Clinical trial results:
A multicenter, open-label, long-term follow-up safety and efficacy study of GLPG0634 treatment in subjects with moderately to severely active rheumatoid arthritis

Summary

EudraCT number	2012-003655-11
Trial protocol	BE LV HU DE BG CZ FR
Global end of trial date	19 January 2023

Results information

Result version number	v1 (current)
This version publication date	27 January 2024
First version publication date	27 January 2024

Trial information

Trial identification

Sponsor protocol code	GLPG0634-CL-205

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02065700
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	19 January 2023
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	19 January 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective is to evaluate the long-term safety and tolerability of filgotinib for the treatment of rheumatoid arthritis (RA).

Protection of trial subjects:

Before initiation of the study at each study center, the protocol, the informed consent form (ICF), other written material given to the participants, and any other relevant study documentation was to be submitted to the appropriate Independent Ethics Committee (IEC)/Institutional Review Board (IRB). Written approval of the study and all relevant study information was to be obtained before the study center could be initiated or the study medication was released to the investigator. Any necessary extensions or renewals of IEC/IRB approval were to be obtained for changes to the study such as modification of the protocol, the ICF or other study documentation. The written approval of the IEC/IRB together with the approved ICF was to be filed in the study files. The investigator was to promptly report to the IEC/IRB any new information that could have adversely affected the safety of the participants or the conduct of the study. The investigator was to submit written summaries of the study status to the IEC/IRB as required. On completion of the study, the IEC/IRB was to be notified that the study had ended.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	25 February 2014
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Argentina: 67
Country: Number of subjects enrolled	Mexico: 66
Country: Number of subjects enrolled	Chile: 46
Country: Number of subjects enrolled	Colombia: 44
Country: Number of subjects enrolled	Guatemala: 38
Country: Number of subjects enrolled	Poland: 76
Country: Number of subjects enrolled	Hungary: 51
Country: Number of subjects enrolled	Bulgaria: 31
Country: Number of subjects enrolled	Latvia: 27
Country: Number of subjects enrolled	Romania: 4
Country: Number of subjects enrolled	Russian Federation: 65
Country: Number of subjects enrolled	Ukraine: 63
Country: Number of subjects enrolled	Moldova, Republic of: 24
Country: Number of subjects enrolled	United States: 92

Country: Number of subjects enrolled	Czechia: 10
Country: Number of subjects enrolled	Spain: 9
Country: Number of subjects enrolled	Australia: 5
Country: Number of subjects enrolled	New Zealand: 8
Country: Number of subjects enrolled	Belgium: 5
Country: Number of subjects enrolled	Israel: 4
Country: Number of subjects enrolled	Germany: 3
Country: Number of subjects enrolled	France: 1
Worldwide total number of subjects	739
EEA total number of subjects	217

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)	626
From 65 to 84 years	113
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants with moderately to severely active rheumatoid arthritis were enrolled in this study.

Pre-assignment

Screening details:

Participants from the previous core studies (GLPG0634-CL-203 [2012-003635-31] or GLPG0634-CL-204 [2012-003654-86]) were roll-over into this long-term follow-up extension study.

Period 1

Period 1 title	Overall (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Filgotinib Darwin 1

Arm description:

Participants who received placebo in Study GLPG0634-CL-203 (2012-003635-31) were randomized to receive oral dose of filgotinib tablet at 100 milligrams (mg) twice daily (b.i.d), or 200 mg once daily (q.d) in this extension study. All other participants (except male participants in United States [US]) continued the same regimen as received in parent study. Male participants in the US were limited to dosing with filgotinib 100 mg q.d due to Food and Drug Administration (FDA) requirement based on a nonclinical finding. Treatment was administered until marketing, local (if applicable) regulatory and/or pertinent local reimbursement approval.
Participants started the study with the same dose level (filgotinib 200 mg per day) and in case of intolerance or safety reasons and as per investigator's discretion, the daily dose of filgotinib was decreased to 100 mg q.d and was returned to 200 mg per day after the reasons for decreasing the dose had resolved and at the investigator's discretion.

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

Dosage and administration details:

Administered as Oral Tablets.

Arm title	Filgotinib Darwin 2

Arm description:

Participants from Study GLPG0634-CL-204 (2012-003654-86) were rolled-over to receive oral dose of filgotinib tablet at 200 mg q.d in this extension study, until marketing, local (if applicable) regulatory and/or pertinent local reimbursement approval.
Participants started the study with the same dose level (filgotinib 200 mg per day) and in case of intolerance or safety reasons and as per investigator's discretion, the daily dose of filgotinib was decreased to 100 mg q.d and was returned to 200 mg per day after the reasons for decreasing the dose had resolved and at the investigator's discretion.

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

Dosage and administration details:
Administered as Oral Tablets.

Number of subjects in period 1	Filgotinib Darwin 1	Filgotinib Darwin 2
Started	497	242
Completed	161	81
Not completed	336	161
Consent withdrawn by subject	90	29
Physician decision	2	-
Use of Non-permitted Concurrent Therapy	3	-
Adverse event, non-fatal	165	101
Treatment Failure	3	2
Other	21	3
Adverse Event and Treatment Failure	-	2
Lost to follow-up	12	9
Sponsor Request	38	15
Noncompliance with Study Procedures	2	-

Baseline characteristics

Reporting groups

Reporting group title	Filgotinib Darwin 1

Reporting group description:

Participants who received placebo in Study GLPG0634-CL-203 (2012-003635-31) were randomized to receive oral dose of filgotinib tablet at 100 milligrams (mg) twice daily (b.i.d), or 200 mg once daily (q.d) in this extension study. All other participants (except male participants in United States [US]) continued the same regimen as received in parent study. Male participants in the US were limited to dosing with filgotinib 100 mg q.d due to Food and Drug Administration (FDA) requirement based on a nonclinical finding. Treatment was administered until marketing, local (if applicable) regulatory and/or pertinent local reimbursement approval.
Participants started the study with the same dose level (filgotinib 200 mg per day) and in case of intolerance or safety reasons and as per investigator's discretion, the daily dose of filgotinib was decreased to 100 mg q.d and was returned to 200 mg per day after the reasons for decreasing the dose had resolved and at the investigator's discretion.

Reporting group title	Filgotinib Darwin 2

Reporting group description:

Participants from Study GLPG0634-CL-204 (2012-003654-86) were rolled-over to receive oral dose of filgotinib tablet at 200 mg q.d in this extension study, until marketing, local (if applicable) regulatory and/or pertinent local reimbursement approval.
Participants started the study with the same dose level (filgotinib 200 mg per day) and in case of intolerance or safety reasons and as per investigator's discretion, the daily dose of filgotinib was decreased to 100 mg q.d and was returned to 200 mg per day after the reasons for decreasing the dose had resolved and at the investigator's discretion.

Reporting group values	Filgotinib Darwin 1	Filgotinib Darwin 2	Total
Number of subjects	497	242	739
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	53	52	
standard deviation	± 11.7	± 12.2	-
Gender categorical Units: Subjects			
Female	405	198	603
Male	92	44	136
Ethnicity Units: Subjects			
Hispanic or Latino	208	85	293
Not Hispanic or Latino	289	157	446
Unknown or Not Reported	0	0	0
Race Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	1	1	2
Native Hawaiian or Other Pacific Islander	0	1	1
Black or African American	3	3	6
White	374	181	555
More than one race	0	0	0

Unknown or Not Reported	119	56	175

End points

End points reporting groups

Reporting group title	Filgotinib Darwin 1

Reporting group description:

Participants who received placebo in Study GLPG0634-CL-203 (2012-003635-31) were randomized to receive oral dose of filgotinib tablet at 100 milligrams (mg) twice daily (b.i.d), or 200 mg once daily (q.d) in this extension study. All other participants (except male participants in United States [US]) continued the same regimen as received in parent study. Male participants in the US were limited to dosing with filgotinib 100 mg q.d due to Food and Drug Administration (FDA) requirement based on a nonclinical finding. Treatment was administered until marketing, local (if applicable) regulatory and/or pertinent local reimbursement approval.
Participants started the study with the same dose level (filgotinib 200 mg per day) and in case of intolerance or safety reasons and as per investigator's discretion, the daily dose of filgotinib was decreased to 100 mg q.d and was returned to 200 mg per day after the reasons for decreasing the dose had resolved and at the investigator's discretion.

Reporting group title	Filgotinib Darwin 2

Reporting group description:

Participants from Study GLPG0634-CL-204 (2012-003654-86) were rolled-over to receive oral dose of filgotinib tablet at 200 mg q.d in this extension study, until marketing, local (if applicable) regulatory and/or pertinent local reimbursement approval.
Participants started the study with the same dose level (filgotinib 200 mg per day) and in case of intolerance or safety reasons and as per investigator's discretion, the daily dose of filgotinib was decreased to 100 mg q.d and was returned to 200 mg per day after the reasons for decreasing the dose had resolved and at the investigator's discretion.

Primary: Number of Participants Experiencing Treatment-Emergent Adverse Events

End point title	Number of Participants Experiencing Treatment-Emergent Adverse Events[1]

End point description:

An Adverse event (AE) was any untoward medical occurrence in a clinical study participant administered a medicinal (investigational or non-investigational) product. An AE does not necessarily have a causal relationship with the treatment. An AE can therefore be any unfavorable and unintended sign (including an abnormal finding), symptom, or disease temporally associated with the use of a medicinal (investigational or non-investigational) product, whether or not related to that medicinal (investigational or non-investigational) product.
Treatment-emergent adverse events (TEAEs) are defined as any AEs with an onset date on or after the filgotinib start date in the core studies or GLPG0634-CL-205 (2012-003655-11), and no later than 30 days after permanent discontinuation of filgotinib in GLPG0634-CL-205 (2012-003655-11).
The Safety Analysis Set included all participants who enrolled in the extension study and received at least one dose of study drug.

End point type	Primary

End point timeframe:

From First dose to Week 437

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 Darwin 1	Filgotinib Darwin 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	497	242		
Units: participants	453	223		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Achieving American College of Rheumatology (ACR)20 Response: Non- Responder Imputation (NRI)

End point title	Percentage of Participants Achieving American College of Rheumatology (ACR)20 Response: Non- Responder Imputation (NRI)

End point description:

The ACR response was a measurement of improvement in multiple disease assessment criteria. The ACR20 response was defined as: 1) ≥ 20% improvement from baseline in swollen joint count 66 (SJC66), and 2) ≥ 20% improvement from baseline in tender joint count 68 (TJC68), and 3) ≥ 20% improvement from baseline in at least 3 of the following 5 items: 1. Pain visual analog scale (VAS) (taken from the Health Assessment Questionnaire - Disability Index [HAQ-DI]), 2.Subject's Global Assessment of Disease Activity (SGA) (VAS), 3. Physician's Global Assessment of Disease Activity (PGA) (VAS), 4. Total HAQ-DI score, and 5. High-Sensitivity C- Reactive Protein (hsCRP).

The Full Analysis Set (FAS) included all participants who enrolled in the extension study and received at least one dose of study drug.

NRI: Participants with missing outcomes were set as nonresponders for binary response measurements.

End point type	Secondary

End point timeframe:

Extension Baseline, Weeks 12, 24, 36, 48, 60, 72, 84, 96, 108, 120, 132, 144, 156, 168, 180, 192, 204, 216, 228, 240, 252, 264, 276, 288, 300, 312, 324, 336, 348, 360, 372, 384, 396, 408

End point values	Filgotinib Darwin 1	Filgotinib Darwin 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	497	242		
Units: Percentage of participants				
number (not applicable)				
Week 12	83.9	83.1		
Week 24	75.3	77.7		
Week 36	75.1	75.2		
Week 48	71.8	71.1		
Week 60	67.8	69.4		
Week 72	68.4	62.4		
Week 84	65.8	64.5		
Week 96	68.2	61.6		
Week 108	61.6	58.3		
Week 120	57.7	59.1		
Week 132	59.0	57.4		
Week 144	56.3	57.4		
Week 156	50.7	50.4		
Week 168	52.3	47.9		

Week 180	52.1	51.7		
Week 192	49.7	48.8		
Week 204	48.9	50.8		
Week 216	45.7	50.8		
Week 228	47.9	48.3		
Week 240	45.5	43.8		
Week 252	42.1	42.1		
Week 264	39.4	40.9		
Week 276	39.6	44.2		
Week 288	36.6	38.8		
Week 300	35.6	39.7		
Week 312	36.8	36.0		
Week 324	36.6	37.2		
Week 336	34.6	35.5		
Week 348	33.2	34.7		
Week 360	31.4	31.4		
Week 372	30.0	28.9		
Week 384	28.0	27.7		
Week 396	26.2	28.5		
Week 408	0.4	0.4		
Extension Baseline	76.5	77.3		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Achieving ACR20 Response: Observed Case (OC)

End point title	Percentage of Participants Achieving ACR20 Response: Observed Case (OC)

End point description:

The ACR response was a measurement of improvement in multiple disease assessment criteria.
The ACR20 response was defined as: 1) ≥ 20% improvement from baseline in SJC66, and 2) ≥ 20% improvement from baseline in tender TJC68, and 3) ≥ 20% improvement from baseline in at least 3 of the following 5 items: 1. Pain VAS (taken from the HAQ-DI), 2.SGA (VAS), 3. PGA (VAS), 4. Total HAQ-DI score, and 5. hsCRP.

FAS with available data was analyzed.

OC: only observed values were used for analysis. No missing data imputation was performed.

Different participants could be analyzed at different timepoints, resulting in overall FAS participants being analyzed.

End point type	Secondary

End point timeframe:

Extension Baseline, Weeks 12, 24, 36, 48, 60, 72, 84, 96, 108, 120, 132, 144, 156, 168, 180, 192, 204, 216, 228, 240, 252, 264, 276, 288, 300, 312, 324, 336, 348, 360, 372, 384, 396, 408

End point values	Filgotinib Darwin 1	Filgotinib Darwin 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	497	242		
Units: Percentage of participants				
number (not applicable)				
Week 12 (n=484, n=230)	86.2	87.4		
Week 24 (n=441, n=210)	84.8	89.5		
Week 36 (n=431, n=204)	86.5	89.2		
Week 48 (n=422, n=198)	84.6	86.9		
Week 60 (n=399, n=185)	84.5	90.8		
Week 72 (n=387, n=172)	87.9	87.8		
Week 84 (n=375, n=170)	87.2	91.8		
Week 96 (n=377, n=163)	89.9	91.4		
Week 108 (n=356, n=158)	86.0	89.2		
Week 120 (n=334, n=157)	85.9	91.1		
Week 132 (n=333, n=151)	88.0	92.1		
Week 144 (n=323, n=155)	86.7	89.7		
Week 156 (n=289, n=136)	87.2	89.7		
Week 168 (n=298, n=138)	87.2	84.1		
Week 180 (n=291, n=141)	89.0	88.7		
Week 192 (n=281, n=133)	87.9	88.7		
Week 204 (n=272, n=134)	89.3	91.8		
Week 216 (n=262, n=132)	86.6	93.2		
Week 228 (n=266, n=126)	89.5	92.9		
Week 240 (n=256, n=119)	88.3	89.1		
Week 252 (n=233, n=111)	89.7	91.9		
Week 264 (n=227, n=109)	86.3	90.8		
Week 276 (n=215, n=114)	91.6	93.9		
Week 288 (n=207, n=110)	87.9	85.5		
Week 300 (n=201, n=105)	88.1	91.4		
Week 312 (n=206, n=100)	88.8	87.0		
Week 324 (n=203, n=104)	89.7	86.5		
Week 336 (n=194, n=97)	88.7	88.7		
Week 348 (n=188, n=92)	87.8	91.3		
Week 360 (n=180, n=86)	86.7	88.4		
Week 372 (n=166, n=82)	89.8	85.4		
Week 384 (n=163, n=79)	85.3	84.8		
Week 396 (n=153, n=75)	85.0	92.0		
Week 408 (n=3, n=2)	66.7	50.0		
Extension Baseline (n=491, n=235)	77.4	79.6		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Achieving ACR50 Response: NRI

End point title	Percentage of Participants Achieving ACR50 Response: NRI

End point description:

The ACR response was a measurement of improvement in multiple disease assessment criteria. ACR50 response was defined as: 1) ≥ 50% improvement from baseline in SJC66, and 2) ≥ 50% improvement from baseline in TJC68, and 3) ≥ 50% improvement from baseline in at least 3 of the following 5 items: 1. Pain VAS (taken from the HAQ-DI) 2.SGA (VAS) 3. PGA (VAS) 4. Total HAQ-DI score 5. hsCRP.

FAS.

NRI: Participants with missing outcomes were set as nonresponders for binary response measurements.

End point type	Secondary

End point timeframe:

Extension Baseline, Weeks 12, 24, 36, 48, 60, 72, 84, 96, 108, 120, 132, 144, 156, 168, 180, 192, 204, 216, 228, 240, 252, 264, 276, 288, 300, 312, 324, 336, 348, 360, 372, 384, 396, 408

End point values	Filgotinib Darwin 1	Filgotinib Darwin 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	497	242		
Units: Percentage of participants				
number (not applicable)				
Week 12	60.8	61.2		
Week 24	56.7	60.3		
Week 36	58.1	60.3		
Week 48	55.9	53.7		
Week 60	53.9	51.2		
Week 72	53.3	47.1		
Week 84	52.9	51.7		
Week 96	55.5	47.1		
Week 108	49.1	43.8		
Week 120	48.7	43.8		
Week 132	47.5	42.1		
Week 144	46.9	43.0		
Week 156	42.3	35.1		
Week 168	43.9	34.7		
Week 180	42.7	38.8		
Week 192	38.4	37.6		
Week 204	37.8	38.4		
Week 216	36.0	35.1		
Week 228	38.4	34.7		
Week 240	34.2	33.9		
Week 252	32.0	32.6		
Week 264	30.6	33.1		
Week 276	29.6	36.0		
Week 288	29.8	33.5		
Week 300	29.2	28.9		
Week 312	29.0	26.9		
Week 324	30.0	28.1		
Week 336	27.4	25.6		
Week 348	27.2	26.4		

Week 360	24.5	24.0		
Week 372	23.7	24.4		
Week 384	21.3	21.5		
Week 396	19.9	20.7		
Week 408	0.4	0.4		
Extension Baseline	48.5	45.0		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Achieving ACR50 Response: OC

End point title	Percentage of Participants Achieving ACR50 Response: OC

End point description:

The ACR response was a measurement of improvement in multiple disease assessment criteria. ACR50 response was defined as: 1) ≥ 50% improvement from baseline in SJC66, and 2) ≥ 50% improvement from baseline in TJC68, and 3) ≥ 50% improvement from baseline in at least 3 of the following 5 items: 1. Pain VAS (taken from the HAQ-DI) 2.SGA (VAS) 3. PGA (VAS) 4. Total HAQ-DI score 5. hsCRP.

FAS with available data was analyzed.

OC: only observed values were used for analysis. No missing data imputation was performed.

Different participants could be analyzed at different timepoints, resulting in overall FAS participants being analyzed.

End point type	Secondary

End point timeframe:

Extension Baseline, Weeks 12, 24, 36, 48, 60, 72, 84, 96, 108, 120, 132, 144, 156, 168, 180, 192, 204, 216, 228, 240, 252, 264, 276, 288, 300, 312, 324, 336, 348, 360, 372, 384, 396, 408

End point values	Filgotinib Darwin 1	Filgotinib Darwin 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	497	242		
Units: Percentage of participants				
number (not applicable)				
Week 12 (n=484, n=231)	62.4	64.1		
Week 24 (n=440, n=211)	64.1	69.2		
Week 36 (n=430, n=204)	67.2	71.6		
Week 48 (n=422, n=199)	65.9	65.3		
Week 60 (n=398, n=187)	67.3	66.3		
Week 72 (n=387, n=173)	68.5	65.9		
Week 84 (n=376, n=170)	69.9	73.5		
Week 96 (n=377, n=164)	73.2	69.5		
Week 108 (n=357, n=159)	68.3	66.7		
Week 120 (n=322, n=157)	72.9	67.5		
Week 132 (n=331, n=153)	71.3	66.7		

Week 144 (n=327, n=154)	71.3	67.5		
Week 156 (n=290, n=135)	72.4	63.0		
Week 168 (n=297, n=138)	73.4	60.9		
Week 180 (n=292, n=140)	72.6	67.1		
Week 192 (n=283, n=134)	67.5	67.9		
Week 204 (n=270, n=134)	69.6	69.4		
Week 216 (n=263, n=132)	68.1	64.4		
Week 228 (n=265, n=126)	72.1	66.7		
Week 240 (n=254, n=118)	66.9	69.5		
Week 252 (n=232, n=111)	68.5	71.2		
Week 264 (n=228, n=107)	66.7	74.8		
Week 276 (n=216, n=114)	68.1	76.3		
Week 288 (n=209, n=110)	70.8	73.6		
Week 300 (n=200, n=105)	72.5	66.7		
Week 312 (n=207, n=101)	69.6	64.4		
Week 324 (n=205, n=104)	72.7	65.4		
Week 336 (n=194, n=97)	70.1	63.9		
Week 348 (n=188, n=92)	71.8	69.6		
Week 360 (n=180, n=86)	67.8	67.4		
Week 372 (n=167, n=83)	70.7	71.1		
Week 384 (n=165, n=80)	64.2	65.0		
Week 396 (n=151, n=77)	65.6	64.9		
Week 408 (n=3, n=2)	66.7	50.0		
Extension Baseline (n=488, n=235)	49.4	46.4		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Achieving ACR70 Response: NRI

End point title	Percentage of Participants Achieving ACR70 Response: NRI

End point description:

The ACR response was a measurement of improvement in multiple disease assessment criteria. ACR70 response was defined as : 1) ≥ 70% improvement from baseline in SJC66, and 2) ≥ 70% improvement from baseline in TJC68, and 3) ≥ 70% improvement from baseline in at least 3 of the following 5 items: 1. Pain VAS (taken from the HAQ-DI), 2.SGA (VAS), 3. PGA (VAS), 4. Total HAQ-DI score, and 5. hsCRP.

FAS.

NRI: Participants with missing outcomes were set as nonresponders for binary response measurements.

End point type	Secondary

End point timeframe:

Extension Baseline, Weeks 12, 24, 36, 48, 60, 72, 84, 96, 108, 120, 132, 144, 156, 168, 180, 192, 204, 216, 228, 240, 252, 264, 276, 288, 300, 312, 324, 336, 348, 360, 372, 384, 396, 408

End point values	Filgotinib Darwin 1	Filgotinib Darwin 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	497	242		
Units: Percentage of participants				
number (not applicable)				
Week 12	36.8	36.4		
Week 24	37.8	39.3		
Week 36	40.6	37.2		
Week 48	39.4	36.4		
Week 60	36.4	34.3		
Week 72	38.0	30.2		
Week 84	36.8	34.3		
Week 96	39.6	28.1		
Week 108	35.4	29.8		
Week 120	36.0	31.0		
Week 132	32.8	29.3		
Week 144	31.6	28.5		
Week 156	26.8	22.3		
Week 168	30.8	24.0		
Week 180	30.8	25.6		
Week 192	26.6	25.2		
Week 204	26.6	24.8		
Week 216	26.4	23.1		
Week 228	27.2	24.4		
Week 240	21.5	21.5		
Week 252	21.7	20.7		
Week 264	23.1	22.7		
Week 276	21.3	24.8		
Week 288	22.1	24.8		
Week 300	22.5	19.8		
Week 312	23.1	19.8		
Week 324	21.5	21.1		
Week 336	20.3	17.8		
Week 348	19.7	19.0		
Week 360	17.7	16.1		
Week 372	16.7	17.4		
Week 384	14.9	14.9		
Week 396	14.9	14.5		
Week 408	0.4	0.4		
Extension Baseline	30.0	23.1		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Achieving ACR70 Response: OC

End point title	Percentage of Participants Achieving ACR70 Response: OC

End point description:

The ACR response was a measurement of improvement in multiple disease assessment criteria. ACR70 response was defined as : 1) ≥ 70% improvement from baseline in SJC66, and 2) ≥ 70% improvement from baseline in TJC68, and 3) ≥ 70% improvement from baseline in at least 3 of the following 5 items: 1. Pain VAS (taken from the HAQ-DI), 2.SGA (VAS), 3. PGA (VAS), 4. Total HAQ-DI score, and 5.hsCRP.

FAS with available data was analyzed.

OC: only observed values were used for analysis. No missing data imputation was performed.

Different participants could be analyzed at different timepoints, resulting in overall FAS participants being analyzed.

End point type	Secondary

End point timeframe:

Extension Baseline, Weeks 12, 24, 36, 48, 60, 72, 84, 96, 108, 120, 132, 144, 156, 168, 180, 192, 204, 216, 228, 240, 252, 264, 276, 288, 300, 312, 324, 336, 348, 360, 372, 384, 396, 408

End point values	Filgotinib Darwin 1	Filgotinib Darwin 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	497	242		
Units: Percentage of participants				
number (not applicable)				
Week 12 (n=486, n=231)	37.7	38.1		
Week 24 (n=440, n=211)	42.7	45.0		
Week 36 (n=431. n=202)	46.9	44.6		
Week 48 (n=421, n=200)	46.6	44.0		
Week 60 (n=398, n=186)	45.5	44.6		
Week 72 (n=388, n=173)	48.7	42.2		
Week 84 (n=374, n=171)	48.9	48.5		
Week 96 (n=375, n=165)	52.5	41.2		
Week 108 (n=354, n=159)	49.7	45.3		
Week 120 (n=333, n=158)	53.8	47.5		
Week 132 (n=333, n=153)	48.9	46.4		
Week 144 (n=325,n=156)	48.3	44.2		
Week 156 (n=292, n=135)	45.5	40.0		
Week 168 (n=297, n=136)	51.5	42.6		
Week 180 (n=292, n=141)	52.4	44.0		
Week 192 (n=283, n=135)	46.6	45.2		
Week 204 (n=269, n= 133)	49.1	45.1		
Week 216 (n=265, n=132)	49.4	42.4		
Week 228 (n=265, n=126)	50.9	46.8		
Week 240 (n=254, n=120)	42.1	43.3		
Week 252 (n=233, n=110)	46.4	45.5		
Week 264 (n=227, n=107)	50.7	51.4		
Week 276 (n=217, n=113)	48.8	53.1		
Week 288 (n=210, n=110)	52.4	54.5		
Week 300 (n=202, n=105)	55.4	45.7		
Week 312 (n=208, n=101)	55.3	47.5		
Week 324 (n=205, n=104)	52.2	49.0		

Week 336 (n=195, n=97)	51.8	44.3		
Week 348 (n=190, n=92)	51.6	50.0		
Week 360 (n=179, n=87)	49.2	44.8		
Week 372 (n=169, n=84)	49.1	50.0		
Week 384 (n=163, n=80)	45.4	45.0		
Week 396 (n=151, n=77)	49.0	45.5		
Week 408 (n=3, n=2)	66.7	50.0		
Extension Baseline: (n=491, n=238)	30.3	23.5		

Statistical analyses

No statistical analyses for this end point

Secondary: ACR N% Improvement (ACR-N) Response: OC

End point title	ACR N% Improvement (ACR-N) Response: OC

End point description:

ACR-N was defined as the smallest percentage improvement from core baseline in SJC66, TJC68 and the median of the following 5 items (Pain VAS [taken from the HAQ-DI], 2.SGA (VAS), 3. PGA (VAS), 4. Total HAQ-DI score, and 5. hsCRP). It had a range between 0 and 100%.

FAS with available data was analyzed.

OC: only observed values were used for analysis. No missing data imputation was performed.

Different participants could be analyzed at different timepoints, resulting in overall FAS participants being analyzed.

End point type	Secondary

End point timeframe:

Extension Baseline, Weeks 12, 24, 36, 48, 60, 72, 84, 96, 108, 120, 132, 144, 156, 168, 180, 192, 204, 216, 228, 240, 252, 264, 276, 288, 300, 312, 324, 336, 348, 360, 372, 384, 396, 408

End point values	Filgotinib Darwin 1	Filgotinib Darwin 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	497	242		
Units: Percentage of improvement				
arithmetic mean (standard deviation)				
Week 12 (n=478, n=226)	56.3 (± 28.43)	56.3 (± 27.13)		
Week 24 (n=435, n=205)	57.9 (± 29.64)	60.8 (± 27.76)		
Week 36 (n=424, n=201)	59.8 (± 29.70)	60.7 (± 27.95)		
Week 48 (n=413, n=196)	59.6 (± 30.69)	58.9 (± 28.65)		
Week 60 (n=388, n=181)	59.9 (± 29.97)	60.1 (± 28.43)		
Week 72 (n=379, n=169)	61.4 (± 28.92)	59.0 (± 28.47)		
Week 84 (n=367, n=168)	61.6 (± 29.07)	63.6 (± 26.74)		
Week 96 (n=370, n=161)	64.8 (± 28.61)	61.2 (± 26.87)		
Week 108 (n=348, n=156)	61.2 (± 30.22)	60.9 (± 28.69)		
Week 120 (n=327, n=155)	63.4 (± 29.25)	61.1 (± 28.72)		
Week 132 (n=325, n=147)	62.3 (± 29.15)	61.3 (± 28.52)		
Week 144 (n=317, n=152)	61.7 (± 28.99)	60.8 (± 29.12)		

Week 156 (n=280, n=132)	61.5 (± 28.05)	58.0 (± 27.70)		
Week 168 (n=283, n=135)	62.8 (± 29.75)	56.9 (± 30.25)		
Week 180 (n=283, n=138)	63.2 (± 28.29)	59.9 (± 29.79)		
Week 192 (n=276, n=131)	60.4 (± 29.15)	61.5 (± 27.30)		
Week 204 (n=264, n= 131)	62.3 (± 28.64)	61.9 (± 26.79)		
Week 216 (n=256, n=130)	61.6 (± 29.87)	61.4 (± 26.86)		
Week 228 (n=259, n=124)	64.2 (± 27.83)	63.0 (± 26.45)		
Week 240 (n=251, n=117)	59.8 (± 28.22)	60.6 (± 28.48)		
Week 252 (n=227, n=107)	62.4 (± 28.71)	62.5 (± 26.24)		
Week 264 (n=221, n=106)	63.4 (± 29.81)	64.4 (± 27.05)		
Week 276 (n=209, n=111)	63.3 (± 28.27)	65.9 (± 25.42)		
Week 288 (n=203, n=107)	65.1 (± 29.68)	63.0 (± 29.82)		
Week 300 (n=196, n=103)	64.9 (± 30.16)	61.9 (± 27.14)		
Week 312 (n=202, n=99)	64.8 (± 29.89)	59.9 (± 30.37)		
Week 324 (n=197, n=101)	65.9 (± 27.39)	61.2 (± 30.98)		
Week 336 (n=189, n=94)	62.7 (± 29.35)	59.8 (± 28.90)		
Week 348 (n=181, n=91)	64.8 (± 29.26)	62.8 (± 28.29)		
Week 360 (n=170, n=80)	62.7 (± 29.81)	61.2 (± 28.32)		
Week 372 (n=152, n=70)	64.2 (± 28.58)	64.6 (± 29.43)		
Week 384 (n=151, n=63)	60.0 (± 30.27)	62.9 (± 30.43)		
Week 396 (n=135, n=57)	61.5 (± 31.34)	64.7 (± 28.98)		
Week 408 (n=3, n=2)	65.9 (± 41.08)	35.4 (± 50.04)		
Extension Baseline: (n=482, n=227)	48.1 (± 30.29)	46.3 (± 27.77)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Core Baseline in Disease Activity Score Based on 28 Joints Using C-reactive Protein (DAS28[CRP]): OC

End point title	Change From Core Baseline in Disease Activity Score Based on 28 Joints Using C-reactive Protein (DAS28[CRP]): OC

End point description:

The DAS28(CRP) was a measure of the participant's disease activity calculated using the TJC (28 joints), SJC (28 joints), SGA [using a VAS on a scale of 0 (very well) to 100 (very poor)] and hsCRP using the formula:

DAS28(CRP) = 0.56 * SQRT (TJC28) + 0.28 * SQRT(SJC28) + 0.36 * Ln(CRP+1) + 0.014 * SGA + 0.96

and the total possible score ranged from 1 to 9.4. Higher values indicated higher disease activity.
A negative change from baseline indicated improvement.

FAS with available data was analyzed.

OC: only observed values were used for analysis. No missing data imputation was performed.

Different participants could be analyzed at different timepoints, resulting in overall FAS participants being analyzed.

End point type	Secondary

End point timeframe:

Core Baseline, Extension Baseline, Weeks 12, 24, 36, 48, 60, 72, 84, 96, 108, 120, 132, 144, 156, 168, 180, 192, 204, 216, 228, 240, 252, 264, 276, 288, 300, 312, 324, 336, 348, 360, 372, 384, 396, 408

End point values	Filgotinib Darwin 1	Filgotinib Darwin 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	497	242		
Units: score on a scale				
arithmetic mean (standard deviation)				
Change from Baseline at Week 12 (n=487, n=232)	-3.1 (± 1.28)	-3.1 (± 1.22)		
Change from Baseline at Week 24 (n=443, n=211)	-3.2 (± 1.29)	-3.2 (± 1.33)		
Change from Baseline at Week 36 (n=434, n=206)	-3.3 (± 1.28)	-3.3 (± 1.22)		
Change from Baseline at Week 48 (n=421, n=201)	-3.3 (± 1.32)	-3.3 (± 1.26)		
Change from Baseline at Week 60 (n=398, n=187)	-3.3 (± 1.22)	-3.4 (± 1.17)		
Change from Baseline at Week 72 (n=386, n=173)	-3.3 (± 1.23)	-3.4 (± 1.21)		
Change from Baseline at Week 84 (n=377, n=172)	-3.4 (± 1.21)	-3.5 (± 1.09)		
Change from Baseline at Week 96 (n=377, n=165)	-3.4 (± 1.22)	-3.4 (± 1.13)		
Change from Baseline at Week 108 (n=356, n=159)	-3.4 (± 1.22)	-3.3 (± 1.21)		
Change from Baseline at Week 120 (n=334, n=159)	-3.4 (± 1.20)	-3.5 (± 1.14)		
Change from Baseline at Week 132 (n=333, n=153)	-3.3 (± 1.21)	-3.5 (± 1.26)		
Change from Baseline at Week 144 (n=325, n=157)	-3.4 (± 1.19)	-3.4 (± 1.15)		
Change from Baseline at Week 156 (n=290, n=136)	-3.4 (± 1.22)	-3.4 (± 1.28)		
Change from Baseline at Week 168 (n=297, n=139)	-3.4 (± 1.27)	-3.4 (± 1.20)		
Change from Baseline at Week 180 (n=292, n=143)	-3.4 (± 1.12)	-3.4 (± 1.21)		
Change from Baseline at Week 192 (n=285, n=135)	-3.3 (± 1.16)	-3.5 (± 1.13)		
Change from Baseline at Week 204 (n=273, n= 135)	-3.4 (± 1.16)	-3.5 (± 1.06)		
Change from Baseline at Week 216 (n=264, n=133)	-3.4 (± 1.16)	-3.5 (± 1.15)		
Change from Baseline at Week 228 (n=267, n=127)	-3.5 (± 1.12)	-3.5 (± 1.09)		
Change from Baseline at Week 240 (n=257, n=122)	-3.4 (± 1.13)	-3.4 (± 1.19)		
Change from Baseline at Week 252 (n=233, n=109)	-3.5 (± 1.11)	-3.6 (± 1.24)		
Change from Baseline at Week 264 (n=227, n=110)	-3.5 (± 1.19)	-3.6 (± 1.20)		
Change from Baseline at Week 276 (n=215, n=114)	-3.5 (± 1.10)	-3.6 (± 1.17)		
Change from Baseline at Week 288 (n=208, n=111)	-3.5 (± 1.22)	-3.6 (± 1.28)		
Change from Baseline at Week 300 (n=202, n=106)	-3.6 (± 1.19)	-3.5 (± 1.23)		

Change from Baseline at Week 312 (n=207, n=101)	-3.5 (± 1.27)	-3.4 (± 1.30)		
Change from Baseline at Week 324 (n=202, n=103)	-3.6 (± 1.14)	-3.5 (± 1.24)		
Change from Baseline at Week 336 (n=194, n=96)	-3.5 (± 1.17)	-3.4 (± 1.16)		
Change from Baseline at Week 348 (n=186, n=93)	-3.5 (± 1.20)	-3.6 (± 1.14)		
Change from Baseline at Week 360 (n=176, n=82)	-3.6 (± 1.21)	-3.4 (± 1.13)		
Change from Baseline at Week 372 (n=155, n=72)	-3.6 (± 1.18)	-3.6 (± 1.26)		
Change from Baseline at Week 384 (n=155, n=64)	-3.4 (± 1.24)	-3.5 (± 1.26)		
Change from Baseline at Week 396 (n=138, n=58)	-3.5 (± 1.38)	-3.8 (± 1.12)		
Change from Baseline at Week 408 (n=3, n=2)	-3.8 (± 0.97)	-2.8 (± 0.25)		
Change at Extension Baseline: (n=491, n=234)	-2.7 (± 1.40)	-2.6 (± 1.28)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Core Baseline in Simple Disease Activity Index (SDAI): OC

End point title	Change From Core Baseline in Simple Disease Activity Index (SDAI): OC

End point description:

SDAI score consisted of following parameters: TJC (28 joints), SJC (28 joints), SGA (0 to 10 cm), PGA (0 to 10 cm), CRP (mg/dL). SDAI = TJC + SJC + SGA + PGA+ CRP. The SDAI score ranged from 0 to approximately 86. Higher SDAI indicated greater disease activity.
A negative change from baseline indicated improvement.

FAS with available data was analyzed.

OC: only observed values were used for analysis. No missing data imputation was performed.

Different participants could be analyzed at different timepoints, resulting in overall FAS participants being analyzed.

End point type	Secondary

End point timeframe:

Core Baseline, Extension Baseline, Weeks 12, 24, 36, 48, 60, 72, 84, 96, 108, 120, 132, 144, 156, 168, 180, 192, 204, 216, 228, 240, 252, 264, 276, 288, 300, 312, 324, 336, 348, 360, 372, 384, 396, 408

End point values	Filgotinib Darwin 1	Filgotinib Darwin 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	497	242		
Units: score on a scale				
arithmetic mean (standard deviation)				
Change from Baseline at Week 12 (n=485, n=228)	-33.4 (± 14.16)	-34.1 (± 13.79)		

Change from Baseline at Week 24 (n=442, n=207)	-34.0 (± 14.19)	-35.0 (± 14.65)		
Change from Baseline at Week 36 (n=432, n=203)	-34.7 (± 13.98)	-35.9 (± 13.42)		
Change from Baseline at Week 48 (n=420, n=197)	-34.7 (± 14.38)	-36.2 (± 14.08)		
Change from Baseline at Week 60 (n=397, n=182)	-35.3 (± 13.57)	-36.3 (± 12.85)		
Change from Baseline at Week 72 (n=385, n=170)	-35.4 (± 13.38)	-36.7 (± 13.41)		
Change from Baseline at Week 84 (n=374, n=169)	-35.6 (± 13.38)	-37.3 (± 13.12)		
Change from Baseline at Week 96 (n=376, n=162)	-36.2 (± 13.31)	-36.8 (± 13.47)		
Change from Baseline at Week 108 (n=354, n=157)	-36.0 (± 13.56)	-36.6 (± 13.65)		
Change from Baseline at Week 120 (n=332, n=156)	-36.1 (± 13.28)	-37.4 (± 12.90)		
Change from Baseline at Week 132 (n=332, n=148)	-35.6 (± 13.38)	-36.9 (± 14.25)		
Change from Baseline at Week 144 (n=323, n=154)	-35.7 (± 13.15)	-36.9 (± 13.12)		
Change from Baseline at Week 156 (n=288, n=134)	-35.5 (± 13.36)	-36.9 (± 14.46)		
Change from Baseline at Week 168 (n=295, n=136)	-35.8 (± 14.18)	-36.9 (± 13.84)		
Change from Baseline at Week 180 (n=291, n=140)	-36.2 (± 12.72)	-36.9 (± 13.33)		
Change from Baseline at Week 192 (n=283, n=132)	-35.5 (± 12.74)	-38.2 (± 13.66)		
Change from Baseline at Week 204 (n=272, n=133)	-35.8 (± 12.78)	-38.5 (± 13.72)		
Change from Baseline at Week 216 (n=262, n=131)	-36.1 (± 12.92)	-38.0 (± 13.85)		
Change from Baseline at Week 228 (n=265, n=125)	-36.8 (± 12.38)	-37.9 (± 12.87)		
Change from Baseline at Week 240 (n=256, n=119)	-35.9 (± 12.69)	-37.1 (± 14.38)		
Change from Baseline at Week 252 (n=232, n=108)	-37.2 (± 12.63)	-38.6 (± 14.85)		
Change from Baseline at Week 264 (n=226, n=107)	-37.3 (± 12.98)	-39.2 (± 14.59)		
Change from Baseline at Week 276 (n=214, n=112)	-37.5 (± 12.18)	-38.6 (± 13.98)		
Change from Baseline at Week 288 (n=207, n=108)	-37.0 (± 13.22)	-38.6 (± 15.09)		
Change from Baseline at Week 300 (n=201, n=103)	-37.5 (± 13.55)	-38.0 (± 15.38)		
Change from Baseline at Week 312 (n=206, n=99)	-37.1 (± 13.71)	-37.7 (± 15.54)		
Change from Baseline at Week 324 (n=201, n=101)	-37.7 (± 13.06)	-38.1 (± 15.56)		
Change from Baseline at Week 336 (n=193, n=94)	-36.7 (± 12.52)	-36.6 (± 14.36)		
Change from Baseline at Week 348 (n=185, n=91)	-37.0 (± 12.53)	-37.2 (± 13.02)		
Change from Baseline at Week 360 (n=175, n=80)	-37.4 (± 12.83)	-36.3 (± 13.05)		
Change from Baseline at Week 372 (n=155, n=70)	-37.3 (± 12.68)	-37.8 (± 13.64)		
Change from Baseline at Week 384 (n=155, n=63)	-36.5 (± 12.64)	-36.5 (± 14.58)		

Change from Baseline at Week 396 (n=138, n=57)	-36.3 (± 14.32)	-39.5 (± 13.50)		
Change from Baseline at Week 408 (n=3, n=2)	-40.4 (± 12.91)	-35.6 (± 5.98)		
Change at Extension Baseline: (n=490, n=230)	-30.2 (± 15.49)	-29.8 (± 14.27)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Core Baseline in Clinical Disease Activity Index (CDAI): OC

End point title	Change From Core Baseline in Clinical Disease Activity Index (CDAI): OC

End point description:

The CDAI was the SDAI modified that excluded CRP and consisted of following parameters: TJC (28 joints), SJC (28 joints), SGA (0 to 10 cm), PGA (0 to 10 cm). SDAI = TJC + SJC + SGA+ PGA. The CDAI score ranged from 0 to approximately 76. Higher CDAI indicated greater disease activity.
A negative change from baseline indicated improvement.

FAS with available data was analyzed.

OC: only observed values were used for analysis. No missing data imputation was performed.

Different participants could be analyzed at different timepoints, resulting in overall FAS participants being analyzed.

End point type	Secondary

End point timeframe:

Core Baseline, Extension Baseline, Weeks 12, 24, 36, 48, 60, 72, 84, 96, 108, 120, 132, 144, 156, 168, 180, 192, 204, 216, 228, 240, 252, 264, 276, 288, 300, 312, 324, 336, 348, 360, 372, 384, 396, 408

End point values	Filgotinib Darwin 1	Filgotinib Darwin 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	497	242		
Units: score on a scale				
arithmetic mean (standard deviation)				
Change from Baseline at Week 12 (n=486, n=229)	-31.8 (± 13.45)	-32.4 (± 12.76)		
Change from Baseline at Week 24 (n=442, n=207)	-32.4 (± 13.63)	-32.9 (± 13.79)		
Change from Baseline at Week 36 (n=432, n=203)	-33.0 (± 13.44)	-33.8 (± 12.51)		
Change from Baseline at Week 48 (n=421, n=197)	-33.1 (± 13.79)	-34.1 (± 13.18)		
Change from Baseline at Week 60 (n=399, n=183)	-33.7 (± 12.97)	-34.2 (± 12.22)		
Change from Baseline at Week 72 (n=386, n=170)	-33.8 (± 12.73)	-34.4 (± 12.57)		
Change from Baseline at Week 84 (n=374, n=169)	-33.9 (± 12.82)	-35.2 (± 12.31)		
Change from Baseline at Week 96 (n=377, n=162)	-34.6 (± 12.76)	-34.7 (± 12.56)		

Change from Baseline at Week 108 (n=355, n=157)	-34.3 (± 12.96)	-34.5 (± 12.92)		
Change from Baseline at Week 120 (n=332, n=156)	-34.5 (± 12.70)	-35.2 (± 11.87)		
Change from Baseline at Week 132 (n=333, n=148)	-34.1 (± 12.82)	-34.7 (± 13.07)		
Change from Baseline at Week 144 (n=323, n=154)	-34.1 (± 12.63)	-34.9 (± 12.12)		
Change from Baseline at Week 156 (n=290, n=134)	-34.0 (± 12.74)	-34.8 (± 13.29)		
Change from Baseline at Week 168 (n=297, n=136)	-34.1 (± 13.64)	-34.8 (± 12.55)		
Change from Baseline at Week 180 (n=291, n=140)	-34.5 (± 12.10)	-34.8 (± 12.39)		
Change from Baseline at Week 192 (n=283, n=132)	-33.9 (± 12.10)	-35.9 (± 12.65)		
Change from Baseline at Week 204 (n=272, n=133)	-34.2 (± 12.26)	-36.3 (± 12.79)		
Change from Baseline at Week 216 (n=262, n=131)	-34.5 (± 12.18)	-36.0 (± 13.00)		
Change from Baseline at Week 228 (n=265, n=125)	-35.2 (± 11.69)	-35.8 (± 11.98)		
Change from Baseline at Week 240 (n=256, n=119)	-34.3 (± 11.99)	-35.2 (± 13.27)		
Change from Baseline at Week 252 (n=235, n=109)	-35.3 (± 11.94)	-36.4 (± 13.55)		
Change from Baseline at Week 264 (n=227, n=108)	-35.6 (± 12.15)	-36.9 (± 13.53)		
Change from Baseline at Week 276 (n=216, n=113)	-35.9 (± 11.38)	-36.4 (± 12.84)		
Change from Baseline at Week 288 (n=208, n=108)	-35.4 (± 12.28)	-36.5 (± 13.47)		
Change from Baseline at Week 300 (n=201, n=103)	-35.8 (± 12.84)	-35.7 (± 14.29)		
Change from Baseline at Week 312 (n=207, n=99)	-35.5 (± 13.10)	-35.5 (± 14.40)		
Change from Baseline at Week 324 (n=202, n=102)	-35.8 (± 12.30)	-36.0 (± 14.37)		
Change from Baseline at Week 336 (n=195, n=96)	-35.0 (± 11.76)	-34.2 (± 13.32)		
Change from Baseline at Week 348 (n=187, n=91)	-35.3 (± 11.70)	-34.8 (± 11.73)		
Change from Baseline at Week 360 (n=180, n=86)	-35.5 (± 12.00)	-34.0 (± 11.54)		
Change from Baseline at Week 372 (n=168, n=83)	-35.4 (± 12.46)	-33.9 (± 12.73)		
Change from Baseline at Week 384 (n=166, n=83)	-34.8 (± 11.82)	-32.6 (± 13.11)		
Change from Baseline at Week 396 (n=154, n=79)	-34.7 (± 13.28)	-34.2 (± 12.55)		
Change from Baseline at Week 408 (n=3, n=2)	-39.2 (± 12.87)	-34.9 (± 6.36)		
Change at Extension Baseline: (n=490, n=233)	-28.8 (± 14.58)	-28.0 (± 13.68)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Achieving European League Against Rheumatism (EULAR) Response: OC

End point title	Percentage of Participants Achieving European League Against Rheumatism (EULAR) Response: OC

End point description:

DAS28(CRP) was categorized into EULAR response categories (none, moderate, good) as follows:
None= Actual DAS28(CRP) ≤ 3.2, > 3.2 to ≤ 5.1, or > 5.1 AND Improvement in DAS28(CRP) from baseline ≤ 6.0 or > 0.6 to ≤ 1.2;
Moderate= Actual DAS28(CRP) ≤ 3.2 AND Improvement in DAS28(CRP) from baseline > 0.6 to ≤ 1.2, Actual DAS28(CRP) > 3.2 to ≤ 5.1 or > 5.1 AND Improvement in DAS28(CRP) from baseline > 1.2, or Actual DAS28(CRP) > 3.2 to ≤ 5.1 AND Improvement in DAS28(CRP) from baseline > 0.6 to ≤ 1.2;
Good= Actual DAS28(CRP) ≤ 3.2 AND Improvement in DAS28(CRP) from baseline > 1.2.

FAS with available data was analyzed.

OC: only observed values were used for analysis. No missing data imputation was performed.

Different participants could be analyzed at different timepoints, resulting in overall FAS participants being analyzed.

End point type	Secondary

End point timeframe:

Extension Baseline, Weeks 12, 24, 36, 48, 60, 72, 84, 96, 108, 120, 132, 144, 156, 168, 180, 192, 204, 216, 228, 240, 252, 264, 276, 288, 300, 312, 324, 336, 348, 360, 372, 384, 396, 408

End point values	Filgotinib Darwin 1	Filgotinib Darwin 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	497	242		
Units: Percentage of participants				
number (not applicable)				
Week 12: Good (n=487, n=232)	59.1	60.3		
Week 12: Moderate (n=487, n=232)	35.5	34.9		
Week 12: None (n=487, n=232)	5.3	4.7		
Week 24: Good (n=443, n=211)	65.2	65.9		
Week 24: Moderate (n=443, n=211)	29.3	28.9		
Week 24: None (n=443, n=211)	5.4	5.2		
Week 36: Good (n=434, n=206)	66.4	66.0		
Week 36: Moderate (n=434, n=206)	29.7	30.6		
Week 36: None (n=434, n=206)	3.9	3.4		
Week 48: Good (n=421, n=201)	67.7	68.7		
Week 48: Moderate (n=421, n=201)	27.8	27.4		
Week 48: None (n=421, n=201)	4.5	4.0		
Week 60: Good (n=398, n=187)	67.8	64.2		
Week 60: Moderate (n=398, n=187)	29.9	34.2		
Week 60: None (n=398, n=187)	2.3	1.6		
Week 72: Good (n=386, n=173)	70.5	65.3		
Week 72: Moderate (n=386, n=173)	26.7	32.9		
Week 72: None (n=386, n=173)	2.8	1.7		
Week 84: Good (n=377, n=172)	70.3	69.8		
Week 84: Moderate (n=377, n=172)	27.6	29.1		
Week 84: None (n=377, n=172)	2.1	1.2		

Week 96: Good (n=377, n=165)	72.9	69.1		
Week 96: Moderate (n=377, n=165)	25.2	27.9		
Week 96: None (n=377, n=165)	1.9	3.0		
Week 108: Good (n=356, n=159)	74.2	66.7		
Week 108: Moderate (n=356, n=159)	23.6	29.6		
Week 108: None (n=356, n=159)	2.2	3.8		
Week 120: Good (n=334, n=159)	74.6	67.9		
Week 120: Moderate (n=334, n=159)	23.7	29.6		
Week 120: None (n=334, n=159)	1.8	2.5		
Week 132: Good (n=333, n=153)	69.1	69.9		
Week 132: Moderate (n=333, n=153)	28.8	27.5		
Week 132: None (n=333, n=153)	2.1	2.6		
Week 144: Good (n=325, n=157)	72.3	65.6		
Week 144: Moderate (n=325, n=157)	25.8	33.1		
Week 144: None (n=325, n=157)	1.8	1.3		
Week 156: Good (n=290, n=136)	69.0	64.7		
Week 156: Moderate (n=290, n=136)	28.3	30.9		
Week 156: None (n=290, n=136)	2.8	4.4		
Week 168: Good (n=297, n=139)	73.4	68.3		
Week 168: Moderate (n=297, n=139)	23.6	29.5		
Week 168: None (n=297, n=139)	3.0	2.2		
Week 180: Good (n=292, n=143)	74.0	68.5		
Week 180: Moderate (n=292, n=143)	25.3	28.7		
Week 180: None (n=292, n=143)	0.7	2.8		
Week 192: Good (n=285, n=135)	71.2	71.1		
Week 192: Moderate (n=285, n=135)	26.3	28.1		
Week 192: None (n=285, n=135)	2.5	0.7		
Week 204: Good (n=273, n=135)	73.3	76.3		
Week 204: Moderate (n=273, n=135)	23.8	22.2		
Week 204: None (n=273, n=135)	2.9	1.5		
Week 216: Good (n=264, n=133)	72.7	69.9		
Week 216: Moderate (n=264, n=133)	26.1	28.6		
Week 216: None (n=264, n=133)	1.1	1.5		
Week 228: Good (n=267, n=127)	76.4	70.1		
Week 228: Moderate (n=267, n=127)	23.6	29.9		
Week 228: None (n=267, n=127)	0	0		
Week 240: Good (n=257, n=122)	73.2	63.1		
Week 240: Moderate (n=257, n=122)	26.1	36.9		
Week 240: None (n=257, n=122)	0.8	0		
Week 252: Good (n=233, n=109)	74.2	73.4		
Week 252: Moderate (n=233, n=109)	24.5	25.7		
Week 252: None (n=233, n=109)	1.3	0.9		
Week 264: Good (n=227, n=110)	74.4	75.5		
Week 264: Moderate (n=227, n=110)	24.2	22.7		
Week 264: None (n=227, n=110)	1.3	1.8		
Week 276: Good (n=215, n=114)	74.4	70.2		
Week 276: Moderate (n=215, n=114)	25.1	28.1		
Week 276: None (n=215, n=114)	0.5	1.8		
Week 288: Good (n=208, n=111)	73.6	73.0		
Week 288: Moderate (n=208, n=111)	24.5	24.3		
Week 288: None (n=208, n=111)	1.9	2.7		
Week 300: Good (n=202, n=106)	74.8	74.5		

Week 300: Moderate (n=202, n=106)	23.8	25.5		
Week 300: None (n=202, n=106)	1.5	0		
Week 312: Good (n=207, n=101)	75.8	66.3		
Week 312: Moderate (n=207, n=101)	22.2	32.7		
Week 312: None (n=207, n=101)	1.9	1.0		
Week 324: Good (n=202, n=103)	75.7	71.8		
Week 324: Moderate (n=202, n=103)	21.8	26.2		
Week 324: None (n=202, n=103)	2.5	1.9		
Week 336: Good (n=194, n=96)	74.2	71.9		
Week 336: Moderate (n=194, n=96)	24.7	26.0		
Week 336: None (n=194, n=96)	1.0	2.1		
Week 348: Good (n=186, n=93)	76.9	78.5		
Week 348: Moderate (n=186, n=93)	21.5	20.4		
Week 348: None (n=186, n=93)	1.6	1.1		
Week 360: Good (n=176, n=82)	73.3	73.2		
Week 360: Moderate (n=176, n=82)	23.9	24.4		
Week 360: None (n=176, n=82)	2.8	2.4		
Week 372: Good (n=155, n=72)	76.8	77.8		
Week 372: Moderate (n=155, n=72)	21.3	18.1		
Week 372: None (n=155, n=72)	1.9	4.2		
Week 384: Good (n=155, n=64)	70.3	78.1		
Week 384: Moderate (n=155, n=64)	28.4	20.3		
Week 384: None (n=155, n=64)	1.3	1.6		
Week 396: Good (n=138, n=58)	73.2	81.0		
Week 396: Moderate (n=138, n=58)	21.7	19.0		
Week 396: None (n=138, n=58)	5.1	0		
Week 408: Good (n=3, n=2)	100.0	50.0		
Week 408: Moderate (n=3, n=2)	0	50.0		
Week 408: None (n=3, n=2)	0	0		
Extension Baseline: Good (n=491, n=234)	46.2	41.5		
Extension Baseline: Moderate (n=491, n=234)	43.6	48.7		
Extension Baseline: None (n=491, n=234)	10.2	9.8		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Achieving ACR/EULAR Remission: NRI

End point title	Percentage of Participants Achieving ACR/EULAR Remission: NRI

End point description:

A participant's disease activity status was defined as being in remission when scores on the TJC28, SJC28, CRP (actual value in mg/dL) and SGA (cm) were all ≤ 1.

FAS.

NRI: Participants with missing outcomes were set as nonresponders for binary response measurements.

End point type	Secondary

End point timeframe:

Extension Baseline, Weeks 12, 24, 36, 48, 60, 72, 84, 96, 108, 120, 132, 144, 156, 168, 180, 192, 204, 216, 228, 240, 252, 264, 276, 288, 300, 312, 324, 336, 348, 360, 372, 384, 396, 408

End point values	Filgotinib Darwin 1	Filgotinib Darwin 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	497	242		
Units: Percentage of participants				
number (not applicable)				
Week 12	13.1	11.6		
Week 24	14.9	15.3		
Week 36	15.3	14.5		
Week 48	17.7	14.0		
Week 60	15.5	12.4		
Week 72	15.5	12.0		
Week 84	15.1	12.4		
Week 96	18.3	11.2		
Week 108	14.9	10.7		
Week 120	12.3	13.2		
Week 132	12.1	12.8		
Week 144	10.5	9.9		
Week 156	10.9	8.3		
Week 168	13.9	7.9		
Week 180	10.3	11.2		
Week 192	10.1	10.7		
Week 204	11.1	9.5		
Week 216	11.5	7.9		
Week 228	11.9	9.9		
Week 240	8.9	7.4		
Week 252	7.8	7.9		
Week 264	11.3	7.4		
Week 276	8.9	9.5		
Week 288	10.1	9.9		
Week 300	10.9	8.7		
Week 312	10.5	7.9		
Week 324	9.5	10.3		
Week 336	8.5	7.4		
Week 348	9.1	9.1		
Week 360	9.3	6.2		
Week 372	8.2	6.6		
Week 384	6.6	4.5		
Week 396	7.8	5.4		
Week 408	0.4	0		
Extension Baseline	10.1	7.4		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Achieving ACR/EULAR Remission: OC

End point title	Percentage of Participants Achieving ACR/EULAR Remission: OC

End point description:

A participant's disease activity status was defined as being in remission when scores on the TJC28, SJC28, CRP (actual value in mg/dL) and SGA (cm) were all ≤ 1.

FAS with available data was analyzed.

OC: only observed values were used for analysis. No missing data imputation was performed.

Different participants could be analyzed at different timepoints, resulting in overall FAS participants being analyzed.

End point type	Secondary

End point timeframe:

Extension Baseline, Weeks 12, 24, 36, 48, 60, 72, 84, 96, 108, 120, 132, 144, 156, 168, 180, 192, 204, 216, 228, 240, 252, 264, 276, 288, 300, 312, 324, 336, 348, 360, 372, 384, 396, 408

End point values	Filgotinib Darwin 1	Filgotinib Darwin 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	497	242		
Units: Percentage of participants				
number (not applicable)				
Week 12 (n=489, n=236)	13.3	11.9		
Week 24 (n=446, n=215)	16.6	17.2		
Week 36 (n=435, n=206)	17.5	17.0		
Week 48 (n=426, n=204)	20.7	16.7		
Week 60 (n=402, n=189)	19.2	15.9		
Week 72 (n=390, n=174)	19.7	16.7		
Week 84 (n=381, n=173)	19.7	17.3		
Week 96 (n=379, n=168)	24.0	16.1		
Week 108 (n=359, n=161)	20.6	16.1		
Week 120 (n=340, n=160)	17.9	20.0		
Week 132 (n=335, n=157)	17.9	19.7		
Week 144 (n=330, n=158)	15.8	15.2		
Week 156 (n=296, n=139)	18.2	14.4		
Week 168 (n=299, n=139)	23.1	13.7		
Week 180 (n=293, n=144)	17.4	18.8		
Week 192 (n=288, n=138)	17.4	18.8		
Week 204 (n=276, n=135)	19.9	17.0		
Week 216 (n=269, n=134)	21.2	14.2		
Week 228 (n=268, n=129)	22.0	18.6		
Week 240 (n=262, n=123)	16.8	14.6		
Week 252 (n=239, n=113)	16.3	16.8		
Week 264 (n=231, n=111)	24.2	16.2		
Week 276 (n=218, n=115)	20.2	20.0		
Week 288 (n=215, n=111)	23.3	21.6		
Week 300 (n=205, n=107)	26.3	19.6		

Week 312 (n=210, n=105)	24.8	18.1		
Week 324 (n=207, n=105)	22.7	23.8		
Week 336 (n=197, n=98)	21.3	18.4		
Week 348 (n=190, n=94)	23.7	23.4		
Week 360 (n=185, n=90)	24.9	16.7		
Week 372 (n=167, n=85)	24.6	18.8		
Week 384 (n=165, n=85)	20.0	12.9		
Week 396 (n=155, n=80)	25.2	16.3		
Week 408 (n=3, n=2)	66.7	0		
Extension Baseline: (n=495, n=240)	10.1	7.5		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Core Baseline in Physical Component Score (PCS) of Quality of Life Using the Short Form-36 (SF-36) Score: OC

End point title	Change From Core Baseline in Physical Component Score (PCS) of Quality of Life Using the Short Form-36 (SF-36) Score: OC

End point description:

The SF-36 was a health-related survey that assesses participant's quality of life and consisted of 36 questions covering 8 health domains: physical functioning, bodily pain, role limitations due to physical problems and emotional problems, general health, mental health, social functioning, vitality, and 2 component scores (Mental Component Score [MCS] and PCS). PCS consisted of physical functioning, bodily pain, role-physical, and general health scales. Each domain was scored by summing the individual items and transforming the scores into a 0 to 100 scale with higher scores indicating better health status or functioning. A positive change from baseline indicated improvement (better health status).

FAS with available data was analyzed.

OC: only observed values were used for analysis. No missing data imputation was performed.

Different participants could be analyzed at different timepoints, resulting in overall FAS participants being analyzed.

End point type	Secondary

End point timeframe:

Core Baseline, Extension Baseline, Weeks 48, 96, 144, 192, 240, 288, 336, 384

End point values	Filgotinib Darwin 1	Filgotinib Darwin 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	497	242		
Units: score on a scale				
arithmetic mean (standard deviation)				
Change from Baseline at Week 48 (n=480, n=227)	11.3 (± 9.45)	11.5 (± 8.74)		
Change from Baseline at Week 96 (n=377, n=168)	12.2 (± 9.70)	11.8 (± 8.87)		
Change from Baseline at Week 144 (n=332, n=153)	11.8 (± 9.86)	12.2 (± 9.21)		
Change from Baseline at Week 192 (n=289, n=140)	11.2 (± 9.21)	11.0 (± 9.40)		

Change from Baseline at Week 240 (n=263, n=125)	10.9 (± 9.58)	11.4 (± 9.29)		
Change from Baseline at Week 288 (n=215, n=109)	13.0 (± 10.71)	13.1 (± 9.50)		
Change from Baseline at Week 336 (n=204, n=104)	12.8 (± 10.12)	12.0 (± 8.79)		
Change from Baseline at Week 384 (n=175, n=90)	11.5 (± 9.97)	11.7 (± 8.00)		
Change at Extension Baseline: (n=490, n=237)	9.2 (± 9.11)	9.5 (± 8.85)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Core Baseline in MCS of Quality of Life Using the SF-36 Scores: OC

End point title	Change From Core Baseline in MCS of Quality of Life Using the SF-36 Scores: OC

End point description:

The SF-36 was a health-related survey that assesses participant's quality of life and consisted of 36 questions covering 8 health domains: physical functioning, bodily pain, role limitations due to physical problems and emotional problems, general health, mental health, social functioning, vitality, and 2 component scores (MCS and PCS). MCS consisted of social functioning, vitality, mental health, and role-emotional scales. Each domain was scored by summing the individual items and transforming the scores into a 0 to 100 scale with higher scores indicating better health status or functioning.
A positive change from baseline indicated improvement (better health status).

FAS with available data was analyzed.

OC: only observed values were used for analysis. No missing data imputation was performed.

Different participants could be analyzed at different timepoints, resulting in overall FAS participants being analyzed.

End point type	Secondary

End point timeframe:

Core Baseline, Extension Baseline, Weeks 48, 96, 144, 192, 240, 288, 336, 384

End point values	Filgotinib Darwin 1	Filgotinib Darwin 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	497	242		
Units: score on a scale				
arithmetic mean (standard deviation)				
Change from Baseline at Week 48 (n=480, n=227)	6.2 (± 10.52)	6.8 (± 10.84)		
Change from Baseline at Week 96 (n=377, n=168)	6.5 (± 10.54)	6.7 (± 10.33)		
Change from Baseline at Week 144 (n=332, n=153)	6.2 (± 10.72)	6.6 (± 10.86)		
Change from Baseline at Week 192 (n=289, n=140)	6.1 (± 11.47)	7.5 (± 11.60)		
Change from Baseline at Week 240 (n=263, n=125)	6.5 (± 11.11)	7.7 (± 11.66)		

Change from Baseline at Week 288 (n=215, n=109)	7.3 (± 11.49)	8.2 (± 11.20)		
Change from Baseline at Week 336 (n=204, n=104)	6.7 (± 10.49)	6.6 (± 13.65)		
Change from Baseline at Week 384 (n=175, n=90)	6.3 (± 11.23)	8.0 (± 10.98)		
Change at Extension Baseline: (n=490, n=237)	6.1 (± 9.67)	7.1 (± 10.01)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Core Baseline in Quality of Life Using Functional Assessment of Chronic Illness Therapy (FACIT) Fatigue Scale: OC

End point title	Change From Core Baseline in Quality of Life Using Functional Assessment of Chronic Illness Therapy (FACIT) Fatigue Scale: OC

End point description:

FACIT-Fatigue scale was a 13-item questionnaire, each scored on a 5-point scale: 0 (Not at all) to 4 (Very much). Negatively stated items were reversed by subtracting the response from "4" before being added to obtain a total score. The sum of all responses resulted in the FACIT-Fatigue score for a total possible score of 0 (worse score) to 52 (better score), with a higher score indicating less fatigue.
A positive change from baseline indicated better quality of life.

FAS with available data was analyzed.

OC: only observed values were used for analysis. No missing data imputation was performed.

Different participants could be analyzed at different timepoints, resulting in overall FAS participants being analyzed.

End point type	Secondary

End point timeframe:

Core Baseline, Extension Baseline, Weeks 48, 96, 144, 192, 240, 288, 336, 384

End point values	Filgotinib Darwin 1	Filgotinib Darwin 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	497	242		
Units: score on a scale				
arithmetic mean (standard deviation)				
Change from Baseline at Week 48 (n=481, n=227)	11.6 (± 11.16)	12.7 (± 11.62)		
Change from Baseline at Week 96 (n=377, n=168)	12.0 (± 11.59)	12.9 (± 10.97)		
Change from Baseline at Week 144 (n=332, n=153)	12.3 (± 11.31)	13.2 (± 11.92)		
Change from Baseline at Week 192 (n=289, n=140)	11.7 (± 11.63)	12.8 (± 11.96)		
Change from Baseline at Week 240 (n=264. n=124)	11.5 (± 11.52)	12.5 (± 11.74)		
Change from Baseline at Week 288 (n=215, n=109)	13.4 (± 13.21)	15.0 (± 12.03)		

Change from Baseline at Week 336 (n=204, n=104)	13.2 (± 12.18)	13.8 (± 12.29)		
Change from Baseline at Week 384 (n=175, n=90)	12.6 (± 13.35)	13.9 (± 10.76)		
Change at Extension Baseline: (n=490, n=237)	10.7 (± 11.06)	12.1 (± 10.71)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From First dose to Week 437

Adverse event reporting additional description:

Safety Analysis Set.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	25.0

Reporting groups

Reporting group title	Filgotinib Darwin 1

Reporting group description:

Participants who received placebo in Study GLPG0634-CL-203 (2012-003635-31) were randomized to receive oral dose of filgotinib tablet at 100 mg b.i.d, or 200 mg q.d in this extension study. All other participants (except male participants in US) continued the same regimen as received in parent study. Male participants in the US were limited to dosing with filgotinib 100 mg q.d due to an FDA requirement based on a nonclinical finding. Treatment was administered until marketing, local (if applicable) regulatory and/or pertinent local reimbursement approval.

Participants started the study with the same dose level (filgotinib 200 mg per day) and in case of intolerance or safety reasons and as per investigator's discretion, the daily dose of filgotinib was decreased to 100 mg q.d and was returned to 200 mg per day after the reasons for decreasing the dose had resolved and at the investigator's discretion.

Reporting group title	Filgotinib Darwin 2

Reporting group description:

Participants from Study GLPG0634-CL-204 (2012-003654-86) were rolled-over to receive oral dose of filgotinib tablet at 200 mg q.d in this extension study, until marketing, local (if applicable) regulatory and/or pertinent local reimbursement approval.

Participants started the study with the same dose level (filgotinib 200 mg per day) and in case of intolerance or safety reasons and as per investigator's discretion, the daily dose of filgotinib was decreased to 100 mg q.d and was returned to 200 mg per day after the reasons for decreasing the dose had resolved and at the investigator's discretion.

Serious adverse events	Filgotinib Darwin 1	Filgotinib Darwin 2	
Total subjects affected by serious adverse events			
subjects affected / exposed	84 / 497 (16.90%)	48 / 242 (19.83%)	
number of deaths (all causes)	8	8	
number of deaths resulting from adverse events	8	8	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Acute leukaemia			
subjects affected / exposed	0 / 497 (0.00%)	1 / 242 (0.41%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	1 / 1	
Brain neoplasm			

subjects affected / exposed	0 / 497 (0.00%)	1 / 242 (0.41%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Breast cancer			
subjects affected / exposed	1 / 497 (0.20%)	0 / 242 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colon cancer			
subjects affected / exposed	1 / 497 (0.20%)	1 / 242 (0.41%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colorectal adenocarcinoma			
subjects affected / exposed	1 / 497 (0.20%)	0 / 242 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colorectal adenoma			
subjects affected / exposed	1 / 497 (0.20%)	0 / 242 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diffuse large B-cell lymphoma			
subjects affected / exposed	1 / 497 (0.20%)	0 / 242 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gallbladder adenocarcinoma			
subjects affected / exposed	0 / 497 (0.00%)	1 / 242 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemangioma of liver			
subjects affected / exposed	0 / 497 (0.00%)	1 / 242 (0.41%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Leiomyosarcoma metastatic			

subjects affected / exposed	1 / 497 (0.20%)	0 / 242 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Lung neoplasm malignant			
subjects affected / exposed	0 / 497 (0.00%)	1 / 242 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Non-Hodgkin's lymphoma			
subjects affected / exposed	0 / 497 (0.00%)	3 / 242 (1.24%)	
occurrences causally related to treatment / all	0 / 0	3 / 3	
deaths causally related to treatment / all	0 / 0	2 / 2	
Prostate cancer			
subjects affected / exposed	1 / 497 (0.20%)	0 / 242 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal cancer			
subjects affected / exposed	0 / 497 (0.00%)	1 / 242 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin cancer			
subjects affected / exposed	1 / 497 (0.20%)	0 / 242 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Soft tissue neoplasm			
subjects affected / exposed	1 / 497 (0.20%)	0 / 242 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Squamous cell carcinoma			
subjects affected / exposed	0 / 497 (0.00%)	2 / 242 (0.83%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Squamous cell carcinoma of lung			

subjects affected / exposed	1 / 497 (0.20%)	0 / 242 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Uterine cancer			
subjects affected / exposed	1 / 497 (0.20%)	0 / 242 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Uterine leiomyoma			
subjects affected / exposed	3 / 497 (0.60%)	0 / 242 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	2 / 497 (0.40%)	0 / 242 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dry gangrene			
subjects affected / exposed	1 / 497 (0.20%)	0 / 242 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertension			
subjects affected / exposed	0 / 497 (0.00%)	1 / 242 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral artery thrombosis			
subjects affected / exposed	1 / 497 (0.20%)	0 / 242 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pregnancy, puerperium and perinatal conditions			
Abortion spontaneous			
subjects affected / exposed	1 / 497 (0.20%)	1 / 242 (0.41%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Pregnancy			
subjects affected / exposed	1 / 497 (0.20%)	0 / 242 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 497 (0.20%)	0 / 242 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Non-cardiac chest pain			
subjects affected / exposed	1 / 497 (0.20%)	0 / 242 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			
subjects affected / exposed	0 / 497 (0.00%)	1 / 242 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Anaphylactic reaction			
subjects affected / exposed	1 / 497 (0.20%)	0 / 242 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Abnormal uterine bleeding			
subjects affected / exposed	1 / 497 (0.20%)	0 / 242 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cervical dysplasia			
subjects affected / exposed	1 / 497 (0.20%)	0 / 242 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colpocele			

subjects affected / exposed	1 / 497 (0.20%)	0 / 242 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endometrial hyperplasia			
subjects affected / exposed	1 / 497 (0.20%)	0 / 242 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Heavy menstrual bleeding			
subjects affected / exposed	1 / 497 (0.20%)	0 / 242 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intermenstrual bleeding			
subjects affected / exposed	1 / 497 (0.20%)	0 / 242 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ovarian cyst			
subjects affected / exposed	1 / 497 (0.20%)	0 / 242 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Acquired diaphragmatic eventration			
subjects affected / exposed	1 / 497 (0.20%)	0 / 242 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Asthmatic crisis			
subjects affected / exposed	1 / 497 (0.20%)	0 / 242 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Caplan's syndrome			
subjects affected / exposed	1 / 497 (0.20%)	0 / 242 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspnoea			

subjects affected / exposed	2 / 497 (0.40%)	0 / 242 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Interstitial lung disease			
subjects affected / exposed	1 / 497 (0.20%)	0 / 242 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			
subjects affected / exposed	2 / 497 (0.40%)	0 / 242 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Pulmonary mass			
subjects affected / exposed	1 / 497 (0.20%)	0 / 242 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Electrocardiogram Q wave abnormal			
subjects affected / exposed	1 / 497 (0.20%)	0 / 242 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Ankle fracture			
subjects affected / exposed	2 / 497 (0.40%)	0 / 242 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Brain contusion			
subjects affected / exposed	0 / 497 (0.00%)	1 / 242 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fall			
subjects affected / exposed	1 / 497 (0.20%)	0 / 242 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Femur fracture			
subjects affected / exposed	3 / 497 (0.60%)	2 / 242 (0.83%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Forearm fracture			
subjects affected / exposed	2 / 497 (0.40%)	0 / 242 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hip fracture			
subjects affected / exposed	2 / 497 (0.40%)	0 / 242 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Humerus fracture			
subjects affected / exposed	0 / 497 (0.00%)	2 / 242 (0.83%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Joint dislocation			
subjects affected / exposed	1 / 497 (0.20%)	0 / 242 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Limb injury			
subjects affected / exposed	1 / 497 (0.20%)	1 / 242 (0.41%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lumbar vertebral fracture			
subjects affected / exposed	0 / 497 (0.00%)	1 / 242 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Periprosthetic fracture			
subjects affected / exposed	1 / 497 (0.20%)	0 / 242 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Postoperative wound complication			

subjects affected / exposed	1 / 497 (0.20%)	0 / 242 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Procedural intestinal perforation			
subjects affected / exposed	1 / 497 (0.20%)	0 / 242 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Shunt occlusion			
subjects affected / exposed	1 / 497 (0.20%)	0 / 242 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin laceration			
subjects affected / exposed	0 / 497 (0.00%)	1 / 242 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal compression fracture			
subjects affected / exposed	1 / 497 (0.20%)	1 / 242 (0.41%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tibia fracture			
subjects affected / exposed	0 / 497 (0.00%)	1 / 242 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper limb fracture			
subjects affected / exposed	0 / 497 (0.00%)	1 / 242 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wrist fracture			
subjects affected / exposed	1 / 497 (0.20%)	0 / 242 (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 coronary syndrome			

subjects affected / exposed	1 / 497 (0.20%)	0 / 242 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute myocardial infarction			
subjects affected / exposed	0 / 497 (0.00%)	1 / 242 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Angina pectoris			
subjects affected / exposed	1 / 497 (0.20%)	0 / 242 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angina unstable			
subjects affected / exposed	2 / 497 (0.40%)	0 / 242 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial fibrillation			
subjects affected / exposed	0 / 497 (0.00%)	1 / 242 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial flutter			
subjects affected / exposed	0 / 497 (0.00%)	1 / 242 (0.41%)	
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	2 / 497 (0.40%)	1 / 242 (0.41%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure congestive			
subjects affected / exposed	1 / 497 (0.20%)	0 / 242 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary artery disease			

subjects affected / exposed	3 / 497 (0.60%)	0 / 242 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pericardial effusion			
subjects affected / exposed	1 / 497 (0.20%)	0 / 242 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ventricular tachycardia			
subjects affected / exposed	1 / 497 (0.20%)	0 / 242 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Cerebrovascular insufficiency			
subjects affected / exposed	0 / 497 (0.00%)	1 / 242 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhagic cerebral infarction			
subjects affected / exposed	1 / 497 (0.20%)	0 / 242 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ischaemic cerebral infarction			
subjects affected / exposed	1 / 497 (0.20%)	0 / 242 (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 / 497 (0.20%)	0 / 242 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Normal pressure hydrocephalus			
subjects affected / exposed	1 / 497 (0.20%)	0 / 242 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Seizure			

subjects affected / exposed	1 / 497 (0.20%)	0 / 242 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subarachnoid haemorrhage			
subjects affected / exposed	0 / 497 (0.00%)	1 / 242 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Blood loss anaemia			
subjects affected / exposed	1 / 497 (0.20%)	0 / 242 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	1 / 497 (0.20%)	1 / 242 (0.41%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vestibular disorder			
subjects affected / exposed	0 / 497 (0.00%)	1 / 242 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Amaurosis fugax			
subjects affected / exposed	1 / 497 (0.20%)	0 / 242 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cataract			
subjects affected / exposed	1 / 497 (0.20%)	1 / 242 (0.41%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Glaucoma			
subjects affected / exposed	1 / 497 (0.20%)	0 / 242 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Lens dislocation			
subjects affected / exposed	0 / 497 (0.00%)	1 / 242 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal hernia			
subjects affected / exposed	1 / 497 (0.20%)	0 / 242 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain lower			
subjects affected / exposed	1 / 497 (0.20%)	0 / 242 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epiploic appendagitis			
subjects affected / exposed	1 / 497 (0.20%)	0 / 242 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis			
subjects affected / exposed	1 / 497 (0.20%)	0 / 242 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis acute			
subjects affected / exposed	1 / 497 (0.20%)	0 / 242 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Proctitis			
subjects affected / exposed	0 / 497 (0.00%)	1 / 242 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Umbilical hernia			
subjects affected / exposed	1 / 497 (0.20%)	0 / 242 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			

Cholelithiasis			
subjects affected / exposed	5 / 497 (1.01%)	1 / 242 (0.41%)	
occurrences causally related to treatment / all	0 / 5	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Actinic keratosis			
subjects affected / exposed	1 / 497 (0.20%)	0 / 242 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin ulcer			
subjects affected / exposed	1 / 497 (0.20%)	0 / 242 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 497 (0.00%)	2 / 242 (0.83%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nephrolithiasis			
subjects affected / exposed	1 / 497 (0.20%)	0 / 242 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal colic			
subjects affected / exposed	1 / 497 (0.20%)	0 / 242 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal cyst			
subjects affected / exposed	0 / 497 (0.00%)	1 / 242 (0.41%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ureterolithiasis			
subjects affected / exposed	1 / 497 (0.20%)	0 / 242 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 497 (0.00%)	1 / 242 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Back pain			
subjects affected / exposed	0 / 497 (0.00%)	1 / 242 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Foot deformity			
subjects affected / exposed	1 / 497 (0.20%)	0 / 242 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteoarthritis			
subjects affected / exposed	7 / 497 (1.41%)	3 / 242 (1.24%)	
occurrences causally related to treatment / all	0 / 9	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteonecrosis			
subjects affected / exposed	0 / 497 (0.00%)	1 / 242 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteonecrosis of jaw			
subjects affected / exposed	0 / 497 (0.00%)	1 / 242 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteopenia			
subjects affected / exposed	0 / 497 (0.00%)	1 / 242 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pathological fracture			
subjects affected / exposed	1 / 497 (0.20%)	0 / 242 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Rheumatoid arthritis			
subjects affected / exposed	1 / 497 (0.20%)	1 / 242 (0.41%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wrist deformity			
subjects affected / exposed	0 / 497 (0.00%)	1 / 242 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Abdominal wall infection			
subjects affected / exposed	1 / 497 (0.20%)	0 / 242 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abscess jaw			
subjects affected / exposed	0 / 497 (0.00%)	1 / 242 (0.41%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arthritis bacterial			
subjects affected / exposed	0 / 497 (0.00%)	1 / 242 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atypical pneumonia			
subjects affected / exposed	1 / 497 (0.20%)	0 / 242 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
COVID-19			
subjects affected / exposed	3 / 497 (0.60%)	1 / 242 (0.41%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
COVID-19 pneumonia			
subjects affected / exposed	6 / 497 (1.21%)	2 / 242 (0.83%)	
occurrences causally related to treatment / all	1 / 6	0 / 2	
deaths causally related to treatment / all	1 / 3	0 / 1	
Diverticulitis			

subjects affected / exposed	1 / 497 (0.20%)	0 / 242 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Escherichia urinary tract infection			
subjects affected / exposed	0 / 497 (0.00%)	1 / 242 (0.41%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
subjects affected / exposed	1 / 497 (0.20%)	1 / 242 (0.41%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Herpes zoster			
subjects affected / exposed	1 / 497 (0.20%)	0 / 242 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Influenza			
subjects affected / exposed	1 / 497 (0.20%)	0 / 242 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower respiratory tract infection			
subjects affected / exposed	1 / 497 (0.20%)	0 / 242 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Medical device site joint infection			
subjects affected / exposed	0 / 497 (0.00%)	1 / 242 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meningitis meningococcal			
subjects affected / exposed	1 / 497 (0.20%)	0 / 242 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	1 / 1	0 / 0	
Ophthalmic herpes zoster			

subjects affected / exposed	1 / 497 (0.20%)	0 / 242 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteomyelitis			
subjects affected / exposed	1 / 497 (0.20%)	0 / 242 (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	7 / 497 (1.41%)	3 / 242 (1.24%)	
occurrences causally related to treatment / all	3 / 7	3 / 3	
deaths causally related to treatment / all	0 / 1	1 / 1	
Pneumonia bacterial			
subjects affected / exposed	0 / 497 (0.00%)	1 / 242 (0.41%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia influenzal			
subjects affected / exposed	2 / 497 (0.40%)	0 / 242 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia viral			
subjects affected / exposed	0 / 497 (0.00%)	1 / 242 (0.41%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis acute			
subjects affected / exposed	0 / 497 (0.00%)	1 / 242 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis chronic			
subjects affected / exposed	0 / 497 (0.00%)	1 / 242 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory tract infection			

subjects affected / exposed	1 / 497 (0.20%)	0 / 242 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sinusitis			
subjects affected / exposed	0 / 497 (0.00%)	1 / 242 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Staphylococcal abscess			
subjects affected / exposed	0 / 497 (0.00%)	1 / 242 (0.41%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Staphylococcal infection			
subjects affected / exposed	0 / 497 (0.00%)	1 / 242 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Staphylococcal sepsis			
subjects affected / exposed	0 / 497 (0.00%)	1 / 242 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tracheobronchitis			
subjects affected / exposed	1 / 497 (0.20%)	0 / 242 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	0 / 497 (0.00%)	2 / 242 (0.83%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urosepsis			
subjects affected / exposed	0 / 497 (0.00%)	1 / 242 (0.41%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	1 / 1	
Wound infection			

subjects affected / exposed	1 / 497 (0.20%)	0 / 242 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Filgotinib Darwin 1	Filgotinib Darwin 2	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	386 / 497 (77.67%)	189 / 242 (78.10%)	
Investigations			
Blood cholesterol increased			
subjects affected / exposed	13 / 497 (2.62%)	23 / 242 (9.50%)	
occurrences (all)	18	42	
Blood creatinine increased			
subjects affected / exposed	13 / 497 (2.62%)	20 / 242 (8.26%)	
occurrences (all)	14	25	
Lymphocyte count decreased			
subjects affected / exposed	20 / 497 (4.02%)	18 / 242 (7.44%)	
occurrences (all)	31	38	
Mycobacterium tuberculosis complex test positive			
subjects affected / exposed	58 / 497 (11.67%)	40 / 242 (16.53%)	
occurrences (all)	59	40	
Vascular disorders			
Hypertension			
subjects affected / exposed	75 / 497 (15.09%)	27 / 242 (11.16%)	
occurrences (all)	83	37	
Nervous system disorders			
Headache			
subjects affected / exposed	34 / 497 (6.84%)	26 / 242 (10.74%)	
occurrences (all)	45	41	
Blood and lymphatic system disorders			
Lymphopenia			
subjects affected / exposed	45 / 497 (9.05%)	23 / 242 (9.50%)	
occurrences (all)	65	33	
Gastrointestinal disorders			

Diarrhoea			
subjects affected / exposed	33 / 497 (6.64%)	12 / 242 (4.96%)	
occurrences (all)	40	13	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	37 / 497 (7.44%)	10 / 242 (4.13%)	
occurrences (all)	41	15	
Rheumatoid arthritis			
subjects affected / exposed	41 / 497 (8.25%)	15 / 242 (6.20%)	
occurrences (all)	78	23	
Infections and infestations			
Bronchitis			
subjects affected / exposed	59 / 497 (11.87%)	19 / 242 (7.85%)	
occurrences (all)	86	22	
COVID-19			
subjects affected / exposed	34 / 497 (6.84%)	10 / 242 (4.13%)	
occurrences (all)	37	10	
Gastroenteritis			
subjects affected / exposed	29 / 497 (5.84%)	8 / 242 (3.31%)	
occurrences (all)	32	10	
Herpes zoster			
subjects affected / exposed	29 / 497 (5.84%)	14 / 242 (5.79%)	
occurrences (all)	32	14	
Influenza			
subjects affected / exposed	30 / 497 (6.04%)	12 / 242 (4.96%)	
occurrences (all)	39	16	
Nasopharyngitis			
subjects affected / exposed	70 / 497 (14.08%)	24 / 242 (9.92%)	
occurrences (all)	112	37	
Pharyngitis			
subjects affected / exposed	31 / 497 (6.24%)	11 / 242 (4.55%)	
occurrences (all)	41	13	
Upper respiratory tract infection			
subjects affected / exposed	57 / 497 (11.47%)	37 / 242 (15.29%)	
occurrences (all)	82	50	
Urinary tract infection			

subjects affected / exposed	72 / 497 (14.49%)	30 / 242 (12.40%)	
occurrences (all)	128	58	
Metabolism and nutrition disorders			
Dyslipidaemia			
subjects affected / exposed	39 / 497 (7.85%)	17 / 242 (7.02%)	
occurrences (all)	53	22	
Hypercholesterolaemia			
subjects affected / exposed	39 / 497 (7.85%)	30 / 242 (12.40%)	
occurrences (all)	54	54	
Hypertriglyceridaemia			
subjects affected / exposed	18 / 497 (3.62%)	13 / 242 (5.37%)	
occurrences (all)	28	44	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
13 March 2014	− Added that a film-coated tablet (25-100 mg per tablet) of the hydrochloride (HCl) salt of GLPG0634 would be available for the study in addition to the oral capsule (10-100 mg per capsule). − Added results of a 39-week toxicity study in dogs. − Refined the inclusion/exclusion criteria with additional criteria to manage the overall health status at Entry Visit. − Refined the individual participant withdrawal criteria to have them fully aligned with the core studies GLPG0634-CL-203 and GLPG0634-CL-204 and to provide further guidance for the investigators. − Added a Data Safety Monitoring Board (DSMB). − Introduced an annual blood tuberculosis (TB) test.
07 October 2016	- The protocol was amended to change sponsorship from Galapagos NV to Gilead Sciences, Inc. − Changed GLPG0634 and G254445 to filgotinib and GS-829845, respectively, throughout the document. − Replaced team members and contact details of Galapagos personnel with those of Gilead personnel and added references to Gilead with respect to sponsorship where applicable. − Included details regarding the Gilead maleate salt tablet formulation and removed references to filgotinib capsules. − Replaced confidentiality statement and signature page text with Gilead-specific requirements and language. − Clarified that "regimen" refers to the actual frequency of active investigational product (IP) intake. − Updated information regarding the anticipated therapeutic daily dose range. − Updated various sections throughout and added an appendix regarding changes to contraceptive requirements to align with filgotinib Phase 3 studies. − Added information regarding study drug interruption. − Clarified procedures for obtaining average serum creatinine values. − Updated guidelines for missed doses to align with filgotinib Phase 3 studies. − Clarified actions that should be taken in case of a positive or confirmed indeterminate TB blood test (QuantiFERON-TB gold test). − Added a visit window of ± 4 days for the Follow-up Visit. − Added requirement of home urine pregnancy testing every 4 weeks during the study for female participants of childbearing potential. − Included investigator instructions on informing male participants of potential fertility risks. − Updated Safety Pharmacology section with current information regarding exposures.

15 March 2018	− Added measurement of weight to all visits after the Entry Visit in order to accurately calculate serum creatinine clearance. − Updated text to reflect the actual number of participants enrolled (739 participants) and sites activated (116 sites). − Updated contact details for Medical Monitor and study personnel. − Updated text to reflect current RA treatment landscape. − Removed information regarding the number of participants who had been dosed with filgotinib. − Updated study duration to 96 months. − Added study drug interruption considerations for participants who test positive for TB based on current guidelines for TB screening for biologics or tofacitinib. − Updated study drug discontinuation criteria to replace creatinine with creatinine clearance as the more accurate measure of kidney function. − Specified that study drug discontinuation consideration for male hormones was to be applied in cases without impairment of testicular function at baseline and with investigator judgment used to determine clinical relevance of the concomitant increase in follicle stimulating hormone (FSH) or luteinizing hormone (LH). − Updated language throughout to align with Gilead filgotinib studies and convention. − Removed details on statistical analyses which were specified in the Statistical Analysis Plan (SAP). − Removed information regarding genomic testing and sample retention from the Informed Consent section. − Clarified definitions for childbearing potential and permanent sterilization. − Updated results from a completed drug-drug interaction study of filgotinib and hormonal contraceptives.
13 May 2021	− The protocol was amended to change sponsorship from Gilead Sciences, Inc. to Galapagos NV. − Contact details were updated due to changes in Medical Monitor, Study Personnel, and the contract research organization. − Safety monitoring components, including information for the DSMB, which was discontinued as of 1-Apr-2021, were updated to align with current practices and safety standards. − Clarification was made to study drug discontinuation criterion regarding serious infections. − Information regarding packaging, labeling, and distribution was updated to align with the change in sponsorship.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

http://www.ncbi.nlm.nih.gov/pubmed/33526618