Clinical trial results:
A Randomized, Double-Blind, Controlled, Multi-Center Study to Evaluate the Efficacy and Safety of Dose De-Escalation of Orally Administered Filgotinib in Subjects With Ulcerative Colitis in Clinical Remission

Summary

EudraCT number	2022-000719-30
Trial protocol	PL CZ FR ES BE IT
Global end of trial date	09 October 2023

Results information

Result version number	v1 (current)
This version publication date	22 September 2024
First version publication date	22 September 2024

Trial information

Trial identification

Sponsor protocol code	GLPG0634-CL-341

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT05479058
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Galapagos NV
Sponsor organisation address	Generaal De Wittelaan L11 A3, Mechelen, Belgium, 2800
Public contact	Galapagos Medical Information, Galapagos NV, medicalinfo@glpg.com
Scientific contact	Galapagos Medical Information, Galapagos NV, medicalinfo@glpg.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	28 June 2024
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	09 October 2023
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To evaluate the efficacy of filgotinib in participants in stable clinical remission on 200 milligrams (mg) filgotinib once daily for whom the dose was decreased to 100 mg once daily compared to participants remaining on 200 mg once daily.

Protection of trial subjects:

This clinical study was conducted in accordance with the ethical principles that have their origin in the "Declaration of Helsinki" and its amendments in force at the time of the clinical study. It was also carried out in conformity with the protocol, the International Council for Harmonisation for Good Clinical Practice (ICH-GCP) Guideline E6 (R2), and local ethical and legal requirements.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	26 July 2022
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Poland: 7
Country: Number of subjects enrolled	Spain: 1
Country: Number of subjects enrolled	Belgium: 4
Country: Number of subjects enrolled	France: 2
Country: Number of subjects enrolled	Germany: 3
Country: Number of subjects enrolled	Korea, Republic of: 1
Country: Number of subjects enrolled	United States: 3
Country: Number of subjects enrolled	United Kingdom: 1
Worldwide total number of subjects	22
EEA total number of subjects	17

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0

Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	17
From 65 to 84 years	5
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants who were in clinical remission with filgotinib 200 mg once daily for at least 2 consecutive quarterly visits in the ongoing long-term extension (LTE) SELECTION-LTE study (GS-US-418-3899; NCT02914535) and who met the eligibility criteria, were rolled over and randomized to this study.

Pre-assignment

Screening details:

The trial was originally designed with the primary endpoint to be assessed at Week 48 after which participants would have received unblinded treatment. Due to early termination, none of the participants completed 48 weeks. All participants participated in blinded treatment period only and the study was unblinded globally after study completion.

Period 1

Period 1 title	Overall (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Carer, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Filgotinib 200 mg

Arm description:

Participants received filgotinib 200 mg and placebo to match filgotinib 100 mg once daily orally.

Arm type	Experimental
Investigational medicinal product name	Filgotinib
Investigational medicinal product code	
Other name	GS-6034, GLPG0634
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Administered orally once daily

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Administered orally once daily

Arm title	Filgotinib 100 mg

Arm description:

Participants received filgotinib 100 mg and placebo to match filgotinib 200 mg once daily orally.

Arm type	Experimental
Investigational medicinal product name	Filgotinib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:
Administered orally once daily

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:
Administered orally once daily

Number of subjects in period 1	Filgotinib 200 mg	Filgotinib 100 mg
Started	11	11
Completed	0	0
Not completed	11	11
Consent withdrawn by subject	1	1
Study terminated by sponsor	10	10

Baseline characteristics

Reporting groups	
Reporting group title	Filgotinib 200 mg
Reporting group description:	
Participants received filgotinib 200 mg and placebo to match filgotinib 100 mg once daily orally.	
Reporting group title	Filgotinib 100 mg
Reporting group description:	
Participants received filgotinib 100 mg and placebo to match filgotinib 200 mg once daily orally.	

Reporting group values	Filgotinib 200 mg	Filgotinib 100 mg	Total
Number of subjects	11	11	22
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	56.5	58.3	
standard deviation	± 8.5	± 10.7	-
Gender categorical Units: Subjects			
Female	8	6	14
Male	3	5	8
Ethnicity Units: Subjects			
Hispanic or Latino	1	0	1
Not Hispanic or Latino	10	11	21
Race Units: Subjects			
Asian	1	0	1
White	10	11	21

End points

End points reporting groups

Reporting group title	Filgotinib 200 mg
Reporting group description:	
Participants received filgotinib 200 mg and placebo to match filgotinib 100 mg once daily orally.	
Reporting group title	Filgotinib 100 mg
Reporting group description:	
Participants received filgotinib 100 mg and placebo to match filgotinib 200 mg once daily orally.	

Primary: Percentage of Participants in Corticosteroid-free Clinical Remission Based on Modified Mayo Clinical Score (mMCS)

End point title	Percentage of Participants in Corticosteroid-free Clinical Remission Based on Modified Mayo Clinical Score (mMCS)[1]

End point description:

The mMCS is a tool designed to measure disease activity for ulcerative colitis. The mMCS was calculated as the sum of the 3 subscores: stool frequency, rectal bleeding, and endoscopy. Each subscore was graded from 0 to 3 with higher scores indicating more severe disease activity. The total mMCS score ranged from 0 to 9 with higher scores indicating more severe disease activity.
The mMCS remission was defined as a total score of score ≤2, with endoscopic subscore of ≤1, stool frequency subscore of ≤1, and a rectal bleeding subscore of 0.
Corticosteroid-free mMCS remission was defined as being free of corticosteroids for at least 12 weeks.

End point type	Primary

End point timeframe:

Week 48

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No participant reached the Week 48 time point, hence the data was not collected and analyzed.

End point values	Filgotinib 200 mg	Filgotinib 100 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[2]	0[3]		
Units: percentage of participants				
number (not applicable)				

Notes:

[2] - Due to early termination, Week 48 time point was not reached. Data was not collected and analyzed.

[3] - Due to early termination, Week 48 time point was not reached. Data was not collected and analyzed.

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Patient-Reported Outcome Based on 2 Items (PRO2) Flare

End point title	Time to Patient-Reported Outcome Based on 2 Items (PRO2) Flare

End point description:

PRO2 flare was defined as a PRO2 score worsening of at least 2 points and an absolute PRO2 score of at least 3, with stool frequency subscore ≥2, and rectal bleeding subscore ≥1.

PRO2 included items of stool frequency and rectal bleeding. The range of each item score was 0 to 3 with higher scores indicating more severe disease.
Participants in the Full Analysis Set (FAS) (all randomized participants who were administered study drug at least once) were analyzed.
'99999' signifies that due to insufficient number of participants with PRO2 flare, the median and 95% CI data could not be calculated.

End point type	Secondary
End point timeframe:	
Baseline up to Week 48	

End point values	Filgotinib 200 mg	Filgotinib 100 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	11		
Units: days				
median (confidence interval 95%)	99999 (99999 to 99999)	99999 (99999 to 99999)		

Statistical analyses

No statistical analyses for this end point

Secondary: Time to ES-Confirmed UC Flare

End point title	Time to ES-Confirmed UC Flare

End point description:

An ES-confirmed UC flare was defined as an increase in rectal bleeding subscore by at least 1 point and an increase in stool frequency subscore by at least 2 points and an increase in endoscopic subscore by at least 1 point. Each subscore graded from 0 to 3 with higher scores indicating more severe disease.
Participants in the FAS were analyzed.
'99999' signifies that due to insufficient number of participants with ES-confirmed UC flare, the median and 95% CI data could not be calculated.

End point type	Secondary
End point timeframe:	
Baseline up to Week 48	

End point values	Filgotinib 200 mg	Filgotinib 100 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	11		
Units: days				
median (confidence interval 95%)	99999 (99999 to 99999)	99999 (99999 to 99999)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in C-Reactive Protein (CRP)

End point title	Change From Baseline in C-Reactive Protein (CRP)

End point description:

CRP is an acute-phase protein which provides an objective criterion of inflammatory activity.
Participants in the FAS with available data were analyzed.
'99999' signifies that data at Week 48 was not collected and analyzed because the study was terminated prior to any participant reaching the Week 48 time point.

End point type	Secondary

End point timeframe:

Baseline, Week 4, Week 12, Week 24, Week 36, and Week 48

End point values	Filgotinib 200 mg	Filgotinib 100 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9	10		
Units: milligrams per liter (mg/L)				
arithmetic mean (standard deviation)				
Change from Baseline at Week 4 (n=9, n=10)	0.166 (± 0.533)	1.713 (± 4.423)		
Change from Baseline at Week 12 (n=6, n=7)	0.532 (± 1.128)	10.406 (± 26.944)		
Change from Baseline at Week 24 (n=5, n=5)	0.156 (± 0.128)	16.002 (± 34.093)		
Change from Baseline at Week 36 (n=3, n=3)	0.367 (± 0.192)	1.443 (± 0.525)		
Change from Baseline at Week 48 (n=0, n=0)	99999 (± 99999)	99999 (± 99999)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Fecal Calprotectin (FCP)

End point title	Change From Baseline in Fecal Calprotectin (FCP)

End point description:

Fecal calprotectin, a very stable biomarker, was a 36 kilodalton calcium and zinc binding protein of S-100 protein family which was neutrophil derived. It represents 60% of cytosolic proteins in neutrophils and was a measurement of neutrophil migration to the gastrointestinal tract.
Participants in the FAS with available data were analyzed.
'99999' signifies that data at Week 48 was not collected and analyzed because the study was terminated prior to any participant reaching the Week 48 time point.

End point type	Secondary

End point timeframe:

Baseline, Week 4, Week 12, Week 24, Week 36, and Week 48

End point values	Filgotinib 200 mg	Filgotinib 100 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7	8		
Units: milligrams per kilogram (mg/kg)				
arithmetic mean (standard deviation)				
Change from Baseline at Week 4 (n=7, n=8)	-27.6 (± 37.2)	142.5 (± 307.7)		
Change from Baseline at Week 12 (n=7, n=5)	-16.7 (± 48.1)	920.6 (± 1996.2)		
Change from Baseline at Week 24 (n=3, n=4)	-52.0 (± 54.6)	374.3 (± 674.8)		
Change from Baseline at Week 36 (n=2, n=3)	-46.5 (± 65.8)	-8.0 (± 70.4)		
Change from Baseline at Week 48 (n=0, n=0)	99999 (± 99999)	99999 (± 99999)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Inflammatory Bowel Disease Questionnaire (IBDQ) Score

End point title	Change From Baseline in Inflammatory Bowel Disease Questionnaire (IBDQ) Score

End point description:

The IBDQ is disease-specific questionnaire used for an assessment of Health Related Quality of Life (HRQoL) in participants with the Inflammatory Bowel Disease (IBD). It comprised of 32 questions divided into four health subscales: bowel symptoms (10 questions); systemic symptoms, including sleep disorders and fatigue (5 questions); emotional function such as depression, aggression, and irritation (12 questions); and social function, meaning the ability to participate in social activities and to work (5 questions). The IBDQ total score was calculated as the sum of the responses (each ranging from 1 [severe problem] to 7 [normal health]) to all 32 questions. Total IBDQ score ranged from 32 to 224 with a higher score indicating a better HRQoL.

End point type	Secondary

End point timeframe:

Baseline, Week 48

End point values	Filgotinib 200 mg	Filgotinib 100 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[4]	0[5]		
Units: score on scale				
arithmetic mean (standard deviation)	()	()		

Notes:

[4] - Due to early termination, Week 48 time point was not reached. Data was not collected and analyzed.
[5] - Due to early termination, Week 48 time point was not reached. Data was not collected and analyzed.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Treatment-Emergent Adverse Events (TEAEs), Treatment-Emergent Serious Adverse Events (SAEs), and TEAEs Leading to Treatment Discontinuation

End point title	Number of Participants With Treatment-Emergent Adverse Events (TEAEs), Treatment-Emergent Serious Adverse Events (SAEs), and TEAEs Leading to Treatment Discontinuation

End point description:

An adverse event (AE) was any untoward medical occurrence, new or worsening of any preexisting condition, in a clinical study participant administered a medicinal product and which did not necessarily had to have a causal relationship with this treatment.
A TEAE was defined as an AE which had a start date equal to or after the date of the first administration of study drug in this study and no later than 30 days after last administration of study drug; And was either a newly reported event, or a worsening of an existing event.
Serious TEAE was defined as a TEAE that Resulted in death and was life-threatening; Required in-patient hospitalization or prolongation of existing hospitalization; Resulted in persistent or significant disability/incapacity; Was a congenital anomaly / birth defect; Was medically significant.
Participants in the Safety Analysis Set (all randomized participants who were administered study drug at least once) were analyzed.

End point type	Secondary

End point timeframe:

Baseline up to Week 48

End point values	Filgotinib 200 mg	Filgotinib 100 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	11		
Units: Participants				
TEAEs	6	6		
Serious TEAEs	0	0		
TEAEs Leading to Treatment Discontinuation	0	0		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Baseline up to Week 48	
Adverse event reporting additional description:	
The Safety Analysis Set included all randomized participants who were administered study drug at least once.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	26.0

Reporting groups	
Reporting group title	Filgotinib 100 mg
Reporting group description:	
Participants received filgotinib 100 mg and placebo to match filgotinib 200 mg once daily orally.	
Reporting group title	Filgotinib 200 mg
Reporting group description:	
Participants received filgotinib 200 mg and placebo to match filgotinib 100 mg once daily orally.	

Serious adverse events	Filgotinib 100 mg	Filgotinib 200 mg	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 11 (0.00%)	0 / 11 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Filgotinib 100 mg	Filgotinib 200 mg	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	6 / 11 (54.55%)	6 / 11 (54.55%)	
Investigations			
Liver function test abnormal			
subjects affected / exposed	1 / 11 (9.09%)	0 / 11 (0.00%)	
occurrences (all)	1	0	
Injury, poisoning and procedural complications			
Tendon rupture			
subjects affected / exposed	0 / 11 (0.00%)	1 / 11 (9.09%)	
occurrences (all)	0	1	

General disorders and administration site conditions			
Influenza like illness			
subjects affected / exposed	0 / 11 (0.00%)	1 / 11 (9.09%)	
occurrences (all)	0	1	
Fatigue			
subjects affected / exposed	1 / 11 (9.09%)	0 / 11 (0.00%)	
occurrences (all)	1	0	
Social circumstances			
Postmenopause			
subjects affected / exposed[1]	1 / 6 (16.67%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal disorders			
Colitis ulcerative			
subjects affected / exposed	2 / 11 (18.18%)	0 / 11 (0.00%)	
occurrences (all)	4	0	
Abdominal pain upper			
subjects affected / exposed	0 / 11 (0.00%)	1 / 11 (9.09%)	
occurrences (all)	0	1	
Diarrhoea			
subjects affected / exposed	2 / 11 (18.18%)	0 / 11 (0.00%)	
occurrences (all)	2	0	
Nausea			
subjects affected / exposed	1 / 11 (9.09%)	0 / 11 (0.00%)	
occurrences (all)	1	0	
Vomiting			
subjects affected / exposed	2 / 11 (18.18%)	0 / 11 (0.00%)	
occurrences (all)	2	0	
Skin and subcutaneous tissue disorders			
Actinic keratosis			
subjects affected / exposed	1 / 11 (9.09%)	0 / 11 (0.00%)	
occurrences (all)	1	0	
Renal and urinary disorders			
Renal colic			
subjects affected / exposed	0 / 11 (0.00%)	1 / 11 (9.09%)	
occurrences (all)	0	1	
Musculoskeletal and connective tissue disorders			

Tendonitis			
subjects affected / exposed	0 / 11 (0.00%)	1 / 11 (9.09%)	
occurrences (all)	0	1	
Bursitis			
subjects affected / exposed	0 / 11 (0.00%)	1 / 11 (9.09%)	
occurrences (all)	0	1	
Back pain			
subjects affected / exposed	0 / 11 (0.00%)	1 / 11 (9.09%)	
occurrences (all)	0	1	
Infections and infestations			
Laryngitis			
subjects affected / exposed	0 / 11 (0.00%)	1 / 11 (9.09%)	
occurrences (all)	0	1	
Gastroenteritis			
subjects affected / exposed	1 / 11 (9.09%)	1 / 11 (9.09%)	
occurrences (all)	1	1	
Conjunctivitis			
subjects affected / exposed	1 / 11 (9.09%)	0 / 11 (0.00%)	
occurrences (all)	1	0	
Campylobacter infection			
subjects affected / exposed	1 / 11 (9.09%)	0 / 11 (0.00%)	
occurrences (all)	1	0	
Sinusitis			
subjects affected / exposed	1 / 11 (9.09%)	0 / 11 (0.00%)	
occurrences (all)	1	0	
Nasopharyngitis			
subjects affected / exposed	1 / 11 (9.09%)	0 / 11 (0.00%)	
occurrences (all)	1	0	
Metabolism and nutrition disorders			
Hypercholesterolaemia			
subjects affected / exposed	0 / 11 (0.00%)	1 / 11 (9.09%)	
occurrences (all)	0	1	
Vitamin D deficiency			
subjects affected / exposed	0 / 11 (0.00%)	1 / 11 (9.09%)	
occurrences (all)	0	1	

Notes:

[1] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: This is a sex-specific AE. Only female participants were at risk.

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
17 March 2023	– Clarifications were added regarding UC flare, biopsies, corticosteroids, food intake, End of treatment visit, unblinding of participants at the study primary analysis endpoint, and hepatitis B virus surveillance. – The eligibility criteria and screening assessments were updated, rescreening allowed, and the screening period was extended. – The definitions of women of childbearing potential and postmenopausal female were changed.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

Study was terminated as the planned number of participants needed to ensure adequate precision in the estimations and to draw meaningful conclusions was unlikely to be met, questioning the scientific value and ethical grounds for study continuation.

Notes: