A Long-Term Extension Study to Evaluate the Safety of Filgotinib in Subjects with Ulcerative Colitis

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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 Gilead-Sponsored filgotinib treatment study in UCThe...

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

Summary

ID

NL-OMON52973

Source
ToetsingOnline

Brief title
GS-US-418-3899

Condition

- Gastrointestinal inflammatory conditions

Synonym
ulceration of the colon, Ulcerative Collitis

Research involving
Human

Sponsors and support

Primary sponsor: Galapagos NV
Source(s) of monetary or material Support: Gilead Sciences Inc.

Intervention

Keyword: Filgotinib, Ulcerative Collitis

Outcome measures

Primary outcome

Efficacy will be evaluated in terms of changes in partial MCS.

Secondary outcome

NVT

Study description

Background summary

Ulcerative colitis (UC) is a chronic, intermittent, relapsing disease characterized by inflammation of the colonic mucosa, which is limited to the colon and rectum. The disease characteristically commences in the rectum and may extend proximally in an uninterrupted pattern into the colon. It can involve the entire colon (pan-colitis), the left colon, or isolated recto-sigmoid disease with patients being equally distributed in those 3 phenotypes. In the United States (US), the prevalence of UC has been estimated to be 238 per 100,000 adults {Kappelman et al 2007}. Europe has the highest reported prevalence values for inflammatory bowel disease (IBD; 505 per 100,000 persons for UC and 322 for Crohn*s Disease [CD]). The incidence and prevalence of inflammatory bowel disease (IBD) appear to be increasing over time globally. The hallmark symptoms of the disease are bloody diarrhea, rectal urgency, and tenesmus. The clinical coursetends to wax and wane with periods of remission interspersed with periods of active disease. Ulcerative colitis may also be associated with extra-intestinal manifestations including ocular lesions, skin lesions, arthritis, and primary sclerosing cholangitis. The exact pathophysiology is not known, but a combination of genetic predisposition and environmental factors appear to contribute to a disordered immune response in these patients {Rutgeerts et al 2005}.

In addition to the abdominal pain and frequent passage of bloody stools that impact activities of daily living and quality of life for patients with UC, the disease also carries with it an increased risk of colorectal cancer due to the chronic inflammation associated with the disease {Velayos et al 2006}. With poorly controlled disease, the rate of developing colorectal cancer increases with time. Ten years after diagnosis, the cumulative probability of developing colorectal cancer is 2% and increases to 18% after 30 years. Overall, the risk of a UC patient developing colorectal cancer may be as high as 23-fold compared to the general population {Triantafillidis et al 2009}. Thus, UC represents a serious, life-threatening disease for which new therapies are needed to interrupt the inflammatory process to prevent disease progression and risk of colorectal cancer.

Treatment of UC is dependent on the severity and the location of disease. Goals of treatment include improved quality of life, reduction in long-term corticosteroid use, and minimization of cancer risk. Mild to moderate distal colitis may be treated with oral aminosalicylates, topical mesalamine, or topical steroids {Kornbluth et al 2010}. For moderate disease, oral corticosteroids, and immunomodulators such as azathioprine and 6-mercaptopurine (6-MP) may be utilized {Danese et al 2011}. For more moderate to severe disease, patients are commonly treated with a tumor necrosis factor-alpha (TNFα) antagonist infusion or injection such as infliximab (Remicade®), adalimumab (Humira®), and golimumab (Simponi®). Vedolizumab (Entyvio®), an injectable integrin α4β7 monoclonal antibody, is also approved for moderately to severely active disease. Ustekinumab (Stelara®, CNTO 1275; an IL-12 and IL-23 monoclonal. antibody), tofacitinb (CP-690,550; JAK1 and JAK3 inhibitor), etrolizumab (PRO145223; monoclonal antibody targeting the β7 subunit of the heterodimeric integrins α4β7 and αEβ7), and ozanimod (RPC1063; selective S1P1 and S1P5 receptor agonist) are currently being tested in Phase 3 clinical trials. Despite several classes of treatment options for patients with UC, there remains an unmet medical need, particularly in the treatment of moderately to severely active

disease. Agents with
novel mechanisms of action that target the inflammatory cascade, with oral dosing and
acceptable immunomodulatory and hematologic effects, remain the most promising option to
address these unmet needs.

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 Gilead-Sponsored filgotinib treatment study in UC

The secondary objective of this study is:
* To evaluate the effect of filgotinib on partial Mayo Clinic Score (MCS)

The exploratory objectives of this study are:
* To evaluate the association of clinical response (based on partial MCS) on systemic or localized inflammatory biomarkers (eg, including but not limited to C-reactive protein [CRP], fecal calprotectin, fecal lactoferrin, and fecal MMP-9)
* To evaluate health-related quality of life (HRQoL)

Study design

Long-term extension study to evaluate the safety of filgotinib administered to subjects with UC.

Intervention

NVT

Study burden and risks

Please refer to the risks section in the ICF for a full overview of the risks associated with Filgotinib.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

1) Must have the ability to understand and sign a written ICF, which must be obtained prior to
initiation of study procedures associated with this trial
2) Must have enrolled in Gilead-sponsored UC parent protocol GS-US-418-3898
3) Must have completed all required procedures or met protocol specified efficacy
discontinuation criteria in a prior Gilead-sponsored filgotinib treatment study for UC
4) 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
5) Male subjects and female subjects of childbearing potential who engage in heterosexual
intercourse must agree to use protocol specified method(s) of contraception
6) Willingness to refrain from live or attenuated vaccines during the study and for 12 weeks
after last dose of study drug

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 the present 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, would make the subject
unsuitable for the study or would prevent compliance with the study protocol
4) 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 35 days of the last dose of the study drug
5) Male subjects unwilling to refrain from sperm donation for at least 90 days after the last dose
of study drug
6) Males or females of reproductive potential who are unwilling to abide by protocol-specified
contraceptive methods
7) Use of prohibited concomitant medications as outlined in the protocol

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):	07-12-2017
Enrollment:	10
Type:	Actual

Medical products/devices used

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

Ethics review

Approved WMO Date:	16-08-2017
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:	05-12-2017
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	22-02-2018
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	12-06-2018
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO	

Date:	12-07-2018
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	14-01-2019
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:	21-03-2019
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	08-10-2019
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	20-12-2019
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:	23-11-2021
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	16-12-2021
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	01-06-2022
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	EUCTR2016-002765-58-NL
ClinicalTrials.gov	NCT02914535

Register	ID
CCMO	NL58871.041.16