Clinical trial results:
A Long-Term Extension Study to Evaluate the Safety of Filgotinib in Subjects with Crohn's Disease

Summary

EudraCT number	2016-002763-34
Trial protocol	HU BG AT CZ GB IS SE GR PT SK DE ES BE NL HR IT
Global end of trial date	01 August 2023

Results information

Result version number	v1 (current)
This version publication date	14 June 2024
First version publication date	14 June 2024

Trial information

Trial identification

Sponsor protocol code	GS-US-419-3896

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02914600
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Galapagos NV
Sponsor organisation address	Generaal De Wittelaan L11 A3, Mechelen, Belgium, 2800
Public contact	Galapagos Medical Information, Galapagos NV, medicalinfo@glpg.com
Scientific contact	Galapagos Medical Information, Galapagos NV, medicalinfo@glpg.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	01 August 2023
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	01 August 2023
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study is to observe the long-term safety of filgotinib in participants who have completed or met protocol specified efficacy discontinuation criteria in a prior filgotinib treatment study in Crohn's disease (CD).

Protection of trial subjects:

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

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	17 March 2017
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Netherlands: 30
Country: Number of subjects enrolled	Poland: 108
Country: Number of subjects enrolled	Portugal: 9
Country: Number of subjects enrolled	Slovakia: 13
Country: Number of subjects enrolled	Spain: 24
Country: Number of subjects enrolled	Sweden: 2
Country: Number of subjects enrolled	United Kingdom: 28
Country: Number of subjects enrolled	Croatia: 1
Country: Number of subjects enrolled	Austria: 9
Country: Number of subjects enrolled	Belgium: 58
Country: Number of subjects enrolled	Czechia: 26
Country: Number of subjects enrolled	France: 99
Country: Number of subjects enrolled	Germany: 71
Country: Number of subjects enrolled	Greece: 1
Country: Number of subjects enrolled	Hungary: 18
Country: Number of subjects enrolled	Ireland: 6
Country: Number of subjects enrolled	Italy: 29

Country: Number of subjects enrolled	United States: 274
Country: Number of subjects enrolled	India: 72
Country: Number of subjects enrolled	Ukraine: 52
Country: Number of subjects enrolled	Japan: 48
Country: Number of subjects enrolled	Canada: 43
Country: Number of subjects enrolled	Australia: 40
Country: Number of subjects enrolled	Russian Federation: 22
Country: Number of subjects enrolled	Israel: 19
Country: Number of subjects enrolled	Korea, Democratic People's Republic of: 11
Country: Number of subjects enrolled	Sri Lanka: 11
Country: Number of subjects enrolled	Switzerland: 10
Country: Number of subjects enrolled	Taiwan: 10
Country: Number of subjects enrolled	Romania: 9
Country: Number of subjects enrolled	Malaysia: 8
Country: Number of subjects enrolled	South Africa: 8
Country: Number of subjects enrolled	New Zealand: 7
Country: Number of subjects enrolled	Georgia: 4
Country: Number of subjects enrolled	Hong Kong: 3
Country: Number of subjects enrolled	Singapore: 3
Country: Number of subjects enrolled	Serbia: 2
Worldwide total number of subjects	1188
EEA total number of subjects	513

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)	1130
From 65 to 84 years	58
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants were enrolled in 37 countries. Participants with CD, who had completed or met protocol-specified efficacy discontinuation criteria from previous parent studies (GS-US-419-4015 [NCT03046056], GS-US-419-4016 [NCT03077412] or GS-US-419-3895 [GLPG0634-CL-309] [NCT02914561]) were rolled-over to this long-term extension study.

Pre-assignment

Screening details:

Sponsor decided not to pursue extension of filgotinib indication for CD, as GS-US-419-3895 did not meet the co-primary endpoint and decided to prematurely terminate the study.

Period 1

Period 1 title	Overall study (overall period)
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Blinding implementation details:

Participants who completed the parent study blinded, received blinded treatment. After un-blinding of the parent study, participants received open-label treatment.

Arms

Are arms mutually exclusive?	Yes
Arm title	Filgotinib 200 mg

Arm description:

Participants who received filgotinib 200 milligrams (mg) blinded and completed the parent study, continued to receive filgotinib 200 mg blinded in this study. After unblinding of the parent study, participants continued open-label on filgotinib 200 mg.
Participants who exited the parent study due to disease worsening or failure to meet response or remission criteria, with the exception of US and Korean males who were not considered dual-biologic refractory, received filgotinib 200 mg open-label in this study.
Treatment was administered orally once a day until filgotinib becomes commercially available or until the early termination (up to 308 weeks).

Arm type	Experimental
Investigational medicinal product name	Filgotinib 200 mg
Investigational medicinal product code	
Other name	GS-6034, GLPG0634, Jyseleca®
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Tablet administered orally once daily.

Arm title	Filgotinib 100 mg

Arm description:

Participants who received filgotinib 100 mg blinded and completed the parent study, continued to receive filgotinib 100 mg blinded in this study. After unblinding of the parent study, participants continued open-label on filgotinib 100 mg.
Male participants from the US & Korea who were not considered dual biologic refractory, and who exited the parent study due to disease worsening or failure to meet response or remission criteria, received filgotinib 100 mg open-label in this study.
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Arm type	Experimental

Investigational medicinal product name	Filgotinib 100 mg
Investigational medicinal product code	
Other name	GS-6034, GLPG0634, Jyseleca®
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Tablet administered orally once daily.

Arm title	Placebo

Arm description:

Participants who received placebo and completed the parent study, continued to receive placebo in this extension study. After un-blinding of the parent study, participants on placebo treatment discontinued study drug and study participation.
Treatment was administered orally once a day until un-blinding of the parent study (up to 308 weeks).

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

Dosage and administration details:

Drug matching tablet administered orally once daily.

Number of subjects in period 1	Filgotinib 200 mg	Filgotinib 100 mg	Placebo
Started	945	119	124
Completed	0	0	0
Not completed	945	119	124
Adverse event, serious fatal	-	1	1
Consent withdrawn by subject	158	20	18
Study Unblinded, participant confirmed on Placebo	-	-	55
Adverse event, non-fatal	298	35	25
Death	3	-	-
Pregnancy	8	-	-
Lost to follow-up	10	4	-
Enrolled but not treated	1	-	-
Investigators discretion	169	14	13
Sponsors decision	287	41	12
Non compliance with study drug	6	1	-
Protocol deviation	5	3	-

Baseline characteristics

Reporting groups

Reporting group title	Filgotinib 200 mg

Reporting group description:

Participants who received filgotinib 200 milligrams (mg) blinded and completed the parent study, continued to receive filgotinib 200 mg blinded in this study. After unblinding of the parent study, participants continued open-label on filgotinib 200 mg.
Participants who exited the parent study due to disease worsening or failure to meet response or remission criteria, with the exception of US and Korean males who were not considered dual-biologic refractory, received filgotinib 200 mg open-label in this study.
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Reporting group title	Filgotinib 100 mg

Reporting group description:

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Male participants from the US & Korea who were not considered dual biologic refractory, and who exited the parent study due to disease worsening or failure to meet response or remission criteria, received filgotinib 100 mg open-label in this study.
Treatment was administered orally once a day until filgotinib becomes commercially available or until the early termination (up to 308 weeks).

Reporting group title	Placebo

Reporting group description:

Participants who received placebo and completed the parent study, continued to receive placebo in this extension study. After un-blinding of the parent study, participants on placebo treatment discontinued study drug and study participation.
Treatment was administered orally once a day until un-blinding of the parent study (up to 308 weeks).

Reporting group values	Filgotinib 200 mg	Filgotinib 100 mg	Placebo
Number of subjects	945	119	124
Age categorical Units: Subjects			
Age continuous Units: years arithmetic mean standard deviation	 39.2 ± 13.60	 46.7 ± 13.28	 42.3 ± 12.42
Gender categorical Units: Subjects			
Female	514	33	56
Male	431	86	68
Ethnicity Units: Subjects			
Hispanic or Latino	18	5	0
Not Hispanic or Latino	905	112	123
Not permitted	22	2	1
Race Units: Subjects			

American Indian or Alaska Native	1	0	0
Asian	137	18	23
Native Hawaiian or Other Pacific Islander	2	0	0
Black or African American	18	10	3
White	740	89	96
Other	6	1	0
Not permitted	41	1	2

Reporting group values	Total		
Number of subjects	1188		
Age categorical			
Units: Subjects			

Age continuous			
Units: years			
arithmetic mean			
standard deviation	-		
Gender categorical			
Units: Subjects			
Female	603		
Male	585		
Ethnicity			
Units: Subjects			
Hispanic or Latino	23		
Not Hispanic or Latino	1140		
Not permitted	25		
Race			
Units: Subjects			
American Indian or Alaska Native	1		
Asian	178		
Native Hawaiian or Other Pacific Islander	2		
Black or African American	31		
White	925		
Other	7		
Not permitted	44		

End points

End points reporting groups

Reporting group title	Filgotinib 200 mg

Reporting group description:

Participants who received filgotinib 200 milligrams (mg) blinded and completed the parent study, continued to receive filgotinib 200 mg blinded in this study. After unblinding of the parent study, participants continued open-label on filgotinib 200 mg.
Participants who exited the parent study due to disease worsening or failure to meet response or remission criteria, with the exception of US and Korean males who were not considered dual-biologic refractory, received filgotinib 200 mg open-label in this study.
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Male participants from the US & Korea who were not considered dual biologic refractory, and who exited the parent study due to disease worsening or failure to meet response or remission criteria, received filgotinib 100 mg open-label in this study.
Treatment was administered orally once a day until filgotinib becomes commercially available or until the early termination (up to 308 weeks).

Reporting group title	Placebo

Reporting group description:

Participants who received placebo and completed the parent study, continued to receive placebo in this extension study. After un-blinding of the parent study, participants on placebo treatment discontinued study drug and study participation.
Treatment was administered orally once a day until un-blinding of the parent study (up to 308 weeks).

Primary: Number of Participants with Treatment Emergent Adverse Events (TEAEs)

End point title	Number of Participants with Treatment Emergent Adverse Events (TEAEs)[1]

End point description:

An AE was defined as any untoward medical occurrence in a participant administered a study drug, and which did not necessarily have a causal relationship with this treatment. An AE could therefore be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease (new or exacerbated) temporally associated with the use of study drug whether or not considered related to the study drug. Treatment-emergent adverse events (TEAEs) were defined as 1 or both of the following:
• Any AEs with an onset date on or after the study drug start date and no later than 30 days after permanent discontinuation of study drug
• Any AEs leading to premature discontinuation of study drug.
The Safety Analysis Set (SAF) included all participants who took at least 1 dose of study drug.

End point type	Primary

End point timeframe:

From the First Dose to Week 312

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analysis was intended to be performed for this endpoint.

End point values	Filgotinib 200 mg	Filgotinib 100 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	944	119	124	
Units: participants	820	103	96	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Patient Reported Outcomes 2 (PRO2) Scores

End point title	Change from Baseline in Patient Reported Outcomes 2 (PRO2) Scores

End point description:

PRO2 was a composite score based on 2 components of the CDAI, the number of liquid or soft stools/day for 7 days, stool frequency and abdominal pain (rated on a scale of 0-3) assessed for 7 days The CDAI system was a composite index of 8 disease activity variables: severity of abdominal pain, general well-being, very soft/liquid stool frequency, extra-intestinal symptoms, need for antidiarrheal drugs, presence of an abdominal mass, body weight and hematocrit. Participants reported information regarding symptoms using a diary. The sub scores of abdominal pain (0-3), general well-being (0-4), and number of very soft or liquid stools were summed over the 7 days prior to each visit. The remaining predictors were noted and weighted to create the total CDAI score ranging from 0-600 with a higher score indicating a worse outcome. Participants from safety analysis set with available data were analysed. Here "99999"signifies that no participants were evaluable for the specified timepoint.

End point type	Secondary

End point timeframe:

Baseline, Week (Wk) 12, Wk 24, Wk 48, Wk 96, Wk 156, Wk 216, Wk 264, and Wk 300

End point values	Filgotinib 200 mg	Filgotinib 100 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	911	113	113	
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline: Liquid/ Soft Stool (n= 911,113,113)	5.6 (± 3.26)	4.0 (± 3.12)	2.2 (± 1.92)	
Change at Wk 12:Liquid/ Soft Stool(n=787,103,103)	-1.6 (± 2.71)	-0.7 (± 2.01)	0.2 (± 1.44)	
Change at Wk 24:Liquid/Soft Stool(n=682,89,89)	-1.8 (± 2.89)	-0.7 (± 2.59)	0.1 (± 1.15)	
Change at Wk 48:Liquid/Soft Stool(n=516,74,81)	-2.0 (± 3.14)	-0.8 (± 2.49)	0.0 (± 1.21)	
Change at Wk 96:Liquid/Soft Stool(n=305,49,53)	-2.2 (± 3.11)	-0.7 (± 2.70)	0.4 (± 2.79)	
Change at Wk 156:Liquid/Soft Stool(n=177,30,26)	-2.4 (± 3.14)	-0.7 (± 3.19)	-0.2 (± 1.63)	
Change at Wk 216:Liquid/Soft Stool(n=82,13,6)	-2.8 (± 3.17)	-1.2 (± 4.10)	1.0 (± 1.41)	
Change at Wk 264:Liquid/Soft Stool(n=20,4,0)	-2.0 (± 2.86)	-4.8 (± 6.18)	99999 (± 99999)	
Change at Wk 300:Liquid/Soft Stool(n=4,0,0)	0.0 (± 2.71)	99999 (± 99999)	99999 (± 99999)	

Baseline: Abdominal Pain(n= 911,113,113)	1.6 (± 0.91)	1.0 (± 0.89)	0.7 (± 0.75)	
Change at Wk 12: Abdominal Pain(n=787,103,103)	-0.6 (± 0.91)	-0.2 (± 0.65)	0.0 (± 0.52)	
Change at Wk 24: Abdominal Pain(n=682,89,89)	-0.7 (± 0.92)	-0.2 (± 0.75)	0.0 (± 0.51)	
Change at Wk 48: Abdominal Pain (n=516,74,81)	-0.8 (± 0.97)	-0.3 (± 0.70)	-0.1 (± 0.54)	
Change at Wk 96: Abdominal Pain (n=305,49,53)	-0.8 (± 1.00)	-0.2 (± 0.73)	-0.1 (± 0.55)	
Change at Wk 156: Abdominal Pain (n=177,30,26)	-0.8 (± 0.98)	-0.2 (± 0.77)	0.0 (± 0.57)	
Change at Wk 216: Abdominal Pain (n=82,13,6)	-0.9 (± 1.05)	-0.5 (± 0.88)	0.0 (± 0.00)	
Change at Wk 264: Abdominal Pain (n=20,4,0)	-0.8 (± 0.64)	-1.3 (± 0.50)	99999 (± 99999)	
Change at Wk 300: Abdominal Pain (n=4,0,0)	-0.3 (± 0.50)	99999 (± 99999)	99999 (± 99999)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in CDAI Scores

End point title	Change from Baseline in CDAI Scores

End point description:

The CDAI system was a composite index of 8 disease activity variables: severity of abdominal pain, general well-being, very soft/liquid stool frequency, extra-intestinal symptoms, need for antidiarrheal drugs, presence of an abdominal mass, body weight and haematocrit. Participants reported information regarding symptoms using a diary. The sub scores of abdominal pain (0-3), general well-being (0-4), and number of very soft or liquid stools were then summed over the 7 days prior to each visit. Additionally, the remaining predictors were also noted and weighted to create the total CDAI score which ranged from 0-600 with a higher score indicating a worse outcome. Participants from safety analysis set with available data were analyzed.
Here "99999"signifies that no participants were evaluable for the specified timepoint.

End point type	Secondary

End point timeframe:

Baseline, Wk 12, Wk 24, Wk 48, Wk 96, Wk 156, Wk 216, Wk 264, and Wk 300

End point values	Filgotinib 200 mg	Filgotinib 100 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	897	110	110	
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline (n= 897,110,110)	280.5 (± 116.58)	189.9 (± 112.73)	120.4 (± 81.33)	
Change at Wk 12 (n=710,94,92)	-86.8 (± 114.02)	-29.1 (± 79.84)	4.2 (± 53.42)	
Change at Wk 24(n=608,84,82)	-98.5 (± 122.68)	-30.8 (± 92.92)	5.7 (± 51.30)	

Change at Wk 48 (n=461,69,71)	-110.2 (± 125.08)	-40.9 (± 91.47)	0.6 (± 49.32)	
Change at Wk 96(n=261,46,45)	-118.6 (± 131.49)	-23.3 (± 91.94)	11.0 (± 69.29)	
Change at Wk 156 (n=154,28,24)	-121.4 (± 132.33)	-33.5 (± 99.15)	0.3 (± 59.27)	
Change at Wk 216 (n=65,13,4)	-137.0 (± 147.14)	-57.5 (± 121.12)	2.5 (± 37.76)	
Change at Wk 264 (n=16,4,0)	-134.8 (± 128.86)	-171.5 (± 141.81)	99999 (± 99999)	
Change at Wk 300 (n=4,0,0)	-32.5 (± 92.99)	99999 (± 99999)	99999 (± 99999)	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
From the First Dose to Week 312	
Adverse event reporting additional description:	
Safety Analysis Set	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	26.0

Reporting groups	
Reporting group title	Filgotinib 100 mg

Reporting group description:

Participants who received filgotinib 100 mg blinded and completed the parent study, continued to receive filgotinib 100 mg blinded in this study. After unblinding of the parent study, participants continued open-label on filgotinib 100 mg.
Male participants from the US & Korea who were not considered dual biologic refractory, and who exited the parent study due to disease worsening or failure to meet response or remission criteria, received filgotinib 100 mg open-label in this study.
Treatment was administered orally once a day until filgotinib becomes commercially available or until the early termination (up to 308 weeks).

Reporting group title	Placebo

Reporting group description:

Participants who received placebo and completed the parent study, continued to receive placebo in this extension study. After unblinding of the parent study, participants on placebo treatment discontinued study drug and study participation.
Treatment was administered orally once a day until unblinding of the parent study.

Reporting group title	Filgotinib 200 mg

Reporting group description:

Participants who received filgotinib 200 milligrams (mg) blinded and completed the parent study, continued to receive filgotinib 200 mg blinded in this study. After unblinding of the parent study, participants continued open-label on filgotinib 200 mg.
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Serious adverse events	Filgotinib 100 mg	Placebo	Filgotinib 200 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	34 / 119 (28.57%)	20 / 124 (16.13%)	284 / 944 (30.08%)
number of deaths (all causes)	2	1	6
number of deaths resulting from adverse events	2	1	5
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Parathyroid tumour benign			

subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	1 / 944 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cervix carcinoma stage 0			
subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	1 / 944 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lip and/or oral cavity cancer			
subjects affected / exposed	1 / 119 (0.84%)	0 / 124 (0.00%)	0 / 944 (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
Lung neoplasm			
subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	1 / 944 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Malignant melanoma stage I			
subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	1 / 944 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nasal sinus cancer			
subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	1 / 944 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Papillary renal cell carcinoma			
subjects affected / exposed	1 / 119 (0.84%)	0 / 124 (0.00%)	0 / 944 (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
Breast cancer			
subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	1 / 944 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Prostate cancer			

subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	1 / 944 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Squamous cell carcinoma of skin			
subjects affected / exposed	1 / 119 (0.84%)	0 / 124 (0.00%)	0 / 944 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tumour inflammation			
subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	1 / 944 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Small cell lung cancer			
subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	1 / 944 (0.11%)
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			
Hypertension			
subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	1 / 944 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombophlebitis			
subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	1 / 944 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pregnancy, puerperium and perinatal conditions			
Abortion spontaneous			
subjects affected / exposed	0 / 119 (0.00%)	1 / 124 (0.81%)	2 / 944 (0.21%)
occurrences causally related to treatment / all	0 / 0	0 / 1	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Asthenia			

subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	1 / 944 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Condition aggravated			
subjects affected / exposed	1 / 119 (0.84%)	0 / 124 (0.00%)	0 / 944 (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
Death			
subjects affected / exposed	1 / 119 (0.84%)	0 / 124 (0.00%)	0 / 944 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Inflammation			
subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	1 / 944 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oedema			
subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	1 / 944 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia			
subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	4 / 944 (0.42%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Bartholin's cyst			
subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	1 / 944 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endometriosis			
subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	1 / 944 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Female genital tract fistula			

subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	1 / 944 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pelvic fluid collection			
subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	1 / 944 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vulvovaginal swelling			
subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	1 / 944 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Pulmonary embolism			
subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	3 / 944 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	3 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	1 / 944 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Asthmatic crisis			
subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	1 / 944 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Asthma			
subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	1 / 944 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute respiratory failure			
subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	1 / 944 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			

Depression			
subjects affected / exposed	0 / 119 (0.00%)	1 / 124 (0.81%)	1 / 944 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute psychosis			
subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	1 / 944 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Adjustment disorder			
subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	1 / 944 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Alcohol abuse			
subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	1 / 944 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Alcoholism			
subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	1 / 944 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Completed suicide			
subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	1 / 944 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Delusional disorder, unspecified type			
subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	1 / 944 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Suicide attempt			
subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	1 / 944 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			

General physical condition abnormal			
subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	1 / 944 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood creatinine increased			
subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	1 / 944 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Fractured sacrum			
subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	1 / 944 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Alcohol poisoning			
subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	1 / 944 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anastomotic leak			
subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	1 / 944 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cervix injury			
subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	1 / 944 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Facial bones fracture			
subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	1 / 944 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fracture of penis			
subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	1 / 944 (0.11%)
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 anastomosis complication			
subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	1 / 944 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Multiple injuries			
subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	1 / 944 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Patella fracture			
subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	1 / 944 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Post-traumatic pain			
subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	1 / 944 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rib fracture			
subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	1 / 944 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Road traffic accident			
subjects affected / exposed	1 / 119 (0.84%)	0 / 124 (0.00%)	2 / 944 (0.21%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Congenital, familial and genetic disorders			
Developmental hip dysplasia			
subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	1 / 944 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hydrocele			
subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	1 / 944 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	1 / 119 (0.84%)	0 / 124 (0.00%)	1 / 944 (0.11%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute coronary syndrome			
subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	1 / 944 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Angina pectoris			
subjects affected / exposed	1 / 119 (0.84%)	0 / 124 (0.00%)	1 / 944 (0.11%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mitral valve incompetence			
subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	1 / 944 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial infarction			
subjects affected / exposed	0 / 119 (0.00%)	1 / 124 (0.81%)	1 / 944 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial ischaemia			
subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	1 / 944 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocarditis			
subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	1 / 944 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coronary artery stenosis			
subjects affected / exposed	1 / 119 (0.84%)	0 / 124 (0.00%)	0 / 944 (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 failure congestive			

subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	1 / 944 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure acute			
subjects affected / exposed	0 / 119 (0.00%)	1 / 124 (0.81%)	1 / 944 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac arrest			
subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	1 / 944 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Atrial fibrillation			
subjects affected / exposed	0 / 119 (0.00%)	1 / 124 (0.81%)	1 / 944 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sinus tachycardia			
subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	1 / 944 (0.11%)
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	0 / 119 (0.00%)	0 / 124 (0.00%)	1 / 944 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Aphasia			
subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	1 / 944 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dizziness			
subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	1 / 944 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Superior sagittal sinus thrombosis			

subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	1 / 944 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Epilepsy			
subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	1 / 944 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Headache			
subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	1 / 944 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peripheral sensory neuropathy			
subjects affected / exposed	1 / 119 (0.84%)	0 / 124 (0.00%)	0 / 944 (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
Psychogenic seizure			
subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	1 / 944 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Serotonin syndrome			
subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	1 / 944 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dysarthria			
subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	1 / 944 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transient ischaemic attack			
subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	2 / 944 (0.21%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			

subjects affected / exposed	1 / 119 (0.84%)	1 / 124 (0.81%)	5 / 944 (0.53%)
occurrences causally related to treatment / all	0 / 1	0 / 1	1 / 7
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lymphadenopathy			
subjects affected / exposed	1 / 119 (0.84%)	0 / 124 (0.00%)	0 / 944 (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			
Vestibular disorder			
subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	1 / 944 (0.11%)
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			
Colitis			
subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	2 / 944 (0.21%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anal stenosis			
subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	2 / 944 (0.21%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anal fistula			
subjects affected / exposed	1 / 119 (0.84%)	1 / 124 (0.81%)	7 / 944 (0.74%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 11
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anal fissure			
subjects affected / exposed	1 / 119 (0.84%)	0 / 124 (0.00%)	1 / 944 (0.11%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain upper			
subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	1 / 944 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain			

subjects affected / exposed	2 / 119 (1.68%)	0 / 124 (0.00%)	17 / 944 (1.80%)
occurrences causally related to treatment / all	0 / 2	0 / 0	1 / 18
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain lower			
subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	1 / 944 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal inflammation			
subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	1 / 944 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastritis			
subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	1 / 944 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Food poisoning			
subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	1 / 944 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Enterocolitis			
subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	1 / 944 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Enteritis			
subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	1 / 944 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dysphagia			
subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	1 / 944 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Duodenitis			

subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	1 / 944 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	2 / 944 (0.21%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dental necrosis			
subjects affected / exposed	1 / 119 (0.84%)	0 / 124 (0.00%)	0 / 944 (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
Dental caries			
subjects affected / exposed	0 / 119 (0.00%)	1 / 124 (0.81%)	0 / 944 (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
Crohn's disease			
subjects affected / exposed	5 / 119 (4.20%)	4 / 124 (3.23%)	101 / 944 (10.70%)
occurrences causally related to treatment / all	0 / 6	0 / 4	5 / 108
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Constipation			
subjects affected / exposed	1 / 119 (0.84%)	0 / 124 (0.00%)	1 / 944 (0.11%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colonic fistula			
subjects affected / exposed	1 / 119 (0.84%)	0 / 124 (0.00%)	0 / 944 (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
Colon dysplasia			
subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	1 / 944 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haematochezia			

subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	1 / 944 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colitis ulcerative			
subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	1 / 944 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hiatus hernia			
subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	1 / 944 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ileal stenosis			
subjects affected / exposed	0 / 119 (0.00%)	1 / 124 (0.81%)	4 / 944 (0.42%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatic cyst			
subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	1 / 944 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nausea			
subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	2 / 944 (0.21%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mechanical ileus			
subjects affected / exposed	0 / 119 (0.00%)	1 / 124 (0.81%)	1 / 944 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Large intestine perforation			
subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	1 / 944 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Large intestinal ulcer			

subjects affected / exposed	0 / 119 (0.00%)	1 / 124 (0.81%)	0 / 944 (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
Large intestinal stenosis			
subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	1 / 944 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Large intestinal obstruction			
subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	1 / 944 (0.11%)
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 stenosis			
subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	2 / 944 (0.21%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal obstruction			
subjects affected / exposed	2 / 119 (1.68%)	0 / 124 (0.00%)	8 / 944 (0.85%)
occurrences causally related to treatment / all	0 / 2	0 / 0	2 / 9
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal mucosal tear			
subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	1 / 944 (0.11%)
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 mass			
subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	1 / 944 (0.11%)
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 haemorrhage			
subjects affected / exposed	0 / 119 (0.00%)	1 / 124 (0.81%)	0 / 944 (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
Intestinal fistula			

subjects affected / exposed	1 / 119 (0.84%)	0 / 124 (0.00%)	1 / 944 (0.11%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Inguinal hernia			
subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	1 / 944 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Impaired gastric emptying			
subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	1 / 944 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	2 / 944 (0.21%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subileus			
subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	4 / 944 (0.42%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Small intestinal stenosis			
subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	2 / 944 (0.21%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Small intestinal perforation			
subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	1 / 944 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Small intestinal obstruction			
subjects affected / exposed	9 / 119 (7.56%)	3 / 124 (2.42%)	11 / 944 (1.17%)
occurrences causally related to treatment / all	1 / 10	0 / 3	0 / 14
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Short-bowel syndrome			

subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	1 / 944 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rectal perforation			
subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	1 / 944 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rectal haemorrhage			
subjects affected / exposed	1 / 119 (0.84%)	0 / 124 (0.00%)	3 / 944 (0.32%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis acute			
subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	2 / 944 (0.21%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis			
subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	1 / 944 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholangitis sclerosing			
subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	1 / 944 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bile duct stone			
subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	2 / 944 (0.21%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Biliary obstruction			
subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	1 / 944 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholecystitis			

subjects affected / exposed	1 / 119 (0.84%)	0 / 124 (0.00%)	1 / 944 (0.11%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholelithiasis			
subjects affected / exposed	0 / 119 (0.00%)	1 / 124 (0.81%)	1 / 944 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Portal vein thrombosis			
subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	1 / 944 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholecystitis acute			
subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	1 / 944 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Diabetic foot			
subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	1 / 944 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Erythema nodosum			
subjects affected / exposed	1 / 119 (0.84%)	0 / 124 (0.00%)	0 / 944 (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
Prurigo			
subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	1 / 944 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Renal failure			
subjects affected / exposed	0 / 119 (0.00%)	1 / 124 (0.81%)	0 / 944 (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
Stag horn calculus			

subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	1 / 944 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nephrolithiasis			
subjects affected / exposed	1 / 119 (0.84%)	0 / 124 (0.00%)	2 / 944 (0.21%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Calculus urinary			
subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	3 / 944 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute kidney injury			
subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	4 / 944 (0.42%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal colic			
subjects affected / exposed	1 / 119 (0.84%)	0 / 124 (0.00%)	1 / 944 (0.11%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ureteric obstruction			
subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	1 / 944 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endocrine disorders			
Goitre			
subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	1 / 944 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Arthritis			
subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	1 / 944 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Back pain			
subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	1 / 944 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intervertebral disc protrusion			
subjects affected / exposed	1 / 119 (0.84%)	0 / 124 (0.00%)	0 / 944 (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
Joint effusion			
subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	1 / 944 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteoarthritis			
subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	3 / 944 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteonecrosis			
subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	1 / 944 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rheumatoid arthritis			
subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	1 / 944 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Campylobacter infection			
subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	1 / 944 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal abscess			
subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	2 / 944 (0.21%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abscess			

subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	1 / 944 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abscess intestinal			
subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	2 / 944 (0.21%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abscess limb			
subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	1 / 944 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anal abscess			
subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	15 / 944 (1.59%)
occurrences causally related to treatment / all	0 / 0	0 / 0	3 / 18
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Appendicitis			
subjects affected / exposed	1 / 119 (0.84%)	0 / 124 (0.00%)	0 / 944 (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
Brain abscess			
subjects affected / exposed	1 / 119 (0.84%)	0 / 124 (0.00%)	0 / 944 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchitis			
subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	1 / 944 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COVID-19			
subjects affected / exposed	0 / 119 (0.00%)	1 / 124 (0.81%)	5 / 944 (0.53%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 5
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
COVID-19 pneumonia			

subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	3 / 944 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Cellulitis			
subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	3 / 944 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Clostridium difficile colitis			
subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	2 / 944 (0.21%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colonic abscess			
subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	2 / 944 (0.21%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diverticulitis			
subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	2 / 944 (0.21%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	2 / 944 (0.21%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Herpes zoster disseminated			
subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	1 / 944 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis viral			
subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	2 / 944 (0.21%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal infection			

subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	1 / 944 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Herpes ophthalmic			
subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	1 / 944 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Herpes zoster			
subjects affected / exposed	1 / 119 (0.84%)	0 / 124 (0.00%)	1 / 944 (0.11%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis cryptosporidial			
subjects affected / exposed	1 / 119 (0.84%)	0 / 124 (0.00%)	0 / 944 (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
Influenza			
subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	1 / 944 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Liver abscess			
subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	1 / 944 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mastitis			
subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	1 / 944 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Perirectal abscess			
subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	3 / 944 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary tuberculosis			

subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	1 / 944 (0.11%)
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			
subjects affected / exposed	1 / 119 (0.84%)	0 / 124 (0.00%)	5 / 944 (0.53%)
occurrences causally related to treatment / all	0 / 1	0 / 0	2 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia haemophilus			
subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	1 / 944 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Post procedural infection			
subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	1 / 944 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psoas abscess			
subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	1 / 944 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peritonitis			
subjects affected / exposed	0 / 119 (0.00%)	1 / 124 (0.81%)	0 / 944 (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
Pyelonephritis acute			
subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	1 / 944 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Salmonellosis			
subjects affected / exposed	1 / 119 (0.84%)	0 / 124 (0.00%)	0 / 944 (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
Sepsis			

subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	1 / 944 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sinusitis			
subjects affected / exposed	1 / 119 (0.84%)	0 / 124 (0.00%)	0 / 944 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Staphylococcal bacteraemia			
subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	1 / 944 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Staphylococcal infection			
subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	1 / 944 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Staphylococcal sepsis			
subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	1 / 944 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Subcutaneous abscess			
subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	1 / 944 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tuberculosis			
subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	1 / 944 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	0 / 119 (0.00%)	1 / 124 (0.81%)	0 / 944 (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
Vulval abscess			

subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	1 / 944 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rectal abscess			
subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	3 / 944 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	1 / 119 (0.84%)	0 / 124 (0.00%)	3 / 944 (0.32%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diabetes mellitus inadequate control			
subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	1 / 944 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Electrolyte imbalance			
subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	1 / 944 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypophosphataemia			
subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	2 / 944 (0.21%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Malnutrition			
subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	2 / 944 (0.21%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypokalaemia			
subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	2 / 944 (0.21%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Frequency threshold for reporting non-serious adverse events: 2 %

Non-serious adverse events	Filgotinib 100 mg	Placebo	Filgotinib 200 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	89 / 119 (74.79%)	78 / 124 (62.90%)	697 / 944 (73.83%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Skin papilloma			
subjects affected / exposed	3 / 119 (2.52%)	0 / 124 (0.00%)	14 / 944 (1.48%)
occurrences (all)	3	0	16
Vascular disorders			
Hypertension			
subjects affected / exposed	8 / 119 (6.72%)	3 / 124 (2.42%)	40 / 944 (4.24%)
occurrences (all)	8	3	41
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	3 / 119 (2.52%)	0 / 124 (0.00%)	65 / 944 (6.89%)
occurrences (all)	4	0	94
Fatigue			
subjects affected / exposed	5 / 119 (4.20%)	4 / 124 (3.23%)	35 / 944 (3.71%)
occurrences (all)	6	6	40
Asthenia			
subjects affected / exposed	1 / 119 (0.84%)	1 / 124 (0.81%)	20 / 944 (2.12%)
occurrences (all)	1	1	24
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	2 / 119 (1.68%)	1 / 124 (0.81%)	21 / 944 (2.22%)
occurrences (all)	2	1	23
Dyspnoea			
subjects affected / exposed	0 / 119 (0.00%)	1 / 124 (0.81%)	21 / 944 (2.22%)
occurrences (all)	0	1	23
Psychiatric disorders			
Anxiety			
subjects affected / exposed	3 / 119 (2.52%)	3 / 124 (2.42%)	24 / 944 (2.54%)
occurrences (all)	3	3	26
Insomnia			

subjects affected / exposed	2 / 119 (1.68%)	0 / 124 (0.00%)	23 / 944 (2.44%)
occurrences (all)	2	0	24
Depression			
subjects affected / exposed	3 / 119 (2.52%)	1 / 124 (0.81%)	20 / 944 (2.12%)
occurrences (all)	3	1	20
Investigations			
Mycobacterium tuberculosis complex test positive			
subjects affected / exposed	0 / 119 (0.00%)	5 / 124 (4.03%)	12 / 944 (1.27%)
occurrences (all)	0	5	12
Weight decreased			
subjects affected / exposed	1 / 119 (0.84%)	2 / 124 (1.61%)	22 / 944 (2.33%)
occurrences (all)	1	2	22
Injury, poisoning and procedural complications			
Procedural pain			
subjects affected / exposed	3 / 119 (2.52%)	0 / 124 (0.00%)	3 / 944 (0.32%)
occurrences (all)	3	0	4
Meniscus injury			
subjects affected / exposed	3 / 119 (2.52%)	1 / 124 (0.81%)	2 / 944 (0.21%)
occurrences (all)	3	1	2
Arthropod bite			
subjects affected / exposed	3 / 119 (2.52%)	0 / 124 (0.00%)	5 / 944 (0.53%)
occurrences (all)	3	0	5
Nervous system disorders			
Headache			
subjects affected / exposed	4 / 119 (3.36%)	11 / 124 (8.87%)	79 / 944 (8.37%)
occurrences (all)	5	12	95
Dizziness			
subjects affected / exposed	1 / 119 (0.84%)	1 / 124 (0.81%)	26 / 944 (2.75%)
occurrences (all)	1	1	28
Blood and lymphatic system disorders			
Lymphopenia			
subjects affected / exposed	2 / 119 (1.68%)	1 / 124 (0.81%)	27 / 944 (2.86%)
occurrences (all)	3	1	34
Iron deficiency anaemia			
subjects affected / exposed	0 / 119 (0.00%)	0 / 124 (0.00%)	22 / 944 (2.33%)
occurrences (all)	0	0	23

Anaemia			
subjects affected / exposed	3 / 119 (2.52%)	5 / 124 (4.03%)	61 / 944 (6.46%)
occurrences (all)	3	5	73
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	5 / 119 (4.20%)	5 / 124 (4.03%)	21 / 944 (2.22%)
occurrences (all)	5	6	27
Anal fistula			
subjects affected / exposed	3 / 119 (2.52%)	5 / 124 (4.03%)	24 / 944 (2.54%)
occurrences (all)	3	5	31
Abdominal pain upper			
subjects affected / exposed	2 / 119 (1.68%)	1 / 124 (0.81%)	24 / 944 (2.54%)
occurrences (all)	2	1	27
Abdominal pain			
subjects affected / exposed	15 / 119 (12.61%)	15 / 124 (12.10%)	93 / 944 (9.85%)
occurrences (all)	19	18	126
Abdominal distension			
subjects affected / exposed	5 / 119 (4.20%)	0 / 124 (0.00%)	17 / 944 (1.80%)
occurrences (all)	5	0	19
Vomiting			
subjects affected / exposed	3 / 119 (2.52%)	3 / 124 (2.42%)	67 / 944 (7.10%)
occurrences (all)	3	3	86
Rectal haemorrhage			
subjects affected / exposed	3 / 119 (2.52%)	1 / 124 (0.81%)	10 / 944 (1.06%)
occurrences (all)	3	1	12
Nausea			
subjects affected / exposed	8 / 119 (6.72%)	4 / 124 (3.23%)	74 / 944 (7.84%)
occurrences (all)	8	6	83
Gastrooesophageal reflux disease			
subjects affected / exposed	3 / 119 (2.52%)	1 / 124 (0.81%)	22 / 944 (2.33%)
occurrences (all)	3	1	24
Gastritis			
subjects affected / exposed	3 / 119 (2.52%)	1 / 124 (0.81%)	16 / 944 (1.69%)
occurrences (all)	3	1	16
Dyspepsia			

subjects affected / exposed	2 / 119 (1.68%)	3 / 124 (2.42%)	29 / 944 (3.07%)
occurrences (all)	2	3	31
Diarrhoea			
subjects affected / exposed	10 / 119 (8.40%)	11 / 124 (8.87%)	54 / 944 (5.72%)
occurrences (all)	13	12	66
Crohn's disease			
subjects affected / exposed	26 / 119 (21.85%)	20 / 124 (16.13%)	210 / 944 (22.25%)
occurrences (all)	36	22	269
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	3 / 119 (2.52%)	1 / 124 (0.81%)	5 / 944 (0.53%)
occurrences (all)	3	1	5
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	7 / 119 (5.88%)	2 / 124 (1.61%)	27 / 944 (2.86%)
occurrences (all)	7	3	29
Dermatitis contact			
subjects affected / exposed	3 / 119 (2.52%)	1 / 124 (0.81%)	2 / 944 (0.21%)
occurrences (all)	3	1	2
Renal and urinary disorders			
Nephrolithiasis			
subjects affected / exposed	7 / 119 (5.88%)	2 / 124 (1.61%)	11 / 944 (1.17%)
occurrences (all)	9	2	11
Musculoskeletal and connective tissue disorders			
Muscle spasms			
subjects affected / exposed	4 / 119 (3.36%)	1 / 124 (0.81%)	15 / 944 (1.59%)
occurrences (all)	4	1	18
Intervertebral disc protrusion			
subjects affected / exposed	3 / 119 (2.52%)	0 / 124 (0.00%)	4 / 944 (0.42%)
occurrences (all)	3	0	4
Back pain			
subjects affected / exposed	4 / 119 (3.36%)	1 / 124 (0.81%)	43 / 944 (4.56%)
occurrences (all)	5	3	53
Arthralgia			
subjects affected / exposed	15 / 119 (12.61%)	1 / 124 (0.81%)	82 / 944 (8.69%)
occurrences (all)	24	3	103

Infections and infestations			
Urinary tract infection			
subjects affected / exposed	8 / 119 (6.72%)	1 / 124 (0.81%)	57 / 944 (6.04%)
occurrences (all)	14	1	82
Upper respiratory tract infection			
subjects affected / exposed	8 / 119 (6.72%)	3 / 124 (2.42%)	57 / 944 (6.04%)
occurrences (all)	9	4	84
Sinusitis			
subjects affected / exposed	7 / 119 (5.88%)	0 / 124 (0.00%)	30 / 944 (3.18%)
occurrences (all)	9	0	35
Pharyngitis			
subjects affected / exposed	1 / 119 (0.84%)	3 / 124 (2.42%)	18 / 944 (1.91%)
occurrences (all)	1	3	22
Oral herpes			
subjects affected / exposed	3 / 119 (2.52%)	0 / 124 (0.00%)	14 / 944 (1.48%)
occurrences (all)	4	0	19
Anal abscess			
subjects affected / exposed	3 / 119 (2.52%)	2 / 124 (1.61%)	16 / 944 (1.69%)
occurrences (all)	3	2	22
Bronchitis			
subjects affected / exposed	5 / 119 (4.20%)	2 / 124 (1.61%)	30 / 944 (3.18%)
occurrences (all)	5	4	37
COVID-19			
subjects affected / exposed	17 / 119 (14.29%)	9 / 124 (7.26%)	127 / 944 (13.45%)
occurrences (all)	17	10	139
Gastroenteritis			
subjects affected / exposed	4 / 119 (3.36%)	1 / 124 (0.81%)	26 / 944 (2.75%)
occurrences (all)	5	1	29
Herpes zoster			
subjects affected / exposed	1 / 119 (0.84%)	1 / 124 (0.81%)	22 / 944 (2.33%)
occurrences (all)	1	1	22
Influenza			
subjects affected / exposed	4 / 119 (3.36%)	4 / 124 (3.23%)	27 / 944 (2.86%)
occurrences (all)	5	6	31
Latent tuberculosis			

subjects affected / exposed	2 / 119 (1.68%)	4 / 124 (3.23%)	14 / 944 (1.48%)
occurrences (all)	2	4	14
Nasopharyngitis			
subjects affected / exposed	13 / 119 (10.92%)	6 / 124 (4.84%)	81 / 944 (8.58%)
occurrences (all)	21	6	101
Metabolism and nutrition disorders			
Folate deficiency			
subjects affected / exposed	3 / 119 (2.52%)	0 / 124 (0.00%)	13 / 944 (1.38%)
occurrences (all)	5	0	14
Hyperlipidaemia			
subjects affected / exposed	4 / 119 (3.36%)	0 / 124 (0.00%)	3 / 944 (0.32%)
occurrences (all)	4	0	3
Hypokalaemia			
subjects affected / exposed	3 / 119 (2.52%)	2 / 124 (1.61%)	22 / 944 (2.33%)
occurrences (all)	4	2	24
Hypophosphataemia			
subjects affected / exposed	1 / 119 (0.84%)	1 / 124 (0.81%)	30 / 944 (3.18%)
occurrences (all)	1	1	35
Iron deficiency			
subjects affected / exposed	1 / 119 (0.84%)	2 / 124 (1.61%)	21 / 944 (2.22%)
occurrences (all)	1	2	23

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
07 September 2016	Amendment 1: Updated Study Procedures Table and footnotes to reflect changes made to weekly visits assessments/procedures in the protocol. Protocol GS-US-419-3896 title changed from Open-Label to Long-Term Extension study.
11 November 2016	Amendment 2: Updated Study Procedures Table to reflect changes made to the study visit assessments/procedures in the protocol.
15 June 2017	Amendment 3: Updates were made in response to the South Korean Ministry of Food and Drug Safety request for the use of 200 mg in males in Korea to be limited to male subjects who had failed 2 classes of biologic therapies (any tumor necrosis factor-alpha [TNFα] antagonist and vedolizumab). Updated sections with emerging relevant clinical and pipeline data, and ensured consistency with Investigator Brochure (IB) Ed 12. Updated Study Procedures Table to reflect changes made to the study visit assessments/procedures in the protocol.
08 March 2018	Amendment 4: Clarification on inclusion/exclusion criteria including those surrounding hepatitis and tuberculosis (TB), clarified Day 1 visit procedures and provided additional flexibility for enhanced safety monitoring (suggested infectious workups for disease worsening). Updated the department name from Drug Safety and Public Health (DSPH) to Pharmacovigilance & Epidemiology (PVE) Updated the Study Procedures Table and footnotes to reflect changes made to the study visit assessments/procedures in the protocol.
09 November 2018	Amendment 5: To allow study-wide unblinding of GSUS- 419-3896 after the parent studies (GSUS- 419-4015, GS-US-419-4016 and GSUS- 419-3895) were unblinded. Inclusion criterion # 2 was amended to include a comprehensive list of the Gilead-sponsored Crohn’s disease (CD) parent studies eligible for roll-over into this long-term extension (LTE) study.
17 April 2019	Amendment 5.1: Updated to allow for continuation of concomitant vedolizumab use in subjects who were previously enrolled in study GS-US-419-4016.
05 September 2019	Amendment 6: Updated duration of treatment to 432 weeks, or until filgotinib becomes commercially available, whichever comes first, to ensure continued access to filgotinib in subjects who have completed the parent study (GS-US-419-3896). Amended study drug interruption or discontinuation criteria to reflect that subjects with newly positive QuantiFERON® TB test (or centrally reported equivalent assay) are now considered for study drug interruption instead of permanent discontinuation.

23 March 2020	Amendment 7: Updated study unblinding language to clarify the unblinding process and to allow subject unblinding once the corresponding parent study (GS-US-419-4015, GS-US-419-4016, or GS-US-419-3895) was unblinded. Updated study drug interruption criteria to allow the investigator to make the assessment of active or latent TB infection based on subject's individual risk factors and further evaluations per standard of care upon seroconversion or sequential indeterminate QuantiFERON® TB tests. Changes were implemented at the request of the United States Food and Drug Administration (US FDA) regarding new safety information of other Janus kinase (JAK) inhibitors on the potential risk of thromboembolic events. A statement was added to clarify the procedures to be followed if the Data Monitoring Committee (DMC) recommended stopping the study due to lack of efficacy.
02 December 2021	Amendment 8: Changed sponsorship from Gilead Sciences, Inc. to Galapagos NV. The Galapagos study number (GLPG0634-CL-310) was added.
23 November 2022	Amendment 9: The duration of treatment and end of study were adapted due to the limited number of subjects expected to continue after 31 January 2025 and to allow subjects from other filgotinib treatment studies for CD to be enrolled into this study. Dose interruption criteria regarding renal impairment and lymphopenia were added to align with the IB Edition 17, 15 Jul 2022. The length of time women of childbearing potential should use effective contraception after cessation of filgotinib treatment was changed to align with the post-treatment visit. The requirements for male condom use and reporting of pregnancies in female partners were removed to align with the IB Edition 17, 15 Jul 2022. Monthly pregnancy testing in clinic was changed to allow at home testing for subjects outside the US to reduce the burden on subjects.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
06 April 2023	After analyzing all available data from the DIVERSITY 1 and DIVERSITY LTE studies, the sponsor decided not to pursue extension of the filgotinib indication for CD and decided to terminate the DIVERSITY LTE study.	-

Notes:

Limitations and caveats

None reported