



Clinical trial results:

A Multicenter, Randomized, Double-Blind, Placebo-Controlled Study of Upadacitinib (ABT-494) for the Induction of Symptomatic and Endoscopic Remission in Subjects with Moderately to Severely Active Crohn's Disease who have Inadequately Responded to or are Intolerant to Immunomodulators or Anti-TNF Therapy

Summary

EudraCT number	2014-003240-12
Trial protocol	BE HU DE ES DK NO SK NL CZ PL IT
Global end of trial date	03 August 2017

Results information

Result version number	v1 (current)
This version publication date	11 August 2018
First version publication date	11 August 2018

Trial information

Trial identification

Sponsor protocol code	M13-740
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02365649
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	AbbVie Deutschland GmbH & Co.KG
Sponsor organisation address	AbbVie House, Vanwall Business Park, Vanwall Road, Maidenhead, Berkshire, United Kingdom, SL6-4UB
Public contact	Fabio Cataldi, AbbVie, fabio.cataldi@abbvie.com
Scientific contact	Fabio Cataldi, AbbVie, fabio.cataldi@abbvie.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	03 August 2017
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	03 August 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The objectives of this study are to determine the efficacy and safety of multiple doses of ABT-494 (upadacitinib) versus placebo and to assess the pharmacokinetics (PK) of ABT-494 following oral administration in subjects with moderately to severely active Crohn's Disease with a history of inadequate response to or intolerance to immunomodulators or anti-TNF therapy.

Protection of trial subjects:

Participant and/or legal guardian read and understood the information provided about the study and gave written permission.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	17 March 2015
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: 2
Country: Number of subjects enrolled	Canada: 26
Country: Number of subjects enrolled	Israel: 4
Country: Number of subjects enrolled	New Zealand: 1
Country: Number of subjects enrolled	United States: 104
Country: Number of subjects enrolled	Netherlands: 9
Country: Number of subjects enrolled	Norway: 2
Country: Number of subjects enrolled	Poland: 7
Country: Number of subjects enrolled	Romania: 5
Country: Number of subjects enrolled	Slovakia: 5
Country: Number of subjects enrolled	Spain: 4
Country: Number of subjects enrolled	United Kingdom: 6
Country: Number of subjects enrolled	Belgium: 9
Country: Number of subjects enrolled	Czech Republic: 3
Country: Number of subjects enrolled	Denmark: 4
Country: Number of subjects enrolled	France: 7
Country: Number of subjects enrolled	Germany: 17
Country: Number of subjects enrolled	Hungary: 2
Country: Number of subjects enrolled	Italy: 3

Worldwide total number of subjects	220
EEA total number of subjects	83

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)	211
From 65 to 84 years	9
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

This multicenter, randomized Phase 2 study included an up to 35-day Screening Period.

Period 1

Period 1 title	Double-Blind Induction (Weeks 1-16)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Investigator, Subject

Blinding implementation details:

The Investigator, study site personnel, the subject and all AbbVie personnel with direct oversight of the conduct and management of the trial (with the exception of AbbVie Drug Supply Management Team) remained blinded to each subject's treatment throughout the course of the study.

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo Twice Daily (BID)

Arm description:

Placebo BID during the 16-week double-blind Induction Phase.

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

Dosage and administration details:

Study drug was taken orally. Subjects were instructed to take 2 daily doses of 2 capsules (4 capsules daily) at approximately the same time each day.

Arm title	Upadacitinib 3 mg BID
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Arm description:

Upadacitinib 3 mg BID during the 16-week double-blind Induction Phase.

Arm type	Experimental
Investigational medicinal product name	upadacitinib 3 mg
Investigational medicinal product code	ABT-494
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Study drug was taken orally. Subjects were instructed to take 2 daily doses of 2 capsules (4 capsules daily) at approximately the same time each day. Placebo was used to maintain the blind.

Investigational medicinal product name	placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Study drug was taken orally. Subjects were instructed to take 2 daily doses of 2 capsules (4 capsules

daily) at approximately the same time each day. Placebo for 3 mg or 12 mg upadacitinib was used in the upadacitinib 3 mg BID, 12 mg BID and 24 mg once daily (QD) arms to maintain the blind.

Arm title	Upadacitinib 6 mg BID
Arm description: Upadacitinib 6 mg BID during the 16-week double-blind Induction Phase.	
Arm type	Experimental
Investigational medicinal product name	upadacitinib 3 mg
Investigational medicinal product code	ABT-494
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use
Dosage and administration details: Study drug was taken orally. Subjects were instructed to take 2 daily doses of 2 capsules (4 capsules daily) at approximately the same time each day.	
Arm title	Upadacitinib 12 mg BID
Arm description: Upadacitinib 12 mg BID during the 16-week double-blind Induction Phase.	
Arm type	Experimental
Investigational medicinal product name	Upadacitinib 12 mg
Investigational medicinal product code	ABT-494
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use
Dosage and administration details: Study drug was taken orally. Subjects were instructed to take 2 daily doses of 2 capsules (4 capsules daily) at approximately the same time each day. Placebo was used to maintain the blind.	
Investigational medicinal product name	placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use
Dosage and administration details: Study drug was taken orally. Subjects were instructed to take 2 daily doses of 2 capsules (4 capsules daily) at approximately the same time each day. Placebo for 3 mg or 12 mg upadacitinib was used in the upadacitinib 3 mg BID, 12 mg BID and 24 mg QD arms to maintain the blind.	
Arm title	Upadacitinib 24 mg BID
Arm description: Upadacitinib 24 mg BID during the 16-week double-blind Induction Phase.	
Arm type	Experimental
Investigational medicinal product name	Upadacitinib 12 mg
Investigational medicinal product code	ABT-494
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use
Dosage and administration details: Study drug was taken orally. Subjects were instructed to take 2 daily doses of 2 capsules (4 capsules daily) at approximately the same time each day.	
Arm title	Upadacitinib 24 mg QD

Arm description:

Upadacitinib 24 mg once daily (consisting of two 12 mg immediate release [IR] doses) during the 16-week double-blind Induction Phase.

Arm type	Experimental
Investigational medicinal product name	Upadacitinib 12 mg
Investigational medicinal product code	ABT-494
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Study drug was taken orally. Subjects were instructed to take 2 daily doses of 2 capsules (4 capsules daily) at approximately the same time each day.

Investigational medicinal product name	placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Study drug was taken orally. Subjects were instructed to take 2 daily doses of 2 capsules (4 capsules daily) at approximately the same time each day. Placebo for 3 mg or 12 mg upadacitinib was used in the upadacitinib 3 mg BID, 12 mg BID, and 24 mg QD arms to maintain the blind.

Number of subjects in period 1	Placebo Twice Daily (BID)	Upadacitinib 3 mg BID	Upadacitinib 6 mg BID
Started	37	39	37
Completed	27	34	33
Not completed	10	5	4
Consent withdrawn by subject	2	-	1
Requires alternative therapy	-	-	-
Subject non-compliance	1	-	-
Not specified	1	-	1
Adverse event	3	4	-
Lost to follow-up	-	-	1
Lack of efficacy	3	1	1

Number of subjects in period 1	Upadacitinib 12 mg BID	Upadacitinib 24 mg BID	Upadacitinib 24 mg QD
Started	36	36	35
Completed	27	29	30
Not completed	9	7	5
Consent withdrawn by subject	-	2	-
Requires alternative therapy	1	-	-
Subject non-compliance	-	1	1
Not specified	-	1	1
Adverse event	7	1	2
Lost to follow-up	-	-	-

Lack of efficacy	1	2	1
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Period 2

Period 2 title	Double-Blind Extension (Weeks 16-52)
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Blinding implementation details:

The Investigator, study site personnel, the subject and all AbbVie personnel with direct oversight of the conduct and management of the trial (with the exception of AbbVie Drug Supply Management Team) remained blinded to each subject's treatment throughout the course of the study.

Arms

Are arms mutually exclusive?	Yes
Arm title	Upadacitinib 3 mg BID

Arm description:

Upadacitinib 3 mg BID during the 36-week double-blind Extension Phase.

Arm type	Experimental
Investigational medicinal product name	upadacitinib 3 mg
Investigational medicinal product code	ABT-494
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Study drug was taken orally. Subjects were instructed to take 2 daily doses of 2 capsules (4 capsules daily) at approximately the same time each day. Placebo was used to maintain the blind.

Investigational medicinal product name	placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Study drug was taken orally. Subjects were instructed to take 2 daily doses of 2 capsules (4 capsules daily) at approximately the same time each day. Placebo for 3 mg or 12 mg upadacitinib was used in the upadacitinib 3 mg BID, 12 mg BID and 24 mg QD arms to maintain the blind.

Arm title	Upadacitinib 6 mg BID
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Arm description:

Upadacitinib 6 mg BID during the 36-week double-blind Extension Phase.

Arm type	Experimental
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Investigational medicinal product name	upadacitinib 3 mg
Investigational medicinal product code	ABT-494
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Study drug was taken orally. Subjects were instructed to take 2 daily doses of 2 capsules (4 capsules daily) at approximately the same time each day.

Arm title	Upadacitinib 12 mg BID
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Arm description:

Upadacitinib 12 mg BID during the 36-week double-blind Extension Phase.

Arm type	Experimental
Investigational medicinal product name	Upadacitinib 12 mg
Investigational medicinal product code	ABT-494
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Study drug was taken orally. Subjects were instructed to take 2 daily doses of 2 capsules (4 capsules daily) at approximately the same time each day. Placebo was used to maintain the blind.

Investigational medicinal product name	placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Study drug was taken orally twice a day for 16 weeks beginning on Baseline. Subjects were instructed to take 2 daily doses of 2 capsules (4 capsules daily) at approximately the same time each day. Placebo for 3 mg or 12 mg upadacitinib was used in the upadacitinib 3 mg BID, 12 mg BID and 24 mg QD arms to maintain the blind.

Arm title	Upadacitinib 24 mg QD
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Arm description:

Upadacitinib 24 mg QD (consisting of two 12 mg IR doses) during the 36-week double-blind Extension Phase.

Arm type	Experimental
Investigational medicinal product name	Upadacitinib 12 mg
Investigational medicinal product code	ABT-494
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Study drug was taken orally. Subjects were instructed to take 2 daily doses of 2 capsules (4 capsules daily) at approximately the same time each day. Placebo was used to maintain the blind.

Investigational medicinal product name	placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Study drug was taken orally. Subjects were instructed to take 2 daily doses of 2 capsules (4 capsules daily) at approximately the same time each day. Placebo for 3 mg or 12 mg upadacitinib was used in the upadacitinib 3 mg BID, 12 mg BID, and 24 mg QD arms to maintain the blind.

Number of subjects in period 2	Upadacitinib 3 mg BID	Upadacitinib 6 mg BID	Upadacitinib 12 mg BID
Started	61	23	59
Completed	43	21	43
Not completed	18	2	16
Consent withdrawn by subject	1	-	2
Requires alternative therapy	2	-	-
Subject non-compliance	2	-	2
Adverse event	6	-	4
Lack of efficacy	7	2	8

Number of subjects in period 2	Upadacitinib 24 mg QD
Started	37
Completed	22
Not completed	15
Consent withdrawn by subject	1
Requires alternative therapy	-
Subject non-compliance	-
Adverse event	4
Lack of efficacy	10

Baseline characteristics

Reporting groups

Reporting group title	Placebo Twice Daily (BID)
Reporting group description: Placebo BID during the 16-week double-blind Induction Phase.	
Reporting group title	Upadacitinib 3 mg BID
Reporting group description: Upadacitinib 3 mg BID during the 16-week double-blind Induction Phase.	
Reporting group title	Upadacitinib 6 mg BID
Reporting group description: Upadacitinib 6 mg BID during the 16-week double-blind Induction Phase.	
Reporting group title	Upadacitinib 12 mg BID
Reporting group description: Upadacitinib 12 mg BID during the 16-week double-blind Induction Phase.	
Reporting group title	Upadacitinib 24 mg BID
Reporting group description: Upadacitinib 24 mg BID during the 16-week double-blind Induction Phase.	
Reporting group title	Upadacitinib 24 mg QD
Reporting group description: Upadacitinib 24 mg once daily (consisting of two 12 mg immediate release [IR] doses) during the 16-week double-blind Induction Phase.	

Reporting group values	Placebo Twice Daily (BID)	Upadacitinib 3 mg BID	Upadacitinib 6 mg BID
Number of subjects	37	39	37
Age categorical			
Units: Subjects			

Age continuous			
Units: years			
arithmetic mean	40.5	39.7	40.5
standard deviation	± 12.14	± 14.03	± 13.41
Gender categorical			
Units: Subjects			
Female	24	19	21
Male	13	20	16
High-sensitivity C-reactive protein (hsCRP)			
Units: mg/L			
arithmetic mean	20.8	23.6	17.9
standard deviation	± 34.29	± 51.43	± 17.92
Fecal Calprotectin			
n=31, 33, 36, 33, 29, 31, respectively, for placebo, upadacitinib 3 mg BID, 6 mg BID, 12 mg BID, 24 mg BID, 24 mg QD.			
Units: mcg/g			
arithmetic mean	1734.7	1925.9	2128.5
standard deviation	± 2444.07	± 2804.07	± 1978.73
Inflammatory Bowel Disease Questionnaire (IBDQ)			
The IBDQ is a disease-specific instrument composed of 32 Likert-scaled items. The total score ranges			

from 32 to 224 using the 7-point response options, with higher scores indicating better health-related quality of life. The IBDQ scale contains 4 component subscales: bowel symptoms, systemic symptoms, emotional function, and social function. Each subscale can be computed with total scores ranging from 10 to 70, 5 to 35, 12 to 84, and 5 to 35, respectively. n=37, 38, 36, 35, 36, 34, respectively, for placebo, upadacitinib 3 mg BID, 6 mg BID, 12 mg BID, 24 mg BID, 24 mg QD.

Units: units on a scale			
arithmetic mean	118.0	115.2	113.7
standard deviation	± 28.45	± 27.48	± 25.86

Reporting group values	Upadacitinib 12 mg BID	Upadacitinib 24 mg BID	Upadacitinib 24 mg QD
Number of subjects	36	36	35
Age categorical			
Units: Subjects			

Age continuous			
Units: years			
arithmetic mean	40.8	42.5	40.2
standard deviation	± 15.18	± 10.02	± 12.60
Gender categorical			
Units: Subjects			
Female	17	25	19
Male	19	11	16
High-sensitivity C-reactive protein (hsCRP)			
Units: mg/L			
arithmetic mean	26.9	17.1	17.1
standard deviation	± 28.86	± 26.49	± 20.83
Fecal Calprotectin			

n=31, 33, 36, 33, 29, 31, respectively, for placebo, upadacitinib 3 mg BID, 6 mg BID, 12 mg BID, 24 mg BID, 24 mg QD.

Units: mcg/g			
arithmetic mean	2067.9	2074.8	1808.7
standard deviation	± 2250.97	± 2324.15	± 2548.11
Inflammatory Bowel Disease Questionnaire (IBDQ)			

The IBDQ is a disease-specific instrument composed of 32 Likert-scaled items. The total score ranges from 32 to 224 using the 7-point response options, with higher scores indicating better health-related quality of life. The IBDQ scale contains 4 component subscales: bowel symptoms, systemic symptoms, emotional function, and social function. Each subscale can be computed with total scores ranging from 10 to 70, 5 to 35, 12 to 84, and 5 to 35, respectively. n=37, 38, 36, 35, 36, 34, respectively, for placebo, upadacitinib 3 mg BID, 6 mg BID, 12 mg BID, 24 mg BID, 24 mg QD.

Units: units on a scale			
arithmetic mean	115.2	113.8	120.7
standard deviation	± 36.05	± 35.97	± 36.25

Reporting group values	Total		
Number of subjects	220		
Age categorical			
Units: Subjects			

Age continuous			
Units: years			
arithmetic mean			
standard deviation	-		

Gender categorical			
Units: Subjects			
Female	125		
Male	95		
High-sensitivity C-reactive protein (hsCRP)			
Units: mg/L			
arithmetic mean			
standard deviation	-		
Fecal Calprotectin			
n=31, 33, 36, 33, 29, 31, respectively, for placebo, upadacitinib 3 mg BID, 6 mg BID, 12 mg BID, 24 mg BID, 24 mg QD.			
Units: mcg/g			
arithmetic mean			
standard deviation	-		
Inflammatory Bowel Disease Questionnaire (IBDQ)			
The IBDQ is a disease-specific instrument composed of 32 Likert-scaled items. The total score ranges from 32 to 224 using the 7-point response options, with higher scores indicating better health-related quality of life. The IBDQ scale contains 4 component subscales: bowel symptoms, systemic symptoms, emotional function, and social function. Each subscale can be computed with total scores ranging from 10 to 70, 5 to 35, 12 to 84, and 5 to 35, respectively. n=37, 38, 36, 35, 36, 34, respectively, for placebo, upadacitinib 3 mg BID, 6 mg BID, 12 mg BID, 24 mg BID, 24 mg QD.			
Units: units on a scale			
arithmetic mean			
standard deviation	-		

End points

End points reporting groups

Reporting group title	Placebo Twice Daily (BID)
Reporting group description: Placebo BID during the 16-week double-blind Induction Phase.	
Reporting group title	Upadacitinib 3 mg BID
Reporting group description: Upadacitinib 3 mg BID during the 16-week double-blind Induction Phase.	
Reporting group title	Upadacitinib 6 mg BID
Reporting group description: Upadacitinib 6 mg BID during the 16-week double-blind Induction Phase.	
Reporting group title	Upadacitinib 12 mg BID
Reporting group description: Upadacitinib 12 mg BID during the 16-week double-blind Induction Phase.	
Reporting group title	Upadacitinib 24 mg BID
Reporting group description: Upadacitinib 24 mg BID during the 16-week double-blind Induction Phase.	
Reporting group title	Upadacitinib 24 mg QD
Reporting group description: Upadacitinib 24 mg once daily (consisting of two 12 mg immediate release [IR] doses) during the 16-week double-blind Induction Phase.	
Reporting group title	Upadacitinib 3 mg BID
Reporting group description: Upadacitinib 3 mg BID during the 36-week double-blind Extension Phase.	
Reporting group title	Upadacitinib 6 mg BID
Reporting group description: Upadacitinib 6 mg BID during the 36-week double-blind Extension Phase.	
Reporting group title	Upadacitinib 12 mg BID
Reporting group description: Upadacitinib 12 mg BID during the 36-week double-blind Extension Phase.	
Reporting group title	Upadacitinib 24 mg QD
Reporting group description: Upadacitinib 24 mg QD (consisting of two 12 mg IR doses) during the 36-week double-blind Extension Phase.	
Subject analysis set title	ITT: 3 mg BID, Upadacitinib in Induction
Subject analysis set type	Intention-to-treat
Subject analysis set description: Includes intent-to-treat responder (ITT-R) and non-responder (ITT-NR) analysis sets: all re-randomized subjects in the double-blind Extension Phase who were responders and nonresponders at Week 16 of the Induction Period, respectively. Includes only ITT subjects who were randomized to upadacitinib at Induction.	
Subject analysis set title	ITT: 6 mg BID, Upadacitinib at Induction
Subject analysis set type	Intention-to-treat
Subject analysis set description: Includes ITT-R and ITT-NR analysis sets: all re-randomized subjects in the double-blind Extension Phase who were responders and nonresponders at Week 16 of the Induction Period, respectively. Includes only ITT subjects who were randomized to upadacitinib at Induction.	
Subject analysis set title	ITT: 12 mg BID, Upadacitinib at Induction
Subject analysis set type	Intention-to-treat
Subject analysis set description: Includes ITT-R and ITT-NR analysis sets: all re-randomized subjects in the double-blind Extension Phase who were responders and nonresponders at Week 16 of the Induction Period, respectively. Includes only	

ITT subjects who were randomized to upadacitinib at Induction.

Subject analysis set title	ITT: 24 mg QD, Upadacitinib at Induction
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Includes ITT-R and ITT-NR analysis sets: all re-randomized subjects in the double-blind Extension Phase who were responders and nonresponders at Week 16 of the Induction Period, respectively. Includes only ITT subjects who were randomized to upadacitinib at Induction.

Subject analysis set title	ITT: 3 mg BID, Placebo in Induction
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Includes ITT-R and ITT-NR analysis sets: all re-randomized subjects in the double-blind Extension Phase who were responders and nonresponders at Week 16 of the Induction Period, respectively. Includes only ITT subjects who were randomized to placebo at Induction.

Subject analysis set title	ITT: 6 mg BID, Placebo at Induction
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Includes ITT-R and ITT-NR analysis sets: all re-randomized subjects in the double-blind Extension Phase who were responders and nonresponders at Week 16 of the Induction Period, respectively. Includes only ITT subjects who were randomized to placebo at Induction.

Subject analysis set title	ITT: 12 mg BID, Placebo at Induction
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Includes ITT-R and ITT-NR analysis sets: all re-randomized subjects in the double-blind Extension Phase who were responders and nonresponders at Week 16 of the Induction Period, respectively. Includes only ITT subjects who were randomized to placebo at Induction.

Subject analysis set title	ITT: 24 mg QD, Placebo at Induction
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Includes ITT-R and ITT-NR analysis sets: all re-randomized subjects in the double-blind Extension Phase who were responders and nonresponders at Week 16 of the Induction Period, respectively. Includes only ITT subjects who were randomized to placebo at Induction.

Primary: Percentage of Subjects Who Achieve Endoscopic Remission at Week 12/16

End point title	Percentage of Subjects Who Achieve Endoscopic Remission at Week 12/16
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End point description:

Endoscopic remission was determined using Simplified Endoscopic Score for Crohn's Disease (SES-CD). SES-CD subscores assess the following: presence and size of ulcers in 5 visualized bowel segments; extent of ulcerated surface in 5 visualized bowel segments; extent of affected surface in 5 visualized bowel segments; presence and type of narrowings in 5 visualized bowel segments. Subscores range from 0 to 15, and are summed for a total SES-CD score ranging from 0 to 56; higher scores indicate greater severity of mucosal inflammation. Endoscopic remission: SES-CD $\leq$ 4 and at least 2-point reduction versus Baseline and no subscore > 1 in any individual variable.

Modified intention to Treat (mITT) Population: all randomized subjects who took at least 1 dose of study drug in the Induction Period. Non-responder imputation.

End point type	Primary
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End point timeframe:

Up to Week 16. (At Baseline, subjects were allocated by randomization 1:1 to have their end of induction colonoscopy done at either Week 12 or Week 16; this endpoint combines the two time points.)

End point values	Placebo Twice Daily (BID)	Upadacitinib 3 mg BID	Upadacitinib 6 mg BID	Upadacitinib 12 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	37	39	37	36
Units: percentage of subjects				
number (not applicable)	0	10.3	8.1	8.3

End point values	Upadacitinib 24 mg BID	Upadacitinib 24 mg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	36	35		
Units: percentage of subjects				
number (not applicable)	22.2	14.3		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Upadacitinib 3 mg BID v Placebo Twice Daily (BID)
Number of subjects included in analysis	76
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.056 ^[1]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted risk difference from placebo
Point estimate	9.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.3
upper limit	20.1

Notes:

[1] - Statistical significance was prespecified at $\alpha = 0.1$. Based on Cochran-Mantel-Haenszel (CMH) test stratified by baseline SES-CD (SES-CD <15 and SES-CD $\geq$ 15).

Statistical analysis title	Statistical Analysis 2
Comparison groups	Placebo Twice Daily (BID) v Upadacitinib 6 mg BID
Number of subjects included in analysis	74
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.108 ^[2]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted risk difference from placebo
Point estimate	7.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.6
upper limit	16.4

Notes:

[2] - Statistical significance was prespecified at $\alpha = 0.1$. Based on CMH test stratified by baseline SES-CD (SES-CD <15 and SES-CD ≥ 15).

Statistical analysis title	Statistical Analysis 3
Comparison groups	Placebo Twice Daily (BID) v Upadacitinib 12 mg BID
Number of subjects included in analysis	73
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.099 ^[3]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted risk difference from placebo
Point estimate	7.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.5
upper limit	16.8

Notes:

[3] - Statistical significance was prespecified at $\alpha = 0.1$. Based on CMH test stratified by baseline SES-CD (SES-CD <15 and SES-CD ≥ 15).

Statistical analysis title	Statistical Analysis 4
Comparison groups	Placebo Twice Daily (BID) v Upadacitinib 24 mg BID
Number of subjects included in analysis	73
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.004 ^[4]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted risk difference from placebo
Point estimate	21
Confidence interval	
level	95 %
sides	2-sided
lower limit	6.8
upper limit	35.2

Notes:

[4] - Statistical significance was prespecified at $\alpha = 0.1$. Based on CMH test stratified by baseline SES-CD (SES-CD <15 and SES-CD ≥ 15).

Statistical analysis title	Statistical Analysis 5
Comparison groups	Placebo Twice Daily (BID) v Upadacitinib 24 mg QD
Number of subjects included in analysis	72
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.025 ^[5]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted risk difference from placebo
Point estimate	13.6

Confidence interval	
level	95 %
sides	2-sided
lower limit	1.8
upper limit	25.5

Notes:

[5] - Statistical significance was prespecified at $\alpha = 0.1$. Based on CMH test stratified by baseline SES-CD (SES-CD <15 and SES-CD ≥ 15).

Primary: Percentage of Subjects Who Achieve Clinical Remission at Week 16

End point title	Percentage of Subjects Who Achieve Clinical Remission at Week 16
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End point description:

Clinical remission: average daily stool frequency ≤ 1.5 and not worse than Baseline AND average daily abdominal pain ≤ 1.0 and not worse than Baseline. The very soft/liquid stool frequency and abdominal pain scores at a visit were the average of the daily values reported during the 7 usable days preceding the scheduled assessment visit. Abdominal Pain was rated on a 4-point scale from 0 (none) to 3 (severe).

mITT Population: all randomized subjects who took at least 1 dose of study drug in the Induction Period. Non-responder imputation.

End point type	Primary
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End point timeframe:

Week 16

End point values	Placebo Twice Daily (BID)	Upadacitinib 3 mg BID	Upadacitinib 6 mg BID	Upadacitinib 12 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	37	39	37	36
Units: percentage of subjects				
number (not applicable)	10.8	12.8	27.0	11.1

End point values	Upadacitinib 24 mg BID	Upadacitinib 24 mg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	36	35		
Units: percentage of subjects				
number (not applicable)	22.2	14.3		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo Twice Daily (BID) v Upadacitinib 3 mg BID

Number of subjects included in analysis	76
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.74 ^[6]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted risk difference from placebo
Point estimate	2.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-12.3
upper limit	17.3

Notes:

[6] - Statistical significance was prespecified at $\alpha = 0.1$. Based on CMH test stratified by baseline SES-CD (SES-CD <15 and SES-CD $\geq$ 15).

Statistical analysis title	Statistical Analysis 2
Comparison groups	Placebo Twice Daily (BID) v Upadacitinib 6 mg BID
Number of subjects included in analysis	74
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.082 ^[7]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted risk difference from placebo
Point estimate	16.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2
upper limit	34.3

Notes:

[7] - Statistical significance was prespecified at $\alpha = 0.1$. Based on CMH test stratified by baseline SES-CD (SES-CD <15 and SES-CD $\geq$ 15).

Statistical analysis title	Statistical Analysis 3
Comparison groups	Placebo Twice Daily (BID) v Upadacitinib 12 mg BID
Number of subjects included in analysis	73
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.952 ^[8]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted risk difference from placebo
Point estimate	0.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-14.1
upper limit	15

Notes:

[8] - Statistical significance was prespecified at $\alpha = 0.1$. Based on CMH test stratified by baseline SES-CD (SES-CD <15 and SES-CD $\geq$ 15).

Statistical analysis title	Statistical Analysis 4
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Comparison groups	Placebo Twice Daily (BID) v Upadacitinib 24 mg BID
Number of subjects included in analysis	73
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.205 ^[9]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted risk difference from placebo
Point estimate	11.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.1
upper limit	28.5

Notes:

[9] - Statistical significance was prespecified at $\alpha = 0.1$. Based on CMH test stratified by baseline SES-CD (SES-CD <15 and SES-CD $\geq$ 15).

Statistical analysis title	Statistical Analysis 5
Comparison groups	Placebo Twice Daily (BID) v Upadacitinib 24 mg QD
Number of subjects included in analysis	72
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.607 ^[10]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted risk difference from placebo
Point estimate	4.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-11.5
upper limit	19.6

Notes:

[10] - Statistical significance was prespecified at $\alpha = 0.1$. Based on CMH test stratified by baseline SES-CD (SES-CD <15 and SES-CD $\geq$ 15).

Secondary: Percentage of Subjects Who Achieve Crohn's Disease Activity Index (CDAI) < 150 at Week 16

End point title	Percentage of Subjects Who Achieve Crohn's Disease Activity Index (CDAI) < 150 at Week 16
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End point description:

CDAI is used to quantify the signs and symptoms of subjects with Crohn's disease. The score includes the frequency of stools, abdominal pain and general well-being as well as the presence of complications, use of antidiarrheals, presence of abdominal mass, hematocrit and weight. CDAI generally ranges from 0 to 600 where higher scores indicate more severe disease. A score below 150 indicates remission.

mITT Population: all randomized subjects who took at least 1 dose of study drug in the Induction Period. Non-responder imputation.

End point type	Secondary
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End point timeframe:

Week 16

End point values	Placebo Twice Daily (BID)	Upadacitinib 3 mg BID	Upadacitinib 6 mg BID	Upadacitinib 12 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	37	39	37	36
Units: percentage of subjects				
number (not applicable)	16.2	20.5	29.7	38.9

End point values	Upadacitinib 24 mg BID	Upadacitinib 24 mg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	36	35		
Units: percentage of subjects				
number (not applicable)	30.6	20.0		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo Twice Daily (BID) v Upadacitinib 3 mg BID
Number of subjects included in analysis	76
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.564 ^[11]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted risk difference from placebo
Point estimate	5.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-12.5
upper limit	22.9

Notes:

[11] - Based on CMH test stratified by baseline SES-CD (SES-CD <15 and SES-CD ≥15).

Statistical analysis title	Statistical Analysis 2
Comparison groups	Placebo Twice Daily (BID) v Upadacitinib 6 mg BID
Number of subjects included in analysis	74
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.221 ^[12]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted risk difference from placebo
Point estimate	12
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.2
upper limit	31.2

Notes:

[12] - Based on CMH test stratified by baseline SES-CD (SES-CD <15 and SES-CD ≥15).

Statistical analysis title	Statistical Analysis 3
Comparison groups	Placebo Twice Daily (BID) v Upadacitinib 12 mg BID
Number of subjects included in analysis	73
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.036 ^[13]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted risk difference from placebo
Point estimate	22.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.4
upper limit	43

Notes:

[13] - Based on CMH test stratified by baseline SES-CD (SES-CD <15 and SES-CD ≥15).

Statistical analysis title	Statistical Analysis 4
Comparison groups	Placebo Twice Daily (BID) v Upadacitinib 24 mg BID
Number of subjects included in analysis	73
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.179 ^[14]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted risk difference from placebo
Point estimate	13.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.2
upper limit	33.1

Notes:

[14] - Based on CMH test stratified by baseline SES-CD (SES-CD <15 and SES-CD ≥15).

Statistical analysis title	Statistical Analysis 5
Comparison groups	Placebo Twice Daily (BID) v Upadacitinib 24 mg QD
Number of subjects included in analysis	72
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.677 ^[15]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted risk difference from placebo
Point estimate	3.9

Confidence interval	
level	95 %
sides	2-sided
lower limit	-14.3
upper limit	22

Notes:

[15] - Based on CMH test stratified by baseline SES-CD (SES-CD <15 and SES-CD ≥15).

Secondary: Percentage of Subjects With a Decrease in CDAI ≥ 70 Points From Baseline at Week 16

End point title	Percentage of Subjects With a Decrease in CDAI ≥ 70 Points From Baseline at Week 16
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End point description:

CDAI is used to quantify the signs and symptoms of subjects with Crohn's disease. The score includes the frequency of stools, abdominal pain and general well-being as well as the presence of complications, use of antidiarrheals, presence of abdominal mass, hematocrit and weight. CDAI generally ranges from 0 to 600 where higher scores indicate more severe disease. A 70-point decrease in the CDAI index refers to improvement in the disease activity from Baseline.

mITT Population: all randomized subjects who took at least 1 dose of study drug in the Induction Period. Non-responder imputation.

End point type	Secondary
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End point timeframe:

Week 16

End point values	Placebo Twice Daily (BID)	Upadacitinib 3 mg BID	Upadacitinib 6 mg BID	Upadacitinib 12 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	37	39	37	36
Units: percentage of subjects				
number (not applicable)	35.1	46.2	54.1	44.4

End point values	Upadacitinib 24 mg BID	Upadacitinib 24 mg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	36	35		
Units: percentage of subjects				
number (not applicable)	61.1	48.6		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo Twice Daily (BID) v Upadacitinib 3 mg BID

Number of subjects included in analysis	76
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.363 ^[16]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted risk difference from placebo
Point estimate	10.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-12
upper limit	32.9

Notes:

[16] - Based on CMH test stratified by baseline SES-CD (SES-CD <15 and SES-CD ≥15).

Statistical analysis title	Statistical Analysis 2
Comparison groups	Placebo Twice Daily (BID) v Upadacitinib 6 mg BID
Number of subjects included in analysis	74
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.137 ^[17]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted risk difference from placebo
Point estimate	17.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.5
upper limit	40

Notes:

[17] - Based on CMH test stratified by baseline SES-CD (SES-CD <15 and SES-CD ≥15).

Statistical analysis title	Statistical Analysis 3
Comparison groups	Placebo Twice Daily (BID) v Upadacitinib 12 mg BID
Number of subjects included in analysis	73
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.512 ^[18]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted risk difference from placebo
Point estimate	7.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-14.9
upper limit	29.9

Notes:

[18] - Based on CMH test stratified by baseline SES-CD (SES-CD <15 and SES-CD ≥15).

Statistical analysis title	Statistical Analysis 4
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Comparison groups	Placebo Twice Daily (BID) v Upadacitinib 24 mg BID
Number of subjects included in analysis	73
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.035 ^[19]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted risk difference from placebo
Point estimate	25
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.8
upper limit	48.2

Notes:

[19] - Based on CMH test stratified by baseline SES-CD (SES-CD <15 and SES-CD ≥15).

Statistical analysis title	Statistical Analysis 5
Comparison groups	Placebo Twice Daily (BID) v Upadacitinib 24 mg QD
Number of subjects included in analysis	72
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.29 ^[20]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted risk difference from placebo
Point estimate	12.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-10.7
upper limit	35.6

Notes:

[20] - Based on CMH test stratified by baseline SES-CD (SES-CD <15 and SES-CD ≥15).

Secondary: Percentage of Subjects Who Achieve Clinical Remission at Week 12

End point title	Percentage of Subjects Who Achieve Clinical Remission at Week 12
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End point description:

Clinical remission: average daily stool frequency ≤ 1.5 and not worse than Baseline AND average daily abdominal pain ≤ 1.0 and not worse than Baseline. The very soft/liquid stool frequency and abdominal pain scores at a visit were the average of the daily values reported during the 7 usable days preceding the scheduled assessment visit. Abdominal Pain was rated on a 4-point scale from 0 (none) to 3 (severe).

mITT Population: all randomized subjects who took at least 1 dose of study drug in the Induction Period. Non-responder imputation.

End point type	Secondary
End point timeframe:	
Week 12	

End point values	Placebo Twice Daily (BID)	Upadacitinib 3 mg BID	Upadacitinib 6 mg BID	Upadacitinib 12 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	37	39	37	36
Units: percentage of subjects				
number (not applicable)	10.8	10.3	29.7	13.9

End point values	Upadacitinib 24 mg BID	Upadacitinib 24 mg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	36	35		
Units: percentage of subjects				
number (not applicable)	25.0	8.6		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo Twice Daily (BID) v Upadacitinib 3 mg BID
Number of subjects included in analysis	76
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.896 ^[21]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted risk difference from placebo
Point estimate	-0.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-15
upper limit	13.1

Notes:

[21] - Based on CMH test stratified by baseline SES-CD (SES-CD <15 and SES-CD ≥15).

Statistical analysis title	Statistical Analysis 2
Comparison groups	Placebo Twice Daily (BID) v Upadacitinib 6 mg BID
Number of subjects included in analysis	74
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.05 ^[22]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted risk difference from placebo
Point estimate	18.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	0
upper limit	37.3

Notes:

[22] - Based on CMH test stratified by baseline SES-CD (SES-CD <15 and SES-CD ≥15).

Statistical analysis title	Statistical Analysis 3
Comparison groups	Placebo Twice Daily (BID) v Upadacitinib 12 mg BID
Number of subjects included in analysis	73
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.702 ^[23]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted risk difference from placebo
Point estimate	3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-12.4
upper limit	18.4

Notes:

[23] - Based on CMH test stratified by baseline SES-CD (SES-CD <15 and SES-CD ≥15).

Statistical analysis title	Statistical Analysis 4
Comparison groups	Placebo Twice Daily (BID) v Upadacitinib 24 mg BID
Number of subjects included in analysis	73
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.117 ^[24]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted risk difference from placebo
Point estimate	14.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.6
upper limit	32.2

Notes:

[24] - Based on CMH test stratified by baseline SES-CD (SES-CD <15 and SES-CD ≥15).

Statistical analysis title	Statistical Analysis 5
Comparison groups	Placebo Twice Daily (BID) v Upadacitinib 24 mg QD
Number of subjects included in analysis	72
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.736 ^[25]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted risk difference from placebo
Point estimate	-2.4

Confidence interval	
level	95 %
sides	2-sided
lower limit	-16.4
upper limit	11.6

Notes:

[25] - Based on CMH test stratified by baseline SES-CD (SES-CD <15 and SES-CD ≥15).

Secondary: Percentage of Subjects Who Achieve Remission at Week 16

End point title	Percentage of Subjects Who Achieve Remission at Week 16
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End point description:

Remission is defined as endoscopic remission at Week 12/16 AND clinical remission at Week 16.

Endoscopic remission: SES-CD ≤ 4 and at least 2-point reduction versus Baseline and no subscore > 1 in any individual variable. Clinical remission: average daily stool frequency ≤ 1.5 and not worse than Baseline AND average daily abdominal pain ≤ 1.0 and not worse than Baseline. The very soft/liquid stool frequency and abdominal pain scores at a visit were the average of the daily values reported during the 7 usable days preceding the scheduled assessment visit. Abdominal Pain was rated on a 4-point scale from 0 (none) to 3 (severe). Details of the SES-CD scale are provided in the description of the first primary endpoint.

mITT Population: all randomized subjects who took at least 1 dose of study drug in the Induction Period. Non-responder imputation.

End point type	Secondary
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End point timeframe:

Week 16

End point values	Placebo Twice Daily (BID)	Upadacitinib 3 mg BID	Upadacitinib 6 mg BID	Upadacitinib 12 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	37	39	37	36
Units: percentage of subjects				
number (not applicable)	0	2.6	5.4	2.8

End point values	Upadacitinib 24 mg BID	Upadacitinib 24 mg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	36	35		
Units: percentage of subjects				
number (not applicable)	8.3	5.7		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo Twice Daily (BID) v Upadacitinib 3 mg BID

Number of subjects included in analysis	76
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.276 ^[26]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted risk difference from placebo
Point estimate	2.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.3
upper limit	8.1

Notes:

[26] - Based on CMH test stratified by baseline SES-CD (SES-CD <15 and SES-CD ≥15).

Statistical analysis title	Statistical Analysis 2
Comparison groups	Placebo Twice Daily (BID) v Upadacitinib 6 mg BID
Number of subjects included in analysis	74
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.195 ^[27]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted risk difference from placebo
Point estimate	4.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.5
upper limit	12.4

Notes:

[27] - Based on CMH test stratified by baseline SES-CD (SES-CD <15 and SES-CD ≥15).

Statistical analysis title	Statistical Analysis 3
Comparison groups	Placebo Twice Daily (BID) v Upadacitinib 12 mg BID
Number of subjects included in analysis	73
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.355 ^[28]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted risk difference from placebo
Point estimate	2.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.9
upper limit	8

Notes:

[28] - Based on CMH test stratified by baseline SES-CD (SES-CD <15 and SES-CD ≥15).

Statistical analysis title	Statistical Analysis 4
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Comparison groups	Placebo Twice Daily (BID) v Upadacitinib 24 mg BID
Number of subjects included in analysis	73
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.099 ^[29]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted risk difference from placebo
Point estimate	7.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.5
upper limit	16.8

Notes:

[29] - Based on CMH test stratified by baseline SES-CD (SES-CD <15 and SES-CD ≥15).

Statistical analysis title	Statistical Analysis 5
Comparison groups	Placebo Twice Daily (BID) v Upadacitinib 24 mg QD
Number of subjects included in analysis	72
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.185 ^[30]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted risk difference from placebo
Point estimate	5.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.5
upper limit	12.9

Notes:

[30] - Based on CMH test stratified by baseline SES-CD (SES-CD <15 and SES-CD ≥15).

Secondary: Percentage of Subjects Who Achieve Response at Week 16

End point title	Percentage of Subjects Who Achieve Response at Week 16
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End point description:

Response is defined as endoscopic response at Week 12/16 AND clinical response at Week 16.

Endoscopic response: SES-CD at least 25% reduction from Baseline. Clinical response: average daily stool frequency at least 30% reduction from Baseline and average daily abdominal pain not worse than Baseline OR average daily abdominal pain at least 30% reduction from Baseline and average daily stool frequency not worse than Baseline. The very soft/liquid stool frequency and abdominal pain scores at a visit were the average of the daily values reported during the 7 usable days preceding the scheduled assessment visit. Abdominal Pain was rated on a 4-point scale from 0 (none) to 3 (severe). Details of the SES-CD scale are provided in the description of the first primary endpoint.

mITT Population: all randomized subjects who took at least 1 dose of study drug in the Induction Period. Non-responder imputation.

End point type	Secondary
End point timeframe:	
Week 16	

End point values	Placebo Twice Daily (BID)	Upadacitinib 3 mg BID	Upadacitinib 6 mg BID	Upadacitinib 12 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	37	39	37	36
Units: percentage of subjects				
number (not applicable)	2.7	15.4	32.4	27.8

End point values	Upadacitinib 24 mg BID	Upadacitinib 24 mg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	36	35		
Units: percentage of subjects				
number (not applicable)	38.9	34.3		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo Twice Daily (BID) v Upadacitinib 3 mg BID
Number of subjects included in analysis	76
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.05 ^[31]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted risk difference from placebo
Point estimate	13.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	0
upper limit	26.5

Notes:

[31] - Based on CMH test stratified by baseline SES-CD (SES-CD <15 and SES-CD ≥15).

Statistical analysis title	Statistical Analysis 2
Comparison groups	Placebo Twice Daily (BID) v Upadacitinib 6 mg BID
Number of subjects included in analysis	74
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.001 ^[32]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted risk difference from placebo
Point estimate	29.5

Confidence interval	
level	95 %
sides	2-sided
lower limit	11.9
upper limit	47.1

Notes:

[32] - Based on CMH test stratified by baseline SES-CD (SES-CD <15 and SES-CD ≥15).

Statistical analysis title	Statistical Analysis 3
Comparison groups	Placebo Twice Daily (BID) v Upadacitinib 12 mg BID
Number of subjects included in analysis	73
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.003 ^[33]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted risk difference from placebo
Point estimate	25.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	8.5
upper limit	42

Notes:

[33] - Based on CMH test stratified by baseline SES-CD (SES-CD <15 and SES-CD ≥15).

Statistical analysis title	Statistical Analysis 4
Comparison groups	Placebo Twice Daily (BID) v Upadacitinib 24 mg BID
Number of subjects included in analysis	73
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 ^[34]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted risk difference from placebo
Point estimate	36.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	17.6
upper limit	55.4

Notes:

[34] - Based on CMH test stratified by baseline SES-CD (SES-CD <15 and SES-CD ≥15).

Statistical analysis title	Statistical Analysis 5
Comparison groups	Placebo Twice Daily (BID) v Upadacitinib 24 mg QD

Number of subjects included in analysis	72
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 ^[35]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted risk difference from placebo
Point estimate	32
Confidence interval	
level	95 %
sides	2-sided
lower limit	13.9
upper limit	50.2

Notes:

[35] - Based on CMH test stratified by baseline SES-CD (SES-CD <15 and SES-CD ≥15).

Secondary: Percentage of Subjects With Endoscopic Response at Week 12/16

End point title	Percentage of Subjects With Endoscopic Response at Week 12/16
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End point description:

Endoscopic response: SES-CD at least 25% reduction from Baseline. Details of the SES-CD scale are provided in the description of the first primary endpoint.

mITT Population: all randomized subjects who took at least 1 dose of study drug in the Induction Period. Non-responder imputation.

End point type	Secondary
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End point timeframe:

Up to Week 16. (At Baseline, patients were allocated by randomization 1:1 to have their end of induction colonoscopy done at either Week 12 or Week 16; this endpoint combines the two time points.)

End point values	Placebo Twice Daily (BID)	Upadacitinib 3 mg BID	Upadacitinib 6 mg BID	Upadacitinib 12 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	37	39	37	36
Units: percentage of subjects				
number (not applicable)	13.5	23.1	43.2	36.1

End point values	Upadacitinib 24 mg BID	Upadacitinib 24 mg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	36	35		
Units: percentage of subjects				
number (not applicable)	50.0	48.6		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo Twice Daily (BID) v Upadacitinib 3 mg BID
Number of subjects included in analysis	76
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.243 ^[36]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted risk difference from placebo
Point estimate	10.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.2
upper limit	28.2

Notes:

[36] - Based on CMH test stratified by baseline SES-CD (SES-CD <15 and SES-CD >=15).

Statistical analysis title	Statistical Analysis 2
Comparison groups	Placebo Twice Daily (BID) v Upadacitinib 6 mg BID
Number of subjects included in analysis	74
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.006 ^[37]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted risk difference from placebo
Point estimate	29.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	8.3
upper limit	49.9

Notes:

[37] - Based on CMH test stratified by baseline SES-CD (SES-CD <15 and SES-CD >=15).

Statistical analysis title	Statistical Analysis 3
Comparison groups	Placebo Twice Daily (BID) v Upadacitinib 12 mg BID
Number of subjects included in analysis	73
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.017 ^[38]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted risk difference from placebo
Point estimate	24.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	4.4
upper limit	44.1

Notes:

[38] - Based on CMH test stratified by baseline SES-CD (SES-CD <15 and SES-CD ≥15).

Statistical analysis title	Statistical Analysis 4
Comparison groups	Placebo Twice Daily (BID) v Upadacitinib 24 mg BID
Number of subjects included in analysis	73
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 ^[39]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted risk difference from placebo
Point estimate	36.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	14.8
upper limit	58.1

Notes:

[39] - Based on CMH test stratified by baseline SES-CD (SES-CD <15 and SES-CD ≥15).

Statistical analysis title	Statistical Analysis 5
Comparison groups	Placebo Twice Daily (BID) v Upadacitinib 24 mg QD
Number of subjects included in analysis	72
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 ^[40]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted risk difference from placebo
Point estimate	36.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	15.2
upper limit	58.3

Notes:

[40] - Based on CMH test stratified by baseline SES-CD (SES-CD <15 and SES-CD ≥15).

Secondary: Percentage of Subjects Who Achieve Clinical Response at Week 16

End point title	Percentage of Subjects Who Achieve Clinical Response at Week 16
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End point description:

Clinical response: average daily stool frequency at least 30% reduction from Baseline and average daily abdominal pain not worse than Baseline OR average daily abdominal pain at least 30% reduction from Baseline and average daily stool frequency not worse than Baseline. The very soft/liquid stool frequency and abdominal pain scores at a visit were the average of the daily values reported during the 7 usable days preceding the scheduled assessment visit. Abdominal Pain was rated on a 4-point scale from 0 (none) to 3 (severe).

mITT Population: all randomized subjects who took at least 1 dose of study drug in the Induction Period. Non-responder imputation.

End point type	Secondary
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End point timeframe:

Week 16

End point values	Placebo Twice Daily (BID)	Upadacitinib 3 mg BID	Upadacitinib 6 mg BID	Upadacitinib 12 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	37	39	37	36
Units: percentage of subjects				
number (not applicable)	32.4	43.6	56.8	47.2

End point values	Upadacitinib 24 mg BID	Upadacitinib 24 mg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	36	35		
Units: percentage of subjects				
number (not applicable)	61.1	48.6		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo Twice Daily (BID) v Upadacitinib 3 mg BID
Number of subjects included in analysis	76
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.353 ^[41]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted risk difference from placebo
Point estimate	10.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-11.7
upper limit	32.7

Notes:

[41] - Based on CMH test stratified by baseline SES-CD (SES-CD <15 and SES-CD ≥15).

Statistical analysis title	Statistical Analysis 2
Comparison groups	Placebo Twice Daily (BID) v Upadacitinib 6 mg BID

Number of subjects included in analysis	74
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.05 ^[42]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted risk difference from placebo
Point estimate	22.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	0
upper limit	45.5

Notes:

[42] - Based on CMH test stratified by baseline SES-CD (SES-CD <15 and SES-CD ≥15).

Statistical analysis title	Statistical Analysis 3
Comparison groups	Placebo Twice Daily (BID) v Upadacitinib 12 mg BID
Number of subjects included in analysis	73
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.268 ^[43]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted risk difference from placebo
Point estimate	12.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-9.6
upper limit	34.6

Notes:

[43] - Based on CMH test stratified by baseline SES-CD (SES-CD <15 and SES-CD ≥15).

Statistical analysis title	Statistical Analysis 4
Comparison groups	Placebo Twice Daily (BID) v Upadacitinib 24 mg BID
Number of subjects included in analysis	73
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.018 ^[44]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted risk difference from placebo
Point estimate	28
Confidence interval	
level	95 %
sides	2-sided
lower limit	4.8
upper limit	51.2

Notes:

[44] - Based on CMH test stratified by baseline SES-CD (SES-CD <15 and SES-CD ≥15).

Statistical analysis title	Statistical Analysis 5
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Comparison groups	Placebo Twice Daily (BID) v Upadacitinib 24 mg QD
Number of subjects included in analysis	72
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.204 ^[45]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted risk difference from placebo
Point estimate	14.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-8.1
upper limit	37.8

Notes:

[45] - Based on CMH test stratified by baseline SES-CD (SES-CD <15 and SES-CD ≥15).

Secondary: Percentage of Subjects With an Average Daily Stool Frequency ≥ 2.5 AND Average Daily Abdominal Pain ≥ 2.0 at Baseline Who Achieve Clinical Remission at Week 16

End point title	Percentage of Subjects With an Average Daily Stool Frequency ≥ 2.5 AND Average Daily Abdominal Pain ≥ 2.0 at Baseline Who Achieve Clinical Remission at Week 16
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End point description:

Clinical remission: average daily stool frequency ≤ 1.5 and not worse than Baseline AND average daily abdominal pain ≤ 1.0 and not worse than Baseline. The very soft/liquid stool frequency and abdominal pain scores at a visit were the average of the daily values reported during the 7 usable days preceding the scheduled assessment visit. Abdominal Pain was rated on a 4-point scale from 0 (none) to 3 (severe).

mITT Population: all randomized subjects who took at least 1 dose of study drug in the Induction Period. Includes only mITT subjects with an average daily stool frequency ≥ 2.5 AND average daily abdominal pain ≥ 2.0 at Baseline. Non-responder imputation.

End point type	Secondary
End point timeframe:	
Week 16	

End point values	Placebo Twice Daily (BID)	Upadacitinib 3 mg BID	Upadacitinib 6 mg BID	Upadacitinib 12 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	14	17	16	18
Units: percentage of subjects				
number (not applicable)	7.1	17.6	18.8	16.7

End point values	Upadacitinib 24 mg BID	Upadacitinib 24 mg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	18		
Units: percentage of subjects				
number (not applicable)	25.0	11.1		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo Twice Daily (BID) v Upadacitinib 3 mg BID
Number of subjects included in analysis	31
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.421 ^[46]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted risk difference from placebo
Point estimate	10
Confidence interval	
level	95 %
sides	2-sided
lower limit	-14.4
upper limit	34.4

Notes:

[46] - Based on CMH test stratified by baseline SES-CD (SES-CD <15 and SES-CD ≥15).

Statistical analysis title	Statistical Analysis 2
Comparison groups	Placebo Twice Daily (BID) v Upadacitinib 6 mg BID
Number of subjects included in analysis	30
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.371 ^[47]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted risk difference from placebo
Point estimate	11.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-13.8
upper limit	36.8

Notes:

[47] - Based on CMH test stratified by baseline SES-CD (SES-CD <15 and SES-CD ≥15).

Statistical analysis title	Statistical Analysis 3
Comparison groups	Placebo Twice Daily (BID) v Upadacitinib 12 mg BID

Number of subjects included in analysis	32
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.445 ^[48]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted risk difference from placebo
Point estimate	9.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-14.4
upper limit	32.8

Notes:

[48] - Based on CMH test stratified by baseline SES-CD (SES-CD <15 and SES-CD ≥15).

Statistical analysis title	Statistical Analysis 4
Comparison groups	Placebo Twice Daily (BID) v Upadacitinib 24 mg BID
Number of subjects included in analysis	26
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.198 ^[49]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted risk difference from placebo
Point estimate	19.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-10.2
upper limit	49.3

Notes:

[49] - Based on CMH test stratified by baseline SES-CD (SES-CD <15 and SES-CD ≥15).

Statistical analysis title	Statistical Analysis 5
Comparison groups	Placebo Twice Daily (BID) v Upadacitinib 24 mg QD
Number of subjects included in analysis	32
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.654 ^[50]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted risk difference from placebo
Point estimate	5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-17
upper limit	27

Notes:

[50] - Based on CMH test stratified by baseline SES-CD (SES-CD <15 and SES-CD ≥15).

Secondary: Percentage of Subjects Taking Corticosteroids at Baseline Who

Discontinued Corticosteroid Use and Achieve CDAI < 150 at Week 16

End point title	Percentage of Subjects Taking Corticosteroids at Baseline Who Discontinued Corticosteroid Use and Achieve CDAI < 150 at Week 16
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End point description:

CDAI is used to quantify the signs and symptoms of subjects with Crohn's disease. The score includes the frequency of stools, abdominal pain and general well-being as well as the presence of complications, use of antidiarrheals, presence of abdominal mass, hematocrit and weight. CDAI generally ranges from 0 to 600 where higher scores indicate more severe disease. A score below 150 indicates remission.

mITT Population: all randomized subjects who took at least 1 dose of study drug in the Induction Period. Includes only subjects taking corticosteroids at Baseline. Non-responder imputation.

End point type	Secondary
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End point timeframe:

Week 16

End point values	Placebo Twice Daily (BID)	Upadacitinib 3 mg BID	Upadacitinib 6 mg BID	Upadacitinib 12 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	15	21	18	17
Units: percentage of subjects				
number (not applicable)	0	19.0	22.2	41.2

End point values	Upadacitinib 24 mg BID	Upadacitinib 24 mg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15	10		
Units: percentage of subjects				
number (not applicable)	33.3	10.0		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo Twice Daily (BID) v Upadacitinib 3 mg BID
Number of subjects included in analysis	36
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.093 ^[51]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted risk difference from placebo
Point estimate	18.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.1
upper limit	40.5

Notes:

[51] - Based on CMH test stratified by baseline SES-CD (SES-CD <15 and SES-CD ≥15).

Statistical analysis title	Statistical Analysis 2
Comparison groups	Placebo Twice Daily (BID) v Upadacitinib 6 mg BID
Number of subjects included in analysis	33
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.176 ^[52]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted risk difference from placebo
Point estimate	13.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.1
upper limit	33.1

Notes:

[52] - Based on CMH test stratified by baseline SES-CD (SES-CD <15 and SES-CD ≥15).

Statistical analysis title	Statistical Analysis 3
Comparison groups	Placebo Twice Daily (BID) v Upadacitinib 12 mg BID
Number of subjects included in analysis	32
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.017 ^[53]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted risk difference from placebo
Point estimate	35.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	6.3
upper limit	65.5

Notes:

[53] - Based on CMH test stratified by baseline SES-CD (SES-CD <15 and SES-CD ≥15).

Statistical analysis title	Statistical Analysis 4
Comparison groups	Placebo Twice Daily (BID) v Upadacitinib 24 mg BID
Number of subjects included in analysis	30
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.044 ^[54]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted risk difference from placebo
Point estimate	26.1

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.7
upper limit	51.5

Notes:

[54] - Based on CMH test stratified by baseline SES-CD (SES-CD <15 and SES-CD ≥15).

Statistical analysis title	Statistical Analysis 5
Comparison groups	Placebo Twice Daily (BID) v Upadacitinib 24 mg QD
Number of subjects included in analysis	25
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.121 ^[55]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted risk difference from placebo
Point estimate	13.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.5
upper limit	29.6

Notes:

[55] - Based on CMH test stratified by baseline SES-CD (SES-CD <15 and SES-CD ≥15).

Secondary: Percentage of Subjects Taking Corticosteroids at Baseline Who Discontinued Corticosteroid Use and Achieve Remission at Week 12/16 and Clinical Remission at Week 16

End point title	Percentage of Subjects Taking Corticosteroids at Baseline Who Discontinued Corticosteroid Use and Achieve Remission at Week 12/16 and Clinical Remission at Week 16
-----------------	---

End point description:

Remission is defined as endoscopic remission at Week 12/16 AND clinical remission at Week 16.

Endoscopic remission: SES-CD ≤ 4 and at least 2-point reduction versus Baseline and no subscore > 1 in any individual variable. Clinical remission: average daily stool frequency ≤ 1.5 and not worse than Baseline AND average daily abdominal pain ≤ 1.0 and not worse than Baseline. The very soft/liquid stool frequency and abdominal pain scores at a visit were the average of the daily values reported during the 7 usable days preceding the scheduled assessment visit. Abdominal Pain was rated on a 4-point scale from 0 (none) to 3 (severe). Details of the SES-CD scale are provided in the description of the first primary endpoint.

mITT Population: all randomized subjects who took at least 1 dose of study drug in the Induction Period. Includes only subjects taking corticosteroids at Baseline. Non-responder imputation.

End point type	Secondary
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End point timeframe:

Up to Week 16. (At Baseline, subjects were allocated by randomization 1:1 to have their end of induction colonoscopy done at either Week 12 or Week 16; this endpoint combines the two time points.)

End point values	Placebo Twice Daily (BID)	Upadacitinib 3 mg BID	Upadacitinib 6 mg BID	Upadacitinib 12 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	15	21	18	17
Units: percentage of subjects				
number (not applicable)	0	0	5.6	5.9

End point values	Upadacitinib 24 mg BID	Upadacitinib 24 mg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15	10		
Units: percentage of subjects				
number (not applicable)	13.3	0		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo Twice Daily (BID) v Upadacitinib 6 mg BID
Number of subjects included in analysis	33
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.564 ^[56]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted risk difference from placebo
Point estimate	3.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-8.1
upper limit	14.9

Notes:

[56] - Based on CMH test stratified by baseline SES-CD (SES-CD <15 and SES-CD ≥15).

Statistical analysis title	Statistical Analysis 2
Comparison groups	Placebo Twice Daily (BID) v Upadacitinib 12 mg BID
Number of subjects included in analysis	32
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.584 ^[57]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted risk difference from placebo
Point estimate	3.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-8.8
upper limit	15.7

Notes:

[57] - Based on CMH test stratified by baseline SES-CD (SES-CD <15 and SES-CD ≥15).

Statistical analysis title	Statistical Analysis 3
Comparison groups	Placebo Twice Daily (BID) v Upadacitinib 24 mg BID
Number of subjects included in analysis	30
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.326 ^[58]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted risk difference from placebo
Point estimate	8.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-8.7
upper limit	26.1

Notes:

[58] - Based on CMH test stratified by baseline SES-CD (SES-CD <15 and SES-CD ≥15).

Secondary: Percentage of Subjects Taking Corticosteroids at Baseline Who Discontinued Corticosteroid Use and Achieve Clinical Remission at Week 16

End point title	Percentage of Subjects Taking Corticosteroids at Baseline Who Discontinued Corticosteroid Use and Achieve Clinical Remission at Week 16
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End point description:

Clinical remission: average daily stool frequency ≤ 1.5 and not worse than Baseline AND average daily abdominal pain ≤ 1.0 and not worse than Baseline. The very soft/liquid stool frequency and abdominal pain scores at a visit were the average of the daily values reported during the 7 usable days preceding the scheduled assessment visit. Abdominal Pain was rated on a 4-point scale from 0 (none) to 3 (severe).

mITT Population: all randomized subjects who took at least 1 dose of study drug in the Induction Period. Includes only subjects taking corticosteroids at Baseline. Non-responder imputation.

End point type	Secondary
End point timeframe:	
Week 16	

End point values	Placebo Twice Daily (BID)	Upadacitinib 3 mg BID	Upadacitinib 6 mg BID	Upadacitinib 12 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	15	21	18	17
Units: percentage of subjects				
number (not applicable)	0	14.3	22.2	11.8

End point values	Upadacitinib 24 mg BID	Upadacitinib 24 mg QD		
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Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15	10		
Units: percentage of subjects				
number (not applicable)	33.3	10.0		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo Twice Daily (BID) v Upadacitinib 3 mg BID
Number of subjects included in analysis	36
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.195 ^[59]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted risk difference from placebo
Point estimate	12.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.2
upper limit	30.7

Notes:

[59] - Based on CMH test stratified by baseline SES-CD (SES-CD <15 and SES-CD ≥15).

Statistical analysis title	Statistical Analysis 2
Comparison groups	Placebo Twice Daily (BID) v Upadacitinib 6 mg BID
Number of subjects included in analysis	33
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.116 ^[60]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted risk difference from placebo
Point estimate	17.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.4
upper limit	40.1

Notes:

[60] - Based on CMH test stratified by baseline SES-CD (SES-CD <15 and SES-CD ≥15).

Statistical analysis title	Statistical Analysis 3
Comparison groups	Placebo Twice Daily (BID) v Upadacitinib 12 mg BID

Number of subjects included in analysis	32
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.178 ^[61]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted risk difference from placebo
Point estimate	12.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.8
upper limit	31.5

Notes:

[61] - Based on CMH test stratified by baseline SES-CD (SES-CD <15 and SES-CD ≥15).

Statistical analysis title	Statistical Analysis 4
Comparison groups	Placebo Twice Daily (BID) v Upadacitinib 24 mg BID
Number of subjects included in analysis	30
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.031 ^[62]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted risk difference from placebo
Point estimate	30.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.8
upper limit	58

Notes:

[62] - Based on CMH test stratified by baseline SES-CD (SES-CD <15 and SES-CD ≥15).

Statistical analysis title	Statistical Analysis 5
Comparison groups	Placebo Twice Daily (BID) v Upadacitinib 24 mg QD
Number of subjects included in analysis	25
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.121 ^[63]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted risk difference from placebo
Point estimate	13.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.5
upper limit	29.6

Notes:

[63] - Based on CMH test stratified by baseline SES-CD (SES-CD <15 and SES-CD ≥15).

Secondary: Percentage of Subjects Taking Corticosteroids at Baseline Who

Discontinued Corticosteroid Use and Achieve Endoscopic Remission at Week 12/16

End point title	Percentage of Subjects Taking Corticosteroids at Baseline Who Discontinued Corticosteroid Use and Achieve Endoscopic Remission at Week 12/16
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End point description:

Endoscopic remission: SES-CD ≤ 4 and at least 2-point reduction versus Baseline and no subscore > 1 in any individual variable. Details of the SES-CD scale are provided in the description of the first primary endpoint.

mITT Population: all randomized subjects who took at least 1 dose of study drug in the Induction Period. Includes only subjects taking corticosteroids at Baseline. Non-responder imputation.

End point type	Secondary
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End point timeframe:

Up to Week 16. (At Baseline, patients were allocated by randomization 1:1 to have their end of induction colonoscopy done at either Week 12 or Week 16; this endpoint combines the two time points.)

End point values	Placebo Twice Daily (BID)	Upadacitinib 3 mg BID	Upadacitinib 6 mg BID	Upadacitinib 12 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	15	21	18	17
Units: percentage of subjects				
number (not applicable)	0	0	11.1	5.9

End point values	Upadacitinib 24 mg BID	Upadacitinib 24 mg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15	10		
Units: percentage of subjects				
number (not applicable)	20.0	10.0		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo Twice Daily (BID) v Upadacitinib 6 mg BID
Number of subjects included in analysis	33
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.392 ^[64]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted risk difference from placebo
Point estimate	6.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-8.7
upper limit	22.2

Notes:

[64] - Based on CMH test stratified by baseline SES-CD (SES-CD <15 and SES-CD ≥15).

Statistical analysis title	Statistical Analysis 2
Comparison groups	Placebo Twice Daily (BID) v Upadacitinib 12 mg BID
Number of subjects included in analysis	32
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.584 ^[65]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted risk difference from placebo
Point estimate	3.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-8.8
upper limit	15.7

Notes:

[65] - Based on CMH test stratified by baseline SES-CD (SES-CD <15 and SES-CD ≥15).

Statistical analysis title	Statistical Analysis 3
Comparison groups	Placebo Twice Daily (BID) v Upadacitinib 24 mg BID
Number of subjects included in analysis	30
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.199 ^[66]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted risk difference from placebo
Point estimate	13
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.8
upper limit	32.9

Notes:

[66] - Based on CMH test stratified by baseline SES-CD (SES-CD <15 and SES-CD ≥15).

Statistical analysis title	Statistical Analysis 4
Comparison groups	Placebo Twice Daily (BID) v Upadacitinib 24 mg QD
Number of subjects included in analysis	25
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.439 ^[67]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted risk difference from placebo
Point estimate	6.9

Confidence interval	
level	95 %
sides	2-sided
lower limit	-10.6
upper limit	24.5

Notes:

[67] - Based on CMH test stratified by baseline SES-CD (SES-CD <15 and SES-CD ≥15).

Secondary: Change from Baseline in Fecal Calprotectin Level Over Time During the Induction Phase

End point title	Change from Baseline in Fecal Calprotectin Level Over Time During the Induction Phase
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End point description:

mITT Population: all randomized subjects who took at least 1 dose of study drug in the Induction Period. Includes only subjects with an assessment at Baseline and Week 16. n=subjects with an assessment at given time point.

End point type	Secondary
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End point timeframe:

Baseline, Week 4, Week 16

End point values	Placebo Twice Daily (BID)	Upadacitinib 3 mg BID	Upadacitinib 6 mg BID	Upadacitinib 12 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	28	26	31	28
Units: µg/g				
arithmetic mean (standard deviation)				
Week 4; n=28, 26, 31, 28, 25, 26	83.7 (± 1024.11)	-310.3 (± 2415.43)	-436.9 (± 1505.75)	-915.7 (± 1600.31)
Week 16; n=18, 21, 21, 19, 12, 19	-128.9 (± 373.53)	-534.5 (± 3279.19)	-429.4 (± 2505.21)	-475.1 (± 2668.93)

End point values	Upadacitinib 24 mg BID	Upadacitinib 24 mg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	25	26		
Units: µg/g				
arithmetic mean (standard deviation)				
Week 4; n=28, 26, 31, 28, 25, 26	-876.2 (± 2240.93)	-255.8 (± 2407.47)		
Week 16; n=18, 21, 21, 19, 12, 19	-828.7 (± 986.09)	-698.4 (± 2228.85)		

Attachments (see zip file)	Table 14.2_1.23.1 stat analysis.docx
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Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in High-Sensitivity C-Reactive Protein (hs-CRP) at Week 16

End point title	Change from Baseline in High-Sensitivity C-Reactive Protein (hs-CRP) at Week 16
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End point description:

mITT Population: all randomized subjects who took at least 1 dose of study drug in the Induction Period. Includes only subjects with an assessment at Baseline and Week 16.

End point type	Secondary
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End point timeframe:

Baseline, Week 16

End point values	Placebo Twice Daily (BID)	Upadacitinib 3 mg BID	Upadacitinib 6 mg BID	Upadacitinib 12 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	29	35	34	31
Units: mg/L				
arithmetic mean (standard deviation)	-0.1 (± 11.96)	-3.0 (± 19.60)	-3.9 (± 19.47)	-6.1 (± 27.02)

End point values	Upadacitinib 24 mg BID	Upadacitinib 24 mg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	27	32		
Units: mg/L				
arithmetic mean (standard deviation)	-14.8 (± 26.38)	-2.7 (± 13.74)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo Twice Daily (BID) v Upadacitinib 3 mg BID
Number of subjects included in analysis	64
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.921 ^[68]
Method	repeated measure model
Parameter estimate	LS Mean Difference
Point estimate	0.5

Confidence interval	
level	95 %
sides	2-sided
lower limit	-9.02
upper limit	9.97

Notes:

[68] - P value for test of difference using the repeated measure model including treatment, Baseline disease severity (SES-CD < 15 and ≥ 15), week, Baseline, interaction of treatment and week. Statistical significance was prespecified at $\alpha = 0.1$.

Statistical analysis title	Statistical Analysis 2
Comparison groups	Placebo Twice Daily (BID) v Upadacitinib 6 mg BID
Number of subjects included in analysis	63
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.75 ^[69]
Method	repeated measure model
Parameter estimate	LS Mean Difference
Point estimate	-1.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-11.19
upper limit	8.08

Notes:

[69] - P value for test of difference using the repeated measure model including treatment, Baseline disease severity (SES-CD < 15 and ≥ 15), week, Baseline, interaction of treatment and week. Statistical significance was prespecified at $\alpha = 0.1$.

Statistical analysis title	Statistical Analysis 3
Comparison groups	Placebo Twice Daily (BID) v Upadacitinib 12 mg BID
Number of subjects included in analysis	60
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7 ^[70]
Method	repeated measure model
Parameter estimate	LS Mean Difference
Point estimate	-1.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-11.7
upper limit	7.87

Notes:

[70] - P value for test of difference using the repeated measure model including treatment, Baseline disease severity (SES-CD < 15 and ≥ 15), week, Baseline, interaction of treatment and week. Statistical significance was prespecified at $\alpha = 0.1$.

Statistical analysis title	Statistical Analysis 4
Comparison groups	Placebo Twice Daily (BID) v Upadacitinib 24 mg BID

Number of subjects included in analysis	56
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.024 ^[71]
Method	repeated measure model
Parameter estimate	LS Mean Difference
Point estimate	-11.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-21.38
upper limit	-1.51

Notes:

[71] - P value for test of difference using the repeated measure model including treatment, Baseline disease severity (SES-CD < 15 and ≥ 15), week, Baseline, interaction of treatment and week. Statistical significance was prespecified at $\alpha = 0.1$.

Statistical analysis title	Statistical Analysis 5
Comparison groups	Placebo Twice Daily (BID) v Upadacitinib 24 mg QD
Number of subjects included in analysis	61
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.845 ^[72]
Method	repeated measure model
Parameter estimate	LS Mean Difference
Point estimate	-1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-10.72
upper limit	8.79

Notes:

[72] - P value for test of difference using the repeated measure model including treatment, Baseline disease severity (SES-CD < 15 and ≥ 15), week, Baseline, interaction of treatment and week. Statistical significance was prespecified at $\alpha = 0.1$.

Secondary: Change From Baseline in Inflammatory Bowel Disease Questionnaire (IBDQ) Over Time During the Induction Phase

End point title	Change From Baseline in Inflammatory Bowel Disease Questionnaire (IBDQ) Over Time During the Induction Phase
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End point description:

The IBDQ is a disease-specific instrument composed of 32 Likert-scaled items. The total score ranges from 32 to 224 using the 7-point response options, with higher scores indicating better health-related quality of life. The IBDQ scale contains 4 component subscales: bowel symptoms, systemic symptoms, emotional function, and social function. Each subscale can be computed with total scores ranging from 10 to 70, 5 to 35, 12 to 84, and 5 to 35, respectively.

mITT Population: all randomized subjects who took at least 1 dose of study drug in the Induction Period. Includes only subjects with an assessment at Baseline and Week 16. n=number of subjects with an assessment at given time point.

End point type	Secondary
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End point timeframe:

Baseline, Week 8, Week 16

End point values	Placebo Twice Daily (BID)	Upadacitinib 3 mg BID	Upadacitinib 6 mg BID	Upadacitinib 12 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	33	36	35	34
Units: units on a scale				
arithmetic mean (standard deviation)				
Week 8; n=33, 36, 35, 34, 31, 33	16.6 (± 25.38)	18.9 (± 40.35)	34.6 (± 36.22)	24.9 (± 30.95)
Week 16; n=29, 35, 33, 28, 29, 32	14.5 (± 29.15)	24.6 (± 42.98)	41.8 (± 47.02)	32.1 (± 38.57)

End point values	Upadacitinib 24 mg BID	Upadacitinib 24 mg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	31	33		
Units: units on a scale				
arithmetic mean (standard deviation)				
Week 8; n=33, 36, 35, 34, 31, 33	39.7 (± 40.76)	23.3 (± 30.34)		
Week 16; n=29, 35, 33, 28, 29, 32	44.4 (± 40.05)	22.5 (± 27.82)		

Attachments (see zip file)	Table 14.2_1.25.1 stat analysis.docx
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Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Isolated Ileal Crohn's Disease at Baseline Who Achieve Remission at Week 16

End point title	Percentage of Subjects With Isolated Ileal Crohn's Disease at Baseline Who Achieve Remission at Week 16
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End point description:

Remission is defined as endoscopic remission AND clinical remission. Endoscopic remission: SES-CD $\leq$ 4 and at least 2-point reduction versus Baseline and no subscore $>$ 1 in any individual variable. Clinical remission: average daily stool frequency $\leq$ 1.5 and not worse than Baseline AND average daily abdominal pain $\leq$ 1.0 and not worse than Baseline. The very soft/liquid stool frequency and abdominal pain scores at a visit were the average of the daily values reported during the 7 usable days preceding the scheduled assessment visit. Abdominal Pain was rated on a 4-point scale from 0 (none) to 3 (severe). Details of the SES-CD scale are provided in the description of the first primary endpoint.

mITT Population: all randomized subjects who took at least 1 dose of study drug in the Induction Period. Only mITT subjects with isolated ileal Crohn's disease at Baseline are included. Non-responder imputation.

End point type	Secondary
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End point timeframe:

Week 16

End point values	Placebo Twice Daily (BID)	Upadacitinib 3 mg BID	Upadacitinib 6 mg BID	Upadacitinib 12 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	9	10	6	5
Units: percentage of subjects				
number (not applicable)	0	20.0	16.7	20.0

End point values	Upadacitinib 24 mg BID	Upadacitinib 24 mg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	10		
Units: percentage of subjects				
number (not applicable)	0	20.0		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo Twice Daily (BID) v Upadacitinib 3 mg BID
Number of subjects included in analysis	19
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.167 ^[73]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted risk difference from placebo
Point estimate	20
Confidence interval	
level	95 %
sides	2-sided
lower limit	-8.4
upper limit	48.4

Notes:

[73] - Based on CMH test stratified by baseline SES-CD (SES-CD <15 and SES-CD ≥15).

Statistical analysis title	Statistical Analysis 2
Comparison groups	Placebo Twice Daily (BID) v Upadacitinib 6 mg BID
Number of subjects included in analysis	15
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.221 ^[74]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted risk difference from placebo
Point estimate	16.7

Confidence interval	
level	95 %
sides	2-sided
lower limit	-10
upper limit	43.3

Notes:

[74] - Based on CMH test stratified by baseline SES-CD (SES-CD <15 and SES-CD ≥15).

Statistical analysis title	Statistical Analysis 3
Comparison groups	Placebo Twice Daily (BID) v Upadacitinib 12 mg BID
Number of subjects included in analysis	14
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.18 ^[75]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted risk difference from placebo
Point estimate	20
Confidence interval	
level	95 %
sides	2-sided
lower limit	-9.2
upper limit	49.2

Notes:

[75] - Based on CMH test stratified by baseline SES-CD (SES-CD <15 and SES-CD ≥15).

Statistical analysis title	Statistical Analysis 4
Comparison groups	Placebo Twice Daily (BID) v Upadacitinib 24 mg QD
Number of subjects included in analysis	19
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.167 ^[76]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted risk difference from placebo
Point estimate	20
Confidence interval	
level	95 %
sides	2-sided
lower limit	-8.4
upper limit	48.4

Notes:

[76] - Based on CMH test stratified by baseline SES-CD (SES-CD <15 and SES-CD ≥15).

Secondary: Percentage of Subjects With a Decrease in CDAI ≥ 100 Points From Baseline at Week 16

End point title	Percentage of Subjects With a Decrease in CDAI ≥ 100 Points From Baseline at Week 16
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End point description:

CDAI is used to quantify the signs and symptoms of subjects with Crohn's disease. The score includes the frequency of stools, abdominal pain and general well-being as well as the presence of complications, use of antidiarrheals, presence of abdominal mass, hematocrit and weight. CDAI generally ranges from 0 to 600 where higher scores indicate more severe disease. A score below 150 indicates remission and a

score above 450 indicates very severe disease.

mITT Population: all randomized subjects who took at least 1 dose of study drug in the Induction Period.
Non-responder imputation.

End point type	Secondary
End point timeframe:	
Week 16	

End point values	Placebo Twice Daily (BID)	Upadacitinib 3 mg BID	Upadacitinib 6 mg BID	Upadacitinib 12 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	37	39	37	36
Units: percentage of subjects				
number (not applicable)	27.0	33.3	40.5	44.4

End point values	Upadacitinib 24 mg BID	Upadacitinib 24 mg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	36	35		
Units: percentage of subjects				
number (not applicable)	55.6	31.4		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo Twice Daily (BID) v Upadacitinib 3 mg BID
Number of subjects included in analysis	76
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.607 ^[77]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted risk difference from placebo
Point estimate	5.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-15.5
upper limit	26.5

Notes:

[77] - Based on CMH test stratified by baseline SES-CD (SES-CD <15 and SES-CD ≥15).

Statistical analysis title	Statistical Analysis 2
Comparison groups	Placebo Twice Daily (BID) v Upadacitinib 6 mg BID

Number of subjects included in analysis	74
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.272 ^[78]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted risk difference from placebo
Point estimate	12.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-9.6
upper limit	33.9

Notes:

[78] - Based on CMH test stratified by baseline SES-CD (SES-CD <15 and SES-CD ≥15).

Statistical analysis title	Statistical Analysis 3
Comparison groups	Placebo Twice Daily (BID) v Upadacitinib 12 mg BID
Number of subjects included in analysis	73
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.157 ^[79]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted risk difference from placebo
Point estimate	15.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.1
upper limit	37.9

Notes:

[79] - Based on CMH test stratified by baseline SES-CD (SES-CD <15 and SES-CD ≥15).

Statistical analysis title	Statistical Analysis 4
Comparison groups	Placebo Twice Daily (BID) v Upadacitinib 24 mg BID
Number of subjects included in analysis	73
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.017 ^[80]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted risk difference from placebo
Point estimate	27.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	4.9
upper limit	50.6

Notes:

[80] - Based on CMH test stratified by baseline SES-CD (SES-CD <15 and SES-CD ≥15).

Statistical analysis title	Statistical Analysis 5
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Comparison groups	Placebo Twice Daily (BID) v Upadacitinib 24 mg QD
Number of subjects included in analysis	72
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.798 ^[81]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted risk difference from placebo
Point estimate	2.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-18.4
upper limit	23.9

Notes:

[81] - Based on CMH test stratified by baseline SES-CD (SES-CD <15 and SES-CD ≥15).

Secondary: Percentage of Subjects Who Achieve > 50% Reduction From Baseline in SES-CD or Endoscopic Remission at Week 12/16

End point title	Percentage of Subjects Who Achieve > 50% Reduction From Baseline in SES-CD or Endoscopic Remission at Week 12/16
-----------------	--

End point description:

Endoscopic remission: SES-CD ≤ 4 and at least two point reduction versus Baseline and no subscore > 1 in any individual variable. Details of the SES-CD scale are provided in the description of the first primary endpoint.

mITT Population: all randomized subjects who took at least 1 dose of study drug in the Induction Period. Non-responder imputation.

End point type	Secondary
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End point timeframe:

Up to Week 16. (At Baseline, patients were allocated by randomization 1:1 to have their end of induction colonoscopy done at either Week 12 or Week 16; this endpoint combines the two time points.)

End point values	Placebo Twice Daily (BID)	Upadacitinib 3 mg BID	Upadacitinib 6 mg BID	Upadacitinib 12 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	37	39	37	36
Units: percentage of subjects				
number (not applicable)	2.7	12.8	18.9	25.0

End point values	Upadacitinib 24 mg BID	Upadacitinib 24 mg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	36	35		
Units: percentage of subjects				
number (not applicable)	36.1	25.7		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo Twice Daily (BID) v Upadacitinib 3 mg BID
Number of subjects included in analysis	76
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.119 ^[82]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted risk difference from placebo
Point estimate	9.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.5
upper limit	22.1

Notes:

[82] - Based on CMH test stratified by baseline SES-CD (SES-CD <15 and SES-CD ≥15).

Statistical analysis title	Statistical Analysis 2
Comparison groups	Placebo Twice Daily (BID) v Upadacitinib 6 mg BID
Number of subjects included in analysis	74
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.034 ^[83]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted risk difference from placebo
Point estimate	15.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.1
upper limit	29.7

Notes:

[83] - Based on CMH test stratified by baseline SES-CD (SES-CD <15 and SES-CD ≥15).

Statistical analysis title	Statistical Analysis 3
Comparison groups	Placebo Twice Daily (BID) v Upadacitinib 12 mg BID

Number of subjects included in analysis	73
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.004 ^[84]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted risk difference from placebo
Point estimate	23.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	7.3
upper limit	39.2

Notes:

[84] - Based on CMH test stratified by baseline SES-CD (SES-CD <15 and SES-CD ≥15).

Statistical analysis title	Statistical Analysis 4
Comparison groups	Placebo Twice Daily (BID) v Upadacitinib 24 mg BID
Number of subjects included in analysis	73
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 ^[85]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted risk difference from placebo
Point estimate	32.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	14.2
upper limit	50.5

Notes:

[85] - Based on CMH test stratified by baseline SES-CD (SES-CD <15 and SES-CD ≥15).

Statistical analysis title	Statistical Analysis 5
Comparison groups	Placebo Twice Daily (BID) v Upadacitinib 24 mg QD
Number of subjects included in analysis	72
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.006 ^[86]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted risk difference from placebo
Point estimate	22.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	6.6
upper limit	39.2

Notes:

[86] - Based on CMH test stratified by baseline SES-CD (SES-CD <15 and SES-CD ≥15).

Secondary: Percentage of Subjects Who Achieve Modified Clinical Remission at

Week 16 Among Subjects With an Average Daily Stool Frequency ≥ 4.0 or Average Daily Abdominal Pain ≥ 2.0 at Baseline

End point title	Percentage of Subjects Who Achieve Modified Clinical Remission at Week 16 Among Subjects With an Average Daily Stool Frequency ≥ 4.0 or Average Daily Abdominal Pain ≥ 2.0 at Baseline
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End point description:

Modified clinical remission was defined as average daily stool frequency ≤ 2.8 and not worse than Baseline and average daily abdominal pain ≤ 1.0 and not worse than Induction Baseline. The very soft/liquid stool frequency and abdominal pain scores at a visit were the average of the daily values reported during the 7 usable days preceding the scheduled assessment visit. Abdominal Pain was rated on a 4-point scale from 0 (none) to 3 (severe).

mITT Population: all randomized subjects who took at least 1 dose of study drug in the Induction Period. Includes only mITT subjects with an average daily stool frequency ≥ 4.0 or average daily abdominal pain ≥ 2.0 at Baseline. Non-responder imputation.

End point type	Secondary
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End point timeframe:

Week 16

End point values	Placebo Twice Daily (BID)	Upadacitinib 3 mg BID	Upadacitinib 6 mg BID	Upadacitinib 12 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	33	38	33	34
Units: percentage of subjects				
number (not applicable)	12.1	15.8	30.3	26.5

End point values	Upadacitinib 24 mg BID	Upadacitinib 24 mg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	30	32		
Units: percentage of subjects				
number (not applicable)	36.7	18.8		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo Twice Daily (BID) v Upadacitinib 3 mg BID
Number of subjects included in analysis	71
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.647 ^[87]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted risk difference from placebo
Point estimate	3.9

Confidence interval	
level	95 %
sides	2-sided
lower limit	-12.7
upper limit	20.5

Notes:

[87] - Based on CMH test stratified by baseline SES-CD (SES-CD <15 and SES-CD ≥15).

Statistical analysis title	Statistical Analysis 2
Comparison groups	Placebo Twice Daily (BID) v Upadacitinib 6 mg BID
Number of subjects included in analysis	66
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.093 ^[88]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted risk difference from placebo
Point estimate	17.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.9
upper limit	37.1

Notes:

[88] - Based on CMH test stratified by baseline SES-CD (SES-CD <15 and SES-CD ≥15).

Statistical analysis title	Statistical Analysis 3
Comparison groups	Placebo Twice Daily (BID) v Upadacitinib 12 mg BID
Number of subjects included in analysis	67
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.165 ^[89]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted risk difference from placebo
Point estimate	13.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.6
upper limit	32.8

Notes:

[89] - Based on CMH test stratified by baseline SES-CD (SES-CD <15 and SES-CD ≥15).

Statistical analysis title	Statistical Analysis 4
Comparison groups	Placebo Twice Daily (BID) v Upadacitinib 24 mg BID

Number of subjects included in analysis	63
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.023 ^[90]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted risk difference from placebo
Point estimate	24.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	3.4
upper limit	46.3

Notes:

[90] - Based on CMH test stratified by baseline SES-CD (SES-CD <15 and SES-CD ≥15).

Statistical analysis title	Statistical Analysis 5
Comparison groups	Placebo Twice Daily (BID) v Upadacitinib 24 mg QD
Number of subjects included in analysis	65
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.448 ^[91]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted risk difference from placebo
Point estimate	7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-11
upper limit	25

Notes:

[91] - Based on CMH test stratified by baseline SES-CD (SES-CD <15 and SES-CD ≥15).

Secondary: Change From Baseline in Abdominal Pain Rating Scale at Week 12

End point title	Change From Baseline in Abdominal Pain Rating Scale at Week 12
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End point description:

Abdominal pain was assessed on an abdominal pain rating scale, where subjects rated their average abdominal pain over the last 24 hours on a scale of 0 (none) to 10 (worst pain imaginable).

mITT Population: all randomized subjects who took at least 1 dose of study drug in the Induction Period. Includes only mITT subjects with an assessment at baseline and given time point. Non-responder imputation.

End point type	Secondary
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End point timeframe:

Baseline, Week 12

End point values	Placebo Twice Daily (BID)	Upadacitinib 3 mg BID	Upadacitinib 6 mg BID	Upadacitinib 12 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	30	35	34	27
Units: units on a scale				
arithmetic mean (standard deviation)	-1.1 (± 1.84)	-1.0 (± 2.61)	-2.6 (± 2.53)	-2.4 (± 3.17)

End point values	Upadacitinib 24 mg BID	Upadacitinib 24 mg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	29	30		
Units: units on a scale				
arithmetic mean (standard deviation)	-2.7 (± 2.52)	-1.0 (± 1.99)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo Twice Daily (BID) v Upadacitinib 3 mg BID
Number of subjects included in analysis	65
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.412 ^[92]
Method	repeated measure model
Parameter estimate	LS Mean Difference
Point estimate	0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.62
upper limit	1.5

Notes:

[92] - P value for test of difference using the repeated measure model including treatment, Baseline disease severity (SES-CD < 15 and ≥ 15), week, Baseline, interaction of treatment and week.

Statistical analysis title	Statistical Analysis 2
Comparison groups	Placebo Twice Daily (BID) v Upadacitinib 6 mg BID
Number of subjects included in analysis	64
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.01 ^[93]
Method	repeated measure model
Parameter estimate	LS Mean Difference
Point estimate	-1.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.47
upper limit	-0.34

Notes:

[93] - P value for test of difference using the repeated measure model including treatment, Baseline disease severity (SES-CD < 15 and ≥ 15), week, Baseline, interaction of treatment and week.

Statistical analysis title	Statistical Analysis 3
Comparison groups	Placebo Twice Daily (BID) v Upadacitinib 12 mg BID
Number of subjects included in analysis	57
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.082 ^[94]
Method	repeated measure model
Parameter estimate	LS Mean Difference
Point estimate	-1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.13
upper limit	0.13

Notes:

[94] - P value for test of difference using the repeated measure model including treatment, Baseline disease severity (SES-CD < 15 and ≥ 15), week, Baseline, interaction of treatment and week.

Statistical analysis title	Statistical Analysis 4
Comparison groups	Placebo Twice Daily (BID) v Upadacitinib 24 mg BID
Number of subjects included in analysis	59
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.004 ^[95]
Method	repeated measure model
Parameter estimate	LS Mean Difference
Point estimate	-1.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.73
upper limit	-0.52

Notes:

[95] - P value for test of difference using the repeated measure model including treatment, Baseline disease severity (SES-CD < 15 and ≥ 15), week, Baseline, interaction of treatment and week.

Statistical analysis title	Statistical Analysis 5
Comparison groups	Placebo Twice Daily (BID) v Upadacitinib 24 mg QD
Number of subjects included in analysis	60
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.766 ^[96]
Method	repeated measure model
Parameter estimate	LS Mean Difference
Point estimate	0.2

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.93
upper limit	1.26

Notes:

[96] - P value for test of difference using the repeated measure model including treatment, Baseline disease severity (SES-CD < 15 and ≥ 15), week, Baseline, interaction of treatment and week.

Secondary: Change From Baseline in Abdominal Pain Rating Scale at Week 16

End point title	Change From Baseline in Abdominal Pain Rating Scale at Week 16
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End point description:

Abdominal pain was assessed on an abdominal pain rating scale, where subjects rated their average abdominal pain over the last 24 hours on a scale of 0 (none) to 10 (worst pain imaginable).

mITT Population: all randomized subjects who took at least 1 dose of study drug in the Induction Period. Includes only mITT subjects with an assessment at Baseline and given time point. Non-responder imputation.

End point type	Secondary
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End point timeframe:

Baseline, Week 16

End point values	Placebo Twice Daily (BID)	Upadacitinib 3 mg BID	Upadacitinib 6 mg BID	Upadacitinib 12 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	28	34	33	26
Units: units on a scale				
arithmetic mean (standard deviation)	-0.9 (± 2.27)	-1.7 (± 3.02)	-2.8 (± 2.77)	-1.7 (± 2.86)

End point values	Upadacitinib 24 mg BID	Upadacitinib 24 mg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	28	28		
Units: units on a scale				
arithmetic mean (standard deviation)	-2.3 (± 2.42)	-1.4 (± 2.15)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo Twice Daily (BID) v Upadacitinib 3 mg BID

Number of subjects included in analysis	62
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.314 ^[97]
Method	mixed effect model repeated measure
Parameter estimate	LS Mean Difference
Point estimate	-0.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.75
upper limit	0.56

Notes:

[97] - P value for test of difference using the repeated measure model including treatment, Baseline disease severity (SES-CD < 15 and ≥ 15), week, Baseline, interaction of treatment and week.

Statistical analysis title	Statistical Analysis 2
Comparison groups	Placebo Twice Daily (BID) v Upadacitinib 6 mg BID
Number of subjects included in analysis	61
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.002 ^[98]
Method	mixed effect model repeated measure
Parameter estimate	LS Mean Difference
Point estimate	-1.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.01
upper limit	-0.68

Notes:

[98] - P value for test of difference using the repeated measure model including treatment, Baseline disease severity (SES-CD < 15 and ≥ 15), week, Baseline, interaction of treatment and week.

Statistical analysis title	Statistical Analysis 3
Comparison groups	Placebo Twice Daily (BID) v Upadacitinib 12 mg BID
Number of subjects included in analysis	54
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.255 ^[99]
Method	mixed effect model repeated measure
Parameter estimate	LS Mean Difference
Point estimate	-0.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.94
upper limit	0.52

Notes:

[99] - P value for test of difference using the repeated measure model including treatment, Baseline disease severity (SES-CD < 15 and ≥ 15), week, Baseline, interaction of treatment and week.

Statistical analysis title	Statistical Analysis 4
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Comparison groups	Placebo Twice Daily (BID) v Upadacitinib 24 mg BID
Number of subjects included in analysis	56
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.022 ^[100]
Method	mixed effect model repeated measure
Parameter estimate	LS Mean Difference
Point estimate	-1.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.61
upper limit	-0.2

Notes:

[100] - P value for test of difference using the repeated measure model including treatment, Baseline disease severity (SES-CD < 15 and ≥ 15), week, Baseline, interaction of treatment and week.

Statistical analysis title	Statistical Analysis 5
Comparison groups	Placebo Twice Daily (BID) v Upadacitinib 24 mg QD
Number of subjects included in analysis	56
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.239 ^[101]
Method	mixed effect model repeated measure
Parameter estimate	LS Mean Difference
Point estimate	-0.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.92
upper limit	0.48

Notes:

[101] - P value for test of difference using the repeated measure model including treatment, Baseline disease severity (SES-CD < 15 and ≥ 15), week, Baseline, interaction of treatment and week.

Secondary: Percentage of Subjects Who Achieve Remission at Week 52

End point title	Percentage of Subjects Who Achieve Remission at Week 52
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End point description:

Remission at Week 52 was defined as both endoscopic remission at Week 52 and clinical remission at Week 52. Endoscopic remission: SES-CD ≤ 4 and at least 2-point reduction versus Baseline and no subscore > 1 in any individual variable. Clinical remission: average daily stool frequency ≤ 1.5 and not worse than Baseline AND average daily abdominal pain ≤ 1.0 and not worse than Baseline. The very soft/liquid stool frequency and abdominal pain scores at a visit were the average of the daily values reported during the 7 usable days preceding the scheduled assessment visit. Abdominal Pain was rated on a 4-point scale from 0 (none) to 3 (severe). See SES-CD description details in the first primary endpoint description of this record.

Non responder imputation. n=total subjects, by Week 16 status (responder/non-responder).

End point type	Secondary
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End point timeframe:

Week 52

End point values	ITT: 3 mg BID, Upadacitinib in Induction	ITT: 6 mg BID, Upadacitinib at Induction	ITT: 12 mg BID, Upadacitinib at Induction	ITT: 24 mg QD, Upadacitinib at Induction
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	52	18	50	33
Units: percentage of subjects				
number (not applicable)				
Responders; n=20, 8, 16, 10, 1, 0, 0, 0	20.0	12.5	25.0	0
Non-responders; n=32, 10, 34, 23, 8, 5, 9, 4	0	0	2.9	13.0
Clinical responders; n=32, 14, 29, 19, 6, 1, 4, 1	12.5	7.1	13.8	15.8
Clinical non-responders; n=20, 4, 21, 14, 3, 4, 5, 3	0	0	1	0

End point values	ITT: 3 mg BID, Placebo in Induction	ITT: 6 mg BID, Placebo at Induction	ITT: 12 mg BID, Placebo at Induction	ITT: 24 mg QD, Placebo at Induction
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	9	5	9	4
Units: percentage of subjects				
number (not applicable)				
Responders; n=20, 8, 16, 10, 1, 0, 0, 0	0	0	0	0
Non-responders; n=32, 10, 34, 23, 8, 5, 9, 4	0	0	0	25.0
Clinical responders; n=32, 14, 29, 19, 6, 1, 4, 1	0	0	0	100
Clinical non-responders; n=20, 4, 21, 14, 3, 4, 5, 3	0	0	0	0

Attachments (see zip file)	Table 14.2_2.1.1.1 stat analysis.docx
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Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects Who Achieve Endoscopic Remission at Week 52

End point title	Percentage of Subjects Who Achieve Endoscopic Remission at Week 52
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End point description:

Endoscopic remission: SES-CD ≤ 4 and at least 2-point reduction versus Baseline and no subscore > 1 in any individual variable. Details of the SES-CD scale are provided in the description of the first primary endpoint.

Non responder imputation. n=total subjects, by Week 16 status (responder/non-responder).

End point type	Secondary
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End point timeframe:

Week 52

End point values	ITT: 3 mg BID, Upadacitinib in Induction	ITT: 6 mg BID, Upadacitinib at Induction	ITT: 12 mg BID, Upadacitinib at Induction	ITT: 24 mg QD, Upadacitinib at Induction
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	52	18	50	33
Units: percentage of subjects				
number (not applicable)				
Responders; n=20, 8, 16, 10, 1, 0, 0, 0	25.0	25.0	37.5	10.0
Non-responders; n=32, 10, 34, 23, 8, 5, 9, 4	3.1	10.0	8.8	17.4
Clinical responders; n=32, 14, 29, 19, 6, 1, 4, 1	15.6	21.4	24.1	26.3
Clinical non-responders; n=20, 4, 21, 14, 3, 4, 5, 3	5.0	0	9.5	0

End point values	ITT: 3 mg BID, Placebo in Induction	ITT: 6 mg BID, Placebo at Induction	ITT: 12 mg BID, Placebo at Induction	ITT: 24 mg QD, Placebo at Induction
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	9	5	9	4
Units: percentage of subjects				
number (not applicable)				
Responders; n=20, 8, 16, 10, 1, 0, 0, 0	0	0	0	0
Non-responders; n=32, 10, 34, 23, 8, 5, 9, 4	0	0	0	25.0
Clinical responders; n=32, 14, 29, 19, 6, 1, 4, 1	0	0	0	100
Clinical non-responders; n=20, 4, 21, 14, 3, 4, 5, 3	0	0	0	0

Attachments (see zip file)	Table 14.2_2.1.2.1 stat analysis.docx
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Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects Who Achieve Both Endoscopic Remission and Modified Clinical Remission at Week 52 Among Subjects With Daily Stool Frequency ≥ 4.0 or Daily Abdominal Pain ≥ 2.0 at Induction Baseline

End point title	Percentage of Subjects Who Achieve Both Endoscopic Remission and Modified Clinical Remission at Week 52 Among Subjects With Daily Stool Frequency ≥ 4.0 or Daily Abdominal Pain ≥ 2.0 at Induction Baseline
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End point description:

Endoscopic remission was defined as SES-CD ≤ 4 and at least 2 points reduction versus induction baseline and no subscore > 1 in any individual variable. Modified clinical remission was defined as average daily stool frequency ≤ 2.8 and not worse than induction baseline AND average daily

abdominal pain ≤ 1.0 and not worse than induction baseline. The very soft/liquid stool frequency and abdominal pain scores at a visit were the average of the daily values reported during the 7 usable days preceding the scheduled assessment visit. Abdominal Pain was rated on a 4-point scale from 0 (none) to 3 (severe). See SES-CD description details in the first primary endpoint description of this record.

Subjects from ITT population with daily stool frequency ≥ 4.0 or daily abdominal pain ≥ 2.0 at Induction Baseline. Non responder imputation. n=total subjects, by Week 16 status (responder/non-responder).

End point type	Secondary
End point timeframe:	
Week 52	

End point values	ITT: 3 mg BID, Upadacitinib in Induction	ITT: 6 mg BID, Upadacitinib at Induction	ITT: 12 mg BID, Upadacitinib at Induction	ITT: 24 mg QD, Upadacitinib at Induction
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	45	17	48	30
Units: percentage of subjects				
number (not applicable)				
Responders; n=17, 8, 15, 10, 1, 0, 0, 0	29.4	12.5	33.3	10.0
Non-responders; n=28, 9, 33, 20, 7, 5, 8, 4	0	0	6.1	15.0
Clinical responders; n=28, 14, 27, 18, 5, 1, 3, 1	17.9	7.1	22.2	22.2
Clinical non-responders; n=17, 3, 21, 12, 3, 4, 5, 3	0	0	4.8	0

End point values	ITT: 3 mg BID, Placebo in Induction	ITT: 6 mg BID, Placebo at Induction	ITT: 12 mg BID, Placebo at Induction	ITT: 24 mg QD, Placebo at Induction
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	8	5	8	4
Units: percentage of subjects				
number (not applicable)				
Responders; n=17, 8, 15, 10, 1, 0, 0, 0	0	0	0	0
Non-responders; n=28, 9, 33, 20, 7, 5, 8, 4	0	0	0	25.0
Clinical responders; n=28, 14, 27, 18, 5, 1, 3, 1	0	0	0	100
Clinical non-responders; n=17, 3, 21, 12, 3, 4, 5, 3	0	0	0	0

Attachments (see zip file)	Table 14.2_2.1.3.1 stat analysis.docx
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Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects Who Achieve Clinical Remission Over Time During Extension Phase

End point title	Percentage of Subjects Who Achieve Clinical Remission Over Time During Extension Phase
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End point description:

Clinical remission was defined as average daily stool frequency ≤ 1.5 and not worse than Induction Baseline and average daily abdominal pain ≤ 1.0 and not worse than Induction Baseline. The very soft/liquid stool frequency and abdominal pain scores at a visit were the average of the daily values reported during the 7 usable days preceding the scheduled assessment visit. Abdominal Pain was rated on a 4-point scale from 0 (none) to 3 (severe).

Non responder imputation. n=total subjects, by Week 16 status (responder/non-responder).

End point type	Secondary
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End point timeframe:

Week 20, Week 28, Week 36, Week 44, Week 52

End point values	ITT: 3 mg BID, Upadacitinib in Induction	ITT: 6 mg BID, Upadacitinib at Induction	ITT: 12 mg BID, Upadacitinib at Induction	ITT: 24 mg QD, Upadacitinib at Induction
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	52	18	50	33
Units: percentage of subjects				
number (not applicable)				
Responders, Week 20; n=20, 8, 16, 10	45.0	37.5	50.0	40.0
Responders, Week 28; n=20, 8, 16, 10	45.0	37.5	56.3	50.0
Responders, Week 36; n=20, 8, 16, 10	40.0	37.5	62.5	30.0
Responders, Week 44; n=20, 8, 16, 10	40.0	12.5	68.8	40.0
Responders, Week 52; n=20, 8, 16, 10	30.0	37.5	62.5	30.0
Non-responders, Week 20; n=32, 10, 34, 23	12.5	40.0	8.8	8.7
Non-responders, Week 28; n=32, 10, 34, 23	12.5	40.0	8.8	13.0
Non-responders, Week 36; n=32, 10, 34, 23	9.4	10.0	2.9	13.0
Non-responders, Week 44; n=32, 10, 34, 23	12.5	20.0	5.9	8.7
Non-responders, Week 52; n=32, 10, 34, 23	9.4	10.0	8.8	13.0
Clinical responders, Week 20; n=32, 14, 29, 19	40.6	50.0	37.9	31.6
Clinical responders, Week 28; n=32, 14, 29, 19	37.5	50.0	41.4	42.1
Clinical responders, Week 36; n=32, 14, 29, 19	34.4	28.6	37.9	31.6
Clinical responders, Week 44; n=32, 14, 29, 19	34.4	21.4	44.8	31.6
Clinical responders, Week 52; n=32, 14, 29, 19	25.0	28.6	41.4	31.6
Clinical non-responders, Week 20; n=20, 4, 21, 14	0	0	0	0
Clinical non-responders, Week 28; n=20, 4, 21, 14	5.0	0	0	0
Clinical non-responders, Week 36; n=20, 4, 21, 14	0	0	0	0

Clinical non-responders, Week 44; n=20, 4, 21, 14	5.0	0	0	0
Clinical non-responders, Week 52; n=20, 4, 21, 14	5.0	0	4.8	0

Attachments (see zip file)	Table 14.2_2.2.1 stat analysis.docx
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Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects Who Maintain Clinical Remission Over Time Among Subjects in Clinical Remission at Week 16

End point title	Percentage of Subjects Who Maintain Clinical Remission Over Time Among Subjects in Clinical Remission at Week 16
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End point description:

Clinical remission was defined as average daily stool frequency ≤ 1.5 and not worse than Induction Baseline and average daily abdominal pain ≤ 1.0 and not worse than Induction Baseline. The very soft/liquid stool frequency and abdominal pain scores at a visit were the average of the daily values reported during the 7 usable days preceding the scheduled assessment visit. Abdominal Pain was rated on a 4-point scale from 0 (none) to 3 (severe).

Subjects from ITT population in clinical remission at Week 16. Non responder imputation. n=total subjects, by Week 16 status (responder/nonresponder).

End point type	Secondary
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End point timeframe:

Week 20, Week 28, Week 36, Week 44, Week 52

End point values	ITT: 3 mg BID, Upadacitinib in Induction	ITT: 6 mg BID, Upadacitinib at Induction	ITT: 12 mg BID, Upadacitinib at Induction	ITT: 24 mg QD, Upadacitinib at Induction
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	13	6	9	4
Units: percentage of subjects				
number (not applicable)				
Responders, Week 20; n=10, 3, 7, 3	80.0	66.7	71.4	100
Responders, Week 28; n=10, 3, 7, 3	90.0	66.7	57.1	100
Responders, Week 36; n=10, 3, 7, 3	80.0	100	71.4	66.7
Responders, Week 44; n=10, 3, 7, 3	80.0	33.3	71.4	66.7
Responders, Week 52; n=10, 3, 7, 3	60.0	66.7	71.4	66.7
Non-responders, Week 20; n=3, 3, 2, 1	66.7	100	50.0	100
Non-responders, Week 28; n=3, 3, 2, 1	66.7	100	50.0	100
Non-responders, Week 36; n=3, 3, 2, 1	66.7	33.3	50.0	100
Non-responders, Week 44; n=3, 3, 2, 1	66.7	66.7	50.0	100
Non-responders, Week 52; n=3, 3, 2, 1	33.3	33.3	0	100
Clinical responders, Week 20; n=13, 6, 9, 4	76.9	83.3	66.7	100
Clinical responders, Week 28; n=13, 6, 9, 4	84.6	83.3	55.6	100

Clinical responders, Week 36; n=13, 6, 9, 4	76.9	66.7	66.7	75.0
Clinical responders, Week 44; n=13, 6, 9, 4	76.9	50.0	66.7	75.0
Clinical responders, Week 52; n=13, 6, 9, 4	53.8	50.0	55.6	75.0
Clinical non-responders, Week 20; n=0, 0, 0, 0	0	0	0	0
Clinical non-responders, Week 28; n=0, 0, 0, 0	0	0	0	0
Clinical non-responders, Week 36; n=0, 0, 0, 0	0	0	0	0
Clinical non-responders, Week 44; n=0, 0, 0, 0	0	0	0	0
Clinical non-responders, Week 52; n=0, 0, 0, 0	0	0	0	0

Attachments (see zip file)	Table 14.2_2.3.1 stat analysis.docx
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Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects Who Achieve Modified Clinical Remission Over Time During Extension Phase Among Subjects With Daily Stool Frequency ≥ 4.0 or Daily Abdominal Pain ≥ 2.0 at Induction Baseline

End point title	Percentage of Subjects Who Achieve Modified Clinical Remission Over Time During Extension Phase Among Subjects With Daily Stool Frequency ≥ 4.0 or Daily Abdominal Pain ≥ 2.0 at Induction Baseline
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End point description:

Modified clinical remission was defined as average daily stool frequency ≤ 2.8 and not worse than Induction Baseline and average daily abdominal pain ≤ 1.0 and not worse than Induction Baseline. The very soft/liquid stool frequency and abdominal pain scores at a visit were the average of the daily values reported during the 7 usable days preceding the scheduled assessment visit. Abdominal Pain was rated on a 4-point scale from 0 (none) to 3 (severe).

Subjects from ITT population with daily stool frequency ≥ 4.0 or daily abdominal pain ≥ 2.0 at Induction Baseline. Non responder imputation. n=total subjects, by Week 16 status (responder/nonresponder).

End point type	Secondary
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End point timeframe:

Week 20, Week 28, Week 36, Week 44, Week 52

End point values	ITT: 3 mg BID, Upadacitinib in Induction	ITT: 6 mg BID, Upadacitinib at Induction	ITT: 12 mg BID, Upadacitinib at Induction	ITT: 24 mg QD, Upadacitinib at Induction
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	22	17	48	30
Units: percentage of subjects				
number (not applicable)				

Responders: Week (Wk) 20; n=17, 8, 15, 10, 1, 0,0,0	47.1	62.5	66.7	60.0
Responders: Wk 28; n=17, 8, 15, 10, 1, 0, 0, 0	70.6	50.0	66.7	60.0
Responders: Wk 36; n=17, 8, 15, 10, 1, 0, 0, 0	58.8	87.5	73.3	30.0
Responders: Wk 44; n=17, 8, 15, 10, 1, 0, 0, 0	47.1	37.5	73.3	40.0
Responders: Wk 52; n=17, 8, 15, 10, 1, 0, 0, 0	41.2	62.5	73.3	40.0
Non-responders: Wk 20; n=28, 9, 33, 20, 7, 5, 8, 4	17.9	44.4	12.1	10.0
Non-responders: Wk 28; n=5, 9, 33, 20, 7, 5, 8, 4	21.4	44.4	9.1	15.0
Non-responders: Wk 36; n=5, 9, 33, 20, 7, 5, 8, 4	14.3	11.1	6.1	15.0
Non-responders: Wk 44; n=5, 9, 33, 20, 7, 5, 8, 4	14.3	22.2	6.1	10.0
Non-responders: Wk 52; n=5, 9, 33, 20, 7, 5, 8, 4	7.1	11.1	12.1	15.0
Clin. responders: Wk 20; n=28, 14, 27, 18, 5,1,3,1	42.9	64.3	51.9	44.4
Clin. responders: Wk 28; n=28, 14, 27, 18, 5,1,3,1	57.1	57.1	48.1	50.0
Clin. responders: Wk 36; n=28, 14, 27, 18, 5,1,3,1	46.4	57.1	48.1	33.3
Clin. responders: Wk 44; n=28, 14, 27, 18, 5,1,3,1	39.3	35.7	48.1	33.3
Clin. responders: Wk 52; n=28, 14, 27, 18, 5,1,3,1	28.6	42.9	51.9	38.9
Clin. non-responders: Wk 20; n=17,3,21,12,3,4,5,3	5.9	0	0	0
Clin. non-responders: Wk 28; n=1,3,21,12,3,4,5,3	11.8	0	0	0
Clin. non-responders: Wk 36; n=1,3,21,12,3,4,5,3	5.9	0	0	0
Clin. non-responders: Wk 44; n=1,3,21,12,3,4,5,3	5.9	0	0	0
Clin. non-responders: Wk 52; n=1,3,21,12,3,4,5,3	5.9	0	4.8	0

End point values	ITT: 3 mg BID, Placebo in Induction	ITT: 6 mg BID, Placebo at Induction	ITT: 12 mg BID, Placebo at Induction	ITT: 24 mg QD, Placebo at Induction
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	8	5	8	4
Units: percentage of subjects				
number (not applicable)				
Responders: Week (Wk) 20; n=17, 8, 15, 10, 1, 0,0,0	0	0	0	0
Responders: Wk 28; n=17, 8, 15, 10, 1, 0, 0, 0	0	0	0	0
Responders: Wk 36; n=17, 8, 15, 10, 1, 0, 0, 0	0	0	0	0
Responders: Wk 44; n=17, 8, 15, 10, 1, 0, 0, 0	0	0	0	0
Responders: Wk 52; n=17, 8, 15, 10, 1, 0, 0, 0	0	0	0	0

Non-responders: Wk 20; n=28, 9, 33, 20, 7, 5, 8, 4	42.9	20.0	25.0	25.0
Non-responders: Wk 28; n=5, 9, 33, 20, 7, 5, 8, 4	42.9	20.0	25.0	50.0
Non-responders: Wk 36; n=5, 9, 33, 20, 7, 5, 8, 4	57.1	20.0	25.0	25.0
Non-responders: Wk 44; n=5, 9, 33, 20, 7, 5, 8, 4	42.9	20.0	37.5	25.0
Non-responders: Wk 52; n=5, 9, 33, 20, 7, 5, 8, 4	28.6	0	37.5	50.0
Clin. responders: Wk 20; n=28, 14, 27, 18, 5,1,3,1	60.0	100	33.3	100
Clin. responders: Wk 28; n=28, 14, 27, 18, 5,1,3,1	60.0	100	33.3	100
Clin. responders: Wk 36; n=28, 14, 27, 18, 5,1,3,1	80.0	100	33.3	100
Clin. responders: Wk 44; n=28, 14, 27, 18, 5,1,3,1	60.0	100	33.3	100
Clin. responders: Wk 52; n=28, 14, 27, 18, 5,1,3,1	40.0	0	33.3	100
Clin. non-responders: Wk 20; n=17,3,21,12,3,4,5,3	0	0	20.0	0
Clin. non-responders: Wk 28; n=1,3,21,12,3,4,5,3	0	0	20.0	33.3
Clin. non-responders: Wk 36; n=1,3,21,12,3,4,5,3	0	0	20.0	0
Clin. non-responders: Wk 44; n=1,3,21,12,3,4,5,3	0	0	40.0	0
Clin. non-responders: Wk 52; n=1,3,21,12,3,4,5,3	0	0	40.0	33.3

Attachments (see zip file)	Table 14.2_2.4.1.1 stat analysis.docx
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Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects Who Achieve Modified Clinical Remission Over Time During Extension Phase Among Subjects In Modified Clinical Remission At Week 16 and Daily Stool Frequency ≥ 4.0 or Daily Abdominal Pain ≥ 2.0 at Induction Baseline

End point title	Percentage of Subjects Who Achieve Modified Clinical Remission Over Time During Extension Phase Among Subjects In Modified Clinical Remission At Week 16 and Daily Stool Frequency ≥ 4.0 or Daily Abdominal Pain ≥ 2.0 at Induction Baseline
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End point description:

Modified clinical remission was defined as average daily stool frequency ≤ 2.8 and not worse than Induction Baseline and average daily abdominal pain ≤ 1.0 and not worse than Induction Baseline. The very soft/liquid stool frequency and abdominal pain scores at a visit were the average of the daily values reported during the 7 usable days preceding the scheduled assessment visit. Abdominal Pain was rated on a 4-point scale from 0 (none) to 3 (severe).

Subjects from ITT population with modified clinical remission at Week 16 and daily stool frequency ≥ 4.0 or daily abdominal pain ≥ 2.0 at Induction Baseline. Non responder imputation. n=total subjects, by Week 16 status (responder/nonresponder).

End point type	Secondary
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End point timeframe:

Week 20, Week 28, Week 36, Week 44, Week 52

End point values	ITT: 3 mg BID, Upadacitinib in Induction	ITT: 6 mg BID, Upadacitinib at Induction	ITT: 12 mg BID, Upadacitinib at Induction	ITT: 24 mg QD, Upadacitinib at Induction
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	15	10	12	5
Units: percentage of subjects				
number (not applicable)				
Responders: Week (Wk) 20; n=12, 5, 10, 4, 0, 0,0,0	66.7	60.0	90.0	100
Responders: Wk 28; n=12, 5, 10, 4, 0, 0, 0, 0	91.7	60.0	90.0	100
Responders: Wk 36; n=12, 5, 10, 4, 0, 0, 0, 0	66.7	100	90.0	75.0
Responders: Wk 44; n=12, 5, 10, 4, 0, 0, 0, 0	66.7	40.0	90.0	75.0
Responders: Wk 52; n=12, 5, 10, 4, 0, 0, 0, 0	58.3	80.0	90.0	75.0
Non-responders: Wk 20; n=3, 5, 2, 1, 2, 0, 1, 1	66.7	80.0	50.0	100
Non-responders: Wk 28; n=3, 5, 2, 1, 2, 0, 1, 1	100	60.0	50.0	100
Non-responders: Wk 36; n=3, 5, 2, 1, 2, 0, 1, 1	66.7	20.0	50.0	100
Non-responders: Wk 44; n=3, 5, 2, 1, 2, 0, 1, 1	66.7	40.0	50.0	100
Non-responders: Wk 52; n=3, 5, 2, 1, 2, 0, 1, 1	33.3	20.0	50.0	100
Clin. responders: Wk 20; n=15, 10, 12, 5, 2, 0,1,1	66.7	70.0	83.3	100
Clin. responders: Wk 28; n=15, 10, 12, 5, 2, 0,1,1	93.3	60.0	83.3	100
Clin. responders: Wk 36; n=15, 10, 12, 5, 2, 0,1,1	66.7	60.0	83.3	80.0
Clin. responders: Wk 44; n=15, 10, 12, 5, 2, 0,1,1	66.7	40.0	83.3	80.0
Clin. responders: Wk 52; n=15, 10, 12, 5, 2, 0,1,1	53.3	50.0	83.3	80.0
Clin. non-responders: Wk 20; n=0, 0, 0, 0, 0,0,0,0	0	0	0	0
Clin. non-responders: Wk 28; n=0, 0, 0, 0, 0,0,0,0	0	0	0	0
Clin. non-responders: Wk 36; n=0, 0, 0, 0, 0,0,0,0	0	0	0	0
Clin. non-responders: Wk 44; n=0, 0, 0, 0, 0,0,0,0	0	0	0	0
Clin. non-responders: Wk 52; n=0, 0, 0, 0, 0,0,0,0	0	0	0	0

End point values	ITT: 3 mg BID, Placebo in	ITT: 6 mg BID, Placebo at	ITT: 12 mg BID, Placebo at	ITT: 24 mg QD, Placebo at
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	Induction	Induction	Induction	Induction
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	2	0 ^[102]	1	1
Units: percentage of subjects				
number (not applicable)				
Responders: Week (Wk) 20; n=12, 5, 10, 4, 0, 0,0,0	0		0	0
Responders: Wk 28; n=12, 5, 10, 4, 0, 0, 0, 0	0		0	0
Responders: Wk 36; n=12, 5, 10, 4, 0, 0, 0, 0	0		0	0
Responders: Wk 44; n=12, 5, 10, 4, 0, 0, 0, 0	0		0	0
Responders: Wk 52; n=12, 5, 10, 4, 0, 0, 0, 0	0		0	0
Non-responders: Wk 20; n=3, 5, 2, 1, 2, 0, 1, 1	100		100	100
Non-responders: Wk 28; n=3, 5, 2, 1, 2, 0, 1, 1	100		100	100
Non-responders: Wk 36; n=3, 5, 2, 1, 2, 0, 1, 1	100		100	100
Non-responders: Wk 44; n=3, 5, 2, 1, 2, 0, 1, 1	50.0		100	100
Non-responders: Wk 52; n=3, 5, 2, 1, 2, 0, 1, 1	50.0		100	100
Clin. responders: Wk 20; n=15, 10, 12, 5, 2, 0,1,1	100		100	100
Clin. responders: Wk 28; n=15, 10, 12, 5, 2, 0,1,1	100		100	100
Clin. responders: Wk 36; n=15, 10, 12, 5, 2, 0,1,1	100		100	100
Clin. responders: Wk 44; n=15, 10, 12, 5, 2, 0,1,1	50.0		100	100
Clin. responders: Wk 52; n=15, 10, 12, 5, 2, 0,1,1	50.0		100	100
Clin. non-responders: Wk 20; n=0, 0, 0, 0, 0,0,0,0	0		0	0
Clin. non-responders: Wk 28; n=0, 0, 0, 0, 0,0,0,0	0		0	0
Clin. non-responders: Wk 36; n=0, 0, 0, 0, 0,0,0,0	0		0	0
Clin. non-responders: Wk 44; n=0, 0, 0, 0, 0,0,0,0	0		0	0
Clin. non-responders: Wk 52; n=0, 0, 0, 0, 0,0,0,0	0		0	0

Notes:

[102] - no subjects met the criteria in this arm

Attachments (see zip file)	Table 14.2_2.5.1.1 stat analysis.docx
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Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects Who Achieve Response at Week 52

End point title	Percentage of Subjects Who Achieve Response at Week 52
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End point description:

Response at Week 52 was defined as both endoscopic response at Week 52 and clinical response at Week 52. Endoscopic response: SES-CD at least 25% reduction from Baseline. Clinical response: average daily stool frequency at least 30% reduction from Induction Baseline and average daily abdominal pain not worse than Induction Baseline OR average daily abdominal pain at least 30% reduction from Induction Baseline and average daily stool frequency not worse than Induction Baseline. The very soft/liquid stool frequency and abdominal pain scores at a visit were the average of the daily values reported during the 7 usable days preceding the scheduled assessment visit. Abdominal Pain was rated on a 4-point scale from 0 (none) to 3 (severe). Details of the SES-CD scale are provided in the description of the first primary endpoint.

Non responder imputation. n=total subjects, by Week 16 status (responder/non-responder).

End point type	Secondary
End point timeframe:	
Week 52	

End point values	ITT: 3 mg BID, Upadacitinib in Induction	ITT: 6 mg BID, Upadacitinib at Induction	ITT: 12 mg BID, Upadacitinib at Induction	ITT: 24 mg QD, Upadacitinib at Induction
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	52	18	50	33
Units: percentage of subjects				
number (not applicable)				
Responders; n=20, 8, 16, 10, 1, 0, 0, 0	50.0	62.5	68.8	40.0
Non-responders; n=32, 10, 34, 23, 8, 5, 9, 4	6.3	10.0	14.7	13.0
Clinical responders; n=32, 14, 29, 19, 6, 1, 4, 1	34.4	42.9	51.7	36.8
Clinical non-responders; n=20, 4, 21, 14, 3, 4, 5, 3	5.0	0	4.8	0

End point values	ITT: 3 mg BID, Placebo in Induction	ITT: 6 mg BID, Placebo at Induction	ITT: 12 mg BID, Placebo at Induction	ITT: 24 mg QD, Placebo at Induction
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	9	5	9	4
Units: percentage of subjects				
number (not applicable)				
Responders; n=20, 8, 16, 10, 1, 0, 0, 0	100	0	0	0
Non-responders; n=32, 10, 34, 23, 8, 5, 9, 4	0	20.0	22.2	25.0
Clinical responders; n=32, 14, 29, 19, 6, 1, 4, 1	16.7	0	0	100
Clinical non-responders; n=20, 4, 21, 14, 3, 4, 5, 3	0	25.0	40.0	0

Attachments (see zip file)	Table 14.2_2.6.1.1 stat analysis.docx
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Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With SES-CD ≤ 2 at Week 52

End point title	Percentage of Subjects With SES-CD ≤ 2 at Week 52
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End point description:

See SES-CD description details in the first primary endpoint description of this record.

Non responder imputation. n=total subjects, by Week 16 status (responder/non-responder).

End point type	Secondary
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End point timeframe:

Week 52

End point values	ITT: 3 mg BID, Upadacitinib in Induction	ITT: 6 mg BID, Upadacitinib at Induction	ITT: 12 mg BID, Upadacitinib at Induction	ITT: 24 mg QD, Upadacitinib at Induction
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	52	18	50	33
Units: percentage of subjects				
number (not applicable)				
Responders; n=20, 8, 16, 10, 1, 0, 0, 0	10.0	12.5	31.3	0
Non-responders; n=32, 10, 34, 23, 8, 5, 9, 4	6.3	0	8.8	8.7
Clinical responders; n=32, 14, 29, 19, 6, 1, 4, 1	6.3	7.1	20.7	10.5
Clinical non-responders;n=20, 4, 21, 14, 3, 4, 5,3	10.0	0	9.5	0

End point values	ITT: 3 mg BID, Placebo in Induction	ITT: 6 mg BID, Placebo at Induction	ITT: 12 mg BID, Placebo at Induction	ITT: 24 mg QD, Placebo at Induction
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	9	5	9	4
Units: percentage of subjects				
number (not applicable)				
Responders; n=20, 8, 16, 10, 1, 0, 0, 0	0	0	0	0
Non-responders; n=32, 10, 34, 23, 8, 5, 9, 4	0	0	0	25.0
Clinical responders; n=32, 14, 29, 19, 6, 1, 4, 1	0	0	0	100
Clinical non-responders;n=20, 4, 21, 14, 3, 4, 5,3	0	0	0	0

Attachments (see zip file)	Table 14.2_2.1.5.1 stat analysis.docx
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Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With SES-CD = 0 at Week 52

End point title	Percentage of Subjects With SES-CD = 0 at Week 52
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End point description:

See SES-CD description details in the first primary endpoint description of this record.

Non responder imputation. n=total subjects, by Week 16 status (responder/non-responder).

End point type	Secondary
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End point timeframe:

Week 52

End point values	ITT: 3 mg BID, Upadacitinib in Induction	ITT: 6 mg BID, Upadacitinib at Induction	ITT: 12 mg BID, Upadacitinib at Induction	ITT: 24 mg QD, Upadacitinib at Induction
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	52	18	50	33
Units: percentage of subjects				
number (not applicable)				
Responders; n=20, 8, 16, 10, 1, 0, 0, 0	10.0	12.5	31.3	0
Non-responders; n=32, 10, 34, 23, 8, 5, 9, 4	3.1	0	8.8	4.3
Clinical responders; n=32, 14, 29, 19, 6, 1, 4, 1	6.3	7.1	20.7	5.3
Clinical non-responders;n=20, 4, 21, 14, 3, 4, 5,3	5.0	0	9.5	0

End point values	ITT: 3 mg BID, Placebo in Induction	ITT: 6 mg BID, Placebo at Induction	ITT: 12 mg BID, Placebo at Induction	ITT: 24 mg QD, Placebo at Induction
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	9	5	9	4
Units: percentage of subjects				
number (not applicable)				
Responders; n=20, 8, 16, 10, 1, 0, 0, 0	0	0	0	0
Non-responders; n=32, 10, 34, 23, 8, 5, 9, 4	0	0	0	0
Clinical responders; n=32, 14, 29, 19, 6, 1, 4, 1	0	0	0	0
Clinical non-responders;n=20, 4, 21, 14, 3, 4, 5,3	0	0	0	0

Attachments (see zip file)	Table 14.2_2.1.7.1 stat analysis.docx
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Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects Who Achieve Endoscopic Response at Week 52

End point title	Percentage of Subjects Who Achieve Endoscopic Response at Week 52
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End point description:

Endoscopic response was defined as SES-CD at least 25% reduction from Induction Baseline. Details of the SES-CD scale are provided in the description of the first primary endpoint.

Non responder imputation. n=total subjects, by Week 16 status (responder/non-responder).

End point type	Secondary
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End point timeframe:

Week 52

End point values	ITT: 3 mg BID, Upadacitinib in Induction	ITT: 6 mg BID, Upadacitinib at Induction	ITT: 12 mg BID, Upadacitinib at Induction	ITT: 24 mg QD, Upadacitinib at Induction
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	52	18	50	33
Units: percentage of subjects				
number (not applicable)				
Responders; n=20, 8, 16, 10, 1, 0, 0, 0	60.0	75.0	75.0	40.0
Non-responders; n=32, 10, 34, 23, 8, 5, 9, 4	15.6	20.0	20.6	17.4
Clinical responders; n=32, 14, 29, 19, 6, 1, 4, 1	40.6	57.1	55.2	42.1
Clinical non-responders; n=20, 4, 21, 14, 3, 4, 5, 3	20.0	0	14.3	0

End point values	ITT: 3 mg BID, Placebo in Induction	ITT: 6 mg BID, Placebo at Induction	ITT: 12 mg BID, Placebo at Induction	ITT: 24 mg QD, Placebo at Induction
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	9	5	9	4
Units: percentage of subjects				
number (not applicable)				
Responders; n=20, 8, 16, 10, 1, 0, 0, 0	100	0	0	0
Non-responders; n=32, 10, 34, 23, 8, 5, 9, 4	0	20.0	22.2	25.0
Clinical responders; n=32, 14, 29, 19, 6, 1, 4, 1	16.7	0	0	100
Clinical non-responders; n=20, 4, 21, 14, 3, 4, 5, 3	0	25.0	40.0	0

Attachments (see zip file)	Table 14.2_2.6.3.1 stat analysis.docx
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Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects Who Achieve Enhanced Endoscopic Response at Week 52

End point title	Percentage of Subjects Who Achieve Enhanced Endoscopic Response at Week 52
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End point description:

Enhanced endoscopic response was defined as SES-CD reduction from Induction Baseline > 50% (or for an Induction Baseline SES-CD of 4, at least a 2 point reduction from Induction Baseline). Details of the SES-CD scale are provided in the description of the first primary endpoint.

Non responder imputation. n=total subjects, by Week 16 status (responder/non-responder).

End point type	Secondary
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End point timeframe:

Week 52

End point values	ITT: 3 mg BID, Upadacitinib in Induction	ITT: 6 mg BID, Upadacitinib at Induction	ITT: 12 mg BID, Upadacitinib at Induction	ITT: 24 mg QD, Upadacitinib at Induction
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	52	18	50	33
Units: percentage of subjects				
number (not applicable)				
Responders; n=20, 8, 16, 10, 1, 0, 0, 0	40.0	50.0	68.8	30.0
Non-responders; n=32, 10, 34, 23, 8, 5, 9, 4	12.5	0	11.8	17.4
Clinical responders; n=32, 14, 29, 19, 6, 1, 4, 1	28.1	28.6	44.8	36.8
Clinical non-responders; n=20, 4, 21, 14, 3, 4, 5, 3	15.0	0	9.5	0

End point values	ITT: 3 mg BID, Placebo in Induction	ITT: 6 mg BID, Placebo at Induction	ITT: 12 mg BID, Placebo at Induction	ITT: 24 mg QD, Placebo at Induction
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	9	5	9	4
Units: percentage of subjects				
number (not applicable)				
Responders; n=20, 8, 16, 10, 1, 0, 0, 0	100	0	0	0
Non-responders; n=32, 10, 34, 23, 8, 5, 9, 4	0	20.0	11.1	25.0
Clinical responders; n=32, 14, 29, 19, 6, 1, 4, 1	16.7	0	0	100
Clinical non-responders; n=20, 4, 21, 14, 3, 4, 5, 3	0	25.0	20.0	0

Attachments (see zip file)	Table 14.2_2.6.5.1 stat analysis.docx
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Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects Who Achieve Endoscopic Improvement at Week 52

End point title	Percentage of Subjects Who Achieve Endoscopic Improvement at Week 52
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End point description:

Endoscopic Improvement: SES-CD reduction from Induction Baseline > 50% or endoscopic remission. Endoscopic remission was defined as SES-CD ≤ 4 and at least 2 points reduction versus Induction Baseline and no subscore > 1 in any individual variable. Details of the SES-CD scale are provided in the description of the first primary endpoint.

Non responder imputation. n=total subjects, by Week 16 status (responder/non-responder).

End point type	Secondary
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End point timeframe:

Week 52

End point values	ITT: 3 mg BID, Upadacitinib in Induction	ITT: 6 mg BID, Upadacitinib at Induction	ITT: 12 mg BID, Upadacitinib at Induction	ITT: 24 mg QD, Upadacitinib at Induction
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	52	18	50	33
Units: percentage of subjects				
number (not applicable)				
Responders; n=20, 8, 16, 10, 1, 0, 0, 0	50.0	50.0	68.8	30.0
Non-responders; n=32, 10, 34, 23, 8, 5, 9, 4	12.5	10.0	11.8	17.4
Clinical responders; n=32, 14, 29, 19, 6, 1, 4, 1	34.4	35.7	44.8	36.8
Clinical non-responders; n=20, 4, 21, 14, 3, 4, 5, 3	15.0	0	9.5	0

End point values	ITT: 3 mg BID, Placebo in Induction	ITT: 6 mg BID, Placebo at Induction	ITT: 12 mg BID, Placebo at Induction	ITT: 24 mg QD, Placebo at Induction
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	9	5	9	4
Units: percentage of subjects				
number (not applicable)				

Responders; n=20, 8, 16, 10, 1, 0, 0, 0	100	0	0	0
Non-responders; n=32, 10, 34, 23, 8, 5, 9, 4	0	20.0	11.1	25.0
Clinical responders; n=32, 14, 29, 19, 6, 1, 4, 1	16.7	0	0	100
Clinical non-responders; n=20, 4, 21, 14, 3, 4, 5, 3	0	25.0	20.0	0

Attachments (see zip file)	Table 14.2_2.7.1.1 stat analysis.docx
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Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects Who Achieve Endoscopic Healing at Week 52

End point title	Percentage of Subjects Who Achieve Endoscopic Healing at Week 52
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End point description:

Endoscopic healing was defined as SES-CD ulcerated surface subscore of 0 in subjects with SES-CD ulcerated surface subscore ≥ 1 at Induction Baseline. Details of the SES-CD scale are provided in the description of the first primary endpoint.

Non responder imputation. n=total subjects, by Week 16 status (responder/non-responder).

End point type	Secondary
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End point timeframe:

Week 52

End point values	ITT: 3 mg BID, Upadacitinib in Induction	ITT: 6 mg BID, Upadacitinib at Induction	ITT: 12 mg BID, Upadacitinib at Induction	ITT: 24 mg QD, Upadacitinib at Induction
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	52	18	50	33
Units: percentage of subjects				
number (not applicable)				
Responders; n=20, 8, 16, 10, 1, 0, 0, 0	15.0	25.0	50.0	0
Non-responders; n=32, 10, 34, 23, 8, 5, 9, 4	9.4	10.0	8.8	8.7
Clinical responders; n=32, 14, 29, 19, 6, 1, 4, 1	9.4	21.4	31.0	10.5
Clinical non-responders; n=20, 4, 21, 14, 3, 4, 5, 3	15.0	0	9.5	0

End point values	ITT: 3 mg BID, Placebo in Induction	ITT: 6 mg BID, Placebo at Induction	ITT: 12 mg BID, Placebo at Induction	ITT: 24 mg QD, Placebo at Induction
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	9	5	9	4

Units: percentage of subjects				
number (not applicable)				
Responders; n=20, 8, 16, 10, 1, 0, 0, 0	0	0	0	0
Non-responders; n=32, 10, 34, 23, 8, 5, 9, 4	0	20.0	0	0
Clinical responders; n=32, 14, 29, 19, 6, 1, 4, 1	0	0	0	0
Clinical non-responders; n=20, 4, 21, 14, 3, 4, 5, 3	0	25.0	0	0

Attachments (see zip file)	Table 14.2_2.6.7.1 stat analysis.docx
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Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects Who Achieve Clinical Response Over Time During Extension Phase

End point title	Percentage of Subjects Who Achieve Clinical Response Over Time During Extension Phase
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End point description:

Clinical response was defined as average daily stool frequency at least 30% reduction from Induction Baseline and average daily abdominal pain not worse than Induction Baseline OR average daily abdominal pain at least 30% reduction from Induction Baseline and average daily stool frequency not worse than Induction Baseline. The very soft/liquid stool frequency and abdominal pain scores at a visit were the average of the daily values reported during the 7 usable days preceding the scheduled assessment visit. Abdominal Pain was rated on a 4-point scale from 0 (none) to 3 (severe).

Non responder imputation. n=total subjects, by Week 16 status (responder/non-responder).

End point type	Secondary
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End point timeframe:

Week 20, Week 28, Week 36, Week 44, Week 52

End point values	ITT: 3 mg BID, Upadacitinib in Induction	ITT: 6 mg BID, Upadacitinib at Induction	ITT: 12 mg BID, Upadacitinib at Induction	ITT: 24 mg QD, Upadacitinib at Induction
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	52	18	50	33
Units: percentage of subjects				
number (not applicable)				
Responders: Week (Wk) 20; n=20, 8, 16, 10, 1,0,0,0	85.0	100	100	80.0
Responders: Wk 28; n=20, 8, 16, 10, 1,0,0,0	85.0	75.0	81.3	60.0
Responders: Wk 36; n=20, 8, 16, 10, 1,0,0,0	75.0	100	75.0	50.0
Responders: Wk 44; n=20, 8, 16, 10, 1,0,0,0	50.0	87.5	81.3	40.0
Responders: Wk 52; n=20, 8, 16, 10, 1,0,0,0	55.0	87.5	68.8	50.0

Non-responders: Wk 20; n=32, 10, 34, 23, 8, 5, 9,4	43.8	60.0	41.2	39.1
Non-responders: Wk 28; n=32, 10, 34, 23, 8, 5, 9,4	40.6	60.0	29.4	26.1
Non-responders: Wk 36; n=32, 10, 34, 23, 8, 5, 9,4	28.1	40.0	26.5	17.4
Non-responders: Wk 44; n=32, 10, 34, 23, 8, 5, 9,4	25.0	30.0	26.5	21.7
Non-responders: Wk 52; n=32, 10, 34, 23, 8, 5, 9,4	21.9	30.0	26.5	13.0
Clin. responders: Wk 20; n=32, 14, 29, 19, 6,1,4,1	78.1	100	93.1	78.9
Clin. responders: Wk 28; n=32, 14, 29, 19, 6,1,4,1	78.1	78.6	69.0	57.9
Clin. responders: Wk 36; n=32, 14, 29, 19, 6,1,4,1	65.6	78.6	65.5	47.4
Clin. responders: Wk 44; n=32, 14, 29, 19, 6,1,4,1	50.0	71.4	72.4	42.1
Clin. responders: Wk 52; n=32, 14, 29, 19, 6,1,4,1	50.0	71.4	62.1	42.1
Clin. non-responders: Wk 20; n=20, 4,21,14,3,4,5,3	30.0	0	14.3	14.3
Clin. non-responders: Wk 28; n=20, 4,21,14,3,4,5,3	25.0	25.0	14.3	7.1
Clin. non-responders: Wk 36; n=20, 4,21,14,3,4,5,3	15.0	25.0	9.5	0
Clin. non-responders: Wk 44; n=20, 4,21,14,3,4,5,3	10.0	0	4.8	7.1
Clin. non-responders: Wk 52; n=20, 4,21,14,3,4,5,3	10.0	0	9.5	0

End point values	ITT: 3 mg BID, Placebo in Induction	ITT: 6 mg BID, Placebo at Induction	ITT: 12 mg BID, Placebo at Induction	ITT: 24 mg QD, Placebo at Induction
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	9	5	9	4
Units: percentage of subjects				
number (not applicable)				
Responders: Week (Wk) 20; n=20, 8, 16, 10, 1,0,0,0	100	0	0	0
Responders: Wk 28; n=20, 8, 16, 10, 1,0,0,0	0	0	0	0
Responders: Wk 36; n=20, 8, 16, 10, 1,0,0,0	100	0	0	0
Responders: Wk 44; n=20, 8, 16, 10, 1,0,0,0	0	0	0	0
Responders: Wk 52; n=20, 8, 16, 10, 1,0,0,0	100	0	0	0
Non-responders: Wk 20; n=32, 10, 34, 23, 8, 5, 9,4	75.0	20.0	33.3	50.0
Non-responders: Wk 28; n=32, 10, 34, 23, 8, 5, 9,4	50.0	20.0	22.2	50.0
Non-responders: Wk 36; n=32, 10, 34, 23, 8, 5, 9,4	50.0	20.0	33.3	25.0
Non-responders: Wk 44; n=32, 10, 34, 23, 8, 5, 9,4	37.5	40.0	33.3	50.0
Non-responders: Wk 52; n=32, 10, 34, 23, 8, 5, 9,4	37.5	40.0	33.3	50.0

Clin. responders: Wk 20; n=32, 14, 29, 19, 6,1,4,1	100	100	25.0	100
Clin. responders: Wk 28; n=32, 14, 29, 19, 6,1,4,1	66.7	100	25.0	100
Clin. responders: Wk 36; n=32, 14, 29, 19, 6,1,4,1	83.3	100	25.0	100
Clin. responders: Wk 44; n=32, 14, 29, 19, 6,1,4,1	50.0	100	25.0	100
Clin. responders: Wk 52; n=32, 14, 29, 19, 6,1,4,1	66.7	100	25.0	100
Clin. non-responders: Wk 20; n=20, 4,21,14,3,4,5,3	33.3	0	40.0	33.3
Clin. non-responders: Wk 28; n=20, 4,21,14,3,4,5,3	0	0	20.0	33.3
Clin. non-responders: Wk 36; n=20, 4,21,14,3,4,5,3	0	0	40.0	0
Clin. non-responders: Wk 44; n=20, 4,21,14,3,4,5,3	0	25.0	40.0	33.3
Clin. non-responders: Wk 52; n=20, 4,21,14,3,4,5,3	0	25.0	40.0	33.3

Attachments (see zip file)	Table 14.2_2.8.1.1 stat analysis.docx
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Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects Who Achieve Enhanced Clinical Response Over Time During Extension Phase

End point title	Percentage of Subjects Who Achieve Enhanced Clinical Response Over Time During Extension Phase
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End point description:

Enhanced clinical response was defined as average daily stool frequency at least 60% reduction from Induction Baseline and average daily abdominal pain not worse than Induction Baseline OR average daily abdominal pain at least 35% reduction from Induction Baseline and average daily stool frequency not worse than Induction Baseline or modified clinical remission (average daily stool frequency ≤ 2.8 and not worse than Induction baseline AND average daily abdominal pain ≤ 1.0 and not worse than Induction baseline). The very soft/liquid stool frequency and abdominal pain scores at a visit were the average of the daily values reported during the 7 usable days preceding the scheduled assessment visit. Abdominal Pain was rated on a 4-point scale from 0 (none) to 3 (severe).

Non responder imputation. n=total subjects, by Week 16 status (responder/non-responder).

End point type	Secondary
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End point timeframe:

Week 20, Week 28, Week 36, Week 44, Week 52

End point values	ITT: 3 mg BID, Upadacitinib in Induction	ITT: 6 mg BID, Upadacitinib at Induction	ITT: 12 mg BID, Upadacitinib at Induction	ITT: 24 mg QD, Upadacitinib at Induction
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	52	18	50	33
Units: percentage of subjects				
number (not applicable)				
Responders: Week (Wk) 20; n=20, 8, 16, 10, 1,0,0,0	70.0	87.5	100	70.0
Responders: Wk 28; n=20, 8, 16, 10, 1,0,0,0	80.0	75.0	81.3	60.0
Responders: Wk 36; n=20, 8, 16, 10, 1,0,0,0	75.0	100	75.0	40.0
Responders: Wk 44; n=20, 8, 16, 10, 1,0,0,0	50.0	62.5	75.0	40.0
Responders: Wk 52; n=20, 8, 16, 10, 1,0,0,0	50.0	87.5	68.8	50.0
Non-responders: Wk 20; n=32, 10, 34, 23, 8, 5, 9,4	34.4	50.0	38.2	26.1
Non-responders: Wk 28; n=32, 10, 34, 23, 8, 5, 9,4	37.5	60.0	29.4	21.7
Non-responders: Wk 36; n=32, 10, 34, 23, 8, 5, 9,4	28.1	40.0	26.5	17.4
Non-responders: Wk 44; n=32, 10, 34, 23, 8, 5, 9,4	21.9	30.0	23.5	21.7
Non-responders: Wk 52; n=32, 10, 34, 23, 8, 5, 9,4	21.9	30.0	26.5	13.0
Clin. responders: Wk 20; n=32, 14, 29, 19, 6,1,4,1	62.5	85.7	93.1	63.2
Clin. responders: Wk 28; n=32, 14, 29, 19, 6,1,4,1	71.9	78.6	69.0	57.9
Clin. responders: Wk 36; n=32, 14, 29, 19, 6,1,4,1	65.6	78.6	65.5	42.1
Clin. responders: Wk 44; n=32, 14, 29, 19, 6,1,4,1	50.0	57.1	65.5	42.1
Clin. responders: Wk 52; n=32, 14, 29, 19, 6,1,4,1	46.9	71.4	62.1	42.1
Clin. non-responders: Wk 20; n=20, 4,21,14,3,4,5,3	25.0	0	9.5	7.1
Clin. non-responders: Wk 28; n=20, 4,21,14,3,4,5,3	25.0	25.0	14.3	0
Clin. non-responders: Wk 36; n=20, 4,21,14,3,4,5,3	15.0	25.0	9.5	0
Clin. non-responders: Wk 44; n=20, 4,21,14,3,4,5,3	5.0	0	4.8	7.1
Clin. non-responders: Wk 52; n=20, 4,21,14,3,4,5,3	10.0	0	9.5	0

End point values	ITT: 3 mg BID, Placebo in Induction	ITT: 6 mg BID, Placebo at Induction	ITT: 12 mg BID, Placebo at Induction	ITT: 24 mg QD, Placebo at Induction
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	9	5	9	4
Units: percentage of subjects				
number (not applicable)				

Responders: Week (Wk) 20; n=20, 8, 16, 10, 1,0,0,0	100	0	0	0
Responders: Wk 28; n=20, 8, 16, 10, 1,0,0,0	0	0	0	0
Responders: Wk 36; n=20, 8, 16, 10, 1,0,0,0	100	0	0	0
Responders: Wk 44; n=20, 8, 16, 10, 1,0,0,0	0	0	0	0
Responders: Wk 52; n=20, 8, 16, 10, 1,0,0,0	100	0	0	0
Non-responders: Wk 20; n=32, 10, 34, 23, 8, 5, 9,4	50.0	20.0	33.3	25.0
Non-responders: Wk 28; n=32, 10, 34, 23, 8, 5, 9,4	50.0	20.0	22.2	50.0
Non-responders: Wk 36; n=32, 10, 34, 23, 8, 5, 9,4	50.0	20.0	33.3	25.0
Non-responders: Wk 44; n=32, 10, 34, 23, 8, 5, 9,4	37.5	20.0	33.3	50.0
Non-responders: Wk 52; n=32, 10, 34, 23, 8, 5, 9,4	37.5	40.0	33.3	50.0
Clin. responders: Wk 20; n=32, 14, 29, 19, 6,1,4,1	83.3	100	25.0	100
Clin. responders: Wk 28; n=32, 14, 29, 19, 6,1,4,1	66.7	100	25.0	100
Clin. responders: Wk 36; n=32, 14, 29, 19, 6,1,4,1	83.3	100	25.0	100
Clin. responders: Wk 44; n=32, 14, 29, 19, 6,1,4,1	50.0	100	25.0	100
Clin. responders: Wk 52; n=32, 14, 29, 19, 6,1,4,1	66.7	100	25.0	100
Clin. non-responders: Wk 20; n=20, 4,21,14,3,4,5,3	0	0	40.0	0
Clin. non-responders: Wk 28; n=20, 4,21,14,3,4,5,3	0	0	20.0	33.3
Clin. non-responders: Wk 36; n=20, 4,21,14,3,4,5,3	0	0	40.0	0
Clin. non-responders: Wk 44; n=20, 4,21,14,3,4,5,3	0	0	40.0	33.3
Clin. non-responders: Wk 52; n=20, 4,21,14,3,4,5,3	0	25.0	40.0	33.3

Attachments (see zip file)	Table 14.2_2.8.3.1 stat analysis.docx
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Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects Who Achieve Enhanced Clinical Response Over Time During Extension Phase Among Subjects In Enhanced Clinical Response At Week 16

End point title	Percentage of Subjects Who Achieve Enhanced Clinical Response Over Time During Extension Phase Among Subjects In Enhanced Clinical Response At Week 16
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End point description:

Enhanced clinical response was defined as average daily stool frequency at least 60% reduction from Induction Baseline and average daily abdominal pain not worse than Induction Baseline or average daily abdominal pain at least 35% reduction from Induction Baseline and average daily stool frequency not

worse than Induction Baseline or modified clinical remission (average daily stool frequency ≤ 2.8 and not worse than Induction baseline AND average daily abdominal pain ≤ 1.0 and not worse than Induction baseline). The very soft/liquid stool frequency and abdominal pain scores at a visit were the average of the daily values reported during the 7 usable days preceding the scheduled assessment visit. Abdominal Pain was rated on a 4-point scale from 0 (none) to 3 (severe).

Subjects from ITT population with enhanced clinical response at Week 16. Non responder imputation. n=total subjects, by Week 16 status (responder/nonresponder).

End point type	Secondary
End point timeframe:	
Week 20, Week 28, Week 36, Week 44, Week 52	

End point values	ITT: 3 mg BID, Upadacitinib in Induction	ITT: 6 mg BID, Upadacitinib at Induction	ITT: 12 mg BID, Upadacitinib at Induction	ITT: 24 mg QD, Upadacitinib at Induction
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	30	13	28	16
Units: percentage of subjects				
number (not applicable)				
Responders: Week (Wk) 20; n=20, 7, 16, 9, 0,0,0,0	70.0	100	100	66.7
Responders: Wk 28; n=20, 7, 16, 9, 0,0,0,0	80.0	71.4	81.3	55.6
Responders: Wk 36; n=20, 7, 16, 9, 0,0,0,0	75.0	100	75.0	33.3
Responders: Wk 44; n=20, 7, 16, 9, 0,0,0,0	50.0	71.4	75.0	33.3
Responders: Wk 52; n=20, 7, 16, 9, 0,0,0,0	50.0	85.7	68.8	44.4
Non-responders: Wk 20; n=10, 6, 12, 7, 4, 1, 2, 1	50.0	83.3	83.3	57.1
Non-responders: Wk 28; n=10, 6, 12, 7, 4, 1, 2, 1	70.0	83.3	58.3	57.1
Non-responders: Wk 36; n=10, 6, 12, 7, 4, 1, 2, 1	50.0	50.0	58.3	57.1
Non-responders: Wk 44; n=10, 6, 12, 7, 4, 1, 2, 1	50.0	50.0	58.3	57.1
Non-responders: Wk 52; n=10, 6, 12, 7, 4, 1, 2, 1	40.0	50.0	58.3	42.9
Clin. responders: Wk 20; n=30, 13, 28, 15, 4,1,2,1	63.3	92.3	92.9	66.7
Clin. responders: Wk 28; n=30, 13, 28, 15, 4,1,2,1	76.7	76.9	71.4	60.0
Clin. responders: Wk 36; n=30, 13, 28, 15, 4,1,2,1	66.7	76.9	67.9	46.7
Clin. responders: Wk 44; n=30, 13, 28, 15, 4,1,2,1	50.0	61.5	67.9	46.7
Clin. responders: Wk 52; n=30, 13, 28, 15, 4,1,2,1	46.7	69.2	64.3	46.7
Clin. non-responders: Wk 20; n=0, 0, 0, 1, 0,0,0,0	0	0	0	0
Clin. non-responders: Wk 28; n=0, 0, 0, 1, 0,0,0,0	0	0	0	0
Clin. non-responders: Wk 36; n=0, 0, 0, 1, 0,0,0,0	0	0	0	0
Clin. non-responders: Wk 44; n=0, 0, 0, 1, 0,0,0,0	0	0	0	0

Clin. non-responders: Wk 52; n=0, 0, 0, 1, 0,0,0,0	0	0	0	0
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End point values	ITT: 3 mg BID, Placebo in Induction	ITT: 6 mg BID, Placebo at Induction	ITT: 12 mg BID, Placebo at Induction	ITT: 24 mg QD, Placebo at Induction
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	4	1	2	1
Units: percentage of subjects				
number (not applicable)				
Responders: Week (Wk) 20; n=20, 7, 16, 9, 0,0,0,0	0	0	0	0
Responders: Wk 28; n=20, 7, 16, 9, 0,0,0,0	0	0	0	0
Responders: Wk 36; n=20, 7, 16, 9, 0,0,0,0	0	0	0	0
Responders: Wk 44; n=20, 7, 16, 9, 0,0,0,0	0	0	0	0
Responders: Wk 52; n=20, 7, 16, 9, 0,0,0,0	0	0	0	0
Non-responders: Wk 20; n=10, 6, 12, 7, 4, 1, 2, 1	100	100	50.0	100
Non-responders: Wk 28; n=10, 6, 12, 7, 4, 1, 2, 1	100	100	50.0	100
Non-responders: Wk 36; n=10, 6, 12, 7, 4, 1, 2, 1	100	100	50.0	100
Non-responders: Wk 44; n=10, 6, 12, 7, 4, 1, 2, 1	75.0	100	50.0	100
Non-responders: Wk 52; n=10, 6, 12, 7, 4, 1, 2, 1	75.0	100	50.0	100
Clin. responders: Wk 20; n=30, 13, 28, 15, 4,1,2,1	100	100	50.0	100
Clin. responders: Wk 28; n=30, 13, 28, 15, 4,1,2,1	100	100	50.0	100
Clin. responders: Wk 36; n=30, 13, 28, 15, 4,1,2,1	100	100	50.0	100
Clin. responders: Wk 44; n=30, 13, 28, 15, 4,1,2,1	75.0	100	50.0	100
Clin. responders: Wk 52; n=30, 13, 28, 15, 4,1,2,1	75.0	100	50.0	100
Clin. non-responders: Wk 20; n=0, 0, 0, 1, 0,0,0,0	0	0	0	0
Clin. non-responders: Wk 28; n=0, 0, 0, 1, 0,0,0,0	0	0	0	0
Clin. non-responders: Wk 36; n=0, 0, 0, 1, 0,0,0,0	0	0	0	0
Clin. non-responders: Wk 44; n=0, 0, 0, 1, 0,0,0,0	0	0	0	0
Clin. non-responders: Wk 52; n=0, 0, 0, 1, 0,0,0,0	0	0	0	0

Attachments (see zip file)	Table 14.2_2.9.1.1 stat analysis.docx
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Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects Who Achieve Clinical Remission Over Time During Extension Phase Among Subjects With an Average Daily Stool Frequency ≥ 2.5 and Average Daily Abdominal Pain ≥ 2.0 at Induction Baseline

End point title	Percentage of Subjects Who Achieve Clinical Remission Over Time During Extension Phase Among Subjects With an Average Daily Stool Frequency ≥ 2.5 and Average Daily Abdominal Pain ≥ 2.0 at Induction Baseline
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End point description:

Clinical remission was defined as average daily stool frequency ≤ 1.5 and not worse than Induction Baseline AND average daily abdominal pain ≤ 1.0 and not worse than Induction Baseline. The very soft/liquid stool frequency and abdominal pain scores at a visit were the average of the daily values reported during the 7 usable days preceding the scheduled assessment visit. Abdominal Pain was rated on a 4-point scale from 0 (none) to 3 (severe).

Subjects from ITT population with mean average daily stool frequency ≥ 2.5 and average daily abdominal pain ≥ 2.0 at Induction Baseline. Non responder imputation. n=total subjects, by Week 16 status (responder/nonresponder).

End point type	Secondary
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End point timeframe:

Week 20, Week 28, Week 36, Week 44, Week 52

End point values	ITT: 3 mg BID, Upadacitinib in Induction	ITT: 6 mg BID, Upadacitinib at Induction	ITT: 12 mg BID, Upadacitinib at Induction	ITT: 24 mg QD, Upadacitinib at Induction
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	23	11	23	14
Units: percentage of subjects				
number (not applicable)				
Responders: Week 20; n=9, 6, 8, 5	44.4	16.7	37.5	20.0
Responders: Week 28; n=9, 6, 8, 5	55.6	16.7	50.0	40.0
Responders: Week 36; n=9, 6, 8, 5	44.4	16.7	50.0	20.0
Responders: Week 44; n=9, 6, 8, 5	44.4	0	50.0	40.0
Responders: Week 52; n=9, 6, 8, 5	33.3	33.3	50.0	20.0
Non-responders: Week 20; n=14, 5, 15, 9	21.4	40.0	6.7	11.1
Non-responders: Week 28; n=14, 5, 15, 9	21.4	40.0	6.7	22.2
Non-responders: Week 36; n=14, 5, 15, 9	21.4	20.0	0	22.2
Non-responders: Week 44; n=14, 5, 15, 9	14.3	20.0	6.7	11.1
Non-responders: Week 52; n=14, 5, 15, 9	7.1	20.0	13.3	22.2
Clinical responders: Week 20; n=17, 10, 15, 9	41.2	30.0	26.7	22.2
Clinical responders: Week 28; n=17, 10, 15, 9	47.1	30.0	33.3	44.4
Clinical responders: Week 36; n=17, 10, 15, 9	41.2	20.0	26.7	33.3
Clinical responders: Week 44; n=17, 10, 15, 9	35.3	10.0	33.3	33.3

Clinical responders: Week 52; n=17, 10, 15, 9	23.5	30.0	40.0	33.3
Clinical non-responders: Week 20; n=6, 1, 8, 5	0	0	0	0
Clinical non-responders: Week 28; n=6, 1, 8, 5	0	0	0	0
Clinical non-responders: Week 36; n=6, 1, 8, 5	0	0	0	0
Clinical non-responders: Week 44; n=6, 1, 8, 5	0	0	0	0
Clinical non-responders: Week 52; n=6, 1, 8, 5	0	0	0	0

Attachments (see zip file)	Table 14.2_2.9.3.1 stat analysis.docx
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Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects Taking Corticosteroids at Induction Baseline Who Discontinued Corticosteroid Use and Achieve CDAI < 150 Over Time

End point title	Percentage of Subjects Taking Corticosteroids at Induction Baseline Who Discontinued Corticosteroid Use and Achieve CDAI < 150 Over Time
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End point description:

CDAI is used to quantify the signs and symptoms of subjects with Crohn's disease. The score includes the frequency of stools, abdominal pain and general well-being as well as the presence of complications, use of antidiarrheals, presence of abdominal mass, hematocrit and weight. CDAI generally ranges from 0 to 600 where higher scores indicate more severe disease. A score below 150 indicates remission.

Subjects from ITT population taking corticosteroids at Induction Baseline. Non responder imputation. n=total subjects, by Week 16 status (responder/nonresponder).

End point type	Secondary
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End point timeframe:

Week 20, Week 28, Week 36, Week 44, Week 52

End point values	ITT: 3 mg BID, Upadacitinib in Induction	ITT: 6 mg BID, Upadacitinib at Induction	ITT: 12 mg BID, Upadacitinib at Induction	ITT: 24 mg QD, Upadacitinib at Induction
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	23	7	20	14
Units: percentage of subjects				
number (not applicable)				
Responders: Week (Wk) 20; n=8, 2, 8, 5, 0, 0, 0, 0	50.0	50.0	75.0	0
Responders: Wk 28; n=8, 2, 8, 5, 0, 0, 0, 0	50.0	50.0	50.0	20.0
Responders: Wk 36; n=8, 2, 8, 5, 0, 0, 0, 0	50.0	100	50.0	0
Responders: Wk 44; n=8, 2, 8, 5, 0, 0, 0, 0	37.5	50.0	50.0	20.0

Responders: Wk 52; n=8, 2, 8, 5, 0, 0, 0, 0	50.0	100	62.5	0
Non-responders: Wk 20; n=15, 5, 12, 9, 5, 0, 3, 3	13.3	40.0	8.3	0
Non-responders: Wk 28; n=15, 5, 12, 9, 5, 0, 3, 3	6.7	40.0	16.7	11.1
Non-responders: Wk 36; n=15, 5, 12, 9, 5, 0, 3, 3	13.3	40.0	8.3	11.1
Non-responders: Wk 44; n=15, 5, 12, 9, 5, 0, 3, 3	26.7	40.0	25.0	11.1
Non-responders: Wk 52; n=15, 5, 12, 9, 5, 0, 3, 3	20.0	40.0	25.0	11.1
Clinical responders: Wk 20; n=15, 6, 14, 8, 2, 0, 1, 0	40.0	50.0	50.0	0
Clinical responders: Wk 28; n=15, 6, 14, 8, 2, 0, 1, 0	33.3	50.0	42.9	25.0
Clinical responders: Wk 36; n=15, 6, 14, 8, 2, 0, 1, 0	40.0	66.7	35.7	12.5
Clinical responders: Wk 44; n=15, 6, 14, 8, 2, 0, 1, 0	40.0	50.0	50.0	25.0
Clinical responders: Wk 52; n=15, 6, 14, 8, 2, 0, 1, 0	46.7	66.7	57.1	12.5
Clinical non-responders: Wk 20; n=8, 1, 6, 6, 3, 0, 2, 3	0	0	0	0
Clinical non-responders: Wk 28; n=8, 1, 6, 6, 3, 0, 2, 3	0	0	0	0
Clinical non-responders: Wk 36; n=8, 1, 6, 6, 3, 0, 2, 3	0	0	0	0
Clinical non-responders: Wk 44; n=8, 1, 6, 6, 3, 0, 2, 3	12.5	0	0	0
Clinical non-responders: Wk 52; n=8, 1, 6, 6, 3, 0, 2, 3	0	0	0	0

End point values	ITT: 3 mg BID, Placebo in Induction	ITT: 6 mg BID, Placebo at Induction	ITT: 12 mg BID, Placebo at Induction	ITT: 24 mg QD, Placebo at Induction
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	5	0 ^[103]	3	3
Units: percentage of subjects				
number (not applicable)				
Responders: Week (Wk) 20; n=8, 2, 8, 5, 0, 0, 0, 0	0		0	0
Responders: Wk 28; n=8, 2, 8, 5, 0, 0, 0, 0	0		0	0
Responders: Wk 36; n=8, 2, 8, 5, 0, 0, 0, 0	0		0	0
Responders: Wk 44; n=8, 2, 8, 5, 0, 0, 0, 0	0		0	0
Responders: Wk 52; n=8, 2, 8, 5, 0, 0, 0, 0	0		0	0
Non-responders: Wk 20; n=15, 5, 12, 9, 5, 0, 3, 3	0		0	0
Non-responders: Wk 28; n=15, 5, 12, 9, 5, 0, 3, 3	0		0	0
Non-responders: Wk 36; n=15, 5, 12, 9, 5, 0, 3, 3	0		0	0
Non-responders: Wk 44; n=15, 5, 12, 9, 5, 0, 3, 3	0		0	0

Non-responders: Wk 52; n=15, 5, 12, 9, 5, 0, 3, 3	0		0	0
Clinical responders: Wk 20; n=15, 6, 14, 8,2,0,1,0	0		0	0
Clinical responders: Wk 28; n=15, 6, 14, 8,2,0,1,0	0		0	0
Clinical responders: Wk 36; n=15, 6, 14, 8,2,0,1,0	0		0	0
Clinical responders: Wk 44; n=15, 6, 14, 8,2,0,1,0	0		0	0
Clinical responders: Wk 52; n=15, 6, 14, 8,2,0,1,0	0		0	0
Clinical non-responders: Wk 20; n=8, 1,6,6,3,0,2,3	0		0	0
Clinical non-responders: Wk 28; n=8, 1,6,6,3,0,2,3	0		0	0
Clinical non-responders: Wk 36; n=8, 1,6,6,3,0,2,3	0		0	0
Clinical non-responders: Wk 44; n=8, 1,6,6,3,0,2,3	0		0	0
Clinical non-responders: Wk 52; n=8, 1,6,6,3,0,2,3	0		0	0

Notes:

[103] - No subjects in this arm were applicable.

Attachments (see zip file)	Table 14.2_2.11.5.1 stat analysis.docx
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Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects Taking Corticosteroids at Induction Baseline Who Discontinued Corticosteroid Use and Achieve Remission At Week 52

End point title	Percentage of Subjects Taking Corticosteroids at Induction Baseline Who Discontinued Corticosteroid Use and Achieve Remission At Week 52
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End point description:

Steroid-free remission at Week 52 was defined as both endoscopic remission at Week 52 and clinical remission at Week 52. Endoscopic remission: SES-CD $\leq$ 4 and at least 2 point reduction versus Induction Baseline and no subscore $>$ 1 in any individual variable. Clinical remission: Average daily stool frequency $\leq$ 1.5 and not worse than baseline AND average daily abdominal pain $\leq$ 1.0 and not worse than Induction Baseline. The very soft/liquid stool frequency and abdominal pain scores at a visit were the average of the daily values reported during the 7 usable days preceding the scheduled assessment visit. Abdominal Pain was rated on a 4-point scale from 0 (none) to 3 (severe). See SES-CD description details in the first primary endpoint description of this record.

Subjects from ITT population taking corticosteroids at Induction Baseline. Non responder imputation. n=total subjects, by Week 16 status (responder/non-responder).

End point type	Secondary
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End point timeframe:

Week 52

End point values	ITT: 3 mg BID, Upadacitinib in Induction	ITT: 6 mg BID, Upadacitinib at Induction	ITT: 12 mg BID, Upadacitinib at Induction	ITT: 24 mg QD, Upadacitinib at Induction
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	23	7	20	14
Units: percentage of subjects				
number (not applicable)				
Responders; n=8, 2, 8, 5, 0, 0, 0, 0	25.0	0	37.5	0
Non-responders; n=15, 5, 12, 9, 5, 0, 3, 3	0	0	0	11.1
Clinical responders; n=15, 6, 14, 8, 2, 0, 1, 0	13.3	0	21.4	12.5
Clinical non-responders; n=8, 1, 6, 6, 3, 0, 2, 3	0	0	0	0

End point values	ITT: 3 mg BID, Placebo in Induction	ITT: 6 mg BID, Placebo at Induction	ITT: 12 mg BID, Placebo at Induction	ITT: 24 mg QD, Placebo at Induction
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	5	0 ^[104]	3	3
Units: percentage of subjects				
number (not applicable)				
Responders; n=8, 2, 8, 5, 0, 0, 0, 0	0		0	0
Non-responders; n=15, 5, 12, 9, 5, 0, 3, 3	0		0	0
Clinical responders; n=15, 6, 14, 8, 2, 0, 1, 0	0		0	0
Clinical non-responders; n=8, 1, 6, 6, 3, 0, 2, 3	0		0	0

Notes:

[104] - No subjects in this arm had were applicable.

Attachments (see zip file)	Table 14.2_2.11.1.1 stat analysis.docx
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Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects Taking Corticosteroids at Induction Baseline Who Discontinued Corticosteroid Use and Achieve Clinical Remission Over Time

End point title	Percentage of Subjects Taking Corticosteroids at Induction Baseline Who Discontinued Corticosteroid Use and Achieve Clinical Remission Over Time
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End point description:

Steroid-free clinical remission was defined as average daily stool frequency ≤ 1.5 and not worse than Induction Baseline AND average daily abdominal pain ≤ 1.0 and not worse than Induction Baseline. The very soft/liquid stool frequency and abdominal pain scores at a visit were the average of the daily values reported during the 7 usable days preceding the scheduled assessment visit. Abdominal Pain was rated on a 4-point scale from 0 (none) to 3 (severe).

Subjects from ITT population taking corticosteroids at Induction Baseline. Non responder imputation. n=total subjects, by Week 16 status (responder/nonresponder).

End point type	Secondary
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End point timeframe:

Week 20, Week 28, Week 36, Week 44, Week 52

End point values	ITT: 3 mg BID, Upadacitinib in Induction	ITT: 6 mg BID, Upadacitinib at Induction	ITT: 12 mg BID, Upadacitinib at Induction	ITT: 24 mg QD, Upadacitinib at Induction
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	23	7	20	14
Units: percentage of subjects				
number (not applicable)				
Responders: Week (Wk) 20; n=8, 2, 8, 5, 0, 0, 0, 0	50.0	50.0	50.0	0
Responders: Wk 28; n=8, 2, 8, 5, 0, 0, 0, 0	37.5	50.0	50.0	20.0
Responders: Wk 36; n=8, 2, 8, 5, 0, 0, 0, 0	37.5	100	62.5	0
Responders: Wk 44; n=8, 2, 8, 5, 0, 0, 0, 0	37.5	0	62.5	20.0
Responders: Wk 52; n=8, 2, 8, 5, 0, 0, 0, 0	25.0	100	62.5	0
Non-responders: Wk 20; n=15, 5, 12, 9, 5, 0, 3, 3	13.3	40.0	0	0
Non-responders: Wk 28; n=15, 5, 12, 9, 5, 0, 3, 3	6.7	40.0	16.7	11.1
Non-responders: Wk 36; n=15, 5, 12, 9, 5, 0, 3, 3	6.7	20.0	0	11.1
Non-responders: Wk 44; n=15, 5, 12, 9, 5, 0, 3, 3	20.0	40.0	0	11.1
Non-responders: Wk 52; n=15, 5, 12, 9, 5, 0, 3, 3	13.3	20.0	8.3	11.1
Clin. responders: Wk 20; n=15, 6, 14, 8, 2, 0,1,0	40.0	50.0	28.6	0
Clin. responders: Wk 28; n=15, 6, 14, 8, 2, 0,1,0	26.7	50.0	42.9	25.0
Clin. responders: Wk 36; n=15, 6, 14, 8, 2, 0,1,0	26.7	50.0	35.7	12.5
Clin. responders: Wk 44; n=15, 6, 14, 8, 2, 0,1,0	40.0	33.3	35.7	25.0
Clin. responders: Wk 52; n=15, 6, 14, 8, 2, 0,1,0	26.7	50.0	42.9	12.5
Clin. non-responders: Wk 20; n=8, 1, 6, 6, 3,0,2,3	0	0	0	0
Clin. non-responders: Wk 28; n=8, 1, 6, 6, 3,0,2,3	0	0	0	0
Clin. non-responders: Wk 36; n=8, 1, 6, 6, 3,0,2,3	0	0	0	0
Clin. non-responders: Wk 44; n=8, 1, 6, 6, 3,0,2,3	0	0	0	0
Clin. non-responders: Wk 52; n=8, 1, 6, 6, 3,0,2,3	0	0	0	0

End point values	ITT: 3 mg BID, Placebo in	ITT: 6 mg BID, Placebo at	ITT: 12 mg BID, Placebo at	ITT: 24 mg QD, Placebo at
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	Induction	Induction	Induction	Induction
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	5	0 ^[105]	3	3
Units: percentage of subjects				
number (not applicable)				
Responders: Week (Wk) 20; n=8, 2, 8, 5, 0, 0, 0, 0	0		0	0
Responders: Wk 28; n=8, 2, 8, 5, 0, 0, 0, 0	0		0	0
Responders: Wk 36; n=8, 2, 8, 5, 0, 0, 0, 0	0		0	0
Responders: Wk 44; n=8, 2, 8, 5, 0, 0, 0, 0	0		0	0
Responders: Wk 52; n=8, 2, 8, 5, 0, 0, 0, 0	0		0	0
Non-responders: Wk 20; n=15, 5, 12, 9, 5, 0, 3, 3	0		0	0
Non-responders: Wk 28; n=15, 5, 12, 9, 5, 0, 3, 3	0		0	0
Non-responders: Wk 36; n=15, 5, 12, 9, 5, 0, 3, 3	0		0	0
Non-responders: Wk 44; n=15, 5, 12, 9, 5, 0, 3, 3	0		0	0
Non-responders: Wk 52; n=15, 5, 12, 9, 5, 0, 3, 3	0		0	0
Clin. responders: Wk 20; n=15, 6, 14, 8, 2, 0,1,0	0		0	0
Clin. responders: Wk 28; n=15, 6, 14, 8, 2, 0,1,0	0		0	0
Clin. responders: Wk 36; n=15, 6, 14, 8, 2, 0,1,0	0		0	0
Clin. responders: Wk 44; n=15, 6, 14, 8, 2, 0,1,0	0		0	0
Clin. responders: Wk 52; n=15, 6, 14, 8, 2, 0,1,0	0		0	0
Clin. non-responders: Wk 20; n=8, 1, 6, 6, 3,0,2,3	0		0	0
Clin. non-responders: Wk 28; n=8, 1, 6, 6, 3,0,2,3	0		0	0
Clin. non-responders: Wk 36; n=8, 1, 6, 6, 3,0,2,3	0		0	0
Clin. non-responders: Wk 44; n=8, 1, 6, 6, 3,0,2,3	0		0	0
Clin. non-responders: Wk 52; n=8, 1, 6, 6, 3,0,2,3	0		0	0

Notes:

[105] - No subjects in this arm were applicable.

Attachments (see zip file)	Table 14.2_2.11.2.1 stat analysis.docx
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Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects Taking Corticosteroids at Induction Baseline and With Daily Stool Frequency ≥ 4.0 or Daily Abdominal Pain ≥ 2.0 at Induction Baseline Who Discontinued Corticosteroid Use and Achieve Modified Clinical Remission Over Time

End point title	Percentage of Subjects Taking Corticosteroids at Induction Baseline and With Daily Stool Frequency ≥ 4.0 or Daily Abdominal Pain ≥ 2.0 at Induction Baseline Who Discontinued Corticosteroid Use and Achieve Modified Clinical Remission Over Time
End point description:	
Steroid-free modified clinical remission was defined as average daily stool frequency ≤ 2.8 and not worse than Induction Baseline AND average daily abdominal pain ≤ 1.0 and not worse than Induction Baseline. The very soft/liquid stool frequency and abdominal pain scores at a visit were the average of the daily values reported during the 7 usable days preceding the scheduled assessment visit. Abdominal Pain was rated on a 4-point scale from 0 (none) to 3 (severe).	
Subjects from ITT population taking corticosteroids at Induction Baseline and Daily Stool Frequency ≥ 4.0 OR Daily Abdominal Pain ≥ 2.0 at Induction Baseline. Non responder imputation. n=total subjects, by Week 16 status (responder/nonresponder).	
End point type	Secondary
End point timeframe:	
Week 20, Week 28, Week 36, Week 44, Week 52	

End point values	ITT: 3 mg BID, Upadacitinib in Induction	ITT: 6 mg BID, Upadacitinib at Induction	ITT: 12 mg BID, Upadacitinib at Induction	ITT: 24 mg QD, Upadacitinib at Induction
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	18	7	20	13
Units: percentage of subjects				
number (not applicable)				
Responders: Week (Wk) 20; n=6, 2, 8, 5, 0, 0, 0, 0	33.3	50.0	62.5	20.0
Responders: Wk 28; n=6, 2, 8, 5, 0, 0, 0, 0	50.0	50.0	62.5	20.0
Responders: Wk 36; n=6, 2, 8, 5, 0, 0, 0, 0	50.0	100	62.5	0
Responders: Wk 44; n=6, 2, 8, 5, 0, 0, 0, 0	33.3	50.0	62.5	20.0
Responders: Wk 52; n=6, 2, 8, 5, 0, 0, 0, 0	33.3	100	62.5	0
Non-responders: Wk 20; n=12, 5, 12, 8, 4, 0, 3, 3	8.3	40.0	8.3	0
Non-responders: Wk 28; n=12, 5, 12, 8, 4, 0, 3, 3	16.7	40.0	16.7	12.5
Non-responders: Wk 36; n=12, 5, 12, 8, 4, 0, 3, 3	8.3	20.0	8.3	12.5
Non-responders: Wk 44; n=12, 5, 12, 8, 4, 0, 3, 3	16.7	40.0	0	12.5
Non-responders: Wk 52; n=12, 5, 12, 8, 4, 0, 3, 3	8.3	20.0	16.7	12.5
Clin. responders: Wk 20; n=12, 6, 14, 7, 1, 0, 1, 0	25.0	50.0	42.9	14.3
Clin. responders: Wk 28; n=12, 6, 14, 7, 1, 0, 1, 0	41.7	50.0	50.0	28.6
Clin. responders: Wk 36; n=12, 6, 14, 7, 1, 0, 1, 0	33.3	50.0	42.9	14.3
Clin. responders: Wk 44; n=12, 6, 14, 7, 1, 0, 1, 0	33.3	50.0	35.7	28.6
Clin. responders: Wk 52; n=12, 6, 14, 7, 1, 0, 1, 0	25.0	50.0	50.0	14.3

Clin. non-responders: Wk 20; n=6, 1, 6, 6, 3,0,2,3	0	0	0	0
Clin. non-responders: Wk 28; n=6, 1, 6, 6, 3,0,2,3	0	0	0	0
Clin. non-responders: Wk 36; n=6, 1, 6, 6, 3,0,2,3	0	0	0	0
Clin. non-responders: Wk 44; n=6, 1, 6, 6, 3,0,2,3	0	0	0	0
Clin. non-responders: Wk 52; n=6, 1, 6, 6, 3,0,2,3	0	0	0	0

End point values	ITT: 3 mg BID, Placebo in Induction	ITT: 6 mg BID, Placebo at Induction	ITT: 12 mg BID, Placebo at Induction	ITT: 24 mg QD, Placebo at Induction
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	4	0 ^[106]	3	3
Units: percentage of subjects				
number (not applicable)				
Responders: Week (Wk) 20; n=6, 2, 8, 5, 0, 0, 0, 0	0		0	0
Responders: Wk 28; n=6, 2, 8, 5, 0, 0, 0, 0	0		0	0
Responders: Wk 36; n=6, 2, 8, 5, 0, 0, 0, 0	0		0	0
Responders: Wk 44; n=6, 2, 8, 5, 0, 0, 0, 0	0		0	0
Responders: Wk 52; n=6, 2, 8, 5, 0, 0, 0, 0	0		0	0
Non-responders: Wk 20; n=12, 5, 12, 8, 4, 0, 3, 3	0		0	0
Non-responders: Wk 28; n=12, 5, 12, 8, 4, 0, 3, 3	0		0	0
Non-responders: Wk 36; n=12, 5, 12, 8, 4, 0, 3, 3	0		0	0
Non-responders: Wk 44; n=12, 5, 12, 8, 4, 0, 3, 3	0		0	0
Non-responders: Wk 52; n=12, 5, 12, 8, 4, 0, 3, 3	0		0	0
Clin. responders: Wk 20; n=12, 6, 14, 7, 1, 0,1,0	0		0	0
Clin. responders: Wk 28; n=12, 6, 14, 7, 1, 0,1,0	0		0	0
Clin. responders: Wk 36; n=12, 6, 14, 7, 1, 0,1,0	0		0	0
Clin. responders: Wk 44; n=12, 6, 14, 7, 1, 0,1,0	0		0	0
Clin. responders: Wk 52; n=12, 6, 14, 7, 1, 0,1,0	0		0	0
Clin. non-responders: Wk 20; n=6, 1, 6, 6, 3,0,2,3	0		0	0
Clin. non-responders: Wk 28; n=6, 1, 6, 6, 3,0,2,3	0		0	0
Clin. non-responders: Wk 36; n=6, 1, 6, 6, 3,0,2,3	0		0	0
Clin. non-responders: Wk 44; n=6, 1, 6, 6, 3,0,2,3	0		0	0
Clin. non-responders: Wk 52; n=6, 1, 6, 6, 3,0,2,3	0		0	0

Notes:

[106] - No subjects in the arm applied.

Attachments (see zip file)	Table 14.2_2.11.3.1 stat analysis.docx
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Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects Taking Corticosteroids at Induction Baseline Who Discontinued Corticosteroid Use and Achieve Endoscopic Remission at Week 52

End point title	Percentage of Subjects Taking Corticosteroids at Induction Baseline Who Discontinued Corticosteroid Use and Achieve Endoscopic Remission at Week 52
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End point description:

Steroid-free endoscopic remission was defined as SES-CD ≤ 4 and at least 2 points reduction versus Induction Baseline and no subscore > 1 in any individual variable. Details of the SES-CD scale are provided in the description of the first primary endpoint.

Subjects from ITT population taking corticosteroids at Induction Baseline. Non responder imputation. n=total subjects, by Week 16 status (responder/nonresponder).

End point type	Secondary
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End point timeframe:

Week 52

End point values	ITT: 3 mg BID, Upadacitinib in Induction	ITT: 6 mg BID, Upadacitinib at Induction	ITT: 12 mg BID, Upadacitinib at Induction	ITT: 24 mg QD, Upadacitinib at Induction
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	23	7	20	14
Units: percentage of subjects				
number (not applicable)				
Responders; n=8, 2, 8, 5, 0, 0, 0, 0	25.0	0	50.0	0
Non-responders; n=15, 5, 12, 9, 5, 0, 3, 3	0	20.0	8.3	11.1
Clinical responders; n=15, 6, 14, 8, 2, 0, 1, 0	13.3	16.7	35.7	12.5
Clinical non-responders; n=8, 1, 6, 6, 3, 0, 2, 3	0	0	0	0

End point values	ITT: 3 mg BID, Placebo in Induction	ITT: 6 mg BID, Placebo at Induction	ITT: 12 mg BID, Placebo at Induction	ITT: 24 mg QD, Placebo at Induction
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	5	0 ^[107]	3	3
Units: percentage of subjects				

number (not applicable)				
Responders; n=8, 2, 8, 5, 0, 0, 0, 0	0		0	0
Non-responders; n=15, 5, 12, 9, 5, 0, 3, 3	0		0	0
Clinical responders; n=15, 6, 14, 8, 2, 0, 1, 0	0		0	0
Clinical non-responders; n=8, 1, 6, 6, 3, 0, 2, 3	0		0	0

Notes:

[107] - No subjects in this arm applied.

Attachments (see zip file)	Table 14.2_2.11.4.1 stat analysis.docx
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Statistical analyses

No statistical analyses for this end point

Secondary: Percentage Of Subjects Who Achieve CDAI < 150 Over Time During Extension Phase

End point title	Percentage Of Subjects Who Achieve CDAI < 150 Over Time During Extension Phase
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End point description:

CDAI is used to quantify the signs and symptoms of subjects with Crohn's disease. The score includes the frequency of stools, abdominal pain and general well-being as well as the presence of complications, use of antidiarrheals, presence of abdominal mass, hematocrit and weight. CDAI generally ranges from 0 to 600 where higher scores indicate more severe disease. A score below 150 indicates remission.

Non responder imputation. n=total subjects, by Week 16 status (responder/non-responder).

End point type	Secondary
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End point timeframe:

Week 20, Week 28, Week 36, Week 44, Week 52

End point values	ITT: 3 mg BID, Upadacitinib in Induction	ITT: 6 mg BID, Upadacitinib at Induction	ITT: 12 mg BID, Upadacitinib at Induction	ITT: 24 mg QD, Upadacitinib at Induction
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	52	18	50	33
Units: percentage of subjects				
number (not applicable)				
Responders: Week (Wk) 20; n=20, 8, 16, 10, 1,0,0,0	65.0	50.0	75.0	50.0
Responders: Wk 28; n=20, 8, 16, 10, 1,0,0,0	75.0	25.0	62.5	60.0
Responders: Wk 36; n=20, 8, 16, 10, 1,0,0,0	70.0	75.0	62.5	30.0
Responders: Wk 44; n=20, 8, 16, 10, 1,0,0,0	45.0	37.5	62.5	40.0
Responders: Wk 52; n=20, 8, 16, 10, 1,0,0,0	55.0	50.0	68.8	40.0
Non-responders: Wk 20; n=32, 10, 34, 23, 8, 5,9,4	28.1	50.0	17.6	8.7
Non-responders: Wk 28; n=32, 10, 34, 23, 8, 5,9,4	15.6	40.0	17.6	13.0

Non-responders: Wk 36; n=32, 10, 34, 23, 8, 5,9,4	15.6	30.0	14.7	13.0
Non-responders: Wk 44; n=32, 10, 34, 23, 8, 5,9,4	18.8	30.0	17.6	8.7
Non-responders: Wk 52; n=32, 10, 34, 23, 8, 5,9,4	9.4	30.0	20.6	13.0
Clin. responders: Wk 20; n=32, 14, 29, 19, 6,1,4,1	59.4	64.3	51.7	36.8
Clin. responders: Wk 28; n=32, 14, 29, 19, 6,1,4,1	56.3	42.9	48.3	47.4
Clin. responders: Wk 36; n=32, 14, 29, 19, 6,1,4,1	59.4	64.3	44.8	31.6
Clin. responders: Wk 44; n=32, 14, 29, 19, 6,1,4,1	40.6	42.9	55.2	31.6
Clin. responders: Wk 52; n=32, 14, 29, 19, 6,1,4,1	43.8	50.0	55.2	36.8
Clin. non-responders: Wk 20; n=20, 4,21,14,3,4,5,3	15.0	0	14.3	0
Clin. non-responders: Wk 28; n=20, 4,21,14,3,4,5,3	10.0	0	9.5	0
Clin. non-responders: Wk 36; n=20, 4,21,14,3,4,5,3	0	0	9.5	0
Clin. non-responders: Wk 44; n=20, 4,21,14,3,4,5,3	10.0	0	0	0
Clin. non-responders: Wk 52; n=20, 4,21,14,3,4,5,3	0	0	9.5	0

End point values	ITT: 3 mg BID, Placebo in Induction	ITT: 6 mg BID, Placebo at Induction	ITT: 12 mg BID, Placebo at Induction	ITT: 24 mg QD, Placebo at Induction
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	9	5	9	4
Units: percentage of subjects				
number (not applicable)				
Responders: Week (Wk) 20; n=20, 8, 16, 10, 1,0,0,0	0	0	0	0
Responders: Wk 28; n=20, 8, 16, 10, 1,0,0,0	0	0	0	0
Responders: Wk 36; n=20, 8, 16, 10, 1,0,0,0	0	0	0	0
Responders: Wk 44; n=20, 8, 16, 10, 1,0,0,0	0	0	0	0
Responders: Wk 52; n=20, 8, 16, 10, 1,0,0,0	0	0	0	0
Non-responders: Wk 20; n=32, 10, 34, 23, 8, 5,9,4	75.0	20.0	11.1	50.0
Non-responders: Wk 28; n=32, 10, 34, 23, 8, 5,9,4	37.5	20.0	22.2	50.0
Non-responders: Wk 36; n=32, 10, 34, 23, 8, 5,9,4	37.5	20.0	33.3	50.0
Non-responders: Wk 44; n=32, 10, 34, 23, 8, 5,9,4	25.0	20.0	33.3	25.0
Non-responders: Wk 52; n=32, 10, 34, 23, 8, 5,9,4	25.0	40.0	33.3	50.0
Clin. responders: Wk 20; n=32, 14, 29, 19, 6,1,4,1	83.3	100	0	100
Clin. responders: Wk 28; n=32, 14, 29, 19, 6,1,4,1	50.0	100	25.0	100

Clin. responders: Wk 36; n=32, 14, 29, 19, 6,1,4,1	50.0	100	25.0	100
Clin. responders: Wk 44; n=32, 14, 29, 19, 6,1,4,1	33.3	100	25.0	100
Clin. responders: Wk 52; n=32, 14, 29, 19, 6,1,4,1	33.3	100	25.0	100
Clin. non-responders: Wk 20; n=20, 4,21,14,3,4,5,3	33.3	0	20.0	33.3
Clin. non-responders: Wk 28; n=20, 4,21,14,3,4,5,3	0	0	20.0	33.3
Clin. non-responders: Wk 36; n=20, 4,21,14,3,4,5,3	0	0	40.0	33.3
Clin. non-responders: Wk 44; n=20, 4,21,14,3,4,5,3	0	0	40.0	0
Clin. non-responders: Wk 52; n=20, 4,21,14,3,4,5,3	0	25.0	40.0	33.3

Attachments (see zip file)	Table 14.2_2.10.1.1 stat analysis.docx
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Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Decrease in CDAI $\geq$ 70 Points From Induction Baseline Over Time During Extension Phase

End point title	Percentage of Subjects With Decrease in CDAI $\geq$ 70 Points From Induction Baseline Over Time During Extension Phase
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End point description:

CDAI is used to quantify the signs and symptoms of subjects with Crohn's disease. The score includes the frequency of stools, abdominal pain and general well-being as well as the presence of complications, use of antidiarrheals, presence of abdominal mass, hematocrit and weight. CDAI generally ranges from 0 to 600 where higher scores indicate more severe disease. A 70-point decrease in the CDAI index refers to improvement in the disease activity from Baseline.

Non responder imputation. n=total subjects, by Week 16 status (responder/non-responder).

End point type	Secondary
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End point timeframe:

Week 20, Week 28, Week 36, Week 44, Week 52

End point values	ITT: 3 mg BID, Upadacitinib in Induction	ITT: 6 mg BID, Upadacitinib at Induction	ITT: 12 mg BID, Upadacitinib at Induction	ITT: 24 mg QD, Upadacitinib at Induction
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	52	18	50	33
Units: percentage of subjects				
number (not applicable)				
Responders: Week (Wk) 20; n=20, 8, 16, 10, 1,0,0,0	80.0	100	93.8	60.0
Responders: Wk 28; n=20, 8, 16, 10, 1,0,0,0	85.0	62.5	68.8	60.0
Responders: Wk 36; n=20, 8, 16, 10, 1,0,0,0	75.0	100	75.0	50.0

Responders: Wk 44; n=20, 8, 16, 10, 1,0,0,0	60.0	87.5	81.3	40.0
Responders: Wk 52; n=20, 8, 16, 10, 1,0,0,0	55.0	75.0	75.0	40.0
Non-responders: Wk 20; n=32, 10, 34, 23, 8, 5,9,4	46.9	70.0	47.1	34.8
Non-responders: Wk 28; n=32, 10, 34, 23, 8, 5,9,4	34.4	60.0	29.4	30.4
Non-responders: Wk 36; n=32, 10, 34, 23, 8, 5,9,4	28.1	50.0	26.5	17.4
Non-responders: Wk 44; n=32, 10, 34, 23, 8, 5,9,4	25.0	30.0	29.4	26.1
Non-responders: Wk 52; n=32, 10, 34, 23, 8, 5,9,4	12.5	40.0	26.5	17.4
Clin. responders: Wk 20; n=32, 14, 29, 19, 6,1,4,1	75.0	100	89.7	63.2
Clin. responders: Wk 28; n=32, 14, 29, 19, 6,1,4,1	75.0	71.4	58.6	57.9
Clin. responders: Wk 36; n=32, 14, 29, 19, 6,1,4,1	65.6	85.7	62.1	42.1
Clin. responders: Wk 44; n=32, 14, 29, 19, 6,1,4,1	56.3	71.4	72.4	42.1
Clin. responders: Wk 52; n=32, 14, 29, 19, 6,1,4,1	46.9	71.4	62.1	36.8
Clin. non-responders: Wk 20; n=20, 4,21,14,3,4,5,3	35.0	25.0	23.8	14.3
Clin. non-responders: Wk 28; n=20, 4,21,14,3,4,5,3	20.0	25.0	19.0	14.3
Clin. non-responders: Wk 36; n=20, 4,21,14,3,4,5,3	15.0	25.0	14.3	7.1
Clin. non-responders: Wk 44; n=20, 4,21,14,3,4,5,3	10.0	0	9.5	14.3
Clin. non-responders: Wk 52; n=20, 4,21,14,3,4,5,3	0	0	14.3	7.1

End point values	ITT: 3 mg BID, Placebo in Induction	ITT: 6 mg BID, Placebo at Induction	ITT: 12 mg BID, Placebo at Induction	ITT: 24 mg QD, Placebo at Induction
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	9	5	9	4
Units: percentage of subjects				
number (not applicable)				
Responders: Week (Wk) 20; n=20, 8, 16, 10, 1,0,0,0	100	0	0	0
Responders: Wk 28; n=20, 8, 16, 10, 1,0,0,0	0	0	0	0
Responders: Wk 36; n=20, 8, 16, 10, 1,0,0,0	100	0	0	0
Responders: Wk 44; n=20, 8, 16, 10, 1,0,0,0	100	0	0	0
Responders: Wk 52; n=20, 8, 16, 10, 1,0,0,0	100	0	0	0
Non-responders: Wk 20; n=32, 10, 34, 23, 8, 5,9,4	75.0	20.0	22.2	50.0
Non-responders: Wk 28; n=32, 10, 34, 23, 8, 5,9,4	50.0	20.0	33.3	50.0
Non-responders: Wk 36; n=32, 10, 34, 23, 8, 5,9,4	50.0	20.0	33.3	50.0

Non-responders: Wk 44; n=32, 10, 34, 23, 8, 5,9,4	37.5	40.0	33.3	25.0
Non-responders: Wk 52; n=32, 10, 34, 23, 8, 5,9,4	37.5	40.0	33.3	50.0
Clin. responders: Wk 20; n=32, 14, 29, 19, 6,1,4,1	100	100	0	100
Clin. responders: Wk 28; n=32, 14, 29, 19, 6,1,4,1	66.7	100	25.0	100
Clin. responders: Wk 36; n=32, 14, 29, 19, 6,1,4,1	83.3	100	25.0	100
Clin. responders: Wk 44; n=32, 14, 29, 19, 6,1,4,1	66.7	100	25.0	100
Clin. responders: Wk 52; n=32, 14, 29, 19, 6,1,4,1	66.7	100	25.0	100
Clin. non-responders: Wk 20; n=20, 4,21,14,3,4,5,3	33.3	0	40.0	33.3
Clin. non-responders: Wk 28; n=20, 4,21,14,3,4,5,3	0	0	40.0	33.3
Clin. non-responders: Wk 36; n=20, 4,21,14,3,4,5,3	0	0	40.0	33.3
Clin. non-responders: Wk 44; n=20, 4,21,14,3,4,5,3	0	25.0	40.0	0
Clin. non-responders: Wk 52; n=20, 4,21,14,3,4,5,3	0	25.0	40.0	33.3

Attachments (see zip file)	Table 14.2_2.10.3.1 stat analysis.docx
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Statistical analyses

No statistical analyses for this end point

Secondary: Change From Induction Baseline in Fecal Calprotectin Level Over Time During Extension Phase

End point title	Change From Induction Baseline in Fecal Calprotectin Level Over Time During Extension Phase
End point description:	
Subjects from ITT population with an assessment at given time point. Last observation carried forward. n=total subjects, by Week 16 status (responder/nonresponder).	
End point type	Secondary
End point timeframe:	
Baseline, Week 28, Week 52	

End point values	ITT: 3 mg BID, Upadacitinib in Induction	ITT: 6 mg BID, Upadacitinib at Induction	ITT: 12 mg BID, Upadacitinib at Induction	ITT: 24 mg QD, Upadacitinib at Induction
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	39	15	30	13
Units: mcg/g				
arithmetic mean (standard deviation)				
Responders: Week (Wk) 28; n=16, 7, 9, 3, 1, 0, 0,0	-153.4 (± 2722.96)	-532.0 (± 519.42)	-2878.6 (± 2584.43)	-3563.7 (± 4747.26)

Responders: Wk 52; n=16, 7, 10, 4, 1, 0, 0,0	-51.9 (± 2650.98)	-524.1 (± 521.31)	-3047.5 (± 2509.27)	-2371.8 (± 2786.97)
Non-responders: Wk 28; n=21, 7, 16, 9, 4, 4, 4, 2	-150.3 (± 958.76)	-148.3 (± 1315.46)	-834.5 (± 3011.51)	-850.2 (± 1821.34)
Non-responders: Wk 52; n=23, 8, 20, 9, 4, 4, 4, 2	-87.2 (± 1494.35)	88.3 (± 1689.67)	-704.0 (± 2801.08)	-562.8 (± 1738.58)
Clin. responders: Wk 28; n=25, 11, 16, 9,4, 1,2,0	-226.2 (± 2261.16)	-424.5 (± 1102.22)	-2794.6 (± 3018.26)	-2099.3 (± 3083.34)
Clin. responders: Wk 52; n=26, 12, 18, 10, 4,1,2,0	1.0 (± 2457.22)	-239.3 (± 1443.14)	-2617.4 (± 3232.04)	-1510.3 (± 2773.90)
Clin. non-responders: Wk 28; n=12, 3, 9, 3,1,3,2,2	3.7 (± 766.69)	-30.7 (± 32.65)	606.0 (± 1133.70)	183.7 (± 443.97)
Clin. non-responders: Wk 52; n=13, 3, 12,3,1,3,2,2	-220.2 (± 514.97)	-30.7 (± 32.65)	213.3 (± 802.34)	183.7 (± 443.97)

End point values	ITT: 3 mg BID, Placebo in Induction	ITT: 6 mg BID, Placebo at Induction	ITT: 12 mg BID, Placebo at Induction	ITT: 24 mg QD, Placebo at Induction
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	5 ^[108]	4 ^[109]	4	2
Units: mcg/g				
arithmetic mean (standard deviation)				
Responders: Week (Wk) 28; n=16, 7, 9, 3, 1, 0, 0,0	-194.0 (± 99999)	0 (± 0)	0 (± 0)	0 (± 0)
Responders: Wk 52; n=16, 7, 10, 4, 1, 0, 0,0	-44.0 (± 99999)	0 (± 0)	0 (± 0)	0 (± 0)
Non-responders: Wk 28; n=21, 7, 16, 9, 4, 4, 4, 2	-16.5 (± 304.33)	-121.0 (± 395.16)	-326.8 (± 817.71)	760.5 (± 1075.51)
Non-responders: Wk 52; n=23, 8, 20, 9, 4, 4, 4, 2	-8.3 (± 344.29)	-121.0 (± 395.16)	-434.0 (± 1030.64)	760.5 (± 1075.51)
Clin. responders: Wk 28; n=25, 11, 16, 9,4, 1,2,0	-65.0 (± 316.06)	-694.0 (± 99999)	117.5 (± 166.17)	0 (± 0)
Clin. responders: Wk 52; n=26, 12, 18, 10, 4,1,2,0	-44.3 (± 350.61)	-694.0 (± 99999)	117.5 (± 166.17)	0 (± 0)
Clin. non-responders: Wk 28; n=12, 3, 9, 3,1,3,2,2	0.0 (± 99999)	70.0 (± 123.85)	-771.0 (± 1090.36)	760.5 (± 1075.51)
Clin. non-responders: Wk 52; n=13, 3, 12,3,1,3,2,2	0.0 (± 99999)	70.0 (± 123.85)	-985.5 (± 1393.71)	760.5 (± 1075.51)

Notes:

[108] - 99999=not applicable (1 subject in arm)

[109] - 99999=not applicable (1 subject in arm)

Attachments (see zip file)	Table 14.2_2.15.1 stat analysis.docx
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Statistical analyses

No statistical analyses for this end point

Secondary: Change from Induction Baseline in hs-CRP Over Time During Extension Phase

End point title	Change from Induction Baseline in hs-CRP Over Time During Extension Phase
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End point description:

Subjects from ITT population with an assessment at given time point. Last observation carried forward.
n=total subjects, by Week 16 status (responder/nonresponder).

End point type	Secondary
End point timeframe:	
Baseline, Week 20, Week 28, Week 36, Week 44, Week 52	

End point values	ITT: 3 mg BID, Upadacitinib in Induction	ITT: 6 mg BID, Upadacitinib at Induction	ITT: 12 mg BID, Upadacitinib at Induction	ITT: 24 mg QD, Upadacitinib at Induction
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	49	18	47	31
Units: mg/L				
arithmetic mean (standard deviation)				
Responders: Week (Wk) 20; n=19, 8, 16, 9, 1, 0,0,0	-9.5 (± 21.77)	-9.4 (± 11.14)	-20.8 (± 19.78)	4.1 (± 36.50)
Responders: Wk 28; n=19, 8, 16, 9, 1, 0,0,0	-6.0 (± 22.53)	-3.6 (± 16.12)	-21.8 (± 17.93)	7.0 (± 35.65)
Responders: Wk 36; n=19, 8, 16, 9, 1, 0,0,0	-1.8 (± 25.57)	-7.2 (± 10.86)	-22.5 (± 18.01)	5.6 (± 35.87)
Responders: Wk 44; n=19, 8, 16, 9, 1, 0,0,0	-5.4 (± 22.95)	-8.5 (± 12.18)	-21.5 (± 19.78)	5.8 (± 35.77)
Responders: Wk 52; n=19, 8, 16, 9, 1, 0,0,0	-4.3 (± 22.68)	-7.0 (± 12.66)	-20.4 (± 18.76)	6.2 (± 35.82)
Non-responders: Wk 20; n=30, 10, 31, 21, 7, 4,7,4	-2.2 (± 9.72)	-1.6 (± 8.24)	-8.5 (± 25.00)	-8.0 (± 18.77)
Non-responders: Wk 28; n=30, 10, 31, 22, 8, 4,7,4	-3.0 (± 9.61)	-0.2 (± 5.92)	-6.4 (± 27.03)	-6.5 (± 20.14)
Non-responders: Wk 36; n=30, 10, 31, 22, 8, 4,7,4	-0.7 (± 8.86)	5.2 (± 15.34)	-7.3 (± 24.87)	0.8 (± 45.98)
Non-responders: Wk 44; n=30, 10, 31, 22, 8, 4,7,4	-1.3 (± 7.82)	11.1 (± 33.68)	-4.1 (± 27.93)	0.9 (± 45.88)
Non-responders: Wk 52; n=30, 10, 31, 22, 8, 4,7,4	-1.2 (± 8.67)	2.8 (± 17.81)	-3.4 (± 32.58)	1.3 (± 45.26)
Clin. responders: Wk 20; n=30, 14, 28, 17, 6,1,3,1	-7.1 (± 18.16)	-6.9 (± 10.80)	-18.0 (± 29.20)	-3.0 (± 31.35)
Clin. responders: Wk 28; n=30, 14, 28, 17, 6,1,3,1	-5.4 (± 19.26)	-2.0 (± 12.93)	-19.2 (± 30.13)	0.0 (± 32.17)
Clin. responders: Wk 36; n=30, 14, 28, 17, 6,1,3,1	-0.8 (± 20.85)	-0.5 (± 16.69)	-18.6 (± 28.62)	9.1 (± 56.33)
Clin. responders: Wk 44; n=30, 14, 28, 17, 6,1,3,1	-3.5 (± 18.87)	3.0 (± 31.54)	-15.3 (± 32.75)	9.3 (± 56.18)
Clin. responders: Wk 52; n=30, 14, 28, 17, 6,1,3,1	-2.8 (± 18.91)	-2.1 (± 18.36)	-13.9 (± 37.06)	10.2 (± 55.66)
Clin. non-responders: Wk 20; n=19, 4,19,13,2,3,4,3	-1.7 (± 10.51)	1.4 (± 2.83)	-4.9 (± 8.36)	-6.2 (± 15.35)
Clin. non-responders: Wk 28; n=20, 4,19,14,3,3,4,3	-2.2 (± 7.71)	-0.6 (± 1.43)	-0.6 (± 6.82)	-5.7 (± 15.26)
Clin. non-responders: Wk 36; n=20, 4,19,14,3,3,4,3	-1.7 (± 8.94)	0.4 (± 0.51)	-3.4 (± 8.04)	-6.1 (± 13.28)
Clin. non-responders: Wk 44; n=20, 4,19,14,3,3,4,3	-1.9 (± 7.83)	0.4 (± 0.51)	-2.3 (± 9.37)	-6.2 (± 13.15)
Clin. non-responders: Wk 52; n=20, 4,19,14,3,3,4,3	-1.9 (± 8.11)	0.4 (± 0.51)	-2.2 (± 9.28)	-6.3 (± 11.71)

End point values	ITT: 3 mg BID, Placebo in Induction	ITT: 6 mg BID, Placebo at Induction	ITT: 12 mg BID, Placebo at Induction	ITT: 24 mg QD, Placebo at Induction
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	9 ^[110]	4 ^[111]	7	4 ^[112]
Units: mg/L				
arithmetic mean (standard deviation)				
Responders: Week (Wk) 20; n=19, 8, 16, 9, 1, 0,0,0	-3.1 (± 99999)	0 (± 0)	0 (± 0)	0 (± 0)
Responders: Wk 28; n=19, 8, 16, 9, 1, 0,0,0	-4.2 (± 99999)	0 (± 0)	0 (± 0)	0 (± 0)
Responders: Wk 36; n=19, 8, 16, 9, 1, 0,0,0	-4.0 (± 99999)	0 (± 0)	0 (± 0)	0 (± 0)
Responders: Wk 44; n=19, 8, 16, 9, 1, 0,0,0	10.6 (± 99999)	0 (± 0)	0 (± 0)	0 (± 0)
Responders: Wk 52; n=19, 8, 16, 9, 1, 0,0,0	0.4 (± 99999)	0 (± 0)	0 (± 0)	0 (± 0)
Non-responders: Wk 20; n=30, 10, 31, 21, 7, 4,7,4	0.3 (± 10.89)	-1.0 (± 0.97)	-6.8 (± 8.82)	-1.5 (± 2.39)
Non-responders: Wk 28; n=30, 10, 31, 22, 8, 4,7,4	0.3 (± 9.78)	-1.1 (± 1.06)	-5.9 (± 6.58)	3.8 (± 9.55)
Non-responders: Wk 36; n=30, 10, 31, 22, 8, 4,7,4	3.3 (± 8.88)	0.5 (± 0.41)	-3.7 (± 7.80)	8.3 (± 12.71)
Non-responders: Wk 44; n=30, 10, 31, 22, 8, 4,7,4	3.0 (± 9.51)	-0.9 (± 0.87)	-4.1 (± 7.12)	5.5 (± 9.39)
Non-responders: Wk 52; n=30, 10, 31, 22, 8, 4,7,4	4.7 (± 11.50)	-0.2 (± 0.42)	-5.1 (± 8.52)	2.5 (± 9.89)
Clin. responders: Wk 20; n=30, 14, 28, 17, 6,1,3,1	-3.8 (± 5.59)	-2.2 (± 99999)	-9.5 (± 12.15)	-4.4 (± 99999)
Clin. responders: Wk 28; n=30, 14, 28, 17, 6,1,3,1	-4.0 (± 4.77)	-2.3 (± 99999)	-6.1 (± 6.32)	-5.3 (± 99999)
Clin. responders: Wk 36; n=30, 14, 28, 17, 6,1,3,1	0.1 (± 5.93)	0.4 (± 99999)	-3.2 (± 9.54)	-4.9 (± 99999)
Clin. responders: Wk 44; n=30, 14, 28, 17, 6,1,3,1	2.2 (± 7.92)	-1.5 (± 99999)	-1.8 (± 7.26)	-3.9 (± 99999)
Clin. responders: Wk 52; n=30, 14, 28, 17, 6,1,3,1	2.7 (± 10.77)	-0.7 (± 99999)	-4.2 (± 11.29)	-4.6 (± 99999)
Clin. non-responders: Wk 20; n=19, 4,19,13,2,3,4,3	10.9 (± 15.47)	-0.6 (± 0.71)	-4.8 (± 6.69)	-0.5 (± 1.68)
Clin. non-responders: Wk 28; n=20, 4,19,14,3,3,4,3	7.3 (± 12.63)	-0.7 (± 0.81)	-5.8 (± 7.73)	6.8 (± 9.10)
Clin. non-responders: Wk 36; n=20, 4,19,14,3,3,4,3	7.3 (± 12.63)	0.6 (± 0.50)	-4.1 (± 7.77)	12.7 (± 11.20)
Clin. non-responders: Wk 44; n=20, 4,19,14,3,3,4,3	7.3 (± 12.63)	-0.7 (± 0.95)	-5.8 (± 7.55)	8.6 (± 8.55)
Clin. non-responders: Wk 52; n=20, 4,19,14,3,3,4,3	7.3 (± 12.63)	0.0 (± 0.33)	-5.8 (± 7.66)	4.9 (± 10.60)

Notes:

[110] - 99999=not applicable (1 subject analyzed)

[111] - 99999=not applicable (1 subject analyzed)

[112] - 99999=not applicable (1 subject analyzed)

Attachments (see zip file)	Table 14.2_2.16.1 stat analysis.docx
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Statistical analyses

No statistical analyses for this end point

Secondary: Change From Induction Baseline in IBDQ at Week 52

End point title	Change From Induction Baseline in IBDQ at Week 52
End point description:	
The IBDQ is a disease-specific instrument composed of 32 Likert-scaled items. The total score ranges from 32 to 224 using the 7-point response options, with higher scores indicating better health-related quality of life. The IBDQ scale contains 4 component subscales: bowel symptoms, systemic symptoms, emotional function, and social function. Each subscale can be computed with total scores ranging from 10 to 70, 5 to 35, 12 to 84, and 5 to 35, respectively.	
Subjects from ITT population with an assessment at given time point. Observed cases. n=total subjects, by Week 16 status (responder/nonresponder).	
End point type	Secondary
End point timeframe:	
Baseline, Week 52	

End point values	ITT: 3 mg BID, Upadacitinib in Induction	ITT: 6 mg BID, Upadacitinib at Induction	ITT: 12 mg BID, Upadacitinib at Induction	ITT: 24 mg QD, Upadacitinib at Induction
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	36	15	38	22
Units: units on a scale				
arithmetic mean (standard deviation)				
Responders; n=14, 8, 14, 7, 1, 0, 0, 0	43.9 (± 38.06)	56.4 (± 14.52)	82.3 (± 35.59)	45.3 (± 49.89)
Non-responders; n=22, 7, 24, 15, 6, 4, 5, 2	20.8 (± 43.58)	26.0 (± 33.14)	25.9 (± 47.05)	2.9 (± 35.25)
Clinical responders; n=22, 13, 23, 14, 5, 1, 2, 1	42.8 (± 44.13)	46.6 (± 27.76)	70.7 (± 46.99)	26.6 (± 53.11)
Clinical non-responders; n=14, 2, 15, 8, 2, 3, 3,1	9.4 (± 31.46)	13.5 (± 19.09)	9.8 (± 30.81)	-1.5 (± 5.81)

End point values	ITT: 3 mg BID, Placebo in Induction	ITT: 6 mg BID, Placebo at Induction	ITT: 12 mg BID, Placebo at Induction	ITT: 24 mg QD, Placebo at Induction
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	7 ^[113]	4 ^[114]	5	2 ^[115]
Units: units on a scale				
arithmetic mean (standard deviation)				
Responders; n=14, 8, 14, 7, 1, 0, 0, 0	-5.0 (± 99999)	0 (± 0)	0 (± 0)	0 (± 0)
Non-responders; n=22, 7, 24, 15, 6, 4, 5, 2	4.8 (± 16.42)	35.5 (± 28.78)	45.4 (± 36.16)	41.5 (± 24.75)
Clinical responders; n=22, 13, 23, 14, 5, 1, 2, 1	4.8 (± 18.70)	68.0 (± 99999)	34.5 (± 4.95)	24.0 (± 99999)
Clinical non-responders; n=14, 2, 15, 8, 2, 3, 3,1	0.0 (± 0.00)	24.6 (± 23.17)	52.7 (± 49.03)	59.0 (± 99999)

Notes:

[113] - 99999=not applicable (1 subject analyzed)

[114] - 99999=not applicable (1 subject analyzed)

[115] - 99999=not applicable (1 subject analyzed)

Statistical analyses

Secondary: Change From Induction Baseline in European Quality of Life (EuroQol) 5 Dimensions Questionnaire (EQ-5D) Index Score at Week 52

End point title	Change From Induction Baseline in European Quality of Life (EuroQol) 5 Dimensions Questionnaire (EQ-5D) Index Score at Week 52
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End point description:

The EQ-5D is a standardized instrument for use as a measure of health-related quality of life. The EQ-5D Index Score has five dimensions of health (mobility, self-care, usual activities, pain/discomfort, and anxiety/depression). Health states are converted into a weighted health state index. These weights lie on a scale on which full health has a value of 1 and dead has a value of 0. A positive change represents an improvement in health-related quality of life.

Subjects from ITT population with an assessment at given time point. Observed cases. n=total subjects, by Week 16 status (responder/nonresponder).

End point type	Secondary
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End point timeframe:

Baseline, Week 52

End point values	ITT: 3 mg BID, Upadacitinib in Induction	ITT: 6 mg BID, Upadacitinib at Induction	ITT: 12 mg BID, Upadacitinib at Induction	ITT: 24 mg QD, Upadacitinib at Induction
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	36	15	38	22
Units: units on a scale				
arithmetic mean (standard deviation)				
Responders; n=14, 8, 14, 7, 1, 0, 0, 0	0.1350 ($\pm$ 0.1473)	0.1673 ($\pm$ 0.1090)	0.2274 ($\pm$ 0.1524)	0.0122 ($\pm$ 0.1276)
Non-responders; n=22, 7, 24, 15, 6, 4, 6, 3	0.0208 ($\pm$ 0.2231)	0.0697 ($\pm$ 0.2091)	0.1090 ($\pm$ 0.1791)	0.0449 ($\pm$ 0.1008)
Clinical responders; n=11, 13, 23, 14, 5, 1, 3, 1	0.1435 ($\pm$ 0.1461)	0.1334 ($\pm$ 0.1740)	0.2306 ($\pm$ 0.1840)	0.0587 ($\pm$ 0.1298)
Clinical non-responders; n=14, 2, 15, 8, 2, 3, 3, 2	-0.0577 ($\pm$ 0.2225)	0.0455 ($\pm$ 0.0643)	0.0330 ($\pm$ 0.0677)	-0.0079 ($\pm$ 0.0228)

End point values	ITT: 3 mg BID, Placebo in Induction	ITT: 6 mg BID, Placebo at Induction	ITT: 12 mg BID, Placebo at Induction	ITT: 24 mg QD, Placebo at Induction
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	7 ^[116]	4 ^[117]	6	3 ^[118]
Units: units on a scale				
arithmetic mean (standard deviation)				
Responders; n=14, 8, 14, 7, 1, 0, 0, 0	0.3260 ($\pm$ 99999)	0 ($\pm$ 0)	0 ($\pm$ 0)	0 ($\pm$ 0)
Non-responders; n=22, 7, 24, 15, 6, 4, 6, 3	0.1288 ($\pm$ 0.1674)	0.1125 ($\pm$ 0.2210)	0.1542 ($\pm$ 0.2377)	0.1187 ($\pm$ 0.1128)
Clinical responders; n=11, 13, 23, 14, 5, 1, 3, 1	0.2198 ($\pm$ 0.1615)	0.4325 ($\pm$ 99999)	0.1758 ($\pm$ 0.3559)	0.1316 ($\pm$ 99999)
Clinical non-responders; n=14, 2, 15, 8, 2, 3, 3, 2	0.0000 ($\pm$ 0.0000)	0.0058 ($\pm$ 0.0708)	0.1325 ($\pm$ 0.1148)	0.1122 ($\pm$ 0.1587)

Notes:

[116] - 99999=not applicable (1 subject was analyzed)

[117] - 99999=not applicable (1 subject was analyzed)

[118] - 99999=not applicable (1 subject was analyzed)

Attachments (see zip file)	Table 14.2_2.19.1 stat analysis EQ-5D.docx
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Statistical analyses

No statistical analyses for this end point

Secondary: Change From Induction Baseline in EQ-5D VAS at Week 52

End point title	Change From Induction Baseline in EQ-5D VAS at Week 52
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End point description:

The EQ-5D is a standardized instrument for use as a measure of health-related quality of life. The EQ-5D VAS is a 20-cm scale with endpoints labeled "best imaginable health" and "worst imaginable health" anchored at 100 and 0, respectively. A positive change represents an improvement in health-related quality of life.

Subjects from ITT population with an assessment at given time point. Observed cases. n=total subjects, by Week 16 status (responder/nonresponder).

End point type	Secondary
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End point timeframe:

Baseline, Week 52

End point values	ITT: 3 mg BID, Upadacitinib in Induction	ITT: 6 mg BID, Upadacitinib at Induction	ITT: 12 mg BID, Upadacitinib at Induction	ITT: 24 mg QD, Upadacitinib at Induction
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	36	15	37	22
Units: units on a scale				
arithmetic mean (standard deviation)				
Responders; n=14, 8, 14, 7, 1, 0, 0, 0	12.9 (± 14.65)	26.9 (± 12.80)	34.8 (± 22.55)	5.0 (± 17.80)
Non-responders; n=22, 7, 23, 15, 6, 4, 6, 3	12.3 (± 24.79)	11.9 (± 18.73)	13.9 (± 27.81)	4.7 (± 14.22)
Clinical responders; n=22, 13, 22, 14, 5, 1, 3, 1	18.2 (± 19.19)	22.2 (± 17.16)	36.1 (± 26.19)	8.1 (± 17.95)
Clinical non-responders; n=14, 2, 15, 8, 2, 3,3,2	3.7 (± 21.79)	5.0 (± 7.07)	0.8 (± 11.72)	-1.0 (± 4.24)

End point values	ITT: 3 mg BID, Placebo in Induction	ITT: 6 mg BID, Placebo at Induction	ITT: 12 mg BID, Placebo at Induction	ITT: 24 mg QD, Placebo at Induction
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	7 ^[119]	4 ^[120]	6	3 ^[121]
Units: units on a scale				
arithmetic mean (standard deviation)				

Responders; n=14, 8, 14, 7, 1, 0, 0, 0	5.0 (± 99999)	0 (± 0)	0 (± 0)	0 (± 0)
Non-responders; n=22, 7, 23, 15, 6, 4, 6, 3	12.2 (± 16.01)	17.5 (± 16.58)	20.3 (± 21.23)	0.0 (± 15.00)
Clinical responders; n=22, 13, 22, 14, 5, 1, 3, 1	15.6 (± 15.63)	40.0 (± 99999)	11.7 (± 16.07)	-15.0 (± 99999)
Clinical non-responders; n=14, 2, 15, 8, 2, 3,3,2	0.0 (± 0.00)	10.0 (± 8.66)	29.0 (± 25.36)	7.5 (± 10.61)

Notes:

[119] - 99999=not applicable (1 subject analyzed)

[120] - 99999=not applicable (1 subject analyzed)

[121] - 99999=not applicable (1 subject analyzed)

Attachments (see zip file)	Table 14.2_2.19.1 stat analysis VAS.docx
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Statistical analyses

No statistical analyses for this end point

Secondary: Cross Tabulation of Induction Baseline and Week 52 in Total Number of Extra-Intestinal Manifestations (EIMs) of Crohn's Disease

End point title	Cross Tabulation of Induction Baseline and Week 52 in Total Number of Extra-Intestinal Manifestations (EIMs) of Crohn's Disease
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End point description:

Presented as percentage of subjects with given number of EIMs at Baseline and Week (Wk) 52. EIMs of Crohn's disease included anemia, autoimmune hepatitis, axial arthropathy, bronchiectasis, chronic obstructive pulmonary disease, episcleritis, erythema nodosum, iritis, nephrolithiasis, oral aphthous ulcers, peripheral arthropathy, primary sclerosing cholangitis, pyoderma gangrenosum, Sweet's syndrome, uveitis, and venous thromboembolism.

Subjects from modified ITT population (all randomized subjects who took at least 1 dose of study drug in the Induction Period). n=total subjects, by number of EIMs at Induction Baseline (BL).

End point type	Secondary
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End point timeframe:

Baseline, Week 52

End point values	Placebo Twice Daily (BID)	Upadacitinib 3 mg BID	Upadacitinib 6 mg BID	Upadacitinib 12 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	37	39	37	36
Units: percentage of subjects				
number (not applicable)				
0 at BL/0 at Wk 52; n=14, 13, 22, 25, 15, 20	85.7	100	86.4	76.0
0 at BL/1 at Wk 52; n=14, 13, 22, 25, 15, 20	7.1	0	9.1	16.0
0 at BL/2 at Wk 52; n=14, 13, 22, 25, 15, 20	0	0	0	0
0 at BL/3 at Wk 52; n=14, 13, 22, 25, 15, 20	0	0	0	0
0 at BL/4 at Wk 52; n=14, 13, 22, 25, 15, 20	0	0	0	0
0 at BL/5 at Wk 52; n=14, 13, 22, 25, 15, 20	0	0	0	0

0 at BL/missing at Wk 52; n=14, 13, 22, 25, 15, 20	7.1	0	4.5	8.0
1 at BL/0 at Wk 52; n=14, 19, 10, 8, 18, 11	42.9	31.6	40.0	62.5
1 at BL/1 at Wk 52; n=14, 19, 10, 8, 18, 11	50.0	57.9	60.0	12.5
1 at BL/2 at Wk 52; n=14, 19, 10, 8, 18, 11	7.1	5.3	0	25.0
1 at BL/3 at Wk 52; n=14, 19, 10, 8, 18, 11	0	0	0	0
1 at BL/4 at Wk 52; n=14, 19, 10, 8, 18, 11	0	0	0	0
1 at BL/5 at Wk 52; n=14, 19, 10, 8, 18, 11	0	0	0	0
1 at BL/missing at Wk 52; n=14, 19, 10, 8, 18, 11	0	5.3	0	0
2 at BL/0 at Wk 52; n=5, 4, 3, 3, 0, 4	20.0	50.0	0	33.3
2 at BL/1 at Wk 52; n=5, 4, 3, 3, 0, 4	0	25.0	66.7	33.3
2 at BL/2 at Wk 52; n=5, 4, 3, 3, 0, 4	60.0	25.0	33.3	33.3
2 at BL/3 at Wk 52; n=5, 4, 3, 3, 0, 4	0	0	0	0
2 at BL/4 at Wk 52; n=5, 4, 3, 3, 0, 4	0	0	0	0
2 at BL/5 at Wk 52; n=5, 4, 3, 3, 0, 4	0	0	0	0
2 at BL/missing at Wk 52; n=5, 4, 3, 3, 0, 4	20.0	0	0	0
3 at BL/0 at Wk 52; n=2, 2, 1, 0, 3, 0	0	50.0	0	0
3 at BL/1 at Wk 52; n=2, 2, 1, 0, 3, 0	50.0	50.0	0	0
3 at BL/2 at Wk 52; n=2, 2, 1, 0, 3, 0	0	0	100	0
3 at BL/3 at Wk 52; n=2, 2, 1, 0, 3, 0	0	0	0	0
3 at BL/4 at Wk 52; n=2, 2, 1, 0, 3, 0	50.0	0	0	0
3 at BL/5 at Wk 52; n=2, 2, 1, 0, 3, 0	0	0	0	0
3 at BL/missing at Wk 52; n=2, 2, 1, 0, 3, 0	0	0	0	0
4 at BL/0 at Wk 52; n=1, 1, 1, 0, 0, 0	0	100	0	0
4 at BL/1 at Wk 52; n=1, 1, 1, 0, 0, 0	0	0	0	0
4 at BL/2 at Wk 52; n=1, 1, 1, 0, 0, 0	0	0	0	0
4 at BL/3 at Wk 52; n=1, 1, 1, 0, 0, 0	0	0	0	0
4 at BL/4 at Wk 52; n=1, 1, 1, 0, 0, 0	100	0	0	0
4 at BL/5 at Wk 52; n=1, 1, 1, 0, 0, 0	0	0	0	0
4 at BL/missing at Wk 52; n=1, 1, 1, 0, 0, 0	0	0	100	0
5 at BL/0 at Wk 52; n=1, 0, 0, 0, 0, 0	0	0	0	0
5 at BL/1 at Wk 52; n=1, 0, 0, 0, 0, 0	0	0	0	0
5 at BL/2 at Wk 52; n=1, 0, 0, 0, 0, 0	0	0	0	0
5 at BL/3 at Wk 52; n=1, 0, 0, 0, 0, 0	0	0	0	0
5 at BL/4 at Wk 52; n=1, 0, 0, 0, 0, 0	0	0	0	0
5 at BL/5 at Wk 52; n=1, 0, 0, 0, 0, 0	100	0	0	0
5 at BL/missing at Wk 52; n=1, 0, 0, 0, 0, 0	0	0	0	0

End point values	Upadacitinib 24 mg BID	Upadacitinib 24 mg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	36	35		

Units: percentage of subjects				
number (not applicable)				
0 at BL/0 at Wk 52; n=14, 13, 22, 25, 15, 20	73.3	85.0		
0 at BL/1 at Wk 52; n=14, 13, 22, 25, 15, 20	13.3	10.0		
0 at BL/2 at Wk 52; n=14, 13, 22, 25, 15, 20	0	0		
0 at BL/3 at Wk 52; n=14, 13, 22, 25, 15, 20	0	0		
0 at BL/4 at Wk 52; n=14, 13, 22, 25, 15, 20	0	0		
0 at BL/5 at Wk 52; n=14, 13, 22, 25, 15, 20	0	0		
0 at BL/missing at Wk 52; n=14, 13, 22, 25, 15, 20	13.3	5.0		
1 at BL/0 at Wk 52; n=14, 19, 10, 8, 18, 11	50.0	54.5		
1 at BL/1 at Wk 52; n=14, 19, 10, 8, 18, 11	33.3	36.4		
1 at BL/2 at Wk 52; n=14, 19, 10, 8, 18, 11	11.1	9.1		
1 at BL/3 at Wk 52; n=14, 19, 10, 8, 18, 11	0	0		
1 at BL/4 at Wk 52; n=14, 19, 10, 8, 18, 11	0	0		
1 at BL/5 at Wk 52; n=14, 19, 10, 8, 18, 11	0	0		
1 at BL/missing at Wk 52; n=14, 19, 10, 8, 18, 11	5.6	0		
2 at BL/0 at Wk 52; n=5, 4, 3, 3, 0, 4	0	25.0		
2 at BL/1 at Wk 52; n=5, 4, 3, 3, 0, 4	0	25.0		
2 at BL/2 at Wk 52; n=5, 4, 3, 3, 0, 4	0	50.0		
2 at BL/3 at Wk 52; n=5, 4, 3, 3, 0, 4	0	0		
2 at BL/4 at Wk 52; n=5, 4, 3, 3, 0, 4	0	0		
2 at BL/5 at Wk 52; n=5, 4, 3, 3, 0, 4	0	0		
2 at BL/missing at Wk 52; n=5, 4, 3, 3, 0, 4	0	0		
3 at BL/0 at Wk 52; n=2, 2, 1, 0, 3, 0	66.7	0		
3 at BL/1 at Wk 52; n=2, 2, 1, 0, 3, 0	0	0		
3 at BL/2 at Wk 52; n=2, 2, 1, 0, 3, 0	33.3	0		
3 at BL/3 at Wk 52; n=2, 2, 1, 0, 3, 0	0	0		
3 at BL/4 at Wk 52; n=2, 2, 1, 0, 3, 0	0	0		
3 at BL/5 at Wk 52; n=2, 2, 1, 0, 3, 0	0	0		
3 at BL/missing at Wk 52; n=2, 2, 1, 0, 3, 0	0	0		
4 at BL/0 at Wk 52; n=1, 1, 1, 0, 0, 0	0	0		
4 at BL/1 at Wk 52; n=1, 1, 1, 0, 0, 0	0	0		
4 at BL/2 at Wk 52; n=1, 1, 1, 0, 0, 0	0	0		
4 at BL/3 at Wk 52; n=1, 1, 1, 0, 0, 0	0	0		
4 at BL/4 at Wk 52; n=1, 1, 1, 0, 0, 0	0	0		
4 at BL/5 at Wk 52; n=1, 1, 1, 0, 0, 0	0	0		
4 at BL/missing at Wk 52; n=1, 1, 1, 0, 0, 0	0	0		
5 at BL/0 at Wk 52; n=1, 0, 0, 0, 0, 0	0	0		
5 at BL/1 at Wk 52; n=1, 0, 0, 0, 0, 0	0	0		
5 at BL/2 at Wk 52; n=1, 0, 0, 0, 0, 0	0	0		

5 at BL/3 at Wk 52; n=1, 0, 0, 0, 0, 0	0	0		
5 at BL/4 at Wk 52; n=1, 0, 0, 0, 0, 0	0	0		
5 at BL/5 at Wk 52; n=1, 0, 0, 0, 0, 0	0	0		
5 at BL/missing at Wk 52; n=1, 0, 0, 0, 0, 0	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects Who Achieve Remission at Week 52 Among Subjects With Isolated Ileal Crohn's Disease at Baseline

End point title	Percentage of Subjects Who Achieve Remission at Week 52 Among Subjects With Isolated Ileal Crohn's Disease at Baseline
End point description:	
Remission at Week 52 is defined as endoscopic remission at Week 52 AND clinical remission at Week 52. Endoscopic remission: SES-CD $\leq$ 4 and at least 2-point reduction versus Baseline and no subscore $>$ 1 in any individual variable. Clinical remission: average daily stool frequency $\leq$ 1.5 and not worse than Baseline AND average daily abdominal pain $\leq$ 1.0 and not worse than Baseline. The very soft/liquid stool frequency and abdominal pain scores at a visit were the average of the daily values reported during the 7 usable days preceding the scheduled assessment visit. Abdominal Pain was rated on a 4-point scale from 0 (none) to 3 (severe). Details of the SES-CD scale are provided in the description of the first primary endpoint.	
Subjects from ITT population with isolated ileal Crohn's disease at Induction Baseline. Non responder imputation. n=total subjects, by Week 16 status (responder/nonresponder).	
End point type	Secondary
End point timeframe:	
Week 52	

End point values	ITT: 3 mg BID, Upadacitinib in Induction	ITT: 6 mg BID, Upadacitinib at Induction	ITT: 12 mg BID, Upadacitinib at Induction	ITT: 24 mg QD, Upadacitinib at Induction
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	15	4	7	3 ^[122]
Units: percentage of subjects				
number (not applicable)				
Responders; n=4, 0, 1, 0, 0, 0, 0, 0	50.0	0	0	0
Non-responders; n=11, 4, 6, 3, 2, 2, 2, 0	0	0	0	0
Clinical responders; n=8, 2, 3, 2, 2, 1, 1, 0	25.0	0	0	0
Clinical non-responders; n=7, 2, 4, 1, 0, 1, 1, 0	0	0	0	0

Notes:

[122] - not applicable in this arm

End point values	ITT: 3 mg BID, Placebo in Induction	ITT: 6 mg BID, Placebo at Induction	ITT: 12 mg BID, Placebo at Induction	ITT: 24 mg QD, Placebo at Induction
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Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	2	2	2	0 ^[123]
Units: percentage of subjects				
number (not applicable)				
Responders; n=4, 0, 1, 0, 0, 0, 0, 0	0	0	0	
Non-responders; n=11, 4, 6, 3, 2, 2, 2, 0	0	0	0	
Clinical responders; n=8, 2, 3, 2, 2, 1, 1, 0	0	0	0	
Clinical non-responders; n=7, 2, 4, 1, 0, 1, 1, 0	0	0	0	

Notes:

[123] - not applicable in this arm

Attachments (see zip file)	Table 14.2_2.5.3.1 stat analysis.docx
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Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects Who Achieve Modified Clinical Remission at Week 52 Among Subjects With Isolated Ileal Crohn's Disease at Baseline And Daily Stool Frequency ≥ 4.0 or Daily Abdominal Pain ≥ 2.0 at Induction Baseline

End point title	Percentage of Subjects Who Achieve Modified Clinical Remission at Week 52 Among Subjects With Isolated Ileal Crohn's Disease at Baseline And Daily Stool Frequency ≥ 4.0 or Daily Abdominal Pain ≥ 2.0 at Induction Baseline
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End point description:

Modified clinical remission was defined as average daily stool frequency ≤ 2.8 and not worse than induction baseline AND average daily abdominal pain ≤ 1.0 and not worse than induction baseline. The very soft/liquid stool frequency and abdominal pain scores at a visit were the average of the daily values reported during the 7 usable days preceding the scheduled assessment visit. Abdominal Pain was rated on a 4-point scale from 0 (none) to 3 (severe).

Subjects from ITT population with isolated ileal Crohn's disease at Induction Baseline and daily stool frequency ≥ 4.0 or daily abdominal pain ≥ 2.0 at Induction Baseline. Non responder imputation. n=total subjects, by Week 16 status (responder/nonresponder).

End point type	Secondary
End point timeframe:	
Week 52	

End point values	ITT: 3 mg BID, Upadacitinib in Induction	ITT: 6 mg BID, Upadacitinib at Induction	ITT: 12 mg BID, Upadacitinib at Induction	ITT: 24 mg QD, Upadacitinib at Induction
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	12	3	7	2
Units: percentage of subjects				
number (not applicable)				
Responders; n=3, 0, 1, 0, 0, 0, 0, 0	66.7	0	0	0
Non-responders; n=9, 3, 6, 2, 2, 2, 2, 0	0	33.3	0	0
Clinical responders; n=6, 2, 3, 1, 2, 1, 1, 0	33.3	50.0	0	0

Clinical non-responders; n=6, 1, 4, 1, 0, 1, 1, 0	0	0	0	0
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End point values	ITT: 3 mg BID, Placebo in Induction	ITT: 6 mg BID, Placebo at Induction	ITT: 12 mg BID, Placebo at Induction	ITT: 24 mg QD, Placebo at Induction
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	2	2	2	0 ^[124]
Units: percentage of subjects				
number (not applicable)				
Responders; n=3, 0, 1, 0, 0, 0, 0, 0	0	0	0	
Non-responders; n=9, 3, 6, 2, 2, 2, 2, 0	50.0	0	0	
Clinical responders; n=6, 2, 3, 1, 2, 1, 1, 0	50.0	0	0	
Clinical non-responders; n=6, 1, 4, 1, 0, 1, 1, 0	0	0	0	

Notes:

[124] - no subjects applicable in this arm

Attachments (see zip file)	Table 14.2_2.5.4.1 stat analysis.docx
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Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Treatment-emergent adverse events AEs (TEAEs): collected from the first dose of study drug through Week 52 plus 30 days.

Adverse event reporting additional description:

For the Extension Phase, a TEAE was defined as any AE with an onset date on or after the first dose of double-blind Extension dose and prior to the open-label dose or up to 30 days after the last dose of double-blind Extension dose if subject discontinued prematurely in the double-blind Extension Phase.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	20.0
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Reporting groups

Reporting group title	Double-Blind Induction Phase: Placebo BID
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Reporting group description:

Placebo BID during the 16-week double-blind Induction Phase.

Reporting group title	Double-Blind Induction Phase: Upadacitinib 3 mg BID
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Reporting group description:

Upadacitinib 3 mg BID during the 16-week double-blind Induction Phase.

Reporting group title	Double-Blind Induction Phase: Upadacitinib 6 mg BID
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Reporting group description:

Upadacitinib 6 mg BID during the 16-week double-blind Induction Phase.

Reporting group title	Double-Blind Induction Phase: Upadacitinib 12 mg BID
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Reporting group description:

Upadacitinib 12 mg BID during the 16-week double-blind Induction Phase.

Reporting group title	Double-Blind Induction Phase: Upadacitinib 24 mg BID
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Reporting group description:

Upadacitinib 24 mg BID during the 16-week double-blind Induction Phase.

Reporting group title	Double-Blind Induction Phase: Upadacitinib 24 mg QD
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Reporting group description:

Upadacitinib 24 mg QD (consisting of two 12 mg IR doses) during the 16-week double-blind Induction Phase.

Reporting group title	Double-Blind Extension Phase: Upadacitinib 3 mg BID
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Reporting group description:

Upadacitinib 3 mg BID during the 36-week double-blind Extension Phase.

Reporting group title	Double-Blind Extension Phase: Upadacitinib 6 mg BID
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Reporting group description:

Upadacitinib 6 mg BID during the 36-week double-blind Extension Phase.

Reporting group title	Double-Blind Extension Phase: Upadacitinib 12 mg BID
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Reporting group description:

Upadacitinib 12 mg BID during the 36-week double-blind Extension Phase.

Reporting group title	Double-Blind Extension Phase: Upadacitinib 24 mg QD
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Reporting group description:

Upadacitinib 24 mg QD (consisting of two 12 mg IR doses) during the 36-week double-blind Extension Phase.

Reporting group title	Open Label (OL) Extension: Upadacitinib 12 mg BID Only
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Reporting group description:

Subjects who met inadequate response criteria at or after Week 20 in the Extension Phase and switched to OL upadacitinib 12 mg BID for the remainder of the Extension Phase.

Reporting group title	OL Extension: Received OL 24 mg BID
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Reporting group description:

Subjects who met inadequate response criteria at or after Week 20 in the Extension Phase and switched to OL upadacitinib 12 mg BID for the remainder of the Extension Phase, and were further dose escalated to OL upadacitinib 24 mg BID after continuing to meet the criteria for inadequate response following a 4-week course of OL upadacitinib 12 mg BID.

Serious adverse events	Double-Blind Induction Phase: Placebo BID	Double-Blind Induction Phase: Upadacitinib 3 mg BID	Double-Blind Induction Phase: Upadacitinib 6 mg BID
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 37 (5.41%)	5 / 39 (12.82%)	2 / 37 (5.41%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Hodgkin's disease			
subjects affected / exposed	0 / 37 (0.00%)	0 / 39 (0.00%)	0 / 37 (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
Malignant neoplasm of thymus			
subjects affected / exposed	0 / 37 (0.00%)	0 / 39 (0.00%)	0 / 37 (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			
Chest pain			
subjects affected / exposed	0 / 37 (0.00%)	0 / 39 (0.00%)	0 / 37 (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
Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure			
subjects affected / exposed	0 / 37 (0.00%)	1 / 39 (2.56%)	0 / 37 (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
Pneumonia aspiration			
subjects affected / exposed	0 / 37 (0.00%)	1 / 39 (2.56%)	0 / 37 (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

Psychiatric disorders			
Bipolar disorder			
subjects affected / exposed	0 / 37 (0.00%)	0 / 39 (0.00%)	0 / 37 (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
Depression			
subjects affected / exposed	0 / 37 (0.00%)	0 / 39 (0.00%)	0 / 37 (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
Suicide attempt			
subjects affected / exposed	0 / 37 (0.00%)	0 / 39 (0.00%)	0 / 37 (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
Investigations			
Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 37 (0.00%)	0 / 39 (0.00%)	0 / 37 (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			
Post procedural haemorrhage			
subjects affected / exposed	0 / 37 (0.00%)	1 / 39 (2.56%)	0 / 37 (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
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	0 / 37 (0.00%)	0 / 39 (0.00%)	0 / 37 (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
Pulseless electrical activity			
subjects affected / exposed	0 / 37 (0.00%)	1 / 39 (2.56%)	0 / 37 (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
Sinus bradycardia			

subjects affected / exposed	0 / 37 (0.00%)	0 / 39 (0.00%)	0 / 37 (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
Sinus tachycardia			
subjects affected / exposed	0 / 37 (0.00%)	0 / 39 (0.00%)	0 / 37 (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
Ventricular tachycardia			
subjects affected / exposed	0 / 37 (0.00%)	0 / 39 (0.00%)	0 / 37 (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
Nervous system disorders			
Syncope			
subjects affected / exposed	0 / 37 (0.00%)	0 / 39 (0.00%)	0 / 37 (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			
Anaemia			
subjects affected / exposed	0 / 37 (0.00%)	0 / 39 (0.00%)	0 / 37 (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	0 / 37 (0.00%)	0 / 39 (0.00%)	0 / 37 (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
Anal fistula			
subjects affected / exposed	0 / 37 (0.00%)	0 / 39 (0.00%)	0 / 37 (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
Anal haemorrhage			
subjects affected / exposed	0 / 37 (0.00%)	0 / 39 (0.00%)	0 / 37 (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

Constipation			
subjects affected / exposed	0 / 37 (0.00%)	0 / 39 (0.00%)	0 / 37 (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	1 / 37 (2.70%)	2 / 39 (5.13%)	2 / 37 (5.41%)
occurrences causally related to treatment / all	1 / 1	0 / 2	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fistula of small intestine			
subjects affected / exposed	0 / 37 (0.00%)	0 / 39 (0.00%)	0 / 37 (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 obstruction			
subjects affected / exposed	0 / 37 (0.00%)	0 / 39 (0.00%)	0 / 37 (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
Ileal perforation			
subjects affected / exposed	0 / 37 (0.00%)	0 / 39 (0.00%)	0 / 37 (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 / 37 (0.00%)	0 / 39 (0.00%)	0 / 37 (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
Intestinal fistula			
subjects affected / exposed	0 / 37 (0.00%)	0 / 39 (0.00%)	0 / 37 (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
Intestinal obstruction			
subjects affected / exposed	0 / 37 (0.00%)	0 / 39 (0.00%)	0 / 37 (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
Intestinal stenosis			

subjects affected / exposed	0 / 37 (0.00%)	0 / 39 (0.00%)	0 / 37 (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
Irritable bowel syndrome			
subjects affected / exposed	0 / 37 (0.00%)	0 / 39 (0.00%)	0 / 37 (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 vein thrombosis			
subjects affected / exposed	0 / 37 (0.00%)	1 / 39 (2.56%)	0 / 37 (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
Peritoneal adhesions			
subjects affected / exposed	0 / 37 (0.00%)	0 / 39 (0.00%)	0 / 37 (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	0 / 37 (0.00%)	0 / 39 (0.00%)	0 / 37 (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 perforation			
subjects affected / exposed	0 / 37 (0.00%)	0 / 39 (0.00%)	0 / 37 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 37 (0.00%)	0 / 39 (0.00%)	0 / 37 (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
Nephrolithiasis			
subjects affected / exposed	0 / 37 (0.00%)	0 / 39 (0.00%)	0 / 37 (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			

Intervertebral disc protrusion			
subjects affected / exposed	0 / 37 (0.00%)	0 / 39 (0.00%)	0 / 37 (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
Osteoarthritis			
subjects affected / exposed	0 / 37 (0.00%)	0 / 39 (0.00%)	0 / 37 (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 / 37 (0.00%)	0 / 39 (0.00%)	0 / 37 (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
Abscess			
subjects affected / exposed	0 / 37 (0.00%)	0 / 39 (0.00%)	0 / 37 (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
Abscess intestinal			
subjects affected / exposed	0 / 37 (0.00%)	0 / 39 (0.00%)	0 / 37 (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
Anal abscess			
subjects affected / exposed	0 / 37 (0.00%)	0 / 39 (0.00%)	0 / 37 (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
Cellulitis			
subjects affected / exposed	0 / 37 (0.00%)	0 / 39 (0.00%)	0 / 37 (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
Escherichia bacteraemia			
subjects affected / exposed	0 / 37 (0.00%)	1 / 39 (2.56%)	0 / 37 (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
Influenza			

subjects affected / exposed	0 / 37 (0.00%)	0 / 39 (0.00%)	0 / 37 (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
Peritonitis			
subjects affected / exposed	0 / 37 (0.00%)	0 / 39 (0.00%)	0 / 37 (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 abscess			
subjects affected / exposed	0 / 37 (0.00%)	0 / 39 (0.00%)	0 / 37 (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
Sepsis			
subjects affected / exposed	0 / 37 (0.00%)	1 / 39 (2.56%)	0 / 37 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subcutaneous abscess			
subjects affected / exposed	0 / 37 (0.00%)	1 / 39 (2.56%)	0 / 37 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	0 / 37 (0.00%)	0 / 39 (0.00%)	0 / 37 (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
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	1 / 37 (2.70%)	0 / 39 (0.00%)	0 / 37 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypokalaemia			
subjects affected / exposed	0 / 37 (0.00%)	0 / 39 (0.00%)	0 / 37 (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
Hypomagnesaemia			

subjects affected / exposed	0 / 37 (0.00%)	0 / 39 (0.00%)	0 / 37 (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	Double-Blind Induction Phase: Upadacitinib 12 mg BID	Double-Blind Induction Phase: Upadacitinib 24 mg BID	Double-Blind Induction Phase: Upadacitinib 24 mg QD
Total subjects affected by serious adverse events			
subjects affected / exposed	10 / 36 (27.78%)	3 / 36 (8.33%)	7 / 35 (20.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Hodgkin's disease			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 35 (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
Malignant neoplasm of thymus			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 35 (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			
Chest pain			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 35 (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
Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 35 (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
Pneumonia aspiration			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 35 (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
Psychiatric disorders			

Bipolar disorder			
subjects affected / exposed	1 / 36 (2.78%)	0 / 36 (0.00%)	0 / 35 (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
Depression			
subjects affected / exposed	1 / 36 (2.78%)	0 / 36 (0.00%)	0 / 35 (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
Suicide attempt			
subjects affected / exposed	0 / 36 (0.00%)	1 / 36 (2.78%)	0 / 35 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Blood creatine phosphokinase increased			
subjects affected / exposed	1 / 36 (2.78%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Post procedural haemorrhage			
subjects affected / exposed	1 / 36 (2.78%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	1 / 36 (2.78%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulseless electrical activity			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 35 (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
Sinus bradycardia			

subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 35 (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
Sinus tachycardia			
subjects affected / exposed	1 / 36 (2.78%)	0 / 36 (0.00%)	0 / 35 (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
Ventricular tachycardia			
subjects affected / exposed	1 / 36 (2.78%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Syncope			
subjects affected / exposed	1 / 36 (2.78%)	0 / 36 (0.00%)	0 / 35 (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			
Anaemia			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 35 (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	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 35 (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
Anal fistula			
subjects affected / exposed	1 / 36 (2.78%)	0 / 36 (0.00%)	0 / 35 (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
Anal haemorrhage			
subjects affected / exposed	1 / 36 (2.78%)	0 / 36 (0.00%)	0 / 35 (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

Constipation			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 35 (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	1 / 36 (2.78%)	2 / 36 (5.56%)	0 / 35 (0.00%)
occurrences causally related to treatment / all	1 / 1	2 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fistula of small intestine			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 35 (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 obstruction			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 35 (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
Ileal perforation			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	1 / 35 (2.86%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ileus			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	1 / 35 (2.86%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal fistula			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	1 / 35 (2.86%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal obstruction			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 35 (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
Intestinal stenosis			

subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 35 (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
Irritable bowel syndrome			
subjects affected / exposed	0 / 36 (0.00%)	1 / 36 (2.78%)	0 / 35 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mesenteric vein thrombosis			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 35 (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
Peritoneal adhesions			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	1 / 35 (2.86%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Small intestinal obstruction			
subjects affected / exposed	1 / 36 (2.78%)	0 / 36 (0.00%)	2 / 35 (5.71%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Small intestinal perforation			
subjects affected / exposed	0 / 36 (0.00%)	1 / 36 (2.78%)	0 / 35 (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
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	1 / 36 (2.78%)	0 / 36 (0.00%)	0 / 35 (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
Nephrolithiasis			
subjects affected / exposed	1 / 36 (2.78%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			

Intervertebral disc protrusion			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 35 (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
Osteoarthritis			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 35 (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 / 36 (0.00%)	0 / 36 (0.00%)	0 / 35 (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
Abscess			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 35 (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
Abscess intestinal			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 35 (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
Anal abscess			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 35 (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
Cellulitis			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 35 (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
Escherichia bacteraemia			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 35 (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
Influenza			

subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 35 (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
Peritonitis			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	1 / 35 (2.86%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rectal abscess			
subjects affected / exposed	1 / 36 (2.78%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	1 / 36 (2.78%)	1 / 36 (2.78%)	1 / 35 (2.86%)
occurrences causally related to treatment / all	1 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subcutaneous abscess			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 35 (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
Urinary tract infection			
subjects affected / exposed	1 / 36 (2.78%)	0 / 36 (0.00%)	1 / 35 (2.86%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 35 (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
Hypokalaemia			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	1 / 35 (2.86%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypomagnesaemia			

subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	1 / 35 (2.86%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Double-Blind Extension Phase: Upadacitinib 3 mg BID	Double-Blind Extension Phase: Upadacitinib 6 mg BID	Double-Blind Extension Phase: Upadacitinib 12 mg BID
Total subjects affected by serious adverse events			
subjects affected / exposed	15 / 60 (25.00%)	2 / 23 (8.70%)	5 / 59 (8.47%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Hodgkin's disease			
subjects affected / exposed	0 / 60 (0.00%)	0 / 23 (0.00%)	1 / 59 (1.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Malignant neoplasm of thymus			
subjects affected / exposed	0 / 60 (0.00%)	0 / 23 (0.00%)	1 / 59 (1.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	0 / 60 (0.00%)	1 / 23 (4.35%)	0 / 59 (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
Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure			
subjects affected / exposed	0 / 60 (0.00%)	0 / 23 (0.00%)	0 / 59 (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
Pneumonia aspiration			
subjects affected / exposed	1 / 60 (1.67%)	0 / 23 (0.00%)	0 / 59 (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
Psychiatric disorders			

Bipolar disorder			
subjects affected / exposed	0 / 60 (0.00%)	0 / 23 (0.00%)	0 / 59 (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
Depression			
subjects affected / exposed	1 / 60 (1.67%)	0 / 23 (0.00%)	0 / 59 (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
Suicide attempt			
subjects affected / exposed	0 / 60 (0.00%)	0 / 23 (0.00%)	0 / 59 (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
Investigations			
Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 60 (0.00%)	0 / 23 (0.00%)	0 / 59 (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			
Post procedural haemorrhage			
subjects affected / exposed	0 / 60 (0.00%)	0 / 23 (0.00%)	0 / 59 (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	0 / 60 (0.00%)	0 / 23 (0.00%)	0 / 59 (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
Pulseless electrical activity			
subjects affected / exposed	0 / 60 (0.00%)	0 / 23 (0.00%)	0 / 59 (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
Sinus bradycardia			

subjects affected / exposed	0 / 60 (0.00%)	0 / 23 (0.00%)	0 / 59 (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
Sinus tachycardia			
subjects affected / exposed	0 / 60 (0.00%)	0 / 23 (0.00%)	0 / 59 (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
Ventricular tachycardia			
subjects affected / exposed	0 / 60 (0.00%)	0 / 23 (0.00%)	0 / 59 (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
Nervous system disorders			
Syncope			
subjects affected / exposed	0 / 60 (0.00%)	0 / 23 (0.00%)	0 / 59 (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			
Anaemia			
subjects affected / exposed	0 / 60 (0.00%)	0 / 23 (0.00%)	1 / 59 (1.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 60 (0.00%)	0 / 23 (0.00%)	1 / 59 (1.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anal fistula			
subjects affected / exposed	0 / 60 (0.00%)	0 / 23 (0.00%)	0 / 59 (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
Anal haemorrhage			
subjects affected / exposed	0 / 60 (0.00%)	0 / 23 (0.00%)	0 / 59 (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

Constipation			
subjects affected / exposed	1 / 60 (1.67%)	0 / 23 (0.00%)	0 / 59 (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
Crohn's disease			
subjects affected / exposed	7 / 60 (11.67%)	0 / 23 (0.00%)	2 / 59 (3.39%)
occurrences causally related to treatment / all	0 / 8	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fistula of small intestine			
subjects affected / exposed	0 / 60 (0.00%)	0 / 23 (0.00%)	0 / 59 (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 obstruction			
subjects affected / exposed	1 / 60 (1.67%)	0 / 23 (0.00%)	0 / 59 (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
Ileal perforation			
subjects affected / exposed	0 / 60 (0.00%)	0 / 23 (0.00%)	0 / 59 (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 / 60 (0.00%)	0 / 23 (0.00%)	0 / 59 (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
Intestinal fistula			
subjects affected / exposed	0 / 60 (0.00%)	0 / 23 (0.00%)	0 / 59 (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
Intestinal obstruction			
subjects affected / exposed	1 / 60 (1.67%)	0 / 23 (0.00%)	0 / 59 (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
Intestinal stenosis			

subjects affected / exposed	1 / 60 (1.67%)	0 / 23 (0.00%)	0 / 59 (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
Irritable bowel syndrome			
subjects affected / exposed	0 / 60 (0.00%)	0 / 23 (0.00%)	0 / 59 (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 vein thrombosis			
subjects affected / exposed	0 / 60 (0.00%)	0 / 23 (0.00%)	0 / 59 (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
Peritoneal adhesions			
subjects affected / exposed	0 / 60 (0.00%)	0 / 23 (0.00%)	0 / 59 (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	2 / 60 (3.33%)	0 / 23 (0.00%)	1 / 59 (1.69%)
occurrences causally related to treatment / all	0 / 4	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Small intestinal perforation			
subjects affected / exposed	0 / 60 (0.00%)	0 / 23 (0.00%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 60 (0.00%)	0 / 23 (0.00%)	0 / 59 (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
Nephrolithiasis			
subjects affected / exposed	0 / 60 (0.00%)	0 / 23 (0.00%)	0 / 59 (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			

Intervertebral disc protrusion			
subjects affected / exposed	1 / 60 (1.67%)	0 / 23 (0.00%)	0 / 59 (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
Osteoarthritis			
subjects affected / exposed	1 / 60 (1.67%)	1 / 23 (4.35%)	0 / 59 (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
Infections and infestations			
Abdominal abscess			
subjects affected / exposed	1 / 60 (1.67%)	0 / 23 (0.00%)	1 / 59 (1.69%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abscess			
subjects affected / exposed	0 / 60 (0.00%)	0 / 23 (0.00%)	0 / 59 (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
Abscess intestinal			
subjects affected / exposed	0 / 60 (0.00%)	0 / 23 (0.00%)	0 / 59 (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
Anal abscess			
subjects affected / exposed	1 / 60 (1.67%)	0 / 23 (0.00%)	0 / 59 (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
Cellulitis			
subjects affected / exposed	1 / 60 (1.67%)	0 / 23 (0.00%)	0 / 59 (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
Escherichia bacteraemia			
subjects affected / exposed	0 / 60 (0.00%)	0 / 23 (0.00%)	0 / 59 (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
Influenza			

subjects affected / exposed	1 / 60 (1.67%)	0 / 23 (0.00%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peritonitis			
subjects affected / exposed	0 / 60 (0.00%)	0 / 23 (0.00%)	0 / 59 (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 abscess			
subjects affected / exposed	0 / 60 (0.00%)	0 / 23 (0.00%)	0 / 59 (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
Sepsis			
subjects affected / exposed	1 / 60 (1.67%)	0 / 23 (0.00%)	0 / 59 (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
Subcutaneous abscess			
subjects affected / exposed	0 / 60 (0.00%)	0 / 23 (0.00%)	0 / 59 (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
Urinary tract infection			
subjects affected / exposed	0 / 60 (0.00%)	0 / 23 (0.00%)	0 / 59 (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
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 60 (0.00%)	0 / 23 (0.00%)	0 / 59 (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
Hypokalaemia			
subjects affected / exposed	0 / 60 (0.00%)	0 / 23 (0.00%)	0 / 59 (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
Hypomagnesaemia			

subjects affected / exposed	0 / 60 (0.00%)	0 / 23 (0.00%)	0 / 59 (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	Double-Blind Extension Phase: Upadacitinib 24 mg QD	Open Label (OL) Extension: Upadacitinib 12 mg BID Only	OL Extension: Received OL 24 mg BID
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 36 (11.11%)	11 / 33 (33.33%)	4 / 27 (14.81%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Hodgkin's disease			
subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	0 / 27 (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
Malignant neoplasm of thymus			
subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	0 / 27 (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			
Chest pain			
subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	0 / 27 (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
Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure			
subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	0 / 27 (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
Pneumonia aspiration			
subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	0 / 27 (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
Psychiatric disorders			

Bipolar disorder			
subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	0 / 27 (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
Depression			
subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	0 / 27 (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
Suicide attempt			
subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	0 / 27 (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
Investigations			
Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	0 / 27 (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			
Post procedural haemorrhage			
subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	0 / 27 (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	0 / 36 (0.00%)	0 / 33 (0.00%)	0 / 27 (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
Pulseless electrical activity			
subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	0 / 27 (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
Sinus bradycardia			

subjects affected / exposed	0 / 36 (0.00%)	1 / 33 (3.03%)	0 / 27 (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
Sinus tachycardia			
subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	0 / 27 (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
Ventricular tachycardia			
subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	0 / 27 (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
Nervous system disorders			
Syncope			
subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	0 / 27 (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			
Anaemia			
subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	0 / 27 (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	2 / 36 (5.56%)	1 / 33 (3.03%)	0 / 27 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anal fistula			
subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	0 / 27 (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
Anal haemorrhage			
subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	0 / 27 (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

Constipation			
subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	0 / 27 (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	4 / 36 (11.11%)	7 / 33 (21.21%)	3 / 27 (11.11%)
occurrences causally related to treatment / all	1 / 4	1 / 9	1 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fistula of small intestine			
subjects affected / exposed	0 / 36 (0.00%)	1 / 33 (3.03%)	0 / 27 (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 obstruction			
subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	0 / 27 (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
Ileal perforation			
subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	0 / 27 (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 / 36 (0.00%)	0 / 33 (0.00%)	0 / 27 (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
Intestinal fistula			
subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	0 / 27 (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
Intestinal obstruction			
subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	0 / 27 (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
Intestinal stenosis			

subjects affected / exposed	0 / 36 (0.00%)	1 / 33 (3.03%)	0 / 27 (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
Irritable bowel syndrome			
subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	0 / 27 (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 vein thrombosis			
subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	0 / 27 (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
Peritoneal adhesions			
subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	0 / 27 (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	0 / 36 (0.00%)	1 / 33 (3.03%)	0 / 27 (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 perforation			
subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	0 / 27 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	0 / 27 (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
Nephrolithiasis			
subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	1 / 27 (3.70%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			

Intervertebral disc protrusion subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	0 / 27 (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
Osteoarthritis subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	0 / 27 (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 / 36 (0.00%)	0 / 33 (0.00%)	1 / 27 (3.70%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abscess subjects affected / exposed	0 / 36 (0.00%)	1 / 33 (3.03%)	0 / 27 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abscess intestinal subjects affected / exposed	0 / 36 (0.00%)	1 / 33 (3.03%)	0 / 27 (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
Anal abscess subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	0 / 27 (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
Cellulitis subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	0 / 27 (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
Escherichia bacteraemia subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	0 / 27 (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
Influenza			

subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	0 / 27 (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
Peritonitis			
subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	0 / 27 (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 abscess			
subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	0 / 27 (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
Sepsis			
subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	0 / 27 (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
Subcutaneous abscess			
subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	0 / 27 (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
Urinary tract infection			
subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	0 / 27 (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
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	0 / 27 (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
Hypokalaemia			
subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	0 / 27 (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
Hypomagnesaemia			

subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	0 / 27 (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

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

Non-serious adverse events	Double-Blind Induction Phase: Placebo BID	Double-Blind Induction Phase: Upadacitinib 3 mg BID	Double-Blind Induction Phase: Upadacitinib 6 mg BID
Total subjects affected by non-serious adverse events			
subjects affected / exposed	25 / 37 (67.57%)	32 / 39 (82.05%)	27 / 37 (72.97%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Lipoma			
subjects affected / exposed	0 / 37 (0.00%)	2 / 39 (5.13%)	0 / 37 (0.00%)
occurrences (all)	0	2	0
Vascular disorders			
Hot flush			
subjects affected / exposed	0 / 37 (0.00%)	2 / 39 (5.13%)	0 / 37 (0.00%)
occurrences (all)	0	2	0
Hypertension			
subjects affected / exposed	0 / 37 (0.00%)	0 / 39 (0.00%)	2 / 37 (5.41%)
occurrences (all)	0	0	2
General disorders and administration site conditions			
Chills			
subjects affected / exposed	1 / 37 (2.70%)	0 / 39 (0.00%)	0 / 37 (0.00%)
occurrences (all)	1	0	0
Fatigue			
subjects affected / exposed	3 / 37 (8.11%)	8 / 39 (20.51%)	2 / 37 (5.41%)
occurrences (all)	3	9	2
Influenza like illness			
subjects affected / exposed	0 / 37 (0.00%)	0 / 39 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0	0
Oedema peripheral			
subjects affected / exposed	0 / 37 (0.00%)	1 / 39 (2.56%)	2 / 37 (5.41%)
occurrences (all)	0	1	2
Pyrexia			

subjects affected / exposed occurrences (all)	3 / 37 (8.11%) 3	5 / 39 (12.82%) 6	0 / 37 (0.00%) 0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 37 (0.00%)	0 / 39 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0	0
Oropharyngeal pain			
subjects affected / exposed	0 / 37 (0.00%)	3 / 39 (7.69%)	2 / 37 (5.41%)
occurrences (all)	0	3	2
Pleural effusion			
subjects affected / exposed	0 / 37 (0.00%)	0 / 39 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Anxiety			
subjects affected / exposed	2 / 37 (5.41%)	0 / 39 (0.00%)	0 / 37 (0.00%)
occurrences (all)	2	0	0
Insomnia			
subjects affected / exposed	0 / 37 (0.00%)	1 / 39 (2.56%)	1 / 37 (2.70%)
occurrences (all)	0	1	1
Investigations			
Blood creatine phosphokinase increased			
subjects affected / exposed	1 / 37 (2.70%)	1 / 39 (2.56%)	1 / 37 (2.70%)
occurrences (all)	1	1	1
C-reactive protein increased			
subjects affected / exposed	0 / 37 (0.00%)	0 / 39 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0	0
Haemoglobin decreased			
subjects affected / exposed	0 / 37 (0.00%)	1 / 39 (2.56%)	1 / 37 (2.70%)
occurrences (all)	0	1	1
Injury, poisoning and procedural complications			
Post procedural haemorrhage			
subjects affected / exposed	0 / 37 (0.00%)	0 / 39 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			

Headache subjects affected / exposed occurrences (all)	3 / 37 (8.11%) 3	7 / 39 (17.95%) 8	7 / 37 (18.92%) 11
Blood and lymphatic system disorders			
Anaemia subjects affected / exposed occurrences (all)	0 / 37 (0.00%) 0	2 / 39 (5.13%) 2	1 / 37 (2.70%) 1
Lymphadenopathy subjects affected / exposed occurrences (all)	1 / 37 (2.70%) 1	2 / 39 (5.13%) 2	0 / 37 (0.00%) 0
Eye disorders			
Eye pain subjects affected / exposed occurrences (all)	0 / 37 (0.00%) 0	2 / 39 (5.13%) 2	0 / 37 (0.00%) 0
Gastrointestinal disorders			
Abdominal pain subjects affected / exposed occurrences (all)	0 / 37 (0.00%) 0	5 / 39 (12.82%) 6	2 / 37 (5.41%) 2
Abdominal pain upper subjects affected / exposed occurrences (all)	2 / 37 (5.41%) 2	0 / 39 (0.00%) 0	0 / 37 (0.00%) 0
Anorectal discomfort subjects affected / exposed occurrences (all)	2 / 37 (5.41%) 2	0 / 39 (0.00%) 0	1 / 37 (2.70%) 1
Constipation subjects affected / exposed occurrences (all)	0 / 37 (0.00%) 0	0 / 39 (0.00%) 0	0 / 37 (0.00%) 0
Crohn's disease subjects affected / exposed occurrences (all)	6 / 37 (16.22%) 6	6 / 39 (15.38%) 6	4 / 37 (10.81%) 4
Diarrhoea subjects affected / exposed occurrences (all)	3 / 37 (8.11%) 3	1 / 39 (2.56%) 1	0 / 37 (0.00%) 0
Dyspepsia subjects affected / exposed occurrences (all)	0 / 37 (0.00%) 0	2 / 39 (5.13%) 2	0 / 37 (0.00%) 0
Flatulence			

subjects affected / exposed	1 / 37 (2.70%)	1 / 39 (2.56%)	0 / 37 (0.00%)
occurrences (all)	1	1	0
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 37 (0.00%)	0 / 39 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0	0
Haematochezia			
subjects affected / exposed	1 / 37 (2.70%)	1 / 39 (2.56%)	0 / 37 (0.00%)
occurrences (all)	1	1	0
Intestinal obstruction			
subjects affected / exposed	2 / 37 (5.41%)	0 / 39 (0.00%)	0 / 37 (0.00%)
occurrences (all)	2	0	0
Nausea			
subjects affected / exposed	3 / 37 (8.11%)	2 / 39 (5.13%)	3 / 37 (8.11%)
occurrences (all)	3	2	4
Proctalgia			
subjects affected / exposed	0 / 37 (0.00%)	3 / 39 (7.69%)	0 / 37 (0.00%)
occurrences (all)	0	3	0
Vomiting			
subjects affected / exposed	1 / 37 (2.70%)	4 / 39 (10.26%)	1 / 37 (2.70%)
occurrences (all)	1	4	1
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	1 / 37 (2.70%)	1 / 39 (2.56%)	2 / 37 (5.41%)
occurrences (all)	1	1	2
Alopecia			
subjects affected / exposed	1 / 37 (2.70%)	0 / 39 (0.00%)	2 / 37 (5.41%)
occurrences (all)	1	0	2
Dermatitis acneiform			
subjects affected / exposed	0 / 37 (0.00%)	0 / 39 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Rash			
subjects affected / exposed	0 / 37 (0.00%)	1 / 39 (2.56%)	0 / 37 (0.00%)
occurrences (all)	0	1	0
Rash erythematous			
subjects affected / exposed	0 / 37 (0.00%)	0 / 39 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0	0

Rosacea			
subjects affected / exposed	0 / 37 (0.00%)	0 / 39 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0	0
Urticaria			
subjects affected / exposed	0 / 37 (0.00%)	0 / 39 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	4 / 37 (10.81%)	2 / 39 (5.13%)	2 / 37 (5.41%)
occurrences (all)	4	2	2
Back pain			
subjects affected / exposed	2 / 37 (5.41%)	1 / 39 (2.56%)	1 / 37 (2.70%)
occurrences (all)	2	1	1
Muscle spasms			
subjects affected / exposed	0 / 37 (0.00%)	1 / 39 (2.56%)	2 / 37 (5.41%)
occurrences (all)	0	1	4
Musculoskeletal pain			
subjects affected / exposed	1 / 37 (2.70%)	0 / 39 (0.00%)	2 / 37 (5.41%)
occurrences (all)	1	0	2
Infections and infestations			
Bronchitis			
subjects affected / exposed	0 / 37 (0.00%)	0 / 39 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0	0
Gastroenteritis			
subjects affected / exposed	1 / 37 (2.70%)	1 / 39 (2.56%)	0 / 37 (0.00%)
occurrences (all)	1	2	0
Influenza			
subjects affected / exposed	0 / 37 (0.00%)	3 / 39 (7.69%)	0 / 37 (0.00%)
occurrences (all)	0	3	0
Lower respiratory tract infection			
subjects affected / exposed	2 / 37 (5.41%)	0 / 39 (0.00%)	0 / 37 (0.00%)
occurrences (all)	2	0	0
Oral herpes			
subjects affected / exposed	0 / 37 (0.00%)	1 / 39 (2.56%)	0 / 37 (0.00%)
occurrences (all)	0	1	0
Pneumonia			

subjects affected / exposed	0 / 37 (0.00%)	0 / 39 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0	0
Sinusitis			
subjects affected / exposed	1 / 37 (2.70%)	0 / 39 (0.00%)	2 / 37 (5.41%)
occurrences (all)	2	0	2
Upper respiratory tract infection			
subjects affected / exposed	2 / 37 (5.41%)	2 / 39 (5.13%)	2 / 37 (5.41%)
occurrences (all)	2	3	2
Urinary tract infection			
subjects affected / exposed	2 / 37 (5.41%)	1 / 39 (2.56%)	4 / 37 (10.81%)
occurrences (all)	2	1	4
Viral upper respiratory tract infection			
subjects affected / exposed	1 / 37 (2.70%)	4 / 39 (10.26%)	4 / 37 (10.81%)
occurrences (all)	2	5	5
Metabolism and nutrition disorders			
Hypokalaemia			
subjects affected / exposed	2 / 37 (5.41%)	1 / 39 (2.56%)	1 / 37 (2.70%)
occurrences (all)	2	1	1
Malnutrition			
subjects affected / exposed	0 / 37 (0.00%)	2 / 39 (5.13%)	0 / 37 (0.00%)
occurrences (all)	0	2	0

Non-serious adverse events	Double-Blind Induction Phase: Upadacitinib 12 mg BID	Double-Blind Induction Phase: Upadacitinib 24 mg BID	Double-Blind Induction Phase: Upadacitinib 24 mg QD
Total subjects affected by non-serious adverse events			
subjects affected / exposed	23 / 36 (63.89%)	28 / 36 (77.78%)	25 / 35 (71.43%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Lipoma			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Vascular disorders			
Hot flush			
subjects affected / exposed	0 / 36 (0.00%)	1 / 36 (2.78%)	0 / 35 (0.00%)
occurrences (all)	0	1	0
Hypertension			

subjects affected / exposed occurrences (all)	1 / 36 (2.78%) 1	0 / 36 (0.00%) 0	2 / 35 (5.71%) 2
General disorders and administration site conditions			
Chills			
subjects affected / exposed	0 / 36 (0.00%)	2 / 36 (5.56%)	0 / 35 (0.00%)
occurrences (all)	0	2	0
Fatigue			
subjects affected / exposed	2 / 36 (5.56%)	4 / 36 (11.11%)	2 / 35 (5.71%)
occurrences (all)	2	4	2
Influenza like illness			
subjects affected / exposed	1 / 36 (2.78%)	2 / 36 (5.56%)	0 / 35 (0.00%)
occurrences (all)	1	2	0
Oedema peripheral			
subjects affected / exposed	1 / 36 (2.78%)	1 / 36 (2.78%)	0 / 35 (0.00%)
occurrences (all)	1	1	0
Pyrexia			
subjects affected / exposed	2 / 36 (5.56%)	1 / 36 (2.78%)	1 / 35 (2.86%)
occurrences (all)	2	2	2
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Oropharyngeal pain			
subjects affected / exposed	0 / 36 (0.00%)	2 / 36 (5.56%)	0 / 35 (0.00%)
occurrences (all)	0	2	0
Pleural effusion			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	2 / 35 (5.71%)
occurrences (all)	0	0	2
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 36 (0.00%)	1 / 36 (2.78%)	2 / 35 (5.71%)
occurrences (all)	0	1	2
Insomnia			
subjects affected / exposed	2 / 36 (5.56%)	2 / 36 (5.56%)	0 / 35 (0.00%)
occurrences (all)	2	2	0
Investigations			

Blood creatine phosphokinase increased subjects affected / exposed occurrences (all)	1 / 36 (2.78%) 1	3 / 36 (8.33%) 3	0 / 35 (0.00%) 0
C-reactive protein increased subjects affected / exposed occurrences (all)	0 / 36 (0.00%) 0	0 / 36 (0.00%) 0	0 / 35 (0.00%) 0
Haemoglobin decreased subjects affected / exposed occurrences (all)	0 / 36 (0.00%) 0	2 / 36 (5.56%) 2	1 / 35 (2.86%) 1
Injury, poisoning and procedural complications Post procedural haemorrhage subjects affected / exposed occurrences (all)	0 / 36 (0.00%) 0	0 / 36 (0.00%) 0	0 / 35 (0.00%) 0
Nervous system disorders Headache subjects affected / exposed occurrences (all)	3 / 36 (8.33%) 3	8 / 36 (22.22%) 9	5 / 35 (14.29%) 5
Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all) Lymphadenopathy subjects affected / exposed occurrences (all)	3 / 36 (8.33%) 3 0 / 36 (0.00%) 0	1 / 36 (2.78%) 1 0 / 36 (0.00%) 0	2 / 35 (5.71%) 3 0 / 35 (0.00%) 0
Eye disorders Eye pain subjects affected / exposed occurrences (all)	0 / 36 (0.00%) 0	0 / 36 (0.00%) 0	0 / 35 (0.00%) 0
Gastrointestinal disorders Abdominal pain subjects affected / exposed occurrences (all) Abdominal pain upper subjects affected / exposed occurrences (all) Anorectal discomfort	6 / 36 (16.67%) 8 1 / 36 (2.78%) 1	2 / 36 (5.56%) 2 0 / 36 (0.00%) 0	5 / 35 (14.29%) 5 1 / 35 (2.86%) 1

subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Constipation			
subjects affected / exposed	0 / 36 (0.00%)	1 / 36 (2.78%)	2 / 35 (5.71%)
occurrences (all)	0	1	3
Crohn's disease			
subjects affected / exposed	7 / 36 (19.44%)	3 / 36 (8.33%)	2 / 35 (5.71%)
occurrences (all)	8	3	2
Diarrhoea			
subjects affected / exposed	3 / 36 (8.33%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	3	0	0
Dyspepsia			
subjects affected / exposed	1 / 36 (2.78%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	1	0	0
Flatulence			
subjects affected / exposed	0 / 36 (0.00%)	3 / 36 (8.33%)	0 / 35 (0.00%)
occurrences (all)	0	3	0
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Haematochezia			
subjects affected / exposed	2 / 36 (5.56%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	2	0	0
Intestinal obstruction			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	3 / 36 (8.33%)	3 / 36 (8.33%)	1 / 35 (2.86%)
occurrences (all)	3	4	1
Proctalgia			
subjects affected / exposed	0 / 36 (0.00%)	1 / 36 (2.78%)	0 / 35 (0.00%)
occurrences (all)	0	1	0
Vomiting			
subjects affected / exposed	3 / 36 (8.33%)	3 / 36 (8.33%)	1 / 35 (2.86%)
occurrences (all)	3	3	1
Skin and subcutaneous tissue disorders			

Acne			
subjects affected / exposed	2 / 36 (5.56%)	3 / 36 (8.33%)	3 / 35 (8.57%)
occurrences (all)	2	3	3
Alopecia			
subjects affected / exposed	0 / 36 (0.00%)	2 / 36 (5.56%)	0 / 35 (0.00%)
occurrences (all)	0	2	0
Dermatitis acneiform			
subjects affected / exposed	2 / 36 (5.56%)	1 / 36 (2.78%)	0 / 35 (0.00%)
occurrences (all)	2	1	0
Rash			
subjects affected / exposed	1 / 36 (2.78%)	0 / 36 (0.00%)	3 / 35 (8.57%)
occurrences (all)	1	0	4
Rash erythematous			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	2 / 35 (5.71%)
occurrences (all)	0	0	2
Rosacea			
subjects affected / exposed	2 / 36 (5.56%)	1 / 36 (2.78%)	0 / 35 (0.00%)
occurrences (all)	2	1	0
Urticaria			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	2 / 35 (5.71%)
occurrences (all)	0	0	2
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 36 (2.78%)	1 / 36 (2.78%)	3 / 35 (8.57%)
occurrences (all)	1	1	3
Back pain			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	1 / 35 (2.86%)
occurrences (all)	0	0	1
Muscle spasms			
subjects affected / exposed	2 / 36 (5.56%)	1 / 36 (2.78%)	1 / 35 (2.86%)
occurrences (all)	2	1	2
Musculoskeletal pain			
subjects affected / exposed	0 / 36 (0.00%)	1 / 36 (2.78%)	0 / 35 (0.00%)
occurrences (all)	0	1	0
Infections and infestations			

Bronchitis			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Gastroenteritis			
subjects affected / exposed	0 / 36 (0.00%)	1 / 36 (2.78%)	2 / 35 (5.71%)
occurrences (all)	0	1	2
Influenza			
subjects affected / exposed	1 / 36 (2.78%)	1 / 36 (2.78%)	0 / 35 (0.00%)
occurrences (all)	1	1	0
Lower respiratory tract infection			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Oral herpes			
subjects affected / exposed	1 / 36 (2.78%)	2 / 36 (5.56%)	0 / 35 (0.00%)
occurrences (all)	1	2	0
Pneumonia			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Sinusitis			
subjects affected / exposed	0 / 36 (0.00%)	2 / 36 (5.56%)	0 / 35 (0.00%)
occurrences (all)	0	2	0
Upper respiratory tract infection			
subjects affected / exposed	4 / 36 (11.11%)	4 / 36 (11.11%)	1 / 35 (2.86%)
occurrences (all)	4	4	2
Urinary tract infection			
subjects affected / exposed	0 / 36 (0.00%)	5 / 36 (13.89%)	2 / 35 (5.71%)
occurrences (all)	0	5	2
Viral upper respiratory tract infection			
subjects affected / exposed	4 / 36 (11.11%)	3 / 36 (8.33%)	2 / 35 (5.71%)
occurrences (all)	4	5	2
Metabolism and nutrition disorders			
Hypokalaemia			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Malnutrition			

subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Double-Blind Extension Phase: Upadacitinib 3 mg BID	Double-Blind Extension Phase: Upadacitinib 6 mg BID	Double-Blind Extension Phase: Upadacitinib 12 mg BID
Total subjects affected by non-serious adverse events			
subjects affected / exposed	31 / 60 (51.67%)	6 / 23 (26.09%)	33 / 59 (55.93%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Lipoma			
subjects affected / exposed	0 / 60 (0.00%)	0 / 23 (0.00%)	0 / 59 (0.00%)
occurrences (all)	0	0	0
Vascular disorders			
Hot flush			
subjects affected / exposed	0 / 60 (0.00%)	0 / 23 (0.00%)	0 / 59 (0.00%)
occurrences (all)	0	0	0
Hypertension			
subjects affected / exposed	0 / 60 (0.00%)	0 / 23 (0.00%)	0 / 59 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Chills			
subjects affected / exposed	0 / 60 (0.00%)	0 / 23 (0.00%)	0 / 59 (0.00%)
occurrences (all)	0	0	0
Fatigue			
subjects affected / exposed	2 / 60 (3.33%)	1 / 23 (4.35%)	2 / 59 (3.39%)
occurrences (all)	2	1	2
Influenza like illness			
subjects affected / exposed	3 / 60 (5.00%)	0 / 23 (0.00%)	0 / 59 (0.00%)
occurrences (all)	3	0	0
Oedema peripheral			
subjects affected / exposed	0 / 60 (0.00%)	0 / 23 (0.00%)	0 / 59 (0.00%)
occurrences (all)	0	0	0
Pyrexia			
subjects affected / exposed	1 / 60 (1.67%)	0 / 23 (0.00%)	3 / 59 (5.08%)
occurrences (all)	2	0	3
Respiratory, thoracic and mediastinal disorders			

Cough subjects affected / exposed occurrences (all)	3 / 60 (5.00%) 3	0 / 23 (0.00%) 0	0 / 59 (0.00%) 0
Oropharyngeal pain subjects affected / exposed occurrences (all)	3 / 60 (5.00%) 3	0 / 23 (0.00%) 0	3 / 59 (5.08%) 4
Pleural effusion subjects affected / exposed occurrences (all)	0 / 60 (0.00%) 0	0 / 23 (0.00%) 0	0 / 59 (0.00%) 0
Psychiatric disorders Anxiety subjects affected / exposed occurrences (all)	0 / 60 (0.00%) 0	0 / 23 (0.00%) 0	0 / 59 (0.00%) 0
Insomnia subjects affected / exposed occurrences (all)	0 / 60 (0.00%) 0	0 / 23 (0.00%) 0	0 / 59 (0.00%) 0
Investigations Blood creatine phosphokinase increased subjects affected / exposed occurrences (all)	4 / 60 (6.67%) 5	1 / 23 (4.35%) 1	2 / 59 (3.39%) 2
C-reactive protein increased subjects affected / exposed occurrences (all)	3 / 60 (5.00%) 3	0 / 23 (0.00%) 0	0 / 59 (0.00%) 0
Haemoglobin decreased subjects affected / exposed occurrences (all)	0 / 60 (0.00%) 0	0 / 23 (0.00%) 0	0 / 59 (0.00%) 0
Injury, poisoning and procedural complications Post procedural haemorrhage subjects affected / exposed occurrences (all)	0 / 60 (0.00%) 0	0 / 23 (0.00%) 0	0 / 59 (0.00%) 0
Nervous system disorders Headache subjects affected / exposed occurrences (all)	0 / 60 (0.00%) 0	1 / 23 (4.35%) 1	5 / 59 (8.47%) 6
Blood and lymphatic system disorders			

Anaemia			
subjects affected / exposed	0 / 60 (0.00%)	0 / 23 (0.00%)	0 / 59 (0.00%)
occurrences (all)	0	0	0
Lymphadenopathy			
subjects affected / exposed	0 / 60 (0.00%)	0 / 23 (0.00%)	0 / 59 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Eye pain			
subjects affected / exposed	0 / 60 (0.00%)	0 / 23 (0.00%)	0 / 59 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	4 / 60 (6.67%)	0 / 23 (0.00%)	1 / 59 (1.69%)
occurrences (all)	4	0	1
Abdominal pain upper			
subjects affected / exposed	3 / 60 (5.00%)	0 / 23 (0.00%)	1 / 59 (1.69%)
occurrences (all)	3	0	1
Anorectal discomfort			
subjects affected / exposed	0 / 60 (0.00%)	0 / 23 (0.00%)	0 / 59 (0.00%)
occurrences (all)	0	0	0
Constipation			
subjects affected / exposed	0 / 60 (0.00%)	0 / 23 (0.00%)	0 / 59 (0.00%)
occurrences (all)	0	0	0
Crohn's disease			
subjects affected / exposed	6 / 60 (10.00%)	2 / 23 (8.70%)	6 / 59 (10.17%)
occurrences (all)	6	2	7
Diarrhoea			
subjects affected / exposed	0 / 60 (0.00%)	0 / 23 (0.00%)	0 / 59 (0.00%)
occurrences (all)	0	0	0
Dyspepsia			
subjects affected / exposed	0 / 60 (0.00%)	0 / 23 (0.00%)	0 / 59 (0.00%)
occurrences (all)	0	0	0
Flatulence			
subjects affected / exposed	0 / 60 (0.00%)	0 / 23 (0.00%)	0 / 59 (0.00%)
occurrences (all)	0	0	0
Gastrooesophageal reflux disease			

subjects affected / exposed	0 / 60 (0.00%)	1 / 23 (4.35%)	2 / 59 (3.39%)
occurrences (all)	0	1	2
Haematochezia			
subjects affected / exposed	0 / 60 (0.00%)	0 / 23 (0.00%)	0 / 59 (0.00%)
occurrences (all)	0	0	0
Intestinal obstruction			
subjects affected / exposed	0 / 60 (0.00%)	0 / 23 (0.00%)	0 / 59 (0.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	1 / 60 (1.67%)	1 / 23 (4.35%)	3 / 59 (5.08%)
occurrences (all)	1	1	3
Proctalgia			
subjects affected / exposed	0 / 60 (0.00%)	0 / 23 (0.00%)	0 / 59 (0.00%)
occurrences (all)	0	0	0
Vomiting			
subjects affected / exposed	1 / 60 (1.67%)	0 / 23 (0.00%)	3 / 59 (5.08%)
occurrences (all)	1	0	3
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	1 / 60 (1.67%)	0 / 23 (0.00%)	4 / 59 (6.78%)
occurrences (all)	1	0	4
Alopecia			
subjects affected / exposed	0 / 60 (0.00%)	0 / 23 (0.00%)	0 / 59 (0.00%)
occurrences (all)	0	0	0
Dermatitis acneiform			
subjects affected / exposed	0 / 60 (0.00%)	0 / 23 (0.00%)	0 / 59 (0.00%)
occurrences (all)	0	0	0
Rash			
subjects affected / exposed	0 / 60 (0.00%)	1 / 23 (4.35%)	3 / 59 (5.08%)
occurrences (all)	0	1	3
Rash erythematous			
subjects affected / exposed	0 / 60 (0.00%)	0 / 23 (0.00%)	0 / 59 (0.00%)
occurrences (all)	0	0	0
Rosacea			
subjects affected / exposed	0 / 60 (0.00%)	0 / 23 (0.00%)	0 / 59 (0.00%)
occurrences (all)	0	0	0

Urticaria subjects affected / exposed occurrences (all)	0 / 60 (0.00%) 0	0 / 23 (0.00%) 0	0 / 59 (0.00%) 0
Musculoskeletal and connective tissue disorders			
Arthralgia subjects affected / exposed occurrences (all)	5 / 60 (8.33%) 5	1 / 23 (4.35%) 1	2 / 59 (3.39%) 2
Back pain subjects affected / exposed occurrences (all)	0 / 60 (0.00%) 0	0 / 23 (0.00%) 0	0 / 59 (0.00%) 0
Muscle spasms subjects affected / exposed occurrences (all)	0 / 60 (0.00%) 0	0 / 23 (0.00%) 0	0 / 59 (0.00%) 0
Musculoskeletal pain subjects affected / exposed occurrences (all)	0 / 60 (0.00%) 0	0 / 23 (0.00%) 0	0 / 59 (0.00%) 0
Infections and infestations			
Bronchitis subjects affected / exposed occurrences (all)	0 / 60 (0.00%) 0	0 / 23 (0.00%) 0	0 / 59 (0.00%) 0
Gastroenteritis subjects affected / exposed occurrences (all)	0 / 60 (0.00%) 0	0 / 23 (0.00%) 0	0 / 59 (0.00%) 0
Influenza subjects affected / exposed occurrences (all)	0 / 60 (0.00%) 0	0 / 23 (0.00%) 0	0 / 59 (0.00%) 0
Lower respiratory tract infection subjects affected / exposed occurrences (all)	0 / 60 (0.00%) 0	0 / 23 (0.00%) 0	0 / 59 (0.00%) 0
Oral herpes subjects affected / exposed occurrences (all)	0 / 60 (0.00%) 0	0 / 23 (0.00%) 0	4 / 59 (6.78%) 4
Pneumonia subjects affected / exposed occurrences (all)	0 / 60 (0.00%) 0	0 / 23 (0.00%) 0	3 / 59 (5.08%) 3
Sinusitis			

subjects affected / exposed occurrences (all)	1 / 60 (1.67%) 1	2 / 23 (8.70%) 2	1 / 59 (1.69%) 1
Upper respiratory tract infection subjects affected / exposed occurrences (all)	3 / 60 (5.00%) 5	1 / 23 (4.35%) 1	4 / 59 (6.78%) 4
Urinary tract infection subjects affected / exposed occurrences (all)	4 / 60 (6.67%) 5	1 / 23 (4.35%) 1	5 / 59 (8.47%) 6
Viral upper respiratory tract infection subjects affected / exposed occurrences (all)	5 / 60 (8.33%) 5	1 / 23 (4.35%) 1	7 / 59 (11.86%) 8
Metabolism and nutrition disorders			
Hypokalaemia subjects affected / exposed occurrences (all)	0 / 60 (0.00%) 0	0 / 23 (0.00%) 0	0 / 59 (0.00%) 0
Malnutrition subjects affected / exposed occurrences (all)	0 / 60 (0.00%) 0	0 / 23 (0.00%) 0	0 / 59 (0.00%) 0

Non-serious adverse events	Double-Blind Extension Phase: Upadacitinib 24 mg QD	Open Label (OL) Extension: Upadacitinib 12 mg BID Only	OL Extension: Received OL 24 mg BID
Total subjects affected by non-serious adverse events subjects affected / exposed	9 / 36 (25.00%)	8 / 33 (24.24%)	17 / 27 (62.96%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps) Lipoma subjects affected / exposed occurrences (all)	0 / 36 (0.00%) 0	0 / 33 (0.00%) 0	0 / 27 (0.00%) 0
Vascular disorders Hot flush subjects affected / exposed occurrences (all)	0 / 36 (0.00%) 0	0 / 33 (0.00%) 0	0 / 27 (0.00%) 0
Hypertension subjects affected / exposed occurrences (all)	0 / 36 (0.00%) 0	0 / 33 (0.00%) 0	0 / 27 (0.00%) 0
General disorders and administration site conditions			

Chills			
subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Fatigue			
subjects affected / exposed	2 / 36 (5.56%)	0 / 33 (0.00%)	0 / 27 (0.00%)
occurrences (all)	2	0	0
Influenza like illness			
subjects affected / exposed	1 / 36 (2.78%)	0 / 33 (0.00%)	0 / 27 (0.00%)
occurrences (all)	1	0	0
Oedema peripheral			
subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Pyrexia			
subjects affected / exposed	1 / 36 (2.78%)	0 / 33 (0.00%)	0 / 27 (0.00%)
occurrences (all)	1	0	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 36 (2.78%)	0 / 33 (0.00%)	0 / 27 (0.00%)
occurrences (all)	1	0	0
Oropharyngeal pain			
subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Pleural effusion			
subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Insomnia			
subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Investigations			
Blood creatine phosphokinase increased			
subjects affected / exposed	1 / 36 (2.78%)	0 / 33 (0.00%)	0 / 27 (0.00%)
occurrences (all)	1	0	0

C-reactive protein increased subjects affected / exposed occurrences (all)	0 / 36 (0.00%) 0	0 / 33 (0.00%) 0	0 / 27 (0.00%) 0
Haemoglobin decreased subjects affected / exposed occurrences (all)	0 / 36 (0.00%) 0	0 / 33 (0.00%) 0	0 / 27 (0.00%) 0
Injury, poisoning and procedural complications Post procedural haemorrhage subjects affected / exposed occurrences (all)	0 / 36 (0.00%) 0	0 / 33 (0.00%) 0	2 / 27 (7.41%) 2
Nervous system disorders Headache subjects affected / exposed occurrences (all)	1 / 36 (2.78%) 1	0 / 33 (0.00%) 0	0 / 27 (0.00%) 0
Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all)	0 / 36 (0.00%) 0	0 / 33 (0.00%) 0	0 / 27 (0.00%) 0
Lymphadenopathy subjects affected / exposed occurrences (all)	0 / 36 (0.00%) 0	0 / 33 (0.00%) 0	0 / 27 (0.00%) 0
Eye disorders Eye pain subjects affected / exposed occurrences (all)	0 / 36 (0.00%) 0	0 / 33 (0.00%) 0	0 / 27 (0.00%) 0
Gastrointestinal disorders Abdominal pain subjects affected / exposed occurrences (all)	0 / 36 (0.00%) 0	0 / 33 (0.00%) 0	0 / 27 (0.00%) 0
Abdominal pain upper subjects affected / exposed occurrences (all)	0 / 36 (0.00%) 0	0 / 33 (0.00%) 0	2 / 27 (7.41%) 2
Anorectal discomfort subjects affected / exposed occurrences (all)	0 / 36 (0.00%) 0	0 / 33 (0.00%) 0	0 / 27 (0.00%) 0
Constipation			

subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Crohn's disease			
subjects affected / exposed	2 / 36 (5.56%)	2 / 33 (6.06%)	3 / 27 (11.11%)
occurrences (all)	2	3	4
Diarrhoea			
subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	2 / 27 (7.41%)
occurrences (all)	0	0	2
Dyspepsia			
subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Flatulence			
subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Gastrooesophageal reflux disease			
subjects affected / exposed	2 / 36 (5.56%)	0 / 33 (0.00%)	0 / 27 (0.00%)
occurrences (all)	2	0	0
Haematochezia			
subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Intestinal obstruction			
subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	1 / 36 (2.78%)	2 / 33 (6.06%)	1 / 27 (3.70%)
occurrences (all)	1	2	1
Proctalgia			
subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Vomiting			
subjects affected / exposed	1 / 36 (2.78%)	1 / 33 (3.03%)	3 / 27 (11.11%)
occurrences (all)	1	1	3
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0

Alopecia			
subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Dermatitis acneiform			
subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Rash			
subjects affected / exposed	2 / 36 (5.56%)	2 / 33 (6.06%)	3 / 27 (11.11%)
occurrences (all)	2	2	3
Rash erythematous			
subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Rosacea			
subjects affected / exposed	2 / 36 (5.56%)	0 / 33 (0.00%)	0 / 27 (0.00%)
occurrences (all)	2	0	0
Urticaria			
subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	2 / 36 (5.56%)	0 / 33 (0.00%)	0 / 27 (0.00%)
occurrences (all)	2	0	0
Back pain			
subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	2 / 27 (7.41%)
occurrences (all)	0	0	2
Muscle spasms			
subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal pain			
subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Bronchitis			
subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	3 / 27 (11.11%)
occurrences (all)	0	0	3
Gastroenteritis			

subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Influenza			
subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Lower respiratory tract infection			
subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Oral herpes			
subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Pneumonia			
subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Sinusitis			
subjects affected / exposed	1 / 36 (2.78%)	0 / 33 (0.00%)	0 / 27 (0.00%)
occurrences (all)	1	0	0
Upper respiratory tract infection			
subjects affected / exposed	2 / 36 (5.56%)	0 / 33 (0.00%)	2 / 27 (7.41%)
occurrences (all)	2	0	2
Urinary tract infection			
subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Viral upper respiratory tract infection			
subjects affected / exposed	2 / 36 (5.56%)	2 / 33 (6.06%)	3 / 27 (11.11%)
occurrences (all)	3	2	3
Metabolism and nutrition disorders			
Hypokalaemia			
subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Malnutrition			
subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
19 February 2015	(19 February 2015, 120 subjects enrolled): Substantive changes were made to allow for extension of the Screening Period as necessary, clarification on approved birth control methods, addition of nitrite and leukocyte tests, and updates to the blinding and toxicity management sections.
20 October 2015	Updated number of study sites to 165. A 6 mg BID group was added to replace the 24 mg QD group in the DB Extension Phase and to replace the 24 mg QD dose with 12 mg BID in the OL Extension Phase for subjects who inadequately responded during the DB Extension Phase, based on recent Phase 2 clinical trial data with upadacitinib in subjects with RA.
05 February 2016	Updated protocol to expand the patient population to include subjects with moderately to severely active CD who are inadequate responders or intolerant to immunomodulators or prior anti-TNF use. Decreased the enrollment threshold for subjects with primary non-response to prior anti-TNF treatment from 35% to 30%.
15 April 2016	Updated definition of inadequate response to: 1) prior immunomodulator therapy; and 2) prior induction therapy with infliximab. Updated stem cell transplant restriction, liver transaminases upper limit of normal (ULN), and the number of subjects participating in the Gene Expression testing to 70 to maintain the sample size accounting for subject drop out and even stratification. Also included clarifications regarding sample collection.
07 November 2016	Updated window for subject rollover to the OL Extension Phase; updated timing of the second interim analysis for the DB Extension Phase; clarifications made regarding required contraception; updated the number of subjects participating in the gene expression testing to 80. Other substantive changes made throughout protocol for clarity.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported