Clinical trial results:
Efficacy and safety of 3 doses of S201086/GLPG1972 administered orally once daily in patients with knee osteoarthritis. A 52-week international, multi-regional, multi-centre, randomised, double-blind, placebo-controlled, dose-ranging study.
ROCCELLA Study

Summary

EudraCT number	2017-004581-10
Trial protocol	ES HU DK PL BG
Global end of trial date	14 July 2020

Results information

Result version number	v1 (current)
This version publication date	06 May 2021
First version publication date	06 May 2021

Trial information

Trial identification

Sponsor protocol code	CL2-201086-002

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03595618
WHO universal trial number (UTN)	U1111-1205-0321

Notes:

Sponsors

Sponsor organisation name	Institut de Recherches Internationales Servier
Sponsor organisation address	50 rue Carnot, Suresnes, France, 92284
Public contact	Neuro-ImmunoInflammation Therapeutic Area, Institut de Recherches Internationales Servier, +33 1 55 72 70 63, clinicaltrials@servier.com
Scientific contact	Neuro-ImmunoInflammation Therapeutic Area, Institut de Recherches Internationales Servier, +33 1 55 72 70 63, clinicaltrials@servier.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	14 July 2020
Is this the analysis of the primary completion data?	Yes
Primary completion date	14 July 2020
Global end of trial reached?	Yes
Global end of trial date	14 July 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To demonstrate the efficacy of at least one dose (among 3 doses) of S201086 compared to placebo after 52 weeks of treatment in reducing cartilage loss measured by cartilage thickness using quantitative magnetic resonance imaging (qMRI) of the central medial tibiofemoral compartment (cMTFC) of the target knee.

Protection of trial subjects:

This study was conducted in accordance with Good Clinical Practice standards, ethical principles stated in the Declaration of Helsinki and applicable regulatory requirements. After the subject has ended his/her participation in the trial, the investigator provided appropriate medication and/or arranged access to appropriate care for the patient.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	14 August 2018
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	Argentina: 67
Country: Number of subjects enrolled	Brazil: 139
Country: Number of subjects enrolled	Canada: 64
Country: Number of subjects enrolled	Japan: 67
Country: Number of subjects enrolled	Korea, Republic of: 31
Country: Number of subjects enrolled	Russian Federation: 38
Country: Number of subjects enrolled	Taiwan: 16
Country: Number of subjects enrolled	United States: 326
Country: Number of subjects enrolled	Denmark: 74
Country: Number of subjects enrolled	Hungary: 32
Country: Number of subjects enrolled	Poland: 52
Country: Number of subjects enrolled	Spain: 26
Worldwide total number of subjects	932
EEA total number of subjects	184

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)	503
From 65 to 84 years	429
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Male or female patients aged from 40 to 75 years with history of knee pain for at least 6 months and on the majority of days (> 50%) during the preceding month, symptom severity defined by a pain ≥ 40 mm and ≤ 90 mm on a 100 mm VAS, diagnosed for knee OA based on clinical and radiological criteria of the American College of Rheumatology.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	S201086/GLPG1972 75mg

Arm description: -

Arm type	Experimental
Investigational medicinal product name	S201086/GLPG1972
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

-S201086/GLPG1972 75 mg/day: From the day of inclusion until the W052 visit, the patient had to take 4 tablets orally once a day with a glass of water preferably in the morning (at the same time), corresponding to 1 tablet of 75 mg + 3 matching tablets of placebo.

Arm title	S201086/GLPG1972 150mg

Arm description: -

Arm type	Experimental
Investigational medicinal product name	S201086/GLPG1972
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

-S201086/GLPG1972 150 mg/day: From the day of inclusion until the W052 visit, the patient had to take 4 tablets orally once a day with a glass of water preferably in the morning (at the same time), corresponding to 2 tablets of 75 mg + 2 matching tablets of placebo.

Arm title	S201086/GLPG1972 300mg

Arm description: -

Arm type	Experimental
Investigational medicinal product name	S201086/GLPG1972
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

-S201086/GLPG1972 300 mg/day: From the day of inclusion until the W052 visit, the patient had to take 4 tablets orally once a day with a glass of water preferably in the morning (at the same time), corresponding to 4 tablets of 75 mg.

Arm title	Placebo
Arm description: -	
Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Placebo: From the day of inclusion until the W052 visit, the patient had to take 4 tablets orally once a day with a glass of water preferably in the morning (at the same time), corresponding to 4 matching tablets of placebo.

Number of subjects in period 1	S201086/GLPG1972 75mg	S201086/GLPG1972 150mg	S201086/GLPG1972 300mg
Started	234	231	233
Completed	191	191	177
Not completed	43	40	56
Adverse event, serious fatal	-	1	-
Consent withdrawn by subject	12	14	14
Physician decision	-	-	1
Adverse event, non-fatal	16	16	20
Other	7	5	10
Lost to follow-up	6	4	5
Protocol deviation	2	-	6

Number of subjects in period 1	Placebo
Started	234
Completed	200
Not completed	34
Adverse event, serious fatal	-
Consent withdrawn by subject	10
Physician decision	2
Adverse event, non-fatal	8
Other	6
Lost to follow-up	6
Protocol deviation	2

Baseline characteristics

Reporting groups	
Reporting group title	S201086/GLPG1972 75mg
Reporting group description: -	
Reporting group title	S201086/GLPG1972 150mg
Reporting group description: -	
Reporting group title	S201086/GLPG1972 300mg
Reporting group description: -	
Reporting group title	Placebo
Reporting group description: -	

Reporting group values	S201086/GLPG1972 75mg	S201086/GLPG1972 150mg	S201086/GLPG1972 300mg
Number of subjects	234	231	233
Age categorical Units: Subjects			
Adults (18-64 years)	125	125	130
From 65-84 years	109	106	103
Age continuous Units: years			
arithmetic mean	62.9	63.2	62.1
standard deviation	± 7.5	± 7.2	± 7.4
Gender categorical Units: Subjects			
Female	164	165	154
Male	70	66	79

Reporting group values	Placebo	Total	
Number of subjects	234	932	
Age categorical Units: Subjects			
Adults (18-64 years)	123	503	
From 65-84 years	111	429	
Age continuous Units: years			
arithmetic mean	63.3		
standard deviation	± 7.1	-	
Gender categorical Units: Subjects			
Female	163	646	
Male	71	286	

End points

End points reporting groups

Reporting group title	S201086/GLPG1972 75mg
Reporting group description: -	
Reporting group title	S201086/GLPG1972 150mg
Reporting group description: -	
Reporting group title	S201086/GLPG1972 300mg
Reporting group description: -	
Reporting group title	Placebo
Reporting group description: -	

Primary: Change from baseline to W052 in cartilage thickness of the central medial tibiofemoral compartment of the target knee by using qMRI (mm)

End point title	Change from baseline to W052 in cartilage thickness of the central medial tibiofemoral compartment of the target knee by using qMRI (mm)

End point description:

End point type	Primary

End point timeframe:

The cartilage thickness was measured at baseline (before inclusion), at the W028 and W052 visits, and at the WD if the time window between WD and the previous qMRI (W000 or W028) was ≥ 2 months .

End point values	S201086/GLPG 1972 75mg	S201086/GLPG 1972 150mg	S201086/GLPG 1972 300mg	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	234[1]	231[2]	233[3]	234[4]
Units: No unit				
arithmetic mean (standard deviation)	-0.06791 (± 0.20169)	-0.09693 (± 0.26839)	-0.08545 (± 0.21697)	-0.11562 (± 0.27275)

Notes:

[1] - Arithmetic mean is based on 162 patients with measured value at baseline and W52

[2] - Arithmetic mean is based on 158 patients with measured value at baseline and W52

[3] - Arithmetic mean is based on 151 patients with measured value at baseline and W52

[4] - Arithmetic mean is based on 172 patients with measured value at baseline and W52

Statistical analyses

Statistical analysis title	S201086/GLPG1972 75mg minus placebo
Comparison groups	S201086/GLPG1972 75mg v Placebo
Number of subjects included in analysis	468
Analysis specification	Pre-specified
Analysis type	superiority[5]
P-value	= 0.165
Method	Mixed-effects model for repeated measure
Parameter estimate	Adjusted mean difference
Point estimate	0.04514

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.00317
upper limit	0.09345
Variability estimate	Standard error of the mean
Dispersion value	0.02465

Notes:

[5] - Estimate of the adjusted difference from baseline to last post baseline value between treatment groups means: each S201086/GLPG1972 dose regimen minus placebo using a MMRM including the fixed, categorical effects of treatment, region, time and treatment-by-time interaction, as well as the continuous, fixed covariates of baseline and time-by-baseline interaction preceded by a Multiple Imputation step for patients without post-baseline measurement.

Statistical analysis title	S201086/GLPG1972 150mg minus placebo
Comparison groups	S201086/GLPG1972 150mg v Placebo
Number of subjects included in analysis	465
Analysis specification	Pre-specified
Analysis type	superiority[6]
P-value	= 0.939
Method	Mixed-effects model for repeated measure
Parameter estimate	Adjusted mean difference
Point estimate	0.012
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.03868
upper limit	0.06267
Variability estimate	Standard error of the mean
Dispersion value	0.02585

Notes:

[6] - Estimate of the adjusted difference from baseline to last post baseline value between treatment groups means: each S201086/GLPG1972 dose regimen minus placebo using a MMRM including the fixed, categorical effects of treatment, region, time and treatment-by-time interaction, as well as the continuous, fixed covariates of baseline and time-by-baseline interaction preceded by a Multiple Imputation step for patients without post-baseline measurement.

Statistical analysis title	S201086/GLPG1972 300mg minus placebo
Comparison groups	S201086/GLPG1972 300mg v Placebo
Number of subjects included in analysis	467
Analysis specification	Pre-specified
Analysis type	superiority[7]
P-value	= 0.682
Method	Mixed-effects model for repeated measure
Parameter estimate	Adjusted mean difference
Point estimate	0.02329
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.02641
upper limit	0.073
Variability estimate	Standard error of the mean
Dispersion value	0.02536

Notes:

[7] - Estimate of the adjusted difference from baseline to last post baseline value between treatment groups means: each S201086/GLPG1972 dose regimen minus placebo using a MMRM including the fixed, categorical effects of treatment, region, time and treatment-by-time interaction, as well as the continuous, fixed covariates of baseline and time-by-baseline interaction preceded by a Multiple Imputation step for patients without post-baseline measurement.

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All adverse events that occurred, worsened or became serious between the first study treatment intake date (included) and the last visit.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	23.0

Reporting groups

Reporting group title	S201086/GLPG1972 75mg
Reporting group description: -	
Reporting group title	S201086/GLPG1972 150mg
Reporting group description: -	
Reporting group title	S201086/GLPG1972 300mg
Reporting group description: -	
Reporting group title	Placebo

Reporting group description: -

Serious adverse events	S201086/GLPG1972 75mg	S201086/GLPG1972 150mg	S201086/GLPG1972 300mg
Total subjects affected by serious adverse events			
subjects affected / exposed	17 / 234 (7.26%)	17 / 231 (7.36%)	18 / 232 (7.76%)
number of deaths (all causes)	0	1	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			
subjects affected / exposed	0 / 234 (0.00%)	0 / 231 (0.00%)	0 / 232 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endometrial adenocarcinoma			
subjects affected / exposed	1 / 234 (0.43%)	0 / 231 (0.00%)	0 / 232 (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
Glottis carcinoma			
subjects affected / exposed	0 / 234 (0.00%)	0 / 231 (0.00%)	0 / 232 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intraductal proliferative breast lesion			

subjects affected / exposed	0 / 234 (0.00%)	0 / 231 (0.00%)	0 / 232 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Invasive ductal breast carcinoma			
subjects affected / exposed	0 / 234 (0.00%)	3 / 231 (1.30%)	0 / 232 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Invasive papillary breast carcinoma			
subjects affected / exposed	0 / 234 (0.00%)	1 / 231 (0.43%)	0 / 232 (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
Malignant melanoma in situ			
subjects affected / exposed	1 / 234 (0.43%)	0 / 231 (0.00%)	0 / 232 (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
Prostate cancer stage II			
subjects affected / exposed	0 / 234 (0.00%)	0 / 231 (0.00%)	1 / 232 (0.43%)
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			
Hypotension			
subjects affected / exposed	0 / 234 (0.00%)	0 / 231 (0.00%)	1 / 232 (0.43%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Orthostatic hypotension			
subjects affected / exposed	0 / 234 (0.00%)	0 / 231 (0.00%)	0 / 232 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Chills			
subjects affected / exposed	1 / 234 (0.43%)	0 / 231 (0.00%)	0 / 232 (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

Non-cardiac chest pain			
subjects affected / exposed	1 / 234 (0.43%)	0 / 231 (0.00%)	0 / 232 (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
Reproductive system and breast disorders			
Ovarian cyst			
subjects affected / exposed	0 / 234 (0.00%)	1 / 231 (0.43%)	0 / 232 (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
Vaginal haemorrhage			
subjects affected / exposed	1 / 234 (0.43%)	0 / 231 (0.00%)	0 / 232 (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
Respiratory, thoracic and mediastinal disorders			
Pulmonary embolism			
subjects affected / exposed	0 / 234 (0.00%)	0 / 231 (0.00%)	1 / 232 (0.43%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Depression suicidal			
subjects affected / exposed	0 / 234 (0.00%)	0 / 231 (0.00%)	1 / 232 (0.43%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Face injury			
subjects affected / exposed	0 / 234 (0.00%)	0 / 231 (0.00%)	1 / 232 (0.43%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fall			
subjects affected / exposed	1 / 234 (0.43%)	0 / 231 (0.00%)	0 / 232 (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
Femur fracture			

subjects affected / exposed	1 / 234 (0.43%)	0 / 231 (0.00%)	0 / 232 (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
Humerus fracture			
subjects affected / exposed	0 / 234 (0.00%)	0 / 231 (0.00%)	0 / 232 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Joint dislocation			
subjects affected / exposed	0 / 234 (0.00%)	0 / 231 (0.00%)	0 / 232 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Procedural pain			
subjects affected / exposed	0 / 234 (0.00%)	0 / 231 (0.00%)	1 / 232 (0.43%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tendon rupture			
subjects affected / exposed	0 / 234 (0.00%)	0 / 231 (0.00%)	1 / 232 (0.43%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wrist fracture			
subjects affected / exposed	1 / 234 (0.43%)	0 / 231 (0.00%)	0 / 232 (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
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	0 / 234 (0.00%)	0 / 231 (0.00%)	0 / 232 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial fibrillation			
subjects affected / exposed	1 / 234 (0.43%)	1 / 231 (0.43%)	1 / 232 (0.43%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial flutter			

subjects affected / exposed	1 / 234 (0.43%)	1 / 231 (0.43%)	0 / 232 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coronary artery occlusion			
subjects affected / exposed	0 / 234 (0.00%)	0 / 231 (0.00%)	0 / 232 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coronary artery stenosis			
subjects affected / exposed	0 / 234 (0.00%)	0 / 231 (0.00%)	0 / 232 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocarditis			
subjects affected / exposed	0 / 234 (0.00%)	0 / 231 (0.00%)	1 / 232 (0.43%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Supraventricular tachycardia			
subjects affected / exposed	1 / 234 (0.43%)	0 / 231 (0.00%)	0 / 232 (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
Nervous system disorders			
Cerebrovascular accident			
subjects affected / exposed	0 / 234 (0.00%)	1 / 231 (0.43%)	0 / 232 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cervical cord compression			
subjects affected / exposed	0 / 234 (0.00%)	0 / 231 (0.00%)	1 / 232 (0.43%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoaesthesia			
subjects affected / exposed	1 / 234 (0.43%)	0 / 231 (0.00%)	0 / 232 (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
Ischaemic stroke			

subjects affected / exposed	2 / 234 (0.85%)	1 / 231 (0.43%)	0 / 232 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sciatica			
subjects affected / exposed	0 / 234 (0.00%)	0 / 231 (0.00%)	1 / 232 (0.43%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
subjects affected / exposed	1 / 234 (0.43%)	0 / 231 (0.00%)	0 / 232 (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
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 234 (0.00%)	1 / 231 (0.43%)	0 / 232 (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
Eye disorders			
Angle closure glaucoma			
subjects affected / exposed	0 / 234 (0.00%)	0 / 231 (0.00%)	0 / 232 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Macular degeneration			
subjects affected / exposed	0 / 234 (0.00%)	0 / 231 (0.00%)	0 / 232 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Retinal detachment			
subjects affected / exposed	0 / 234 (0.00%)	0 / 231 (0.00%)	1 / 232 (0.43%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal incarcerated hernia			
subjects affected / exposed	1 / 234 (0.43%)	0 / 231 (0.00%)	0 / 232 (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

Food poisoning			
subjects affected / exposed	0 / 234 (0.00%)	0 / 231 (0.00%)	1 / 232 (0.43%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal obstruction			
subjects affected / exposed	1 / 234 (0.43%)	0 / 231 (0.00%)	0 / 232 (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
Nausea			
subjects affected / exposed	1 / 234 (0.43%)	0 / 231 (0.00%)	0 / 232 (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
Peritoneal cyst			
subjects affected / exposed	0 / 234 (0.00%)	1 / 231 (0.43%)	0 / 232 (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
Hepatobiliary disorders			
Bile duct stone			
subjects affected / exposed	0 / 234 (0.00%)	0 / 231 (0.00%)	0 / 232 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholecystitis acute			
subjects affected / exposed	0 / 234 (0.00%)	0 / 231 (0.00%)	0 / 232 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholelithiasis			
subjects affected / exposed	0 / 234 (0.00%)	1 / 231 (0.43%)	0 / 232 (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
Drug-induced liver injury			
subjects affected / exposed	0 / 234 (0.00%)	0 / 231 (0.00%)	0 / 232 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			

Acute kidney injury			
subjects affected / exposed	1 / 234 (0.43%)	0 / 231 (0.00%)	1 / 232 (0.43%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ureterolithiasis			
subjects affected / exposed	1 / 234 (0.43%)	0 / 231 (0.00%)	0 / 232 (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
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	2 / 234 (0.85%)	1 / 231 (0.43%)	1 / 232 (0.43%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Back pain			
subjects affected / exposed	0 / 234 (0.00%)	0 / 231 (0.00%)	1 / 232 (0.43%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Joint swelling			
subjects affected / exposed	1 / 234 (0.43%)	0 / 231 (0.00%)	0 / 232 (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
Myopathy			
subjects affected / exposed	0 / 234 (0.00%)	1 / 231 (0.43%)	0 / 232 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteoarthritis			
subjects affected / exposed	2 / 234 (0.85%)	2 / 231 (0.87%)	3 / 232 (1.29%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Appendiceal abscess			
subjects affected / exposed	0 / 234 (0.00%)	0 / 231 (0.00%)	0 / 232 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Bronchitis			
subjects affected / exposed	0 / 234 (0.00%)	1 / 231 (0.43%)	0 / 232 (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
Burn infection			
subjects affected / exposed	0 / 234 (0.00%)	0 / 231 (0.00%)	0 / 232 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COVID-19			
subjects affected / exposed	0 / 234 (0.00%)	1 / 231 (0.43%)	1 / 232 (0.43%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Gastroenteritis			
subjects affected / exposed	0 / 234 (0.00%)	0 / 231 (0.00%)	1 / 232 (0.43%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia bacterial			
subjects affected / exposed	0 / 234 (0.00%)	0 / 231 (0.00%)	1 / 232 (0.43%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis			
subjects affected / exposed	1 / 234 (0.43%)	0 / 231 (0.00%)	0 / 232 (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
Urinary tract infection			
subjects affected / exposed	1 / 234 (0.43%)	0 / 231 (0.00%)	0 / 232 (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
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 234 (0.00%)	0 / 231 (0.00%)	1 / 232 (0.43%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypercalcaemia			

subjects affected / exposed	1 / 234 (0.43%)	0 / 231 (0.00%)	0 / 232 (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

Serious adverse events	Placebo		
Total subjects affected by serious adverse events			
subjects affected / exposed	18 / 234 (7.69%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			
subjects affected / exposed	1 / 234 (0.43%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Endometrial adenocarcinoma			
subjects affected / exposed	0 / 234 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Glottis carcinoma			
subjects affected / exposed	1 / 234 (0.43%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Intraductal proliferative breast lesion			
subjects affected / exposed	1 / 234 (0.43%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Invasive ductal breast carcinoma			
subjects affected / exposed	1 / 234 (0.43%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Invasive papillary breast carcinoma			
subjects affected / exposed	0 / 234 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Malignant melanoma in situ			
subjects affected / exposed	0 / 234 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Prostate cancer stage II			
subjects affected / exposed	0 / 234 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Hypotension			
subjects affected / exposed	1 / 234 (0.43%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Orthostatic hypotension			
subjects affected / exposed	1 / 234 (0.43%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Chills			
subjects affected / exposed	0 / 234 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Non-cardiac chest pain			
subjects affected / exposed	0 / 234 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Reproductive system and breast disorders			
Ovarian cyst			
subjects affected / exposed	0 / 234 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vaginal haemorrhage			

subjects affected / exposed	0 / 234 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Pulmonary embolism			
subjects affected / exposed	0 / 234 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Depression suicidal			
subjects affected / exposed	0 / 234 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Face injury			
subjects affected / exposed	0 / 234 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Fall			
subjects affected / exposed	0 / 234 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Femur fracture			
subjects affected / exposed	0 / 234 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Humerus fracture			
subjects affected / exposed	1 / 234 (0.43%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Joint dislocation			

subjects affected / exposed	1 / 234 (0.43%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Procedural pain				
subjects affected / exposed	0 / 234 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Tendon rupture				
subjects affected / exposed	0 / 234 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Wrist fracture				
subjects affected / exposed	0 / 234 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardiac disorders				
Acute myocardial infarction				
subjects affected / exposed	2 / 234 (0.85%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 0			
Atrial fibrillation				
subjects affected / exposed	0 / 234 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Atrial flutter				
subjects affected / exposed	0 / 234 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Coronary artery occlusion				
subjects affected / exposed	1 / 234 (0.43%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Coronary artery stenosis				

subjects affected / exposed	1 / 234 (0.43%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Myocarditis				
subjects affected / exposed	0 / 234 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Supraventricular tachycardia				
subjects affected / exposed	0 / 234 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Nervous system disorders				
Cerebrovascular accident				
subjects affected / exposed	0 / 234 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cervical cord compression				
subjects affected / exposed	0 / 234 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hypoaesthesia				
subjects affected / exposed	0 / 234 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Ischaemic stroke				
subjects affected / exposed	1 / 234 (0.43%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Sciatica				
subjects affected / exposed	0 / 234 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Syncope				

subjects affected / exposed	1 / 234 (0.43%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 234 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Eye disorders			
Angle closure glaucoma			
subjects affected / exposed	1 / 234 (0.43%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Macular degeneration			
subjects affected / exposed	1 / 234 (0.43%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Retinal detachment			
subjects affected / exposed	0 / 234 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Abdominal incarcerated hernia			
subjects affected / exposed	0 / 234 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Food poisoning			
subjects affected / exposed	0 / 234 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Intestinal obstruction			
subjects affected / exposed	0 / 234 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Nausea			
subjects affected / exposed	0 / 234 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Peritoneal cyst			
subjects affected / exposed	0 / 234 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Bile duct stone			
subjects affected / exposed	1 / 234 (0.43%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cholecystitis acute			
subjects affected / exposed	2 / 234 (0.85%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Cholelithiasis			
subjects affected / exposed	0 / 234 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Drug-induced liver injury			
subjects affected / exposed	1 / 234 (0.43%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 234 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Ureterolithiasis			
subjects affected / exposed	0 / 234 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 234 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Back pain			
subjects affected / exposed	0 / 234 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Joint swelling			
subjects affected / exposed	0 / 234 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Myopathy			
subjects affected / exposed	0 / 234 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Osteoarthritis			
subjects affected / exposed	0 / 234 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Appendiceal abscess			
subjects affected / exposed	1 / 234 (0.43%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Bronchitis			
subjects affected / exposed	0 / 234 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Burn infection			
subjects affected / exposed	1 / 234 (0.43%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

COVID-19				
subjects affected / exposed	0 / 234 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastroenteritis				
subjects affected / exposed	0 / 234 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumonia bacterial				
subjects affected / exposed	0 / 234 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pyelonephritis				
subjects affected / exposed	0 / 234 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Urinary tract infection				
subjects affected / exposed	0 / 234 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Metabolism and nutrition disorders				
Dehydration				
subjects affected / exposed	0 / 234 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hypercalcaemia				
subjects affected / exposed	0 / 234 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			

Frequency threshold for reporting non-serious adverse events: 3 %

Non-serious adverse events	S201086/GLPG1972 75mg	S201086/GLPG1972 150mg	S201086/GLPG1972 300mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	171 / 234 (73.08%)	176 / 231 (76.19%)	170 / 232 (73.28%)
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	4 / 234 (1.71%)	3 / 231 (1.30%)	10 / 232 (4.31%)
occurrences (all)	4	4	10
Aspartate aminotransferase increased			
subjects affected / exposed	4 / 234 (1.71%)	2 / 231 (0.87%)	10 / 232 (4.31%)
occurrences (all)	4	2	10
Blood creatine phosphokinase increased			
subjects affected / exposed	12 / 234 (5.13%)	7 / 231 (3.03%)	9 / 232 (3.88%)
occurrences (all)	12	7	9
C-reactive protein increased			
subjects affected / exposed	1 / 234 (0.43%)	1 / 231 (0.43%)	9 / 232 (3.88%)
occurrences (all)	1	1	9
Gamma-glutamyltransferase increased			
subjects affected / exposed	3 / 234 (1.28%)	2 / 231 (0.87%)	16 / 232 (6.90%)
occurrences (all)	3	2	16
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	4 / 234 (1.71%)	7 / 231 (3.03%)	6 / 232 (2.59%)
occurrences (all)	6	8	6
Fall			
subjects affected / exposed	14 / 234 (5.98%)	20 / 231 (8.66%)	16 / 232 (6.90%)
occurrences (all)	16	23	17
Vascular disorders			
Hypertension			
subjects affected / exposed	6 / 234 (2.56%)	9 / 231 (3.90%)	12 / 232 (5.17%)
occurrences (all)	6	9	13
Nervous system disorders			
Headache			
subjects affected / exposed	15 / 234 (6.41%)	12 / 231 (5.19%)	11 / 232 (4.74%)
occurrences (all)	16	14	11
General disorders and administration site conditions			

Oedema peripheral			
subjects affected / exposed	6 / 234 (2.56%)	4 / 231 (1.73%)	2 / 232 (0.86%)
occurrences (all)	6	4	2
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	3 / 234 (1.28%)	7 / 231 (3.03%)	4 / 232 (1.72%)
occurrences (all)	3	7	5
Nausea			
subjects affected / exposed	3 / 234 (1.28%)	7 / 231 (3.03%)	11 / 232 (4.74%)
occurrences (all)	3	8	12
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	26 / 234 (11.11%)	34 / 231 (14.72%)	26 / 232 (11.21%)
occurrences (all)	30	39	31
Back pain			
subjects affected / exposed	11 / 234 (4.70%)	10 / 231 (4.33%)	6 / 232 (2.59%)
occurrences (all)	12	10	6
Joint swelling			
subjects affected / exposed	3 / 234 (1.28%)	7 / 231 (3.03%)	4 / 232 (1.72%)
occurrences (all)	3	7	4
Musculoskeletal pain			
subjects affected / exposed	3 / 234 (1.28%)	4 / 231 (1.73%)	8 / 232 (3.45%)
occurrences (all)	4	5	8
Osteoarthritis			
subjects affected / exposed	6 / 234 (2.56%)	10 / 231 (4.33%)	8 / 232 (3.45%)
occurrences (all)	6	11	8
Pain in extremity			
subjects affected / exposed	5 / 234 (2.14%)	7 / 231 (3.03%)	6 / 232 (2.59%)
occurrences (all)	5	7	6
Infections and infestations			
Bronchitis			
subjects affected / exposed	8 / 234 (3.42%)	7 / 231 (3.03%)	5 / 232 (2.16%)
occurrences (all)	9	7	5
Influenza			
subjects affected / exposed	8 / 234 (3.42%)	4 / 231 (1.73%)	3 / 232 (1.29%)
occurrences (all)	8	4	3

Nasopharyngitis			
subjects affected / exposed	21 / 234 (8.97%)	16 / 231 (6.93%)	22 / 232 (9.48%)
occurrences (all)	23	16	26
Upper respiratory tract infection			
subjects affected / exposed	7 / 234 (2.99%)	12 / 231 (5.19%)	6 / 232 (2.59%)
occurrences (all)	7	20	7
Urinary tract infection			
subjects affected / exposed	6 / 234 (2.56%)	5 / 231 (2.16%)	4 / 232 (1.72%)
occurrences (all)	8	8	4
Metabolism and nutrition disorders			
Hypercholesterolaemia			
subjects affected / exposed	3 / 234 (1.28%)	7 / 231 (3.03%)	4 / 232 (1.72%)
occurrences (all)	3	7	4

Non-serious adverse events	Placebo		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	170 / 234 (72.65%)		
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	7 / 234 (2.99%)		
occurrences (all)	7		
Aspartate aminotransferase increased			
subjects affected / exposed	6 / 234 (2.56%)		
occurrences (all)	6		
Blood creatine phosphokinase increased			
subjects affected / exposed	8 / 234 (3.42%)		
occurrences (all)	9		
C-reactive protein increased			
subjects affected / exposed	2 / 234 (0.85%)		
occurrences (all)	2		
Gamma-glutamyltransferase increased			
subjects affected / exposed	4 / 234 (1.71%)		
occurrences (all)	4		
Injury, poisoning and procedural complications			

Contusion subjects affected / exposed occurrences (all) Fall subjects affected / exposed occurrences (all)	6 / 234 (2.56%) 7 13 / 234 (5.56%) 16		
Vascular disorders Hypertension subjects affected / exposed occurrences (all)	16 / 234 (6.84%) 16		
Nervous system disorders Headache subjects affected / exposed occurrences (all)	9 / 234 (3.85%) 9		
General disorders and administration site conditions Oedema peripheral subjects affected / exposed occurrences (all)	8 / 234 (3.42%) 8		
Gastrointestinal disorders Diarrhoea subjects affected / exposed occurrences (all) Nausea subjects affected / exposed occurrences (all)	7 / 234 (2.99%) 7 5 / 234 (2.14%) 6		
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all) Back pain subjects affected / exposed occurrences (all) Joint swelling subjects affected / exposed occurrences (all) Musculoskeletal pain	19 / 234 (8.12%) 20 19 / 234 (8.12%) 21 4 / 234 (1.71%) 4		

subjects affected / exposed	5 / 234 (2.14%)		
occurrences (all)	5		
Osteoarthritis			
subjects affected / exposed	10 / 234 (4.27%)		
occurrences (all)	12		
Pain in extremity			
subjects affected / exposed	4 / 234 (1.71%)		
occurrences (all)	4		
Infections and infestations			
Bronchitis			
subjects affected / exposed	6 / 234 (2.56%)		
occurrences (all)	6		
Influenza			
subjects affected / exposed	7 / 234 (2.99%)		
occurrences (all)	7		
Nasopharyngitis			
subjects affected / exposed	20 / 234 (8.55%)		
occurrences (all)	28		
Upper respiratory tract infection			
subjects affected / exposed	10 / 234 (4.27%)		
occurrences (all)	13		
Urinary tract infection			
subjects affected / exposed	8 / 234 (3.42%)		
occurrences (all)	8		
Metabolism and nutrition disorders			
Hypercholesterolaemia			
subjects affected / exposed	7 / 234 (2.99%)		
occurrences (all)	7		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
11 July 2018	-Amendment No. 1 was applicable in all countries. The main changes included: - Increase of the age of female patients of non-childbearing potential to 50 years old instead of 40 years old (inclusion criterion n°1) (except for female patients surgically sterile) as requested by USA IRB. - Addition of information regarding the management of an overdose of S201086/GLPG1972 as requested by Health Canada. - Addition of one withdrawal criterion "delta > 60 ms over baseline value (inclusion) with regards to ECG parameters as beside the absolute values on QTcF the delta is also an important parameter to evaluate for the safety of the patient. - Implementation of an evaluation of the consistency of the primary analysis' results between Japanese patients and non-Japanese patients as recommended by the Pharmaceuticals and Medical Devices Agency (Japanese Competent Authorities). The initial randomisation list was stratified on 2 strata (Asia vs Rest of the World). In order to ensure balanced Japanese patients between treatment groups, the stratification factors of the randomisation list were modified accordingly (3 strata in the randomisation list: Japan vs South Korea/Taiwan vs Rest of the World). - Clarification of the choice of the target knee in inclusion criterion n°9.
12 March 2019	Amendment No. 2 was applicable in all countries. It mainly concerned the widening of the recruitment: - Clarification and/or modification of inclusion criteria n°7, 9 and exclusion criteria n°24, 25, 27, 28, 29, 31, 32, 33, 38, 40, 44. - Update of forbidden/authorised concomitant treatments with regards to database reference.

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.

Due to the exceptional circumstances in relation to the COVID-19 pandemic, the Sponsor decided in accordance with competent regulatory authorities' guidelines to implement some precautionary measures in order to mitigate the risk of infection.

Notes: