receive placebo/ustekinumab.

Phase 3 treatment groups

Phase 3 (GALAXI 2 and 3): Group 1 and Group 2 (Guselkumab):
Participants will receive guselkumab by intravenous (IV) infusion, followed by guselkumab by subcutaneous (SC) injection. Participants who are eligible and willing to continue guselkumab may enter the LTE phase and continue to receive guselkumab.
Note: Guselkumab dose regimens for Phase 3 evaluation will be determined based on the results of the Phase 2 study.

Phase 3 (GALAXI 2 and 3): Group 3 (Ustekinumab):
Participants will receive ustekinumab by intravenous (IV) infusion, followed by subcutaneous (SC) injection. Participants who are eligible and willing to continue ustekinumab may enter the LTE phase and continue to receive ustekinumab.

Phase 3 (GALAXI 2 and 3): Group 4 (Placebo/Ustekinumab):
Participants will receive placebo administered by intravenous (IV) infusion. At Week 12, non-responders will receive active treatment (ustekinumab) administered by intravenous (IV) infusion followed by subcutaneous (SC) injection. Participants who are eligible and willing to continue placebo/ustekinumab may enter the LTE and continue to receive placebo/ustekinumab.

Study burden and risks

In general, study participants may experience physical or psychological discomfort from the study tests, study procedures, interviews and questionnaires; and each study participant may have a different experience. In addition, study particpants may experience side effects from the study medication. For a discussion of the Sponsor*s benefit-risk assessment please refer to Section 2.3 of the Protocol.

Number of visits:
-Max 39 over the course of study participation

Chest X-ray: 1 time at screening.

ECG: 1 time at screening.

Blood draws for efficacy, safety, biomarkers etc. evaluation: max 41 over course of study participation.

QuantiFERON-TB blood test: 1 time at screening; additional testing may apply if necessary due to initial findings.

Urine test for pregnancy: Urine pregnancy test for females of childbearing potential before each study intervention (max 38 visits).

Video Ileocolonoscopy with Biopsies: max 4 times for all participants over course of study participation. 1 additional optional time point for participants who consent to the sub-study.

Physical examination: max. 39 times over course of study participation.

Interviews and questionnaires: max 39 over course of study participation

Stool samples for screening eligibility and biomarkers: max 14 over course of study participation

Fistula assessment: max 27 times.

Contacts

Public
Janssen-Cilag

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Beerse 2340
BE
Scientific
Janssen-Cilag

Turnhoutseweg 30
Beerse 2340
BE

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

Have screening laboratory test results within the protocol specified parameters; Female participants of childbearing potential must have a negative urine pregnancy test result at screening and baseline; Participants must have demonstrated intolerance or inadequate response to conventional or to biologic therapy for CD.

Exclusion criteria

Current diagnosis of ulcerative colitis or indeterminate colitis; Has complications of Crohn*s disease, such as symptomatic strictures or stenoses, short gut syndrome, or any other manifestation; On unstable doses of concomitant Crohn's disease therapy; Receipt of Crohn*s disease approved biologic agents, investigational agents, or procedures outside of permitted timeframe as specified in the protocol; Prior exposure to p40 inhibitors or p19 inhibitors; Any medical contraindications preventing study participation; During the 6 weeks prior to baseline, have had ANY of (a) confirmed SARS-CoV-2 (COVID-19) infection (test positive), OR (b) suspected SARS-CoV-2 infection (clinical features without documented test results), OR (c) close contact with a person with known or suspected SARS-CoV-2 infection (see Protocol Appendix 27Apr2020 for exceptions and notes).

Study design

Design

Study phase:	2
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	03-10-2019
Enrollment:	19
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	STELARA®
Generic name:	Ustekinumab
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	TREMFYA®
Generic name:	Guselkumab
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	30-04-2018
Application type:	First submission
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	10-09-2018

Application type:	First submission
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	03-10-2018
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	24-10-2018
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	04-02-2019
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	15-02-2019
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	28-02-2019
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	05-03-2019
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	16-05-2019
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	23-05-2019
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	05-06-2019

Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	10-06-2019
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	18-09-2019
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	21-10-2019
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	23-10-2019
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	04-11-2019
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	18-12-2019
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	19-12-2019
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	08-04-2020
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	14-04-2020

Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	19-06-2020
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	26-06-2020
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	25-08-2020
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	20-01-2021
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	27-01-2021
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	06-06-2021
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	14-06-2021
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	09-07-2021
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	26-07-2021

Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	09-09-2021
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	22-09-2021
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	06-10-2021
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	19-10-2021
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	09-11-2021
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	15-11-2021
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	21-02-2022
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	19-03-2022
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	04-04-2022

Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	30-04-2022
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	09-06-2022
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	23-08-2022
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	05-09-2022
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	21-11-2022
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	28-11-2022
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	17-10-2023
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	09-11-2023
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	21-03-2024

Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	18-04-2024
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	03-05-2024
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)

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	clintrials.gov. NCT number is NCT03466411
EU-CTR	CTIS2023-504736-18-00
EudraCT	EUCTR2017-002195-13-NL
CCMO	NL64944.028.18