Clinical trial results:
A Phase 2a, Double-Blind, Randomized, Placebo-Controlled, Parallel Group Study to Evaluate the Efficacy and Safety of Oral PF-06651600 and PF-06700841 as Induction and Open Label Extension Treatment in Subjects With Moderate to Severe Crohn's Disease

Summary

EudraCT number	2017-003359-43
Trial protocol	LT DE SK AT PL HU ES CZ BE HR IT
Global end of trial date	19 October 2023

Results information

Result version number	v1 (current)
This version publication date	23 October 2024
First version publication date	23 October 2024

Trial information

Trial identification

Sponsor protocol code	B7981007

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03395184
WHO universal trial number (UTN)	-
Other trial identifiers	PIZZICATO: Other Study ID

Notes:

Sponsors

Sponsor organisation name	Pfizer Inc.
Sponsor organisation address	235 E 42nd Street, New York, United States, NY 10017
Public contact	Pfizer ClinicalTrials.gov Call Center, Pfizer Inc., 001 8007181021, ClinicalTrials.gov_Inquiries@pfizer.com
Scientific contact	Pfizer ClinicalTrials.gov Call Center, Pfizer Inc., 001 8007181021, ClinicalTrials.gov_Inquiries@pfizer.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	06 April 2024
Is this the analysis of the primary completion data?	No

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

Notes:

General information about the trial

Main objective of the trial:

Induction Period: To evaluate the efficacy of PF-06651600 (ritlecitinib) and PF-06700841 (brepocitinib) compared to placebo at Week 12 in participants with moderate to severe Crohn's disease (CD).
Open label extension (OLE) period: To assess the safety and tolerability of PF-06651600 and PF-06700841 therapy during open label extension period for subjects with moderate to severe CD.

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and in compliance with all International Council for Harmonization (ICH) Good Clinical Practice (GCP) Guidelines. All the local regulatory requirements pertinent to safety of trials subjects were followed.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	02 February 2018
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Australia: 5
Country: Number of subjects enrolled	Bosnia and Herzegovina: 1
Country: Number of subjects enrolled	Canada: 4
Country: Number of subjects enrolled	Czechia: 6
Country: Number of subjects enrolled	Germany: 16
Country: Number of subjects enrolled	Georgia: 3
Country: Number of subjects enrolled	Hungary: 2
Country: Number of subjects enrolled	Italy: 15
Country: Number of subjects enrolled	Belgium: 9
Country: Number of subjects enrolled	Saudi Arabia: 1
Country: Number of subjects enrolled	Spain: 9
Country: Number of subjects enrolled	Lebanon: 7
Country: Number of subjects enrolled	Austria: 2
Country: Number of subjects enrolled	Korea, Republic of: 15
Country: Number of subjects enrolled	Poland: 39
Country: Number of subjects enrolled	Serbia: 4
Country: Number of subjects enrolled	South Africa: 2
Country: Number of subjects enrolled	Tunisia: 1
Country: Number of subjects enrolled	Türkiye: 6

Country: Number of subjects enrolled	Russian Federation: 24
Country: Number of subjects enrolled	Slovakia: 8
Country: Number of subjects enrolled	Switzerland: 4
Country: Number of subjects enrolled	Ukraine: 9
Country: Number of subjects enrolled	United Arab Emirates: 1
Country: Number of subjects enrolled	United States: 51
Worldwide total number of subjects	244
EEA total number of subjects	106

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)	240
From 65 to 84 years	4
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study consisted of a 12-weeks induction period and a 52-weeks open label extension (OLE) period. The participants who completed induction period, entered the 52-week OLE period.

Pre-assignment

Screening details:

A total of 645 participants were screened across 26 countries of which 401 were screen failures and 244 participants were randomized in the study.

Period 1

Period 1 title	Induction Period (Up to 12 weeks)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	Induction Period: Placebo QD

Arm description:

Participants received placebo matched to either PF-06651600 (ritlecitinib) or PF-06700841 (brepocitinib) once daily (QD) orally for 12 weeks in induction period.

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

Dosage and administration details:

Single dose of placebo QD orally for 12 weeks.

Arm title	Induction period: Ritlecitinib 200 mg/50 mg QD

Arm description:

Participants received PF-06651600 (ritlecitinib) 200 milligrams (mg) once daily orally for 8 weeks followed by ritlecitinib 50 mg QD orally for 4 weeks in induction period.

Arm type	Experimental
Investigational medicinal product name	Ritlecitinib
Investigational medicinal product code	PF-06651600
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Single dose of PF-06651600 (ritlecitinib) 200 mg QD orally for 8 weeks followed by ritlecitinib 50 mg QD orally for 4 weeks administered as 50 mg tablets.

Arm title	Induction period: Brepocitinib 60 mg QD

Arm description:

Participants received PF-06700841 (brepocitinib) 60 mg QD orally for 12 weeks in induction period.

Arm type	Experimental

Investigational medicinal product name	Brepocitinib
Investigational medicinal product code	PF-06700841
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Single dose of PF-06700841 (brepocitinib) 60 mg QD orally for 12 weeks administered as 25 mg and 5 mg tablets.

Number of subjects in period 1	Induction Period: Placebo QD	Induction period: Ritlecitinib 200 mg/50 mg QD	Induction period: Brepocitinib 60 mg QD
Started	79	93	72
Completed	68	84	65
Not completed	11	9	7
Consent withdrawn by subject	2	2	-
Adverse events	6	4	4
No longer met eligibility criteria	-	2	1
Unspecified	1	-	-
Lost to follow-up	-	1	-
Lack of efficacy	2	-	2

Period 2

Period 2 title	OLE Period (Up to 52 weeks)
Is this the baseline period?	No
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	OLE Period: Placebo QD -> Ritlecitinib 50 mg QD

Arm description:

Participants who received placebo matched to ritlecitinib during the induction period were administered ritlecitinib 50 mg QD orally for 52 weeks in OLE period.

Arm type	Experimental
Investigational medicinal product name	Ritlecitinib
Investigational medicinal product code	PF-06651600
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Single dose of PF-06651600 (ritlecitinib) 50 mg QD orally for 52 weeks

Arm title	OLE Period: Ritlecitinib 200 mg/50mgQD->Ritlecitinib 50mgQD

Arm description:

Participants who received ritlecitinib 200 mg /50 mg QD in the induction period continued to receive ritlecitinib 50 mg QD for 52 weeks in OLE period.

Arm type	Experimental
Investigational medicinal product name	Ritlecitinib
Investigational medicinal product code	PF-06651600
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Single dose of PF-06651600 (ritlecitinib) 50 mg QD orally for 52 weeks administered as 50 mg tablets.

Arm title	OLE Period: Placebo QD -> Brepocitinib 30 mg QD

Arm description:

Participants who received placebo matched to brepocitinib in the induction period were administered brepocitinib 30 mg QD orally for 52 weeks in OLE period.

Arm type	Experimental
Investigational medicinal product name	Brepocitinib
Investigational medicinal product code	PF-06700841
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Single dose of PF-06700841 (brepocitinib) 30 mg QD orally for 52 weeks administered as 25 mg and 5 mg tablets.

Arm title	OLE Period: Brepocitinib 60 mg QD -> Brepocitinib 30 mg QD

Arm description:

Participants who received brepocitinib 60 mg QD in the induction period were administered brepocitinib 30 mg QD for 52 weeks in OLE period.

Arm type	Experimental
Investigational medicinal product name	Brepocitinib
Investigational medicinal product code	PF-06700841
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Single dose of PF-06700841 (brepocitinib) 30 mg QD orally for 12 weeks administered as 25 mg and 5 mg tablets.

Number of subjects in period 2[1]	OLE Period: Placebo QD -> Ritlecitinib 50 mg QD	OLE Period: Ritlecitinib 200 mg/50mgQD->Ritlecitinib 50mgQD	OLE Period: Placebo QD -> Brepocitinib 30 mg QD
Started	36	84	32
Completed	20	45	21
Not completed	16	39	11
Consent withdrawn by subject	3	11	3
Adverse events	7	13	4
No longer met eligibility criteria	1	-	1

Unspecified	-	2	-
Lost to follow-up	-	2	-
Lack of efficacy	5	11	3

Number of subjects in period 2[1]	OLE Period: Brepocitinib 60 mg QD -> Brepocitinib 30 mg QD
Started	64
Completed	34
Not completed	30
Consent withdrawn by subject	8
Adverse events	15
No longer met eligibility criteria	-
Unspecified	2
Lost to follow-up	-
Lack of efficacy	5

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.
Justification: Not all participants chose to participate in the extension phase

Baseline characteristics

Reporting groups	
Reporting group title	Induction Period: Placebo QD
Reporting group description:	
Participants received placebo matched to either PF-06651600 (ritlecitinib) or PF-06700841 (brepocitinib) once daily (QD) orally for 12 weeks in induction period.	
Reporting group title	Induction period: Ritlecitinib 200 mg/50 mg QD
Reporting group description:	
Participants received PF-06651600 (ritlecitinib) 200 milligrams (mg) once daily orally for 8 weeks followed by ritlecitinib 50 mg QD orally for 4 weeks in induction period.	
Reporting group title	Induction period: Brepocitinib 60 mg QD
Reporting group description:	
Participants received PF-06700841 (brepocitinib) 60 mg QD orally for 12 weeks in induction period.	

Reporting group values	Induction Period: Placebo QD	Induction period: Ritlecitinib 200 mg/50 mg QD	Induction period: Brepocitinib 60 mg QD
Number of subjects	79	93	72
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	77	92	71
From 65-84 years	2	1	1
85 years and over	0	0	0
Age Continuous Units: Years			
arithmetic mean	36.1	34.6	36.5
standard deviation	± 13.03	± 10.64	± 12.70
Sex: Female, Male Units: Participants			
Female	37	41	29
Male	42	52	43
Race Units: Subjects			
White	71	84	61
Black or African American	0	0	2
Asian	5	6	7
Multiracial	1	1	1
Not reported	2	2	1
Ethinicity Units: Subjects			
Hispanic or Latino	2	1	1
Not Hispanic or Latino	75	91	69

Not reported	2	1	2

Reporting group values	Total		
Number of subjects	244		
Age categorical Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	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)	240		
From 65-84 years	4		
85 years and over	0		
Age Continuous Units: Years			
arithmetic mean			
standard deviation	-		
Sex: Female, Male Units: Participants			
Female	107		
Male	137		
Race Units: Subjects			
White	216		
Black or African American	2		
Asian	18		
Multiracial	3		
Not reported	5		
Ethinicity Units: Subjects			
Hispanic or Latino	4		
Not Hispanic or Latino	235		
Not reported	5		

End points

End points reporting groups

Reporting group title	Induction Period: Placebo QD
Reporting group description:	
Participants received placebo matched to either PF-06651600 (ritlecitinib) or PF-06700841 (brepocitinib) once daily (QD) orally for 12 weeks in induction period.	
Reporting group title	Induction period: Ritlecitinib 200 mg/50 mg QD
Reporting group description:	
Participants received PF-06651600 (ritlecitinib) 200 milligrams (mg) once daily orally for 8 weeks followed by ritlecitinib 50 mg QD orally for 4 weeks in induction period.	
Reporting group title	Induction period: Brepocitinib 60 mg QD
Reporting group description:	
Participants received PF-06700841 (brepocitinib) 60 mg QD orally for 12 weeks in induction period.	
Reporting group title	OLE Period: Placebo QD -> Ritlecitinib 50 mg QD
Reporting group description:	
Participants who received placebo matched to ritlecitinib during the induction period were administered ritlecitinib 50 mg QD orally for 52 weeks in OLE period.	
Reporting group title	OLE Period: Ritlecitinib 200 mg/50mgQD->Ritlecitinib 50mgQD
Reporting group description:	
Participants who received ritlecitinib 200 mg /50 mg QD in the induction period continued to receive ritlecitinib 50 mg QD for 52 weeks in OLE period.	
Reporting group title	OLE Period: Placebo QD -> Brepocitinib 30 mg QD
Reporting group description:	
Participants who received placebo matched to brepocitinib in the induction period were administered brepocitinib 30 mg QD orally for 52 weeks in OLE period.	
Reporting group title	OLE Period: Brepocitinib 60 mg QD -> Brepocitinib 30 mg QD
Reporting group description:	
Participants who received brepocitinib 60 mg QD in the induction period were administered brepocitinib 30 mg QD for 52 weeks in OLE period.	

Primary: Percentage of Participants Achieving Greater Than or Equal to (>=) 50 Percent (%) Reduction in Simple Endoscopic Score for Crohn’s Disease (SES CD50) at Week 12: Induction Period

End point title	Percentage of Participants Achieving Greater Than or Equal to (>=) 50 Percent (%) Reduction in Simple Endoscopic Score for Crohn’s Disease (SES CD50) at Week 12: Induction Period
End point description:	
SES CD50: 50% improvement from baseline(B) in SES-CD. B: last measurement prior to first dosing on Day1. Following bowel segments(S) were used: Ileum, right colon(C),transverse C, left C & rectum. Each S assessed for 4 domains: presence of ulcers(U), Ulcerated surface,affected surface & presence of narrowing,each scored on scale; 0-3. Presence of U score: 0=none,1=small U:(0.1-0.5cm),2=Large U(0.5-2cm),3=very large U(>2cm); Uted surface score:0=none,1=<10%,2=10-30%&3=>30%; affected surface score: 0=unaffected S,1=<50%,2=50-75%&3=>75%;presence of narrowing score:0=none,1=single,can be passed(CNB), 2=multiple,CNB&3=cannot be passed.Total SES CD score determined by sum of each domain score for all 5 bowel S, ranged;0-60,higher score=more severe disease. FAS=all randomized participants who received at least one dose of randomized investigational drug. Participants who received placebo in induction period were analyzed as single reporting group. N=participants evaluable for this endpoint.	
End point type	Primary
End point timeframe:	
Week 12	

End point values	Induction Period: Placebo QD	Induction period: Ritlecitinib 200 mg/50 mg QD	Induction period: Brepocitinib 60 mg QD	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	78	92	71	
Units: Percentage of participants				
number (confidence interval 90%)	12.8 (7.1 to 19.9)	27.2 (19.6 to 35.7)	33.8 (25.1 to 43.1)	

Statistical analyses

Statistical analysis title	Placebo QD versus Brepocitinib 60 mg QD
Statistical analysis description:	
Analysis: Cochran Mantel Hansel (CMH) with test treatment & baseline disease activity/extent as factors, & baseline SES-CD score as covariate.	
Comparison groups	Induction Period: Placebo QD v Induction period: Brepocitinib 60 mg QD
Number of subjects included in analysis	149
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0012
Method	Min risk weight method(Mehrotra&Railkar)
Parameter estimate	Percentage risk difference
Point estimate	21.4
Confidence interval	
level	90 %
sides	2-sided
lower limit	10
upper limit	32.9

Statistical analysis title	Placebo QD versus Ritlecitinib 200 mg/50 mg QD
Statistical analysis description:	
Analysis: Cochran Mantel Hansel (CMH) with test treatment & baseline disease activity/extent as factors, & baseline SES-CD score as covariate.	
Comparison groups	Induction Period: Placebo QD v Induction period: Ritlecitinib 200 mg/50 mg QD
Number of subjects included in analysis	170
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0119
Method	Min risk weight method(Mehrotra-Railkar)
Parameter estimate	Percentage risk difference
Point estimate	14.3

Confidence interval	
level	90 %
sides	2-sided
lower limit	4
upper limit	24.5

Primary: Number of Participants With Laboratory Test Abnormalities During OLE Period

End point title	Number of Participants With Laboratory Test Abnormalities During OLE Period[1]

End point description:

Pre-specified criteria for lab abnormalities included- hematology: hemoglobin(Hb), erythrocytes(ery),hematocrit:<0.8*lower limit of normal(LLN);reticulocytes: <0.5*LLN, >1.5*upper limit of normal(ULN); ery mean corpuscular(EMC) volume:<0.9*ULN, >1.11*ULN;EMC Hb:<0.9*LLN; platelets:>1.75*ULN; leukocytes(10^9/L): <0.6*LLN,>1.5*ULN;lymphocyte,neutrophil(10^9/L):<0.8*LLN,>1.2*ULN;basophil,eosinophil,monocyte (10^9/L):>1.2*ULN. Chemistry:bilirubin(mg/dL),aspartate aminotransferase(AT),alanine AT(units per litre)>3.0*ULN; protein, albumin(g/dL):<0.8*LLN;creatinine,triglycerides (mg/dL):>1.3*ULN; urate(mg/dL):>1.2*ULN,potassium(mEq/L):<0.9*LLN;calcium (mg/dL): <0.9*LLN,>1.1*ULN. Urinalysis:pH>8;urine,glucose,protein(mg/dl);ketones,nitrite, urine Hb(scalar):>=1. Number of participants with any lab abnormality meeting pre-specified criteria are reported. Safety analysis set(SAS)=participants who received at least one dose of the investigational drug. N=participants

End point type	Primary

End point timeframe:

From start of study intervention in OLE period up to 4 weeks after last dose of study intervention (up to 56 weeks)

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 planned for this endpoint

End point values	OLE Period: Placebo QD -> Ritlecitinib 50 mg QD	OLE Period: Ritlecitinib 200 mg/50mgQD->Ritlecitinib 50mgQD	OLE Period: Placebo QD -> Brepocitinib 30 mg QD	OLE Period: Brepocitinib 60 mg QD -> Brepocitinib 30 mg QD
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	36	83	32	63
Units: Participants	33	76	26	56

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants According to Categorization of Vital Signs During OLE Period

End point title	Number of Participants According to Categorization of Vital Signs During OLE Period[2]

End point description:

Vital signs including blood pressure (diastolic blood pressure [DBP], systolic blood pressure [SBP], and pulse rate [PR]) were measured in a supine position using automated devices. DBP included value < 50 (millimeter of mercury [mmHg]), change >=20 (mmHg) increase and change >=20 (mmHg) decrease; SBP: value < 90 (mmHg), change >= 30 (mmHg) increase and change >= 30 (mmHg) decrease; PR:

value > 120 (beats per minute [bpm]). SAS included all those participants who received at least one dose of the investigational drug (ritlecitinib, brepocitinib, or placebo). Here, Number of Participants Analyzed signifies participants evaluable for this endpoint.

End point type	Primary

End point timeframe:

From start of study intervention in OLE period up to 4 weeks after last dose of study intervention (up to 56 weeks)

Notes:

[2] - 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 planned for this endpoint

End point values	OLE Period: Placebo QD -> Ritlecitinib 50 mg QD	OLE Period: Ritlecitinib 200 mg/50mgQD->Ritlecitinib 50mgQD	OLE Period: Placebo QD -> Brepocitinib 30 mg QD	OLE Period: Brepocitinib 60 mg QD -> Brepocitinib 30 mg QD
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	36	83	32	63
Units: Participants				
DBP; value < 50 (mmHg)	0	2	0	1
DBP; change >=20 (mmHg) increase	4	6	2	6
DBP; change >=20 (mmHg) decrease	1	4	3	8
PR; value > 120 (bpm)	0	1	0	0
SBP; value < 90 (mmHg)	0	2	0	1
SBP; change >= 30 (mmHg) increase	1	2	0	5
SBP; change >= 30 (mmHg) decrease	3	0	3	2

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants With Abnormal Clinically Significant Electrocardiogram Findings During OLE Period

End point title	Number of Participants With Abnormal Clinically Significant Electrocardiogram Findings During OLE Period[3]

End point description:

Single twelve lead ECGs were obtained using an automated ECG machine after participant had rested quietly for at least 10 minutes in a supine position. QTc prolongations were defined as a QTc >=480 milli second (msec) or an absolute change in QTc greater than (>) 60 msec. Clinically significant ECG findings were determined by the investigator. SAS included all those participants who received at least one dose of the investigational drug (ritlecitinib, brepocitinib, or placebo). Here, Number of Participants Analyzed signifies participants evaluable for this endpoint.

End point type	Primary

End point timeframe:

From start of study intervention in OLE period up to 4 weeks after last dose of study intervention (up to 56 weeks)

Notes:

[3] - 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 planned for this endpoint

End point values	OLE Period: Placebo QD -> Ritlecitinib 50 mg QD	OLE Period: Ritlecitinib 200 mg/50mgQD->Ritlecitinib 50mgQD	OLE Period: Placebo QD -> Brepocitinib 30 mg QD	OLE Period: Brepocitinib 60 mg QD -> Brepocitinib 30 mg QD
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	23	50	21	40
Units: Participants	0	0	0	1

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants With Treatment Emergent Adverse Events (TEAEs) During OLE Period

End point title	Number of Participants With Treatment Emergent Adverse Events (TEAEs) During OLE Period[4]

End point description:

An adverse event (AE) was any untoward medical occurrence in a study participant administered a study intervention; the event need not necessarily have a causal relationship with the treatment or usage. An AE was considered TEAE to a given treatment if the event started during the effective duration of treatment regardless of whether a similar event of equal or greater severity existed in the baseline period. SAS included all those participants who received at least one dose of the investigational drug (ritlecitinib, brepocitinib, or placebo).

End point type	Primary

End point timeframe:

From start of study intervention in OLE period up to 4 weeks after last dose of study intervention (up to 56 weeks)

Notes:

[4] - 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 planned for this endpoint

End point values	OLE Period: Placebo QD -> Ritlecitinib 50 mg QD	OLE Period: Ritlecitinib 200 mg/50mgQD->Ritlecitinib 50mgQD	OLE Period: Placebo QD -> Brepocitinib 30 mg QD	OLE Period: Brepocitinib 60 mg QD -> Brepocitinib 30 mg QD
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	36	84	32	64
Units: Participants	32	58	25	54

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants With Treatment Emergent Serious Adverse Events (TESAE) During OLE Period

End point title	Number of Participants With Treatment Emergent Serious Adverse Events (TESAE) During OLE Period[5]

End point description:

A serious adverse event (SAE) was any untoward medical occurrence at any dose that: resulted in

death; was life-threatening (immediate risk of death); required inpatient hospitalization or prolongation of existing hospitalization; resulted in persistent or significant disability/incapacity (substantial disruption of the ability to conduct normal life functions) or resulted in congenital anomaly/birth defect or was considered an important medical event. An SAE was considered as TESAE if the event started during the effective duration of treatment regardless of whether a similar event of equal or greater severity existed in the baseline period. SAS included all those participants who received at least one dose of the investigational drug (ritlecitinib, brepocitinib, or placebo).

End point type	Primary

End point timeframe:

From start of study intervention in OLE period up to 4 weeks after last dose of study intervention (up to 56 weeks)

Notes:

[5] - 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 planned for this endpoint

End point values	OLE Period: Placebo QD -> Ritlecitinib 50 mg QD	OLE Period: Ritlecitinib 200 mg/50mgQD->Ritlecitinib 50mgQD	OLE Period: Placebo QD -> Brepocitinib 30 mg QD	OLE Period: Brepocitinib 60 mg QD -> Brepocitinib 30 mg QD
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	36	84	32	64
Units: Participants	6	10	5	16

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants With Discontinuations due to Adverse Events During OLE Period

End point title	Number of Participants With Discontinuations due to Adverse Events During OLE Period[6]

End point description:

An AE was any untoward medical occurrence in a study participant administered a study intervention; the event need not necessarily have a causal relationship with the treatment or usage. Discontinuations from study due to TEAEs were defined as participants with an AE record indicating the AE caused permanent discontinuation from the study but action taken with study treatment was not drug withdrawn. Permanent discontinuations from any study intervention due to TEAEs were defined as participants with an AE record indicating that action taken with study treatment was drug withdrawn. In this endpoint number of participants with discontinuation from study due to AEs and permanent discontinuation from study intervention due to AEs are reported. SAS included all those participants who received at least one dose of the investigational drug (ritlecitinib, brepocitinib, or placebo).

End point type	Primary

End point timeframe:

From start of study intervention in OLE period up to 4 weeks after last dose of study intervention (up to 56 weeks)

Notes:

[6] - 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 planned for this endpoint

End point values	OLE Period: Placebo QD -> Ritlecitinib 50 mg QD	OLE Period: Ritlecitinib 200 mg/50mgQD->Ritlecitinib 50mgQD	OLE Period: Placebo QD -> Brepocitinib 30 mg QD	OLE Period: Brepocitinib 60 mg QD -> Brepocitinib 30 mg QD
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	36	84	32	64
Units: Participants				
Discontinuation from study due to TEAEs	0	1	0	0
PD from any study intervention due to TEAEs	7	13	4	15

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants According to Categorization of Vital Signs During Induction Period

End point title	Number of Participants According to Categorization of Vital Signs During Induction Period

End point description:

Vital signs including blood pressure (diastolic blood pressure [DBP], systolic blood pressure [SBP], and pulse rate [PR]) were measured in a supine position using automated devices. DBP included value < 50 (mmHg), change >=20 (mmHg) increase and change >=20 (mmHg) decrease; SBP: value < 90 (mmHg), change >= 30 (mmHg) increase and PR: value > 120 (bpm). SAS included all those participants who received at least one dose of the investigational drug (ritlecitinib, brepocitinib, or placebo). Participants who received placebo in induction period were analyzed as a single reporting group. Here, n= number of participants evaluable for specific rows.

End point type	Secondary

End point timeframe:

From start of study intervention on Day 1 up to Week 12

End point values	Induction Period: Placebo QD	Induction period: Ritlecitinib 200 mg/50 mg QD	Induction period: Brepocitinib 60 mg QD	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	79	93	72	
Units: Participants				
DBP; value < 50 (mmHg) (n=79,93,72)	1	0	0	
DBP; change >=20 (mmHg) increase (n=78,92,72)	4	2	4	
DBP; change >=20 (mmHg) decrease (n=78,92,72)	4	2	4	
Pulse rate; value > 120 (bpm) (n=79,93,72)	4	1	0	
SBP; value < 90 (mmHg) (n=79,93,72)	0	3	0	
SBP; change >= 30 (mmHg) increase (n=78,92,72)	3	2	7	
SBP; change >= 30 (mmHg) decrease (n=78,92,72)	0	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Laboratory Test Abnormalities During Induction Period

End point title	Number of Participants With Laboratory Test Abnormalities During Induction Period

End point description:

Pre-specified criteria for lab abnormalities included- hematology: hemoglobin(Hb), erythrocytes(ery), hematocrit:<0.8*LLN; reticulocytes: <0.5*LLN, >1.5*ULN; ery mean corpuscular(EMC) volume:<0.9*ULN, >1.11*ULN;EMC Hb:<0.9*LLN; platelets:>1.75*ULN; leukocytes(10^9/L): <0.6*LLN,>1.5*ULN; lymphocyte, neutrophil(10^9/L):<0.8*LLN,>1.2*ULN; basophil, eosinophil, monocyte (10^9/L):>1.2*ULN. Chemistry: bilirubin (mg/dL), aspartate aminotransferase (AT), alanine AT (units per litre)>3.0*ULN; protein, albumin(g/dL): <0.8*LLN; creatinine, triglycerides (mg/dL) :>1.3*ULN; urate(mg/dL):>1.2*ULN, potassium (mEq/L):<0.9*LLN; calcium (mg/dL): <0.9*LLN,>1.1*ULN. Urinalysis: pH>8; urine, glucose, protein(mg/dl); ketones, nitrite, urine Hb(scalar):>=1. Number of participants with any lab abnormality meeting pre-specified criteria are reported. SAS was used. Participants who received placebo in induction period were analyzed as a single reporting group. N=participants evaluable for this endpoint.

End point type	Secondary

End point timeframe:

From start of study intervention on Day 1 up to Week 12

End point values	Induction Period: Placebo QD	Induction period: Ritlecitinib 200 mg/50 mg QD	Induction period: Brepocitinib 60 mg QD	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	78	92	72	
Units: Participants	67	72	61	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Treatment Emergent Adverse Events (TEAEs) During Induction Period

End point title	Number of Participants With Treatment Emergent Adverse Events (TEAEs) During Induction Period

End point description:

An AE was any untoward medical occurrence in a study participant administered a study intervention; the event need not necessarily have a causal relationship with the treatment or usage. An AE was considered TEAE to a given treatment if the event started during the effective duration of treatment regardless of whether a similar event of equal or greater severity existed in the baseline period. SAS

included all those participants who received at least one dose of the investigational drug (ritlecitinib, brepocitinib, or placebo). Participants who received placebo in induction period were analyzed as a single reporting group.

End point type	Secondary

End point timeframe:

From start of study intervention on Day 1 up to Week 12

End point values	Induction Period: Placebo QD	Induction period: Ritlecitinib 200 mg/50 mg QD	Induction period: Brepocitinib 60 mg QD	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	79	93	72	
Units: Participants	51	46	49	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Abnormal Clinically Significant Electrocardiogram Findings During Induction Period

End point title	Number of Participants With Abnormal Clinically Significant Electrocardiogram Findings During Induction Period

End point description:

Single twelve lead ECGs were obtained using an automated ECG machine after participant had rested quietly for at least 10 minutes in a supine position. QTc prolongations were defined as a QTc greater than or equal to (>=)480 milli second (msec) or an absolute change in QTc greater than (>)60 msec. Clinically significant ECG findings were determined by the investigator. SAS included all those participants who received at least one dose of the investigational drug (ritlecitinib, brepocitinib, or placebo). Participants who received placebo in induction period were analyzed as a single reporting group. Here Number of Participants Analyzed signifies number of participants evaluable for this endpoint.

End point type	Secondary

End point timeframe:

From start of study intervention on Day 1 up to Week 12

End point values	Induction Period: Placebo QD	Induction period: Ritlecitinib 200 mg/50 mg QD	Induction period: Brepocitinib 60 mg QD	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	68	83	63	
Units: Participants	1	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants Discontinuation due to Adverse Events During Induction Period

End point title	Number of Participants Discontinuation due to Adverse Events During Induction Period

End point description:

An AE was any untoward medical occurrence in a study participant administered a study intervention; the event need not necessarily have a causal relationship with the treatment or usage. Discontinuations from study due to TEAEs were defined as participants with an AE record indicating the AE caused permanent discontinuation from the study but action taken with study treatment was not drug withdrawn. Permanent discontinuations from any study intervention due to TEAEs were defined as participants with an AE record indicating that action taken with study treatment was drug withdrawn. In this endpoint number of participants with discontinuation from study due to AEs and permanent discontinuation from study intervention due to AEs are reported. SAS included all those participants who received at least one dose of the investigational drug (ritlecitinib, brepocitinib, or placebo). Participants who received placebo in induction period were analyzed as a single reporting group.

End point type	Secondary

End point timeframe:

From start of study intervention on Day 1 up to Week 12

End point values	Induction Period: Placebo QD	Induction period: Ritlecitinib 200 mg/50 mg QD	Induction period: Brepocitinib 60 mg QD	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	79	93	72	
Units: Participants				
Discontinuations from study due to TEAEs	0	1	0	
PD from any study intervention due to TEAEs	6	4	4	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Treatment Emergent Serious Adverse Events (TESAE) During Induction Period

End point title	Number of Participants With Treatment Emergent Serious Adverse Events (TESAE) During Induction Period

End point description:

A SAE was any untoward medical occurrence at any dose that: resulted in death; was life-threatening (immediate risk of death); required inpatient hospitalization or prolongation of existing hospitalization; resulted in persistent or significant disability/incapacity (substantial disruption of the ability to conduct normal life functions) or resulted in congenital anomaly/birth defect or was considered an important medical event. An SAE was considered as TESAE if the event started during the effective duration of treatment regardless of whether a similar event of equal or greater severity existed in the baseline period. SAS included all those participants who received at least one dose of the investigational drug (ritlecitinib, brepocitinib, or placebo). Participants who received placebo in induction period were analyzed as a single reporting group.

End point type	Secondary

End point timeframe:

From start of study intervention on Day 1 up to Week 12

End point values	Induction Period: Placebo QD	Induction period: Ritlecitinib 200 mg/50 mg QD	Induction period: Brepocitinib 60 mg QD	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	79	93	72	
Units: Participants	6	4	4	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants who Achieved Clinically Meaningful Endoscopic Improvement (CMEI) (Reduction of >=3 Points From Baseline in SES-CD Score) at Week 12: Induction Period

End point title	Percentage of Participants who Achieved Clinically Meaningful Endoscopic Improvement (CMEI) (Reduction of >=3 Points From Baseline in SES-CD Score) at Week 12: Induction Period

End point description:

CMEI was defined as reduction of >=3 points from baseline in SES-CD score as assessed by centrally read SES-CD score. Baseline: last measurement prior to first dosing on Day1. Following bowel segments were used for calculating SES-CD scores: Ileum, right C, transverse C, left C and rectum. Each segment assessed for 4 domains: presence of ulcers(U), ulcerated surface, affected surface & presence of narrowing, each scored on scale:0-3, higher scores=more severe condition. Presence of U score: 0=none,1=small U: (0.1-0.5cm),2=Large U(0.5-2cm),3=very large U(>2cm); ulcerated surface score: 0=none,1=<10%,2=10-30% & 3=>30%; affected surface score: 0=unaffected segment, 1=<50%, 2=50-75% & 3=>75%; presence of narrowing score: 0=none,1=single, can be passed, 2=multiple, can be passed & 3=cannot be passed. Total SES CD score was determined by sum of each domain score for all 5 bowel segments & ranged: 0-60, higher score=more severe disease. FAS. N=participants evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Week 12

End point values	Induction Period: Placebo QD	Induction period: Ritlecitinib 200 mg/50 mg QD	Induction period: Brepocitinib 60 mg QD	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	78	92	71	
Units: Percentage of participants				
number (confidence interval 90%)	29.5 (21.7 to 38.9)	42.4 (34.2 to 51.5)	57.7 (47.6 to 67.2)	

Statistical analyses

Statistical analysis title	Placebo QD versus Brepocitinib 60 mg QD

Statistical analysis description:

Analysis: Cochran Mantel Hansel (CMH) with test treatment & baseline disease activity/extent as factors, & baseline SES-CD score as covariate.

Comparison groups	Induction Period: Placebo QD v Induction period: Brepocitinib 60 mg QD
Number of subjects included in analysis	149
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0001
Method	Min risk weight method(Mehrotra&Railkar)
Parameter estimate	Percentage risk difference
Point estimate	29.7
Confidence interval	
level	90 %
sides	2-sided
lower limit	17.2
upper limit	42.2

Statistical analysis title	Placebo QD versus Ritlecitinib 200 mg/50 mg QD

Statistical analysis description:

Analysis: Cochran Mantel Hansel (CMH) with test treatment & baseline disease activity/extent as factors, & baseline SES-CD score as covariate.

Comparison groups	Induction Period: Placebo QD v Induction period: Ritlecitinib 200 mg/50 mg QD
Number of subjects included in analysis	170
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.039
Method	Min risk weight method(Mehrotra&Railkar)
Parameter estimate	Percentage risk difference
Point estimate	13.3
Confidence interval	
level	90 %
sides	2-sided
lower limit	1
upper limit	25.7

Secondary: Number of Participants With Serious Infections During Induction Period

End point title	Number of Participants With Serious Infections During Induction Period

End point description:

Participants were monitored for development of any infection (viral, bacterial & fungal). Serious infections were treated infections that required parenteral antimicrobial therapy and were present with positive pre-treatment culture and required hospitalization for treatment/met other criteria that required infection to be classified as SAE. An SAE was any untoward medical occurrence at any dose that: resulted in death; is life-threatening; requires inpatient hospitalization/prolongation of existing hospitalization; resulted in persistent or significant disability/incapacity/results in congenital

anomaly/birth defect. Treated infections were infections that required antimicrobial therapy by any route of administration/required any surgical intervention (e.g., incision and drainage). SAS was used for analysis. Participants who received placebo in induction period were analyzed as a single reporting group.

End point type	Secondary

End point timeframe:

From start of study intervention on Day 1 up to Week 12

End point values	Induction Period: Placebo QD	Induction period: Ritlecitinib 200 mg/50 mg QD	Induction period: Brepocitinib 60 mg QD	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	79	93	72	
Units: Participants	0	1	2	

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change From Baseline in SES-CD Score at Week 12: Induction Period

End point title	Mean Change From Baseline in SES-CD Score at Week 12: Induction Period

End point description:

Mean change from baseline in SES-CD score: Week 12 analyzed using analysis of covariance(ANCOVA)model with treatment,baseline disease activity/extent as factors, baseline SES CD score as covariate. Baseline=last measurement prior to first dosing on Day 1. Following bowel segments used for calculating SES-CD scores: Ileum,right C,transverse C,left C,rectum. Each segment assessed for 4 domains:presence of ulcers,ulcerated surface,affected surface,presence of narrowing,each score on a scale of 0-3,higher scores=more severe condition. Presence of U score:0=none,1=small U:(0.1-0.5cm),2=large U(0.5-2cm),3=very large U(>2 cm);ulcerated surface score:0=none,1=<10%,2=10-30%,3=>30%;affected surface score:0=unaffected segment,1=<50%, 2=50-75%,3=>75%;presence of narrowing score:0=none,1=single,CNB,2=multiple CNB,3=cannot be passed. Total SES CD score=sum of each domain score for all 5 bowel segments,range: 0-60, higher score =more severe disease. FAS. N= participants evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Baseline and Week 12

End point values	Induction Period: Placebo QD	Induction period: Ritlecitinib 200 mg/50 mg QD	Induction period: Brepocitinib 60 mg QD	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	68	82	63	
Units: Units on a scale				
least squares mean (confidence interval 90%)	-0.1 (-1.32 to 1.12)	-3.1 (-4.22 to -2.02)	-5.0 (-6.36 to -3.72)	

Statistical analyses

Statistical analysis title	Placebo QD versus Brepocitinib 60 mg QD
Statistical analysis description: Analysis: ANCOVA model with treatment and baseline disease activity/extent as factors, and baseline SES CD score as a covariate.	
Comparison groups	Induction Period: Placebo QD v Induction period: Brepocitinib 60 mg QD
Number of subjects included in analysis	131
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	-4.9
Confidence interval	
level	90 %
sides	2-sided
lower limit	-6.62
upper limit	-3.26

Statistical analysis title	Placebo QD versus Ritlecitinib 200 mg/50 mg QD
Statistical analysis description: Analysis: Analysis of covariance (ANCOVA) model with treatment and baseline disease activity/extent as factors, and baseline SES CD score as a covariate.	
Comparison groups	Induction Period: Placebo QD v Induction period: Ritlecitinib 200 mg/50 mg QD
Number of subjects included in analysis	150
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0007
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	-3
Confidence interval	
level	90 %
sides	2-sided
lower limit	-4.55
upper limit	-1.48

Secondary: Percentage of Participants Achieving >=25% Reduction in SES-CD from

Baseline (SES-CD 25) at Week 12: Induction Period

End point title	Percentage of Participants Achieving >=25% Reduction in SES-CD from Baseline (SES-CD 25) at Week 12: Induction Period

End point description:

SES CD25 was defined as >=25% improvement from baseline in SES CD. Baseline: last measurement prior to first dosing on Day1. Following bowel segments were used for calculating SES-CD scores: Ileum, right C, transverse C, left C and rectum. Each segment assessed for 4 domains: presence of ulcers, ulcerated surface, affected surface and presence of narrowing, each scored on a scale of 0 to 3, higher scores=more severe condition. Presence of ulcers score: 0=none, 1=small ulcer: (0.1-0.5 cm), 2=Large ulcer(0.5-2 cm), 3=very large ulcer(>2 cm); ulcerated surface score: 0=none, 1=<10%, 2=10-30% and 3=>30%; affected surface score: 0=unaffected segment, 1=<50%, 2=50-75% and 3=>75%; presence of narrowing score: 0=none,1=single, can be passed, 2=multiple, can be passed and 3=cannot be passed. Total SES CD score was determined by sum of each domain score for all 5 bowel segments and ranged from 0-60, higher score indicating more severe disease. FAS. N=participants evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Week 12

End point values	Induction Period: Placebo QD	Induction period: Ritlecitinib 200 mg/50 mg QD	Induction period: Brepocitinib 60 mg QD	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	78	92	71	
Units: Percentage of participants				
number (confidence interval 90%)	25.6 (17.7 to 34.3)	39.1 (30.6 to 47.4)	56.3 (46.2 to 66.4)	

Statistical analyses

Statistical analysis title	Placebo QD versus Ritlecitinib 200 mg/50 mg QD

Statistical analysis description:

Analysis: CMH with test treatment & baseline disease activity/extent as factors, & baseline SES-CD score as covariate.

Comparison groups	Induction Period: Placebo QD v Induction period: Ritlecitinib 200 mg/50 mg QD
Number of subjects included in analysis	170
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0279
Method	Min risk weight method(Mehrotra&Railkar)
Parameter estimate	Percentage risk difference
Point estimate	13.9
Confidence interval	
level	90 %
sides	2-sided
lower limit	2.1
upper limit	25.6

Statistical analysis title	Placebo QD versus Brepocitinib 60 mg QD
Statistical analysis description:	
Analysis: CMH with test treatment & baseline disease activity/extent as factors, & baseline SES-CD score as covariate.	
Comparison groups	Induction Period: Placebo QD v Induction period: Brepocitinib 60 mg QD
Number of subjects included in analysis	149
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001
Method	Min risk weight method(Mehrotra&Railkar)
Parameter estimate	Percentage risk difference
Point estimate	31.5
Confidence interval	
level	90 %
sides	2-sided
lower limit	19.1
upper limit	43.9

Secondary: Percentage of Participants Achieving Endoscopic Remission at Week 12: Induction Period

End point title	Percentage of Participants Achieving Endoscopic Remission at Week 12: Induction Period
End point description:	
Endoscopic remission was defined as SES-CD score of <= 2. Following bowel segments were used for calculating SES-CD scores: Ileum, right C, transverse C, left C and rectum. Each segment assessed for four domains: presence of ulcers, ulcerated surface, affected surface and presence of narrowing, each scored on a scale of 0 to 3, higher scores indicated more severe condition. Presence of ulcers score: 0=none, 1=small ulcer: (0.1-0.5 cm), 2=Large ulcer(0.5-2 cm), 3=very large ulcer(>2 cm); ulcerated surface score: 0=none, 1=<10%, 2=10-30% and 3=>30%; affected surface score: 0=unaffected segment, 1=<50%, 2=50-75% and 3=>75%; presence of narrowing score: 0=none,1=single, can be passed, 2=multiple, can be passed and 3=cannot be passed. Total SES CD score was determined by sum of each domain score for all 5 bowel segments and ranged from 0 to 60, higher score indicating more severe disease. FAS. N=participants evaluable for this endpoint.	
End point type	Secondary
End point timeframe:	
Week 12	

End point values	Induction Period: Placebo QD	Induction period: Ritlecitinib 200 mg/50 mg QD	Induction period: Brepocitinib 60 mg QD	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	78	92	71	
Units: Percentage of participants				
number (confidence interval 90%)	5.1 (2.3 to 11.2)	7.6 (4.0 to 13.2)	12.7 (7.2 to 20.8)	

Statistical analyses

Statistical analysis title	Placebo QD versus Brepocitinib 60 mg QD
Statistical analysis description:	
Analysis: CMH with test treatment & baseline disease activity/extent as factors, & baseline SES-CD score as covariate.	
Comparison groups	Induction Period: Placebo QD v Induction period: Brepocitinib 60 mg QD
Number of subjects included in analysis	149
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0449
Method	Min risk weight method(Mehrotra&Railkar)
Parameter estimate	Percentage risk difference
Point estimate	7.4
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.4
upper limit	15.2

Statistical analysis title	Placebo QD versus Ritlecitinib 200 mg/50 mg QD
Statistical analysis description:	
Analysis: CMH with test treatment & baseline disease activity/extent as factors, & baseline SES-CD score as covariate.	
Comparison groups	Induction Period: Placebo QD v Induction period: Ritlecitinib 200 mg/50 mg QD
Number of subjects included in analysis	170
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.2922
Method	Min risk weight method(Mehrotra&Railkar)
Parameter estimate	Percentage risk difference
Point estimate	2.5
Confidence interval	
level	90 %
sides	2-sided
lower limit	-4.3
upper limit	9.3

Secondary: Percentage of Participants Achieving Mucosal Healing at Week 12:

Induction Period

End point title	Percentage of Participants Achieving Mucosal Healing at Week 12: Induction Period

End point description:

Mucosal healing was defined as complete absence of ulcers. FAS included all randomized participants who received at least one dose of the randomized investigational drug (ritlecitinib, brepocitinib, or placebo). Participants who received placebo in induction period were analyzed as a single reporting group. Here, Number of Participants Analyzed signifies participants evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Week 12

End point values	Induction Period: Placebo QD	Induction period: Ritlecitinib 200 mg/50 mg QD	Induction period: Brepocitinib 60 mg QD	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	78	92	71	
Units: Percentage of participants				
number (confidence interval 90%)	5.1 (2.3 to 11.2)	10.9 (6.1 to 17.7)	16.9 (10.1 to 25.8)	

Statistical analyses

Statistical analysis title	Placebo QD versus Brepocitinib 60 mg QD

Statistical analysis description:

Analysis was performed using CMH with test treatment & baseline disease activity/extent as factors, and baseline SES CD score as a covariate.

Comparison groups	Induction Period: Placebo QD v Induction period: Brepocitinib 60 mg QD
Number of subjects included in analysis	149
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0111
Method	Percentage risk difference
Parameter estimate	Risk difference (RD)
Point estimate	11.8
Confidence interval	
level	90 %
sides	2-sided
lower limit	2.8
upper limit	20.9

Statistical analysis title	Placebo QD versus Ritlecitinib 200 mg/50 mg QD

Statistical analysis description:

Analysis was performed using CMH with test treatment & baseline disease activity/extent as factors, and baseline SES CD score as a covariate.

Comparison groups	Induction Period: Placebo QD v Induction period: Ritlecitinib 200 mg/50 mg QD
Number of subjects included in analysis	170
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0998
Method	Min risk weight method(Mehrotra&Railkar)
Parameter estimate	Percentage risk difference
Point estimate	5.8
Confidence interval	
level	90 %
sides	2-sided
lower limit	-1.6
upper limit	13.3

Secondary: Percentage of Participants Achieving SES CD 25 and SES CD 50 at Week 64 Among Participants who Achieved SES CD 25 and SES CD 50 at Week 12 (Baseline of OLE Period): OLE Period

End point title	Percentage of Participants Achieving SES CD 25 and SES CD 50 at Week 64 Among Participants who Achieved SES CD 25 and SES CD 50 at Week 12 (Baseline of OLE Period): OLE Period

End point description:

SES CD50 and SES CD25: 50% & 25% improvement from baseline, respectively. Baseline: last measurement prior to first dosing on Day1 of Week 12. Following bowel segments were used for calculating SES-CD scores: Ileum, right C, transverse C, left C and rectum. Each segment assessed for 4 domains: presence of U, ulcerated surface, affected surface & presence of narrowing, each scored on scale of 0 to 3, higher scores=more severe condition. Presence of U score: 0=none, 1=small U: (0.1-0.5 cm), 2=Large U(0.5-2 cm), 3=very large U(>2 cm); ulcerated surface score: 0=none, 1=<10%, 2=10-30% & 3=>30%; affected surface score: 0=unaffected segment, 1=<50%, 2=50-75% and 3=>75%; presence of narrowing score: 0=none,1=single, CNB, 2=multiple, CNB and 3=cannot be passed. Total SES CD score was determined by sum of each domain score for all 5 bowel segments & ranged, 0-60, higher score=more severe disease. FAS. N=participants evaluable for this endpoint & n= participants evaluable for specified rows.

End point type	Secondary

End point timeframe:

Week 64 (Week 52 of OLE period)

End point values	OLE Period: Placebo QD -> Ritlecitinib 50 mg QD	OLE Period: Ritlecitinib 200 mg/50mgQD->Ritlecitinib 50mgQD	OLE Period: Placebo QD -> Brepocitinib 30 mg QD	OLE Period: Brepocitinib 60 mg QD -> Brepocitinib 30 mg QD
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	8	31	11	38
Units: Percentage of participants				
number (confidence interval 90%)				
SES-CD 25 (n=8,31,11,38)	25.0 (6.9 to 58.2)	41.9 (26.9 to 57.9)	54.5 (30.2 to 80.0)	42.1 (28.5 to 56.7)
SES-CD 50 (n=4,22,6,22)	25.0 (2.6 to 68.0)	36.4 (19.6 to 55.6)	50.0 (20.1 to 79.9)	36.4 (19.6 to 55.6)

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Achieving CMEI at Week 64 Among Participants who Achieved CMEI response at Week 12 (Baseline of OLE Period): OLE Period

End point title	Percentage of Participants Achieving CMEI at Week 64 Among Participants who Achieved CMEI response at Week 12 (Baseline of OLE Period): OLE Period

End point description:

CMEI was defined as reduction of >=3 points from baseline as assessed by centrally read SES CD score. Baseline: last measurement prior to first dosing on Day 1 of Week 12. Following bowel segments were used for calculating SES-CD scores: Ileum, right C, transverse C, left C and rectum. Each segment assessed for 4 domains: presence of U, ulcerated surface, affected surface and presence of narrowing, each scored on scale of 0-3, higher scores=more severe condition. Presence of ulcers score: 0=none,1=small U: (0.1-0.5 cm),2=Large U(0.5-2 cm),3=very large U(>2 cm); ulcerated surface score: 0=none,1=<10%, 2=10-30% and 3=>30%; affected surface score: 0=unaffected segment, 1=<50%, 2=50-75% and 3=>75%; presence of narrowing score: 0=none,1=single, CNB, 2=multiple, CNB & 3=cannot be passed. Total SES CD score was determined by sum of each domain score for all 5 bowel segments and ranged from 0-60, higher score = more severe disease. FAS. N=participants evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Week 64 (Week 52 of OLE period)

End point values	OLE Period: Placebo QD -> Ritlecitinib 50 mg QD	OLE Period: Ritlecitinib 200 mg/50mgQD->Ritlecitinib 50mgQD	OLE Period: Placebo QD -> Brepocitinib 30 mg QD	OLE Period: Brepocitinib 60 mg QD -> Brepocitinib 30 mg QD
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	11	34	11	38
Units: Percentage of participants				
number (confidence interval 90%)	27.3 (10.5 to 56.4)	44.1 (30.7 to 59.5)	54.5 (30.2 to 80.0)	42.1 (28.5 to 56.7)

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Induction Period(P): From start of study intervention on Day1 upto Week12(for maximum duration:12weeks); OLE P: From start of study intervention in OLE period (Week12) upto 4weeks after last dose of study intervention on Week64(for max. duration:56weeks)

Adverse event reporting additional description:

Same event may appear as both non-SAE and SAE. However, what is presented are distinct events. An event may be categorized as serious in one participant and non-serious in another participants, or one participant may have experienced both serious and non-serious event during the study.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	26.1

Reporting groups

Reporting group title	Induction Period: Placebo QD

Reporting group description:

Participants received placebo matched to either PF-06651600 (ritlecitinib) or PF-06700841 (brepocitinib) once daily (QD) orally for 12 weeks in induction period.

Reporting group title	Induction period: Ritlecitinib 200 mg/50 mg QD

Reporting group description:

Participants received PF-06651600 (ritlecitinib) 200 milligrams (mg) once daily orally for 8 weeks followed by ritlecitinib 50 mg QD orally for 4 weeks in induction period.

Reporting group title	Induction period: Brepocitinib 60 mg QD

Reporting group description:

Participants received PF-06700841 (brepocitinib) 60 mg QD orally for 12 weeks in induction period.

Reporting group title	OLE Period: Brepocitinib 60 mg QD -> Brepocitinib 30 mg QD

Reporting group description:

Participants who received brepocitinib 60 mg QD in the induction period were administered brepocitinib 30 mg QD for 52 weeks in OLE period.

Reporting group title	OLE Period:Ritlecitinib 200 mg/50 mg QD->Ritlecitinib 50 mgQD

Reporting group description:

Participants who received ritlecitinib 200 mg /50 mg QD in the induction period were administered ritlecitinib 50 mg QD for 52 weeks in OLE period.

Reporting group title	OLE Period: Placebo QD -> Brepocitinib 30 mg QD

Reporting group description:

Participants who received placebo matched to brepocitinib in the induction period were administered brepocitinib 30 mg QD orally for 52 weeks in OLE period.

Reporting group title	OLE Period: Placebo QD -> Ritlecitinib 50 mg QD

Reporting group description:

Participants who received placebo matched to ritlecitinib during the induction phase were administered ritlecitinib 50 mg QD orally for 52 weeks in OLE period.

Serious adverse events	Induction Period: Placebo QD	Induction period: Ritlecitinib 200 mg/50 mg QD	Induction period: Brepocitinib 60 mg QD
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 79 (7.59%)	4 / 93 (4.30%)	4 / 72 (5.56%)
number of deaths (all causes)	0	0	0

number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Cervix carcinoma			
subjects affected / exposed	0 / 79 (0.00%)	0 / 93 (0.00%)	0 / 72 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Parathyroid tumour benign			
subjects affected / exposed	0 / 79 (0.00%)	0 / 93 (0.00%)	0 / 72 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thyroid adenoma			
subjects affected / exposed	0 / 79 (0.00%)	0 / 93 (0.00%)	0 / 72 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Humerus fracture			
subjects affected / exposed	0 / 79 (0.00%)	0 / 93 (0.00%)	0 / 72 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 79 (0.00%)	0 / 93 (0.00%)	1 / 72 (1.39%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	0 / 79 (0.00%)	0 / 93 (0.00%)	0 / 72 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Lymphopenia			
subjects affected / exposed	0 / 79 (0.00%)	0 / 93 (0.00%)	0 / 72 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Anaemia			
subjects affected / exposed	1 / 79 (1.27%)	0 / 93 (0.00%)	0 / 72 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 79 (0.00%)	1 / 93 (1.08%)	0 / 72 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 79 (0.00%)	0 / 93 (0.00%)	0 / 72 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
subjects affected / exposed	0 / 79 (0.00%)	0 / 93 (0.00%)	0 / 72 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Crohn's disease			
subjects affected / exposed	5 / 79 (6.33%)	2 / 93 (2.15%)	0 / 72 (0.00%)
occurrences causally related to treatment / all	0 / 5	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Constipation			
subjects affected / exposed	0 / 79 (0.00%)	0 / 93 (0.00%)	0 / 72 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ileus			
subjects affected / exposed	0 / 79 (0.00%)	0 / 93 (0.00%)	0 / 72 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nausea			
subjects affected / exposed	0 / 79 (0.00%)	0 / 93 (0.00%)	0 / 72 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Ileus paralytic			
subjects affected / exposed	0 / 79 (0.00%)	0 / 93 (0.00%)	0 / 72 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rectal ulcer			
subjects affected / exposed	0 / 79 (0.00%)	1 / 93 (1.08%)	0 / 72 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Small intestinal obstruction			
subjects affected / exposed	0 / 79 (0.00%)	0 / 93 (0.00%)	0 / 72 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	0 / 79 (0.00%)	0 / 93 (0.00%)	0 / 72 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subileus			
subjects affected / exposed	0 / 79 (0.00%)	0 / 93 (0.00%)	0 / 72 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Female genital tract fistula			
subjects affected / exposed	0 / 79 (0.00%)	0 / 93 (0.00%)	0 / 72 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Musculoskeletal chest pain			
subjects affected / exposed	0 / 79 (0.00%)	0 / 93 (0.00%)	1 / 72 (1.39%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Abdominal abscess			

subjects affected / exposed	0 / 79 (0.00%)	0 / 93 (0.00%)	0 / 72 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastritis viral			
subjects affected / exposed	0 / 79 (0.00%)	0 / 93 (0.00%)	0 / 72 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cytomegalovirus infection			
subjects affected / exposed	0 / 79 (0.00%)	1 / 93 (1.08%)	1 / 72 (1.39%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cytomegalovirus colitis			
subjects affected / exposed	0 / 79 (0.00%)	0 / 93 (0.00%)	1 / 72 (1.39%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Clostridium difficile colitis			
subjects affected / exposed	0 / 79 (0.00%)	0 / 93 (0.00%)	0 / 72 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bartholin's abscess			
subjects affected / exposed	0 / 79 (0.00%)	0 / 93 (0.00%)	0 / 72 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tonsillitis			
subjects affected / exposed	0 / 79 (0.00%)	0 / 93 (0.00%)	0 / 72 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Kidney infection			
subjects affected / exposed	0 / 79 (0.00%)	0 / 93 (0.00%)	0 / 72 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mesenteric abscess			

subjects affected / exposed	0 / 79 (0.00%)	0 / 93 (0.00%)	0 / 72 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	OLE Period: Brepocitinib 60 mg QD -> Brepocitinib 30 mg QD	OLE Period:Ritlecitinib 200 mg/50 mg QD->Ritlecitinib 50 mgQD	OLE Period: Placebo QD -> Brepocitinib 30 mg QD
Total subjects affected by serious adverse events			
subjects affected / exposed	16 / 64 (25.00%)	10 / 84 (11.90%)	5 / 32 (15.63%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Cervix carcinoma			
subjects affected / exposed	0 / 64 (0.00%)	0 / 84 (0.00%)	1 / 32 (3.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Parathyroid tumour benign			
subjects affected / exposed	1 / 64 (1.56%)	0 / 84 (0.00%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thyroid adenoma			
subjects affected / exposed	1 / 64 (1.56%)	0 / 84 (0.00%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Humerus fracture			
subjects affected / exposed	0 / 64 (0.00%)	0 / 84 (0.00%)	1 / 32 (3.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 64 (0.00%)	0 / 84 (0.00%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			

Acute myocardial infarction			
subjects affected / exposed	1 / 64 (1.56%)	0 / 84 (0.00%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Lymphopenia			
subjects affected / exposed	0 / 64 (0.00%)	1 / 84 (1.19%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anaemia			
subjects affected / exposed	0 / 64 (0.00%)	0 / 84 (0.00%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 64 (0.00%)	0 / 84 (0.00%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 64 (1.56%)	0 / 84 (0.00%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
subjects affected / exposed	0 / 64 (0.00%)	0 / 84 (0.00%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Crohn's disease			
subjects affected / exposed	7 / 64 (10.94%)	5 / 84 (5.95%)	3 / 32 (9.38%)
occurrences causally related to treatment / all	0 / 7	0 / 6	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Constipation			

subjects affected / exposed	1 / 64 (1.56%)	0 / 84 (0.00%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ileus			
subjects affected / exposed	1 / 64 (1.56%)	1 / 84 (1.19%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nausea			
subjects affected / exposed	0 / 64 (0.00%)	1 / 84 (1.19%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ileus paralytic			
subjects affected / exposed	0 / 64 (0.00%)	1 / 84 (1.19%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rectal ulcer			
subjects affected / exposed	0 / 64 (0.00%)	0 / 84 (0.00%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Small intestinal obstruction			
subjects affected / exposed	1 / 64 (1.56%)	1 / 84 (1.19%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	0 / 64 (0.00%)	1 / 84 (1.19%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subileus			
subjects affected / exposed	1 / 64 (1.56%)	0 / 84 (0.00%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Female genital tract fistula			

subjects affected / exposed	0 / 64 (0.00%)	1 / 84 (1.19%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Musculoskeletal chest pain			
subjects affected / exposed	0 / 64 (0.00%)	0 / 84 (0.00%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Abdominal abscess			
subjects affected / exposed	0 / 64 (0.00%)	1 / 84 (1.19%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastritis viral			
subjects affected / exposed	1 / 64 (1.56%)	0 / 84 (0.00%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cytomegalovirus infection			
subjects affected / exposed	0 / 64 (0.00%)	0 / 84 (0.00%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cytomegalovirus colitis			
subjects affected / exposed	0 / 64 (0.00%)	0 / 84 (0.00%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Clostridium difficile colitis			
subjects affected / exposed	0 / 64 (0.00%)	0 / 84 (0.00%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bartholin's abscess			
subjects affected / exposed	0 / 64 (0.00%)	1 / 84 (1.19%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Tonsillitis			
subjects affected / exposed	0 / 64 (0.00%)	1 / 84 (1.19%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Kidney infection			
subjects affected / exposed	1 / 64 (1.56%)	0 / 84 (0.00%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mesenteric abscess			
subjects affected / exposed	0 / 64 (0.00%)	0 / 84 (0.00%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	OLE Period: Placebo QD -> Ritlecitinib 50 mg QD		
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 36 (16.67%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Cervix carcinoma			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Parathyroid tumour benign			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Thyroid adenoma			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Humerus fracture			

subjects affected / exposed	0 / 36 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Lymphopenia			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Anaemia			
subjects affected / exposed	1 / 36 (2.78%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 36 (2.78%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Diarrhoea			

subjects affected / exposed	1 / 36 (2.78%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Crohn's disease				
subjects affected / exposed	3 / 36 (8.33%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Constipation				
subjects affected / exposed	0 / 36 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Ileus				
subjects affected / exposed	0 / 36 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Nausea				
subjects affected / exposed	0 / 36 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Ileus paralytic				
subjects affected / exposed	0 / 36 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Rectal ulcer				
subjects affected / exposed	0 / 36 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Small intestinal obstruction				
subjects affected / exposed	0 / 36 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Vomiting				

subjects affected / exposed	0 / 36 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Subileus				
subjects affected / exposed	0 / 36 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Reproductive system and breast disorders				
Female genital tract fistula				
subjects affected / exposed	0 / 36 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Musculoskeletal and connective tissue disorders				
Musculoskeletal chest pain				
subjects affected / exposed	0 / 36 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Infections and infestations				
Abdominal abscess				
subjects affected / exposed	0 / 36 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastritis viral				
subjects affected / exposed	0 / 36 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cytomegalovirus infection				
subjects affected / exposed	0 / 36 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cytomegalovirus colitis				

subjects affected / exposed	0 / 36 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Clostridium difficile colitis			
subjects affected / exposed	1 / 36 (2.78%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Bartholin's abscess			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Tonsillitis			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Kidney infection			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Mesenteric abscess			
subjects affected / exposed	1 / 36 (2.78%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Induction Period: Placebo QD	Induction period: Ritlecitinib 200 mg/50 mg QD	Induction period: Brepocitinib 60 mg QD
Total subjects affected by non-serious adverse events			
subjects affected / exposed	20 / 79 (25.32%)	20 / 93 (21.51%)	17 / 72 (23.61%)
Investigations			
SARS-CoV-2 test positive			
subjects affected / exposed	3 / 79 (3.80%)	6 / 93 (6.45%)	1 / 72 (1.39%)
occurrences (all)	3	6	1

Blood creatinine increased			
subjects affected / exposed	0 / 79 (0.00%)	0 / 93 (0.00%)	0 / 72 (0.00%)
occurrences (all)	0	0	0
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 79 (0.00%)	0 / 93 (0.00%)	0 / 72 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Hypoaesthesia			
subjects affected / exposed	0 / 79 (0.00%)	0 / 93 (0.00%)	0 / 72 (0.00%)
occurrences (all)	0	0	0
Headache			
subjects affected / exposed	4 / 79 (5.06%)	3 / 93 (3.23%)	5 / 72 (6.94%)
occurrences (all)	4	5	5
Blood and lymphatic system disorders			
Lymphopenia			
subjects affected / exposed	1 / 79 (1.27%)	3 / 93 (3.23%)	4 / 72 (5.56%)
occurrences (all)	1	5	7
Anaemia			
subjects affected / exposed	0 / 79 (0.00%)	0 / 93 (0.00%)	0 / 72 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 79 (0.00%)	0 / 93 (0.00%)	0 / 72 (0.00%)
occurrences (all)	0	0	0
Peripheral swelling			
subjects affected / exposed	0 / 79 (0.00%)	0 / 93 (0.00%)	0 / 72 (0.00%)
occurrences (all)	0	0	0
Fatigue			
subjects affected / exposed	0 / 79 (0.00%)	0 / 93 (0.00%)	0 / 72 (0.00%)
occurrences (all)	0	0	0
Ear and labyrinth disorders			
Tinnitus			
subjects affected / exposed	0 / 79 (0.00%)	0 / 93 (0.00%)	0 / 72 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			

Abdominal pain			
subjects affected / exposed	1 / 79 (1.27%)	2 / 93 (2.15%)	4 / 72 (5.56%)
occurrences (all)	1	2	4
Abdominal pain lower			
subjects affected / exposed	0 / 79 (0.00%)	0 / 93 (0.00%)	0 / 72 (0.00%)
occurrences (all)	0	0	0
Aphthous ulcer			
subjects affected / exposed	0 / 79 (0.00%)	0 / 93 (0.00%)	0 / 72 (0.00%)
occurrences (all)	0	0	0
Crohn's disease			
subjects affected / exposed	4 / 79 (5.06%)	2 / 93 (2.15%)	2 / 72 (2.78%)
occurrences (all)	4	2	2
Diarrhoea			
subjects affected / exposed	0 / 79 (0.00%)	0 / 93 (0.00%)	0 / 72 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain			
subjects affected / exposed	0 / 79 (0.00%)	0 / 93 (0.00%)	0 / 72 (0.00%)
occurrences (all)	0	0	0
Cough			
subjects affected / exposed	0 / 79 (0.00%)	0 / 93 (0.00%)	0 / 72 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	0 / 79 (0.00%)	1 / 93 (1.08%)	4 / 72 (5.56%)
occurrences (all)	0	1	4
Rash			
subjects affected / exposed	0 / 79 (0.00%)	0 / 93 (0.00%)	0 / 72 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Insomnia			
subjects affected / exposed	0 / 79 (0.00%)	0 / 93 (0.00%)	0 / 72 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Myalgia			

subjects affected / exposed	0 / 79 (0.00%)	0 / 93 (0.00%)	0 / 72 (0.00%)
occurrences (all)	0	0	0
Muscle spasms			
subjects affected / exposed	0 / 79 (0.00%)	0 / 93 (0.00%)	0 / 72 (0.00%)
occurrences (all)	0	0	0
Arthralgia			
subjects affected / exposed	4 / 79 (5.06%)	3 / 93 (3.23%)	2 / 72 (2.78%)
occurrences (all)	4	3	2
Infections and infestations			
Influenza			
subjects affected / exposed	0 / 79 (0.00%)	0 / 93 (0.00%)	0 / 72 (0.00%)
occurrences (all)	0	0	0
Gastroenteritis			
subjects affected / exposed	0 / 79 (0.00%)	0 / 93 (0.00%)	0 / 72 (0.00%)
occurrences (all)	0	0	0
Folliculitis			
subjects affected / exposed	0 / 79 (0.00%)	0 / 93 (0.00%)	0 / 72 (0.00%)
occurrences (all)	0	0	0
Urinary tract infection			
subjects affected / exposed	0 / 79 (0.00%)	0 / 93 (0.00%)	0 / 72 (0.00%)
occurrences (all)	0	0	0
Upper respiratory tract infection			
subjects affected / exposed	4 / 79 (5.06%)	2 / 93 (2.15%)	0 / 72 (0.00%)
occurrences (all)	6	2	0
Respiratory tract infection			
subjects affected / exposed	0 / 79 (0.00%)	0 / 93 (0.00%)	0 / 72 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	OLE Period: Brepocitinib 60 mg QD -> Brepocitinib 30 mg QD	OLE Period:Ritlecitinib 200 mg/50 mg QD->Ritlecitinib 50 mgQD	OLE Period: Placebo QD -> Brepocitinib 30 mg QD
Total subjects affected by non-serious adverse events			
subjects affected / exposed	31 / 64 (48.44%)	34 / 84 (40.48%)	19 / 32 (59.38%)
Investigations			
SARS-CoV-2 test positive			
subjects affected / exposed	8 / 64 (12.50%)	4 / 84 (4.76%)	4 / 32 (12.50%)
occurrences (all)	8	4	5

Blood creatinine increased			
subjects affected / exposed	0 / 64 (0.00%)	0 / 84 (0.00%)	2 / 32 (6.25%)
occurrences (all)	0	0	2
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 64 (1.56%)	0 / 84 (0.00%)	0 / 32 (0.00%)
occurrences (all)	1	0	0
Nervous system disorders			
Hypoaesthesia			
subjects affected / exposed	0 / 64 (0.00%)	0 / 84 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Headache			
subjects affected / exposed	2 / 64 (3.13%)	1 / 84 (1.19%)	2 / 32 (6.25%)
occurrences (all)	2	6	2
Blood and lymphatic system disorders			
Lymphopenia			
subjects affected / exposed	0 / 64 (0.00%)	0 / 84 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Anaemia			
subjects affected / exposed	2 / 64 (3.13%)	0 / 84 (0.00%)	2 / 32 (6.25%)
occurrences (all)	2	0	2
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	3 / 64 (4.69%)	2 / 84 (2.38%)	1 / 32 (3.13%)
occurrences (all)	3	2	3
Peripheral swelling			
subjects affected / exposed	0 / 64 (0.00%)	0 / 84 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Fatigue			
subjects affected / exposed	0 / 64 (0.00%)	2 / 84 (2.38%)	1 / 32 (3.13%)
occurrences (all)	0	2	1
Ear and labyrinth disorders			
Tinnitus			
subjects affected / exposed	0 / 64 (0.00%)	1 / 84 (1.19%)	0 / 32 (0.00%)
occurrences (all)	0	1	0
Gastrointestinal disorders			

Abdominal pain			
subjects affected / exposed	6 / 64 (9.38%)	5 / 84 (5.95%)	4 / 32 (12.50%)
occurrences (all)	6	6	4
Abdominal pain lower			
subjects affected / exposed	0 / 64 (0.00%)	0 / 84 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Aphthous ulcer			
subjects affected / exposed	1 / 64 (1.56%)	0 / 84 (0.00%)	0 / 32 (0.00%)
occurrences (all)	1	0	0
Crohn's disease			
subjects affected / exposed	4 / 64 (6.25%)	9 / 84 (10.71%)	2 / 32 (6.25%)
occurrences (all)	4	11	2
Diarrhoea			
subjects affected / exposed	0 / 64 (0.00%)	3 / 84 (3.57%)	0 / 32 (0.00%)
occurrences (all)	0	3	0
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain			
subjects affected / exposed	0 / 64 (0.00%)	0 / 84 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Cough			
subjects affected / exposed	2 / 64 (3.13%)	1 / 84 (1.19%)	0 / 32 (0.00%)
occurrences (all)	2	1	0
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	2 / 64 (3.13%)	1 / 84 (1.19%)	1 / 32 (3.13%)
occurrences (all)	3	1	1
Rash			
subjects affected / exposed	3 / 64 (4.69%)	0 / 84 (0.00%)	2 / 32 (6.25%)
occurrences (all)	4	0	2
Psychiatric disorders			
Insomnia			
subjects affected / exposed	0 / 64 (0.00%)	0 / 84 (0.00%)	1 / 32 (3.13%)
occurrences (all)	0	0	1
Musculoskeletal and connective tissue disorders			
Myalgia			

subjects affected / exposed	0 / 64 (0.00%)	0 / 84 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Muscle spasms			
subjects affected / exposed	0 / 64 (0.00%)	2 / 84 (2.38%)	0 / 32 (0.00%)
occurrences (all)	0	2	0
Arthralgia			
subjects affected / exposed	4 / 64 (6.25%)	1 / 84 (1.19%)	1 / 32 (3.13%)
occurrences (all)	4	1	1
Infections and infestations			
Influenza			
subjects affected / exposed	0 / 64 (0.00%)	2 / 84 (2.38%)	0 / 32 (0.00%)
occurrences (all)	0	2	0
Gastroenteritis			
subjects affected / exposed	1 / 64 (1.56%)	0 / 84 (0.00%)	0 / 32 (0.00%)
occurrences (all)	1	0	0
Folliculitis			
subjects affected / exposed	1 / 64 (1.56%)	0 / 84 (0.00%)	2 / 32 (6.25%)
occurrences (all)	1	0	2
Urinary tract infection			
subjects affected / exposed	0 / 64 (0.00%)	1 / 84 (1.19%)	1 / 32 (3.13%)
occurrences (all)	0	1	1
Upper respiratory tract infection			
subjects affected / exposed	2 / 64 (3.13%)	3 / 84 (3.57%)	2 / 32 (6.25%)
occurrences (all)	2	4	2
Respiratory tract infection			
subjects affected / exposed	0 / 64 (0.00%)	3 / 84 (3.57%)	0 / 32 (0.00%)
occurrences (all)	0	3	0

Non-serious adverse events	OLE Period: Placebo QD -> Ritlecitinib 50 mg QD		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	29 / 36 (80.56%)		
Investigations			
SARS-CoV-2 test positive			
subjects affected / exposed	6 / 36 (16.67%)		
occurrences (all)	6		
Blood creatinine increased			

subjects affected / exposed occurrences (all)	0 / 36 (0.00%) 0		
Vascular disorders Hypertension subjects affected / exposed occurrences (all)	 2 / 36 (5.56%) 2		
Nervous system disorders Hypoaesthesia subjects affected / exposed occurrences (all) Headache subjects affected / exposed occurrences (all)	 2 / 36 (5.56%) 2 1 / 36 (2.78%) 1		
Blood and lymphatic system disorders Lymphopenia subjects affected / exposed occurrences (all) Anaemia subjects affected / exposed occurrences (all)	 0 / 36 (0.00%) 0 3 / 36 (8.33%) 3		
General disorders and administration site conditions Pyrexia subjects affected / exposed occurrences (all) Peripheral swelling subjects affected / exposed occurrences (all) Fatigue subjects affected / exposed occurrences (all)	 3 / 36 (8.33%) 3 2 / 36 (5.56%) 2 3 / 36 (8.33%) 4		
Ear and labyrinth disorders Tinnitus subjects affected / exposed occurrences (all)	 3 / 36 (8.33%) 3		
Gastrointestinal disorders			

Abdominal pain subjects affected / exposed occurrences (all)	4 / 36 (11.11%) 4		
Abdominal pain lower subjects affected / exposed occurrences (all)	2 / 36 (5.56%) 2		
Aphthous ulcer subjects affected / exposed occurrences (all)	2 / 36 (5.56%) 2		
Crohn's disease subjects affected / exposed occurrences (all)	4 / 36 (11.11%) 4		
Diarrhoea subjects affected / exposed occurrences (all)	2 / 36 (5.56%) 2		
Respiratory, thoracic and mediastinal disorders Oropharyngeal pain subjects affected / exposed occurrences (all)	3 / 36 (8.33%) 3		
Cough subjects affected / exposed occurrences (all)	2 / 36 (5.56%) 2		
Skin and subcutaneous tissue disorders Acne subjects affected / exposed occurrences (all)	4 / 36 (11.11%) 4		
Rash subjects affected / exposed occurrences (all)	1 / 36 (2.78%) 1		
Psychiatric disorders Insomnia subjects affected / exposed occurrences (all)	4 / 36 (11.11%) 4		
Musculoskeletal and connective tissue disorders Myalgia			

subjects affected / exposed	3 / 36 (8.33%)		
occurrences (all)	3		
Muscle spasms			
subjects affected / exposed	2 / 36 (5.56%)		
occurrences (all)	2		
Arthralgia			
subjects affected / exposed	2 / 36 (5.56%)		
occurrences (all)	3		
Infections and infestations			
Influenza			
subjects affected / exposed	3 / 36 (8.33%)		
occurrences (all)	3		
Gastroenteritis			
subjects affected / exposed	3 / 36 (8.33%)		
occurrences (all)	3		
Folliculitis			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences (all)	0		
Urinary tract infection			
subjects affected / exposed	2 / 36 (5.56%)		
occurrences (all)	2		
Upper respiratory tract infection			
subjects affected / exposed	1 / 36 (2.78%)		
occurrences (all)	1		
Respiratory tract infection			
subjects affected / exposed	2 / 36 (5.56%)		
occurrences (all)	2		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
27 November 2017	Amendment 1: (The OLE SOA was updated to add ECG monitoring at Weeks 32, 48 and 64. This update is to ensure subject safety during the study. The induction SOA is being revised to clarify that PGIS will be collected continuously for 12 weeks throughout the induction phase (including at Week 2). The induction SOA, footnote j, is being revised to clarify that fasting lipid profile will be assessed from Baseline visit. The induction and OLE SOAs are being updated to add: Review and report to the Sponsor of any incidental endoscopic findings reported by Robarts that are deemed clinically significant by the PI/sites.
15 March 2018	Amendment 2: To address the VHP (VoluntaryHarmonization Procedure) request, theprotocol summary, Section 2.2, andSection 9.5.2 are updated to add a secondaryobjective and endpoint to assess theproportion of patients who maintain response after the induction period. To address the VHP request, Section 4.1 isupdated to clarify that inclusion criterion number 5 should be met only after the usual clinical practice in each center has been fulfilled, which may involve administration of more than one line of previous treatment. To address the VHP request, Section 4.2 is updated to exclude subjects with heart failure (NYHA III, NYHA IV). To address the VHP request, Section 4.4.1 is updated to add that male subject must refrain from donating sperm during the study and for 90 days after the last dose of investigational product. To address the VHP request, Section 5.9.2 is updated to add that subjects requiring a second step up in corticosteroid usage will be required to discontinue the study.
24 August 2018	Amendment 3: Section 4.2, exclusion criteria 11 is being updated to clarify that subjects with adenomatous polyps finding at screening will be eligible if the polyps have been completely removed and subjects are free of polyps at baseline. Section 4.2, Exclusion criterion 14 and Section 7.1.6 Screening for Clostridium Difficile are revised to permit treatment and re-testing or re-screening of subjects and to allow subjects with appropriately resolved infection to enter the study. Section 4.2, Exclusion criterion 16 is revised to allow subjects adequately treated for latent and/or active tuberculosis infection to enter the study. Section 4.2, Exclusion criterion 33 is revised to correct that "ALT or AST ≥1.5 times > ULN" not "ALT and AST ≥1.5 times ULN "will be exclusionary. Section 4.4.1 and Exclusion criterion 27 are being updated to align with the Clinical Trials Facilitation Group (CTFG) European guidance of the Heads of Medicines Agencies (HMA) and TransCelerate initiative across Pharma. Section 5.9.3, is updated to clarify the timeframe in which the listed medications are not permitted for those for which the information is not already stated.
27 July 2021	Amendment 5: Sections Summary, 1, 1.3.2, 1.4.2, 1.5.3, 1.6, 1.6.2.2, 2.1, 3.1, 4.3, 5.4.1: updated to eliminate the PF-06700841 (brepocitinib) active and corresponding (brepocitinib) placebo arms.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported