



Clinical trial results:

An exploratory, randomized, double-blind, placebo-controlled, multicenter study to evaluate the efficacy, safety, tolerability and pharmacokinetics of orally administered GLPG2737 for 52 weeks, followed by an open-label extension period of 52 weeks in subjects with autosomal dominant polycystic kidney disease

Summary

EudraCT number	2019-003521-21
Trial protocol	BE NL DE ES CZ IT
Global end of trial date	04 April 2023

Results information

Result version number	v1 (current)
This version publication date	11 April 2024
First version publication date	11 April 2024

Trial information

Trial identification

Sponsor protocol code	GLPG2737-CL-203
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04578548
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	04 April 2023
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	04 April 2023
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To characterize the effect of GLPG2737 on growth in total kidney volume (TKV) compared to placebo, safety and tolerability of oral doses of GLPG2737 compared to placebo.

Protection of trial subjects:

This study is being conducted under a US investigational new drug (IND) application and in accordance with recognized international scientific and ethical standards, including but not limited to the International Council for Harmonisation (ICH) guideline for Good Clinical Practice (GCP), and the original principles embodied in the Declaration of Helsinki. These standards are consistent with the requirements of the US Code of Federal Regulations (CFR) Title 21, Part 312 (21CFR312), and the EU Clinical Trials Directive 2001/20/EC as well as other local legislation.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	10 November 2020
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	Netherlands: 10
Country: Number of subjects enrolled	Poland: 15
Country: Number of subjects enrolled	Spain: 19
Country: Number of subjects enrolled	Belgium: 1
Country: Number of subjects enrolled	Czechia: 9
Country: Number of subjects enrolled	Germany: 1
Country: Number of subjects enrolled	Italy: 11
Worldwide total number of subjects	66
EEA total number of subjects	66

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)	66
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants with autosomal dominant polycystic kidney disease (ADPKD) were enrolled. The study was conducted at 20 sites in 7 countries i.e. Belgium, Czech Republic, Germany, Italy, Netherlands, Poland, and Spain. Of these 20 activated sites, 3 sites did not enroll any participants. 89 participants were screened, out of which 66 were randomized.

Pre-assignment

Screening details:

Participants who met protocol eligibility criteria were assigned to GLPG2737 or placebo in the double-blind (DB) treatment period and open-label extension (OLE) period. The study was prematurely terminated on 02 March 2023, due to the lack of efficacy of GLPG2737, making the expected benefit-risk balance negative.

Period 1

Period 1 title	Double-blind treatment period (52 weeks)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Carer

Arms

Are arms mutually exclusive?	Yes
Arm title	GLPG2737 During DB

Arm description:

Participants received 150 milligrams (mg) GLPG2737 capsules orally once daily for 52 weeks in the DB treatment period.

Arm type	Experimental
Investigational medicinal product name	GLPG2737
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Capsules administered orally for 52 weeks.

Arm title	Placebo During DB
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Arm description:

Participants received placebo matched to GLPG2737 capsules orally once daily for 52 weeks in the DB treatment period.

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

Dosage and administration details:

Capsules administered orally for 52 weeks.

Number of subjects in period 1	GLPG2737 During DB	Placebo During DB
Started	44	22
Completed	41	20
Not completed	3	2
Consent withdrawn by subject	1	-
Lost to follow-up	1	1
Non compliance with study drug	1	1

Period 2

Period 2 title	Open-Label treatment period (52 weeks)
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	GLPG2737 During DB + During OLE

Arm description:

Eligible participants who received GLPG2737 in DB period were rolled over to an OLE period to receive 150 mg GLPG2737 capsules orally once daily for 52 weeks.

Arm type	Experimental
Investigational medicinal product name	GLPG2737
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Capsules administered orally.

Arm title	Placebo During DB + GLPG2737 During OLE
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Arm description:

Eligible participants who received placebo in DB period were rolled over to an OLE period to receive 150 mg GLPG2737 capsules orally once daily for 52 weeks.

Arm type	Experimental
Investigational medicinal product name	GLPG2737
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Capsules administered orally

Number of subjects in period 2 ^[1]	GLPG2737 During DB + During OLE	Placebo During DB + GLPG2737 During OLE
Started	39	20
Completed	3	4
Not completed	36	16
Consent withdrawn by subject	1	-
Adverse event, non-fatal	1	1
Study terminated by sponsor	34	15

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: Not all participants who completed the DB treatment period entered the OLE treatment period

Baseline characteristics

Reporting groups

Reporting group title	GLPG2737 During DB
Reporting group description:	
Participants received 150 milligrams (mg) GLPG2737 capsules orally once daily for 52 weeks in the DB treatment period.	

Reporting group title	Placebo During DB
Reporting group description:	
Participants received placebo matched to GLPG2737 capsules orally once daily for 52 weeks in the DB treatment period.	

Reporting group values	GLPG2737 During DB	Placebo During DB	Total
Number of subjects	44	22	66
Age categorical			
Units: Subjects			

Age continuous			
Units: years			
arithmetic mean	40.6	39.6	
standard deviation	± 6.3	± 6.2	-
Gender categorical			
Units: Subjects			
Female	24	8	32
Male	20	14	34
Ethnicity (NIH/OMB)			
Units: Subjects			
Hispanic or Latino	9	2	11
Not Hispanic or Latino	35	20	55
Other	0	0	0
Race (NIH/OMB)			
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	44	22	66
More than one race	0	0	0
Unknown or Not Reported	0	0	0
Height-Adjusted Total Kidney Volume(htTKV) (n=41, 20)			
htTKV is used in participants with ADPKD disease to predict the onset of renal insufficiency. htTKV was calculated using TKV (in milliliter [mL]) obtained from magnetic resonance imaging (MRI) divided by height (in meter [m]). MRI Baseline: For MRI assessments, all non-missing values before the first study drug administration in the study +14 days (included) was considered as the primary baseline definition. Participants with MRI baseline (41 for GLPG2737 and 20 for placebo) were analyzed.			
Units: mL/m			
arithmetic mean	1069.18	1439.23	
standard deviation	± 438.06	± 737.67	-
Estimated Glomerular filtration rate			

(GFR)			
eGFR is a test that measures level of kidney function and determines your stage of kidney disease. eGFR was based on chronic kidney disease-Epidemiology (CKD-EPI) formula (2009) calculated from serum creatinine concentrations. eGFR was measured as milliliters per minute per 1.73 square meter (mL/min/1.73 m^2).			
Units: mL/min/1.73 m^2			
arithmetic mean	55.5	51.6	
standard deviation	± 16.3	± 15.6	-

End points

End points reporting groups

Reporting group title	GLPG2737 During DB
Reporting group description: Participants received 150 milligrams (mg) GLPG2737 capsules orally once daily for 52 weeks in the DB treatment period.	
Reporting group title	Placebo During DB
Reporting group description: Participants received placebo matched to GLPG2737 capsules orally once daily for 52 weeks in the DB treatment period.	
Reporting group title	GLPG2737 During DB + During OLE
Reporting group description: Eligible participants who received GLPG2737 in DB period were rolled over to an OLE period to receive 150 mg GLPG2737 capsules orally once daily for 52 weeks.	
Reporting group title	Placebo During DB + GLPG2737 During OLE
Reporting group description: Eligible participants who received placebo in DB period were rolled over to an OLE period to receive 150 mg GLPG2737 capsules orally once daily for 52 weeks.	

Primary: DB Period: Mean Percent Change From MRI Baseline in htTKV

End point title	DB Period: Mean Percent Change From MRI Baseline in htTKV
End point description: htTKV is used in participants with ADPKD disease to predict the onset of renal insufficiency. htTKV was calculated using TKV (in mL) obtained from MRI divided by height (in m). MRI Baseline: For MRI assessments, all non-missing values before the first study drug administration in the study +14 days (included) was considered as the primary baseline definition. Results were derived by mean of the individual slopes (i.e. using all MRI performed between baseline and Week 52). Full Analysis Set (FAS): All randomized participants who received at least one dose of study drug.	
End point type	Primary
End point timeframe: MRI Baseline up to Week 52	

End point values	GLPG2737 During DB	Placebo During DB		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	44	22		
Units: percent change				
geometric mean (confidence interval 95%)	8.18 (6.04 to 10.36)	9.17 (6.05 to 12.38)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Statistical analysis description: Based on a random coefficient regression model (linear slope model) on htTKV log-transformed values with time (in weeks) as a continuous variable, treatment, time-by-treatment interaction and a random	

intercept and slope. The treatment effect was determined by using estimated slopes for each treatment group on the basis of the time-by-treatment interaction term from the mixed model.

Comparison groups	GLPG2737 During DB v Placebo During DB
Number of subjects included in analysis	66
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.606
Method	Random coefficient regression model
Parameter estimate	Geometric Mean Difference
Point estimate	-0.91
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.34
upper limit	2.64

Primary: DB Period: Number of Participants with Treatment-Emergent Adverse Events (TEAEs) and Serious TEAEs

End point title	DB Period: Number of Participants with Treatment-Emergent Adverse Events (TEAEs) and Serious TEAEs ^[1]
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End point description:

AE is any untoward medical occurrence in a participant administered a study drug, and which does not necessarily have to have causal relationship with this treatment. AE can therefore be any unfavorable/unintended sign (including an abnormal laboratory finding), symptom, or disease (new or exacerbated) temporally associated with the use of study drug, whether or not considered related to it. Serious adverse event (SAE) is defined as any untoward medical occurrence that results in death, is life-threatening, requires inpatient hospitalization or prolongation of existing hospitalization, results in persistent or significant disability/incapacity, congenital anomaly/birth defect or other medically important event. TEAE is defined as AE observed after starting administration of study drug until 30 days after last DB dose or 1 day before OLE dose, whichever occurred first. Safety Analysis Set (SAS): All randomized participants who received at least one dose of study drug.

End point type	Primary
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End point timeframe:

From first dose to Week 56

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: The statistical analysis was not planned to be carried out.

End point values	GLPG2737 During DB	Placebo During DB		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	44	22		
Units: participants				
number (not applicable)				
TEAEs	44	22		
Serious TEAEs	1	3		

Statistical analyses

Secondary: DB Period: Mean Change From Baseline in eGFR

End point title	DB Period: Mean Change From Baseline in eGFR
End point description: The eGFR is a test that measures level of kidney function and determines the stage of kidney disease. eGFR was based on CKD-EPI formula (2009) calculated from serum creatinine concentrations. Results were derived by mean of the individual slopes (i.e. using data between baseline and Week 52). FAS.	
End point type	Secondary
End point timeframe: Baseline up to Week 52	

End point values	GLPG2737 During DB	Placebo During DB		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	44	22		
Units: mL/min/1.73m ²				
least squares mean (confidence interval 95%)	-5.44 (-7.34 to -3.54)	-3.13 (-5.87 to -0.39)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Statistical analysis description: Least-squares mean difference (95% CI) from a random coefficient regression model (linear slope model) on eGFR values with time (in weeks) as a continuous variable, the time-by-treatment interaction and a random intercept and slope. The treatment effect was determined by using estimated slopes for each treatment group on the basis of the time-by-treatment interaction term from the mixed model.	
Comparison groups	GLPG2737 During DB v Placebo During DB
Number of subjects included in analysis	66
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.171
Method	Random coefficient regression model
Parameter estimate	Least-squares mean difference
Point estimate	-2.31
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.64
upper limit	1.02

Secondary: DB Period: Area Under the Plasma Concentration-Time Curve During a Dosing Interval (AUC_{tau}) of GLPG2737 and its metabolite

End point title	DB Period: Area Under the Plasma Concentration-Time Curve
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End point description:

AUC0-tau described the area under the curve limited to the end of a dosing interval. The metabolite of GLPG2737 is M4. Pharmacokinetic Analysis Set (PKAS): All randomized participants who received at least one dose of study drug for which plasma concentration data was available to facilitate development of the Population PK model and for whom the time of the dose on the days of PK sampling was known.

End point type Secondary

End point timeframe:

Predose (within 30 minutes prior to dosing), 1, 1.5, 2, 3, 4, 5, 6, 7 hours post dose through Week 52

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: For PK analysis only the GLPG2737 arm was analyzed.

End point values	GLPG2737 During DB			
Subject group type	Reporting group			
Number of subjects analysed	44			
Units: nanogram* hour per milliliter (ng*h/mL)				
geometric mean (confidence interval 95%)				
GLPG2737	18500 (17500 to 19500)			
Metabolite M4	18700 (17400 to 20200)			

Statistical analyses

No statistical analyses for this end point

Secondary: DB Period: Maximum Observed Plasma Concentration (Cmax) of GLPG2737 and its metabolite

End point title DB Period: Maximum Observed Plasma Concentration (Cmax) of GLPG2737 and its metabolite^[3]

End point description:

Cmax is the maximum observed plasma concentration of the drug. The metabolite of GLPG2737 is M4. PKAS.

End point type Secondary

End point timeframe:

Predose (within 30 minutes prior to dosing), 1, 1.5, 2, 3, 4, 5, 6, 7 hours post dose through Week 52

Notes:

[3] - 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: For PK analysis only the GLPG2737 arm was analyzed.

End point values	GLPG2737 During DB			
Subject group type	Reporting group			
Number of subjects analysed	44			
Units: ng/mL				
geometric mean (confidence interval 95%)				

GLPG2737	1160 (1110 to 1220)			
Metabolite M4	873 (813 to 939)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

DB Period: From first dose to Week 56

OLE Period: From first dose to Week 56

Adverse event reporting additional description:

DB Period: SAS.

OLE Period: All OLE enrolled participants who received one dose of study drug during the OLE period.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	25.1
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Reporting groups

Reporting group title	GLPG2737 During DB + During OLE
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Reporting group description:

Participants received 150 mg GLPG2737 capsules orally once daily for 52 weeks in the DB treatment period. Eligible participants were rolled over to an OLE period to receive 150 mg GLPG2737 capsules orally once daily for 52 weeks.

Reporting group title	Placebo During DB + GLPG2737 During OLE
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Reporting group description:

Eligible participants from Placebo DB were rolled over to an OLE period to receive 150 mg GLPG2737 capsules orally once daily for 52 weeks.

Reporting group title	Placebo During DB
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Reporting group description:

Participants received placebo matched to GLPG2737 capsules orally once daily for 52 weeks in the DB treatment period.

Serious adverse events	GLPG2737 During DB + During OLE	Placebo During DB + GLPG2737 During OLE	Placebo During DB
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 44 (6.82%)	2 / 20 (10.00%)	3 / 22 (13.64%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Lung neoplasm malignant			
subjects affected / exposed	1 / 44 (2.27%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Uterine leiomyoma			

subjects affected / exposed	0 / 44 (0.00%)	0 / 20 (0.00%)	1 / 22 (4.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Hypertensive emergency			
subjects affected / exposed	0 / 44 (0.00%)	0 / 20 (0.00%)	1 / 22 (4.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Ventricular extrasystoles			
subjects affected / exposed	0 / 44 (0.00%)	0 / 20 (0.00%)	1 / 22 (4.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Cyst rupture			
subjects affected / exposed	0 / 44 (0.00%)	1 / 20 (5.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	1 / 44 (2.27%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Renal cyst			
subjects affected / exposed	0 / 44 (0.00%)	1 / 20 (5.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Hepatic cyst infection			
subjects affected / exposed	1 / 44 (2.27%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal abscess			

subjects affected / exposed	0 / 44 (0.00%)	0 / 20 (0.00%)	1 / 22 (4.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal cyst infection			
subjects affected / exposed	1 / 44 (2.27%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	GLPG2737 During DB + During OLE	Placebo During DB + GLPG2737 During OLE	Placebo During DB
Total subjects affected by non-serious adverse events			
subjects affected / exposed	44 / 44 (100.00%)	15 / 20 (75.00%)	22 / 22 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Uterine leiomyoma			
subjects affected / exposed	0 / 44 (0.00%)	0 / 20 (0.00%)	1 / 22 (4.55%)
occurrences (all)	0	0	2
Vascular disorders			
Hypertension			
subjects affected / exposed	13 / 44 (29.55%)	0 / 20 (0.00%)	4 / 22 (18.18%)
occurrences (all)	16	0	4
Hypotension			
subjects affected / exposed	1 / 44 (2.27%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Orthostatic hypotension			
subjects affected / exposed	1 / 44 (2.27%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Raynaud's phenomenon			
subjects affected / exposed	1 / 44 (2.27%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Pregnancy, puerperium and perinatal conditions			
Pregnancy			
subjects affected / exposed	1 / 44 (2.27%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0

General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	2 / 44 (4.55%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences (all)	4	0	0
Asthenia			
subjects affected / exposed	3 / 44 (6.82%)	0 / 20 (0.00%)	3 / 22 (13.64%)
occurrences (all)	3	0	3
Malaise			
subjects affected / exposed	2 / 44 (4.55%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences (all)	2	0	0
Injection site pain			
subjects affected / exposed	1 / 44 (2.27%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Oedema mucosal			
subjects affected / exposed	1 / 44 (2.27%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Oedema peripheral			
subjects affected / exposed	3 / 44 (6.82%)	0 / 20 (0.00%)	1 / 22 (4.55%)
occurrences (all)	4	0	2
Peripheral swelling			
subjects affected / exposed	1 / 44 (2.27%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences (all)	2	0	0
Pyrexia			
subjects affected / exposed	6 / 44 (13.64%)	0 / 20 (0.00%)	2 / 22 (9.09%)
occurrences (all)	10	0	3
Thirst			
subjects affected / exposed	1 / 44 (2.27%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Vaccination site pain			
subjects affected / exposed	1 / 44 (2.27%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Discomfort			
subjects affected / exposed	1 / 44 (2.27%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Drug intolerance			

subjects affected / exposed	1 / 44 (2.27%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Fatigue			
subjects affected / exposed	5 / 44 (11.36%)	0 / 20 (0.00%)	3 / 22 (13.64%)
occurrences (all)	6	0	4
Hyperthermia			
subjects affected / exposed	1 / 44 (2.27%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Influenza like illness			
subjects affected / exposed	1 / 44 (2.27%)	0 / 20 (0.00%)	1 / 22 (4.55%)
occurrences (all)	1	0	1
Non-cardiac chest pain			
subjects affected / exposed	1 / 44 (2.27%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	1 / 44 (2.27%)	1 / 20 (5.00%)	1 / 22 (4.55%)
occurrences (all)	1	1	1
Rubber sensitivity			
subjects affected / exposed	1 / 44 (2.27%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Seasonal allergy			
subjects affected / exposed	2 / 44 (4.55%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences (all)	3	0	0
Reproductive system and breast disorders			
Amenorrhoea			
subjects affected / exposed	1 / 44 (2.27%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Dysmenorrhoea			
subjects affected / exposed	1 / 44 (2.27%)	0 / 20 (0.00%)	1 / 22 (4.55%)
occurrences (all)	1	0	1
Erectile dysfunction			
subjects affected / exposed	1 / 44 (2.27%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Heavy menstrual bleeding			

subjects affected / exposed	1 / 44 (2.27%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Prostatitis			
subjects affected / exposed	1 / 44 (2.27%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Ovarian cyst			
subjects affected / exposed	1 / 44 (2.27%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain			
subjects affected / exposed	8 / 44 (18.18%)	1 / 20 (5.00%)	2 / 22 (9.09%)
occurrences (all)	11	1	3
Chronic obstructive pulmonary disease			
subjects affected / exposed	1 / 44 (2.27%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Cough			
subjects affected / exposed	3 / 44 (6.82%)	1 / 20 (5.00%)	3 / 22 (13.64%)
occurrences (all)	4	1	3
Dyspnoea			
subjects affected / exposed	0 / 44 (0.00%)	0 / 20 (0.00%)	1 / 22 (4.55%)
occurrences (all)	0	0	1
Epistaxis			
subjects affected / exposed	0 / 44 (0.00%)	0 / 20 (0.00%)	2 / 22 (9.09%)
occurrences (all)	0	0	2
Mediastinal cyst			
subjects affected / exposed	0 / 44 (0.00%)	0 / 20 (0.00%)	1 / 22 (4.55%)
occurrences (all)	0	0	1
Rhinitis allergic			
subjects affected / exposed	1 / 44 (2.27%)	0 / 20 (0.00%)	1 / 22 (4.55%)
occurrences (all)	1	0	1
Rhinorrhoea			
subjects affected / exposed	2 / 44 (4.55%)	0 / 20 (0.00%)	3 / 22 (13.64%)
occurrences (all)	2	0	3
Psychiatric disorders			

Stress			
subjects affected / exposed	0 / 44 (0.00%)	0 / 20 (0.00%)	1 / 22 (4.55%)
occurrences (all)	0	0	1
Anxiety			
subjects affected / exposed	1 / 44 (2.27%)	0 / 20 (0.00%)	1 / 22 (4.55%)
occurrences (all)	1	0	1
Insomnia			
subjects affected / exposed	1 / 44 (2.27%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Panic attack			
subjects affected / exposed	1 / 44 (2.27%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Investigations			
Amylase increased			
subjects affected / exposed	1 / 44 (2.27%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Aortic bruit			
subjects affected / exposed	1 / 44 (2.27%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Blood pressure increased			
subjects affected / exposed	0 / 44 (0.00%)	0 / 20 (0.00%)	1 / 22 (4.55%)
occurrences (all)	0	0	1
Lipase increased			
subjects affected / exposed	1 / 44 (2.27%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	1 / 44 (2.27%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences (all)	2	0	0
Arthropod bite			
subjects affected / exposed	1 / 44 (2.27%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Arthropod sting			
subjects affected / exposed	1 / 44 (2.27%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Chillblains			

subjects affected / exposed	0 / 44 (0.00%)	0 / 20 (0.00%)	1 / 22 (4.55%)
occurrences (all)	0	0	1
Clavicle fracture			
subjects affected / exposed	0 / 44 (0.00%)	0 / 20 (0.00%)	1 / 22 (4.55%)
occurrences (all)	0	0	1
Fall			
subjects affected / exposed	0 / 44 (0.00%)	0 / 20 (0.00%)	2 / 22 (9.09%)
occurrences (all)	0	0	2
Ligament sprain			
subjects affected / exposed	1 / 44 (2.27%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Limb fracture			
subjects affected / exposed	0 / 44 (0.00%)	0 / 20 (0.00%)	1 / 22 (4.55%)
occurrences (all)	0	0	1
Limb injury			
subjects affected / exposed	0 / 44 (0.00%)	1 / 20 (5.00%)	0 / 22 (0.00%)
occurrences (all)	0	1	0
Muscle strain			
subjects affected / exposed	1 / 44 (2.27%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Post procedural hemorrhage			
subjects affected / exposed	1 / 44 (2.27%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Post vaccination syndrome			
subjects affected / exposed	0 / 44 (0.00%)	0 / 20 (0.00%)	2 / 22 (9.09%)
occurrences (all)	0	0	3
Post-traumatic pain			
subjects affected / exposed	0 / 44 (0.00%)	0 / 20 (0.00%)	2 / 22 (9.09%)
occurrences (all)	0	0	2
Skin abrasion			
subjects affected / exposed	0 / 44 (0.00%)	0 / 20 (0.00%)	1 / 22 (4.55%)
occurrences (all)	0	0	1
Traumatic renal injury			
subjects affected / exposed	0 / 44 (0.00%)	0 / 20 (0.00%)	1 / 22 (4.55%)
occurrences (all)	0	0	1
Vaccination complication			

subjects affected / exposed	4 / 44 (9.09%)	0 / 20 (0.00%)	1 / 22 (4.55%)
occurrences (all)	9	0	1
Haematuria traumatic			
subjects affected / exposed	0 / 44 (0.00%)	0 / 20 (0.00%)	2 / 22 (9.09%)
occurrences (all)	0	0	2
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	1 / 44 (2.27%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences (all)	2	0	0
Ventricular extrasystoles			
subjects affected / exposed	1 / 44 (2.27%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Defect conduction intraventricular			
subjects affected / exposed	1 / 44 (2.27%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Palpitations			
subjects affected / exposed	2 / 44 (4.55%)	0 / 20 (0.00%)	1 / 22 (4.55%)
occurrences (all)	3	0	1
Supraventricular tachycardia			
subjects affected / exposed	1 / 44 (2.27%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Tachycardia			
subjects affected / exposed	0 / 44 (0.00%)	0 / 20 (0.00%)	1 / 22 (4.55%)
occurrences (all)	0	0	1
Bradycardia			
subjects affected / exposed	0 / 44 (0.00%)	0 / 20 (0.00%)	1 / 22 (4.55%)
occurrences (all)	0	0	1
Nervous system disorders			
Cerebellar infarction			
subjects affected / exposed	1 / 44 (2.27%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Dizziness			
subjects affected / exposed	4 / 44 (9.09%)	0 / 20 (0.00%)	1 / 22 (4.55%)
occurrences (all)	5	0	1
Headache			

subjects affected / exposed	11 / 44 (25.00%)	0 / 20 (0.00%)	8 / 22 (36.36%)
occurrences (all)	44	0	18
Hypoaesthesia			
subjects affected / exposed	1 / 44 (2.27%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Paraesthesia			
subjects affected / exposed	1 / 44 (2.27%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Sciatica			
subjects affected / exposed	1 / 44 (2.27%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 44 (2.27%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Lymphopenia			
subjects affected / exposed	1 / 44 (2.27%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Iron deficiency anaemia			
subjects affected / exposed	2 / 44 (4.55%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences (all)	2	0	0
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	2 / 44 (4.55%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences (all)	2	0	0
Tinnitus			
subjects affected / exposed	1 / 44 (2.27%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Eye disorders			
Blepharospasm			
subjects affected / exposed	1 / 44 (2.27%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Conjunctival haemorrhage			
subjects affected / exposed	0 / 44 (0.00%)	0 / 20 (0.00%)	1 / 22 (4.55%)
occurrences (all)	0	0	1
Gastrointestinal disorders			

Gingival swelling			
subjects affected / exposed	1 / 44 (2.27%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Abdominal discomfort			
subjects affected / exposed	1 / 44 (2.27%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Abdominal distension			
subjects affected / exposed	1 / 44 (2.27%)	0 / 20 (0.00%)	1 / 22 (4.55%)
occurrences (all)	1	0	1
Abdominal pain			
subjects affected / exposed	3 / 44 (6.82%)	0 / 20 (0.00%)	2 / 22 (9.09%)
occurrences (all)	7	0	6
Abdominal pain lower			
subjects affected / exposed	1 / 44 (2.27%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Abdominal pain upper			
subjects affected / exposed	3 / 44 (6.82%)	0 / 20 (0.00%)	3 / 22 (13.64%)
occurrences (all)	5	0	3
Chronic gastritis			
subjects affected / exposed	1 / 44 (2.27%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Constipation			
subjects affected / exposed	1 / 44 (2.27%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Diarrhoea			
subjects affected / exposed	4 / 44 (9.09%)	1 / 20 (5.00%)	2 / 22 (9.09%)
occurrences (all)	6	1	3
Dry mouth			
subjects affected / exposed	11 / 44 (25.00%)	1 / 20 (5.00%)	1 / 22 (4.55%)
occurrences (all)	21	1	1
Dyspepsia			
subjects affected / exposed	5 / 44 (11.36%)	0 / 20 (0.00%)	1 / 22 (4.55%)
occurrences (all)	5	0	2
Flatulence			
subjects affected / exposed	1 / 44 (2.27%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0

Gastritis			
subjects affected / exposed	0 / 44 (0.00%)	1 / 20 (5.00%)	2 / 22 (9.09%)
occurrences (all)	0	2	2
Gastrooesophageal reflux disease			
subjects affected / exposed	3 / 44 (6.82%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences (all)	7	0	0
Hiatus hernia			
subjects affected / exposed	1 / 44 (2.27%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Nausea			
subjects affected / exposed	1 / 44 (2.27%)	0 / 20 (0.00%)	2 / 22 (9.09%)
occurrences (all)	1	0	4
Odynophagia			
subjects affected / exposed	0 / 44 (0.00%)	0 / 20 (0.00%)	1 / 22 (4.55%)
occurrences (all)	0	0	2
Oesophageal pain			
subjects affected / exposed	1 / 44 (2.27%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Stomatitis			
subjects affected / exposed	1 / 44 (2.27%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Toothache			
subjects affected / exposed	4 / 44 (9.09%)	1 / 20 (5.00%)	2 / 22 (9.09%)
occurrences (all)	8	1	2
Umbilical hernia			
subjects affected / exposed	1 / 44 (2.27%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Vomiting			
subjects affected / exposed	1 / 44 (2.27%)	0 / 20 (0.00%)	1 / 22 (4.55%)
occurrences (all)	1	0	1
Lip dry			
subjects affected / exposed	1 / 44 (2.27%)	0 / 20 (0.00%)	1 / 22 (4.55%)
occurrences (all)	1	0	1
Hepatobiliary disorders			
Gallbladder polyp			

subjects affected / exposed occurrences (all)	0 / 44 (0.00%) 0	0 / 20 (0.00%) 0	1 / 22 (4.55%) 1
Hepatic cyst subjects affected / exposed occurrences (all)	1 / 44 (2.27%) 1	0 / 20 (0.00%) 0	0 / 22 (0.00%) 0
Skin and subcutaneous tissue disorders			
Dry skin subjects affected / exposed occurrences (all)	1 / 44 (2.27%) 1	0 / 20 (0.00%) 0	1 / 22 (4.55%) 1
Hair texture abnormal subjects affected / exposed occurrences (all)	1 / 44 (2.27%) 1	0 / 20 (0.00%) 0	0 / 22 (0.00%) 0
Pruritus subjects affected / exposed occurrences (all)	2 / 44 (4.55%) 2	0 / 20 (0.00%) 0	0 / 22 (0.00%) 0
Rash subjects affected / exposed occurrences (all)	2 / 44 (4.55%) 2	0 / 20 (0.00%) 0	0 / 22 (0.00%) 0
Skin depigmentation subjects affected / exposed occurrences (all)	1 / 44 (2.27%) 1	0 / 20 (0.00%) 0	0 / 22 (0.00%) 0
Skin mass subjects affected / exposed occurrences (all)	0 / 44 (0.00%) 0	0 / 20 (0.00%) 0	1 / 22 (4.55%) 1
Renal and urinary disorders			
Renal cyst ruptured subjects affected / exposed occurrences (all)	1 / 44 (2.27%) 2	0 / 20 (0.00%) 0	1 / 22 (4.55%) 1
Albuminuria subjects affected / exposed occurrences (all)	1 / 44 (2.27%) 1	0 / 20 (0.00%) 0	0 / 22 (0.00%) 0
Dysuria subjects affected / exposed occurrences (all)	1 / 44 (2.27%) 1	0 / 20 (0.00%) 0	0 / 22 (0.00%) 0
Haematuria			

subjects affected / exposed	4 / 44 (9.09%)	0 / 20 (0.00%)	1 / 22 (4.55%)
occurrences (all)	11	0	1
Micturition urgency			
subjects affected / exposed	1 / 44 (2.27%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Nephrolithiasis			
subjects affected / exposed	0 / 44 (0.00%)	0 / 20 (0.00%)	1 / 22 (4.55%)
occurrences (all)	0	0	2
Renal cyst			
subjects affected / exposed	0 / 44 (0.00%)	1 / 20 (5.00%)	0 / 22 (0.00%)
occurrences (all)	0	1	0
Renal cyst haemorrhage			
subjects affected / exposed	1 / 44 (2.27%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences (all)	2	0	0
Renal impairment			
subjects affected / exposed	4 / 44 (9.09%)	2 / 20 (10.00%)	2 / 22 (9.09%)
occurrences (all)	4	2	2
Renal pain			
subjects affected / exposed	8 / 44 (18.18%)	2 / 20 (10.00%)	6 / 22 (27.27%)
occurrences (all)	15	2	19
Renal injury			
subjects affected / exposed	0 / 44 (0.00%)	0 / 20 (0.00%)	1 / 22 (4.55%)
occurrences (all)	0	0	1
Endocrine disorders			
Goitre			
subjects affected / exposed	0 / 44 (0.00%)	0 / 20 (0.00%)	1 / 22 (4.55%)
occurrences (all)	0	0	1
Hyperparathyroidism secondary			
subjects affected / exposed	1 / 44 (2.27%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal and connective tissue disorders			
Plantar fasciitis			
subjects affected / exposed	0 / 44 (0.00%)	1 / 20 (5.00%)	1 / 22 (4.55%)
occurrences (all)	0	1	1
Arthralgia			

subjects affected / exposed	3 / 44 (6.82%)	0 / 20 (0.00%)	2 / 22 (9.09%)
occurrences (all)	5	0	2
Back pain			
subjects affected / exposed	8 / 44 (18.18%)	0 / 20 (0.00%)	4 / 22 (18.18%)
occurrences (all)	10	0	9
Flank pain			
subjects affected / exposed	3 / 44 (6.82%)	0 / 20 (0.00%)	2 / 22 (9.09%)
occurrences (all)	6	0	3
Limb discomfort			
subjects affected / exposed	1 / 44 (2.27%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Muscle spasms			
subjects affected / exposed	1 / 44 (2.27%)	0 / 20 (0.00%)	1 / 22 (4.55%)
occurrences (all)	1	0	1
Musculoskeletal chest pain			
subjects affected / exposed	2 / 44 (4.55%)	0 / 20 (0.00%)	2 / 22 (9.09%)
occurrences (all)	5	0	2
Myalgia			
subjects affected / exposed	2 / 44 (4.55%)	0 / 20 (0.00%)	1 / 22 (4.55%)
occurrences (all)	2	0	1
Neck pain			
subjects affected / exposed	1 / 44 (2.27%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Pain in extremity			
subjects affected / exposed	3 / 44 (6.82%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences (all)	3	0	0
Rotator cuff syndrome			
subjects affected / exposed	2 / 44 (4.55%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences (all)	2	0	0
Tendonitis			
subjects affected / exposed	2 / 44 (4.55%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences (all)	2	0	0
Infections and infestations			
Acarodermatitis			
subjects affected / exposed	1 / 44 (2.27%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0

Abdominal infection			
subjects affected / exposed	0 / 44 (0.00%)	0 / 20 (0.00%)	1 / 22 (4.55%)
occurrences (all)	0	0	1
Bacterial vulvovaginitis			
subjects affected / exposed	1 / 44 (2.27%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Bronchitis			
subjects affected / exposed	4 / 44 (9.09%)	2 / 20 (10.00%)	1 / 22 (4.55%)
occurrences (all)	4	2	1
COVID-19			
subjects affected / exposed	21 / 44 (47.73%)	1 / 20 (5.00%)	5 / 22 (22.73%)
occurrences (all)	25	1	5
Cystitis			
subjects affected / exposed	1 / 44 (2.27%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences (all)	2	0	0
Ear infection			
subjects affected / exposed	0 / 44 (0.00%)	0 / 20 (0.00%)	1 / 22 (4.55%)
occurrences (all)	0	0	1
Folliculitis			
subjects affected / exposed	1 / 44 (2.27%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Gardnerella infection			
subjects affected / exposed	1 / 44 (2.27%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Gastric infection			
subjects affected / exposed	1 / 44 (2.27%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Gastroenteritis			
subjects affected / exposed	3 / 44 (6.82%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences (all)	3	0	0
Gastroenteritis viral			
subjects affected / exposed	2 / 44 (4.55%)	0 / 20 (0.00%)	1 / 22 (4.55%)
occurrences (all)	2	0	1
Gastrointestinal infection			
subjects affected / exposed	0 / 44 (0.00%)	0 / 20 (0.00%)	1 / 22 (4.55%)
occurrences (all)	0	0	1

Helicobacter gastritis			
subjects affected / exposed	1 / 44 (2.27%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Hepatic cyst infection			
subjects affected / exposed	1 / 44 (2.27%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences (all)	2	0	0
Hordeolum			
subjects affected / exposed	0 / 44 (0.00%)	0 / 20 (0.00%)	1 / 22 (4.55%)
occurrences (all)	0	0	1
Influenza			
subjects affected / exposed	8 / 44 (18.18%)	1 / 20 (5.00%)	2 / 22 (9.09%)
occurrences (all)	10	1	3
Lower respiratory tract infection			
subjects affected / exposed	1 / 44 (2.27%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Nasopharyngitis			
subjects affected / exposed	10 / 44 (22.73%)	2 / 20 (10.00%)	5 / 22 (22.73%)
occurrences (all)	16	2	7
Norovirus infection			
subjects affected / exposed	1 / 44 (2.27%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Oral herpes			
subjects affected / exposed	2 / 44 (4.55%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences (all)	3	0	0
Otitis externa			
subjects affected / exposed	1 / 44 (2.27%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Otitis media			
subjects affected / exposed	1 / 44 (2.27%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Peritonsillar abscess			
subjects affected / exposed	1 / 44 (2.27%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Pharyngitis			
subjects affected / exposed	1 / 44 (2.27%)	1 / 20 (5.00%)	0 / 22 (0.00%)
occurrences (all)	1	1	0

Phlebitis infective			
subjects affected / exposed	1 / 44 (2.27%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Renal cyst infection			
subjects affected / exposed	1 / 44 (2.27%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences (all)	2	0	0
Rhinitis			
subjects affected / exposed	0 / 44 (0.00%)	0 / 20 (0.00%)	1 / 22 (4.55%)
occurrences (all)	0	0	1
Sinusitis			
subjects affected / exposed	3 / 44 (6.82%)	0 / 20 (0.00%)	1 / 22 (4.55%)
occurrences (all)	3	0	1
Tonsillitis			
subjects affected / exposed	2 / 44 (4.55%)	1 / 20 (5.00%)	1 / 22 (4.55%)
occurrences (all)	2	1	1
Tooth abscess			
subjects affected / exposed	2 / 44 (4.55%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences (all)	3	0	0
Upper respiratory tract infection			
subjects affected / exposed	5 / 44 (11.36%)	5 / 20 (25.00%)	3 / 22 (13.64%)
occurrences (all)	8	6	3
Urinary tract infection			
subjects affected / exposed	1 / 44 (2.27%)	0 / 20 (0.00%)	2 / 22 (9.09%)
occurrences (all)	1	0	2
Viral infection			
subjects affected / exposed	1 / 44 (2.27%)	0 / 20 (0.00%)	1 / 22 (4.55%)
occurrences (all)	1	0	1
Wound infection			
subjects affected / exposed	1 / 44 (2.27%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Otitis media acute			
subjects affected / exposed	1 / 44 (2.27%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Metabolism and nutrition disorders			
Dyslipidaemia			

subjects affected / exposed	1 / 44 (2.27%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Gout			
subjects affected / exposed	1 / 44 (2.27%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Hypercholesterolaemia			
subjects affected / exposed	1 / 44 (2.27%)	0 / 20 (0.00%)	1 / 22 (4.55%)
occurrences (all)	1	0	1
Hyperkalaemia			
subjects affected / exposed	2 / 44 (4.55%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences (all)	2	0	0
Hyperlipasaemia			
subjects affected / exposed	1 / 44 (2.27%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Hypertriglyceridaemia			
subjects affected / exposed	1 / 44 (2.27%)	0 / 20 (0.00%)	1 / 22 (4.55%)
occurrences (all)	1	0	2
Hyperuricaemia			
subjects affected / exposed	4 / 44 (9.09%)	0 / 20 (0.00%)	1 / 22 (4.55%)
occurrences (all)	4	0	1
Hypokalaemia			
subjects affected / exposed	1 / 44 (2.27%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Metabolic acidosis			
subjects affected / exposed	0 / 44 (0.00%)	1 / 20 (5.00%)	0 / 22 (0.00%)
occurrences (all)	0	1	0
Polydipsia			
subjects affected / exposed	1 / 44 (2.27%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
18 December 2019	Clarification of prohibited medication was added.
11 February 2020	Update of CSP in order to extend treatment period from 24 weeks to 52 weeks.
25 June 2020	Change in contraceptive language, mitigation on the SARS-CoV-2 pandemic, updated wording related to IDMC, collection and storage of biological samples.
13 August 2021	Incorporation of an open label extension period, removal of the interim analysis in combination with a change in the composition from iDMC to DMC, clarification on vaccinations including covid vaccination, and operational changes (including update of timing of MRI assessments).
20 December 2021	The CSP was updated to change the composition of the DMC by removing the sponsor's representative to create a fully independent DMC.

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.

The early termination was decided due to the lack of efficacy of GLPG2737, making the expected benefit-risk balance negative.

Notes: