Clinical trial results:
GALACTIC-1- A randomized, double-blind, multicentre, parallel, placebo-controlled Phase 2b study in subjects with idiopathic pulmonary fibrosis (IPF) investigating the efficacy and safety of TD139, an inhaled galectin-3 inhibitor administered via a dry powder inhaler over 52 weeks

Summary

EudraCT number	2018-002664-73
Trial protocol	IE GB FR PL ES BE IT
Global end of trial date	17 May 2023

Results information

Result version number	v1 (current)
This version publication date	19 May 2024
First version publication date	19 May 2024

Trial information

Trial identification

Sponsor protocol code	GALACTIC-1

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03832946
WHO universal trial number (UTN)	-
Other trial identifiers	124075: IND

Notes:

Sponsors

Sponsor organisation name	Galecto Biotech AB
Sponsor organisation address	Ole Maaloes Vej 3, Copenhagen, Denmark, DK
Public contact	Chief Medical Officer, Galecto Biotech AB, Clinicaltrials@galecto.com
Scientific contact	Chief Medical Officer, Galecto Biotech AB, Clinicaltrials@galecto.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	13 October 2023
Is this the analysis of the primary completion data?	Yes
Primary completion date	17 May 2023
Global end of trial reached?	Yes
Global end of trial date	17 May 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the study was to evaluate the effect of GB0139 3 mg dry powder for inhalation compared with placebo over a 52-week treatment period on the annual rate of decline in forced vital capacity (FVC) in participants with IPF who were not treated with or could not tolerate nintedanib or pirfenidone.
The secondary objective of the study was to further characterise the effect of GB0139 3 mg compared with placebo over a 52-week treatment period on FVC, also on the quality of life, time to respiratory-related hospitalisations and all-cause mortality.

Protection of trial subjects:

This study was conducted in accordance with the International Council on Harmonisation (ICH) Good Clinical Practice, and the principles of the Declaration of Helsinki. All the local regulatory requirements pertinent to safety of trial subjects were also followed during the conduct of the trial.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	20 February 2019
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	Poland: 11
Country: Number of subjects enrolled	Spain: 5
Country: Number of subjects enrolled	United Kingdom: 42
Country: Number of subjects enrolled	France: 7
Country: Number of subjects enrolled	Germany: 6
Country: Number of subjects enrolled	Ireland: 2
Country: Number of subjects enrolled	Italy: 3
Country: Number of subjects enrolled	United States: 47
Country: Number of subjects enrolled	Australia: 9
Country: Number of subjects enrolled	Canada: 2
Country: Number of subjects enrolled	Georgia: 9
Country: Number of subjects enrolled	Israel: 15
Country: Number of subjects enrolled	Ukraine: 6
Country: Number of subjects enrolled	Russian Federation: 8
Worldwide total number of subjects	172
EEA total number of subjects	34

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)	23
From 65 to 84 years	144
85 years and over	5

Subject disposition

Recruitment

Recruitment details:

This study included participants with a diagnosis of IPF and was conducted in 16 countries (including Belarus where no participants were randomised and Belgium where no participants were enrolled after a change in trial design in protocol version 6.0)

Pre-assignment

Screening details:

825 participants were screened. 426 were enrolled and randomised. 424 received placebo or GB0139. By protocol amendment 6.0 the participants on SOC and the 10 mg arm were excluded. 173 participants were enrolled and randomised according to protocol v.6.0. 1 was randomised by error and didn't receive treatment. A population of 172 is presented here.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	GB0139 3 mg

Arm description:

Participants received 3 mg GB0139 administered as inhalation once a day for 52 Weeks. Participants were neither treated with nintedanib nor pirfenidone during the trial.

Arm type	Experimental
Investigational medicinal product name	Olitigaltin
Investigational medicinal product code	GB0139
Other name	TD139
Pharmaceutical forms	Capsule, hard
Routes of administration	Inhalation use

Dosage and administration details:

GB0139 3 mg was administered by inhalation once a day as two 1.5 mg capsules for 52 weeks. The study treatment was administered using the Plastiape RS01 Monodose DPI device.

Arm title	Placebo

Arm description:

Participants received placebo administered as inhalation once a day for 52 Weeks. Participants were neither treated with nintedanib nor pirfenidone during the trial.

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

Dosage and administration details:

Placebo was administered by inhalation once a day as two capsules for 52 weeks. The study treatment was administered using the Plastiape RS01 Monodose DPI device.

Number of subjects in period 1	GB0139 3 mg	Placebo
Started	102	70
Completed	55	38
Not completed	47	32
Consent withdrawn by subject	12	9
Adverse event	3	1
Lost to follow-up	1	-
Protocol change forbidding nintedanib/pirfenidone	30	22
Lack of efficacy	1	-

Baseline characteristics

Reporting groups	
Reporting group title	GB0139 3 mg
Reporting group description:	
Participants received 3 mg GB0139 administered as inhalation once a day for 52 Weeks. Participants were neither treated with nintedanib nor pirfenidone during the trial.	
Reporting group title	Placebo
Reporting group description:	
Participants received placebo administered as inhalation once a day for 52 Weeks. Participants were neither treated with nintedanib nor pirfenidone during the trial.	

Reporting group values	GB0139 3 mg	Placebo	Total
Number of subjects	102	70	172
Age categorical Units: Subjects			
< 70 Years	34	26	60
≥ 70 Years	68	44	112
Age continuous Units: years			
arithmetic mean	72.5	71.7	
standard deviation	± 7.56	± 7.36	-
Gender categorical Units: Subjects			
Female	27	22	49
Male	75	48	123

Subject analysis sets	
Subject analysis set title	Primary Population
Subject analysis set type	Modified intention-to-treat
Subject analysis set description:	
Patients randomised and received at least one dose of study drug.	
Subject analysis set title	Safety Population
Subject analysis set type	Safety analysis
Subject analysis set description:	
Patients randomised and received at least one dose of study drug and grouped by treatment received.	

Reporting group values	Primary Population	Safety Population	
Number of subjects	172	172	
Age categorical Units: Subjects			
< 70 Years	60	60	
≥ 70 Years	112	112	
Age continuous Units: years			
arithmetic mean			
standard deviation	±	±	

Gender categorical Units: Subjects			
Female	49	49	
Male	123	123	

End points

End points reporting groups

Reporting group title	GB0139 3 mg
Reporting group description:	
Participants received 3 mg GB0139 administered as inhalation once a day for 52 Weeks. Participants were neither treated with nintedanib nor pirfenidone during the trial.	
Reporting group title	Placebo
Reporting group description:	
Participants received placebo administered as inhalation once a day for 52 Weeks. Participants were neither treated with nintedanib nor pirfenidone during the trial.	
Subject analysis set title	Primary Population
Subject analysis set type	Modified intention-to-treat
Subject analysis set description:	
Patients randomised and received at least one dose of study drug.	
Subject analysis set title	Safety Population
Subject analysis set type	Safety analysis
Subject analysis set description:	
Patients randomised and received at least one dose of study drug and grouped by treatment received.	

Primary: Annual Rate of Decline in Forced Vital Capacity (FVC)

End point title	Annual Rate of Decline in Forced Vital Capacity (FVC)
End point description:	
End point type	Primary
End point timeframe:	
52 weeks	

End point values	GB0139 3 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	100	68		
Units: mL				
least squares mean (confidence interval 95%)	-316.60 (-394.86 to -238.35)	-127.41 (-221.12 to -33.71)		

Statistical analyses

Statistical analysis title	Primary
Statistical analysis description:	
Comparing GB0139 vs. placebo	
Comparison groups	GB0139 3 mg v Placebo

Number of subjects included in analysis	168
Analysis specification	Pre-specified
Analysis type	superiority[1]
P-value	= 0.003
Method	Coefficient Regression Model
Parameter estimate	Least Squares (LS) mean difference
Point estimate	-189.19
Confidence interval	
level	95 %
sides	2-sided
lower limit	-311.28
upper limit	-67.1

Notes:

[1] - Coefficient Regression Model

Secondary: Proportion of participants with an absolute decline from baseline in FVC (% predicted) of ≤10% at Week 52

End point title	Proportion of participants with an absolute decline from baseline in FVC (% predicted) of ≤10% at Week 52

End point description:

End point type	Secondary

End point timeframe:

52 weeks

End point values	GB0139 3 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	102	70		
Units: Participants	43	39		

Statistical analyses

Statistical analysis title	Main

Statistical analysis description:

Comparing GB0139 vs. placebo

Comparison groups	GB0139 3 mg v Placebo
Number of subjects included in analysis	172
Analysis specification	Pre-specified
Analysis type	superiority[2]
P-value	= 0.074
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.57

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.31
upper limit	1.06

Notes:

[2] - Regression, logistic

Secondary: Time to first hospitalisation (respiratory related, including acute exacerbation of IPF)

End point title	Time to first hospitalisation (respiratory related, including acute exacerbation of IPF)

End point description:

End point type	Secondary

End point timeframe:

52 weeks

End point values	GB0139 3 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	102	70		
Units: Participants	17	5		

Statistical analyses

Statistical analysis title	Main
Statistical analysis description:	
Comparing GB0139 vs. placebo	
Comparison groups	GB0139 3 mg v Placebo
Number of subjects included in analysis	172
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.081
Method	Cox proportional hazards model
Parameter estimate	Hazard ratio (HR)
Point estimate	2.44
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.9
upper limit	6.62

Secondary: Time to death (all causes)

End point title	Time to death (all causes)
End point description:	

End point type	Secondary
End point timeframe:	
52 weeks	

End point values	GB0139 3 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	102	70		
Units: Participants	7	4		

Statistical analyses

Statistical analysis title	Main
Statistical analysis description:	
Comparing GB0139 vs. placebo	
Comparison groups	GB0139 3 mg v Placebo
Number of subjects included in analysis	172
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.656
Method	Cox proportional hazards model
Parameter estimate	Hazard ratio (HR)
Point estimate	1.32
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.39
upper limit	4.53

Secondary: Assessment of Respiratory Related Quality of Life Using the St. George's Respiratory Questionnaire (SGRQ)

End point title	Assessment of Respiratory Related Quality of Life Using the St. George's Respiratory Questionnaire (SGRQ)
End point description:	
Change from baseline in the SGRQ total score. The SGRQ is a 50-item questionnaire split into three domains: symptoms, activity and impact. Weighting of both individual domains and the total score produces a range from 0 to 100, with higher scores indicating a poorer health-related quality of life.	
End point type	Secondary
End point timeframe:	
52 weeks	

End point values	GB0139 3 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	102	70		
Units: Score on a scale				
least squares mean (standard deviation)	5.687 (± 25.5537)	-6.198 (± 20.0903)		

Statistical analyses

Statistical analysis title	Main
Statistical analysis description: Comparing GB0139 vs. placebo	
Comparison groups	GB0139 3 mg v Placebo
Number of subjects included in analysis	172
Analysis specification	Pre-specified
Analysis type	superiority[3]
P-value	= 0.019
Method	Mixed models analysis
Parameter estimate	Least Squares (LS) mean difference
Point estimate	7.132
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.18
upper limit	13.084

Notes:

[3] - 116 subjects reached this stage

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
52 weeks (Includes all AEs with a start date up to and including Day 379 (52 weeks + 14 days)	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	26.0

Reporting groups	
Reporting group title	GB0139 3 mg
Reporting group description:	
Participants received 3 mg GB0139 administered as inhalation once a day for 52 Weeks. Participants were neither treated with nintedanib nor pirfenidone during the trial.	
Reporting group title	Placebo
Reporting group description:	
Participants received placebo administered as inhalation once a day for 52 Weeks. Participants were neither treated with nintedanib nor pirfenidone during the trial.	

Serious adverse events	GB0139 3 mg	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	24 / 102 (23.53%)	11 / 70 (15.71%)	
number of deaths (all causes)	8	5	
number of deaths resulting from adverse events	6	5	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Colon cancer			
subjects affected / exposed	0 / 102 (0.00%)	1 / 70 (1.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung adenocarcinoma			
subjects affected / exposed	0 / 102 (0.00%)	1 / 70 (1.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung neoplasm malignant			
subjects affected / exposed	0 / 102 (0.00%)	1 / 70 (1.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Metastases to skin			

subjects affected / exposed	1 / 102 (0.98%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neuroendocrine tumour of the lung			
subjects affected / exposed	1 / 102 (0.98%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prostate cancer			
subjects affected / exposed	0 / 102 (0.00%)	1 / 70 (1.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Injury, poisoning and procedural complications			
Abdominal injury			
subjects affected / exposed	1 / 102 (0.98%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Craniocerebral injury			
subjects affected / exposed	1 / 102 (0.98%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hip fracture			
subjects affected / exposed	0 / 102 (0.00%)	1 / 70 (1.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rib fracture			
subjects affected / exposed	1 / 102 (0.98%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Peripheral ischaemia			
subjects affected / exposed	1 / 102 (0.98%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	1 / 102 (0.98%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angina pectoris			
subjects affected / exposed	0 / 102 (0.00%)	1 / 70 (1.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrioventricular block complete			
subjects affected / exposed	0 / 102 (0.00%)	1 / 70 (1.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac Arrest			
subjects affected / exposed	1 / 102 (0.98%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Coronary artery disease			
subjects affected / exposed	1 / 102 (0.98%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ventricular fibrillation			
subjects affected / exposed	1 / 102 (0.98%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Nervous system disorders			
Cerebral microangiopathy			
subjects affected / exposed	1 / 102 (0.98%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebrovascular accident			
subjects affected / exposed	1 / 102 (0.98%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Ischaemic stroke			
subjects affected / exposed	1 / 102 (0.98%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Pernicious anaemia			
subjects affected / exposed	0 / 102 (0.00%)	1 / 70 (1.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	1 / 102 (0.98%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperthermia			
subjects affected / exposed	0 / 102 (0.00%)	1 / 70 (1.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Necrosis			
subjects affected / exposed	1 / 102 (0.98%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sudden death			
subjects affected / exposed	0 / 102 (0.00%)	1 / 70 (1.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Respiratory, thoracic and mediastinal disorders			
Acute respiratory distress syndrome			
subjects affected / exposed	1 / 102 (0.98%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Acute respiratory failure			

subjects affected / exposed	2 / 102 (1.96%)	1 / 70 (1.43%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 1	
Dyspnoea			
subjects affected / exposed	2 / 102 (1.96%)	1 / 70 (1.43%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemoptysis			
subjects affected / exposed	0 / 102 (0.00%)	1 / 70 (1.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Idiopathic pulmonary fibrosis			
subjects affected / exposed	8 / 102 (7.84%)	1 / 70 (1.43%)	
occurrences causally related to treatment / all	1 / 10	0 / 1	
deaths causally related to treatment / all	0 / 2	0 / 1	
Pneumothorax			
subjects affected / exposed	0 / 102 (0.00%)	1 / 70 (1.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	1 / 102 (0.98%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Cellulitis			
subjects affected / exposed	0 / 102 (0.00%)	1 / 70 (1.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronavirus infection			
subjects affected / exposed	1 / 102 (0.98%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
COVID-19			

subjects affected / exposed	4 / 102 (3.92%)	1 / 70 (1.43%)	
occurrences causally related to treatment / all	0 / 4	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
COVID-19 pneumonia			
subjects affected / exposed	2 / 102 (1.96%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Localised infection			
subjects affected / exposed	1 / 102 (0.98%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	4 / 102 (3.92%)	1 / 70 (1.43%)	
occurrences causally related to treatment / all	0 / 4	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Sepsis			
subjects affected / exposed	2 / 102 (1.96%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Septic shock			
subjects affected / exposed	2 / 102 (1.96%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	GB0139 3 mg	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	80 / 102 (78.43%)	50 / 70 (71.43%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal Cell Carcinoma			
subjects affected / exposed	2 / 102 (1.96%)	1 / 70 (1.43%)	
occurrences (all)	2	1	
Monoclonal Gammopathy			

subjects affected / exposed	0 / 102 (0.00%)	1 / 70 (1.43%)	
occurrences (all)	0	1	
Seborrhoeic keratosis			
subjects affected / exposed	1 / 102 (0.98%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Vascular disorders			
Aortic arteriosclerosis			
subjects affected / exposed	1 / 102 (0.98%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Haematoma			
subjects affected / exposed	1 / 102 (0.98%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Hypertension			
subjects affected / exposed	3 / 102 (2.94%)	0 / 70 (0.00%)	
occurrences (all)	3	0	
Hypotension			
subjects affected / exposed	1 / 102 (0.98%)	1 / 70 (1.43%)	
occurrences (all)	1	1	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	4 / 102 (3.92%)	0 / 70 (0.00%)	
occurrences (all)	4	0	
Fatigue			
subjects affected / exposed	2 / 102 (1.96%)	5 / 70 (7.14%)	
occurrences (all)	2	5	
Feeling Cold			
subjects affected / exposed	1 / 102 (0.98%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Influenza Like Illness			
subjects affected / exposed	1 / 102 (0.98%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Malaise			
subjects affected / exposed	1 / 102 (0.98%)	0 / 70 (0.00%)	
occurrences (all)	2	0	
Oedema Peripheral			

subjects affected / exposed	4 / 102 (3.92%)	2 / 70 (2.86%)	
occurrences (all)	4	2	
Pyrexia			
subjects affected / exposed	2 / 102 (1.96%)	1 / 70 (1.43%)	
occurrences (all)	2	1	
Vaccination Site Pain			
subjects affected / exposed	1 / 102 (0.98%)	0 / 70 (0.00%)	
occurrences (all)	2	0	
Vaccination Site Rash			
subjects affected / exposed	1 / 102 (0.98%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Immune system disorders			
Autoimmune Disorder			
subjects affected / exposed	0 / 102 (0.00%)	1 / 70 (1.43%)	
occurrences (all)	0	1	
Seasonal Allergy			
subjects affected / exposed	0 / 102 (0.00%)	1 / 70 (1.43%)	
occurrences (all)	0	1	
Reproductive system and breast disorders			
Benign prostatic hyperplasia			
subjects affected / exposed	1 / 102 (0.98%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Prostatic atrophy			
subjects affected / exposed	1 / 102 (0.98%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Prostatomegaly			
subjects affected / exposed	0 / 102 (0.00%)	1 / 70 (1.43%)	
occurrences (all)	0	1	
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	2 / 102 (1.96%)	0 / 70 (0.00%)	
occurrences (all)	2	0	
Bronchial Obstruction			
subjects affected / exposed	1 / 102 (0.98%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Cough			

subjects affected / exposed	17 / 102 (16.67%)	9 / 70 (12.86%)	
occurrences (all)	24	9	
Dysphonia			
subjects affected / exposed	1 / 102 (0.98%)	1 / 70 (1.43%)	
occurrences (all)	1	1	
Dyspnoea			
subjects affected / exposed	11 / 102 (10.78%)	5 / 70 (7.14%)	
occurrences (all)	14	5	
Dyspnoea Exertional			
subjects affected / exposed	1 / 102 (0.98%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Epistaxis			
subjects affected / exposed	3 / 102 (2.94%)	0 / 70 (0.00%)	
occurrences (all)	3	0	
Haemoptysis			
subjects affected / exposed	0 / 102 (0.00%)	1 / 70 (1.43%)	
occurrences (all)	0	2	
Hypoxia			
subjects affected / exposed	3 / 102 (2.94%)	1 / 70 (1.43%)	
occurrences (all)	3	1	
Idiopathic Pulmonary Fibrosis			
subjects affected / exposed	5 / 102 (4.90%)	3 / 70 (4.29%)	
occurrences (all)	6	3	
Nasal Congestion			
subjects affected / exposed	1 / 102 (0.98%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Oropharyngeal pain			
subjects affected / exposed	1 / 102 (0.98%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Pleuritic Pain			
subjects affected / exposed	0 / 102 (0.00%)	1 / 70 (1.43%)	
occurrences (all)	0	1	
Productive cough			
subjects affected / exposed	6 / 102 (5.88%)	2 / 70 (2.86%)	
occurrences (all)	6	2	
Pulmonary Embolism			

subjects affected / exposed	1 / 102 (0.98%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Pulmonary Mass			
subjects affected / exposed	0 / 102 (0.00%)	1 / 70 (1.43%)	
occurrences (all)	0	1	
Respiratory tract congestion			
subjects affected / exposed	0 / 102 (0.00%)	1 / 70 (1.43%)	
occurrences (all)	0	1	
Rhinitis allergic			
subjects affected / exposed	1 / 102 (0.98%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Sputum discoloured			
subjects affected / exposed	1 / 102 (0.98%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Sputum Increased			
subjects affected / exposed	2 / 102 (1.96%)	0 / 70 (0.00%)	
occurrences (all)	2	0	
Wheezing			
subjects affected / exposed	1 / 102 (0.98%)	1 / 70 (1.43%)	
occurrences (all)	2	1	
Psoriasis			
subjects affected / exposed	0 / 102 (0.00%)	1 / 70 (1.43%)	
occurrences (all)	0	1	
Psychiatric disorders			
Anxiety			
subjects affected / exposed	3 / 102 (2.94%)	0 / 70 (0.00%)	
occurrences (all)	3	0	
Insomnia			
subjects affected / exposed	1 / 102 (0.98%)	2 / 70 (2.86%)	
occurrences (all)	1	2	
Restlessness			
subjects affected / exposed	0 / 102 (0.00%)	1 / 70 (1.43%)	
occurrences (all)	0	1	
Sleep Disorder			
subjects affected / exposed	0 / 102 (0.00%)	1 / 70 (1.43%)	
occurrences (all)	0	1	

Suicidal Ideation			
subjects affected / exposed	1 / 102 (0.98%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Investigations			
Anticoagulation drug level above therapeutic			
subjects affected / exposed	1 / 102 (0.98%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Blood glucose increased			
subjects affected / exposed	1 / 102 (0.98%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Forced vital capacity decreased			
subjects affected / exposed	2 / 102 (1.96%)	2 / 70 (2.86%)	
occurrences (all)	2	2	
Heart rate increased			
subjects affected / exposed	1 / 102 (0.98%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Occult blood positive			
subjects affected / exposed	0 / 102 (0.00%)	1 / 70 (1.43%)	
occurrences (all)	0	1	
Weight decreased			
subjects affected / exposed	4 / 102 (3.92%)	3 / 70 (4.29%)	
occurrences (all)	4	3	
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	1 / 102 (0.98%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Eye Injury			
subjects affected / exposed	1 / 102 (0.98%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Eyelid Contusion			
subjects affected / exposed	1 / 102 (0.98%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Fall			
subjects affected / exposed	3 / 102 (2.94%)	0 / 70 (0.00%)	
occurrences (all)	5	0	
Limb Injury			

subjects affected / exposed	2 / 102 (1.96%)	0 / 70 (0.00%)	
occurrences (all)	2	0	
Muscle Injury			
subjects affected / exposed	1 / 102 (0.98%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Procedural Pain			
subjects affected / exposed	0 / 102 (0.00%)	1 / 70 (1.43%)	
occurrences (all)	0	1	
Rib Fracture			
subjects affected / exposed	1 / 102 (0.98%)	0 / 70 (0.00%)	
occurrences (all)	2	0	
Road traffic accident			
subjects affected / exposed	1 / 102 (0.98%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Skin Laceration			
subjects affected / exposed	2 / 102 (1.96%)	0 / 70 (0.00%)	
occurrences (all)	2	0	
Soft tissue injury			
subjects affected / exposed	1 / 102 (0.98%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Spinal compression fracture			
subjects affected / exposed	1 / 102 (0.98%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Tendon rupture			
subjects affected / exposed	1 / 102 (0.98%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Thermal burn			
subjects affected / exposed	1 / 102 (0.98%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Vaccination complication			
subjects affected / exposed	1 / 102 (0.98%)	1 / 70 (1.43%)	
occurrences (all)	1	3	
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	0 / 102 (0.00%)	1 / 70 (1.43%)	
occurrences (all)	0	1	

Arteriosclerosis coronary artery			
subjects affected / exposed	1 / 102 (0.98%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Atrial fibrillation			
subjects affected / exposed	2 / 102 (1.96%)	1 / 70 (1.43%)	
occurrences (all)	2	1	
Atrioventricular block first degree			
subjects affected / exposed	1 / 102 (0.98%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Bradycardia			
subjects affected / exposed	0 / 102 (0.00%)	1 / 70 (1.43%)	
occurrences (all)	0	1	
Bundle branch block left			
subjects affected / exposed	1 / 102 (0.98%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Cardiac failure			
subjects affected / exposed	1 / 102 (0.98%)	1 / 70 (1.43%)	
occurrences (all)	1	1	
Coronary artery disease			
subjects affected / exposed	1 / 102 (0.98%)	1 / 70 (1.43%)	
occurrences (all)	1	1	
Myocardial hypoxia			
subjects affected / exposed	1 / 102 (0.98%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Palpitations			
subjects affected / exposed	1 / 102 (0.98%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Sinus bradycardia			
subjects affected / exposed	1 / 102 (0.98%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Tachycardia			
subjects affected / exposed	2 / 102 (1.96%)	1 / 70 (1.43%)	
occurrences (all)	2	1	
Nervous system disorders			
Dizziness			

subjects affected / exposed	4 / 102 (3.92%)	2 / 70 (2.86%)	
occurrences (all)	4	2	
Essential Tremor			
subjects affected / exposed	0 / 102 (0.00%)	1 / 70 (1.43%)	
occurrences (all)	0	1	
Headache			
subjects affected / exposed	7 / 102 (6.86%)	2 / 70 (2.86%)	
occurrences (all)	7	5	
Hemiparesis			
subjects affected / exposed	1 / 102 (0.98%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Lethargy			
subjects affected / exposed	1 / 102 (0.98%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Memory Impairment			
subjects affected / exposed	1 / 102 (0.98%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Mental impairment			
subjects affected / exposed	0 / 102 (0.00%)	1 / 70 (1.43%)	
occurrences (all)	0	1	
Neuropathy peripheral			
subjects affected / exposed	1 / 102 (0.98%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Paraesthesia			
subjects affected / exposed	1 / 102 (0.98%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Presyncope			
subjects affected / exposed	1 / 102 (0.98%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Sciatica			
subjects affected / exposed	1 / 102 (0.98%)	1 / 70 (1.43%)	
occurrences (all)	1	1	
Sensory Loss			
subjects affected / exposed	1 / 102 (0.98%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Tremor			

subjects affected / exposed	1 / 102 (0.98%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Blood and lymphatic system disorders			
Leukocytosis			
subjects affected / exposed	0 / 102 (0.00%)	1 / 70 (1.43%)	
occurrences (all)	0	1	
Neutrophilia			
subjects affected / exposed	0 / 102 (0.00%)	1 / 70 (1.43%)	
occurrences (all)	0	1	
Polycythaemia			
subjects affected / exposed	0 / 102 (0.00%)	1 / 70 (1.43%)	
occurrences (all)	0	1	
Ear and labyrinth disorders			
Excessive cerumen production			
subjects affected / exposed	1 / 102 (0.98%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Vertigo positional			
subjects affected / exposed	1 / 102 (0.98%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Eye disorders			
Cataract			
subjects affected / exposed	1 / 102 (0.98%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Dry eye			
subjects affected / exposed	1 / 102 (0.98%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Epiretinal membrane			
subjects affected / exposed	0 / 102 (0.00%)	1 / 70 (1.43%)	
occurrences (all)	0	1	
Episcleritis			
subjects affected / exposed	0 / 102 (0.00%)	1 / 70 (1.43%)	
occurrences (all)	0	1	
Eye haematoma			
subjects affected / exposed	1 / 102 (0.98%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Eye pain			

subjects affected / exposed	1 / 102 (0.98%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal disorders			
Abdominal Distension			
subjects affected / exposed	1 / 102 (0.98%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Abdominal Pain			
subjects affected / exposed	2 / 102 (1.96%)	1 / 70 (1.43%)	
occurrences (all)	3	1	
Constipation			
subjects affected / exposed	4 / 102 (3.92%)	0 / 70 (0.00%)	
occurrences (all)	4	0	
Diarrhoea			
subjects affected / exposed	8 / 102 (7.84%)	2 / 70 (2.86%)	
occurrences (all)	13	2	
Diverticulum intestinal			
subjects affected / exposed	1 / 102 (0.98%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Dyspepsia			
subjects affected / exposed	1 / 102 (0.98%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Eructation			
subjects affected / exposed	1 / 102 (0.98%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Flatulence			
subjects affected / exposed	1 / 102 (0.98%)	1 / 70 (1.43%)	
occurrences (all)	1	1	
Gastritis			
subjects affected / exposed	0 / 102 (0.00%)	1 / 70 (1.43%)	
occurrences (all)	0	1	
Gastrooesophageal reflux disease			
subjects affected / exposed	3 / 102 (2.94%)	0 / 70 (0.00%)	
occurrences (all)	3	0	
Gingival Cyst			
subjects affected / exposed	1 / 102 (0.98%)	0 / 70 (0.00%)	
occurrences (all)	1	0	

Hiatus Hernia			
subjects affected / exposed	1 / 102 (0.98%)	0 / 70 (0.00%)	
occurrences (all)	2	0	
Inguinal Hernia			
subjects affected / exposed	0 / 102 (0.00%)	1 / 70 (1.43%)	
occurrences (all)	0	1	
Mouth Ulceration			
subjects affected / exposed	1 / 102 (0.98%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Nausea			
subjects affected / exposed	3 / 102 (2.94%)	0 / 70 (0.00%)	
occurrences (all)	6	0	
Reflux Gastritis			
subjects affected / exposed	0 / 102 (0.00%)	1 / 70 (1.43%)	
occurrences (all)	0	1	
Vomiting			
subjects affected / exposed	1 / 102 (0.98%)	1 / 70 (1.43%)	
occurrences (all)	1	1	
Skin and subcutaneous tissue disorders			
Eczema			
subjects affected / exposed	0 / 102 (0.00%)	1 / 70 (1.43%)	
occurrences (all)	0	1	
Hyperhidrosis			
subjects affected / exposed	1 / 102 (0.98%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Rash			
subjects affected / exposed	2 / 102 (1.96%)	0 / 70 (0.00%)	
occurrences (all)	2	0	
Rash macular			
subjects affected / exposed	0 / 102 (0.00%)	1 / 70 (1.43%)	
occurrences (all)	0	1	
Rash maculo-papular			
subjects affected / exposed	1 / 102 (0.98%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Renal and urinary disorders			

Acute Kidney Injury			
subjects affected / exposed	0 / 102 (0.00%)	1 / 70 (1.43%)	
occurrences (all)	0	1	
Haematuria			
subjects affected / exposed	0 / 102 (0.00%)	1 / 70 (1.43%)	
occurrences (all)	0	1	
Nephrolithiasis			
subjects affected / exposed	1 / 102 (0.98%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Renal Cyst			
subjects affected / exposed	1 / 102 (0.98%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Renal Failure			
subjects affected / exposed	0 / 102 (0.00%)	1 / 70 (1.43%)	
occurrences (all)	0	1	
Endocrine disorders			
Goitre			
subjects affected / exposed	0 / 102 (0.00%)	1 / 70 (1.43%)	
occurrences (all)	0	1	
Hypothyroidism			
subjects affected / exposed	1 / 102 (0.98%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	3 / 102 (2.94%)	2 / 70 (2.86%)	
occurrences (all)	3	2	
Back pain			
subjects affected / exposed	5 / 102 (4.90%)	3 / 70 (4.29%)	
occurrences (all)	5	3	
Chest wall haematoma			
subjects affected / exposed	1 / 102 (0.98%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Joint stiffness			
subjects affected / exposed	1 / 102 (0.98%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Joint Swelling			

subjects affected / exposed	1 / 102 (0.98%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Limb mass			
subjects affected / exposed	1 / 102 (0.98%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Muscle Spasms			
subjects affected / exposed	1 / 102 (0.98%)	1 / 70 (1.43%)	
occurrences (all)	1	1	
Muscular weakness			
subjects affected / exposed	1 / 102 (0.98%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal chest pain			
subjects affected / exposed	2 / 102 (1.96%)	0 / 70 (0.00%)	
occurrences (all)	2	0	
Musculoskeletal Discomfort			
subjects affected / exposed	0 / 102 (0.00%)	1 / 70 (1.43%)	
occurrences (all)	0	1	
Musculoskeletal pain			
subjects affected / exposed	1 / 102 (0.98%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal stiffness			
subjects affected / exposed	1 / 102 (0.98%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Myalgia			
subjects affected / exposed	0 / 102 (0.00%)	2 / 70 (2.86%)	
occurrences (all)	0	2	
Pain in extremity			
subjects affected / exposed	1 / 102 (0.98%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Polymyalgia rheumatica			
subjects affected / exposed	0 / 102 (0.00%)	1 / 70 (1.43%)	
occurrences (all)	0	1	
Rotator cuff syndrome			
subjects affected / exposed	1 / 102 (0.98%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Infections and infestations			

Acarodermatitis			
subjects affected / exposed	1 / 102 (0.98%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Bronchitis			
subjects affected / exposed	6 / 102 (5.88%)	3 / 70 (4.29%)	
occurrences (all)	8	4	
Bronchitis Bacterial			
subjects affected / exposed	1 / 102 (0.98%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
COVID-19			
subjects affected / exposed	13 / 102 (12.75%)	3 / 70 (4.29%)	
occurrences (all)	14	4	
COVID-19 Pneumonia			
subjects affected / exposed	0 / 102 (0.00%)	1 / 70 (1.43%)	
occurrences (all)	0	1	
Cellulitis			
subjects affected / exposed	0 / 102 (0.00%)	1 / 70 (1.43%)	
occurrences (all)	0	1	
Coronavirus Infection			
subjects affected / exposed	1 / 102 (0.98%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Cystitis			
subjects affected / exposed	0 / 102 (0.00%)	1 / 70 (1.43%)	
occurrences (all)	0	1	
Escherichia urinary tract infection			
subjects affected / exposed	0 / 102 (0.00%)	1 / 70 (1.43%)	
occurrences (all)	0	1	
Gastroenteritis			
subjects affected / exposed	1 / 102 (0.98%)	1 / 70 (1.43%)	
occurrences (all)	1	1	
Gingivitis			
subjects affected / exposed	1 / 102 (0.98%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Helicobacter Infection			
subjects affected / exposed	0 / 102 (0.00%)	1 / 70 (1.43%)	
occurrences (all)	0	1	

Influenza			
subjects affected / exposed	1 / 102 (0.98%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Localised Infection			
subjects affected / exposed	1 / 102 (0.98%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Lower Respiratory Tract Infection			
subjects affected / exposed	12 / 102 (11.76%)	3 / 70 (4.29%)	
occurrences (all)	19	3	
Nasopharyngitis			
subjects affected / exposed	4 / 102 (3.92%)	3 / 70 (4.29%)	
occurrences (all)	7	4	
Oral herpes			
subjects affected / exposed	0 / 102 (0.00%)	1 / 70 (1.43%)	
occurrences (all)	0	1	
Pharyngitis			
subjects affected / exposed	1 / 102 (0.98%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Pneumonia			
subjects affected / exposed	1 / 102 (0.98%)	1 / 70 (1.43%)	
occurrences (all)	1	1	
Postoperative wound infection			
subjects affected / exposed	0 / 102 (0.00%)	1 / 70 (1.43%)	
occurrences (all)	0	1	
Root canal infection			
subjects affected / exposed	1 / 102 (0.98%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Tooth Abcess			
subjects affected / exposed	3 / 102 (2.94%)	0 / 70 (0.00%)	
occurrences (all)	3	0	
Tooth infection			
subjects affected / exposed	2 / 102 (1.96%)	1 / 70 (1.43%)	
occurrences (all)	2	1	
Tracheitis			
subjects affected / exposed	1 / 102 (0.98%)	1 / 70 (1.43%)	
occurrences (all)	1	1	

Upper Respiratory Tract Infection			
subjects affected / exposed	5 / 102 (4.90%)	4 / 70 (5.71%)	
occurrences (all)	6	4	
Urinary tract infection			
subjects affected / exposed	5 / 102 (4.90%)	1 / 70 (1.43%)	
occurrences (all)	8	2	
Viral Infection			
subjects affected / exposed	0 / 102 (0.00%)	1 / 70 (1.43%)	
occurrences (all)	0	1	
Viral Upper Respiratory Tract Infection			
subjects affected / exposed	0 / 102 (0.00%)	1 / 70 (1.43%)	
occurrences (all)	0	1	
Metabolism and nutrition disorders			
Abnormal loss of weight			
subjects affected / exposed	1 / 102 (0.98%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Decreased Appetite			
subjects affected / exposed	4 / 102 (3.92%)	3 / 70 (4.29%)	
occurrences (all)	4	3	
Folate deficiency			
subjects affected / exposed	0 / 102 (0.00%)	1 / 70 (1.43%)	
occurrences (all)	0	1	
Glucose tolerance impaired			
subjects affected / exposed	1 / 102 (0.98%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Gout			
subjects affected / exposed	2 / 102 (1.96%)	1 / 70 (1.43%)	
occurrences (all)	3	2	
Hyperkalaemia			
subjects affected / exposed	0 / 102 (0.00%)	1 / 70 (1.43%)	
occurrences (all)	0	1	
Increased appetite			
subjects affected / exposed	0 / 102 (0.00%)	1 / 70 (1.43%)	
occurrences (all)	0	1	
Iron deficiency			

subjects affected / exposed	1 / 102 (0.98%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Malnutrition			
subjects affected / exposed	1 / 102 (0.98%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Type 2 Diabetes mellitus			
subjects affected / exposed	1 / 102 (0.98%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Vitamin D deficiency			
subjects affected / exposed	1 / 102 (0.98%)	0 / 70 (0.00%)	
occurrences (all)	1	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
15 November 2018	Protocol version 2.0: Removal of 12-week time limit for participants to be on stable background treatment, as the time needed to stabilise a participant on treatment can vary and should be the judgment of the principal investigator (treating physician) rather than within a prescribed time limit.
10 December 2018	Protocol version 3.0 Update to events schedule: - Laboratory test will be performed at Visit 2 (baseline) as, given length of screening window, it is considered appropriate to have a baseline sample immediately prior to the commencement of dosing. - Participants should be observed for 1 hour after the first dose to monitor for any acute adverse effects of study drug administration (e.g., bronchospasm), per a comment from the Food and Drug Administration regarding potential for bronchospasm.
05 July 2019	Protocol version 4.0: - Amendment to inclusion criteria 1, regarding the HRCT scan, to allow participants with a HRCT scan older than 12 months to undergo a HRCT scan and be considered for enrolment. - Dosing instructions changed from 2 inhalations with each capsule to 1 to 3 inhalations, to clarify that up to 3 inhalations may be required for proper dosing. HRCT=high resolution computerised tomography
22 April 2020	Global Addendum 1 and 2, dated 22 April 2020 and 31 March 2021, respectively: Amended due to the global coronavirus disease pandemic and its potential impact on participant safety, eligibility and recruitment, as follows: - Use of telephone clinical assessments in lieu of on-site visits, where not safe or feasible - If not randomised within the 12-week screening window, the participant could return for a rescreen once safe. - Completion of home-based spirometry and HRQoL questionnaires/dyspnoea assessments via iPad or 'interview mode'. - Pregnancy monitoring at home and communicated during telephone assessments. HRQoL=health-related quality of life
23 June 2020	Protocol version 5.0: - Removal of stratified randomisation by SoC and increase in site number due to difficulties with enrolment in an acceptable timeframe, with no change in planned total number of participants. - Update to exclusion criteria to allow patients with squamous cell carcinoma to enrol, as no risk is foreseen. - Diffusion capacity for carbon monoxide and 6MWT added to withdrawal assessments as they are important assessments for IPF. - Addition and clarification of rescreen procedures to be performed which included DLCO and spirometry. SoC=standard of care; 6MWT=6-minute walk test; IPF=idiopathic pulmonary fibrosis; DLCO=diffusion capacity for carbon monoxide;

07 April 2021	Protocol version 6.0: - Following the DSMB's recommendation, participants on SoC/approved treatment for IPF were excluded, and the GB0139 10 mg treatment arm was removed. Eligible participants were to be randomised in a 2:1 ratio to 1 of the 2 treatment arms, 3 mg and placebo, to maintain the chance (2/3) of receiving an active treatment at randomisation for individual participants, compared with the previous design - The primary objective was updated to reflect to the current study design - Key secondary endpoints were updated to include: - Change from baseline in SGRQ total score at Week 52 - Moved time to first hospitalisation, respiratory related to the key secondary endpoints - Exploratory endpoints were updated to include: - Time to initiation of pirfenidone or nintedanib treatment for SoC2 participants up to the time when SoC1 and SoC2 were removed - Time to termination of pirfenidone or nintedanib treatment for SoC1 participants up to the time when SoC1 and SoC2 were removed - Screening period duration was updated to 6 weeks - Change of follow-up to be conducted by phone call from 1 week and up to 2 weeks after the last study visit - Exclusion criteria were updated to exclude participants from the trial that: - Currently receiving nintedanib and pirfenidone - Previously using GB0139 or were randomised in GALACTIC-1 - Previously used nintedanib or pirfenidone within 7 days of initiation of screening - Previously used investigational drugs within 30 days of initiation of screening - Participate in another clinical trial - Have hypersensitivity to the active substance (GB0139) or the excipient (lactose) - Duration of IPF diagnosis to screening was changed from 3 to 5 years to facilitate enrolment under the updated patient selection criteria - Coronavirus disease vaccines were added under permitted medications No participants in Belgium enrolled in new trial design DSMB=Drug Safety Monitoring Board;SGRQ=St. George's Respiratory Questionnaire
28 January 2022	Protocol version 7.0: - Exclusion criterion number 11 was updated to exclude only participants participating in another interventional clinical trial, based on the study investigator's suggestion. - Correction of secondary endpoint – proportion of participants with an absolute decline from baseline in FVC% pred of ≤10% and ≤5 at Week 52 (from >10% and >5%, respectively). The revised wording is a definition of a responder, rather than a progressor. - Sample size justification updated. The level of significance and power of the study were revised to be more reflective of a Phase 2 study. As a result of increasing the significance level to 10% and reducing the power to 75%, the sample size decreased to 141 participants. The level of confidence was changed from 95% to 90% to reflect the new level of significance. - Time to termination of pirfenidone or nintedanib treatment was removed from exploratory endpoints as the use of these drugs had been systematically curtailed, so was no longer relevant. FVC=forced vital capacity

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.

A 10 mg dose arm and concomitant use of nintedanib and pirfinidone were removed from the trial design (protocol v. 6.0). The results presented reflects the modified trial design.

Notes: