Clinical trial results:
A Randomized, Double-Blind, Placebo-Controlled, Multicenter Study to Evaluate the Efficacy, Safety, Tolerability, Pharmacokinetics, and Pharmacodynamics of Orally Administered GLPG3970 for 12 Weeks in Adult Subjects With Active Primary Sjögren's Syndrome

Summary

EudraCT number	2020-003298-22
Trial protocol	FR DE HU GR ES
Global end of trial date	27 December 2021

Results information

Result version number	v1 (current)
This version publication date	15 December 2022
First version publication date	15 December 2022

Trial information

Trial identification

Sponsor protocol code	GLPG3970-CL-207

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04700280
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 April 2022
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	27 December 2021
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the study was to evaluate the efficacy of GLPG3970 compared to placebo on the signs and symptoms of primary Sjogren's Syndrome (pSS). The study also evaluated the safety and tolerability of GLPG3970 compared to placebo.

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 (2013 version). 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	28 January 2021
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Ukraine: 3
Country: Number of subjects enrolled	Poland: 23
Country: Number of subjects enrolled	Germany: 1
Country: Number of subjects enrolled	Greece: 1
Country: Number of subjects enrolled	Hungary: 3
Worldwide total number of subjects	31
EEA total number of subjects	28

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)	29
From 65 to 84 years	2
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants were enrolled at 10 clinical study sites across 5 countries (1 in Germany, 1 in Greece, 1 in Hungary, 6 in Poland, and 1 in Ukraine).

Pre-assignment

Screening details:

A total of 69 participants were screened. Of these, 31 participants were randomized and treated in the study.

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 GLPG3970 400 milligram (mg) (2 *200 mg tablet), orally, once daily for 12 weeks.

Arm type	Experimental
Investigational medicinal product name	GLPG3970
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

GLPG3970 was administered per dose and schedule specified in the arm description.

Arm title	Placebo

Arm description:

Participants received placebo matched to GLPG3970 tablet, orally, once daily for 12 weeks.

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

Dosage and administration details:

Placebo matched to GLPG3970 was administered per schedule specified in the arm description.

Number of subjects in period 1	GLPG3970	Placebo
Started	20	11
Completed	9	8
Not completed	11	3
Adverse event, non-fatal	4	-
Study terminated by sponsor	5	3
Other than specified	1	-
Lack of efficacy	1	-

Baseline characteristics

Reporting groups	
Reporting group title	GLPG3970
Reporting group description:	
Participants received GLPG3970 400 milligram (mg) (2 *200 mg tablet), orally, once daily for 12 weeks.	
Reporting group title	Placebo
Reporting group description:	
Participants received placebo matched to GLPG3970 tablet, orally, once daily for 12 weeks.	

Reporting group values	GLPG3970	Placebo	Total
Number of subjects	20	11	31
Age categorical Units: Subjects			
Adults (18-64 years)	19	10	29
From 65-74 years	1	1	2
Age continuous Units: years			
arithmetic mean	49.6	47.4	
standard deviation	± 10.3	± 10.0	-
Gender categorical Units: Subjects			
Female	19	10	29
Male	1	1	2
Ethnicity Units: Subjects			
Hispanic or Latino	0	0	0
Not Hispanic or Latino	20	11	31
Unknown or Not Reported	0	0	0
Race Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	0	0	0
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	0	0
White	20	11	31
More than one race	0	0	0
Unknown or Not Reported	0	0	0
European League Against Rheumatism (EULAR) Sjögren's Syndrome Disease Activity Index (ESSDAI) Score			
ESSDAI includes 12 domains: constitutional, lymphadenopathy and lymphoma, glandular, articular, cutaneous, pulmonary,renal, muscular, peripheral nervous system, central nervous system [CNS], hematological, biological. Each of the domains was assessed for activity level: no, low, moderate, high. Each domain score was obtained by multiplying the activity level with domain weight (range: 1 to 6), and assigned a numerical score. Sum of all individual weighted domain scores = 0 (best) to 123 (worst activity). A higher score indicated more disease activity.			
Units: score on a scale			
arithmetic mean	12.5	8.3	
standard deviation	± 6.6	± 2.4	-

End points

End points reporting groups

Reporting group title	GLPG3970
Reporting group description:	
Participants received GLPG3970 400 milligram (mg) (2 *200 mg tablet), orally, once daily for 12 weeks.	
Reporting group title	Placebo
Reporting group description:	
Participants received placebo matched to GLPG3970 tablet, orally, once daily for 12 weeks.	

Primary: Change From Baseline in ESSDAI Score at Week 12

End point title	Change From Baseline in ESSDAI Score at Week 12
End point description:	
ESSDAI, a systemic disease activity index to assess 12 domains (constitutional, lymphadenopathy and lymphoma, glandular, articular, cutaneous, pulmonary, renal, muscular, peripheral nervous system, central nervous system [CNS], hematological, biological) in participants with pSS. Each of the domains was assessed for activity level (no, low, moderate, high). Each domain score was obtained by multiplying the activity level with domain weight (range:1 to 6), and assigned a numerical score. Sum of all individual weighted domain scores was overall score (range:0[best] to 123[worst activity]), higher score indicated more disease activity. A clinically meaningful reduction from baseline (≥3 points) indicated improvement of symptoms. Least squares (LS) mean was calculated using mixed models for repeated measures (MMRM). Participants in the full analysis set (FAS: all randomized participants who received at least one dose of study drug) with available data were analyzed.	
End point type	Primary
End point timeframe:	
Baseline, Week 12	

End point values	GLPG3970	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	8	5		
Units: score on a scale				
least squares mean (standard error)	-4.4 (± 1.56)	-3.0 (± 2.03)		

Statistical analyses

Statistical analysis title	GLPG3970 vs Placebo
Comparison groups	GLPG3970 v Placebo
Number of subjects included in analysis	13
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.617
Method	Mixed models analysis
Parameter estimate	LS Mean Difference
Point estimate	-1.4

Confidence interval	
level	90 %
sides	2-sided
lower limit	-6.2
upper limit	3.4
Variability estimate	Standard error of the mean
Dispersion value	2.69

Primary: Number of Participants Who Experienced Treatment Emergent Adverse Events (TEAEs) by Severity

End point title	Number of Participants Who Experienced Treatment Emergent Adverse Events (TEAEs) by Severity[1]

End point description:

An adverse event (AE) was any untoward medical occurrence in a participant administered study drug and which did not necessarily have a causal relationship with study drug. The severity of AEs was graded using the Common Terminology Criteria for Adverse Events (CTCAE) current version at the time of assessment. The maximum intensity of the AE were Grade 1 (mild), Grade 2 (moderate), Grade 3 (severe), Grade 4 (life-threatening), or Grade 5 (fatal). A TEAE was any AE with an onset date on or after the first dose of GLPG3970 and no later than 30 days after last dose of GLPG3970, or any worsening of any AE on or after the GLPG3970 start date. The safety analysis set included all randomized participants who received at least one dose of study drug.

End point type	Primary

End point timeframe:

From first dose of study drug up to 30 days after last dose of study drug (maximum duration=16 weeks)

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: Statistical analysis was not planned for primary endpoint related to safety.

End point values	GLPG3970	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	20	11		
Units: participants				
Mild	3	4		
Moderate	5	3		
Severe	3	0		
Life-threatening	0	0		
Death	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in EULAR Sjögren's Syndrome Patient Reported Index (ESSPRI) Score at Weeks 4, 8, and 12

End point title	Change From Baseline in EULAR Sjögren's Syndrome Patient Reported Index (ESSPRI) Score at Weeks 4, 8, and 12

End point description:

The ESSPRI is a participant-reported questionnaire to assess subjective participant symptoms and includes 3 domains (dryness, pain, and fatigue). Each domain was scored on scale of 0-10 (0 = no

symptom at all and 10 = worst symptom imaginable), and an overall score was calculated as the mean of the 3 individual domains where all domains carry the same weight. Minimum score can be 0 and maximum score can be 10. A higher score indicates worst symptom. A clinically significant reduction from baseline of the ESSPRI score (at least one point or 15% of the baseline value) indicated the improvement of symptoms. Participants in the FAS with available data were analyzed.

End point type	Secondary

End point timeframe:

Baseline, Weeks 4, 8, and 12

End point values	GLPG3970	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	19	11		
Units: score on a scale				
least squares mean (standard error)				
Change at Week 4 (n=19, 11)	-1.25 (± 0.37)	-0.60 (± 0.49)		
Change at Week 8 (n=17, 8)	-2.05 (± 0.41)	-1.28 (± 0.56)		
Change at Week 12 (n=11, 8)	-2.15 (± 0.59)	-1.79 (± 0.70)		

Statistical analyses

Statistical analysis title	Week 4: GLPG3970 vs Placebo

Statistical analysis description:

Number of participants included in analysis were 30.

Comparison groups	GLPG3970 v Placebo
Number of subjects included in analysis	30
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3089
Method	Mixed models analysis
Parameter estimate	LS Mean Difference
Point estimate	-0.64
Confidence interval	
level	90 %
sides	2-sided
lower limit	-1.7
upper limit	0.41
Variability estimate	Standard error of the mean
Dispersion value	0.62

Statistical analysis title	Week 8: GLPG3970 vs Placebo

Statistical analysis description:

Number of participants included in analysis were 25.

Comparison groups	GLPG3970 v Placebo

Number of subjects included in analysis	30
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2834
Method	Mixed models analysis
Parameter estimate	LS Mean Difference
Point estimate	-0.77
Confidence interval	
level	90 %
sides	2-sided
lower limit	-1.97
upper limit	0.43
Variability estimate	Standard error of the mean
Dispersion value	0.71

Statistical analysis title	Week 12: GLPG3970 vs Placebo
Statistical analysis description:	
Number of participants included in analysis were 19.	
Comparison groups	GLPG3970 v Placebo
Number of subjects included in analysis	30
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7109
Method	Mixed models analysis
Parameter estimate	LS Mean Difference
Point estimate	-0.36
Confidence interval	
level	90 %
sides	2-sided
lower limit	-2.02
upper limit	1.3
Variability estimate	Standard error of the mean
Dispersion value	0.95

Secondary: Change From Baseline in ESSDAI Score at Weeks 4, 8, and 12

End point title	Change From Baseline in ESSDAI Score at Weeks 4, 8, and 12

End point description:

The ESSDAI is a systemic disease activity index to assess 12 domains (organ systems: constitutional, lymphadenopathy and lymphoma, glandular, articular, cutaneous, pulmonary, renal, muscular, peripheral nervous system, CNS, hematological, biological) in participants with pSS. Each of the domains was assessed for activity level (no, low, moderate, and high). Each domain score was obtained by multiplying the activity level with the domain weight, ranged from 1 to 6, and assigned a numerical score based on pre-determined weighting of each individual domain. The sum of all individual weighted domain scores was the overall score, ranged from 0 (best) to 123 (worst activity). A higher score indicated more disease activity. A clinically meaningful reduction from baseline (≥3 points) indicated the improvement of symptoms. Participants in the FAS with available data were analyzed. Results of Week 12 is presented in primary endpoint 1.

End point type	Secondary

End point timeframe:
Baseline, Weeks 4, 8, and 12

End point values	GLPG3970	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15	7		
Units: score on a scale				
least squares mean (standard error)				
Change at Week 4 (n=9, 6)	-1.7 (± 1.17)	-1.4 (± 1.32)		
Change at Week 8 (n=15, 7)	-3.5 (± 1.28)	-4.0 (± 2.02)		

Statistical analyses

Statistical analysis title	Week 4: GLPG3970 vs Placebo
Statistical analysis description: Number of participants included in analysis were 15.	
Comparison groups	GLPG3970 v Placebo
Number of subjects included in analysis	22
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.859
Method	Mixed models analysis
Parameter estimate	LS Mean Difference
Point estimate	-0.3
Confidence interval	
level	90 %
sides	2-sided
lower limit	-3.6
upper limit	2.9
Variability estimate	Standard error of the mean
Dispersion value	1.81

Statistical analysis title	Week 8: GLPG3970 vs Placebo
Statistical analysis description: Number of participants included in analysis were 22.	
Comparison groups	GLPG3970 v Placebo
Number of subjects included in analysis	22
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.837
Method	Mixed models analysis
Parameter estimate	LS Mean Difference
Point estimate	0.5

Confidence interval	
level	90 %
sides	2-sided
lower limit	-3.8
upper limit	4.8
Variability estimate	Standard error of the mean
Dispersion value	2.46

Secondary: Observed Pre-dose Plasma Concentration (Ctrough) of GLPG3970

End point title	Observed Pre-dose Plasma Concentration (Ctrough) of GLPG3970[2]

End point description:

Plasma concentration of GLPG3970 observed at pre-dose in nanogram per milliliter (ng/mL), obtained directly from the observed concentration versus time data. The pharmacokinetic (PK) analysis set included all randomized participant who received at least 1 dose of study drug and for which plasma concentration data were available. Number of participants with available data were analyzed.

End point type	Secondary

End point timeframe:

Pre-dose (within 30 minutes prior to dosing) on Weeks 1, 4, 8, and 12

Notes:

[2] - 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	20			
Units: ng/mL				
geometric mean (geometric coefficient of variation)				
Week 1 (n=16)	77.6 (± 64.7)			
Week 4 (n=15)	70.4 (± 108)			
Week 8 (n=9)	65 (± 265)			
Week 12 (n=7)	66 (± 219)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
From first dose of study drug up to 30 days after last dose of study drug (maximum duration=16 weeks)	
Assessment type	Systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	23.1
Reporting groups	
Reporting group title	GLPG3970
Reporting group description:	
Participants received GLPG3970 400 mg (2 *200 mg tablet), orally, once daily for 12 weeks.	
Reporting group title	Placebo
Reporting group description:	
Participants received placebo matched to GLPG3970 tablet, orally, once daily for 12 weeks.	

Serious adverse events	GLPG3970	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 20 (10.00%)	0 / 11 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Hepatobiliary disorders			
Drug-induced liver injury			
subjects affected / exposed	1 / 20 (5.00%)	0 / 11 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Liver injury			
subjects affected / exposed	1 / 20 (5.00%)	0 / 11 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	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	10 / 20 (50.00%)	7 / 11 (63.64%)	
Investigations			

Alanine aminotransferase increased			
subjects affected / exposed	1 / 20 (5.00%)	0 / 11 (0.00%)	
occurrences (all)	1	0	
Activated partial thromboplastin time prolonged			
subjects affected / exposed	0 / 20 (0.00%)	1 / 11 (9.09%)	
occurrences (all)	0	1	
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 20 (5.00%)	0 / 11 (0.00%)	
occurrences (all)	1	0	
Blood creatine phosphokinase increased			
subjects affected / exposed	1 / 20 (5.00%)	0 / 11 (0.00%)	
occurrences (all)	1	0	
Epstein-Barr virus antibody positive			
subjects affected / exposed	1 / 20 (5.00%)	0 / 11 (0.00%)	
occurrences (all)	1	0	
International normalised ratio increased			
subjects affected / exposed	0 / 20 (0.00%)	1 / 11 (9.09%)	
occurrences (all)	0	1	
Lipase increased			
subjects affected / exposed	1 / 20 (5.00%)	0 / 11 (0.00%)	
occurrences (all)	1	0	
Pancreatic enzymes increased			
subjects affected / exposed	1 / 20 (5.00%)	0 / 11 (0.00%)	
occurrences (all)	1	0	
Injury, poisoning and procedural complications			
Arthropod bite			
subjects affected / exposed	0 / 20 (0.00%)	1 / 11 (9.09%)	
occurrences (all)	0	1	
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 20 (5.00%)	1 / 11 (9.09%)	
occurrences (all)	1	1	
Blood and lymphatic system disorders			

Leukopenia			
subjects affected / exposed	0 / 20 (0.00%)	1 / 11 (9.09%)	
occurrences (all)	0	2	
Thrombocytopenia			
subjects affected / exposed	0 / 20 (0.00%)	1 / 11 (9.09%)	
occurrences (all)	0	1	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	0 / 20 (0.00%)	1 / 11 (9.09%)	
occurrences (all)	0	1	
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	2 / 20 (10.00%)	0 / 11 (0.00%)	
occurrences (all)	2	0	
Oral mucosa erosion			
subjects affected / exposed	0 / 20 (0.00%)	1 / 11 (9.09%)	
occurrences (all)	0	1	
Vomiting			
subjects affected / exposed	2 / 20 (10.00%)	0 / 11 (0.00%)	
occurrences (all)	2	0	
Respiratory, thoracic and mediastinal disorders			
Dysphonia			
subjects affected / exposed	1 / 20 (5.00%)	0 / 11 (0.00%)	
occurrences (all)	1	0	
Oropharyngeal pain			
subjects affected / exposed	0 / 20 (0.00%)	1 / 11 (9.09%)	
occurrences (all)	0	1	
Hepatobiliary disorders			
Liver injury			
subjects affected / exposed	1 / 20 (5.00%)	0 / 11 (0.00%)	
occurrences (all)	1	0	
Skin and subcutaneous tissue disorders			
Drug eruption			
subjects affected / exposed	1 / 20 (5.00%)	0 / 11 (0.00%)	
occurrences (all)	1	0	
Rash pruritic			

subjects affected / exposed	1 / 20 (5.00%)	0 / 11 (0.00%)	
occurrences (all)	1	0	
Skin reaction			
subjects affected / exposed	0 / 20 (0.00%)	1 / 11 (9.09%)	
occurrences (all)	0	1	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 20 (0.00%)	1 / 11 (9.09%)	
occurrences (all)	0	2	
Infections and infestations			
Fungal pharyngitis			
subjects affected / exposed	1 / 20 (5.00%)	0 / 11 (0.00%)	
occurrences (all)	1	0	
Nasopharyngitis			
subjects affected / exposed	1 / 20 (5.00%)	0 / 11 (0.00%)	
occurrences (all)	1	0	
Oral herpes			
subjects affected / exposed	0 / 20 (0.00%)	1 / 11 (9.09%)	
occurrences (all)	0	1	
Otitis media			
subjects affected / exposed	1 / 20 (5.00%)	0 / 11 (0.00%)	
occurrences (all)	1	0	
Upper respiratory tract infection			
subjects affected / exposed	1 / 20 (5.00%)	0 / 11 (0.00%)	
occurrences (all)	1	0	
Urinary tract infection			
subjects affected / exposed	0 / 20 (0.00%)	1 / 11 (9.09%)	
occurrences (all)	0	1	
Metabolism and nutrition disorders			
Vitamin D deficiency			
subjects affected / exposed	0 / 20 (0.00%)	1 / 11 (9.09%)	
occurrences (all)	0	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
04 March 2021	The protocol was amended in alignment with the newly identified potential risk of QT prolongation.
12 May 2021	The protocol was amended to closer monitor the new potential risk of QT prolongation.

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.

There were limitations in the dataset, given the small number of participants completing the treatment period due to early termination of the study.

Notes: