Clinical trial results:
A Randomized, Double-blind, Placebo-controlled, Multicenter Study to Evaluate the Safety, Tolerability, Efficacy, and Pharmacokinetics of GLPG3970, Administered Orally for 6 Weeks in Adult Subjects With Moderately to Severely Active Ulcerative Colitis

Summary

EudraCT number	2020-000659-11
Trial protocol	PL
Global end of trial date	31 May 2021

Results information

Result version number	v1 (current)
This version publication date	13 May 2022
First version publication date	13 May 2022

Trial information

Trial identification

Sponsor protocol code	GLPG3970-CL-210

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04577794
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	31 May 2021
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	31 May 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the effect of GLPG3970 compared to placebo on the signs and symptoms of ulcerative colitis (UC) in participants with moderately to severely active UC.

Protection of trial subjects:

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 (2013 version). It was also carried out in conformity with the protocol, the International Council for Harmonization for Good Clinical Practice (ICH-GCP) Guideline E6 (R2), and local ethical and legal requirements. The investigator informed the subjects of the risks and benefits of the clinical study. The subjects were informed that they could withdraw from the clinical study at any time for any reason. Consent was obtained in writing prior to any clinical study-related activities; the investigator retained a copy of the ICFs, which are available to the sponsor for review. The subjects were covered by the sponsor's insurance according to local legal requirements.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	05 October 2020
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	Georgia: 5
Country: Number of subjects enrolled	Moldova, Republic of: 6
Country: Number of subjects enrolled	Ukraine: 15
Country: Number of subjects enrolled	Poland: 5
Worldwide total number of subjects	31
EEA total number of subjects	5

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	0

months)	
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	31
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Study was conducted across 4 countries (Georgia, the Republic of Moldova, Poland, and Ukraine).

Pre-assignment

Screening details:

A total of 65 participants were screened, out of which 31 were randomized and treated.

Period 1

Period 1 title	Overall study (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	GLPG3970

Arm description:

Participants received 400 milligrams (mg) GLPG3970 oral solution, once daily (QD) for a period of 6 weeks.

Arm type	Experimental
Investigational medicinal product name	GLPG3970
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solvent for oral solution
Routes of administration	Oral use

Dosage and administration details:

Participants received 400 mg GLPG3970 reconstituted oral solution, QD for a period of 6 weeks.

Arm title	Placebo

Arm description:

Participants received GLPG3970 matching placebo oral solution, QD for a period of 6 weeks.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solvent for oral solution
Routes of administration	Oral use

Dosage and administration details:

Participants received GLPG3970 matching placebo reconstituted oral solution, QD for a period of 6 weeks.

Number of subjects in period 1	GLPG3970	Placebo
Started	21	10
Completed	20	9
Not completed	1	1
Adverse event, non-fatal	1	1

Baseline characteristics

Reporting groups	
Reporting group title	GLPG3970
Reporting group description:	
Participants received 400 milligrams (mg) GLPG3970 oral solution, once daily (QD) for a period of 6 weeks.	
Reporting group title	Placebo
Reporting group description:	
Participants received GLPG3970 matching placebo oral solution, QD for a period of 6 weeks.	

Reporting group values	GLPG3970	Placebo	Total
Number of subjects	21	10	31
Age categorical Units: Subjects			
Adults (18-64 years)	21	10	31
Age continuous Units: years			
arithmetic mean	39.7	37.8	
standard deviation	± 10.9	± 5.8	-
Gender categorical Units: Subjects			
Female	5	1	6
Male	16	9	25
Ethnicity Units: Subjects			
Not Hispanic or Latino	21	10	31
Race Units: Subjects			
White	21	10	31
Total Mayo Clinical Score (MCS)			
The MCS is the primary tool for assessing ulcerative colitis activity. Total MCS is the sum of 4 subscores (i.e., stool frequency, rectal bleeding, endoscopic findings, and a physician's global assessment); each rated on a scale from 0 (normal) to 3 (severe). The total MCS value ranges from 0 to 12, with higher scores indicating more severe disease.			
Units: units on a scale			
arithmetic mean	8.5	8.2	
standard deviation	± 1.2	± 1.3	-

End points

End points reporting groups

Reporting group title	GLPG3970
Reporting group description:	
Participants received 400 milligrams (mg) GLPG3970 oral solution, once daily (QD) for a period of 6 weeks.	
Reporting group title	Placebo
Reporting group description:	
Participants received GLPG3970 matching placebo oral solution, QD for a period of 6 weeks.	

Primary: Change From Baseline in Total MCS at Week 6

End point title	Change From Baseline in Total MCS at Week 6
End point description:	
The MCS is the primary tool for assessing ulcerative colitis activity. Total MCS is the sum of 4 subscores (i.e., stool frequency, rectal bleeding, endoscopic findings, and a physician's global assessment); each rated on a scale from 0 (normal) to 3 (severe). The total MCS value ranges from 0 to 12, with higher scores indicating more severe disease. Missing data were imputed using Rubin's multiple imputation. Analysis Population: Full analysis set consisted of all randomized participants who received at least 1 dose of investigational product (IP). Participants with available data at specified timepoint were included.	
End point type	Primary
End point timeframe:	
Baseline and Week 6	

End point values	GLPG3970	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	18	9		
Units: units on a scale				
least squares mean (standard error)	-2.6 (± 0.57)	-2.6 (± 0.85)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Statistical analysis description:	
An analysis of covariance (ANCOVA) was used with a multiple imputation method to handle missing values, with treatment as fixed effect and baseline score as covariate.	
Comparison groups	GLPG3970 v Placebo
Number of subjects included in analysis	27
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.981
Method	ANCOVA
Parameter estimate	Least square (LS) mean difference
Point estimate	0

Confidence interval	
level	90 %
sides	2-sided
lower limit	-1.7
upper limit	1.7
Variability estimate	Standard error of the mean
Dispersion value	1.02

Secondary: Number of Participants With Treatment-Emergent Adverse Events (TEAEs)

End point title	Number of Participants With Treatment-Emergent Adverse Events (TEAEs)

End point description:

Treatment-Emergent Adverse Events (TEAEs) were defined as
• Any adverse event (AE) with an onset date on or after the IP start date and no later than 14 days after last dose of IP, or worsening of any AE on or after the IP start date.
• Improvement or no change of any ongoing AEs on or after the IP start date are not considered treatment-emergent. If an AE was ongoing at the time of first IP intake and if there was no change or an improvement in its toxicity grade or its seriousness status, this AE was not considered as treatment-emergent.
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.
Analysis Population: Participants in the safety analysis set were analyzed.

End point type	Secondary

End point timeframe:

First dose date up to 14 days after the last dose of study drug (up to 57 days)

End point values	GLPG3970	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	21	10		
Units: participants				
TEAEs	11	3		
Serious TEAEs	0	0		
TEAEs leading to death	0	0		
Treatment-related TEAEs	4	1		
TEAEs leading to study drug discontinuation	1	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Plasma Concentration (Ctrough) of GLPG3970

End point title	Plasma Concentration (Ctrough) of GLPG3970[1]

End point description:

Ctrough was defined as plasma concentration level at the end of the dosing interval.
Analysis Population: Pharmacokinetic analysis set consisted of all participants who received at least 1 dose of IP with available plasma concentration data. Participants with available plasma concentration at specified time point were included.

End point type	Secondary

End point timeframe:

Day 15: pre-dose; Day 29: pre-dose; Day 43: pre-dose

Notes:

[1] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The endpoint assessed plasma concentration (Ctrough) of GLPG3970. Therefore, it is applicable for GLPG3970 arm only.

End point values	GLPG3970			
Subject group type	Reporting group			
Number of subjects analysed	16[2]			
Units: nanograms per milliliter (ng/mL)				
geometric mean (geometric coefficient of variation)				
Day 15: Pre-dose	73.2 (± 145)			
Day 29: Pre-dose	55.9 (± 65.3)			
Day 43: Pre-dose	84.9 (± 107)			

Notes:

[2] - n = 16 at Day 15, 15 at Day 29, and 11 at Day 43

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
First dose date up to 14 days after the last dose of study drug (up to 57 days)	
Adverse event reporting additional description:	
Participants in the safety analysis set were analyzed.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	23.0

Reporting groups	
Reporting group title	GLPG3970
Reporting group description:	
Participants received 400 mg GLPG3970 oral solution, QD for a period of 6 weeks.	
Reporting group title	Placebo
Reporting group description:	
Participants received GLPG3970 matching placebo oral solution, QD for a period of 6 weeks.	

Serious adverse events	GLPG3970	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 21 (0.00%)	0 / 10 (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	GLPG3970	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	11 / 21 (52.38%)	3 / 10 (30.00%)	
Investigations			
Amylase increased			
subjects affected / exposed	2 / 21 (9.52%)	0 / 10 (0.00%)	
occurrences (all)	2	0	
Blood bilirubin increased			
subjects affected / exposed	0 / 21 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Blood lactate dehydrogenase decreased			

subjects affected / exposed	1 / 21 (4.76%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Lipase increased			
subjects affected / exposed	3 / 21 (14.29%)	0 / 10 (0.00%)	
occurrences (all)	4	0	
Lymphocyte count decreased			
subjects affected / exposed	1 / 21 (4.76%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Neutrophil count decreased			
subjects affected / exposed	0 / 21 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
SARS-CoV-2 test positive			
subjects affected / exposed	1 / 21 (4.76%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 21 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
General disorders and administration site conditions			
Pain			
subjects affected / exposed	1 / 21 (4.76%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Pyrexia			
subjects affected / exposed	1 / 21 (4.76%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 21 (4.76%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Flatulence			
subjects affected / exposed	1 / 21 (4.76%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Abdominal pain upper			
subjects affected / exposed	1 / 21 (4.76%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Frequent bowel movements			

subjects affected / exposed	1 / 21 (4.76%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Haematochezia			
subjects affected / exposed	2 / 21 (9.52%)	0 / 10 (0.00%)	
occurrences (all)	2	0	
Nausea			
subjects affected / exposed	4 / 21 (19.05%)	0 / 10 (0.00%)	
occurrences (all)	4	0	
Stomatitis			
subjects affected / exposed	1 / 21 (4.76%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Reproductive system and breast disorders			
Pelvic cyst			
subjects affected / exposed	1 / 21 (4.76%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Skin and subcutaneous tissue disorders			
Erythema			
subjects affected / exposed	1 / 21 (4.76%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Rash			
subjects affected / exposed	1 / 21 (4.76%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Renal and urinary disorders			
Nephrolithiasis			
subjects affected / exposed	1 / 21 (4.76%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal and connective tissue disorders			
Musculoskeletal chest pain			
subjects affected / exposed	1 / 21 (4.76%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Back pain			
subjects affected / exposed	0 / 21 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Metabolism and nutrition disorders			
Hyperkalaemia			

subjects affected / exposed occurrences (all)	1 / 21 (4.76%) 1	0 / 10 (0.00%) 0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported