An Long-Term Extension Study to Evaluate the Safety of Filgotinib in Subjects with Crohn*s Disease

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The primary objective of this study is:- To observe the long-term safety of filgotinib in subjects who have completed or met protocol specified efficacy discontinuation criteria in a prior filgotinib treatment study for CDThe secondary objective of...

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

Summary

ID

NL-OMON54703

Source
ToetsingOnline

Brief title
GS-US-419-3896

Condition

- Gastrointestinal inflammatory conditions

Synonym
Crohn syndrome, regional enteritis

Research involving
Human

Sponsors and support

Primary sponsor: Galapagos NV
Source(s) of monetary or material Support: Galapagos NV

Intervention

Keyword: Crohn's Disease, Filgotinib, Long Term Extension Study

Outcome measures

Primary outcome

The primary endpoint is safety. Safety will be evaluated through AEs, clinical laboratory tests, and vital signs. Safety endpoints will be analyzed by the number and percent of subjects with events or abnormalities for categorical values or standard descriptive statistics (n, mean, standard deviation [SD], median, 1st quartile [Q1], 3rd quartile [Q3], minimum, maximum) for continuous data.

Secondary outcome

The secondary efficacy endpoints of change from baseline in PRO2 and CDAI scores, and exploratory endpoints of change in HRQoL scores will be summarized using standard descriptive statistics (n, mean, SD, median, Q1, Q3, minimum, maximum).

Study description

Background summary

A significant change in CD management and therapeutic strategy has occurred over the last decade. Recent therapeutic goals extend beyond symptomatic control and include long-term mucosal and endoscopic remission. The ultimate aim is to change the natural course of the disease by slowing down or halting its progression, thus avoiding surgery or hospitalization. This is believed to be achieved by utilizing earlier, aggressive, and goal-directed therapy. Risk assessment and prediction by means of complex clinical, biochemical, and endoscopic markers has become the key to patient management, therapy optimization, and prediction of the outcome and side effects of medical therapy. Many new treatments focus

on inhibiting, suppressing, or altering T-cell differentiation and homing.
Three monoclonal antibodies which inhibit tumor
necrosis factor-alpha (TNFα), are currently marketed for the treatment of CD: infliximab (Remicade®), adalimumab (Humira® [approved in US and European Union {EU}]) and certolizumab pegol (Cimzia® [approved in US]). More recently, vedolizumab (Entivyo® [approved in US and EU]), a monoclonal antibody against α4β7 integrin was approved by US Food and Drug Administration (FDA) and European Medicines Agency (EMA). Other approaches include the administration of cytokines to stimulate innate immunity and the use of prebiotics to alter the gut flora. Blocking the interleukin (IL)-6 signaling pathway is also considered a possible therapeutic strategy for CD: tocilizumab (RoActemra®), an anti-IL-6R monoclonal antibody (mAb), showed promising results in an early pilot study {Ito et al 2004} and a Phase 2 study is currently ongoing with the anti-IL-6 mAb PF-04236921. In addition, an oral antisense oligonucleotide (GED-0301) is being evaluated for the treatment of CD showed
encouraging results in a Phase 2 study. Other new treatments being tested in clinical trials includes janus kinase (JAK) inhibitors (eg, upadacitinib, tofacitinib), IL-12/23 antagonist (ustekinumab [Stelara]), and a matrix metallopeptidase-9 (MMP-9) inhibitor (GS-5745).
Leukocytapheresis therapy may be used in Japan {Fukunaga et al 2012}. Despite currently available therapies, long-term or durable remission rates are still low at approximately 20%. Furthermore, the risk of infection, and in rare cases malignancy, limits the long-term use or use in vulnerable populations (eg, children and those with comorbid disorders). Therefore, a need still exists for safer and durable efficacious therapies for moderately to severely active CD.

Study objective

The primary objective of this study is:
- To observe the long-term safety of filgotinib in subjects who have completed or met protocol specified efficacy discontinuation criteria in a prior filgotinib treatment study for CD
The secondary objective of this study is:
- To evaluate the effect of filgotinib on Patient Reported Outcomes (PRO2) and Crohn*s Disease Activity Index (CDAI) scores

Study design

This is a long-term extension study. Some subjects will receive open-label drug and some will receive blinded dosing until subject*s treatment in the corresponding parent study is unblinded. In general, subjects who fully complete a parent study blinded will continue blinded dosing at thsame regimen in the present study on 200 mg filgotinib, 100 mg filgotinib, or placebo. After the corresponding parent study (GS-US-419-4015, GS-US-419-4016, or GS-US-419-3895, or other Gilead/ Galapagos-sponsored filgotinib treatment study) is unblinded, subjects enrolled in the present study may be unblinded.

Subjects who enroll from a parent study and receive blinded treatment in the DIVERSITY LTE study will have their DIVERSITY
LTE treatment assignment unblinded when the parent study is unblinded. Subjects will continue on the same dose of open-label filgotinib as they had been receiving in blinded treatment. Subjects on placebo treatment will discontinue study drug and study participation. Subjects who exit a parent study due to disease worsening or failure to meet response or remission criteria will receive open-label 200 mg filgotinib.

Intervention

NA

Study burden and risks

An overview of risks of study medication and procedures can be found in ICF

Contacts

Public
Galapagos NV

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NA NA
BE
Scientific
Galapagos NV

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NA NA
BE

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

1) Must have the ability to understand and sign a written informed consent form (ICF), which must be obtained prior to initiation of study procedures associated with this trial
2) Criterion modified per amendment 9
2.1) Must have enrolled in a CD parent protocol, GS-US-4194015, GS-US-419-4016 or GS-US-419-3895 or any other Gilead/Galapagos-sponsored filgotinib treatment study for CD
3) Females of childbearing potential must have a negative pregnancy test at Day 1 and must agree to continued monthly pregnancy testing during use of filgotinib treatment
4) Criterion modified per amendment 9
4.1) Female subjects of childbearing potential who engage in heterosexual intercourse must agree to use protocol specified method(s) of contraception for the duration described in the protocol
5) Willingness to refrain from live or attenuated vaccines during the study and for 12 weeks after last dose of study drug
6) Must have completed all required procedures or met protocol specified efficacy discontinuation criteria in a prior filgotinib treatment study for CD

Exclusion criteria

1) Subjects who are discontinued from a parent study for reasons other than disease worsening or lack of response or remission; eg, subjects who discontinue for safety or tolerability issues are
not eligible for this study
2) Known hypersensitivity to the study drug
3) Any chronic medical condition (including, but not limited to, cardiac or pulmonary disease, alcohol or drug abuse) that, in the opinion of the Investigator or Sponsor, would make the subject unsuitable
for the study or would prevent compliance with the study protocol
4) Criterion modified per amendment 9
4.1) Females who may wish to become pregnant and/or plan to undergo egg donation or egg harvesting for the purpose of current or future fertilization during the course of the study and for at least 30 days after the last dose of study drug
5) Criterion deleted per amendment 9
6) Criterion deleted per amendment 9
6.1) Females of reproductive potential who are unwilling to abide by

protocol-specified contraceptive methods as defined in the protocol
7) Use of prohibited concomitant medications as outlined in Section 5.4.2

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	14-08-2018
Enrollment:	15
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Filgotinib
Generic name:	Filgotinib

Ethics review

Approved WMO

Date:	14-08-2017
Application type:	First submission
Review commission:	METC NedMec

Approved WMO

Date:	06-11-2017
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	04-12-2017
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	13-12-2017
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	11-06-2018
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	12-07-2018
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	07-01-2019
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	30-01-2019
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	13-03-2019
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	04-04-2019
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO	

Date:	08-10-2019
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	07-11-2019
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	19-05-2020
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	23-10-2020
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	27-10-2020
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	10-10-2021
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	03-11-2021
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	18-03-2022
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	01-06-2022
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO	

Date:	10-02-2023
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	03-03-2023
Application type:	Amendment
Review commission:	METC NedMec

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	EUCTR2016-002763-34-NL
ClinicalTrials.gov	NCT02914600
CCMO	NL59097.041.17