Clinical trial results:
A Multicenter, Randomized, Double-Blind, Placebo-Controlled Study to Evaluate the Safety and Efficacy of Upadacitinib (ABT-494) for Induction and Maintenance Therapy in Subjects With Moderately to Severely Active Ulcerative Colitis

Summary

EudraCT number	2016-000641-31
Trial protocol	SK NL FI HU CZ SE PL IE PT DE LV LT AT GR BE EE NO ES GB FR HR IT RO
Global end of trial date	13 December 2021

Results information

Result version number	v1 (current)
This version publication date	19 June 2022
First version publication date	19 June 2022

Trial information

Trial identification

Sponsor protocol code	M14-234

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02819635
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	Global Medical Services, AbbVie , 001 8006339110, abbvieclinicaltrials@abbvie.com
Scientific contact	Global Medical Services, AbbVie, 001 8006339110, abbvieclinicaltrials@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?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	13 December 2021
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	13 December 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

This study was comprised of three substudies.

Substudy 1 (SS1) was a Phase 2b dose-ranging study designed to evaluate the efficacy and safety of different doses of UPA (7.5, 15, 30, and 45 mg) compared to placebo as 8-week induction therapy in subjects with moderately to severely active ulcerative colitis (UC).

Substudy 2 (SS2) was a two-part Phase 3 dose-confirming study designed to evaluate the efficacy and safety of oral administration of UPA 45 mg compared to placebo as induction therapy for up to 16 weeks in subjects with moderately to severely active UC.

Substudy 3 (SS3) was a Phase 3 maintenance study designed to evaluate the efficacy and safety of UPA 15 and 30 mg once daily (QD) compared to placebo in achieving clinical remission per Adapted Mayo score in subjects with moderately to severely active UC who achieved clinical response per Adapted Mayo score following induction therapy from SS1, SS2, or Study M14-675 (NCT03653026).

Protection of trial subjects:

The investigator or his/her representative explained the nature of the study to the subject and answer all questions regarding this study. Prior to any study-related screening procedures being performed on the subject, the informed consent statement was to be reviewed and signed and dated by the subject, the person who administered the informed consent, and any other signatories according to local requirements.

For US subjects: at Week 8 or Week 16 (Substudy 1 or 2 or Study M14-675), subjects who will continue into Substudy 3 were to sign and date a study specific Independent Ethics Committee/Institutional Review Board (IEC/IRB) approved Informed Consent Form before Substudy 3 procedures are performed.

For adolescent subjects, the investigator or his/her representative explained the nature of the study and optional exploratory research samples to the subject and the subject's parent/legal guardian and answered all questions regarding this study. Adolescent subjects were to be included in all discussions in order to obtain verbal or written assent. Prior to any study-related screening procedures being performed on the subject, the informed consent statement was to be reviewed, signed and dated by the subject's parent/legal guardian, the person who administered the informed consent, and any other signatories according to local requirements. Additionally, in keeping with each institution's IRB/IEC requirements, an informed assent form may also have been obtained by each subject prior to any study-related procedures being performed. If a subject attained legal age during the course of the study, that subject was to be re-consented.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	26 September 2016
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	Argentina: 12
Country: Number of subjects enrolled	Australia: 10
Country: Number of subjects enrolled	Austria: 11
Country: Number of subjects enrolled	Belgium: 18
Country: Number of subjects enrolled	Bosnia and Herzegovina: 4
Country: Number of subjects enrolled	Brazil: 12
Country: Number of subjects enrolled	Canada: 114
Country: Number of subjects enrolled	Chile: 2
Country: Number of subjects enrolled	China: 40
Country: Number of subjects enrolled	Colombia: 2
Country: Number of subjects enrolled	Croatia: 5
Country: Number of subjects enrolled	Czechia: 14
Country: Number of subjects enrolled	Estonia: 24
Country: Number of subjects enrolled	Finland: 9
Country: Number of subjects enrolled	France: 28
Country: Number of subjects enrolled	Germany: 17
Country: Number of subjects enrolled	Greece: 4
Country: Number of subjects enrolled	Hungary: 13
Country: Number of subjects enrolled	Ireland: 8
Country: Number of subjects enrolled	Israel: 11
Country: Number of subjects enrolled	Italy: 63
Country: Number of subjects enrolled	Japan: 198
Country: Number of subjects enrolled	Korea, Republic of: 36
Country: Number of subjects enrolled	Latvia: 17
Country: Number of subjects enrolled	Lithuania: 11
Country: Number of subjects enrolled	Malaysia: 6
Country: Number of subjects enrolled	Mexico: 8
Country: Number of subjects enrolled	Netherlands: 25
Country: Number of subjects enrolled	Norway: 29
Country: Number of subjects enrolled	Poland: 34
Country: Number of subjects enrolled	Portugal: 14
Country: Number of subjects enrolled	Puerto Rico: 2
Country: Number of subjects enrolled	Russian Federation: 50
Country: Number of subjects enrolled	Serbia: 31
Country: Number of subjects enrolled	Singapore: 1
Country: Number of subjects enrolled	Slovakia: 16
Country: Number of subjects enrolled	South Africa: 35
Country: Number of subjects enrolled	Spain: 5
Country: Number of subjects enrolled	Switzerland: 34
Country: Number of subjects enrolled	Taiwan: 24
Country: Number of subjects enrolled	Turkey: 8
Country: Number of subjects enrolled	Ukraine: 6

Country: Number of subjects enrolled	United Kingdom: 18
Country: Number of subjects enrolled	United States: 273
Worldwide total number of subjects	1302
EEA total number of subjects	365

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)	6
Adults (18-64 years)	1183
From 65 to 84 years	113
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Intent-to-treat (ITT): Substudy 1 (randomized subjects who rcvd at least 1 dose of study drug in Substudy 1); Substudy 2 (randomized subjects who rcvd at least 1 dose of double-blinded study drug in Part 1 and those who rcvd at least 1 dose of upadacitinib 45 mg in Part 2); Substudy 3 (subjects who rcvd at least 1 dose of study drug in Substudy 3)

Period 1

Period 1 title	Substudy 1 and Substudy 2, Part 1
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	SS1: Placebo

Arm description:

During the 8-week induction phase in Substudy 1, participants received placebo for upadacitinib film-coated tablets once daily by mouth (QD) for 8 weeks.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

During the 8-week induction phase in Substudy 1, participants received placebo for upadacitinib film-coated tablets once daily by mouth (QD) for 8 weeks.

Arm title	SS1: Upadacitinib 7.5 mg

Arm description:

During the 8-week induction phase in Substudy 1, participants received 7.5 mg upadacitinib film-coated tablets once daily by mouth (QD) for 8 weeks.

Arm type	Experimental
Investigational medicinal product name	Upadacitinib
Investigational medicinal product code	
Other name	ABT-494, RINVOQ
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Participants received 7.5 mg upadacitinib film-coated tablets once daily by mouth (QD) for 8 weeks.

Arm title	SS1: Upadacitinib 15 mg

Arm description:

During the 8-week induction phase in Substudy 1, participants received 15 mg upadacitinib film-coated

tablets once daily by mouth (QD) for 8 weeks.

Arm type	Experimental
Investigational medicinal product name	Upadacitinib
Investigational medicinal product code	
Other name	ABT-494, RINVOQ
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Participants received 15 mg upadacitinib film-coated tablets once daily by mouth (QD) for 8 weeks.

Arm title	SS1: Upadacitinib 30 mg

Arm description:

During the 8-week induction phase in Substudy 1, participants received 30 mg upadacitinib film-coated tablets once daily by mouth (QD) for 8 weeks. Additional participants were enrolled during the Substudy 1 analysis period and received 30 mg upadacitinib film-coated tablets once daily by mouth (QD) for 4 weeks.

Arm type	Experimental
Investigational medicinal product name	Upadacitinib
Investigational medicinal product code	
Other name	ABT-494, RINVOQ
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Participants received 30 mg upadacitinib film-coated tablets once daily by mouth (QD) for 8 weeks during the Induction Phase. Additional participants were enrolled during the Substudy 1 analysis period and received 30 mg upadacitinib film-coated tablets once daily by mouth (QD) for 4 weeks.

Arm title	SS1: Upadacitinib 45 mg

Arm description:

During the 8-week induction phase in Substudy 1, participants received 45 mg upadacitinib film-coated tablets once daily by mouth (QD) for 8 weeks. Additional participants were enrolled during the Substudy 1 analysis period and received 45 mg upadacitinib film-coated tablets once daily by mouth (QD) for 4 weeks.

Arm type	Experimental
Investigational medicinal product name	Upadacitinib
Investigational medicinal product code	
Other name	ABT-494, RINVOQ
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Participants received 45 mg upadacitinib film-coated tablets once daily by mouth (QD) for 8 weeks during the Induction Phase. Additional participants were enrolled during the Substudy 1 analysis period and received 45 mg upadacitinib film-coated tablets once daily by mouth (QD) for 4 weeks.

Arm title	SS2: Placebo/Upadacitinib 45 mg

Arm description:

During the Substudy 2 Part 1 induction period, participants received placebo for upadacitinib film-coated tablets once daily by mouth (QD) for 8 weeks. Participants who did not achieve clinical response at Week 8 of Part 1 were enrolled in an open-label extended treatment period and received 45 mg

upadacitinib film-coated tablets once daily by mouth (QD) for an additional 8 weeks.

Arm type	Experimental
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

During the Substudy 2 Part 1 induction period, participants received placebo for upadacitinib film-coated tablets once daily by mouth (QD) for 8 weeks.

Investigational medicinal product name	Upadacitinib
Investigational medicinal product code	
Other name	ABT-494, RINVOQ
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Participants who did not achieve clinical response at Week 8 of Part 1 were enrolled in an open-label extended treatment period and received 45 mg upadacitinib film-coated tablets once daily by mouth (QD) for an additional 8 weeks.

Arm title	SS2: Upadacitinib 45 mg/Upadacitinib 45 mg

Arm description:

During the Substudy 2 Part 1 induction period, participants received 45 mg upadacitinib film-coated tablets once daily by mouth (QD) for 8 weeks. Participants who did not achieve clinical response at Week 8 of Part 1 were enrolled in an open-label expended treatment period and received 45 mg upadacitinib film-coated tablets once daily by mouth (QD) for an additional 8 weeks.

Arm type	Experimental
Investigational medicinal product name	Upadacitinib
Investigational medicinal product code	
Other name	ABT-494, RINVOQ
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

During the Substudy 2 Part 1 induction period, participants received 45 mg upadacitinib film-coated tablets once daily by mouth (QD) for 8 weeks.

Arm title	SS3: M14-675 Clinical Responders

Arm description:

Participants in Study M14-675 (NCT03653026) who achieved clinical response defined by Adapted Mayo Score at Week 8 or Week 16 in that study and did not meet any study discontinuation criteria were eligible to enroll into Substudy 3. Participants were treated with a blinded treatment assignment (15 mg upadacitinib film-coated tablets once daily by mouth [QD], or 30 mg upadacitinib film-coated tablets QD, or placebo for upadacitinib film-coated tablets QD) for up to 52 weeks.

Arm type	Experimental

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Participants in Study M14-675 (NCT03653026) who achieved clinical response defined by Adapted Mayo Score at Week 8 or Week 16 in that\ study and did not meet any study discontinuation criteria were eligible to enroll into Substudy 3. Participants were re-randomized and treated with placebo for upadacitinib film-coated tablets QD) for up to 52 weeks.

Investigational medicinal product name	Upadacitinib
Investigational medicinal product code	
Other name	ABT-494, RINVOQ
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Participants in Study M14-675 (NCT03653026) who achieved clinical response defined by Adapted Mayo Score at Week 8 or Week 16 in that study and did not meet any study discontinuation criteria were eligible to enroll into Substudy 3. Participants were re-randomized and treated with a blinded treatment assignment (15 mg upadacitinib film-coated tablets once daily by mouth [QD], or 30 mg upadacitinib film-coated tablets QD for up to 52 weeks.

Number of subjects in period 1	SS1: Placebo	SS1: Upadacitinib 7.5 mg	SS1: Upadacitinib 15 mg
Started	46	47	49
Completed	41	45	45
Not completed	5	2	4
Adverse event, non-fatal	3	1	3
COVID-19 Logistical Restrictions	-	-	-
Other, not specified	2	1	1
Withdrew consent	-	-	-
Lost to follow-up	-	-	-

Number of subjects in period 1	SS1: Upadacitinib 30 mg	SS1: Upadacitinib 45 mg	SS2: Placebo/Upadacitinib 45 mg
Started	117	123	155
Completed	105	113	135
Not completed	12	10	20
Adverse event, non-fatal	5	4	9
COVID-19 Logistical Restrictions	-	-	-
Other, not specified	7	5	7
Withdrew consent	-	1	3
Lost to follow-up	-	-	1

Number of subjects in period 1	SS2: Upadacitinib 45 mg/Upadacitinib 45 mg	SS3: M14-675 Clinical Responders
Started	319	446
Completed	306	446
Not completed	13	0
Adverse event, non-fatal	6	-
COVID-19 Logistical Restrictions	1	-
Other, not specified	3	-
Withdrew consent	2	-
Lost to follow-up	1	-

Period 2

Period 2 title	Substudy 3
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	SS3: Placebo

Arm description:

Participants who achieved clinical response in Substudy 1, Substudy 2, or Study M14-675 at either Week 8 or Week 16, while receiving upadacitinib 15, 30, or 45 mg QD and those who achieved clinical response while receiving upadacitinib 15 mg QD in Substudy 1 and were randomized to placebo QD in Substudy 3 for up to 52 weeks. In addition, participants who received double-blind placebo QD treatment for 8 weeks during Substudy 1, Substudy 2 Part 1, or Study M14-675 Part 1 and achieved clinical response at Week 8 continued to receive blinded placebo QD in Substudy 3 for up to 52 weeks.

Arm type	Experimental
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Participants received placebo QD in Substudy 3 for up to 52 weeks.

Arm title	SS3: UPA 7.5 mg

Arm description:

Participants who received double-blinded treatment of upadacitinib 7.5 mg QD for 8 weeks during Substudy 1 and achieved clinical response at Week 8 continued to receive blinded treatment of upadacitinib 7.5 mg QD in Substudy 3 for up to 52 weeks.

Arm type	Experimental

Investigational medicinal product name	Upadacitinib
Investigational medicinal product code	
Other name	ABT-494, RINVOQ
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Participants received 7.5 mg upadacitinib film-coated tablets once daily by mouth (QD) for up to 52 weeks.

Arm title	SS3: UPA 15 mg

Arm description:

Participants who achieved clinical response in Substudy 1, Substudy 2, or Study M14-675 at either Week 8 or Week 16, while receiving upadacitinib 15, 30, or 45 mg QD and those who achieved clinical response while receiving upadacitinib 15 mg QD in Substudy 1 and were randomized to upadacitinib 15 mg QD in Substudy 3 for up to 52 weeks. In addition, participants who received upadacitinib 45 mg QD in Induction Phase and did not achieve clinical response and received upadacitinib 45 mg QD in Extended Treatment in Substudy 2 Part 2 or in Study M14-675 Part 2 and achieved clinical response at Week 16 and were randomized to upadacitinib 15 mg QD in Substudy 3.

Arm type	Experimental
Investigational medicinal product name	Upadacitinib
Investigational medicinal product code	
Other name	ABT-494, RINVOQ
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Participants received 15 mg upadacitinib film-coated tablets once daily by mouth (QD) for up to 52 weeks.

Arm title	SS3: UPA 30 mg

Arm description:

Participants who achieved clinical response in Substudy 1, Substudy 2, or Study M14-675 at either Week 8 or Week 16, while receiving upadacitinib 15, 30, or 45 mg QD and those who achieved clinical response while receiving upadacitinib 15 mg QD in Substudy 1 and were randomized to upadacitinib 30 mg QD in Substudy 3 for up to 52 weeks. In addition, participants who received upadacitinib 45 mg QD in Induction Phase and did not achieve clinical response and received upadacitinib 45 mg QD in Extended Treatment in Substudy 2 Part 2 or in Study M14-675 Part 2 and achieved clinical response at Week 16 and were randomized to upadacitinib 30 mg QD in Substudy 3.

Arm type	Experimental
Investigational medicinal product name	Upadacitinib
Investigational medicinal product code	
Other name	ABT-494, RINVOQ
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Participants received 30 mg upadacitinib film-coated tablets once daily by mouth (QD) for up to 52 weeks.

Number of subjects in period 2[1]	SS3: Placebo	SS3: UPA 7.5 mg	SS3: UPA 15 mg
Started	386	20	324
Completed	140	11	218
Not completed	246	9	106
Adverse event, non-fatal	32	3	12
COVID-19 Logistical Restrictions	-	-	-
Other, not specified	202	5	89
Withdrew consent	11	1	4
Lost to follow-up	1	-	1

Number of subjects in period 2[1]	SS3: UPA 30 mg
Started	316
Completed	248
Not completed	68
Adverse event, non-fatal	18
COVID-19 Logistical Restrictions	1
Other, not specified	39
Withdrew consent	9
Lost to follow-up	1

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.
Justification: Substudy 3 was a Phase 3 maintenance study designed to evaluate the efficacy and safety of upadacitinib 15 and 30 mg once daily (QD) compared to placebo in achieving clinical remission per Adapted Mayo score in participants with moderately to severely active UC who achieved clinical response per Adapted Mayo score following induction therapy from Substudy 1, Substudy 2, or Study M14-675.

Period 3

Period 3 title	Substudy 2, Part 2
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	SS2: Placebo/Upadacitinib 45 mg

Arm description:

During the Substudy 2 Part 1 induction period, participants received placebo for upadacitinib film-coated tablets once daily by mouth (QD) for 8 weeks. Participants who did not achieve clinical response at Week 8 of Part 1 were enrolled in an open-label extended treatment period and received 45 mg upadacitinib film-coated tablets once daily by mouth (QD) for an additional 8 weeks in Part 2 of the study.

Arm type	Experimental

Investigational medicinal product name	Upadacitinib
Investigational medicinal product code	
Other name	ABT-494, RINVOQ
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Participants who did not achieve clinical response at Week 8 of Part 1 were enrolled in an open-label extended treatment period and received 45 mg upadacitinib film-coated tablets once daily by mouth (QD) for an additional 8 weeks in Part 2 of the study.

Arm title	SS2: Upadacitinib 45 mg/Upadacitinib 45 mg

Arm description:

During the Substudy 2 Part 1 induction period, participants received 45 mg upadacitinib film-coated tablets once daily by mouth (QD) for 8 weeks. Participants who did not achieve clinical response at Week 8 of Part 1 were enrolled in an open-label expended treatment period and received 45 mg upadacitinib film-coated tablets once daily by mouth (QD) for an additional 8 weeks in Part 2 of the study.

Arm type	Experimental
Investigational medicinal product name	Upadacitinib
Investigational medicinal product code	
Other name	ABT-494, RINVOQ
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Participants who did not achieve clinical response at Week 8 of Part 1 were enrolled in an open-label extended treatment period and received 45 mg upadacitinib film-coated tablets once daily by mouth (QD) for an additional 8 weeks in Part 2 of the study.

Number of subjects in period 3[2]	SS2: Placebo/Upadacitinib 45 mg	SS2: Upadacitinib 45 mg/Upadacitinib 45 mg
Started	85	59
Completed	74	47
Not completed	11	12
Adverse event, non-fatal	4	-
COVID-19 Logistical Restrictions	-	2
Other, not specified	4	8
Withdrew consent	3	1
Lost to follow-up	-	1

Notes:

[2] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.
Justification: Substudy 2 Part 2 was an open-label, 8-week extended treatment period for clinical non-

responders from Part 1 of Substudy 2.

Baseline characteristics

Reporting groups

Reporting group title	SS1: Placebo

Reporting group description:

During the 8-week induction phase in Substudy 1, participants received placebo for upadacitinib film-coated tablets once daily by mouth (QD) for 8 weeks.

Reporting group title	SS1: Upadacitinib 7.5 mg

Reporting group description:

During the 8-week induction phase in Substudy 1, participants received 7.5 mg upadacitinib film-coated tablets once daily by mouth (QD) for 8 weeks.

Reporting group title	SS1: Upadacitinib 15 mg

Reporting group description:

During the 8-week induction phase in Substudy 1, participants received 15 mg upadacitinib film-coated tablets once daily by mouth (QD) for 8 weeks.

Reporting group title	SS1: Upadacitinib 30 mg

Reporting group description:

During the 8-week induction phase in Substudy 1, participants received 30 mg upadacitinib film-coated tablets once daily by mouth (QD) for 8 weeks. Additional participants were enrolled during the Substudy 1 analysis period and received 30 mg upadacitinib film-coated tablets once daily by mouth (QD) for 4 weeks.

Reporting group title	SS1: Upadacitinib 45 mg

Reporting group description:

During the 8-week induction phase in Substudy 1, participants received 45 mg upadacitinib film-coated tablets once daily by mouth (QD) for 8 weeks. Additional participants were enrolled during the Substudy 1 analysis period and received 45 mg upadacitinib film-coated tablets once daily by mouth (QD) for 4 weeks.

Reporting group title	SS2: Placebo/Upadacitinib 45 mg

Reporting group description:

During the Substudy 2 Part 1 induction period, participants received placebo for upadacitinib film-coated tablets once daily by mouth (QD) for 8 weeks. Participants who did not achieve clinical response at Week 8 of Part 1 were enrolled in an open-label extended treatment period and received 45 mg upadacitinib film-coated tablets once daily by mouth (QD) for an additional 8 weeks.

Reporting group title	SS2: Upadacitinib 45 mg/Upadacitinib 45 mg

Reporting group description:

During the Substudy 2 Part 1 induction period, participants received 45 mg upadacitinib film-coated tablets once daily by mouth (QD) for 8 weeks. Participants who did not achieve clinical response at Week 8 of Part 1 were enrolled in an open-label expended treatment period and received 45 mg upadacitinib film-coated tablets once daily by mouth (QD) for an additional 8 weeks.

Reporting group title	SS3: M14-675 Clinical Responders

Reporting group description:

Participants in Study M14-675 (NCT03653026) who achieved clinical response defined by Adapted Mayo Score at Week 8 or Week 16 in that study and did not meet any study discontinuation criteria were eligible to enroll into Substudy 3. Participants were treated with a blinded treatment assignment (15 mg upadacitinib film-coated tablets once daily by mouth [QD], or 30 mg upadacitinib film-coated tablets QD, or placebo for upadacitinib film-coated tablets QD) for up to 52 weeks.

Reporting group values	SS1: Placebo	SS1: Upadacitinib 7.5 mg	SS1: Upadacitinib 15 mg
Number of subjects	46	47	49
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	42.3	41.7	46.0
standard deviation	± 13.29	± 14.58	± 13.58
Gender categorical Units: Subjects			
Female	17	24	19
Male	29	23	30
Race/Ethnicity Units: Subjects			
White	37	36	38
Black or African American	0	3	1
Asian	8	7	10
American Indian or Alaska Native	0	0	0
Native Hawaiian or Other Pacific Islander	0	0	0
Multiple	1	1	0
Previous Biologic Use Units: Subjects			
Yes	35	36	38
No	11	11	11
Not recorded	0	0	0
Biologicinadequate Responder (BioIR) Status			
Biologic-inadequate responders (Bio-IR) are defined as participants who had inadequate response, loss of response, or intolerance to biologic therapy. Non-biologic-inadequate responders (non-bio-IR) are defined as participants who had inadequate response, loss of response, or intolerance to conventional therapy but had not failed biologic therapy.			
Units: Subjects			
Bio-IR	0	0	0
Non-Bio-IR	0	0	0
Not recorded	46	47	49
Baseline Corticosteroid Use Units: Subjects			
Yes	26	24	27
No	20	23	22
Average Stool Frequency Subscore			
Measure Description: Participants recorded stool frequency using an electronic subject diary on a daily basis. The stool frequency subscore (SFS) ranges from 0 to 3 according to the following scale: Score 0: Normal number of stools Score 1: 1 to 2 stools more than normal Score 2: 3 to 4 stools more than normal Score 3: 5 or more stools more than normal Participants with available data; Group 5 (n=122), Group 7 (n=318), Group 8 (n=445)			

Units: units on a scale			
arithmetic mean	2.56	2.62	2.68
standard deviation	± 0.667	± 0.600	± 0.565
Average Rectal Bleeding Subscore			
Participants recorded rectal bleeding in an electronic subject diary on a daily basis. The rectal bleeding subscore ranges from 0 to 3 according to the following scale: Score 0: No blood seen Score 1: Streaks of blood with stool less than half the time Score 2: Obvious blood with stool most of the time Score 3: Blood alone passed Participants with available data; Group 5 (n=122), Group 7 (n=318), Group 8 (n=445)			
Units: units on a scale			
arithmetic mean	1.66	1.61	1.55
standard deviation	± 1.034	± 1.027	± 0.915
Average Endoscopy Subscore			
Findings on endoscopy were scored according to the following: Score 0: Normal or inactive disease Score 1: Mild disease (erythema, decreased vascular pattern) Score 2: Moderate disease (marked erythema, lack of vascular pattern, any friability, erosions) Score 3: Severe disease (spontaneous bleeding, ulceration)			
Units: units on a scale			
arithmetic mean	2.8	2.8	2.8
standard deviation	± 0.43	± 0.40	± 0.39

Reporting group values	SS1: Upadacitinib 30 mg	SS1: Upadacitinib 45 mg	SS2: Placebo/Upadacitinib 45 mg
Number of subjects	117	123	155
Age categorical			
Units: Subjects			
Age continuous			
Units: years			
arithmetic mean	42.9	41.6	44.3
standard deviation	± 14.44	± 14.19	± 14.64
Gender categorical			
Units: Subjects			
Female	47	44	58
Male	70	79	97
Race/Ethnicity			
Units: Subjects			
White	88	90	101
Black or African American	3	2	4
Asian	23	28	46
American Indian or Alaska Native	1	0	2
Native Hawaiian or Other Pacific Islander	0	0	0
Multiple	2	3	2
Previous Biologic Use			
Units: Subjects			
Yes	87	92	0
No	30	31	0

Not recorded	0	0	155
Biologicinadequate Responder (BioIR) Status			
Biologic-inadequate responders (Bio-IR) are defined as participants who had inadequate response, loss of response, or intolerance to biologic therapy. Non-biologic-inadequate responders (non-bio-IR) are defined as participants who had inadequate response, loss of response, or intolerance to conventional therapy but had not failed biologic therapy.			
Units: Subjects			
Bio-IR	0	0	79
Non-Bio-IR	0	0	76
Not recorded	117	123	0
Baseline Corticosteroid Use Units: Subjects			
Yes	51	53	62
No	66	70	93
Average Stool Frequency Subscore			
Measure Description: Participants recorded stool frequency using an electronic subject diary on a daily basis. The stool frequency subscore (SFS) ranges from 0 to 3 according to the following scale: Score 0: Normal number of stools Score 1: 1 to 2 stools more than normal Score 2: 3 to 4 stools more than normal Score 3: 5 or more stools more than normal Participants with available data; Group 5 (n=122), Group 7 (n=318), Group 8 (n=445)			
Units: units on a scale			
arithmetic mean	2.61	2.58	2.52
standard deviation	± 0.613	± 0.648	± 0.668
Average Rectal Bleeding Subscore			
Participants recorded rectal bleeding in an electronic subject diary on a daily basis. The rectal bleeding subscore ranges from 0 to 3 according to the following scale: Score 0: No blood seen Score 1: Streaks of blood with stool less than half the time Score 2: Obvious blood with stool most of the time Score 3: Blood alone passed Participants with available data; Group 5 (n=122), Group 7 (n=318), Group 8 (n=445)			
Units: units on a scale			
arithmetic mean	1.51	1.49	1.76
standard deviation	± 0.975	± 0.960	± 0.994
Average Endoscopy Subscore			
Findings on endoscopy were scored according to the following: Score 0: Normal or inactive disease Score 1: Mild disease (erythema, decreased vascular pattern) Score 2: Moderate disease (marked erythema, lack of vascular pattern, any friability, erosions) Score 3: Severe disease (spontaneous bleeding, ulceration)			
Units: units on a scale			
arithmetic mean	2.7	2.7	2.7
standard deviation	± 0.47	± 0.48	± 0.47

Reporting group values	SS2: Upadacitinib 45 mg/Upadacitinib 45 mg	SS3: M14-675 Clinical Responders	Total
Number of subjects	319	446	1302

Age categorical Units: Subjects			

Age continuous Units: years			
arithmetic mean	43.6	42.1	
standard deviation	± 14.04	± 14.42	-
Gender categorical Units: Subjects			
Female	121	170	500
Male	198	276	802
Race/Ethnicity Units: Subjects			
White	206	302	898
Black or African American	12	15	40
Asian	95	124	341
American Indian or Alaska Native	0	1	4
Native Hawaiian or Other Pacific Islander	1	1	2
Multiple	5	3	17
Previous Biologic Use Units: Subjects			
Yes	0	0	288
No	0	0	94
Not recorded	319	446	920
Biologicinadequate Responder (BioIR) Status			
Biologic-inadequate responders (Bio-IR) are defined as participants who had inadequate response, loss of response, or intolerance to biologic therapy. Non-biologic-inadequate responders (non-bio-IR) are defined as participants who had inadequate response, loss of response, or intolerance to conventional therapy but had not failed biologic therapy.			
Units: Subjects			
Bio-IR	168	221	468
Non-Bio-IR	151	225	452
Not recorded	0	0	382
Baseline Corticosteroid Use Units: Subjects			
Yes	124	173	540
No	195	273	762
Average Stool Frequency Subscore			
Measure Description: Participants recorded stool frequency using an electronic subject diary on a daily basis. The stool frequency subscore (SFS) ranges from 0 to 3 according to the following scale: Score 0: Normal number of stools Score 1: 1 to 2 stools more than normal Score 2: 3 to 4 stools more than normal Score 3: 5 or more stools more than normal Participants with available data; Group 5 (n=122), Group 7 (n=318), Group 8 (n=445)			
Units: units on a scale			
arithmetic mean	2.60	2.55	
standard deviation	± 0.624	± 0.623	-

Average Rectal Bleeding Subscore			
Participants recorded rectal bleeding in an electronic subject diary on a daily basis. The rectal bleeding subscore ranges from 0 to 3 according to the following scale: Score 0: No blood seen Score 1: Streaks of blood with stool less than half the time Score 2: Obvious blood with stool most of the time Score 3: Blood alone passed Participants with available data; Group 5 (n=122), Group 7 (n=318), Group 8 (n=445)			
Units: units on a scale			
arithmetic mean	1.71	1.77	
standard deviation	± 1.046	± 0.990	-
Average Endoscopy Subscore			
Findings on endoscopy were scored according to the following: Score 0: Normal or inactive disease Score 1: Mild disease (erythema, decreased vascular pattern) Score 2: Moderate disease (marked erythema, lack of vascular pattern, any friability, erosions) Score 3: Severe disease (spontaneous bleeding, ulceration)			
Units: units on a scale			
arithmetic mean	2.7	2.7	
standard deviation	± 0.46	± 0.47	-

End points reporting groups

Reporting group title	SS1: Placebo

Reporting group description:

During the 8-week induction phase in Substudy 1, participants received placebo for upadacitinib film-coated tablets once daily by mouth (QD) for 8 weeks.

Reporting group title	SS1: Upadacitinib 7.5 mg

Reporting group description:

During the 8-week induction phase in Substudy 1, participants received 7.5 mg upadacitinib film-coated tablets once daily by mouth (QD) for 8 weeks.

Reporting group title	SS1: Upadacitinib 15 mg

Reporting group description:

During the 8-week induction phase in Substudy 1, participants received 15 mg upadacitinib film-coated tablets once daily by mouth (QD) for 8 weeks.

Reporting group title	SS1: Upadacitinib 30 mg

Reporting group description:

During the 8-week induction phase in Substudy 1, participants received 30 mg upadacitinib film-coated tablets once daily by mouth (QD) for 8 weeks. Additional participants were enrolled during the Substudy 1 analysis period and received 30 mg upadacitinib film-coated tablets once daily by mouth (QD) for 4 weeks.

Reporting group title	SS1: Upadacitinib 45 mg

Reporting group description:

During the 8-week induction phase in Substudy 1, participants received 45 mg upadacitinib film-coated tablets once daily by mouth (QD) for 8 weeks. Additional participants were enrolled during the Substudy 1 analysis period and received 45 mg upadacitinib film-coated tablets once daily by mouth (QD) for 4 weeks.

Reporting group title	SS2: Placebo/Upadacitinib 45 mg

Reporting group description:

During the Substudy 2 Part 1 induction period, participants received placebo for upadacitinib film-coated tablets once daily by mouth (QD) for 8 weeks. Participants who did not achieve clinical response at Week 8 of Part 1 were enrolled in an open-label extended treatment period and received 45 mg upadacitinib film-coated tablets once daily by mouth (QD) for an additional 8 weeks.

Reporting group title	SS2: Upadacitinib 45 mg/Upadacitinib 45 mg

Reporting group description:

During the Substudy 2 Part 1 induction period, participants received 45 mg upadacitinib film-coated tablets once daily by mouth (QD) for 8 weeks. Participants who did not achieve clinical response at Week 8 of Part 1 were enrolled in an open-label expended treatment period and received 45 mg upadacitinib film-coated tablets once daily by mouth (QD) for an additional 8 weeks.

Reporting group title	SS3: M14-675 Clinical Responders

Reporting group description:

Participants in Study M14-675 (NCT03653026) who achieved clinical response defined by Adapted Mayo Score at Week 8 or Week 16 in that study and did not meet any study discontinuation criteria were eligible to enroll into Substudy 3. Participants were treated with a blinded treatment assignment (15 mg upadacitinib film-coated tablets once daily by mouth [QD], or 30 mg upadacitinib film-coated tablets QD, or placebo for upadacitinib film-coated tablets QD) for up to 52 weeks.

Reporting group title	SS3: Placebo

Reporting group description:

Participants who achieved clinical response in Substudy 1, Substudy 2, or Study M14-675 at either Week 8 or Week 16, while receiving upadacitinib 15, 30, or 45 mg QD and those who achieved clinical response while receiving upadacitinib 15 mg QD in Substudy 1 and were randomized to placebo QD in

Substudy 3 for up to 52 weeks. In addition, participants who received double-blind placebo QD treatment for 8 weeks during Substudy 1, Substudy 2 Part 1, or Study M14-675 Part 1 and achieved clinical response at Week 8 continued to receive blinded placebo QD in Substudy 3 for up to 52 weeks.

Reporting group title	SS3: UPA 7.5 mg

Reporting group description:

Participants who received double-blinded treatment of upadacitinib 7.5 mg QD for 8 weeks during Substudy 1 and achieved clinical response at Week 8 continued to receive blinded treatment of upadacitinib 7.5 mg QD in Substudy 3 for up to 52 weeks.

Reporting group title	SS3: UPA 15 mg

Reporting group description:

Participants who achieved clinical response in Substudy 1, Substudy 2, or Study M14-675 at either Week 8 or Week 16, while receiving upadacitinib 15, 30, or 45 mg QD and those who achieved clinical response while receiving upadacitinib 15 mg QD in Substudy 1 and were randomized to upadacitinib 15 mg QD in Substudy 3 for up to 52 weeks. In addition, participants who received upadacitinib 45 mg QD in Induction Phase and did not achieve clinical response and received upadacitinib 45 mg QD in Extended Treatment in Substudy 2 Part 2 or in Study M14-675 Part 2 and achieved clinical response at Week 16 and were randomized to upadacitinib 15 mg QD in Substudy 3.

Reporting group title	SS3: UPA 30 mg

Reporting group description:

Participants who achieved clinical response in Substudy 1, Substudy 2, or Study M14-675 at either Week 8 or Week 16, while receiving upadacitinib 15, 30, or 45 mg QD and those who achieved clinical response while receiving upadacitinib 15 mg QD in Substudy 1 and were randomized to upadacitinib 30 mg QD in Substudy 3 for up to 52 weeks. In addition, participants who received upadacitinib 45 mg QD in Induction Phase and did not achieve clinical response and received upadacitinib 45 mg QD in Extended Treatment in Substudy 2 Part 2 or in Study M14-675 Part 2 and achieved clinical response at Week 16 and were randomized to upadacitinib 30 mg QD in Substudy 3.

Reporting group title	SS2: Placebo/Upadacitinib 45 mg

Reporting group description:

During the Substudy 2 Part 1 induction period, participants received placebo for upadacitinib film-coated tablets once daily by mouth (QD) for 8 weeks. Participants who did not achieve clinical response at Week 8 of Part 1 were enrolled in an open-label extended treatment period and received 45 mg upadacitinib film-coated tablets once daily by mouth (QD) for an additional 8 weeks in Part 2 of the study.

Reporting group title	SS2: Upadacitinib 45 mg/Upadacitinib 45 mg

Reporting group description:

During the Substudy 2 Part 1 induction period, participants received 45 mg upadacitinib film-coated tablets once daily by mouth (QD) for 8 weeks. Participants who did not achieve clinical response at Week 8 of Part 1 were enrolled in an open-label expended treatment period and received 45 mg upadacitinib film-coated tablets once daily by mouth (QD) for an additional 8 weeks in Part 2 of the study.

Subject analysis set title	SS2: Placebo
Subject analysis set type	Intention-to-treat

Subject analysis set description:

During the Substudy 2 Part 1 induction period, participants received placebo for upadacitinib film-coated tablets once daily by mouth (QD) for 8 weeks.

Subject analysis set title	SS2: Upadacitinib 45 mg
Subject analysis set type	Intention-to-treat

Subject analysis set description:

During the Substudy 2 Part 1 induction period, participants received 45 mg upadacitinib film-coated tablets once daily by mouth (QD) for 8 weeks.

Subject analysis set title	SS3: Placebo
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Participants who achieved clinical response in Substudy 1, Substudy 2, or Study M14-675 at Week 8, while receiving upadacitinib 15, 30, or 45 mg QD and were randomized to placebo QD in Substudy 3 for up to 52 weeks. In addition, participants who received double-blind placebo QD treatment for 8 weeks during Substudy 1, Substudy 2 Part 1, or Study M14-675 Part 1 and achieved clinical response at Week 8 continued to receive blinded placebo QD in Substudy 3 for up to 52 weeks.

Subject analysis set title	SS3: UPA 15 mg
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Participants who achieved clinical response in Substudy 1, Substudy 2, or Study M14-675 at Week 8 while receiving upadacitinib 15, 30, or 45 mg QD and were randomized to upadacitinib 15 mg QD in Substudy 3 for up to 52 weeks

Subject analysis set title	SS3: UPA 30 mg
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Participants who achieved clinical response in Substudy 1, Substudy 2, or Study M14-675 at Week 8 while receiving upadacitinib 15, 30, or 45 mg QD and were randomized to upadacitinib 30 mg QD in Substudy 3 for up to 52 weeks

Primary: Substudy 1: Percentage Of Participants Who Achieved Clinical Remission Per Adapted Mayo Score at Week 8

End point title	Substudy 1: Percentage Of Participants Who Achieved Clinical Remission Per Adapted Mayo Score at Week 8[1]

End point description:

The Adapted Mayo Score is a composite score of UC disease activity based on the following 3 subscores:

1. Stool frequency subscore (SFS), scored from 0 (normal number of stools) to 3 (5 or more stools more than normal)
2. Rectal bleeding subscore (RBS), scored from 0 (no blood seen) to 3 (blood alone passed)
3. Endoscopic subscore, scored from 0 (normal or inactive disease) to 3 (severe disease, spontaneous bleeding, ulceration)

The overall Adapted Mayo score ranges from 0 to 9 where higher scores represent more severe disease. For Substudy 1, clinical remission is defined as SFS ≤ 1, RBS of 0, and endoscopic subscore ≤ 1.

End point type	Primary

End point timeframe:

At Week 8

Notes:

[1] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint included Substudy 1, Part 1 participants.

End point values	SS1: Placebo	SS1: Upadacitinib 7.5 mg	SS1: Upadacitinib 15 mg	SS1: Upadacitinib 30 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	46[2]	47[3]	49[4]	52[5]
Units: percentage of participants				
number (not applicable)	0	8.5	14.3	13.5

Notes:

[2] - SS1 main subjects (ITT1A) randomized to ≥1 study drug dose during Pt 1; NRI used for missing values
[3] - SS1 main subjects (ITT1A) randomized to ≥1 study drug dose during Pt 1; NRI used for missing values

[4] - SS1 main subjects (ITT1A) randomized to ≥1 study drug dose during Pt 1; NRI used for missing values
[5] - SS1 main subjects (ITT1A) randomized to ≥1 study drug dose during Pt 1; NRI used for missing values

End point values	SS1: Upadacitinib 45 mg			
Subject group type	Reporting group			
Number of subjects analysed	56[6]			
Units: percentage of participants				
number (not applicable)	21.4			

Notes:
[6] - SS1 main subjects (ITT1A) randomized to ≥1 study drug dose during Pt 1; NRI used for missing values

Statistical analyses

Statistical analysis title	Substudy 1: Upadacitinib 7.5 mg vs Placebo
Comparison groups	SS1: Placebo v SS1: Upadacitinib 7.5 mg
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority[7]
P-value	= 0.049 [8]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted risk difference (%)
Point estimate	8.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	0
upper limit	16.8

Notes:
[7] - The primary and ranked secondary efficacy endpoints were tested with multiplicity adjustment using a fixed-sequence multiple testing procedure to ensure a strong control of family-wise type I error rate at significance level alpha = 0.05 (2-sided).

[8] - Stratified by previous biologic use, baseline corticosteroid use and baseline Adapted Mayo score (≤ 7 and > 7)

Statistical analysis title	Substudy 1: Upadacitinib 15 mg vs Placebo
Comparison groups	SS1: Placebo v SS1: Upadacitinib 15 mg
Number of subjects included in analysis	95
Analysis specification	Pre-specified
Analysis type	superiority[9]
P-value	= 0.01 [10]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted risk difference (%)
Point estimate	13.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	3.3
upper limit	23.8

Notes:

[9] - The primary and ranked secondary efficacy endpoints were tested with multiplicity adjustment using a fixed-sequence multiple testing procedure to ensure a strong control of family-wise type I error rate at significance level alpha = 0.05 (2-sided).

[10] - Stratified by previous biologic use, baseline corticosteroid use and baseline Adapted Mayo score (≤ 7 and > 7)

Statistical analysis title	Substudy 1: Upadacitinib 30 mg vs Placebo
Comparison groups	SS1: Placebo v SS1: Upadacitinib 30 mg
Number of subjects included in analysis	98
Analysis specification	Pre-specified
Analysis type	superiority[11]
P-value	= 0.007 [12]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted risk difference (%)
Point estimate	13.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	3.8
upper limit	23.9

Notes:

[11] - The primary and ranked secondary efficacy endpoints were tested with multiplicity adjustment using a fixed-sequence multiple testing procedure to ensure a strong control of family-wise type I error rate at significance level alpha = 0.05 (2-sided).

[12] - Stratified by previous biologic use, baseline corticosteroid use and baseline Adapted Mayo score (≤ 7 and > 7)

Statistical analysis title	Substudy 1: Upadacitinib 45 mg vs Placebo
Comparison groups	SS1: Placebo v SS1: Upadacitinib 45 mg
Number of subjects included in analysis	102
Analysis specification	Pre-specified
Analysis type	superiority[13]
P-value	< 0.001 [14]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted risk difference (%)
Point estimate	21.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	8.6
upper limit	33.6

Notes:

[13] - The primary and ranked secondary efficacy endpoints were tested with multiplicity adjustment using a fixed-sequence multiple testing procedure to ensure a strong control of family-wise type I error rate at significance level alpha = 0.05 (2-sided).

[14] - Stratified by previous biologic use, baseline corticosteroid use and baseline Adapted Mayo score (≤ 7 and > 7)

Primary: Substudy 2: Percentage Of Participants Who Achieved Clinical Remission Per Adapted Mayo Score at Week 8

End point title	Substudy 2: Percentage Of Participants Who Achieved Clinical Remission Per Adapted Mayo Score at Week 8

End point description:

The Adapted Mayo Score is a composite score of UC disease activity based on the following 3 subscores:
1. Stool frequency subscore (SFS), scored from 0 (normal number of stools) to 3 (5 or more stools more than normal)
2. Rectal bleeding subscore (RBS), scored from 0 (no blood seen) to 3 (blood alone passed)
3. Endoscopic subscore, scored from 0 (normal or inactive disease) to 3 (severe disease, spontaneous bleeding, ulceration)

The overall Adapted Mayo score ranges from 0 to 9 where higher scores represent more severe disease. For Substudy 2, clinical remission is defined as SFS ≤ 1 and not greater than Baseline, RBS of 0, and endoscopic subscore ≤ 1. In Substudy 2, evidence of friability during endoscopy in participants with otherwise "mild" endoscopic activity conferred an endoscopic subscore of 2.

Participants were analyzed according to the treatment groups to which they were randomized.

End point type	Primary

End point timeframe:

At Week 8

End point values	SS2: Placebo	SS2: Upadacitinib 45 mg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	154[15]	319[16]		
Units: percentage of participants				
number (not applicable)	4.8	26.1		

Notes:

[15] - SS2 (ITT1): randomized to ≥1 dose of study drug during Pt 1. NRI with MI due to COVID-19 (NRI-C)
[16] - SS2 (ITT1): randomized to ≥1 dose of study drug during Pt 1. NRI with MI due to COVID-19 (NRI-C)

Statistical analyses

Statistical analysis title	Substudy 2: Upadacitinib 45 mg vs Placebo
Comparison groups	SS2: Upadacitinib 45 mg v SS2: Placebo
Number of subjects included in analysis	473
Analysis specification	Pre-specified
Analysis type	superiority[17]
P-value	< 0.001 [18]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted risk difference (%)
Point estimate	21.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	15.8
upper limit	27.4

Notes:

[17] - The primary and ranked secondary efficacy endpoints were tested with multiplicity adjustment using a fixed-sequence multiple testing procedure to ensure a strong control of family-wise type I error rate at significance level alpha = 0.05 (2-sided).

[18] - Stratified by bio-IR status (bio-IR vs. non-bio-IR), Baseline corticosteroid use (yes vs. no) and Baseline Adapted Mayo score (≤ 7 vs. > 7)

Primary: Substudy 3: Percentage Of Participants Who Achieved Clinical Remission Per Adapted Mayo Score at Week 52

End point title	Substudy 3: Percentage Of Participants Who Achieved Clinical Remission Per Adapted Mayo Score at Week 52

End point description:

The Adapted Mayo Score is a composite score of UC disease activity based on the following 3 subscores:
1. Stool frequency subscore (SFS), scored from 0 (normal number of stools) to 3 (5 or more stools more than normal).
2. Rectal bleeding subscore (RBS), scored from 0 (no blood seen) to 3 (blood alone passed).
3. Endoscopic subscore, scored from 0 (normal or inactive disease) to 3 (severe disease, spontaneous bleeding, ulceration).

The overall Adapted Mayo score ranges from 0 to 9 where higher scores represent more severe disease. For Substudy 3, clinical remission is defined as SFS ≤ 1 and not greater than Baseline, RBS of 0, and endoscopic subscore ≤ 1. In addition, evidence of friability during endoscopy in participants with otherwise "mild" endoscopic activity conferred an endoscopic subscore of 2.

End point type	Primary

End point timeframe:

At Week 52

End point values	SS3: Placebo	SS3: UPA 15 mg	SS3: UPA 30 mg	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	149[19]	148[20]	154[21]	
Units: percentage of participants				
number (confidence interval 95%)	12.1 (6.9 to 17.4)	42.3 (34.3 to 50.3)	51.7 (43.6 to 59.8)	

Notes:

[19] - SS3 ITT_A:1st 451 Upa 45 mg 8-wk responders; 52-wk tx Cohort 1, NRI with MI due to COVID-19- NRI-C

[20] - SS3 ITT_A:1st 451 Upa 45 mg 8-wk responders; 52-wk tx Cohort 1, NRI with MI due to COVID-19- NRI-C

[21] - SS3 ITT_A:1st 451 Upa 45 mg 8-wk responders; 52-wk tx Cohort 1, NRI with MI due to COVID-19- NRI-C

Statistical analyses

Statistical analysis title	Substudy 3: Upadacitinib 15 mg vs Placebo
Comparison groups	SS3: Placebo v SS3: UPA 15 mg
Number of subjects included in analysis	297
Analysis specification	Pre-specified
Analysis type	superiority[22]
P-value	< 0.001 [23]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted risk difference (%)
Point estimate	30.7

Confidence interval	
level	95 %
sides	2-sided
lower limit	21.7
upper limit	39.8

Notes:

[22] - The primary and ranked secondary efficacy endpoints were tested with multiplicity adjustment using a fixed-sequence multiple testing procedure to ensure a strong control of family-wise type I error rate at significance level alpha = 0.05 (2-sided).

[23] - Stratified by Bio-IR (Bio-IR/Non-Bio-IR) at Baseline of Induction Study; clinical remission at Week 0 (yes/no); corticosteroid use at Week 0 (yes/no)

Statistical analysis title	Substudy 3: Upadacitinib 30 mg vs Placebo
Comparison groups	SS3: Placebo v SS3: UPA 30 mg
Number of subjects included in analysis	303
Analysis specification	Pre-specified
Analysis type	superiority[24]
P-value	< 0.001 [25]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted risk difference (%)
Point estimate	39
Confidence interval	
level	95 %
sides	2-sided
lower limit	29.7
upper limit	48.2

Notes:

[24] - The primary and ranked secondary efficacy endpoints were tested with multiplicity adjustment using a fixed-sequence multiple testing procedure to ensure a strong control of family-wise type I error rate at significance level alpha = 0.05 (2-sided).

[25] - Stratified by Bio-IR (Bio-IR/Non-Bio-IR) at Baseline of Induction Study; clinical remission at Week 0 (yes/no); corticosteroid use at Week 0 (yes/no)

Secondary: Substudy 1: Percentage Of Participants With Endoscopic Improvement at Week 8

End point title	Substudy 1: Percentage Of Participants With Endoscopic Improvement at Week 8[26]

End point description:

Endoscopic improvement is defined as an endoscopic subscore of 0 or 1. Endoscopies were assessed by a blinded central reader and scored according to the following scale: 0 = Normal or inactive disease; 1 = Mild disease (erythema, decreased vascular pattern); 2 = Moderate disease (marked erythema, lack of vascular pattern, any friability, erosions); 3 = Severe disease (spontaneous bleeding, ulceration).

End point type	Secondary

End point timeframe:

At Week 8

Notes:

[26] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint included Substudy 1, Part 1 participants.

End point values	SS1: Placebo	SS1: Upadacitinib 7.5 mg	SS1: Upadacitinib 15 mg	SS1: Upadacitinib 30 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	46[27]	47[28]	49[29]	52[30]
Units: percentage of participants				
number (not applicable)	2.2	14.9	30.6	26.9

Notes:

[27] - SS1 main subjects (ITT1A) randomized to ≥1 study drug dose during Pt 1; NRI used for missing values
[28] - SS1 main subjects (ITT1A) randomized to ≥1 study drug dose during Pt 1; NRI used for missing values
[29] - SS1 main subjects (ITT1A) randomized to ≥1 study drug dose during Pt 1; NRI used for missing values
[30] - SS1 main subjects (ITT1A) randomized to ≥1 study drug dose during Pt 1; NRI used for missing values

End point values	SS1: Upadacitinib 45 mg			
Subject group type	Reporting group			
Number of subjects analysed	56[31]			
Units: percentage of participants				
number (not applicable)	35.7			

Notes:

[31] - SS1 main subjects (ITT1A) randomized to ≥1 study drug dose during Pt 1; NRI used for missing values

Statistical analyses

Statistical analysis title	Substudy 1: Upadacitinib 7.5 mg vs Placebo
Comparison groups	SS1: Placebo v SS1: Upadacitinib 7.5 mg
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority[32]
P-value	= 0.03 [33]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted risk difference (%)
Point estimate	13.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.2
upper limit	25

Notes:

[32] - The primary and ranked secondary efficacy endpoints were tested with multiplicity adjustment using a fixed-sequence multiple testing procedure to ensure a strong control of family-wise type I error rate at significance level alpha = 0.05 (2-sided).

[33] - Stratified by previous biologic use, baseline corticosteroid use and baseline Adapted Mayo score (≤ 7 and > 7)

Statistical analysis title	Substudy 1: Upadacitinib 15 mg vs Placebo
Comparison groups	SS1: Placebo v SS1: Upadacitinib 15 mg

Number of subjects included in analysis	95
Analysis specification	Pre-specified
Analysis type	superiority[34]
P-value	< 0.001 [35]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted risk difference (%)
Point estimate	27.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	13.1
upper limit	42.1

Notes:

[34] - The primary and ranked secondary efficacy endpoints were tested with multiplicity adjustment using a fixed-sequence multiple testing procedure to ensure a strong control of family-wise type I error rate at significance level alpha = 0.05 (2-sided).

[35] - Stratified by previous biologic use, baseline corticosteroid use and baseline Adapted Mayo score (≤ 7 and > 7)

Statistical analysis title	Substudy 1: Upadacitinib 30 mg vs Placebo
Comparison groups	SS1: Placebo v SS1: Upadacitinib 30 mg
Number of subjects included in analysis	98
Analysis specification	Pre-specified
Analysis type	superiority[36]
P-value	< 0.001 [37]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted risk difference (%)
Point estimate	26.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	12.3
upper limit	40.8

Notes:

[36] - The primary and ranked secondary efficacy endpoints were tested with multiplicity adjustment using a fixed-sequence multiple testing procedure to ensure a strong control of family-wise type I error rate at significance level alpha = 0.05 (2-sided).

[37] - Stratified by previous biologic use, baseline corticosteroid use and baseline Adapted Mayo score (≤ 7 and > 7)

Statistical analysis title	Substudy 1: Upadacitinib 45 mg vs Placebo
Comparison groups	SS1: Upadacitinib 45 mg v SS1: Placebo
Number of subjects included in analysis	102
Analysis specification	Pre-specified
Analysis type	superiority[38]
P-value	< 0.001 [39]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted risk difference (%)
Point estimate	35.4

Confidence interval	
level	95 %
sides	2-sided
lower limit	19.2
upper limit	51.7

Notes:

[38] - The primary and ranked secondary efficacy endpoints were tested with multiplicity adjustment using a fixed-sequence multiple testing procedure to ensure a strong control of family-wise type I error rate at significance level alpha = 0.05 (2-sided).

[39] - Stratified by previous biologic use, baseline corticosteroid use and baseline Adapted Mayo score (≤ 7 and > 7)

Secondary: Substudy 1: Percentage Of Participants Achieving Clinical Remission Per Full Mayo Score at Week 8

End point title	Substudy 1: Percentage Of Participants Achieving Clinical Remission Per Full Mayo Score at Week 8[40]

End point description:

The Mayo score is a tool designed to measure disease activity for ulcerative colitis. The Full Mayo score (FMS) ranges from 0 (normal or inactive disease) to 12 (severe disease) and is calculated as the sum of 4 subscores (stool frequency, rectal bleeding, endoscopy [confirmed by a central reader], and physician's global assessment), each of which ranges from 0 (normal) to 3 (severe disease). Negative changes indicate improvement. Clinical remission per FMS is defined as Mayo Score ≤ 2 and no individual subscore > 1.

End point type	Secondary

End point timeframe:

At Week 8

Notes:

[40] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint included Substudy 1, Part 1 participants.

End point values	SS1: Placebo	SS1: Upadacitinib 7.5 mg	SS1: Upadacitinib 15 mg	SS1: Upadacitinib 30 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	46[41]	47[42]	49[43]	52[44]
Units: percentage of participants				
number (not applicable)	0	10.6	10.2	11.5

Notes:

[41] - SS1 main subjects (ITT1A) randomized to ≥1 study drug dose during Pt 1; NRI used for missing values
[42] - SS1 main subjects (ITT1A) randomized to ≥1 study drug dose during Pt 1; NRI used for missing values
[43] - SS1 main subjects (ITT1A) randomized to ≥1 study drug dose during Pt 1; NRI used for missing values
[44] - SS1 main subjects (ITT1A) randomized to ≥1 study drug dose during Pt 1; NRI used for missing values

End point values	SS1: Upadacitinib 45 mg			
Subject group type	Reporting group			
Number of subjects analysed	56			
Units: percentage of participants				
number (not applicable)	19.6			

Statistical analyses

Statistical analysis title	Substudy 1: Upadacitinib 7.5 mg vs Placebo
Comparison groups	SS1: Placebo v SS1: Upadacitinib 7.5 mg
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority[45]
P-value	= 0.021 [46]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted risk difference (%)
Point estimate	11
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.7
upper limit	20.4

Notes:

[45] - The primary and ranked secondary efficacy endpoints were tested with multiplicity adjustment using a fixed-sequence multiple testing procedure to ensure a strong control of family-wise type I error rate at significance level alpha = 0.05 (2-sided).

[46] - Stratified by previous biologic use, baseline corticosteroid use and baseline Adapted Mayo score (≤ 7 and > 7)

Statistical analysis title	Substudy 1: Upadacitinib 15 mg vs Placebo
Comparison groups	SS1: Placebo v SS1: Upadacitinib 15 mg
Number of subjects included in analysis	95
Analysis specification	Pre-specified
Analysis type	superiority[47]
P-value	= 0.024 [48]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted risk difference (%)
Point estimate	9.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.3
upper limit	18

Notes:

[47] - The primary and ranked secondary efficacy endpoints were tested with multiplicity adjustment using a fixed-sequence multiple testing procedure to ensure a strong control of family-wise type I error rate at significance level alpha = 0.05 (2-sided).

[48] - Stratified by previous biologic use, baseline corticosteroid use and baseline Adapted Mayo score (≤ 7 and > 7)

Statistical analysis title	Substudy 1: Upadacitinib 30 mg vs Placebo

Comparison groups	SS1: Placebo v SS1: Upadacitinib 30 mg
Number of subjects included in analysis	98
Analysis specification	Pre-specified
Analysis type	superiority[49]
P-value	= 0.015 [50]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted risk difference (%)
Point estimate	12.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.3
upper limit	22

Notes:

[49] - The primary and ranked secondary efficacy endpoints were tested with multiplicity adjustment using a fixed-sequence multiple testing procedure to ensure a strong control of family-wise type I error rate at significance level alpha = 0.05 (2-sided).

[50] - Stratified by previous biologic use, baseline corticosteroid use and baseline Adapted Mayo score (≤ 7 and > 7)

Statistical analysis title	Substudy 1: Upadacitinib 45 mg vs Placebo
Comparison groups	SS1: Placebo v SS1: Upadacitinib 45 mg
Number of subjects included in analysis	102
Analysis specification	Pre-specified
Analysis type	superiority[51]
P-value	= 0.001 [52]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted risk difference (%)
Point estimate	20.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	8
upper limit	32.1

Notes:

[51] - The primary and ranked secondary efficacy endpoints were tested with multiplicity adjustment using a fixed-sequence multiple testing procedure to ensure a strong control of family-wise type I error rate at significance level alpha = 0.05 (2-sided).

[52] - Stratified by previous biologic use, baseline corticosteroid use and baseline Adapted Mayo score (≤ 7 and > 7)

Secondary: Substudy 1: Percentage Of Participants Achieving Clinical Response Per Adapted Mayo Score at Week 8

End point title	Substudy 1: Percentage Of Participants Achieving Clinical Response Per Adapted Mayo Score at Week 8[53]

End point description:

The Adapted Mayo Score is a composite score of UC disease activity based on the following 3 subscores:
1. Stool frequency subscore (SFS), scored from 0 (normal number of stools) to 3 (5 or more stools more than normal).
2. Rectal bleeding subscore (RBS), scored from 0 (no blood seen) to 3 (blood alone passed).
3. Endoscopic subscore, scored from 0 (normal or inactive disease) to 3 (severe disease, spontaneous bleeding, ulceration).

The overall Adapted Mayo score ranges from 0 to 9 where higher scores represent more severe disease.

Clinical response is defined as a decrease from baseline in the Adapted Mayo score ≥ 2 points and ≥ 30% from baseline, and a decrease in RBS ≥ 1 or an absolute RBS ≤ 1).

End point type	Secondary

End point timeframe:

At Week 8

Notes:

[53] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint included Substudy 1, Part 1 participants.

End point values	SS1: Placebo	SS1: Upadacitinib 7.5 mg	SS1: Upadacitinib 15 mg	SS1: Upadacitinib 30 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	46[54]	47[55]	49[56]	52[57]
Units: percentage of participants				
number (not applicable)	13.0	29.8	49.0	46.2

Notes:

[54] - SS1 main subjects (ITT1A) randomized to ≥1 study drug dose during Pt 1; NRI used for missing values
[55] - SS1 main subjects (ITT1A) randomized to ≥1 study drug dose during Pt 1; NRI used for missing values
[56] - SS1 main subjects (ITT1A) randomized to ≥1 study drug dose during Pt 1; NRI used for missing values
[57] - SS1 main subjects (ITT1A) randomized to ≥1 study drug dose during Pt 1; NRI used for missing values

End point values	SS1: Upadacitinib 45 mg			
Subject group type	Reporting group			
Number of subjects analysed	56[58]			
Units: percentage of participants				
number (not applicable)	55.4			

Notes:

[58] - SS1 main subjects (ITT1A) randomized to ≥1 study drug dose during Pt 1; NRI used for missing values

Statistical analyses

Statistical analysis title	Substudy 1: Upadacitinib 7.5 mg vs Placebo
Comparison groups	SS1: Placebo v SS1: Upadacitinib 7.5 mg
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority[59]
P-value	= 0.038 [60]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted risk difference (%)
Point estimate	16.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.9
upper limit	32.5

Notes:

[59] - The primary and ranked secondary efficacy endpoints were tested with multiplicity adjustment using a fixed-sequence multiple testing procedure to ensure a strong control of family-wise type I error rate at significance level alpha = 0.05 (2-sided).

[60] - Stratified by previous biologic use, baseline corticosteroid use and baseline Adapted Mayo score (≤ 7 and > 7)

Statistical analysis title	Substudy 1: Upadacitinib 15 mg vs Placebo
Comparison groups	SS1: Placebo v SS1: Upadacitinib 15 mg
Number of subjects included in analysis	95
Analysis specification	Pre-specified
Analysis type	superiority[61]
P-value	< 0.001 [62]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted risk difference (%)
Point estimate	35.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	17.5
upper limit	52.8

Notes:

[61] - The primary and ranked secondary efficacy endpoints were tested with multiplicity adjustment using a fixed-sequence multiple testing procedure to ensure a strong control of family-wise type I error rate at significance level alpha = 0.05 (2-sided).

[62] - Stratified by previous biologic use, baseline corticosteroid use and baseline Adapted Mayo score (≤ 7 and > 7)

Statistical analysis title	Substudy 1: Upadacitinib 30 mg vs Placebo
Comparison groups	SS1: Placebo v SS1: Upadacitinib 30 mg
Number of subjects included in analysis	98
Analysis specification	Pre-specified
Analysis type	superiority[63]
P-value	< 0.001 [64]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted risk difference (%)
Point estimate	33.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	16.3
upper limit	50.8

Notes:

[63] - The primary and ranked secondary efficacy endpoints were tested with multiplicity adjustment using a fixed-sequence multiple testing procedure to ensure a strong control of family-wise type I error rate at significance level alpha = 0.05 (2-sided).

[64] - Stratified by previous biologic use, baseline corticosteroid use and baseline Adapted Mayo score (≤ 7 and > 7)

Statistical analysis title	Substudy 1: Upadacitinib 45 mg vs Placebo
Comparison groups	SS1: Placebo v SS1: Upadacitinib 45 mg

Number of subjects included in analysis	102
Analysis specification	Pre-specified
Analysis type	superiority[65]
P-value	< 0.001 [66]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted risk difference (%)
Point estimate	45.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	26.2
upper limit	63.9

Notes:

[65] - The primary and ranked secondary efficacy endpoints were tested with multiplicity adjustment using a fixed-sequence multiple testing procedure to ensure a strong control of family-wise type I error rate at significance level alpha = 0.05 (2-sided).

[66] - Stratified by previous biologic use, baseline corticosteroid use and baseline Adapted Mayo score (≤ 7 and > 7)

Secondary: Substudy 1: Percentage Of Participants Achieving Clinical Response Per Partial Mayo Score at Week 2

End point title	Substudy 1: Percentage Of Participants Achieving Clinical Response Per Partial Mayo Score at Week 2[67]

End point description:

The Partial Mayo Score is a composite score of UC disease activity based on the following 2 subscores:
1. Stool frequency subscore (SFS), scored from 0 (normal number of stools) to 3 (5 or more stools more than normal).
2. Rectal bleeding subscore (RBS), scored from 0 (no blood seen) to 3 (blood alone passed).

The overall Partial Mayo score ranges from 0 to 6 with higher scores representing more severe disease.

Clinical response per Partial Mayo Score is defined as a decrease in Partial Adapted Mayo score ≥ 2 points and ≥ 30% from Baseline, plus a decrease in RBS ≥ 1 or an absolute RBS ≤ 1.

End point type	Secondary

End point timeframe:

At Week 2

Notes:

[67] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint included Substudy 1, Part 1 participants.

End point values	SS1: Placebo	SS1: Upadacitinib 7.5 mg	SS1: Upadacitinib 15 mg	SS1: Upadacitinib 30 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	46[68]	47[69]	49[70]	52[71]
Units: percentage of participants				
number (not applicable)	17.4	23.4	34.7	36.5

Notes:

[68] - SS1 main subjects (ITT1A) randomized to ≥1 study drug dose during Pt 1; NRI used for missing values
[69] - SS1 main subjects (ITT1A) randomized to ≥1 study drug dose during Pt 1; NRI used for missing values

[70] - SS1 main subjects (ITT1A) randomized to ≥1 study drug dose during Pt 1; NRI used for missing values
[71] - SS1 main subjects (ITT1A) randomized to ≥1 study drug dose during Pt 1; NRI used for missing values

End point values	SS1: Upadacitinib 45 mg			
Subject group type	Reporting group			
Number of subjects analysed	56[72]			
Units: percentage of participants				
number (not applicable)	55.4			

Notes:
[72] - SS1 main subjects (ITT1A) randomized to ≥1 study drug dose during Pt 1; NRI used for missing values

Statistical analyses

Statistical analysis title	Substudy 1: Upadacitinib 7.5 mg vs Placebo
Comparison groups	SS1: Placebo v SS1: Upadacitinib 7.5 mg
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority[73]
P-value	= 0.495 [74]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted risk difference (%)
Point estimate	5.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-11.1
upper limit	22.9

Notes:
[73] - The primary and ranked secondary efficacy endpoints were tested with multiplicity adjustment using a fixed-sequence multiple testing procedure to ensure a strong control of family-wise type I error rate at significance level alpha = 0.05 (2-sided).

[74] - Stratified by previous biologic use, baseline corticosteroid use and baseline Adapted Mayo score (≤ 7 and > 7)

Statistical analysis title	Substudy 1: Upadacitinib 15 mg vs Placebo
Comparison groups	SS1: Placebo v SS1: Upadacitinib 15 mg
Number of subjects included in analysis	95
Analysis specification	Pre-specified
Analysis type	superiority[75]
P-value	= 0.074 [76]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted risk difference (%)
Point estimate	15.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.6
upper limit	33.4

Notes:

[75] - The primary and ranked secondary efficacy endpoints were tested with multiplicity adjustment using a fixed-sequence multiple testing procedure to ensure a strong control of family-wise type I error rate at significance level alpha = 0.05 (2-sided).

[76] - Stratified by previous biologic use, baseline corticosteroid use and baseline Adapted Mayo score (≤ 7 and > 7)

Statistical analysis title	Substudy 1: Upadacitinib 30 mg vs Placebo
Comparison groups	SS1: Placebo v SS1: Upadacitinib 30 mg
Number of subjects included in analysis	98
Analysis specification	Pre-specified
Analysis type	superiority[77]
P-value	= 0.033 [78]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted risk difference (%)
Point estimate	19.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.6
upper limit	36.9

Notes:

[77] - The primary and ranked secondary efficacy endpoints were tested with multiplicity adjustment using a fixed-sequence multiple testing procedure to ensure a strong control of family-wise type I error rate at significance level alpha = 0.05 (2-sided).

[78] - Stratified by previous biologic use, baseline corticosteroid use and baseline Adapted Mayo score (≤ 7 and > 7)

Statistical analysis title	Substudy 1: Upadacitinib 45 mg vs Placebo
Comparison groups	SS1: Placebo v SS1: Upadacitinib 45 mg
Number of subjects included in analysis	102
Analysis specification	Pre-specified
Analysis type	superiority[79]
P-value	< 0.001 [80]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted risk difference (%)
Point estimate	40.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	20.5
upper limit	59.7

Notes:

[79] - The primary and ranked secondary efficacy endpoints were tested with multiplicity adjustment using a fixed-sequence multiple testing procedure to ensure a strong control of family-wise type I error rate at significance level alpha = 0.05 (2-sided).

[80] - Stratified by previous biologic use, baseline corticosteroid use and baseline Adapted Mayo score (≤ 7 and > 7)

Secondary: Substudy 1: Change in Full Mayo Score From Baseline to Week 8

End point title	Substudy 1: Change in Full Mayo Score From Baseline to Week

	8[81]

End point description:

The Mayo score is a tool designed to measure disease activity for ulcerative colitis. The Full Mayo score (FMS) ranges from 0 (normal or inactive disease) to 12 (severe disease) and is calculated as the sum of 4 subscores (stool frequency, rectal bleeding, endoscopy [confirmed by a central reader], and physician's global assessment), each of which ranges from 0 (normal) to 3 (severe disease). Negative changes indicate improvement. Clinical remission per FMS is defined as Mayo Score ≤ 2 and no individual subscore > 1.

End point type	Secondary

End point timeframe:

Baseline (Week 0), Week 8

Notes:

[81] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint included Substudy 1, Part 1 participants.

End point values	SS1: Placebo	SS1: Upadacitinib 7.5 mg	SS1: Upadacitinib 15 mg	SS1: Upadacitinib 30 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	41[82]	43[83]	44[84]	44[85]
Units: units on a scale				
arithmetic mean (standard deviation)	-0.741 (± 2.3302)	-2.870 (± 2.9685)	-3.589 (± 2.4984)	-4.211 (± 3.0886)

Notes:

[82] - SS1 main subjects (ITT1A) randomized to ≥1 study drug dose during Pt 1; LOCF used for missing data
[83] - SS1 main subjects (ITT1A) randomized to ≥1 study drug dose during Pt 1; LOCF used for missing data
[84] - SS1 main subjects (ITT1A) randomized to ≥1 study drug dose during Pt 1; LOCF used for missing data
[85] - SS1 main subjects (ITT1A) randomized to ≥1 study drug dose during Pt 1; LOCF used for missing data

End point values	SS1: Upadacitinib 45 mg			
Subject group type	Reporting group			
Number of subjects analysed	48[86]			
Units: units on a scale				
arithmetic mean (standard deviation)	-4.606 (± 2.8976)			

Notes:

[86] - SS1 main subjects (ITT1A) randomized to ≥1 study drug dose during Pt 1; LOCF used for missing data

Statistical analyses

Statistical analysis title	Substudy 1: Upadacitinib 7.5 mg vs Placebo
Comparison groups	SS1: Placebo v SS1: Upadacitinib 7.5 mg

Number of subjects included in analysis	84
Analysis specification	Pre-specified
Analysis type	superiority[87]
P-value	< 0.001 [88]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-2.142
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.2323
upper limit	-1.052

Notes:

[87] - The primary and ranked secondary efficacy endpoints were tested with multiplicity adjustment using a fixed-sequence multiple testing procedure to ensure a strong control of family-wise type I error rate at significance level alpha = 0.05 (2-sided).

[88] - Stratified by previous biologic use, Baseline corticosteroid use, Baseline Adapted Mayo score (<= 7 and > 7)), and Baseline value as covariate.

Statistical analysis title	Substudy 1: Upadacitinib 15 mg vs Placebo
Comparison groups	SS1: Placebo v SS1: Upadacitinib 15 mg
Number of subjects included in analysis	85
Analysis specification	Pre-specified
Analysis type	superiority[89]
P-value	< 0.001 [90]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-2.938
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.0284
upper limit	-1.8478

Notes:

[89] - The primary and ranked secondary efficacy endpoints were tested with multiplicity adjustment using a fixed-sequence multiple testing procedure to ensure a strong control of family-wise type I error rate at significance level alpha = 0.05 (2-sided).

[90] - Stratified by previous biologic use, Baseline corticosteroid use, Baseline Adapted Mayo score (<= 7 and > 7)), and Baseline value as covariate.

Statistical analysis title	Substudy 1: Upadacitinib 30 mg vs Placebo
Comparison groups	SS1: Placebo v SS1: Upadacitinib 30 mg
Number of subjects included in analysis	85
Analysis specification	Pre-specified
Analysis type	superiority[91]
P-value	< 0.001 [92]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-3.736

Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.8247
upper limit	-2.647

Notes:

[91] - The primary and ranked secondary efficacy endpoints were tested with multiplicity adjustment using a fixed-sequence multiple testing procedure to ensure a strong control of family-wise type I error rate at significance level alpha = 0.05 (2-sided).

[92] - Stratified by previous biologic use, Baseline corticosteroid use, Baseline Adapted Mayo score (<= 7 and > 7)), and Baseline value as covariate.

Statistical analysis title	Substudy 1: Upadacitinib 45 mg vs Placebo
Comparison groups	SS1: Upadacitinib 45 mg v SS1: Placebo
Number of subjects included in analysis	89
Analysis specification	Pre-specified
Analysis type	superiority[93]
P-value	< 0.001 [94]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-4.061
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.1252
upper limit	-2.9974

Notes:

[93] - The primary and ranked secondary efficacy endpoints were tested with multiplicity adjustment using a fixed-sequence multiple testing procedure to ensure a strong control of family-wise type I error rate at significance level alpha = 0.05 (2-sided).

[94] - Stratified by previous biologic use, Baseline corticosteroid use, Baseline Adapted Mayo score (<= 7 and > 7)), and Baseline value as covariate.

Secondary: Substudy 1: Percentage Of Participants With Endoscopic Remission at Week 8

End point title	Substudy 1: Percentage Of Participants With Endoscopic Remission at Week 8[95]

End point description:

Endoscopic remission is defined as an endoscopic subscore of 0. Endoscopies were assessed by a blinded central reader and scored according to the following scale: 0 = Normal or inactive disease; 1 = Mild disease (erythema, decreased vascular pattern); 2 = Moderate disease (marked erythema, lack of vascular pattern, any friability, erosions); 3 = Severe disease (spontaneous bleeding, ulceration).

End point type	Secondary

End point timeframe:

At Week 8

Notes:

[95] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint included Substudy 1, Part 1 participants.

End point values	SS1: Placebo	SS1: Upadacitinib 7.5 mg	SS1: Upadacitinib 15 mg	SS1: Upadacitinib 30 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	46[96]	47[97]	49[98]	52[99]
Units: percentage of participants				
number (not applicable)	0	6.4	4.1	9.6

Notes:

[96] - SS1 main subjects (ITT1A) randomized to ≥1 study drug dose during Pt 1; NRI used for missing values
[97] - SS1 main subjects (ITT1A) randomized to ≥1 study drug dose during Pt 1; NRI used for missing values
[98] - SS1 main subjects (ITT1A) randomized to ≥1 study drug dose during Pt 1; NRI used for missing values
[99] - SS1 main subjects (ITT1A) randomized to ≥1 study drug dose during Pt 1; NRI used for missing values

End point values	SS1: Upadacitinib 45 mg			
Subject group type	Reporting group			
Number of subjects analysed	56[100]			
Units: percentage of participants				
number (not applicable)	17.9			

Notes:

[100] - SS1 main subjects (ITT1A) randomized to ≥1 study drug dose during Pt 1; NRI used for missing values

Statistical analyses

Statistical analysis title	Substudy 1: Upadacitinib 7.5 mg vs Placebo
Comparison groups	SS1: Placebo v SS1: Upadacitinib 7.5 mg
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority[101]
P-value	= 0.075 [102]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted risk difference (%)
Point estimate	6.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.7
upper limit	13.9

Notes:

[101] - The primary and ranked secondary efficacy endpoints were tested with multiplicity adjustment using a fixed-sequence multiple testing procedure to ensure a strong control of family-wise type I error rate at significance level alpha = 0.05 (2-sided).

[102] - Stratified by previous biologic use, baseline corticosteroid use and baseline Adapted Mayo score (≤ 7 and > 7)

Statistical analysis title	Substudy 1: Upadacitinib 15 mg vs Placebo
Comparison groups	SS1: Placebo v SS1: Upadacitinib 15 mg

Number of subjects included in analysis	95
Analysis specification	Pre-specified
Analysis type	superiority[103]
P-value	= 0.199 [104]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted risk difference (%)
Point estimate	3.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2
upper limit	9.6

Notes:

[103] - The primary and ranked secondary efficacy endpoints were tested with multiplicity adjustment using a fixed-sequence multiple testing procedure to ensure a strong control of family-wise type I error rate at significance level alpha = 0.05 (2-sided).

[104] - Stratified by previous biologic use, baseline corticosteroid use and baseline Adapted Mayo score (≤ 7 and > 7)

Statistical analysis title	Substudy 1: Upadacitinib 30 mg vs Placebo
Comparison groups	SS1: Placebo v SS1: Upadacitinib 30 mg
Number of subjects included in analysis	98
Analysis specification	Pre-specified
Analysis type	superiority[105]
P-value	= 0.015 [106]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted risk difference (%)
Point estimate	11.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.2
upper limit	20

Notes:

[105] - The primary and ranked secondary efficacy endpoints were tested with multiplicity adjustment using a fixed-sequence multiple testing procedure to ensure a strong control of family-wise type I error rate at significance level alpha = 0.05 (2-sided).

[106] - Stratified by previous biologic use, baseline corticosteroid use and baseline Adapted Mayo score (≤ 7 and > 7)

Statistical analysis title	Substudy 1: Upadacitinib 45 mg vs Placebo
Comparison groups	SS1: Placebo v SS1: Upadacitinib 45 mg
Number of subjects included in analysis	102
Analysis specification	Pre-specified
Analysis type	superiority[107]
P-value	= 0.004 [108]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted risk difference (%)
Point estimate	17.8

Confidence interval	
level	95 %
sides	2-sided
lower limit	5.8
upper limit	29.9

Notes:

[107] - The primary and ranked secondary efficacy endpoints were tested with multiplicity adjustment using a fixed-sequence multiple testing procedure to ensure a strong control of family-wise type I error rate at significance level alpha = 0.05 (2-sided).

[108] - Stratified by previous biologic use, baseline corticosteroid use and baseline Adapted Mayo score (≤ 7 and > 7)

Secondary: Substudy 1: Percentage Of Participants Who Achieved Histologic Improvement at Week 8

End point title	Substudy 1: Percentage Of Participants Who Achieved Histologic Improvement at Week 8[109]

End point description:

The Geboes histologic index includes seven histological features (architectural change, chronic inflammatory infiltrate, lamina propria neutrophils and eosinophils, neutrophils in epithelium, crypt destruction and erosion or ulcers). The Geboes score has 6 grades, each with 3-5 subgrades: Grade 0, structural change only; Grade 1, chronic inflammation; Grade 2, lamina propria neutrophils and eosinophils; Grade 3, neutrophils in epithelium; Grade 4, crypt destruction; and Grade 5, erosions or ulceration.

Histologic improvement was defined as decrease from baseline in Geboes score.

End point type	Secondary

End point timeframe:

At Week 8

Notes:

[109] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint included Substudy 1, Part 1 participants.

End point values	SS1: Placebo	SS1: Upadacitinib 7.5 mg	SS1: Upadacitinib 15 mg	SS1: Upadacitinib 30 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	46[110]	47[111]	49[112]	52[113]
Units: percentage of participants				
number (not applicable)	6.5	31.9	51.0	44.2

Notes:

[110] - SS1 main subjects (ITT1A) randomized to ≥1 study drug dose during Pt 1; NRI used for missing values
[111] - SS1 main subjects (ITT1A) randomized to ≥1 study drug dose during Pt 1; NRI used for missing values
[112] - SS1 main subjects (ITT1A) randomized to ≥1 study drug dose during Pt 1; NRI used for missing values
[113] - SS1 main subjects (ITT1A) randomized to ≥1 study drug dose during Pt 1; NRI used for missing values

End point values	SS1: Upadacitinib 45 mg			
Subject group type	Reporting group			
Number of subjects analysed	56[114]			

Units: percentage of participants				
number (not applicable)	48.2			

Notes:

[114] - SS1 main subjects (ITT1A) randomized to ≥1 study drug dose during Pt 1; NRI used for missing values

Statistical analyses

Statistical analysis title	Substudy 1: Upadacitinib 7.5 mg vs Placebo
Comparison groups	SS1: Placebo v SS1: Upadacitinib 7.5 mg
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority[115]
P-value	= 0.003 [116]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted risk difference (%)
Point estimate	25.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	8.9
upper limit	42.3

Notes:

[115] - The primary and ranked secondary efficacy endpoints were tested with multiplicity adjustment using a fixed-sequence multiple testing procedure to ensure a strong control of family-wise type I error rate at significance level alpha = 0.05 (2-sided).

[116] - Stratified by previous biologic use, baseline corticosteroid use and baseline Adapted Mayo score (≤ 7 and > 7)

Statistical analysis title	Substudy 1: Upadacitinib 15 mg vs Placebo
Comparison groups	SS1: Placebo v SS1: Upadacitinib 15 mg
Number of subjects included in analysis	95
Analysis specification	Pre-specified
Analysis type	superiority[117]
P-value	< 0.001 [118]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted risk difference (%)
Point estimate	43.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	25.4
upper limit	61.8

Notes:

[117] - The primary and ranked secondary efficacy endpoints were tested with multiplicity adjustment using a fixed-sequence multiple testing procedure to ensure a strong control of family-wise type I error rate at significance level alpha = 0.05 (2-sided).

[118] - Stratified by previous biologic use, baseline corticosteroid use and baseline Adapted Mayo score (≤ 7 and > 7)

Statistical analysis title	Substudy 1: Upadacitinib 30 mg vs Placebo

Comparison groups	SS1: Placebo v SS1: Upadacitinib 30 mg
Number of subjects included in analysis	98
Analysis specification	Pre-specified
Analysis type	superiority[119]
P-value	< 0.001 [120]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted risk difference (%)
Point estimate	39.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	21.3
upper limit	57.5

Notes:

[119] - The primary and ranked secondary efficacy endpoints were tested with multiplicity adjustment using a fixed-sequence multiple testing procedure to ensure a strong control of family-wise type I error rate at significance level alpha = 0.05 (2-sided).

[120] - Stratified by previous biologic use, baseline corticosteroid use and baseline Adapted Mayo score (≤ 7 and > 7)

Statistical analysis title	Substudy 1: Upadacitinib 45 mg vs Placebo
Comparison groups	SS1: Placebo v SS1: Upadacitinib 45 mg
Number of subjects included in analysis	102
Analysis specification	Pre-specified
Analysis type	superiority[121]
P-value	< 0.001 [122]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted risk difference (%)
Point estimate	43.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	24.4
upper limit	61.9

Notes:

[121] - The primary and ranked secondary efficacy endpoints were tested with multiplicity adjustment using a fixed-sequence multiple testing procedure to ensure a strong control of family-wise type I error rate at significance level alpha = 0.05 (2-sided).

[122] - Stratified by previous biologic use, baseline corticosteroid use and baseline Adapted Mayo score (≤ 7 and > 7)

Secondary: Substudy 2: Percentage Of Participants With Endoscopic Improvement at Week 8

End point title	Substudy 2: Percentage Of Participants With Endoscopic Improvement at Week 8

End point description:

Endoscopic improvement is defined as an endoscopic subscore of 0 or 1. Endoscopies were assessed by a blinded central reader and scored according to the following scale: 0 = Normal or inactive disease; 1 = Mild disease (erythema, decreased vascular pattern); 2 = Moderate disease (marked erythema, lack of vascular pattern, any friability, erosions); 3 = Severe disease (spontaneous bleeding, ulceration).

End point type	Secondary

End point timeframe:

At Week 8

End point values	SS2: Placebo	SS2: Upadacitinib 45 mg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	154[123]	319[124]		
Units: percentage of participants				
number (confidence interval 95%)	7.4 (3.2 to 11.5)	36.3 (31.0 to 41.7)		

Notes:

[123] - SS2 (ITT1): randomized to ≥1 dose of study drug during Pt 1. NRI with MI due to COVID-19 (NRI-C)

[124] - SS2 (ITT1): randomized to ≥1 dose of study drug during Pt 1. NRI with MI due to COVID-19 (NRI-C)

Statistical analyses

Statistical analysis title	Substudy 2: Upadacitinib 45 mg vs Placebo
Comparison groups	SS2: Placebo v SS2: Upadacitinib 45 mg
Number of subjects included in analysis	473
Analysis specification	Pre-specified
Analysis type	superiority[125]
P-value	< 0.001 [126]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted risk difference (%)
Point estimate	29.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	22.6
upper limit	35.9

Notes:

[125] - The primary and ranked secondary efficacy endpoints were tested with multiplicity adjustment using a fixed-sequence multiple testing procedure to ensure a strong control of family-wise type I error rate at significance level alpha = 0.05 (2-sided).

[126] - Stratified by bio-IR status (bio-IR vs. non-bio-IR), Baseline corticosteroid use (yes or no) and Baseline Adapted Mayo score (≤ 7 vs. > 7)

Secondary: Substudy 2: Percentage Of Participants With Endoscopic Remission at Week 8

End point title	Substudy 2: Percentage Of Participants With Endoscopic Remission at Week 8

End point description:

Endoscopic remission is defined as an endoscopic subscore of 0. Endoscopies were assessed by a blinded central reader and scored according to the following scale: 0 = Normal or inactive disease; 1 = Mild disease (erythema, decreased vascular pattern); 2 = Moderate disease (marked erythema, lack of vascular pattern, any friability, erosions); 3 = Severe disease (spontaneous bleeding, ulceration).

End point type	Secondary

End point timeframe:

At Week 8

End point values	SS2: Placebo	SS2: Upadacitinib 45 mg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	154[127]	319[128]		
Units: percentage of participants				
number (confidence interval 95%)	1.3 (0.0 to 3.1)	13.7 (9.9 to 17.6)		

Notes:

[127] - SS2 (ITT1): randomized to ≥1 dose of study drug during Pt 1. NRI with MI due to COVID-19 (NRI-C)

[128] - SS2 (ITT1): randomized to ≥1 dose of study drug during Pt 1. NRI with MI due to COVID-19 (NRI-C)

Statistical analyses

Statistical analysis title	Substudy 2: Upadacitinib 45 mg vs Placebo
Comparison groups	SS2: Upadacitinib 45 mg v SS2: Placebo
Number of subjects included in analysis	473
Analysis specification	Pre-specified
Analysis type	superiority[129]
P-value	< 0.001 [130]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted risk difference (%)
Point estimate	12.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	8.4
upper limit	17

Notes:

[129] - The primary and ranked secondary efficacy endpoints were tested with multiplicity adjustment using a fixed-sequence multiple testing procedure to ensure a strong control of family-wise type I error rate at significance level alpha = 0.05 (2-sided).

[130] - Stratified by bio-IR status (bio-IR vs. non-bio-IR), Baseline corticosteroid use (yes or no) and Baseline Adapted Mayo score (≤ 7 vs. > 7)

Secondary: Substudy 2: Percentage Of Participants Achieving Clinical Response Per Adapted Mayo Score at Week 8

End point title	Substudy 2: Percentage Of Participants Achieving Clinical Response Per Adapted Mayo Score at Week 8

End point description:

The Adapted Mayo Score is a composite score of UC disease activity based on the following 3 subscores:
1. Stool frequency subscore (SFS), scored from 0 (normal number of stools) to 3 (5 or more stools more than normal).
2. Rectal bleeding subscore (RBS), scored from 0 (no blood seen) to 3 (blood alone passed).
3. Endoscopic subscore, scored from 0 (normal or inactive disease) to 3 (severe disease, spontaneous bleeding, ulceration).

The overall Adapted Mayo score ranges from 0 to 9 where higher scores represent more severe disease.

Clinical response is defined as a decrease from baseline in the Adapted Mayo score ≥ 2 points and ≥ 30% from baseline, and a decrease in RBS ≥ 1 or an absolute RBS ≤ 1).

End point type	Secondary

End point timeframe:

At Week 8

End point values	SS2: Placebo	SS2: Upadacitinib 45 mg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	154[131]	319[132]		
Units: percentage of participants				
number (confidence interval 95%)	27.3 (20.2 to 34.3)	72.6 (67.7 to 77.5)		

Notes:

[131] - SS2 (ITT1): randomized to ≥1 dose of study drug during Pt 1. NRI with MI due to COVID-19 (NRI-C)
[132] - SS2 (ITT1): randomized to ≥1 dose of study drug during Pt 1. NRI with MI due to COVID-19 (NRI-C)

Statistical analyses

Statistical analysis title	Substudy 2: Upadacitinib 45 mg vs Placebo
Comparison groups	SS2: Placebo v SS2: Upadacitinib 45 mg
Number of subjects included in analysis	473
Analysis specification	Pre-specified
Analysis type	superiority[133]
P-value	< 0.001 [134]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted risk difference (%)
Point estimate	46.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	38.4
upper limit	54.2

Notes:

[133] - The primary and ranked secondary efficacy endpoints were tested with multiplicity adjustment using a fixed-sequence multiple testing procedure to ensure a strong control of family-wise type I error rate at significance level alpha = 0.05 (2-sided).

[134] - Stratified by bio-IR status (bio-IR vs. non-bio-IR), Baseline corticosteroid use (yes or no) and Baseline Adapted Mayo score (≤ 7 vs. > 7)

Secondary: Substudy 2: Percentage Of Participants Achieving Clinical Response Per Partial Mayo Score at Week 2

End point title	Substudy 2: Percentage Of Participants Achieving Clinical Response Per Partial Mayo Score at Week 2

End point description:

The Partial Mayo Score is a composite score of UC disease activity based on the following 2 subscores:
1. Stool frequency subscore (SFS), scored from 0 (normal number of stools) to 3 (5 or more stools more than normal).

2. Rectal bleeding subscore (RBS), scored from 0 (no blood seen) to 3 (blood alone passed).

The overall Partial Mayo score ranges from 0 to 6 with higher scores representing more severe disease.

Clinical response per Partial Mayo Score is defined as a decrease from Baseline ≥ 1 point and ≥ 30% from Baseline, plus a decrease in RBS ≥ 1 or an absolute RBS ≤ 1.

End point type	Secondary

End point timeframe:

At Week 2

End point values	SS2: Placebo	SS2: Upadacitinib 45 mg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	154[135]	319[136]		
Units: percentage of participants				
number (confidence interval 95%)	27.3 (20.2 to 34.3)	60.1 (54.7 to 65.5)		

Notes:

[135] - SS2 (ITT1): randomized to ≥1 dose of study drug during Pt 1. NRI with MI due to COVID-19 (NRI-C)
[136] - SS2 (ITT1): randomized to ≥1 dose of study drug during Pt 1. NRI with MI due to COVID-19 (NRI-C)

Statistical analyses

Statistical analysis title	Substudy 2: Upadacitinib 45 mg vs Placebo
Comparison groups	SS2: Placebo v SS2: Upadacitinib 45 mg
Number of subjects included in analysis	473
Analysis specification	Pre-specified
Analysis type	superiority[137]
P-value	< 0.001 [138]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted risk difference (%)
Point estimate	33.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	24.8
upper limit	41.8

Notes:

[137] - The primary and ranked secondary efficacy endpoints were tested with multiplicity adjustment using a fixed-sequence multiple testing procedure to ensure a strong control of family-wise type I error rate at significance level alpha = 0.05 (2-sided).

[138] - Stratified by bio-IR status (bio-IR vs. non-bio-IR), Baseline corticosteroid use (yes or no) and Baseline Adapted Mayo score (≤ 7 vs. > 7)

Secondary: Substudy 2: Percentage Of Participants Who Achieved Histologic-Endoscopic Mucosal Improvement at Week 8

End point title	Substudy 2: Percentage Of Participants Who Achieved Histologic-Endoscopic Mucosal Improvement at Week 8

End point description:

Histologic-endoscopic mucosal improvement is defined as an endoscopic subscore of 0 or 1 and a Geboes score ≤ 3.1.

The endoscopic subscore ranges from 0 (normal or inactive disease) to 3 (severe disease with spontaneous bleeding, ulceration).

The Geboes histologic index includes seven histological features (architectural change, chronic inflammatory infiltrate, lamina propria neutrophils and eosinophils, neutrophils in epithelium, crypt destruction and erosion or ulcers). The Geboes score has 6 grades, each with 3-5 subgrades: Grade 0, structural change only; Grade 1, chronic inflammation; Grade 2, lamina propria neutrophils and eosinophils; Grade 3, neutrophils in epithelium; Grade 4, crypt destruction; and Grade 5, erosions or ulceration.

End point type	Secondary

End point timeframe:

At Week 8

End point values	SS2: Placebo	SS2: Upadacitinib 45 mg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	154[139]	319[140]		
Units: percentage of participants				
number (confidence interval 95%)	6.6 (2.6 to 10.5)	30.1 (25.0 to 35.1)		

Notes:

[139] - SS2 (ITT1): randomized to ≥1 dose of study drug during Pt 1. NRI with MI due to COVID-19 (NRI-C)
[140] - SS2 (ITT1): randomized to ≥1 dose of study drug during Pt 1. NRI with MI due to COVID-19 (NRI-C)

Statistical analyses

Statistical analysis title	Substudy 2: Upadacitinib 45 mg vs Placebo
Comparison groups	SS2: Placebo v SS2: Upadacitinib 45 mg
Number of subjects included in analysis	473
Analysis specification	Pre-specified
Analysis type	superiority[141]
P-value	< 0.001 [142]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted risk difference (%)
Point estimate	23.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	17.5
upper limit	30

Notes:

[141] - The primary and ranked secondary efficacy endpoints were tested with multiplicity adjustment using a fixed-sequence multiple testing procedure to ensure a strong control of family-wise type I error rate at significance level alpha = 0.05 (2-sided).

[142] - Stratified by bio-IR status (bio-IR vs. non-bio-IR), Baseline corticosteroid use (yes or no) and

Baseline Adapted Mayo score (≤ 7 vs. > 7)

Secondary: Substudy 2: Percentage Of Participants Who Report No Bowel Urgency at Week 8

End point title	Substudy 2: Percentage Of Participants Who Report No Bowel Urgency at Week 8

End point description:

Bowel urgency was assessed by participants in a subject diary completed once a day.

End point type	Secondary

End point timeframe:

At Week 8

End point values	SS2: Placebo	SS2: Upadacitinib 45 mg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	154[143]	319[144]		
Units: percentage of participants				
number (confidence interval 95%)	21.4 (14.9 to 27.9)	48.4 (42.9 to 53.9)		

Notes:

[143] - SS2 (ITT1): randomized to ≥1 dose of study drug during Pt 1. NRI with MI due to COVID-19 (NRI-C)
[144] - SS2 (ITT1): randomized to ≥1 dose of study drug during Pt 1. NRI with MI due to COVID-19 (NRI-C)

Statistical analyses

Statistical analysis title	Substudy 2: Upadacitinib 45 mg vs Placebo
Comparison groups	SS2: Placebo v SS2: Upadacitinib 45 mg
Number of subjects included in analysis	473
Analysis specification	Pre-specified
Analysis type	superiority[145]
P-value	< 0.001 [146]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted risk difference (%)
Point estimate	27.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	19.2
upper limit	35.6

Notes:

[145] - The primary and ranked secondary efficacy endpoints were tested with multiplicity adjustment using a fixed-sequence multiple testing procedure to ensure a strong control of family-wise type I error rate at significance level alpha = 0.05 (2-sided).

[146] - Stratified by bio-IR status (bio-IR vs. non-bio-IR), Baseline corticosteroid use (yes or no) and Baseline Adapted Mayo score (≤ 7 vs. > 7)

Secondary: Substudy 2: Percentage Of Participants Who Reported No Abdominal Pain at Week 8

End point title	Substudy 2: Percentage Of Participants Who Reported No Abdominal Pain at Week 8

End point description:

Abdominal pain was assessed by participants in a subject diary completed once a day.

End point type	Secondary

End point timeframe:

At Week 8

End point values	SS2: Placebo	SS2: Upadacitinib 45 mg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	154[147]	319[148]		
Units: percentage of participants				
number (confidence interval 95%)	23.4 (16.7 to 30.1)	46.6 (41.1 to 52.1)		

Notes:

[147] - SS2 (ITT1): randomized to ≥1 dose of study drug during Pt 1. NRI with MI due to COVID-19 (NRI-C)
[148] - SS2 (ITT1): randomized to ≥1 dose of study drug during Pt 1. NRI with MI due to COVID-19 (NRI-C)

Statistical analyses

Statistical analysis title	Substudy 2: Upadacitinib 45 mg vs Placebo
Comparison groups	SS2: Placebo v SS2: Upadacitinib 45 mg
Number of subjects included in analysis	473
Analysis specification	Pre-specified
Analysis type	superiority[149]
P-value	< 0.001 [150]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted risk difference (%)
Point estimate	23.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	15.1
upper limit	32.1

Notes:

[149] - The primary and ranked secondary efficacy endpoints were tested with multiplicity adjustment using a fixed-sequence multiple testing procedure to ensure a strong control of family-wise type I error rate at significance level alpha = 0.05 (2-sided).

[150] - Stratified by bio-IR status (bio-IR vs. non-bio-IR), Baseline corticosteroid use (yes or no) and Baseline Adapted Mayo score (≤ 7 vs. > 7)

Secondary: Substudy 2: Percentage Of Participants Who Achieved Histologic Improvement at Week 8

End point title	Substudy 2: Percentage Of Participants Who Achieved Histologic Improvement at Week 8

End point description:

The Geboes histologic index includes seven histological features (architectural change, chronic inflammatory infiltrate, lamina propria neutrophils and eosinophils, neutrophils in epithelium, crypt destruction and erosion or ulcers). The Geboes score has 6 grades, each with 3-5 subgrades: Grade 0, structural change only; Grade 1, chronic inflammation; Grade 2, lamina propria neutrophils and eosinophils; Grade 3, neutrophils in epithelium; Grade 4, crypt destruction; and Grade 5, erosions or ulceration. Histologic improvement was defined as decrease from baseline in Geboes score.

End point type	Secondary

End point timeframe:

At Week 8

End point values	SS2: Placebo	SS2: Upadacitinib 45 mg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	154[151]	319[152]		
Units: percentage of participants				
number (confidence interval 95%)	22.5 (15.9 to 29.1)	55.0 (49.5 to 60.5)		

Notes:

[151] - SS2 (ITT1): randomized to ≥1 dose of study drug during Pt 1. NRI with MI due to COVID-19 (NRI-C)
[152] - SS2 (ITT1): randomized to ≥1 dose of study drug during Pt 1. NRI with MI due to COVID-19 (NRI-C)

Statistical analyses

Statistical analysis title	Substudy 2: Upadacitinib 45 mg vs Placebo
Comparison groups	SS2: Placebo v SS2: Upadacitinib 45 mg
Number of subjects included in analysis	473
Analysis specification	Pre-specified
Analysis type	superiority[153]
P-value	< 0.001 [154]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted risk difference (%)
Point estimate	32.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	23.8
upper limit	40.7

Notes:

[153] - The primary and ranked secondary efficacy endpoints were tested with multiplicity adjustment using a fixed-sequence multiple testing procedure to ensure a strong control of family-wise type I error rate at significance level alpha = 0.05 (2-sided).

[154] - Stratified by bio-IR status (bio-IR vs. non-bio-IR), Baseline corticosteroid use (yes or no) and Baseline Adapted Mayo score (≤ 7 vs. > 7)

Secondary: Substudy 2: Change From Baseline in Inflammatory Bowel Disease Questionnaire (IBDQ) Total Score at Week 8

End point title	Substudy 2: Change From Baseline in Inflammatory Bowel Disease Questionnaire (IBDQ) Total Score at Week 8

End point description:

The Inflammatory Bowel Disease Questionnaire (IBDQ) is used to assess health-related quality of life (HRQoL) in patients with ulcerative colitis. It consists of 32 questions evaluating bowel and systemic symptoms, as well as emotional and social functions. Each question is answered on a scale from 1 (worst) to 7 (best). The total score ranges from 32 to 224 with higher scores indicating better health-related quality of life. A positive change from Baseline indicates improvement.

End point type	Secondary

End point timeframe:

Baseline (Week 0), Week 8

End point values	SS2: Placebo	SS2: Upadacitinib 45 mg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	125[155]	292[156]		
Units: units on a scale				
least squares mean (confidence interval 95%)	21.7 (16.03 to 27.28)	55.3 (51.54 to 59.15)		

Notes:

[155] - SS2 ITT1 w/ available data; MMRM anal; data after occurrence of UC-related corticosteroids event exc

[156] - SS2 ITT1 w/ available data; MMRM anal; data after occurrence of UC-related corticosteroids event exc

Statistical analyses

Statistical analysis title	Substudy 2: Upadacitinib 45 mg vs Placebo
Comparison groups	SS2: Placebo v SS2: Upadacitinib 45 mg
Number of subjects included in analysis	417
Analysis specification	Pre-specified
Analysis type	superiority[157]
P-value	< 0.001 [158]
Method	Mixed-effect model repeated measurement
Parameter estimate	LS Mean Difference
Point estimate	33.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	27.02
upper limit	40.36
Variability estimate	Standard error of the mean
Dispersion value	3.39

Notes:

[157] - The primary and ranked secondary efficacy endpoints were tested with multiplicity adjustment using a fixed-sequence multiple testing procedure to ensure a strong control of family-wise type I error rate at significance level alpha = 0.05 (2-sided).

[158] - MMRM with Baseline, treatment, visit, treatment-by-visit interaction, and strata (Baseline Adapted Mayo score, corticosteroid use, and bio-IR status).

Secondary: Substudy 2: Percentage Of Participants With Mucosal Healing at Week 8

End point title	Substudy 2: Percentage Of Participants With Mucosal Healing at Week 8

End point description:

Mucosal healing is defined as an endoscopic score of 0 and Geboes score < 2.0. The endoscopic subscore ranges from 0 (normal or inactive disease) to 3 (severe disease with spontaneous bleeding, ulceration).

The Geboes histologic index includes seven histological features (architectural change, chronic inflammatory infiltrate, lamina propria neutrophils and eosinophils, neutrophils in epithelium, crypt destruction and erosion or ulcers). The Geboes score has 6 grades, each with 3-5 subgrades: Grade 0, structural change only; Grade 1, chronic inflammation; Grade 2, lamina propria neutrophils and eosinophils; Grade 3, neutrophils in epithelium; Grade 4, crypt destruction; and Grade 5, erosions or ulceration.

End point type	Secondary

End point timeframe:

At Week 8

End point values	SS2: Placebo	SS2: Upadacitinib 45 mg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	154[159]	319[160]		
Units: percentage of participants				
number (confidence interval 95%)	1.3 (0.0 to 3.1)	10.7 (7.3 to 14.1)		

Notes:

[159] - SS2 (ITT1): randomized to ≥1 dose of study drug during Pt 1. NRI with MI due to COVID-19 (NRI-C)
[160] - SS2 (ITT1): randomized to ≥1 dose of study drug during Pt 1. NRI with MI due to COVID-19 (NRI-C)

Statistical analyses

Statistical analysis title	Substudy 2: Upadacitinib 45 mg vs Placebo
Comparison groups	SS2: Placebo v SS2: Upadacitinib 45 mg
Number of subjects included in analysis	473
Analysis specification	Pre-specified
Analysis type	superiority[161]
P-value	< 0.001 [162]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted risk difference (%)
Point estimate	9.7

Confidence interval	
level	95 %
sides	2-sided
lower limit	5.7
upper limit	13.7

Notes:

[161] - The primary and ranked secondary efficacy endpoints were tested with multiplicity adjustment using a fixed-sequence multiple testing procedure to ensure a strong control of family-wise type I error rate at significance level alpha = 0.05 (2-sided).

[162] - Stratified by Baseline corticosteroid use (yes or no), Baseline Adapted Mayo score (≤ 7 or > 7), and bio-IR status (bio-IR or non-bio-IR)

Secondary: Substudy 2: Change From Baseline in Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F) Score at Week 8

End point title	Substudy 2: Change From Baseline in Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F) Score at Week 8

End point description:

The FACIT fatigue questionnaire was developed to assess fatigue associated with anemia. It consists of 13 fatigue-related questions. Each question is answered on a 5-point Likert scale: 0 (not at all); 1 (a little bit); 2 (somewhat); 3 (quite a bit); and 4 (very much). The total score ranges from 0 to 52, where higher scores represent less fatigue, and a positive change from Baseline indicates improvement.

End point type	Secondary

End point timeframe:

Baseline (Week 0), Week 8

End point values	SS2: Placebo	SS2: Upadacitinib 45 mg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	125[163]	291[164]		
Units: units on a scale				
least squares mean (confidence interval 95%)	2.8 (1.23 to 4.44)	9.5 (8.44 to 10.61)		

Notes:

[163] - SS2 ITT1 w/ available data; MMRM anal; data after occurrence of UC-related corticosteroids event exc

[164] - SS2 ITT1 w/ available data; MMRM anal; data after occurrence of UC-related corticosteroids event exc

Statistical analyses

Statistical analysis title	Substudy 2: Upadacitinib 45 mg vs Placebo
Comparison groups	SS2: Placebo v SS2: Upadacitinib 45 mg
Number of subjects included in analysis	416
Analysis specification	Pre-specified
Analysis type	superiority[165]
P-value	< 0.001 [166]
Method	Mixed-effect model repeated measurement
Parameter estimate	LS Mean Difference
Point estimate	6.7

Confidence interval	
level	95 %
sides	2-sided
lower limit	4.79
upper limit	8.59
Variability estimate	Standard error of the mean
Dispersion value	0.97

Notes:

[165] - The primary and ranked secondary efficacy endpoints were tested with multiplicity adjustment using a fixed-sequence multiple testing procedure to ensure a strong control of family-wise type I error rate at significance level alpha = 0.05 (2-sided).

[166] - MMRM with Baseline, treatment, visit, treatment-by-visit interaction, and strata (Baseline Adapted Mayo score, corticosteroid use, and bio-IR status)

Secondary: Substudy 3: Percentage Of Participants With Endoscopic Improvement at Week 52

End point title	Substudy 3: Percentage Of Participants With Endoscopic Improvement at Week 52

End point description:

Endoscopic improvement is defined as an endoscopic subscore of 0 or 1. Endoscopies were assessed by a blinded central reader and scored according to the following scale: 0 = Normal or inactive disease; 1 = Mild disease (erythema, decreased vascular pattern); 2 = Moderate disease (marked erythema, lack of vascular pattern, any friability, erosions); 3 = Severe disease (spontaneous bleeding, ulceration).

End point type	Secondary

End point timeframe:

At Week 52

End point values	SS3: Placebo	SS3: UPA 15 mg	SS3: UPA 30 mg	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	149[167]	148[168]	154[169]	
Units: percentage of participants				
number (confidence interval 95%)	14.5 (8.7 to 20.3)	48.7 (40.5 to 56.8)	61.6 (53.6 to 69.6)	

Notes:

[167] - SS3 ITT_A:1st 451 Upa 45 mg 8-wk responders; 52-wk tx Cohort 1, NRI with MI due to COVID-19- NRI-C

[168] - SS3 ITT_A:1st 451 Upa 45 mg 8-wk responders; 52-wk tx Cohort 1, NRI with MI due to COVID-19- NRI-C

[169] - SS3 ITT_A:1st 451 Upa 45 mg 8-wk responders; 52-wk tx Cohort 1, NRI with MI due to COVID-19- NRI-C

Statistical analyses

Statistical analysis title	Substudy 3: Upadacitinib 15 mg vs Placebo
Comparison groups	SS3: Placebo v SS3: UPA 15 mg

Number of subjects included in analysis	297
Analysis specification	Pre-specified
Analysis type	superiority[170]
P-value	< 0.001 [171]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted risk difference (%)
Point estimate	34.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	25.1
upper limit	43.7

Notes:

[170] - The primary and ranked secondary efficacy endpoints were tested with graphical multiplicity adjustment to ensure a strong control of family-wise type I error rate at significance level α= 0.05 (2-sided).

[171] - Stratified by Bio-IR (Bio-IR/Non-Bio-IR) at Induction Study Baseline; clinical remission at Week 0 (yes/no); corticosteroid use at Week 0 (yes/no)

Statistical analysis title	Substudy 3: Upadacitinib 30 mg vs Placebo
Comparison groups	SS3: Placebo v SS3: UPA 30 mg
Number of subjects included in analysis	303
Analysis specification	Pre-specified
Analysis type	superiority[172]
P-value	< 0.001 [173]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted risk difference (%)
Point estimate	46.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	36.7
upper limit	55.8

Notes:

[172] - The primary and ranked secondary efficacy endpoints were tested with graphical multiplicity adjustment to ensure a strong control of family-wise type I error rate at significance level α= 0.05 (2-sided).

[173] - Stratified by Bio-IR (Bio-IR/Non-Bio-IR) at Induction Study Baseline; clinical remission at Week 0 (yes/no); corticosteroid use at Week 0 (yes/no)

Secondary: Substudy 3: Percentage of Participants With Clinical Remission Per Adapted Mayo Score at Week 52 Among Those Who Achieved Clinical Remission at the End of the Induction Treatment

End point title	Substudy 3: Percentage of Participants With Clinical Remission Per Adapted Mayo Score at Week 52 Among Those Who Achieved Clinical Remission at the End of the Induction Treatment

End point description:

The Adapted Mayo Score is a composite score of UC disease activity based on the following 3 subscores:
1. Stool frequency subscore (SFS), scored from 0 (normal number of stools) to 3 (5 or more stools more than normal).
2. Rectal bleeding subscore (RBS), scored from 0 (no blood seen) to 3 (blood alone passed).
3. Endoscopic subscore, scored from 0 (normal or inactive disease) to 3 (severe disease, spontaneous bleeding, ulceration).

The overall Adapted Mayo score ranges from 0 to 9 where higher scores represent more severe disease.

For Substudy 3, clinical remission is defined as SFS ≤ 1 and not greater than Baseline, RBS of 0, and endoscopic subscore ≤ 1. In addition, evidence of friability during endoscopy in participants with otherwise "mild" endoscopic activity conferred an endoscopic subscore of 2.

End point type	Secondary

End point timeframe:

At Week 52

End point values	SS3: Placebo	SS3: UPA 15 mg	SS3: UPA 30 mg	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	54[174]	47[175]	58[176]	
Units: percentage of participants				
number (confidence interval 95%)	22.2 (11.1 to 33.3)	59.2 (45.1 to 73.4)	69.7 (57.7 to 81.8)	

Notes:

[174] - SS3 ITT_A:1st 451 Upa 45 mg 8-wk responders; 52-wk tx Cohort 1, NRI with MI due to COVID-19- NRI-C

[175] - SS3 ITT_A:1st 451 Upa 45 mg 8-wk responders; 52-wk tx Cohort 1, NRI with MI due to COVID-19- NRI-C

[176] - SS3 ITT_A:1st 451 Upa 45 mg 8-wk responders; 52-wk tx Cohort 1, NRI with MI due to COVID-19- NRI-C

Statistical analyses

Statistical analysis title	Substudy 3: Upadacitinib 15 mg vs Placebo
Comparison groups	SS3: Placebo v SS3: UPA 15 mg
Number of subjects included in analysis	101
Analysis specification	Pre-specified
Analysis type	superiority[177]
P-value	< 0.001 [178]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted risk difference (%)
Point estimate	37.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	20.3
upper limit	54.6

Notes:

[177] - The primary and ranked secondary efficacy endpoints were tested with graphical multiplicity adjustment to ensure a strong control of family-wise type I error rate at significance level α= 0.05 (2-sided).

[178] - Stratified by Bio-IR (Bio-IR/Non-Bio-IR) at Induction Study Baseline; clinical remission at Week 0 (yes/no); corticosteroid use at Week 0 (yes/no)

Statistical analysis title	Substudy 3: Upadacitinib 30 mg vs Placebo
Comparison groups	SS3: Placebo v SS3: UPA 30 mg

Number of subjects included in analysis	112
Analysis specification	Pre-specified
Analysis type	superiority[179]
P-value	< 0.001 [180]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted risk difference (%)
Point estimate	47
Confidence interval	
level	95 %
sides	2-sided
lower limit	30.7
upper limit	63.3

Notes:

[179] - The primary and ranked secondary efficacy endpoints were tested with graphical multiplicity adjustment to ensure a strong control of family-wise type I error rate at significance level α= 0.05 (2-sided).

[180] - Stratified by Bio-IR (Bio-IR/Non-Bio-IR) at Induction Study Baseline; clinical remission at Week 0 (yes/no); corticosteroid use at Week 0 (yes/no)

Secondary: Substudy 3: Percentage of Participants Who Achieved Clinical Remission Per Adapted Mayo Score at Wk 52 and Were Corticosteroid Free for ≥ 90 Days Immediately Preceding Wk 52 Among Those Who Achieved Clinical Remission at the End of the Induction Treatment

End point title	Substudy 3: Percentage of Participants Who Achieved Clinical Remission Per Adapted Mayo Score at Wk 52 and Were Corticosteroid Free for ≥ 90 Days Immediately Preceding Wk 52 Among Those Who Achieved Clinical Remission at the End of the Induction Treatment

End point description:

The Adapted Mayo Score is a composite score of UC disease activity based on the following 3 subscores:
1. Stool frequency subscore (SFS), scored from 0 (normal number of stools) to 3 (5 or more stools more than normal).
2. Rectal bleeding subscore (RBS), scored from 0 (no blood seen) to 3 (blood alone passed).
3. Endoscopic subscore, scored from 0 (normal or inactive disease) to 3 (severe disease, spontaneous bleeding, ulceration).

The overall Adapted Mayo score ranges from 0 to 9 where higher scores represent more severe disease.

For Substudy 3, clinical remission is defined as SFS ≤ 1 and not greater than Baseline, RBS of 0, and endoscopic subscore ≤ 1. In addition, evidence of friability during endoscopy in participants with otherwise "mild" endoscopic activity conferred an endoscopic subscore of 2.

End point type	Secondary

End point timeframe:

At Week 52

End point values	SS3: Placebo	SS3: UPA 15 mg	SS3: UPA 30 mg	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	54[181]	47[182]	58[183]	
Units: percentage of participants				
number (confidence interval 95%)	22.2 (11.1 to 33.3)	57.1 (42.9 to 71.3)	68.0 (55.8 to 80.2)	

Notes:

[181] - SS3 ITT_A:1st 451 Upa 45 mg 8-wk responders; 52-wk tx Cohort 1, NRI with MI due to COVID-19- NRI-C
[182] - SS3 ITT_A:1st 451 Upa 45 mg 8-wk responders; 52-wk tx Cohort 1, NRI with MI due to COVID-19- NRI-C
[183] - SS3 ITT_A:1st 451 Upa 45 mg 8-wk responders; 52-wk tx Cohort 1, NRI with MI due to COVID-19- NRI-C

Statistical analyses

Statistical analysis title	Substudy 3: Upadacitinib 15 mg vs Placebo
Comparison groups	SS3: Placebo v SS3: UPA 15 mg
Number of subjects included in analysis	101
Analysis specification	Pre-specified
Analysis type	superiority[184]
P-value	< 0.001 [185]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted risk difference (%)
Point estimate	35.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	18.2
upper limit	52.7

Notes:

[184] - The primary and ranked secondary efficacy endpoints were tested with graphical multiplicity adjustment to ensure a strong control of family-wise type I error rate at significance level α= 0.05 (2-sided).

[185] - Stratified by Bio-IR (Bio-IR/Non-Bio-IR) at Induction Study Baseline; clinical remission at Week 0 (yes/no); corticosteroid use at Week 0 (yes/no)

Statistical analysis title	Substudy 3: Upadacitinib 30 mg vs Placebo
Comparison groups	SS3: Placebo v SS3: UPA 30 mg
Number of subjects included in analysis	112
Analysis specification	Pre-specified
Analysis type	superiority[186]
P-value	< 0.001 [187]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted risk difference (%)
Point estimate	45.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	28.7
upper limit	61.6

Notes:

[186] - The primary and ranked secondary efficacy endpoints were tested with graphical multiplicity adjustment to ensure a strong control of family-wise type I error rate at significance level α= 0.05 (2-sided).

[187] - Stratified by Bio-IR (Bio-IR/Non-Bio-IR) at Induction Study Baseline; clinical remission at Week 0 (yes/no); corticosteroid use at Week 0 (yes/no)

Secondary: Substudy 3: Percentage of Participants With Endoscopic Improvement at

Wk 52 Among Those Who Achieved Endoscopic Improvement at the End of the Induction Treatment

End point title	Substudy 3: Percentage of Participants With Endoscopic Improvement at Wk 52 Among Those Who Achieved Endoscopic Improvement at the End of the Induction Treatment

End point description:

Endoscopic improvement is defined as an endoscopic subscore of 0 or 1. Endoscopies were assessed by a blinded central reader and scored according to the following scale: 0 = Normal or inactive disease; 1 = Mild disease (erythema, decreased vascular pattern); 2 = Moderate disease (marked erythema, lack of vascular pattern, any friability, erosions); 3 = Severe disease (spontaneous bleeding, ulceration).

End point type	Secondary

End point timeframe:

At Week 52

End point values	SS3: Placebo	SS3: UPA 15 mg	SS3: UPA 30 mg	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	73[188]	63[189]	79[190]	
Units: percentage of participants				
number (confidence interval 95%)	19.2 (9.9 to 28.4)	61.6 (49.6 to 73.7)	69.5 (59.1 to 80.0)	

Notes:

[188] - SS3 ITT_A:1st 451 Upa 45 mg 8-wk responders; 52-wk tx Cohort 1, NRI with MI due to COVID-19- NRI-C

[189] - SS3 ITT_A:1st 451 Upa 45 mg 8-wk responders; 52-wk tx Cohort 1, NRI with MI due to COVID-19- NRI-C

[190] - SS3 ITT_A:1st 451 Upa 45 mg 8-wk responders; 52-wk tx Cohort 1, NRI with MI due to COVID-19- NRI-C

Statistical analyses

Statistical analysis title	Substudy 3: Upadacitinib 15 mg vs Placebo
Comparison groups	SS3: Placebo v SS3: UPA 15 mg
Number of subjects included in analysis	136
Analysis specification	Pre-specified
Analysis type	superiority[191]
P-value	< 0.001 [192]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted risk difference (%)
Point estimate	42
Confidence interval	
level	95 %
sides	2-sided
lower limit	27.8
upper limit	56.2

Notes:

[191] - The primary and ranked secondary efficacy endpoints were tested with graphical multiplicity adjustment to ensure a strong control of family-wise type I error rate at significance level α= 0.05 (2-sided).

[192] - Stratified by Bio-IR (Bio-IR/Non-Bio-IR) at Induction Study Baseline; clinical remission at Week 0 (yes/no); corticosteroid use at Week 0 (yes/no)

Statistical analysis title	Substudy 3: Upadacitinib 30 mg vs Placebo
Comparison groups	SS3: Placebo v SS3: UPA 30 mg
Number of subjects included in analysis	152
Analysis specification	Pre-specified
Analysis type	superiority[193]
P-value	< 0.001 [194]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted risk difference (%)
Point estimate	48.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	35.5
upper limit	61.7

Notes:

[193] - The primary and ranked secondary efficacy endpoints were tested with graphical multiplicity adjustment to ensure a strong control of family-wise type I error rate at significance level α= 0.05 (2-sided).
[194] - Stratified by Bio-IR (Bio-IR/Non-Bio-IR) at Induction Study Baseline; clinical remission at Week 0 (yes/no); corticosteroid use at Week 0 (yes/no)

Secondary: Substudy 3: Percentage Of Participants With Endoscopic Remission At Week 52

End point title	Substudy 3: Percentage Of Participants With Endoscopic Remission At Week 52

End point description:

Endoscopic remission is defined as an endoscopic subscore of 0. Endoscopies were assessed by a blinded central reader and scored according to the following scale: 0 = Normal or inactive disease; 1 = Mild disease (erythema, decreased vascular pattern); 2 = Moderate disease (marked erythema, lack of vascular pattern, any friability, erosions); 3 = Severe disease (spontaneous bleeding, ulceration).

End point type	Secondary

End point timeframe:

At Week 52

End point values	SS3: Placebo	SS3: UPA 15 mg	SS3: UPA 30 mg	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	149[195]	148	154[196]	
Units: percentage of participants				
number (confidence interval 95%)	5.6 (1.8 to 9.3)	24.2 (17.3 to 31.2)	25.9 (18.8 to 33.0)	

Notes:

[195] - SS3 ITT_A:1st 451 Upa 45 mg 8-wk responders; 52-wk tx Cohort 1, NRI with MI due to COVID-19- NRI-C
[196] - SS3 ITT_A:1st 451 Upa 45 mg 8-wk responders; 52-wk tx Cohort 1, NRI with MI due to COVID-19- NRI-C

Statistical analyses

Statistical analysis title	Substudy 3: Upadacitinib 15 mg vs Placebo
Comparison groups	SS3: Placebo v SS3: UPA 15 mg
Number of subjects included in analysis	297
Analysis specification	Pre-specified
Analysis type	superiority[197]
P-value	< 0.001 [198]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted risk difference (%)
Point estimate	18.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	11
upper limit	26.4

Notes:

[197] - The primary and ranked secondary efficacy endpoints were tested with graphical multiplicity adjustment to ensure a strong control of family-wise type I error rate at significance level α= 0.05 (2-sided).

[198] - Stratified by Bio-IR (Bio-IR/Non-Bio-IR) at Induction Study Baseline; clinical remission at Week 0 (yes/no); corticosteroid use at Week 0 (yes/no)

Statistical analysis title	Substudy 3: Upadacitinib 30 mg vs Placebo
Comparison groups	SS3: Placebo v SS3: UPA 30 mg
Number of subjects included in analysis	303
Analysis specification	Pre-specified
Analysis type	superiority[199]
P-value	< 0.001 [200]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted risk difference (%)
Point estimate	19.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	11.7
upper limit	27.2

Notes:

[199] - The primary and ranked secondary efficacy endpoints were tested with graphical multiplicity adjustment to ensure a strong control of family-wise type I error rate at significance level α= 0.05 (2-sided).

[200] - Stratified by Bio-IR (Bio-IR/Non-Bio-IR) at Induction Study Baseline; clinical remission at Week 0 (yes/no); corticosteroid use at Week 0 (yes/no)

Secondary: Substudy 3: Percentage Of Participants Who Maintained Clinical Response Per Adapted Mayo Score at Wk 52 Among Those Who Achieved Clinical Response at the End of the Induction Treatment

End point title	Substudy 3: Percentage Of Participants Who Maintained Clinical Response Per Adapted Mayo Score at Wk 52 Among Those Who Achieved Clinical Response at the End of the Induction Treatment

End point description:

The Adapted Mayo Score is a composite score of UC disease activity based on the following 3 subscores:

1. Stool frequency subscore (SFS), scored from 0 (normal number of stools) to 3 (5 or more stools more than normal).
2. Rectal bleeding subscore (RBS), scored from 0 (no blood seen) to 3 (blood alone passed).
3. Endoscopic subscore, scored from 0 (normal or inactive disease) to 3 (severe disease, spontaneous bleeding, ulceration).

The overall Adapted Mayo score ranges from 0 to 9 where higher scores represent more severe disease. Clinical response is defined as a decrease from baseline in the Adapted Mayo score ≥ 2 points and ≥ 30% from baseline, and a decrease in RBS ≥ 1 or an absolute RBS ≤ 1).

End point type	Secondary

End point timeframe:

At Week 52

End point values	SS3: Placebo	SS3: UPA 15 mg	SS3: UPA 30 mg	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	134[201]	135[202]	144[203]	
Units: percentage of participants				
number (confidence interval 95%)	18.8 (12.1 to 25.5)	63.0 (54.8 to 71.1)	76.6 (69.6 to 83.6)	

Notes:

[201] - SS3 ITT_A:1st 451 Upa 45 mg 8-wk responders; 52-wk tx Cohort 1, NRI with MI due to COVID-19- NRI-C

[202] - SS3 ITT_A:1st 451 Upa 45 mg 8-wk responders; 52-wk tx Cohort 1, NRI with MI due to COVID-19- NRI-C

[203] - SS3 ITT_A:1st 451 Upa 45 mg 8-wk responders; 52-wk tx Cohort 1, NRI with MI due to COVID-19- NRI-C

Statistical analyses

Statistical analysis title	Substudy 3: Upadacitinib 15 mg vs Placebo
Comparison groups	SS3: Placebo v SS3: UPA 15 mg
Number of subjects included in analysis	269
Analysis specification	Pre-specified
Analysis type	superiority[204]
P-value	< 0.001 [205]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted risk difference (%)
Point estimate	44.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	34.5
upper limit	54.7

Notes:

[204] - The primary and ranked secondary efficacy endpoints were tested with graphical multiplicity adjustment to ensure a strong control of family-wise type I error rate at significance level α= 0.05 (2-sided).

[205] - Stratified by Bio-IR (Bio-IR/Non-Bio-IR) at Induction Study Baseline; clinical remission at Week 0 (yes/no); corticosteroid use at Week 0 (yes/no)

Statistical analysis title	Substudy 3: Upadacitinib 30 mg vs Placebo
Comparison groups	SS3: Placebo v SS3: UPA 30 mg
Number of subjects included in analysis	278
Analysis specification	Pre-specified
Analysis type	superiority[206]
P-value	< 0.001 [207]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted risk difference (%)
Point estimate	56.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	47.2
upper limit	66

Notes:

[206] - The primary and ranked secondary efficacy endpoints were tested with graphical multiplicity adjustment to ensure a strong control of family-wise type I error rate at significance level α= 0.05 (2-sided).

[207] - Stratified by Bio-IR (Bio-IR/Non-Bio-IR) at Induction Study Baseline; clinical remission at Week 0 (yes/no); corticosteroid use at Week 0 (yes/no)

Secondary: Substudy 3: Percentage Of Participants Who Achieved Histologic-Endoscopic Mucosal Improvement at Week 52

End point title	Substudy 3: Percentage Of Participants Who Achieved Histologic-Endoscopic Mucosal Improvement at Week 52

End point description:

Histologic-endoscopic mucosal improvement is defined as an endoscopic subscore of 0 or 1 and a Geboes score ≤ 3.1.

The endoscopic subscore ranges from 0 (normal or inactive disease) to 3 (severe disease with spontaneous bleeding, ulceration).

The Geboes histologic index includes seven histological features (architectural change, chronic inflammatory infiltrate, lamina propria neutrophils and eosinophils, neutrophils in epithelium, crypt destruction and erosion or ulcers). The Geboes score has 6 grades, each with 3-5 subgrades: Grade 0, structural change only; Grade 1, chronic inflammation; Grade 2, lamina propria neutrophils and eosinophils; Grade 3, neutrophils in epithelium; Grade 4, crypt destruction; and Grade 5, erosions or ulceration.

End point type	Secondary

End point timeframe:

At Week 52

End point values	SS3: Placebo	SS3: UPA 15 mg	SS3: UPA 30 mg	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	149[208]	148[209]	154[210]	
Units: percentage of participants				
number (confidence interval 95%)	11.9 (6.7 to 17.2)	35.0 (27.1 to 42.8)	49.8 (41.5 to 58.0)	

Notes:

[208] - SS3 ITT_A:1st 451 Upa 45 mg 8-wk responders; 52-wk tx Cohort 1, NRI with MI due to COVID-19- NRI-C

[209] - SS3 ITT_A:1st 451 Upa 45 mg 8-wk responders; 52-wk tx Cohort 1, NRI with MI due to COVID-19- NRI-C

[210] - SS3 ITT_A:1st 451 Upa 45 mg 8-wk responders; 52-wk tx Cohort 1, NRI with MI due to COVID-19- NRI-C

Statistical analyses

Statistical analysis title	Substudy 3: Upadacitinib 15 mg vs Placebo
Comparison groups	SS3: Placebo v SS3: UPA 15 mg
Number of subjects included in analysis	297
Analysis specification	Pre-specified
Analysis type	superiority[211]
P-value	< 0.001 [212]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted risk difference (%)
Point estimate	23.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	14.8
upper limit	32.8

Notes:

[211] - The primary and ranked secondary efficacy endpoints were tested with graphical multiplicity adjustment to ensure a strong control of family-wise type I error rate at significance level α= 0.05 (2-sided).

[212] - Stratified by Bio-IR (Bio-IR/Non-Bio-IR) at Induction Study Baseline; clinical remission at Week 0 (yes/no); corticosteroid use at Week 0 (yes/no)

Statistical analysis title	Substudy 3: Upadacitinib 30 mg vs Placebo
Comparison groups	SS3: Placebo v SS3: UPA 30 mg
Number of subjects included in analysis	303
Analysis specification	Pre-specified
Analysis type	superiority[213]
P-value	< 0.001 [214]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted risk difference (%)
Point estimate	37.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	27.8
upper limit	46.8

Notes:

[213] - The primary and ranked secondary efficacy endpoints were tested with graphical multiplicity adjustment to ensure a strong control of family-wise type I error rate at significance level α= 0.05 (2-sided).

[214] - Stratified by Bio-IR (Bio-IR/Non-Bio-IR) at Induction Study Baseline; clinical remission at Week 0 (yes/no); corticosteroid use at Week 0 (yes/no)

Secondary: Substudy 3: Change From Baseline in Inflammatory Bowel Disease Questionnaire (IBDQ) Total Score at Week 52

End point title	Substudy 3: Change From Baseline in Inflammatory Bowel Disease Questionnaire (IBDQ) Total Score at Week 52

End point description:

The Inflammatory Bowel Disease Questionnaire (IBDQ) is used to assess health-related quality of life (HRQoL) in patients with ulcerative colitis. It consists of 32 questions evaluating bowel and systemic symptoms, as well as emotional and social functions. Each question is answered on a scale from 1 (worst) to 7 (best). The total score ranges from 32 to 224 with higher scores indicating better health-related quality of life. A positive change from Baseline indicates improvement.

End point type	Secondary

End point timeframe:

Baseline (Week 0), Week 52

End point values	SS3: Placebo	SS3: UPA 15 mg	SS3: UPA 30 mg	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	149[215]	148[216]	154[217]	
Units: units on a scale				
least squares mean (confidence interval 95%)	17.9 (10.79 to 25.00)	49.2 (42.59 to 55.89)	58.9 (52.14 to 65.59)	

Notes:

[215] - SS3 ITT_A w/ available data; Baseline= last non-missing value prior to 1st induction dose; RTB-MI

[216] - SS3 ITT_A w/ available data; Baseline= last non-missing value prior to 1st induction dose; RTB-MI

[217] - SS3 ITT_A w/ available data; Baseline= last non-missing value prior to 1st induction dose; RTB-MI

Statistical analyses

Statistical analysis title	Substudy 3: Upadacitinib 15 mg vs Placebo
Comparison groups	SS3: Placebo v SS3: UPA 15 mg
Number of subjects included in analysis	297
Analysis specification	Pre-specified
Analysis type	superiority[218]
P-value	< 0.001 [219]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	31.3

Confidence interval	
level	95 %
sides	2-sided
lower limit	21.98
upper limit	40.7
Variability estimate	Standard error of the mean
Dispersion value	4.77

Notes:

[218] - The primary and ranked secondary efficacy endpoints were tested with graphical multiplicity adjustment to ensure a strong control of family-wise type I error rate at significance level α= 0.05 (2-sided).

[219] - Stratified by corticosteroid use at Week 0 (yes/no); clinical remission status at Week 0 (yes/no); Bio-IR status at Baseline (Bio-IR or Non-Bio-IR)

Statistical analysis title	Substudy 3: Upadacitinib 30 mg vs Placebo
Comparison groups	SS3: Placebo v SS3: UPA 30 mg
Number of subjects included in analysis	303
Analysis specification	Pre-specified
Analysis type	superiority[220]
P-value	< 0.001 [221]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	41
Confidence interval	
level	95 %
sides	2-sided
lower limit	31.39
upper limit	50.55
Variability estimate	Standard error of the mean
Dispersion value	4.88

Notes:

[220] - The primary and ranked secondary efficacy endpoints were tested with graphical multiplicity adjustment to ensure a strong control of family-wise type I error rate at significance level α= 0.05 (2-sided).

[221] - Stratified by corticosteroid use at Week 0 (yes/no); clinical remission status at Week 0 (yes/no); Bio-IR status at Baseline (Bio-IR or Non-Bio-IR)

Secondary: Substudy 3: Percentage Of Participants With Mucosal Healing at Week 52

End point title	Substudy 3: Percentage Of Participants With Mucosal Healing at Week 52

End point description:

Mucosal healing is defined as an endoscopic score of 0 and Geboes score < 2.0. The endoscopic subscore ranges from 0 (normal or inactive disease) to 3 (severe disease with spontaneous bleeding, ulceration).

The Geboes histologic index includes seven histological features (architectural change, chronic inflammatory infiltrate, lamina propria neutrophils and eosinophils, neutrophils in epithelium, crypt destruction and erosion or ulcers). The Geboes score has 6 grades, each with 3-5 subgrades: Grade 0, structural change only; Grade 1, chronic inflammation; Grade 2, lamina propria neutrophils and eosinophils; Grade 3, neutrophils in epithelium; Grade 4, crypt destruction; and Grade 5, erosions or ulceration.

End point type	Secondary

End point timeframe:

At Week 52

End point values	SS3: Placebo	SS3: UPA 15 mg	SS3: UPA 30 mg	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	149[222]	148[223]	154[224]	
Units: percentage of participants				
number (confidence interval 95%)	4.7 (1.3 to 8.2)	17.6 (11.4 to 23.8)	19.0 (12.6 to 25.4)	

Notes:

[222] - SS3 ITT_A:1st 451 Upa 45 mg 8-wk responders; 52-wk tx Cohort 1, NRI with MI due to COVID-19- NRI-C

[223] - SS3 ITT_A:1st 451 Upa 45 mg 8-wk responders; 52-wk tx Cohort 1, NRI with MI due to COVID-19- NRI-C

[224] - SS3 ITT_A:1st 451 Upa 45 mg 8-wk responders; 52-wk tx Cohort 1, NRI with MI due to COVID-19- NRI-C

Statistical analyses

Statistical analysis title	Substudy 3: Upadacitinib 15 mg vs Placebo
Comparison groups	SS3: Placebo v SS3: UPA 15 mg
Number of subjects included in analysis	297
Analysis specification	Pre-specified
Analysis type	superiority[225]
P-value	< 0.001 [226]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted risk difference (%)
Point estimate	13
Confidence interval	
level	95 %
sides	2-sided
lower limit	6
upper limit	20

Notes:

[225] - The primary and ranked secondary efficacy endpoints were tested with graphical multiplicity adjustment to ensure a strong control of family-wise type I error rate at significance level α= 0.05 (2-sided).

[226] - Stratified by Bio-IR (Bio-IR/Non-Bio-IR) at Induction Study Baseline; clinical remission at Week 0 (yes/no); corticosteroid use at Week 0 (yes/no)

Statistical analysis title	Substudy 3: Upadacitinib 30 mg vs Placebo
Comparison groups	SS3: Placebo v SS3: UPA 30 mg
Number of subjects included in analysis	303
Analysis specification	Pre-specified
Analysis type	superiority[227]
P-value	< 0.001 [228]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted risk difference (%)
Point estimate	13.6

Confidence interval	
level	95 %
sides	2-sided
lower limit	6.6
upper limit	20.6

Notes:

[227] - The primary and ranked secondary efficacy endpoints were tested with graphical multiplicity adjustment to ensure a strong control of family-wise type I error rate at significance level α= 0.05 (2-sided).

[228] - Stratified by Bio-IR (Bio-IR/Non-Bio-IR) at Induction Study Baseline; clinical remission at Week 0 (yes/no); corticosteroid use at Week 0 (yes/no)

Secondary: Substudy 3: Percentage Of Participants Who Reported No Bowel Urgency at Week 52

End point title	Substudy 3: Percentage Of Participants Who Reported No Bowel Urgency at Week 52

End point description:

Bowel urgency was assessed by participants in a subject diary completed once a day.

End point type	Secondary

End point timeframe:

At Week 52

End point values	SS3: Placebo	SS3: UPA 15 mg	SS3: UPA 30 mg	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	149[229]	148[230]	154[231]	
Units: percentage of participants				
number (confidence interval 95%)	17.4 (11.4 to 23.5)	56.1 (48.1 to 64.1)	63.6 (56.0 to 71.2)	

Notes:

[229] - SS3 ITT_A:1st 451 Upa 45 mg 8-wk responders; 52-wk tx Cohort 1, NRI with MI due to COVID-19- NRI-C

[230] - SS3 ITT_A:1st 451 Upa 45 mg 8-wk responders; 52-wk tx Cohort 1, NRI with MI due to COVID-19- NRI-C

[231] - SS3 ITT_A:1st 451 Upa 45 mg 8-wk responders; 52-wk tx Cohort 1, NRI with MI due to COVID-19- NRI-C

Statistical analyses

Statistical analysis title	Substudy 3: Upadacitinib 15 mg vs Placebo
Comparison groups	SS3: Placebo v SS3: UPA 15 mg
Number of subjects included in analysis	297
Analysis specification	Pre-specified
Analysis type	superiority[232]
P-value	< 0.001 [233]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted risk difference (%)
Point estimate	38.7

Confidence interval	
level	95 %
sides	2-sided
lower limit	28.9
upper limit	48.5

Notes:

[232] - The primary and ranked secondary efficacy endpoints were tested with graphical multiplicity adjustment to ensure a strong control of family-wise type I error rate at significance level α= 0.05 (2-sided).

[233] - Stratified by Bio-IR (Bio-IR/Non-Bio-IR) at Induction Study Baseline; clinical remission at Week 0 (yes/no); corticosteroid use at Week 0 (yes/no)

Statistical analysis title	Substudy 3: Upadacitinib 30 mg vs Placebo
Comparison groups	SS3: Placebo v SS3: UPA 30 mg
Number of subjects included in analysis	303
Analysis specification	Pre-specified
Analysis type	superiority[234]
P-value	< 0.001 [235]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted risk difference (%)
Point estimate	45.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	35.5
upper limit	54.8

Notes:

[234] - The primary and ranked secondary efficacy endpoints were tested with graphical multiplicity adjustment to ensure a strong control of family-wise type I error rate at significance level α= 0.05 (2-sided).

[235] - Stratified by Bio-IR (Bio-IR/Non-Bio-IR) at Induction Study Baseline; clinical remission at Week 0 (yes/no); corticosteroid use at Week 0 (yes/no)

Secondary: Substudy 3: Percentage Of Participants Who Reported No Abdominal Pain at Week 52

End point title	Substudy 3: Percentage Of Participants Who Reported No Abdominal Pain at Week 52

End point description:

Abdominal pain was assessed by participants in a subject diary completed once a day.

End point type	Secondary

End point timeframe:

At Week 52

End point values	SS3: Placebo	SS3: UPA 15 mg	SS3: UPA 30 mg	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	149[236]	148[237]	154[238]	
Units: percentage of participants				
number (confidence interval 95%)	20.8 (14.2 to 27.3)	45.9 (37.9 to 54.0)	55.3 (47.4 to 63.2)	

Notes:

[236] - SS3 ITT_A:1st 451 Upa 45 mg 8-wk responders; 52-wk tx Cohort 1, NRI with MI due to COVID-19- NRI-C

[237] - SS3 ITT_A:1st 451 Upa 45 mg 8-wk responders; 52-wk tx Cohort 1, NRI with MI due to COVID-19- NRI-C

[238] - SS3 ITT_A:1st 451 Upa 45 mg 8-wk responders; 52-wk tx Cohort 1, NRI with MI due to COVID-19- NRI-C

Statistical analyses

Statistical analysis title	Substudy 3: Upadacitinib 15 mg vs Placebo
Comparison groups	SS3: Placebo v SS3: UPA 15 mg
Number of subjects included in analysis	297
Analysis specification	Pre-specified
Analysis type	superiority[239]
P-value	< 0.001 [240]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted risk difference (%)
Point estimate	24.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	14.2
upper limit	34.5

Notes:

[239] - The primary and ranked secondary efficacy endpoints were tested with graphical multiplicity adjustment to ensure a strong control of family-wise type I error rate at significance level α= 0.05 (2-sided).

[240] - Stratified by Bio-IR (Bio-IR/Non-Bio-IR) at Induction Study Baseline; clinical remission at Week 0 (yes/no); corticosteroid use at Week 0 (yes/no)

Statistical analysis title	Substudy 3: Upadacitinib 30 mg vs Placebo
Comparison groups	SS3: Placebo v SS3: UPA 30 mg
Number of subjects included in analysis	303
Analysis specification	Pre-specified
Analysis type	superiority[241]
P-value	< 0.001 [242]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Adjusted risk difference (%)
Point estimate	33.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	23.6
upper limit	43.9

Notes:

[241] - The primary and ranked secondary efficacy endpoints were tested with graphical multiplicity adjustment to ensure a strong control of family-wise type I error rate at significance level α= 0.05 (2-sided).

[242] - Stratified by Bio-IR (Bio-IR/Non-Bio-IR) at Induction Study Baseline; clinical remission at Week 0 (yes/no); corticosteroid use at Week 0 (yes/no)

Secondary: Substudy 3: Change From Baseline in Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F) Score at Week 52

End point title	Substudy 3: Change From Baseline in Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F) Score at Week 52

End point description:

The FACIT fatigue questionnaire was developed to assess fatigue associated with anemia. It consists of 13 fatigue-related questions. Each question is answered on a 5-point Likert scale: 0 (not at all); 1 (a little bit); 2 (somewhat); 3 (quite a bit); and 4 (very much). The total score ranges from 0 to 52, where higher scores represent less fatigue, and a positive change from Baseline indicates improvement.

End point type	Secondary

End point timeframe:

Baseline (Week 0), Week 52

End point values	SS3: Placebo	SS3: UPA 15 mg	SS3: UPA 30 mg	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	149[243]	148[244]	154[245]	
Units: units on a scale				
least squares mean (confidence interval 95%)	3.7 (1.88 to 5.43)	8.7 (7.01 to 10.49)	9.5 (7.80 to 11.22)	

Notes:

[243] - SS3 ITT_A w/ available data; Baseline= last non-missing value prior to 1st induction dose; RTB-MI

[244] - SS3 ITT_A w/ available data; Baseline= last non-missing value prior to 1st induction dose; RTB-MI

[245] - SS3 ITT_A w/ available data; Baseline= last non-missing value prior to 1st induction dose; RTB-MI

Statistical analyses

Statistical analysis title	Substudy 3: Upadacitinib 15 mg vs Placebo
Comparison groups	SS3: Placebo v SS3: UPA 15 mg
Number of subjects included in analysis	297
Analysis specification	Pre-specified
Analysis type	superiority[246]
P-value	< 0.001 [247]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	5.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.67
upper limit	7.52

Notes:

[246] - The primary and ranked secondary efficacy endpoints were tested with graphical multiplicity adjustment to ensure a strong control of family-wise type I error rate at significance level α= 0.05 (2-sided).

[247] - Stratified by corticosteroid use at Week 0 (yes/no); clinical remission status at Week 0 (yes/no); Bio-IR status at Baseline (Bio-IR or Non-Bio-IR)

Statistical analysis title	Substudy 3: Upadacitinib 30 mg vs Placebo
Comparison groups	SS3: Placebo v SS3: UPA 30 mg
Number of subjects included in analysis	303
Analysis specification	Pre-specified
Analysis type	superiority[248]
P-value	< 0.001 [249]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	5.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	3.44
upper limit	8.27

Notes:

[248] - The primary and ranked secondary efficacy endpoints were tested with graphical multiplicity adjustment to ensure a strong control of family-wise type I error rate at significance level α= 0.05 (2-sided).

[249] - Stratified by corticosteroid use at Week 0 (yes/no); clinical remission status at Week 0 (yes/no); Bio-IR status at Baseline (Bio-IR or Non-Bio-IR)

Adverse events information

Timeframe for reporting adverse events:

All-cause mortality from enrollment to study end: median follow-up was ≤ 57, 61, and 364 days (SS 1, 2, and 3). TEAEs/SAEs collected from 1st dose of study drug until 30 days after last dose; mean duration was ≤ 57, 56, and 364 days for SS 1, 2, and 3.

Adverse event reporting additional description:

For safety analyses, participants were assigned to a treatment group based on the treatment actually received, regardless of the treatment randomized. The "as treated" group was determined by the most frequent dose regimen received in the analysis period.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	23.0

Reporting groups

Reporting group title	SS1: Upadacitinib 7.5 mg

Reporting group description:

During the 8-week induction phase in Substudy 1, participants received 7.5 mg upadacitinib film-coated tablets once daily by mouth (QD) for 8 weeks.

Reporting group title	SS1: Placebo

Reporting group description:

During the 8-week induction phase in Substudy 1, participants received placebo for upadacitinib film-coated tablets once daily by mouth (QD) for 8 weeks.

Reporting group title	SS1: Upadacitinib 30 mg

Reporting group description:

During the 8-week induction phase in Substudy 1, participants received 30 mg upadacitinib film-coated tablets once daily by mouth (QD) for 8 weeks. Additional participants were enrolled during the Substudy 1 analysis period and received 30 mg upadacitinib film-coated tablets once daily by mouth (QD) for 4 weeks.

Reporting group title	SS1: Upadacitinib 15 mg

Reporting group description:

During the 8-week induction phase in Substudy 1, participants received 15 mg upadacitinib film-coated tablets once daily by mouth (QD) for 8 weeks.

Reporting group title	SS1: Upadacitinib 45 mg

Reporting group description:

During the 8-week induction phase in Substudy 1, participants received 45 mg upadacitinib film-coated tablets once daily by mouth (QD) for 8 weeks. Additional participants were enrolled during the Substudy 1 analysis period and received 45 mg upadacitinib film-coated tablets once daily by mouth (QD) for 4 weeks.

Reporting group title	SS2: Placebo

Reporting group description:

During the Substudy 2 Part 1 induction period, participants received placebo for upadacitinib film-coated tablets once daily by mouth (QD) for 8 weeks.

Reporting group title	SS3: Upadacitinib 15 mg

Reporting group description:

Participants who achieved clinical response in Substudy 1, Substudy 2, or Study M14-675 at either Week 8 or Week 16, while receiving upadacitinib 15, 30, or 45 mg QD and those who achieved clinical response while receiving upadacitinib 15 mg QD in Substudy 1 and were randomized to upadacitinib 15 mg QD in Substudy 3 for up to 52 weeks. In addition, participants who received upadacitinib 45 mg QD in Induction Phase and did not achieve clinical response and received upadacitinib 45 mg QD in Extended Treatment in Substudy 2 Part 2 or in Study M14-675 Part 2 and achieved clinical response at Week 16 and were randomized to upadacitinib 15 mg QD in Substudy 3.

Reporting group title	SS3: Placebo

Reporting group description:

Participants who achieved clinical response in Substudy 1, Substudy 2, or Study M14-675 at either Week 8 or Week 16, while receiving upadacitinib 15, 30, or 45 mg QD and those who achieved clinical response while receiving upadacitinib 15 mg QD in Substudy 1 and were randomized to placebo QD in Substudy 3 for up to 52 weeks. In addition, participants who received double-blind placebo QD treatment for 8 weeks during Substudy
1, Substudy 2 Part 1, or Study M14-675 Part 1 and achieved clinical response at Week 8 continued to receive blinded placebo QD in Substudy 3 for up to 52 weeks.

Reporting group title	SS2: Upadacitinib 45 mg/Upadacitinib 45 mg

Reporting group description:

During the Substudy 2 Part 1 induction period, participants received 45 mg upadacitinib film-coated tablets once daily by mouth (QD) for 8 weeks. Participants who did not achieve clinical response at Week 8 of Part 1 were enrolled in an open-label expended treatment period and received 45 mg upadacitinib film-coated tablets once daily by mouth (QD) for an additional 8 weeks.

Reporting group title	SS2: Upadacitinib 45 mg

Reporting group description:

During the Substudy 2 Part 1 induction period, participants received 45 mg upadacitinib film-coated tablets once daily by mouth (QD) for 8 weeks.

Reporting group title	SS2: Placebo/Upadacitinib 45 mg

Reporting group description:

During the Substudy 2 Part 1 induction period, participants received placebo for upadacitinib film-coated tablets once daily by mouth (QD) for 8 weeks. Participants who did not achieve clinical response at Week 8 of Part 1 were enrolled in an open-label extended treatment period and received 45 mg upadacitinib film-coated tablets once daily by mouth (QD) for an additional 8 weeks.

Reporting group title	SS3: Upadacitinib 30 mg

Reporting group description:

Participants who achieved clinical response in Substudy 1, Substudy 2, or Study M14-675 at either Week 8 or Week 16, while receiving upadacitinib 15, 30, or 45 mg QD and those who achieved clinical response while receiving upadacitinib 15 mg QD in Substudy 1 and were randomized to upadacitinib 30 mg QD in Substudy 3 for up to 52 weeks. In addition, participants who received upadacitinib 45 mg QD in Induction Phase and did not achieve clinical response and received upadacitinib 45 mg QD in Extended Treatment in Substudy 2 Part 2 or in Study M14-675 Part 2 and achieved clinical response at Week 16 and were randomized to upadacitinib 30 mg QD in Substudy 3.

Reporting group title	SS3: Upadacitinib 7.5 mg

Reporting group description:

Participants who received double-blinded treatment of upadacitinib 7.5 mg QD for 8 weeks during Substudy 1 and achieved clinical response at Week 8 continued to receive blinded treatment of upadacitinib 7.5 mg QD in Substudy 3 for up to 52 weeks.

Serious adverse events	SS1: Upadacitinib 7.5 mg	SS1: Placebo	SS1: Upadacitinib 30 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 47 (0.00%)	5 / 46 (10.87%)	5 / 117 (4.27%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
ADENOCARCINOMA OF COLON			
subjects affected / exposed	0 / 47 (0.00%)	0 / 46 (0.00%)	0 / 117 (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
BASAL CELL CARCINOMA			

subjects affected / exposed	0 / 47 (0.00%)	0 / 46 (0.00%)	0 / 117 (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
INVASIVE BREAST CARCINOMA			
subjects affected / exposed	0 / 47 (0.00%)	0 / 46 (0.00%)	0 / 117 (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
SEBORRHOEIC KERATOSIS			
subjects affected / exposed	0 / 47 (0.00%)	0 / 46 (0.00%)	0 / 117 (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 CELL CARCINOMA			
subjects affected / exposed	0 / 47 (0.00%)	0 / 46 (0.00%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
DEEP VEIN THROMBOSIS			
subjects affected / exposed	0 / 47 (0.00%)	0 / 46 (0.00%)	0 / 117 (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
HYPOTENSION			
subjects affected / exposed	0 / 47 (0.00%)	0 / 46 (0.00%)	0 / 117 (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
Surgical and medical procedures			
ABORTION INDUCED			
subjects affected / exposed	0 / 47 (0.00%)	0 / 46 (0.00%)	0 / 117 (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			
DEVICE INTOLERANCE			
subjects affected / exposed	0 / 47 (0.00%)	0 / 46 (0.00%)	0 / 117 (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

PYREXIA			
subjects affected / exposed	0 / 47 (0.00%)	0 / 46 (0.00%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
CERVICAL DYSPLASIA			
subjects affected / exposed	0 / 47 (0.00%)	0 / 46 (0.00%)	0 / 117 (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 / 47 (0.00%)	0 / 46 (0.00%)	0 / 117 (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
CHRONIC OBSTRUCTIVE PULMONARY DISEASE			
subjects affected / exposed	0 / 47 (0.00%)	0 / 46 (0.00%)	0 / 117 (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
INTERSTITIAL LUNG DISEASE			
subjects affected / exposed	0 / 47 (0.00%)	0 / 46 (0.00%)	0 / 117 (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
NONINFECTIVE BRONCHITIS			
subjects affected / exposed	0 / 47 (0.00%)	0 / 46 (0.00%)	0 / 117 (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
PULMONARY EMBOLISM			
subjects affected / exposed	0 / 47 (0.00%)	0 / 46 (0.00%)	0 / 117 (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			
ANXIETY			

subjects affected / exposed	0 / 47 (0.00%)	0 / 46 (0.00%)	0 / 117 (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 / 47 (0.00%)	0 / 46 (0.00%)	0 / 117 (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
MENTAL DISORDER			
subjects affected / exposed	0 / 47 (0.00%)	0 / 46 (0.00%)	0 / 117 (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
SUICIDAL IDEATION			
subjects affected / exposed	0 / 47 (0.00%)	0 / 46 (0.00%)	0 / 117 (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			
ASPARTATE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	0 / 47 (0.00%)	0 / 46 (0.00%)	0 / 117 (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			
HIP FRACTURE			
subjects affected / exposed	0 / 47 (0.00%)	0 / 46 (0.00%)	0 / 117 (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
PULMONARY CONTUSION			
subjects affected / exposed	0 / 47 (0.00%)	0 / 46 (0.00%)	0 / 117 (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
SKIN LACERATION			
subjects affected / exposed	0 / 47 (0.00%)	0 / 46 (0.00%)	0 / 117 (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

THORACIC VERTEBRAL FRACTURE			
subjects affected / exposed	0 / 47 (0.00%)	0 / 46 (0.00%)	0 / 117 (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 / 47 (0.00%)	0 / 46 (0.00%)	0 / 117 (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
ATRIAL FIBRILLATION			
subjects affected / exposed	0 / 47 (0.00%)	0 / 46 (0.00%)	0 / 117 (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			
CARPAL TUNNEL SYNDROME			
subjects affected / exposed	0 / 47 (0.00%)	0 / 46 (0.00%)	0 / 117 (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
CEREBROVASCULAR ACCIDENT			
subjects affected / exposed	0 / 47 (0.00%)	0 / 46 (0.00%)	0 / 117 (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
SUBARACHNOID HAEMORRHAGE			
subjects affected / exposed	0 / 47 (0.00%)	0 / 46 (0.00%)	0 / 117 (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 / 47 (0.00%)	0 / 46 (0.00%)	0 / 117 (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
IRON DEFICIENCY ANAEMIA			

subjects affected / exposed	0 / 47 (0.00%)	0 / 46 (0.00%)	0 / 117 (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
Eye disorders			
CATARACT			
subjects affected / exposed	0 / 47 (0.00%)	0 / 46 (0.00%)	0 / 117 (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 / 47 (0.00%)	0 / 46 (0.00%)	0 / 117 (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 / 47 (0.00%)	0 / 46 (0.00%)	0 / 117 (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
COLITIS			
subjects affected / exposed	0 / 47 (0.00%)	0 / 46 (0.00%)	0 / 117 (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
COLITIS ULCERATIVE			
subjects affected / exposed	0 / 47 (0.00%)	2 / 46 (4.35%)	4 / 117 (3.42%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COLON DYSPLASIA			
subjects affected / exposed	0 / 47 (0.00%)	0 / 46 (0.00%)	0 / 117 (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
DIAPHRAGMATIC HERNIA			
subjects affected / exposed	0 / 47 (0.00%)	0 / 46 (0.00%)	0 / 117 (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 / 47 (0.00%)	0 / 46 (0.00%)	1 / 117 (0.85%)
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 / 47 (0.00%)	0 / 46 (0.00%)	0 / 117 (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
PANCREATITIS			
subjects affected / exposed	0 / 47 (0.00%)	0 / 46 (0.00%)	0 / 117 (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
Hepatobiliary disorders			
HEPATITIS			
subjects affected / exposed	0 / 47 (0.00%)	0 / 46 (0.00%)	0 / 117 (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
LIVER DISORDER			
subjects affected / exposed	0 / 47 (0.00%)	0 / 46 (0.00%)	0 / 117 (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
Skin and subcutaneous tissue disorders			
ERYTHEMA NODOSUM			
subjects affected / exposed	0 / 47 (0.00%)	0 / 46 (0.00%)	0 / 117 (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
PANNICULITIS			
subjects affected / exposed	0 / 47 (0.00%)	0 / 46 (0.00%)	0 / 117 (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
SKIN ULCER			
subjects affected / exposed	0 / 47 (0.00%)	0 / 46 (0.00%)	0 / 117 (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			

CYSTITIS HAEMORRHAGIC			
subjects affected / exposed	0 / 47 (0.00%)	0 / 46 (0.00%)	1 / 117 (0.85%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
URINARY RETENTION			
subjects affected / exposed	0 / 47 (0.00%)	0 / 46 (0.00%)	0 / 117 (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			
ARTHRITIS			
subjects affected / exposed	0 / 47 (0.00%)	0 / 46 (0.00%)	0 / 117 (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
CHONDROMALACIA			
subjects affected / exposed	0 / 47 (0.00%)	0 / 46 (0.00%)	0 / 117 (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 / 47 (0.00%)	0 / 46 (0.00%)	0 / 117 (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
ACUTE ENDOCARDITIS			
subjects affected / exposed	0 / 47 (0.00%)	0 / 46 (0.00%)	0 / 117 (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 / 47 (0.00%)	0 / 46 (0.00%)	0 / 117 (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
APPENDICITIS			
subjects affected / exposed	0 / 47 (0.00%)	0 / 46 (0.00%)	0 / 117 (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

ARTHRITIS BACTERIAL			
subjects affected / exposed	0 / 47 (0.00%)	0 / 46 (0.00%)	0 / 117 (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
BREAST ABSCESS			
subjects affected / exposed	0 / 47 (0.00%)	0 / 46 (0.00%)	0 / 117 (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
BRONCHITIS			
subjects affected / exposed	0 / 47 (0.00%)	0 / 46 (0.00%)	0 / 117 (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
BURSITIS INFECTIVE			
subjects affected / exposed	0 / 47 (0.00%)	0 / 46 (0.00%)	0 / 117 (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 / 47 (0.00%)	1 / 46 (2.17%)	0 / 117 (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
CLOSTRIDIUM DIFFICILE INFECTION			
subjects affected / exposed	0 / 47 (0.00%)	0 / 46 (0.00%)	0 / 117 (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
COVID-19			
subjects affected / exposed	0 / 47 (0.00%)	0 / 46 (0.00%)	0 / 117 (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
COVID-19 PNEUMONIA			
subjects affected / exposed	0 / 47 (0.00%)	0 / 46 (0.00%)	0 / 117 (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
GASTROENTERITIS NOROVIRUS			

subjects affected / exposed	0 / 47 (0.00%)	0 / 46 (0.00%)	0 / 117 (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
HERPES ZOSTER			
subjects affected / exposed	0 / 47 (0.00%)	0 / 46 (0.00%)	0 / 117 (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
HERPES ZOSTER MENINGITIS			
subjects affected / exposed	0 / 47 (0.00%)	0 / 46 (0.00%)	0 / 117 (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
INFECTIOUS MONONUCLEOSIS			
subjects affected / exposed	0 / 47 (0.00%)	0 / 46 (0.00%)	0 / 117 (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 / 47 (0.00%)	0 / 46 (0.00%)	0 / 117 (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
LARGE INTESTINE INFECTION			
subjects affected / exposed	0 / 47 (0.00%)	0 / 46 (0.00%)	0 / 117 (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
MASTITIS			
subjects affected / exposed	0 / 47 (0.00%)	0 / 46 (0.00%)	0 / 117 (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
MUSCLE ABSCESS			
subjects affected / exposed	0 / 47 (0.00%)	0 / 46 (0.00%)	0 / 117 (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
PNEUMOCYSTIS JIROVECII PNEUMONIA			

subjects affected / exposed	0 / 47 (0.00%)	0 / 46 (0.00%)	0 / 117 (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			
subjects affected / exposed	0 / 47 (0.00%)	0 / 46 (0.00%)	0 / 117 (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 CRYPTOCOCCAL			
subjects affected / exposed	0 / 47 (0.00%)	0 / 46 (0.00%)	0 / 117 (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 PNEUMOCOCCAL			
subjects affected / exposed	0 / 47 (0.00%)	0 / 46 (0.00%)	0 / 117 (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
POST PROCEDURAL INFECTION			
subjects affected / exposed	0 / 47 (0.00%)	0 / 46 (0.00%)	0 / 117 (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 SYNCYTIAL VIRUS INFECTION			
subjects affected / exposed	0 / 47 (0.00%)	0 / 46 (0.00%)	0 / 117 (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 / 47 (0.00%)	0 / 46 (0.00%)	0 / 117 (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
SINUSITIS			
subjects affected / exposed	0 / 47 (0.00%)	1 / 46 (2.17%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
TONSILLITIS			

subjects affected / exposed	0 / 47 (0.00%)	0 / 46 (0.00%)	0 / 117 (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
UROSEPSIS			
subjects affected / exposed	0 / 47 (0.00%)	0 / 46 (0.00%)	0 / 117 (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
VIRAL INFECTION			
subjects affected / exposed	0 / 47 (0.00%)	0 / 46 (0.00%)	0 / 117 (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
VIRAL PHARYNGITIS			
subjects affected / exposed	0 / 47 (0.00%)	0 / 46 (0.00%)	0 / 117 (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			
HYPOALBUMINAEMIA			
subjects affected / exposed	0 / 47 (0.00%)	0 / 46 (0.00%)	0 / 117 (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
HYPOPHOSPHATAEMIA			
subjects affected / exposed	0 / 47 (0.00%)	1 / 46 (2.17%)	0 / 117 (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

Serious adverse events	SS1: Upadacitinib 15 mg	SS1: Upadacitinib 45 mg	SS2: Placebo
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 49 (4.08%)	6 / 123 (4.88%)	9 / 155 (5.81%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
ADENOCARCINOMA OF COLON			

subjects affected / exposed	0 / 49 (0.00%)	0 / 123 (0.00%)	0 / 155 (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
BASAL CELL CARCINOMA			
subjects affected / exposed	0 / 49 (0.00%)	0 / 123 (0.00%)	0 / 155 (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
INVASIVE BREAST CARCINOMA			
subjects affected / exposed	0 / 49 (0.00%)	0 / 123 (0.00%)	0 / 155 (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
SEBORRHOEIC KERATOSIS			
subjects affected / exposed	0 / 49 (0.00%)	0 / 123 (0.00%)	0 / 155 (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 CELL CARCINOMA			
subjects affected / exposed	0 / 49 (0.00%)	0 / 123 (0.00%)	0 / 155 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
DEEP VEIN THROMBOSIS			
subjects affected / exposed	0 / 49 (0.00%)	1 / 123 (0.81%)	0 / 155 (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
HYPOTENSION			
subjects affected / exposed	0 / 49 (0.00%)	0 / 123 (0.00%)	0 / 155 (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
Surgical and medical procedures			
ABORTION INDUCED			
subjects affected / exposed	0 / 49 (0.00%)	0 / 123 (0.00%)	0 / 155 (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			
DEVICE INTOLERANCE			
subjects affected / exposed	0 / 49 (0.00%)	0 / 123 (0.00%)	0 / 155 (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
PYREXIA			
subjects affected / exposed	0 / 49 (0.00%)	1 / 123 (0.81%)	0 / 155 (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
Reproductive system and breast disorders			
CERVICAL DYSPLASIA			
subjects affected / exposed	0 / 49 (0.00%)	0 / 123 (0.00%)	0 / 155 (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 / 49 (0.00%)	0 / 123 (0.00%)	0 / 155 (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
CHRONIC OBSTRUCTIVE PULMONARY DISEASE			
subjects affected / exposed	0 / 49 (0.00%)	0 / 123 (0.00%)	0 / 155 (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
INTERSTITIAL LUNG DISEASE			
subjects affected / exposed	0 / 49 (0.00%)	0 / 123 (0.00%)	0 / 155 (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
NONINFECTIVE BRONCHITIS			
subjects affected / exposed	0 / 49 (0.00%)	0 / 123 (0.00%)	0 / 155 (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
PULMONARY EMBOLISM			

subjects affected / exposed	0 / 49 (0.00%)	1 / 123 (0.81%)	0 / 155 (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
Psychiatric disorders			
ANXIETY			
subjects affected / exposed	0 / 49 (0.00%)	0 / 123 (0.00%)	0 / 155 (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 / 49 (0.00%)	0 / 123 (0.00%)	0 / 155 (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
MENTAL DISORDER			
subjects affected / exposed	0 / 49 (0.00%)	0 / 123 (0.00%)	0 / 155 (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
SUICIDAL IDEATION			
subjects affected / exposed	0 / 49 (0.00%)	0 / 123 (0.00%)	0 / 155 (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			
ASPARTATE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	0 / 49 (0.00%)	1 / 123 (0.81%)	0 / 155 (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
Injury, poisoning and procedural complications			
HIP FRACTURE			
subjects affected / exposed	0 / 49 (0.00%)	0 / 123 (0.00%)	0 / 155 (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
PULMONARY CONTUSION			

subjects affected / exposed	0 / 49 (0.00%)	0 / 123 (0.00%)	0 / 155 (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
SKIN LACERATION			
subjects affected / exposed	0 / 49 (0.00%)	0 / 123 (0.00%)	0 / 155 (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
THORACIC VERTEBRAL FRACTURE			
subjects affected / exposed	0 / 49 (0.00%)	0 / 123 (0.00%)	0 / 155 (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 / 49 (0.00%)	0 / 123 (0.00%)	0 / 155 (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
ATRIAL FIBRILLATION			
subjects affected / exposed	0 / 49 (0.00%)	0 / 123 (0.00%)	0 / 155 (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			
CARPAL TUNNEL SYNDROME			
subjects affected / exposed	0 / 49 (0.00%)	0 / 123 (0.00%)	0 / 155 (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
CEREBROVASCULAR ACCIDENT			
subjects affected / exposed	0 / 49 (0.00%)	0 / 123 (0.00%)	0 / 155 (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
SUBARACHNOID HAEMORRHAGE			
subjects affected / exposed	0 / 49 (0.00%)	0 / 123 (0.00%)	0 / 155 (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 / 49 (0.00%)	0 / 123 (0.00%)	0 / 155 (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
IRON DEFICIENCY ANAEMIA			
subjects affected / exposed	0 / 49 (0.00%)	0 / 123 (0.00%)	0 / 155 (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
Eye disorders			
CATARACT			
subjects affected / exposed	0 / 49 (0.00%)	0 / 123 (0.00%)	0 / 155 (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 / 49 (0.00%)	1 / 123 (0.81%)	0 / 155 (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 FISTULA			
subjects affected / exposed	0 / 49 (0.00%)	0 / 123 (0.00%)	0 / 155 (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
COLITIS			
subjects affected / exposed	0 / 49 (0.00%)	0 / 123 (0.00%)	1 / 155 (0.65%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COLITIS ULCERATIVE			
subjects affected / exposed	1 / 49 (2.04%)	3 / 123 (2.44%)	5 / 155 (3.23%)
occurrences causally related to treatment / all	0 / 1	1 / 3	3 / 6
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COLON DYSPLASIA			
subjects affected / exposed	0 / 49 (0.00%)	1 / 123 (0.81%)	0 / 155 (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

DIAPHRAGMATIC HERNIA			
subjects affected / exposed	0 / 49 (0.00%)	0 / 123 (0.00%)	1 / 155 (0.65%)
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 / 49 (0.00%)	0 / 123 (0.00%)	0 / 155 (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 / 49 (0.00%)	0 / 123 (0.00%)	0 / 155 (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
PANCREATITIS			
subjects affected / exposed	0 / 49 (0.00%)	0 / 123 (0.00%)	0 / 155 (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
Hepatobiliary disorders			
HEPATITIS			
subjects affected / exposed	0 / 49 (0.00%)	0 / 123 (0.00%)	0 / 155 (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
LIVER DISORDER			
subjects affected / exposed	0 / 49 (0.00%)	0 / 123 (0.00%)	0 / 155 (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
Skin and subcutaneous tissue disorders			
ERYTHEMA NODOSUM			
subjects affected / exposed	0 / 49 (0.00%)	0 / 123 (0.00%)	0 / 155 (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
PANNICULITIS			
subjects affected / exposed	0 / 49 (0.00%)	0 / 123 (0.00%)	0 / 155 (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

SKIN ULCER			
subjects affected / exposed	0 / 49 (0.00%)	0 / 123 (0.00%)	0 / 155 (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			
CYSTITIS HAEMORRHAGIC			
subjects affected / exposed	0 / 49 (0.00%)	0 / 123 (0.00%)	0 / 155 (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 RETENTION			
subjects affected / exposed	0 / 49 (0.00%)	0 / 123 (0.00%)	0 / 155 (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			
ARTHRITIS			
subjects affected / exposed	0 / 49 (0.00%)	0 / 123 (0.00%)	0 / 155 (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
CHONDROMALACIA			
subjects affected / exposed	0 / 49 (0.00%)	0 / 123 (0.00%)	0 / 155 (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 / 49 (0.00%)	0 / 123 (0.00%)	0 / 155 (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
ACUTE ENDOCARDITIS			
subjects affected / exposed	0 / 49 (0.00%)	0 / 123 (0.00%)	0 / 155 (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 / 49 (0.00%)	0 / 123 (0.00%)	0 / 155 (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
APPENDICITIS			
subjects affected / exposed	0 / 49 (0.00%)	0 / 123 (0.00%)	0 / 155 (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
ARTHRITIS BACTERIAL			
subjects affected / exposed	0 / 49 (0.00%)	0 / 123 (0.00%)	0 / 155 (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
BREAST ABSCESS			
subjects affected / exposed	0 / 49 (0.00%)	0 / 123 (0.00%)	0 / 155 (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
BRONCHITIS			
subjects affected / exposed	0 / 49 (0.00%)	0 / 123 (0.00%)	0 / 155 (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
BURSITIS INFECTIVE			
subjects affected / exposed	0 / 49 (0.00%)	0 / 123 (0.00%)	0 / 155 (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 / 49 (0.00%)	0 / 123 (0.00%)	1 / 155 (0.65%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CLOSTRIDIUM DIFFICILE INFECTION			
subjects affected / exposed	0 / 49 (0.00%)	0 / 123 (0.00%)	0 / 155 (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
COVID-19			

subjects affected / exposed	0 / 49 (0.00%)	0 / 123 (0.00%)	0 / 155 (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
COVID-19 PNEUMONIA			
subjects affected / exposed	0 / 49 (0.00%)	0 / 123 (0.00%)	0 / 155 (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
GASTROENTERITIS NOROVIRUS			
subjects affected / exposed	0 / 49 (0.00%)	0 / 123 (0.00%)	0 / 155 (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
HERPES ZOSTER			
subjects affected / exposed	0 / 49 (0.00%)	0 / 123 (0.00%)	0 / 155 (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
HERPES ZOSTER MENINGITIS			
subjects affected / exposed	0 / 49 (0.00%)	0 / 123 (0.00%)	0 / 155 (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
INFECTIOUS MONONUCLEOSIS			
subjects affected / exposed	0 / 49 (0.00%)	0 / 123 (0.00%)	0 / 155 (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 / 49 (0.00%)	0 / 123 (0.00%)	0 / 155 (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
LARGE INTESTINE INFECTION			
subjects affected / exposed	0 / 49 (0.00%)	0 / 123 (0.00%)	0 / 155 (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
MASTITIS			

subjects affected / exposed	0 / 49 (0.00%)	0 / 123 (0.00%)	0 / 155 (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
MUSCLE ABSCESS			
subjects affected / exposed	0 / 49 (0.00%)	0 / 123 (0.00%)	1 / 155 (0.65%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PNEUMOCYSTIS JIROVECII PNEUMONIA			
subjects affected / exposed	0 / 49 (0.00%)	0 / 123 (0.00%)	0 / 155 (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			
subjects affected / exposed	0 / 49 (0.00%)	0 / 123 (0.00%)	0 / 155 (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 CRYPTOCOCCAL			
subjects affected / exposed	0 / 49 (0.00%)	0 / 123 (0.00%)	0 / 155 (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 PNEUMOCOCCAL			
subjects affected / exposed	0 / 49 (0.00%)	0 / 123 (0.00%)	0 / 155 (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
POST PROCEDURAL INFECTION			
subjects affected / exposed	0 / 49 (0.00%)	0 / 123 (0.00%)	0 / 155 (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 SYNCYTIAL VIRUS INFECTION			
subjects affected / exposed	0 / 49 (0.00%)	1 / 123 (0.81%)	0 / 155 (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
SEPSIS			

subjects affected / exposed	0 / 49 (0.00%)	1 / 123 (0.81%)	0 / 155 (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
SINUSITIS			
subjects affected / exposed	0 / 49 (0.00%)	0 / 123 (0.00%)	0 / 155 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
TONSILLITIS			
subjects affected / exposed	0 / 49 (0.00%)	0 / 123 (0.00%)	0 / 155 (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
UROSEPSIS			
subjects affected / exposed	1 / 49 (2.04%)	0 / 123 (0.00%)	0 / 155 (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
VIRAL INFECTION			
subjects affected / exposed	0 / 49 (0.00%)	0 / 123 (0.00%)	0 / 155 (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
VIRAL PHARYNGITIS			
subjects affected / exposed	0 / 49 (0.00%)	1 / 123 (0.81%)	0 / 155 (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
Metabolism and nutrition disorders			
HYPOALBUMINAEMIA			
subjects affected / exposed	0 / 49 (0.00%)	0 / 123 (0.00%)	1 / 155 (0.65%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HYPOPHOSPHATAEMIA			
subjects affected / exposed	0 / 49 (0.00%)	0 / 123 (0.00%)	0 / 155 (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	SS3: Upadacitinib	SS3: Placebo	SS2: Upadacitinib

	15 mg		45 mg/Upadacitinib 45 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	24 / 323 (7.43%)	32 / 385 (8.31%)	2 / 59 (3.39%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
ADENOCARCINOMA OF COLON			
subjects affected / exposed	0 / 323 (0.00%)	0 / 385 (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
BASAL CELL CARCINOMA			
subjects affected / exposed	0 / 323 (0.00%)	0 / 385 (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
INVASIVE BREAST CARCINOMA			
subjects affected / exposed	1 / 323 (0.31%)	1 / 385 (0.26%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SEBORRHOEIC KERATOSIS			
subjects affected / exposed	0 / 323 (0.00%)	0 / 385 (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 CELL CARCINOMA			
subjects affected / exposed	0 / 323 (0.00%)	0 / 385 (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
Vascular disorders			
DEEP VEIN THROMBOSIS			
subjects affected / exposed	0 / 323 (0.00%)	1 / 385 (0.26%)	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
HYPOTENSION			

subjects affected / exposed	0 / 323 (0.00%)	0 / 385 (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
Surgical and medical procedures			
ABORTION INDUCED			
subjects affected / exposed	2 / 323 (0.62%)	0 / 385 (0.00%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
DEVICE INTOLERANCE			
subjects affected / exposed	0 / 323 (0.00%)	1 / 385 (0.26%)	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
PYREXIA			
subjects affected / exposed	0 / 323 (0.00%)	1 / 385 (0.26%)	0 / 59 (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
Reproductive system and breast disorders			
CERVICAL DYSPLASIA			
subjects affected / exposed	0 / 323 (0.00%)	0 / 385 (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
Respiratory, thoracic and mediastinal disorders			
ACUTE RESPIRATORY FAILURE			
subjects affected / exposed	0 / 323 (0.00%)	1 / 385 (0.26%)	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
CHRONIC OBSTRUCTIVE PULMONARY DISEASE			
subjects affected / exposed	1 / 323 (0.31%)	0 / 385 (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
INTERSTITIAL LUNG DISEASE			

subjects affected / exposed	0 / 323 (0.00%)	1 / 385 (0.26%)	0 / 59 (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
NONINFECTIVE BRONCHITIS			
subjects affected / exposed	0 / 323 (0.00%)	0 / 385 (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
PULMONARY EMBOLISM			
subjects affected / exposed	2 / 323 (0.62%)	0 / 385 (0.00%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
ANXIETY			
subjects affected / exposed	0 / 323 (0.00%)	1 / 385 (0.26%)	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
DEPRESSION			
subjects affected / exposed	0 / 323 (0.00%)	1 / 385 (0.26%)	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
MENTAL DISORDER			
subjects affected / exposed	0 / 323 (0.00%)	1 / 385 (0.26%)	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
SUICIDAL IDEATION			
subjects affected / exposed	0 / 323 (0.00%)	1 / 385 (0.26%)	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
Investigations			
ASPARTATE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	0 / 323 (0.00%)	0 / 385 (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			
HIP FRACTURE			
subjects affected / exposed	0 / 323 (0.00%)	1 / 385 (0.26%)	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
PULMONARY CONTUSION			
subjects affected / exposed	1 / 323 (0.31%)	0 / 385 (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
SKIN LACERATION			
subjects affected / exposed	1 / 323 (0.31%)	0 / 385 (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
THORACIC VERTEBRAL FRACTURE			
subjects affected / exposed	1 / 323 (0.31%)	0 / 385 (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
Cardiac disorders			
ACUTE MYOCARDIAL INFARCTION			
subjects affected / exposed	0 / 323 (0.00%)	1 / 385 (0.26%)	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
ATRIAL FIBRILLATION			
subjects affected / exposed	0 / 323 (0.00%)	1 / 385 (0.26%)	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
Nervous system disorders			
CARPAL TUNNEL SYNDROME			
subjects affected / exposed	0 / 323 (0.00%)	1 / 385 (0.26%)	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
CEREBROVASCULAR ACCIDENT			

subjects affected / exposed	0 / 323 (0.00%)	0 / 385 (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
SUBARACHNOID HAEMORRHAGE			
subjects affected / exposed	0 / 323 (0.00%)	0 / 385 (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 / 323 (0.00%)	0 / 385 (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
IRON DEFICIENCY ANAEMIA			
subjects affected / exposed	0 / 323 (0.00%)	1 / 385 (0.26%)	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
Eye disorders			
CATARACT			
subjects affected / exposed	1 / 323 (0.31%)	0 / 385 (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
Gastrointestinal disorders			
ABDOMINAL PAIN			
subjects affected / exposed	0 / 323 (0.00%)	0 / 385 (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 FISTULA			
subjects affected / exposed	0 / 323 (0.00%)	0 / 385 (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
COLITIS			
subjects affected / exposed	0 / 323 (0.00%)	1 / 385 (0.26%)	0 / 59 (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

COLITIS ULCERATIVE			
subjects affected / exposed	1 / 323 (0.31%)	9 / 385 (2.34%)	1 / 59 (1.69%)
occurrences causally related to treatment / all	0 / 1	4 / 9	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COLON DYSPLASIA			
subjects affected / exposed	0 / 323 (0.00%)	0 / 385 (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
DIAPHRAGMATIC HERNIA			
subjects affected / exposed	0 / 323 (0.00%)	0 / 385 (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 / 323 (0.00%)	0 / 385 (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	0 / 323 (0.00%)	1 / 385 (0.26%)	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
PANCREATITIS			
subjects affected / exposed	0 / 323 (0.00%)	1 / 385 (0.26%)	0 / 59 (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
Hepatobiliary disorders			
HEPATITIS			
subjects affected / exposed	1 / 323 (0.31%)	0 / 385 (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
LIVER DISORDER			
subjects affected / exposed	0 / 323 (0.00%)	0 / 385 (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
Skin and subcutaneous tissue disorders			

ERYTHEMA NODOSUM			
subjects affected / exposed	0 / 323 (0.00%)	1 / 385 (0.26%)	0 / 59 (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
PANNICULITIS			
subjects affected / exposed	1 / 323 (0.31%)	0 / 385 (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
SKIN ULCER			
subjects affected / exposed	0 / 323 (0.00%)	1 / 385 (0.26%)	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
Renal and urinary disorders			
CYSTITIS HAEMORRHAGIC			
subjects affected / exposed	0 / 323 (0.00%)	0 / 385 (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 RETENTION			
subjects affected / exposed	1 / 323 (0.31%)	0 / 385 (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
Musculoskeletal and connective tissue disorders			
ARTHRITIS			
subjects affected / exposed	1 / 323 (0.31%)	0 / 385 (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
CHONDROMALACIA			
subjects affected / exposed	0 / 323 (0.00%)	0 / 385 (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
Infections and infestations			
ABDOMINAL ABSCESS			

subjects affected / exposed	0 / 323 (0.00%)	1 / 385 (0.26%)	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
ACUTE ENDOCARDITIS			
subjects affected / exposed	0 / 323 (0.00%)	1 / 385 (0.26%)	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
ANAL ABSCESS			
subjects affected / exposed	1 / 323 (0.31%)	0 / 385 (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
APPENDICITIS			
subjects affected / exposed	0 / 323 (0.00%)	0 / 385 (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
ARTHRITIS BACTERIAL			
subjects affected / exposed	1 / 323 (0.31%)	0 / 385 (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
BREAST ABSCESS			
subjects affected / exposed	1 / 323 (0.31%)	0 / 385 (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
BRONCHITIS			
subjects affected / exposed	1 / 323 (0.31%)	0 / 385 (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
BURSITIS INFECTIVE			
subjects affected / exposed	0 / 323 (0.00%)	0 / 385 (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
CELLULITIS			

subjects affected / exposed	0 / 323 (0.00%)	1 / 385 (0.26%)	0 / 59 (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
CLOSTRIDIUM DIFFICILE INFECTION			
subjects affected / exposed	1 / 323 (0.31%)	1 / 385 (0.26%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COVID-19			
subjects affected / exposed	0 / 323 (0.00%)	0 / 385 (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
COVID-19 PNEUMONIA			
subjects affected / exposed	2 / 323 (0.62%)	1 / 385 (0.26%)	0 / 59 (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
GASTROENTERITIS NOROVIRUS			
subjects affected / exposed	0 / 323 (0.00%)	0 / 385 (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
HERPES ZOSTER			
subjects affected / exposed	1 / 323 (0.31%)	0 / 385 (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
HERPES ZOSTER MENINGITIS			
subjects affected / exposed	0 / 323 (0.00%)	0 / 385 (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
INFECTIOUS MONONUCLEOSIS			
subjects affected / exposed	1 / 323 (0.31%)	0 / 385 (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
INFLUENZA			

subjects affected / exposed	1 / 323 (0.31%)	0 / 385 (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
LARGE INTESTINE INFECTION			
subjects affected / exposed	1 / 323 (0.31%)	0 / 385 (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
MASTITIS			
subjects affected / exposed	1 / 323 (0.31%)	0 / 385 (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
MUSCLE ABSCESS			
subjects affected / exposed	0 / 323 (0.00%)	0 / 385 (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
PNEUMOCYSTIS JIROVECII PNEUMONIA			
subjects affected / exposed	0 / 323 (0.00%)	1 / 385 (0.26%)	0 / 59 (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
PNEUMONIA			
subjects affected / exposed	0 / 323 (0.00%)	3 / 385 (0.78%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PNEUMONIA CRYPTOCOCCAL			
subjects affected / exposed	0 / 323 (0.00%)	0 / 385 (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 PNEUMOCOCCAL			
subjects affected / exposed	1 / 323 (0.31%)	0 / 385 (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
POST PROCEDURAL INFECTION			

subjects affected / exposed	0 / 323 (0.00%)	1 / 385 (0.26%)	0 / 59 (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
RESPIRATORY SYNCYTIAL VIRUS INFECTION			
subjects affected / exposed	0 / 323 (0.00%)	0 / 385 (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	0 / 323 (0.00%)	0 / 385 (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
SINUSITIS			
subjects affected / exposed	0 / 323 (0.00%)	0 / 385 (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
TONSILLITIS			
subjects affected / exposed	0 / 323 (0.00%)	1 / 385 (0.26%)	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
UROSEPSIS			
subjects affected / exposed	0 / 323 (0.00%)	0 / 385 (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
VIRAL INFECTION			
subjects affected / exposed	0 / 323 (0.00%)	0 / 385 (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
VIRAL PHARYNGITIS			
subjects affected / exposed	0 / 323 (0.00%)	0 / 385 (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			
HYPOALBUMINAEMIA			

subjects affected / exposed	0 / 323 (0.00%)	0 / 385 (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
HYPOPHOSPHATAEMIA			
subjects affected / exposed	0 / 323 (0.00%)	0 / 385 (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	SS2: Upadacitinib 45 mg	SS2: Placebo/Upadacitinib 45 mg	SS3: Upadacitinib 30 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	8 / 319 (2.51%)	2 / 85 (2.35%)	25 / 316 (7.91%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
ADENOCARCINOMA OF COLON			
subjects affected / exposed	0 / 319 (0.00%)	0 / 85 (0.00%)	1 / 316 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BASAL CELL CARCINOMA			
subjects affected / exposed	0 / 319 (0.00%)	0 / 85 (0.00%)	1 / 316 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
INVASIVE BREAST CARCINOMA			
subjects affected / exposed	0 / 319 (0.00%)	0 / 85 (0.00%)	0 / 316 (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
SEBORRHOEIC KERATOSIS			
subjects affected / exposed	0 / 319 (0.00%)	0 / 85 (0.00%)	1 / 316 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SMALL CELL CARCINOMA			

subjects affected / exposed	0 / 319 (0.00%)	0 / 85 (0.00%)	1 / 316 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
DEEP VEIN THROMBOSIS			
subjects affected / exposed	0 / 319 (0.00%)	0 / 85 (0.00%)	0 / 316 (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
HYPOTENSION			
subjects affected / exposed	0 / 319 (0.00%)	0 / 85 (0.00%)	0 / 316 (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
Surgical and medical procedures			
ABORTION INDUCED			
subjects affected / exposed	0 / 319 (0.00%)	0 / 85 (0.00%)	0 / 316 (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			
DEVICE INTOLERANCE			
subjects affected / exposed	0 / 319 (0.00%)	0 / 85 (0.00%)	0 / 316 (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
PYREXIA			
subjects affected / exposed	1 / 319 (0.31%)	0 / 85 (0.00%)	0 / 316 (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
Reproductive system and breast disorders			
CERVICAL DYSPLASIA			
subjects affected / exposed	0 / 319 (0.00%)	0 / 85 (0.00%)	2 / 316 (0.63%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
ACUTE RESPIRATORY FAILURE			

subjects affected / exposed	0 / 319 (0.00%)	0 / 85 (0.00%)	1 / 316 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CHRONIC OBSTRUCTIVE PULMONARY DISEASE			
subjects affected / exposed	0 / 319 (0.00%)	0 / 85 (0.00%)	0 / 316 (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
INTERSTITIAL LUNG DISEASE			
subjects affected / exposed	0 / 319 (0.00%)	0 / 85 (0.00%)	0 / 316 (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
NONINFECTIVE BRONCHITIS			
subjects affected / exposed	0 / 319 (0.00%)	0 / 85 (0.00%)	1 / 316 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PULMONARY EMBOLISM			
subjects affected / exposed	0 / 319 (0.00%)	0 / 85 (0.00%)	0 / 316 (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			
ANXIETY			
subjects affected / exposed	0 / 319 (0.00%)	0 / 85 (0.00%)	1 / 316 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DEPRESSION			
subjects affected / exposed	0 / 319 (0.00%)	0 / 85 (0.00%)	1 / 316 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
MENTAL DISORDER			
subjects affected / exposed	0 / 319 (0.00%)	0 / 85 (0.00%)	0 / 316 (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
SUICIDAL IDEATION			

subjects affected / exposed	0 / 319 (0.00%)	0 / 85 (0.00%)	0 / 316 (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			
ASPARTATE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	0 / 319 (0.00%)	0 / 85 (0.00%)	0 / 316 (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			
HIP FRACTURE			
subjects affected / exposed	0 / 319 (0.00%)	0 / 85 (0.00%)	0 / 316 (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
PULMONARY CONTUSION			
subjects affected / exposed	0 / 319 (0.00%)	0 / 85 (0.00%)	0 / 316 (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
SKIN LACERATION			
subjects affected / exposed	0 / 319 (0.00%)	0 / 85 (0.00%)	0 / 316 (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
THORACIC VERTEBRAL FRACTURE			
subjects affected / exposed	0 / 319 (0.00%)	0 / 85 (0.00%)	0 / 316 (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 / 319 (0.00%)	0 / 85 (0.00%)	0 / 316 (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
ATRIAL FIBRILLATION			

subjects affected / exposed	0 / 319 (0.00%)	0 / 85 (0.00%)	0 / 316 (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			
CARPAL TUNNEL SYNDROME			
subjects affected / exposed	0 / 319 (0.00%)	0 / 85 (0.00%)	0 / 316 (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
CEREBROVASCULAR ACCIDENT			
subjects affected / exposed	0 / 319 (0.00%)	0 / 85 (0.00%)	1 / 316 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SUBARACHNOID HAEMORRHAGE			
subjects affected / exposed	0 / 319 (0.00%)	0 / 85 (0.00%)	1 / 316 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
ANAEMIA			
subjects affected / exposed	0 / 319 (0.00%)	2 / 85 (2.35%)	1 / 316 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
IRON DEFICIENCY ANAEMIA			
subjects affected / exposed	0 / 319 (0.00%)	0 / 85 (0.00%)	0 / 316 (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
Eye disorders			
CATARACT			
subjects affected / exposed	0 / 319 (0.00%)	0 / 85 (0.00%)	0 / 316 (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 / 319 (0.00%)	0 / 85 (0.00%)	0 / 316 (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 / 319 (0.00%)	0 / 85 (0.00%)	1 / 316 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COLITIS			
subjects affected / exposed	0 / 319 (0.00%)	0 / 85 (0.00%)	0 / 316 (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
COLITIS ULCERATIVE			
subjects affected / exposed	2 / 319 (0.63%)	1 / 85 (1.18%)	3 / 316 (0.95%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COLON DYSPLASIA			
subjects affected / exposed	0 / 319 (0.00%)	0 / 85 (0.00%)	0 / 316 (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
DIAPHRAGMATIC HERNIA			
subjects affected / exposed	0 / 319 (0.00%)	0 / 85 (0.00%)	0 / 316 (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 / 319 (0.00%)	0 / 85 (0.00%)	0 / 316 (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 / 319 (0.00%)	0 / 85 (0.00%)	0 / 316 (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
PANCREATITIS			

subjects affected / exposed	0 / 319 (0.00%)	0 / 85 (0.00%)	0 / 316 (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
Hepatobiliary disorders			
HEPATITIS			
subjects affected / exposed	0 / 319 (0.00%)	0 / 85 (0.00%)	0 / 316 (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
LIVER DISORDER			
subjects affected / exposed	0 / 319 (0.00%)	0 / 85 (0.00%)	1 / 316 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
ERYTHEMA NODOSUM			
subjects affected / exposed	0 / 319 (0.00%)	0 / 85 (0.00%)	0 / 316 (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
PANNICULITIS			
subjects affected / exposed	0 / 319 (0.00%)	0 / 85 (0.00%)	0 / 316 (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
SKIN ULCER			
subjects affected / exposed	0 / 319 (0.00%)	0 / 85 (0.00%)	0 / 316 (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			
CYSTITIS HAEMORRHAGIC			
subjects affected / exposed	0 / 319 (0.00%)	0 / 85 (0.00%)	0 / 316 (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 RETENTION			
subjects affected / exposed	0 / 319 (0.00%)	0 / 85 (0.00%)	0 / 316 (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			
ARTHRITIS			
subjects affected / exposed	0 / 319 (0.00%)	0 / 85 (0.00%)	0 / 316 (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
CHONDROMALACIA			
subjects affected / exposed	0 / 319 (0.00%)	0 / 85 (0.00%)	1 / 316 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
ABDOMINAL ABSCESS			
subjects affected / exposed	0 / 319 (0.00%)	0 / 85 (0.00%)	0 / 316 (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
ACUTE ENDOCARDITIS			
subjects affected / exposed	0 / 319 (0.00%)	0 / 85 (0.00%)	0 / 316 (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 / 319 (0.00%)	0 / 85 (0.00%)	0 / 316 (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
APPENDICITIS			
subjects affected / exposed	2 / 319 (0.63%)	0 / 85 (0.00%)	0 / 316 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ARTHRITIS BACTERIAL			
subjects affected / exposed	0 / 319 (0.00%)	0 / 85 (0.00%)	0 / 316 (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
BREAST ABSCESS			
subjects affected / exposed	0 / 319 (0.00%)	0 / 85 (0.00%)	0 / 316 (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

BRONCHITIS			
subjects affected / exposed	0 / 319 (0.00%)	0 / 85 (0.00%)	0 / 316 (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
BURSITIS INFECTIVE			
subjects affected / exposed	0 / 319 (0.00%)	0 / 85 (0.00%)	1 / 316 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CELLULITIS			
subjects affected / exposed	0 / 319 (0.00%)	0 / 85 (0.00%)	0 / 316 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CLOSTRIDIUM DIFFICILE INFECTION			
subjects affected / exposed	0 / 319 (0.00%)	0 / 85 (0.00%)	0 / 316 (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
COVID-19			
subjects affected / exposed	0 / 319 (0.00%)	0 / 85 (0.00%)	1 / 316 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COVID-19 PNEUMONIA			
subjects affected / exposed	0 / 319 (0.00%)	0 / 85 (0.00%)	2 / 316 (0.63%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
GASTROENTERITIS NOROVIRUS			
subjects affected / exposed	1 / 319 (0.31%)	0 / 85 (0.00%)	0 / 316 (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
HERPES ZOSTER			
subjects affected / exposed	0 / 319 (0.00%)	0 / 85 (0.00%)	1 / 316 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HERPES ZOSTER MENINGITIS			

subjects affected / exposed	0 / 319 (0.00%)	0 / 85 (0.00%)	1 / 316 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
INFECTIOUS MONONUCLEOSIS			
subjects affected / exposed	0 / 319 (0.00%)	0 / 85 (0.00%)	0 / 316 (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 / 319 (0.00%)	0 / 85 (0.00%)	0 / 316 (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
LARGE INTESTINE INFECTION			
subjects affected / exposed	0 / 319 (0.00%)	0 / 85 (0.00%)	0 / 316 (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
MASTITIS			
subjects affected / exposed	0 / 319 (0.00%)	0 / 85 (0.00%)	0 / 316 (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
MUSCLE ABSCESS			
subjects affected / exposed	0 / 319 (0.00%)	0 / 85 (0.00%)	0 / 316 (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
PNEUMOCYSTIS JIROVECII PNEUMONIA			
subjects affected / exposed	0 / 319 (0.00%)	0 / 85 (0.00%)	0 / 316 (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			
subjects affected / exposed	1 / 319 (0.31%)	0 / 85 (0.00%)	1 / 316 (0.32%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PNEUMONIA CRYPTOCOCCAL			

subjects affected / exposed	0 / 319 (0.00%)	0 / 85 (0.00%)	2 / 316 (0.63%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PNEUMONIA PNEUMOCOCCAL			
subjects affected / exposed	0 / 319 (0.00%)	0 / 85 (0.00%)	0 / 316 (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
POST PROCEDURAL INFECTION			
subjects affected / exposed	0 / 319 (0.00%)	0 / 85 (0.00%)	0 / 316 (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 SYNCYTIAL VIRUS INFECTION			
subjects affected / exposed	0 / 319 (0.00%)	0 / 85 (0.00%)	0 / 316 (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 / 319 (0.00%)	0 / 85 (0.00%)	0 / 316 (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
SINUSITIS			
subjects affected / exposed	0 / 319 (0.00%)	0 / 85 (0.00%)	0 / 316 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
TONSILLITIS			
subjects affected / exposed	0 / 319 (0.00%)	0 / 85 (0.00%)	0 / 316 (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
UROSEPSIS			
subjects affected / exposed	0 / 319 (0.00%)	0 / 85 (0.00%)	0 / 316 (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
VIRAL INFECTION			

subjects affected / exposed	1 / 319 (0.31%)	0 / 85 (0.00%)	0 / 316 (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
VIRAL PHARYNGITIS			
subjects affected / exposed	0 / 319 (0.00%)	0 / 85 (0.00%)	0 / 316 (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			
HYPOALBUMINAEMIA			
subjects affected / exposed	0 / 319 (0.00%)	0 / 85 (0.00%)	0 / 316 (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
HYPOPHOSPHATAEMIA			
subjects affected / exposed	0 / 319 (0.00%)	0 / 85 (0.00%)	0 / 316 (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	SS3: Upadacitinib 7.5 mg		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 20 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
ADENOCARCINOMA OF COLON			
subjects affected / exposed	0 / 20 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
BASAL CELL CARCINOMA			
subjects affected / exposed	0 / 20 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
INVASIVE BREAST CARCINOMA			

subjects affected / exposed	0 / 20 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
SEBORRHOEIC KERATOSIS			
subjects affected / exposed	0 / 20 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
SMALL CELL CARCINOMA			
subjects affected / exposed	0 / 20 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
DEEP VEIN THROMBOSIS			
subjects affected / exposed	0 / 20 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
HYPOTENSION			
subjects affected / exposed	0 / 20 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Surgical and medical procedures			
ABORTION INDUCED			
subjects affected / exposed	0 / 20 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
DEVICE INTOLERANCE			
subjects affected / exposed	0 / 20 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
PYREXIA			
subjects affected / exposed	0 / 20 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Reproductive system and breast disorders			
CERVICAL DYSPLASIA			
subjects affected / exposed	0 / 20 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
ACUTE RESPIRATORY FAILURE			
subjects affected / exposed	0 / 20 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
CHRONIC OBSTRUCTIVE PULMONARY DISEASE			
subjects affected / exposed	0 / 20 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
INTERSTITIAL LUNG DISEASE			
subjects affected / exposed	0 / 20 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
NONINFECTIVE BRONCHITIS			
subjects affected / exposed	0 / 20 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
PULMONARY EMBOLISM			
subjects affected / exposed	0 / 20 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
ANXIETY			
subjects affected / exposed	0 / 20 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
DEPRESSION			

subjects affected / exposed	0 / 20 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
MENTAL DISORDER				
subjects affected / exposed	0 / 20 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
SUICIDAL IDEATION				
subjects affected / exposed	0 / 20 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Investigations				
ASPARTATE AMINOTRANSFERASE INCREASED				
subjects affected / exposed	0 / 20 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Injury, poisoning and procedural complications				
HIP FRACTURE				
subjects affected / exposed	0 / 20 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
PULMONARY CONTUSION				
subjects affected / exposed	0 / 20 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
SKIN LACERATION				
subjects affected / exposed	0 / 20 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
THORACIC VERTEBRAL FRACTURE				
subjects affected / exposed	0 / 20 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			

Cardiac disorders			
ACUTE MYOCARDIAL INFARCTION			
subjects affected / exposed	0 / 20 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
ATRIAL FIBRILLATION			
subjects affected / exposed	0 / 20 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
CARPAL TUNNEL SYNDROME			
subjects affected / exposed	0 / 20 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
CEREBROVASCULAR ACCIDENT			
subjects affected / exposed	0 / 20 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
SUBARACHNOID HAEMORRHAGE			
subjects affected / exposed	0 / 20 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
ANAEMIA			
subjects affected / exposed	0 / 20 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
IRON DEFICIENCY ANAEMIA			
subjects affected / exposed	0 / 20 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Eye disorders			
CATARACT			

subjects affected / exposed	0 / 20 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal disorders				
ABDOMINAL PAIN				
subjects affected / exposed	0 / 20 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
ANAL FISTULA				
subjects affected / exposed	0 / 20 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
COLITIS				
subjects affected / exposed	0 / 20 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
COLITIS ULCERATIVE				
subjects affected / exposed	0 / 20 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
COLON DYSPLASIA				
subjects affected / exposed	0 / 20 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
DIAPHRAGMATIC HERNIA				
subjects affected / exposed	0 / 20 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
ILEUS				
subjects affected / exposed	0 / 20 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
INTESTINAL OBSTRUCTION				

subjects affected / exposed	0 / 20 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
PANCREATITIS			
subjects affected / exposed	0 / 20 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
HEPATITIS			
subjects affected / exposed	0 / 20 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
LIVER DISORDER			
subjects affected / exposed	0 / 20 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
ERYTHEMA NODOSUM			
subjects affected / exposed	0 / 20 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
PANNICULITIS			
subjects affected / exposed	0 / 20 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
SKIN ULCER			
subjects affected / exposed	0 / 20 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
CYSTITIS HAEMORRHAGIC			
subjects affected / exposed	0 / 20 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

URINARY RETENTION				
subjects affected / exposed	0 / 20 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Musculoskeletal and connective tissue disorders				
ARTHRITIS				
subjects affected / exposed	0 / 20 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
CHONDROMALACIA				
subjects affected / exposed	0 / 20 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Infections and infestations				
ABDOMINAL ABSCESS				
subjects affected / exposed	0 / 20 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
ACUTE ENDOCARDITIS				
subjects affected / exposed	0 / 20 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
ANAL ABSCESS				
subjects affected / exposed	0 / 20 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
APPENDICITIS				
subjects affected / exposed	0 / 20 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
ARTHRITIS BACTERIAL				
subjects affected / exposed	0 / 20 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			

BREAST ABSCESS				
subjects affected / exposed	0 / 20 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
BRONCHITIS				
subjects affected / exposed	0 / 20 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
BURSITIS INFECTIVE				
subjects affected / exposed	0 / 20 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
CELLULITIS				
subjects affected / exposed	0 / 20 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
CLOSTRIDIUM DIFFICILE INFECTION				
subjects affected / exposed	0 / 20 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
COVID-19				
subjects affected / exposed	0 / 20 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
COVID-19 PNEUMONIA				
subjects affected / exposed	0 / 20 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
GASTROENTERITIS NOROVIRUS				
subjects affected / exposed	0 / 20 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
HERPES ZOSTER				

subjects affected / exposed	0 / 20 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
HERPES ZOSTER MENINGITIS				
subjects affected / exposed	0 / 20 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
INFECTIOUS MONONUCLEOSIS				
subjects affected / exposed	0 / 20 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
INFLUENZA				
subjects affected / exposed	0 / 20 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
LARGE INTESTINE INFECTION				
subjects affected / exposed	0 / 20 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
MASTITIS				
subjects affected / exposed	0 / 20 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
MUSCLE ABSCESS				
subjects affected / exposed	0 / 20 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
PNEUMOCYSTIS JIROVECII PNEUMONIA				
subjects affected / exposed	0 / 20 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
PNEUMONIA				

subjects affected / exposed	0 / 20 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
PNEUMONIA CRYPTOCOCCAL				
subjects affected / exposed	0 / 20 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
PNEUMONIA PNEUMOCOCCAL				
subjects affected / exposed	0 / 20 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
POST PROCEDURAL INFECTION				
subjects affected / exposed	0 / 20 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
RESPIRATORY SYNCYTIAL VIRUS INFECTION				
subjects affected / exposed	0 / 20 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
SEPSIS				
subjects affected / exposed	0 / 20 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
SINUSITIS				
subjects affected / exposed	0 / 20 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
TONSILLITIS				
subjects affected / exposed	0 / 20 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
UROSEPSIS				

subjects affected / exposed	0 / 20 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
VIRAL INFECTION			
subjects affected / exposed	0 / 20 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
VIRAL PHARYNGITIS			
subjects affected / exposed	0 / 20 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
HYPOALBUMINAEMIA			
subjects affected / exposed	0 / 20 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
HYPOPHOSPHATAEMIA			
subjects affected / exposed	0 / 20 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	SS1: Upadacitinib 7.5 mg	SS1: Placebo	SS1: Upadacitinib 30 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	18 / 47 (38.30%)	27 / 46 (58.70%)	58 / 117 (49.57%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
MALIGNANT MELANOMA			
subjects affected / exposed	0 / 47 (0.00%)	0 / 46 (0.00%)	0 / 117 (0.00%)
occurrences (all)	0	0	0
MELANOCYTIC NAEVUS			
subjects affected / exposed	1 / 47 (2.13%)	0 / 46 (0.00%)	0 / 117 (0.00%)
occurrences (all)	1	0	0
SKIN PAPILLOMA			

subjects affected / exposed	0 / 47 (0.00%)	0 / 46 (0.00%)	0 / 117 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
INFLUENZA LIKE ILLNESS			
subjects affected / exposed	1 / 47 (2.13%)	1 / 46 (2.17%)	1 / 117 (0.85%)
occurrences (all)	1	1	1
PSEUDOPOLYP			
subjects affected / exposed	0 / 47 (0.00%)	0 / 46 (0.00%)	1 / 117 (0.85%)
occurrences (all)	0	0	1
PYREXIA			
subjects affected / exposed	1 / 47 (2.13%)	1 / 46 (2.17%)	5 / 117 (4.27%)
occurrences (all)	1	1	5
Respiratory, thoracic and mediastinal disorders			
ASTHMA			
subjects affected / exposed	0 / 47 (0.00%)	0 / 46 (0.00%)	0 / 117 (0.00%)
occurrences (all)	0	0	0
COUGH			
subjects affected / exposed	1 / 47 (2.13%)	1 / 46 (2.17%)	3 / 117 (2.56%)
occurrences (all)	1	1	3
NASAL CONGESTION			
subjects affected / exposed	0 / 47 (0.00%)	0 / 46 (0.00%)	1 / 117 (0.85%)
occurrences (all)	0	0	1
OROPHARYNGEAL PAIN			
subjects affected / exposed	1 / 47 (2.13%)	0 / 46 (0.00%)	4 / 117 (3.42%)
occurrences (all)	1	0	4
PULMONARY MASS			
subjects affected / exposed	0 / 47 (0.00%)	0 / 46 (0.00%)	0 / 117 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
DEPRESSED MOOD			
subjects affected / exposed	0 / 47 (0.00%)	0 / 46 (0.00%)	0 / 117 (0.00%)
occurrences (all)	0	0	0
IRRITABILITY			
subjects affected / exposed	0 / 47 (0.00%)	0 / 46 (0.00%)	0 / 117 (0.00%)
occurrences (all)	0	0	0
Investigations			

BLOOD CREATINE PHOSPHOKINASE INCREASED			
subjects affected / exposed	0 / 47 (0.00%)	0 / 46 (0.00%)	4 / 117 (3.42%)
occurrences (all)	0	0	4
HAEMOGLOBIN DECREASED			
subjects affected / exposed	1 / 47 (2.13%)	0 / 46 (0.00%)	0 / 117 (0.00%)
occurrences (all)	1	0	0
LYMPHOCYTE COUNT DECREASED			
subjects affected / exposed	0 / 47 (0.00%)	0 / 46 (0.00%)	1 / 117 (0.85%)
occurrences (all)	0	0	1
LYMPHOCYTE COUNT INCREASED			
subjects affected / exposed	0 / 47 (0.00%)	0 / 46 (0.00%)	0 / 117 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
ACCIDENTAL OVERDOSE			
subjects affected / exposed	0 / 47 (0.00%)	3 / 46 (6.52%)	5 / 117 (4.27%)
occurrences (all)	0	3	5
FALL			
subjects affected / exposed	0 / 47 (0.00%)	0 / 46 (0.00%)	0 / 117 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
HEADACHE			
subjects affected / exposed	4 / 47 (8.51%)	5 / 46 (10.87%)	9 / 117 (7.69%)
occurrences (all)	4	5	9
Blood and lymphatic system disorders			
ANAEMIA			
subjects affected / exposed	0 / 47 (0.00%)	3 / 46 (6.52%)	4 / 117 (3.42%)
occurrences (all)	0	3	4
LYMPHOPENIA			
subjects affected / exposed	0 / 47 (0.00%)	0 / 46 (0.00%)	1 / 117 (0.85%)
occurrences (all)	0	0	1
Ear and labyrinth disorders			
CERUMEN IMPACTION			
subjects affected / exposed	0 / 47 (0.00%)	0 / 46 (0.00%)	0 / 117 (0.00%)
occurrences (all)	0	0	0
Eye disorders			

CATARACT			
subjects affected / exposed	0 / 47 (0.00%)	0 / 46 (0.00%)	0 / 117 (0.00%)
occurrences (all)	0	0	0
VISUAL IMPAIRMENT			
subjects affected / exposed	0 / 47 (0.00%)	0 / 46 (0.00%)	0 / 117 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
ABDOMINAL DISTENSION			
subjects affected / exposed	3 / 47 (6.38%)	0 / 46 (0.00%)	0 / 117 (0.00%)
occurrences (all)	3	0	0
ABDOMINAL PAIN			
subjects affected / exposed	0 / 47 (0.00%)	1 / 46 (2.17%)	1 / 117 (0.85%)
occurrences (all)	0	1	1
ABDOMINAL TENDERNESS			
subjects affected / exposed	0 / 47 (0.00%)	1 / 46 (2.17%)	1 / 117 (0.85%)
occurrences (all)	0	1	1
APHTHOUS ULCER			
subjects affected / exposed	0 / 47 (0.00%)	0 / 46 (0.00%)	0 / 117 (0.00%)
occurrences (all)	0	0	0
COLITIS ULCERATIVE			
subjects affected / exposed	1 / 47 (2.13%)	4 / 46 (8.70%)	4 / 117 (3.42%)
occurrences (all)	1	4	4
CONSTIPATION			
subjects affected / exposed	0 / 47 (0.00%)	1 / 46 (2.17%)	1 / 117 (0.85%)
occurrences (all)	0	1	1
DIARRHOEA			
subjects affected / exposed	0 / 47 (0.00%)	0 / 46 (0.00%)	0 / 117 (0.00%)
occurrences (all)	0	0	0
NAUSEA			
subjects affected / exposed	1 / 47 (2.13%)	2 / 46 (4.35%)	8 / 117 (6.84%)
occurrences (all)	1	2	8
PERIANAL ERYTHEMA			
subjects affected / exposed	0 / 47 (0.00%)	0 / 46 (0.00%)	0 / 117 (0.00%)
occurrences (all)	0	0	0
VOMITING			

subjects affected / exposed	1 / 47 (2.13%)	1 / 46 (2.17%)	1 / 117 (0.85%)
occurrences (all)	1	1	1
Skin and subcutaneous tissue disorders			
ACNE			
subjects affected / exposed	1 / 47 (2.13%)	0 / 46 (0.00%)	6 / 117 (5.13%)
occurrences (all)	1	0	6
DERMATITIS ACNEIFORM			
subjects affected / exposed	0 / 47 (0.00%)	0 / 46 (0.00%)	2 / 117 (1.71%)
occurrences (all)	0	0	2
PRURITUS			
subjects affected / exposed	0 / 47 (0.00%)	1 / 46 (2.17%)	1 / 117 (0.85%)
occurrences (all)	0	1	1
RASH			
subjects affected / exposed	1 / 47 (2.13%)	0 / 46 (0.00%)	5 / 117 (4.27%)
occurrences (all)	1	0	5
ROSACEA			
subjects affected / exposed	0 / 47 (0.00%)	0 / 46 (0.00%)	1 / 117 (0.85%)
occurrences (all)	0	0	1
Musculoskeletal and connective tissue disorders			
ARTHRALGIA			
subjects affected / exposed	2 / 47 (4.26%)	1 / 46 (2.17%)	2 / 117 (1.71%)
occurrences (all)	2	1	2
BACK PAIN			
subjects affected / exposed	0 / 47 (0.00%)	1 / 46 (2.17%)	2 / 117 (1.71%)
occurrences (all)	0	1	2
BURSITIS			
subjects affected / exposed	0 / 47 (0.00%)	0 / 46 (0.00%)	0 / 117 (0.00%)
occurrences (all)	0	0	0
MUSCLE SPASMS			
subjects affected / exposed	0 / 47 (0.00%)	1 / 46 (2.17%)	2 / 117 (1.71%)
occurrences (all)	0	1	2
MUSCULOSKELETAL PAIN			
subjects affected / exposed	0 / 47 (0.00%)	1 / 46 (2.17%)	1 / 117 (0.85%)
occurrences (all)	0	1	1
OSTEOPENIA			

subjects affected / exposed	0 / 47 (0.00%)	0 / 46 (0.00%)	0 / 117 (0.00%)
occurrences (all)	0	0	0
PAIN IN EXTREMITY			
subjects affected / exposed	0 / 47 (0.00%)	3 / 46 (6.52%)	0 / 117 (0.00%)
occurrences (all)	0	3	0
Infections and infestations			
BRONCHITIS			
subjects affected / exposed	0 / 47 (0.00%)	2 / 46 (4.35%)	2 / 117 (1.71%)
occurrences (all)	0	2	2
CYSTITIS			
subjects affected / exposed	1 / 47 (2.13%)	0 / 46 (0.00%)	1 / 117 (0.85%)
occurrences (all)	1	0	1
EAR INFECTION			
subjects affected / exposed	0 / 47 (0.00%)	0 / 46 (0.00%)	1 / 117 (0.85%)
occurrences (all)	0	0	1
HERPES ZOSTER			
subjects affected / exposed	0 / 47 (0.00%)	0 / 46 (0.00%)	0 / 117 (0.00%)
occurrences (all)	0	0	0
INFLUENZA			
subjects affected / exposed	0 / 47 (0.00%)	0 / 46 (0.00%)	2 / 117 (1.71%)
occurrences (all)	0	0	2
NASOPHARYNGITIS			
subjects affected / exposed	1 / 47 (2.13%)	3 / 46 (6.52%)	3 / 117 (2.56%)
occurrences (all)	1	3	3
ORAL HERPES			
subjects affected / exposed	0 / 47 (0.00%)	1 / 46 (2.17%)	2 / 117 (1.71%)
occurrences (all)	0	1	2
PULPITIS DENTAL			
subjects affected / exposed	0 / 47 (0.00%)	0 / 46 (0.00%)	0 / 117 (0.00%)
occurrences (all)	0	0	0
RESPIRATORY TRACT INFECTION VIRAL			
subjects affected / exposed	0 / 47 (0.00%)	0 / 46 (0.00%)	0 / 117 (0.00%)
occurrences (all)	0	0	0
SKIN CANDIDA			

subjects affected / exposed	0 / 47 (0.00%)	0 / 46 (0.00%)	0 / 117 (0.00%)
occurrences (all)	0	0	0
UPPER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	1 / 47 (2.13%)	0 / 46 (0.00%)	3 / 117 (2.56%)
occurrences (all)	1	0	3
URINARY TRACT INFECTION			
subjects affected / exposed	1 / 47 (2.13%)	0 / 46 (0.00%)	3 / 117 (2.56%)
occurrences (all)	1	0	3
VAGINAL INFECTION			
subjects affected / exposed	0 / 47 (0.00%)	0 / 46 (0.00%)	0 / 117 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
DECREASED APPETITE			
subjects affected / exposed	0 / 47 (0.00%)	2 / 46 (4.35%)	0 / 117 (0.00%)
occurrences (all)	0	2	0
HYPOKALAEMIA			
subjects affected / exposed	1 / 47 (2.13%)	0 / 46 (0.00%)	1 / 117 (0.85%)
occurrences (all)	1	0	1
IRON DEFICIENCY			
subjects affected / exposed	0 / 47 (0.00%)	1 / 46 (2.17%)	0 / 117 (0.00%)
occurrences (all)	0	1	0

Non-serious adverse events	SS1: Upadacitinib 15 mg	SS1: Upadacitinib 45 mg	SS2: Placebo
Total subjects affected by non-serious adverse events			
subjects affected / exposed	22 / 49 (44.90%)	50 / 123 (40.65%)	62 / 155 (40.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
MALIGNANT MELANOMA			
subjects affected / exposed	0 / 49 (0.00%)	0 / 123 (0.00%)	0 / 155 (0.00%)
occurrences (all)	0	0	0
MELANOCYTIC NAEVUS			
subjects affected / exposed	0 / 49 (0.00%)	0 / 123 (0.00%)	0 / 155 (0.00%)
occurrences (all)	0	0	0
SKIN PAPILLOMA			
subjects affected / exposed	0 / 49 (0.00%)	0 / 123 (0.00%)	0 / 155 (0.00%)
occurrences (all)	0	0	0
General disorders and administration			

site conditions			
INFLUENZA LIKE ILLNESS			
subjects affected / exposed	0 / 49 (0.00%)	0 / 123 (0.00%)	0 / 155 (0.00%)
occurrences (all)	0	0	0
PSEUDOPOLYP			
subjects affected / exposed	0 / 49 (0.00%)	0 / 123 (0.00%)	0 / 155 (0.00%)
occurrences (all)	0	0	0
PYREXIA			
subjects affected / exposed	0 / 49 (0.00%)	1 / 123 (0.81%)	2 / 155 (1.29%)
occurrences (all)	0	1	3
Respiratory, thoracic and mediastinal disorders			
ASTHMA			
subjects affected / exposed	0 / 49 (0.00%)	0 / 123 (0.00%)	0 / 155 (0.00%)
occurrences (all)	0	0	0
COUGH			
subjects affected / exposed	1 / 49 (2.04%)	4 / 123 (3.25%)	2 / 155 (1.29%)
occurrences (all)	1	4	2
NASAL CONGESTION			
subjects affected / exposed	0 / 49 (0.00%)	0 / 123 (0.00%)	0 / 155 (0.00%)
occurrences (all)	0	0	0
OROPHARYNGEAL PAIN			
subjects affected / exposed	2 / 49 (4.08%)	0 / 123 (0.00%)	1 / 155 (0.65%)
occurrences (all)	2	0	1
PULMONARY MASS			
subjects affected / exposed	0 / 49 (0.00%)	0 / 123 (0.00%)	2 / 155 (1.29%)
occurrences (all)	0	0	2
Psychiatric disorders			
DEPRESSED MOOD			
subjects affected / exposed	0 / 49 (0.00%)	0 / 123 (0.00%)	0 / 155 (0.00%)
occurrences (all)	0	0	0
IRRITABILITY			
subjects affected / exposed	0 / 49 (0.00%)	0 / 123 (0.00%)	0 / 155 (0.00%)
occurrences (all)	0	0	0
Investigations			
BLOOD CREATINE PHOSPHOKINASE INCREASED			

subjects affected / exposed	3 / 49 (6.12%)	8 / 123 (6.50%)	3 / 155 (1.94%)
occurrences (all)	3	8	3
HAEMOGLOBIN DECREASED			
subjects affected / exposed	1 / 49 (2.04%)	2 / 123 (1.63%)	3 / 155 (1.94%)
occurrences (all)	1	2	4
LYMPHOCYTE COUNT DECREASED			
subjects affected / exposed	1 / 49 (2.04%)	2 / 123 (1.63%)	0 / 155 (0.00%)
occurrences (all)	1	2	0
LYMPHOCYTE COUNT INCREASED			
subjects affected / exposed	0 / 49 (0.00%)	0 / 123 (0.00%)	0 / 155 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
ACCIDENTAL OVERDOSE			
subjects affected / exposed	2 / 49 (4.08%)	3 / 123 (2.44%)	0 / 155 (0.00%)
occurrences (all)	2	3	0
FALL			
subjects affected / exposed	0 / 49 (0.00%)	0 / 123 (0.00%)	0 / 155 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
HEADACHE			
subjects affected / exposed	4 / 49 (8.16%)	8 / 123 (6.50%)	4 / 155 (2.58%)
occurrences (all)	4	9	4
Blood and lymphatic system disorders			
ANAEMIA			
subjects affected / exposed	3 / 49 (6.12%)	1 / 123 (0.81%)	9 / 155 (5.81%)
occurrences (all)	3	1	9
LYMPHOPENIA			
subjects affected / exposed	0 / 49 (0.00%)	1 / 123 (0.81%)	1 / 155 (0.65%)
occurrences (all)	0	1	1
Ear and labyrinth disorders			
CERUMEN IMPACTION			
subjects affected / exposed	0 / 49 (0.00%)	0 / 123 (0.00%)	0 / 155 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
CATARACT			

subjects affected / exposed	0 / 49 (0.00%)	0 / 123 (0.00%)	0 / 155 (0.00%)
occurrences (all)	0	0	0
VISUAL IMPAIRMENT			
subjects affected / exposed	0 / 49 (0.00%)	0 / 123 (0.00%)	0 / 155 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
ABDOMINAL DISTENSION			
subjects affected / exposed	1 / 49 (2.04%)	1 / 123 (0.81%)	0 / 155 (0.00%)
occurrences (all)	1	1	0
ABDOMINAL PAIN			
subjects affected / exposed	1 / 49 (2.04%)	3 / 123 (2.44%)	1 / 155 (0.65%)
occurrences (all)	1	3	1
ABDOMINAL TENDERNESS			
subjects affected / exposed	0 / 49 (0.00%)	3 / 123 (2.44%)	0 / 155 (0.00%)
occurrences (all)	0	3	0
APHTHOUS ULCER			
subjects affected / exposed	0 / 49 (0.00%)	0 / 123 (0.00%)	0 / 155 (0.00%)
occurrences (all)	0	0	0
COLITIS ULCERATIVE			
subjects affected / exposed	2 / 49 (4.08%)	3 / 123 (2.44%)	16 / 155 (10.32%)
occurrences (all)	2	3	16
CONSTIPATION			
subjects affected / exposed	0 / 49 (0.00%)	1 / 123 (0.81%)	0 / 155 (0.00%)
occurrences (all)	0	1	0
DIARRHOEA			
subjects affected / exposed	0 / 49 (0.00%)	2 / 123 (1.63%)	0 / 155 (0.00%)
occurrences (all)	0	2	0
NAUSEA			
subjects affected / exposed	1 / 49 (2.04%)	0 / 123 (0.00%)	3 / 155 (1.94%)
occurrences (all)	1	0	3
PERIANAL ERYTHEMA			
subjects affected / exposed	0 / 49 (0.00%)	0 / 123 (0.00%)	0 / 155 (0.00%)
occurrences (all)	0	0	0
VOMITING			
subjects affected / exposed	1 / 49 (2.04%)	0 / 123 (0.00%)	0 / 155 (0.00%)
occurrences (all)	1	0	0

Skin and subcutaneous tissue disorders			
ACNE			
subjects affected / exposed	1 / 49 (2.04%)	6 / 123 (4.88%)	1 / 155 (0.65%)
occurrences (all)	1	6	1
DERMATITIS ACNEIFORM			
subjects affected / exposed	0 / 49 (0.00%)	0 / 123 (0.00%)	1 / 155 (0.65%)
occurrences (all)	0	0	1
PRURITUS			
subjects affected / exposed	0 / 49 (0.00%)	0 / 123 (0.00%)	4 / 155 (2.58%)
occurrences (all)	0	0	4
RASH			
subjects affected / exposed	0 / 49 (0.00%)	1 / 123 (0.81%)	1 / 155 (0.65%)
occurrences (all)	0	1	1
ROSACEA			
subjects affected / exposed	0 / 49 (0.00%)	0 / 123 (0.00%)	0 / 155 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
ARTHRALGIA			
subjects affected / exposed	0 / 49 (0.00%)	3 / 123 (2.44%)	7 / 155 (4.52%)
occurrences (all)	0	3	7
BACK PAIN			
subjects affected / exposed	0 / 49 (0.00%)	1 / 123 (0.81%)	1 / 155 (0.65%)
occurrences (all)	0	1	1
BURSITIS			
subjects affected / exposed	1 / 49 (2.04%)	0 / 123 (0.00%)	0 / 155 (0.00%)
occurrences (all)	1	0	0
MUSCLE SPASMS			
subjects affected / exposed	1 / 49 (2.04%)	2 / 123 (1.63%)	1 / 155 (0.65%)
occurrences (all)	1	2	1
MUSCULOSKELETAL PAIN			
subjects affected / exposed	0 / 49 (0.00%)	0 / 123 (0.00%)	0 / 155 (0.00%)
occurrences (all)	0	0	0
OSTEOPENIA			
subjects affected / exposed	0 / 49 (0.00%)	0 / 123 (0.00%)	1 / 155 (0.65%)
occurrences (all)	0	0	1
PAIN IN EXTREMITY			

subjects affected / exposed	0 / 49 (0.00%)	2 / 123 (1.63%)	1 / 155 (0.65%)
occurrences (all)	0	2	1
Infections and infestations			
BRONCHITIS			
subjects affected / exposed	0 / 49 (0.00%)	0 / 123 (0.00%)	0 / 155 (0.00%)
occurrences (all)	0	0	0
CYSTITIS			
subjects affected / exposed	0 / 49 (0.00%)	0 / 123 (0.00%)	0 / 155 (0.00%)
occurrences (all)	0	0	0
EAR INFECTION			
subjects affected / exposed	0 / 49 (0.00%)	0 / 123 (0.00%)	2 / 155 (1.29%)
occurrences (all)	0	0	2
HERPES ZOSTER			
subjects affected / exposed	0 / 49 (0.00%)	0 / 123 (0.00%)	0 / 155 (0.00%)
occurrences (all)	0	0	0
INFLUENZA			
subjects affected / exposed	0 / 49 (0.00%)	3 / 123 (2.44%)	1 / 155 (0.65%)
occurrences (all)	0	3	1
NASOPHARYNGITIS			
subjects affected / exposed	3 / 49 (6.12%)	4 / 123 (3.25%)	6 / 155 (3.87%)
occurrences (all)	3	4	6
ORAL HERPES			
subjects affected / exposed	0 / 49 (0.00%)	1 / 123 (0.81%)	0 / 155 (0.00%)
occurrences (all)	0	1	0
PULPITIS DENTAL			
subjects affected / exposed	0 / 49 (0.00%)	0 / 123 (0.00%)	0 / 155 (0.00%)
occurrences (all)	0	0	0
RESPIRATORY TRACT INFECTION VIRAL			
subjects affected / exposed	0 / 49 (0.00%)	0 / 123 (0.00%)	1 / 155 (0.65%)
occurrences (all)	0	0	1
SKIN CANDIDA			
subjects affected / exposed	0 / 49 (0.00%)	0 / 123 (0.00%)	0 / 155 (0.00%)
occurrences (all)	0	0	0
UPPER RESPIRATORY TRACT INFECTION			

subjects affected / exposed	4 / 49 (8.16%)	6 / 123 (4.88%)	6 / 155 (3.87%)
occurrences (all)	4	7	6
URINARY TRACT INFECTION			
subjects affected / exposed	0 / 49 (0.00%)	1 / 123 (0.81%)	3 / 155 (1.94%)
occurrences (all)	0	1	3
VAGINAL INFECTION			
subjects affected / exposed	0 / 49 (0.00%)	0 / 123 (0.00%)	0 / 155 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
DECREASED APPETITE			
subjects affected / exposed	1 / 49 (2.04%)	0 / 123 (0.00%)	1 / 155 (0.65%)
occurrences (all)	1	0	1
HYPOKALAEMIA			
subjects affected / exposed	0 / 49 (0.00%)	0 / 123 (0.00%)	0 / 155 (0.00%)
occurrences (all)	0	0	0
IRON DEFICIENCY			
subjects affected / exposed	0 / 49 (0.00%)	1 / 123 (0.81%)	2 / 155 (1.29%)
occurrences (all)	0	1	2

Non-serious adverse events	SS3: Upadacitinib 15 mg	SS3: Placebo	SS2: Upadacitinib 45 mg/Upadacitinib 45 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	181 / 323 (56.04%)	216 / 385 (56.10%)	17 / 59 (28.81%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
MALIGNANT MELANOMA			
subjects affected / exposed	0 / 323 (0.00%)	0 / 385 (0.00%)	0 / 59 (0.00%)
occurrences (all)	0	0	0
MELANOCYTIC NAEVUS			
subjects affected / exposed	1 / 323 (0.31%)	0 / 385 (0.00%)	0 / 59 (0.00%)
occurrences (all)	1	0	0
SKIN PAPILLOMA			
subjects affected / exposed	0 / 323 (0.00%)	0 / 385 (0.00%)	0 / 59 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
INFLUENZA LIKE ILLNESS			

subjects affected / exposed	0 / 323 (0.00%)	2 / 385 (0.52%)	0 / 59 (0.00%)
occurrences (all)	0	2	0
PSEUDOPOLYP			
subjects affected / exposed	0 / 323 (0.00%)	0 / 385 (0.00%)	0 / 59 (0.00%)
occurrences (all)	0	0	0
PYREXIA			
subjects affected / exposed	10 / 323 (3.10%)	11 / 385 (2.86%)	0 / 59 (0.00%)
occurrences (all)	10	13	0
Respiratory, thoracic and mediastinal disorders			
ASTHMA			
subjects affected / exposed	1 / 323 (0.31%)	0 / 385 (0.00%)	0 / 59 (0.00%)
occurrences (all)	1	0	0
COUGH			
subjects affected / exposed	6 / 323 (1.86%)	6 / 385 (1.56%)	1 / 59 (1.69%)
occurrences (all)	6	6	1
NASAL CONGESTION			
subjects affected / exposed	1 / 323 (0.31%)	3 / 385 (0.78%)	0 / 59 (0.00%)
occurrences (all)	1	3	0
OROPHARYNGEAL PAIN			
subjects affected / exposed	5 / 323 (1.55%)	6 / 385 (1.56%)	0 / 59 (0.00%)
occurrences (all)	5	6	0
PULMONARY MASS			
subjects affected / exposed	0 / 323 (0.00%)	0 / 385 (0.00%)	0 / 59 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
DEPRESSED MOOD			
subjects affected / exposed	0 / 323 (0.00%)	0 / 385 (0.00%)	0 / 59 (0.00%)
occurrences (all)	0	0	0
IRRITABILITY			
subjects affected / exposed	1 / 323 (0.31%)	2 / 385 (0.52%)	0 / 59 (0.00%)
occurrences (all)	1	2	0
Investigations			
BLOOD CREATINE PHOSPHOKINASE INCREASED			
subjects affected / exposed	20 / 323 (6.19%)	7 / 385 (1.82%)	4 / 59 (6.78%)
occurrences (all)	21	7	4
HAEMOGLOBIN DECREASED			

subjects affected / exposed	2 / 323 (0.62%)	1 / 385 (0.26%)	1 / 59 (1.69%)
occurrences (all)	2	1	1
LYMPHOCYTE COUNT DECREASED			
subjects affected / exposed	6 / 323 (1.86%)	3 / 385 (0.78%)	1 / 59 (1.69%)
occurrences (all)	7	3	1
LYMPHOCYTE COUNT INCREASED			
subjects affected / exposed	1 / 323 (0.31%)	1 / 385 (0.26%)	0 / 59 (0.00%)
occurrences (all)	1	1	0
Injury, poisoning and procedural complications			
ACCIDENTAL OVERDOSE			
subjects affected / exposed	0 / 323 (0.00%)	0 / 385 (0.00%)	0 / 59 (0.00%)
occurrences (all)	0	0	0
FALL			
subjects affected / exposed	0 / 323 (0.00%)	0 / 385 (0.00%)	0 / 59 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
HEADACHE			
subjects affected / exposed	10 / 323 (3.10%)	16 / 385 (4.16%)	2 / 59 (3.39%)
occurrences (all)	10	16	3
Blood and lymphatic system disorders			
ANAEMIA			
subjects affected / exposed	11 / 323 (3.41%)	20 / 385 (5.19%)	1 / 59 (1.69%)
occurrences (all)	12	24	1
LYMPHOPENIA			
subjects affected / exposed	3 / 323 (0.93%)	3 / 385 (0.78%)	0 / 59 (0.00%)
occurrences (all)	4	4	0
Ear and labyrinth disorders			
CERUMEN IMPACTION			
subjects affected / exposed	0 / 323 (0.00%)	0 / 385 (0.00%)	0 / 59 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
CATARACT			
subjects affected / exposed	1 / 323 (0.31%)	2 / 385 (0.52%)	0 / 59 (0.00%)
occurrences (all)	1	2	0
VISUAL IMPAIRMENT			

subjects affected / exposed	0 / 323 (0.00%)	0 / 385 (0.00%)	0 / 59 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
ABDOMINAL DISTENSION			
subjects affected / exposed	2 / 323 (0.62%)	2 / 385 (0.52%)	0 / 59 (0.00%)
occurrences (all)	2	2	0
ABDOMINAL PAIN			
subjects affected / exposed	8 / 323 (2.48%)	8 / 385 (2.08%)	2 / 59 (3.39%)
occurrences (all)	9	8	2
ABDOMINAL TENDERNESS			
subjects affected / exposed	0 / 323 (0.00%)	0 / 385 (0.00%)	0 / 59 (0.00%)
occurrences (all)	0	0	0
APHTHOUS ULCER			
subjects affected / exposed	1 / 323 (0.31%)	3 / 385 (0.78%)	0 / 59 (0.00%)
occurrences (all)	1	4	0
COLITIS ULCERATIVE			
subjects affected / exposed	40 / 323 (12.38%)	101 / 385 (26.23%)	1 / 59 (1.69%)
occurrences (all)	47	110	1
CONSTIPATION			
subjects affected / exposed	4 / 323 (1.24%)	2 / 385 (0.52%)	0 / 59 (0.00%)
occurrences (all)	5	2	0
DIARRHOEA			
subjects affected / exposed	2 / 323 (0.62%)	4 / 385 (1.04%)	0 / 59 (0.00%)
occurrences (all)	2	4	0
NAUSEA			
subjects affected / exposed	6 / 323 (1.86%)	6 / 385 (1.56%)	0 / 59 (0.00%)
occurrences (all)	6	7	0
PERIANAL ERYTHEMA			
subjects affected / exposed	0 / 323 (0.00%)	0 / 385 (0.00%)	0 / 59 (0.00%)
occurrences (all)	0	0	0
VOMITING			
subjects affected / exposed	1 / 323 (0.31%)	1 / 385 (0.26%)	0 / 59 (0.00%)
occurrences (all)	1	1	0
Skin and subcutaneous tissue disorders			
ACNE			

subjects affected / exposed	7 / 323 (2.17%)	8 / 385 (2.08%)	1 / 59 (1.69%)
occurrences (all)	8	8	1
DERMATITIS ACNEIFORM			
subjects affected / exposed	1 / 323 (0.31%)	0 / 385 (0.00%)	0 / 59 (0.00%)
occurrences (all)	1	0	0
PRURITUS			
subjects affected / exposed	2 / 323 (0.62%)	9 / 385 (2.34%)	0 / 59 (0.00%)
occurrences (all)	2	12	0
RASH			
subjects affected / exposed	9 / 323 (2.79%)	14 / 385 (3.64%)	1 / 59 (1.69%)
occurrences (all)	9	14	1
ROSACEA			
subjects affected / exposed	4 / 323 (1.24%)	1 / 385 (0.26%)	0 / 59 (0.00%)
occurrences (all)	4	1	0
Musculoskeletal and connective tissue disorders			
ARTHRALGIA			
subjects affected / exposed	19 / 323 (5.88%)	28 / 385 (7.27%)	0 / 59 (0.00%)
occurrences (all)	19	28	0
BACK PAIN			
subjects affected / exposed	11 / 323 (3.41%)	15 / 385 (3.90%)	0 / 59 (0.00%)
occurrences (all)	11	15	0
BURSITIS			
subjects affected / exposed	0 / 323 (0.00%)	0 / 385 (0.00%)	0 / 59 (0.00%)
occurrences (all)	0	0	0
MUSCLE SPASMS			
subjects affected / exposed	0 / 323 (0.00%)	0 / 385 (0.00%)	0 / 59 (0.00%)
occurrences (all)	0	0	0
MUSCULOSKELETAL PAIN			
subjects affected / exposed	2 / 323 (0.62%)	3 / 385 (0.78%)	0 / 59 (0.00%)
occurrences (all)	2	3	0
OSTEOPENIA			
subjects affected / exposed	1 / 323 (0.31%)	0 / 385 (0.00%)	0 / 59 (0.00%)
occurrences (all)	1	0	0
PAIN IN EXTREMITY			

subjects affected / exposed	1 / 323 (0.31%)	4 / 385 (1.04%)	0 / 59 (0.00%)
occurrences (all)	1	4	0
Infections and infestations			
BRONCHITIS			
subjects affected / exposed	4 / 323 (1.24%)	4 / 385 (1.04%)	0 / 59 (0.00%)
occurrences (all)	4	4	0
CYSTITIS			
subjects affected / exposed	3 / 323 (0.93%)	1 / 385 (0.26%)	0 / 59 (0.00%)
occurrences (all)	3	1	0
EAR INFECTION			
subjects affected / exposed	3 / 323 (0.93%)	0 / 385 (0.00%)	1 / 59 (1.69%)
occurrences (all)	3	0	1
HERPES ZOSTER			
subjects affected / exposed	10 / 323 (3.10%)	0 / 385 (0.00%)	3 / 59 (5.08%)
occurrences (all)	10	0	3
INFLUENZA			
subjects affected / exposed	10 / 323 (3.10%)	4 / 385 (1.04%)	0 / 59 (0.00%)
occurrences (all)	10	4	0
NASOPHARYNGITIS			
subjects affected / exposed	31 / 323 (9.60%)	27 / 385 (7.01%)	1 / 59 (1.69%)
occurrences (all)	40	28	1
ORAL HERPES			
subjects affected / exposed	6 / 323 (1.86%)	7 / 385 (1.82%)	0 / 59 (0.00%)
occurrences (all)	8	8	0
PULPITIS DENTAL			
subjects affected / exposed	1 / 323 (0.31%)	0 / 385 (0.00%)	0 / 59 (0.00%)
occurrences (all)	1	0	0
RESPIRATORY TRACT INFECTION VIRAL			
subjects affected / exposed	4 / 323 (1.24%)	1 / 385 (0.26%)	0 / 59 (0.00%)
occurrences (all)	4	1	0
SKIN CANDIDA			
subjects affected / exposed	0 / 323 (0.00%)	0 / 385 (0.00%)	0 / 59 (0.00%)
occurrences (all)	0	0	0
UPPER RESPIRATORY TRACT INFECTION			

subjects affected / exposed	19 / 323 (5.88%)	11 / 385 (2.86%)	0 / 59 (0.00%)
occurrences (all)	20	12	0
URINARY TRACT INFECTION			
subjects affected / exposed	10 / 323 (3.10%)	9 / 385 (2.34%)	0 / 59 (0.00%)
occurrences (all)	13	10	0
VAGINAL INFECTION			
subjects affected / exposed	0 / 323 (0.00%)	0 / 385 (0.00%)	0 / 59 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
DECREASED APPETITE			
subjects affected / exposed	1 / 323 (0.31%)	2 / 385 (0.52%)	0 / 59 (0.00%)
occurrences (all)	1	2	0
HYPOKALAEMIA			
subjects affected / exposed	3 / 323 (0.93%)	5 / 385 (1.30%)	0 / 59 (0.00%)
occurrences (all)	3	5	0
IRON DEFICIENCY			
subjects affected / exposed	0 / 323 (0.00%)	2 / 385 (0.52%)	0 / 59 (0.00%)
occurrences (all)	0	2	0

Non-serious adverse events	SS2: Upadacitinib 45 mg	SS2: Placebo/Upadacitinib 45 mg	SS3: Upadacitinib 30 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	121 / 319 (37.93%)	36 / 85 (42.35%)	166 / 316 (52.53%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
MALIGNANT MELANOMA			
subjects affected / exposed	0 / 319 (0.00%)	0 / 85 (0.00%)	0 / 316 (0.00%)
occurrences (all)	0	0	0
MELANOCYTIC NAEVUS			
subjects affected / exposed	0 / 319 (0.00%)	0 / 85 (0.00%)	0 / 316 (0.00%)
occurrences (all)	0	0	0
SKIN PAPILLOMA			
subjects affected / exposed	2 / 319 (0.63%)	0 / 85 (0.00%)	1 / 316 (0.32%)
occurrences (all)	2	0	2
General disorders and administration site conditions			
INFLUENZA LIKE ILLNESS			

subjects affected / exposed	0 / 319 (0.00%)	0 / 85 (0.00%)	2 / 316 (0.63%)
occurrences (all)	0	0	2
PSEUDOPOLYP			
subjects affected / exposed	0 / 319 (0.00%)	0 / 85 (0.00%)	0 / 316 (0.00%)
occurrences (all)	0	0	0
PYREXIA			
subjects affected / exposed	8 / 319 (2.51%)	6 / 85 (7.06%)	18 / 316 (5.70%)
occurrences (all)	8	7	19
Respiratory, thoracic and mediastinal disorders			
ASTHMA			
subjects affected / exposed	0 / 319 (0.00%)	0 / 85 (0.00%)	1 / 316 (0.32%)
occurrences (all)	0	0	1
COUGH			
subjects affected / exposed	5 / 319 (1.57%)	2 / 85 (2.35%)	4 / 316 (1.27%)
occurrences (all)	5	2	5
NASAL CONGESTION			
subjects affected / exposed	0 / 319 (0.00%)	1 / 85 (1.18%)	2 / 316 (0.63%)
occurrences (all)	0	1	2
OROPHARYNGEAL PAIN			
subjects affected / exposed	6 / 319 (1.88%)	1 / 85 (1.18%)	8 / 316 (2.53%)
occurrences (all)	6	1	8
PULMONARY MASS			
subjects affected / exposed	1 / 319 (0.31%)	0 / 85 (0.00%)	0 / 316 (0.00%)
occurrences (all)	1	0	0
Psychiatric disorders			
DEPRESSED MOOD			
subjects affected / exposed	0 / 319 (0.00%)	0 / 85 (0.00%)	1 / 316 (0.32%)
occurrences (all)	0	0	1
IRRITABILITY			
subjects affected / exposed	0 / 319 (0.00%)	0 / 85 (0.00%)	0 / 316 (0.00%)
occurrences (all)	0	0	0
Investigations			
BLOOD CREATINE PHOSPHOKINASE INCREASED			
subjects affected / exposed	16 / 319 (5.02%)	5 / 85 (5.88%)	21 / 316 (6.65%)
occurrences (all)	18	5	25
HAEMOGLOBIN DECREASED			

subjects affected / exposed	0 / 319 (0.00%)	0 / 85 (0.00%)	2 / 316 (0.63%)
occurrences (all)	0	0	3
LYMPHOCYTE COUNT DECREASED			
subjects affected / exposed	3 / 319 (0.94%)	0 / 85 (0.00%)	5 / 316 (1.58%)
occurrences (all)	3	0	6
LYMPHOCYTE COUNT INCREASED			
subjects affected / exposed	3 / 319 (0.94%)	0 / 85 (0.00%)	2 / 316 (0.63%)
occurrences (all)	3	0	2
Injury, poisoning and procedural complications			
ACCIDENTAL OVERDOSE			
subjects affected / exposed	0 / 319 (0.00%)	0 / 85 (0.00%)	0 / 316 (0.00%)
occurrences (all)	0	0	0
FALL			
subjects affected / exposed	0 / 319 (0.00%)	0 / 85 (0.00%)	1 / 316 (0.32%)
occurrences (all)	0	0	1
Nervous system disorders			
HEADACHE			
subjects affected / exposed	13 / 319 (4.08%)	4 / 85 (4.71%)	14 / 316 (4.43%)
occurrences (all)	16	4	16
Blood and lymphatic system disorders			
ANAEMIA			
subjects affected / exposed	8 / 319 (2.51%)	5 / 85 (5.88%)	7 / 316 (2.22%)
occurrences (all)	8	5	7
LYMPHOPENIA			
subjects affected / exposed	6 / 319 (1.88%)	0 / 85 (0.00%)	1 / 316 (0.32%)
occurrences (all)	7	0	1
Ear and labyrinth disorders			
CERUMEN IMPACTION			
subjects affected / exposed	0 / 319 (0.00%)	0 / 85 (0.00%)	0 / 316 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
CATARACT			
subjects affected / exposed	1 / 319 (0.31%)	1 / 85 (1.18%)	2 / 316 (0.63%)
occurrences (all)	1	1	2
VISUAL IMPAIRMENT			

subjects affected / exposed	0 / 319 (0.00%)	0 / 85 (0.00%)	0 / 316 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
ABDOMINAL DISTENSION			
subjects affected / exposed	3 / 319 (0.94%)	1 / 85 (1.18%)	5 / 316 (1.58%)
occurrences (all)	4	1	5
ABDOMINAL PAIN			
subjects affected / exposed	4 / 319 (1.25%)	1 / 85 (1.18%)	5 / 316 (1.58%)
occurrences (all)	5	1	5
ABDOMINAL TENDERNESS			
subjects affected / exposed	0 / 319 (0.00%)	0 / 85 (0.00%)	2 / 316 (0.63%)
occurrences (all)	0	0	2
APHTHOUS ULCER			
subjects affected / exposed	2 / 319 (0.63%)	0 / 85 (0.00%)	4 / 316 (1.27%)
occurrences (all)	2	0	4
COLITIS ULCERATIVE			
subjects affected / exposed	1 / 319 (0.31%)	2 / 85 (2.35%)	24 / 316 (7.59%)
occurrences (all)	1	2	25
CONSTIPATION			
subjects affected / exposed	6 / 319 (1.88%)	2 / 85 (2.35%)	7 / 316 (2.22%)
occurrences (all)	6	2	7
DIARRHOEA			
subjects affected / exposed	1 / 319 (0.31%)	0 / 85 (0.00%)	2 / 316 (0.63%)
occurrences (all)	1	0	2
NAUSEA			
subjects affected / exposed	4 / 319 (1.25%)	1 / 85 (1.18%)	7 / 316 (2.22%)
occurrences (all)	5	1	7
PERIANAL ERYTHEMA			
subjects affected / exposed	0 / 319 (0.00%)	0 / 85 (0.00%)	0 / 316 (0.00%)
occurrences (all)	0	0	0
VOMITING			
subjects affected / exposed	2 / 319 (0.63%)	1 / 85 (1.18%)	3 / 316 (0.95%)
occurrences (all)	2	1	3
Skin and subcutaneous tissue disorders			
ACNE			

subjects affected / exposed	15 / 319 (4.70%)	2 / 85 (2.35%)	11 / 316 (3.48%)
occurrences (all)	15	2	14
DERMATITIS ACNEIFORM			
subjects affected / exposed	4 / 319 (1.25%)	0 / 85 (0.00%)	0 / 316 (0.00%)
occurrences (all)	4	0	0
PRURITUS			
subjects affected / exposed	1 / 319 (0.31%)	0 / 85 (0.00%)	2 / 316 (0.63%)
occurrences (all)	1	0	2
RASH			
subjects affected / exposed	8 / 319 (2.51%)	0 / 85 (0.00%)	14 / 316 (4.43%)
occurrences (all)	8	0	15
ROSACEA			
subjects affected / exposed	0 / 319 (0.00%)	0 / 85 (0.00%)	1 / 316 (0.32%)
occurrences (all)	0	0	1
Musculoskeletal and connective tissue disorders			
ARTHRALGIA			
subjects affected / exposed	5 / 319 (1.57%)	0 / 85 (0.00%)	8 / 316 (2.53%)
occurrences (all)	5	0	9
BACK PAIN			
subjects affected / exposed	3 / 319 (0.94%)	1 / 85 (1.18%)	4 / 316 (1.27%)
occurrences (all)	3	1	4
BURSITIS			
subjects affected / exposed	0 / 319 (0.00%)	0 / 85 (0.00%)	1 / 316 (0.32%)
occurrences (all)	0	0	1
MUSCLE SPASMS			
subjects affected / exposed	1 / 319 (0.31%)	2 / 85 (2.35%)	0 / 316 (0.00%)
occurrences (all)	1	2	0
MUSCULOSKELETAL PAIN			
subjects affected / exposed	1 / 319 (0.31%)	0 / 85 (0.00%)	1 / 316 (0.32%)
occurrences (all)	1	0	1
OSTEOPENIA			
subjects affected / exposed	0 / 319 (0.00%)	0 / 85 (0.00%)	2 / 316 (0.63%)
occurrences (all)	0	0	2
PAIN IN EXTREMITY			

subjects affected / exposed	1 / 319 (0.31%)	2 / 85 (2.35%)	6 / 316 (1.90%)
occurrences (all)	1	2	6
Infections and infestations			
BRONCHITIS			
subjects affected / exposed	0 / 319 (0.00%)	2 / 85 (2.35%)	2 / 316 (0.63%)
occurrences (all)	0	2	2
CYSTITIS			
subjects affected / exposed	1 / 319 (0.31%)	1 / 85 (1.18%)	2 / 316 (0.63%)
occurrences (all)	1	1	3
EAR INFECTION			
subjects affected / exposed	0 / 319 (0.00%)	0 / 85 (0.00%)	3 / 316 (0.95%)
occurrences (all)	0	0	3
HERPES ZOSTER			
subjects affected / exposed	1 / 319 (0.31%)	5 / 85 (5.88%)	15 / 316 (4.75%)
occurrences (all)	1	5	16
INFLUENZA			
subjects affected / exposed	3 / 319 (0.94%)	1 / 85 (1.18%)	8 / 316 (2.53%)
occurrences (all)	3	1	10
NASOPHARYNGITIS			
subjects affected / exposed	15 / 319 (4.70%)	4 / 85 (4.71%)	30 / 316 (9.49%)
occurrences (all)	16	4	43
ORAL HERPES			
subjects affected / exposed	4 / 319 (1.25%)	2 / 85 (2.35%)	9 / 316 (2.85%)
occurrences (all)	4	2	11
PULPITIS DENTAL			
subjects affected / exposed	0 / 319 (0.00%)	0 / 85 (0.00%)	1 / 316 (0.32%)
occurrences (all)	0	0	1
RESPIRATORY TRACT INFECTION VIRAL			
subjects affected / exposed	1 / 319 (0.31%)	0 / 85 (0.00%)	0 / 316 (0.00%)
occurrences (all)	1	0	0
SKIN CANDIDA			
subjects affected / exposed	0 / 319 (0.00%)	0 / 85 (0.00%)	0 / 316 (0.00%)
occurrences (all)	0	0	0
UPPER RESPIRATORY TRACT INFECTION			

subjects affected / exposed	8 / 319 (2.51%)	0 / 85 (0.00%)	15 / 316 (4.75%)
occurrences (all)	9	0	18
URINARY TRACT INFECTION			
subjects affected / exposed	3 / 319 (0.94%)	2 / 85 (2.35%)	4 / 316 (1.27%)
occurrences (all)	3	3	6
VAGINAL INFECTION			
subjects affected / exposed	0 / 319 (0.00%)	0 / 85 (0.00%)	0 / 316 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
DECREASED APPETITE			
subjects affected / exposed	0 / 319 (0.00%)	0 / 85 (0.00%)	0 / 316 (0.00%)
occurrences (all)	0	0	0
HYPOKALAEMIA			
subjects affected / exposed	1 / 319 (0.31%)	0 / 85 (0.00%)	0 / 316 (0.00%)
occurrences (all)	1	0	0
IRON DEFICIENCY			
subjects affected / exposed	0 / 319 (0.00%)	0 / 85 (0.00%)	1 / 316 (0.32%)
occurrences (all)	0	0	1

Non-serious adverse events	SS3: Upadacitinib 7.5 mg		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	18 / 20 (90.00%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
MALIGNANT MELANOMA			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
MELANOCYTIC NAEVUS			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
SKIN PAPILLOMA			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
General disorders and administration site conditions			
INFLUENZA LIKE ILLNESS			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		

PSEUDOPOLYP			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
PYREXIA			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Respiratory, thoracic and mediastinal disorders			
ASTHMA			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	2		
COUGH			
subjects affected / exposed	2 / 20 (10.00%)		
occurrences (all)	2		
NASAL CONGESTION			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
OROPHARYNGEAL PAIN			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
PULMONARY MASS			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	2		
Psychiatric disorders			
DEPRESSED MOOD			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
IRRITABILITY			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Investigations			
BLOOD CREATINE PHOSPHOKINASE INCREASED			
subjects affected / exposed	0 / 20 (0.00%)		
occurrences (all)	0		
HAEMOGLOBIN DECREASED			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		

LYMPHOCYTE COUNT DECREASED subjects affected / exposed occurrences (all) LYMPHOCYTE COUNT INCREASED subjects affected / exposed occurrences (all)	 1 / 20 (5.00%) 1 1 / 20 (5.00%) 1		
Injury, poisoning and procedural complications ACCIDENTAL OVERDOSE subjects affected / exposed occurrences (all) FALL subjects affected / exposed occurrences (all)	 0 / 20 (0.00%) 0 1 / 20 (5.00%) 1		
Nervous system disorders HEADACHE subjects affected / exposed occurrences (all)	 0 / 20 (0.00%) 0		
Blood and lymphatic system disorders ANAEMIA subjects affected / exposed occurrences (all) LYMPHOPENIA subjects affected / exposed occurrences (all)	 1 / 20 (5.00%) 2 1 / 20 (5.00%) 1		
Ear and labyrinth disorders CERUMEN IMPACTION subjects affected / exposed occurrences (all)	 1 / 20 (5.00%) 1		
Eye disorders CATARACT subjects affected / exposed occurrences (all) VISUAL IMPAIRMENT subjects affected / exposed occurrences (all)	 1 / 20 (5.00%) 2 1 / 20 (5.00%) 1		
Gastrointestinal disorders			

ABDOMINAL DISTENSION			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
ABDOMINAL PAIN			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	2		
ABDOMINAL TENDERNESS			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
APHTHOUS ULCER			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
COLITIS ULCERATIVE			
subjects affected / exposed	3 / 20 (15.00%)		
occurrences (all)	3		
CONSTIPATION			
subjects affected / exposed	2 / 20 (10.00%)		
occurrences (all)	2		
DIARRHOEA			
subjects affected / exposed	2 / 20 (10.00%)		
occurrences (all)	2		
NAUSEA			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
PERIANAL ERYTHEMA			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
VOMITING			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Skin and subcutaneous tissue disorders			
ACNE			
subjects affected / exposed	0 / 20 (0.00%)		
occurrences (all)	0		
DERMATITIS ACNEIFORM			

subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
PRURITUS			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
RASH			
subjects affected / exposed	2 / 20 (10.00%)		
occurrences (all)	2		
ROSACEA			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Musculoskeletal and connective tissue disorders			
ARTHRALGIA			
subjects affected / exposed	4 / 20 (20.00%)		
occurrences (all)	5		
BACK PAIN			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
BURSITIS			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
MUSCLE SPASMS			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
MUSCULOSKELETAL PAIN			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
OSTEOPENIA			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
PAIN IN EXTREMITY			
subjects affected / exposed	0 / 20 (0.00%)		
occurrences (all)	0		
Infections and infestations			

BRONCHITIS				
subjects affected / exposed	1 / 20 (5.00%)			
occurrences (all)	1			
CYSTITIS				
subjects affected / exposed	1 / 20 (5.00%)			
occurrences (all)	1			
EAR INFECTION				
subjects affected / exposed	1 / 20 (5.00%)			
occurrences (all)	1			
HERPES ZOSTER				
subjects affected / exposed	0 / 20 (0.00%)			
occurrences (all)	0			
INFLUENZA				
subjects affected / exposed	1 / 20 (5.00%)			
occurrences (all)	2			
NASOPHARYNGITIS				
subjects affected / exposed	0 / 20 (0.00%)			
occurrences (all)	0			
ORAL HERPES				
subjects affected / exposed	1 / 20 (5.00%)			
occurrences (all)	1			
PULPITIS DENTAL				
subjects affected / exposed	1 / 20 (5.00%)			
occurrences (all)	1			
RESPIRATORY TRACT INFECTION VIRAL				
subjects affected / exposed	1 / 20 (5.00%)			
occurrences (all)	1			
SKIN CANDIDA				
subjects affected / exposed	1 / 20 (5.00%)			
occurrences (all)	1			
UPPER RESPIRATORY TRACT INFECTION				
subjects affected / exposed	2 / 20 (10.00%)			
occurrences (all)	2			
URINARY TRACT INFECTION				

subjects affected / exposed	2 / 20 (10.00%)		
occurrences (all)	2		
VAGINAL INFECTION			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Metabolism and nutrition disorders			
DECREASED APPETITE			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
HYPOKALAEMIA			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
IRON DEFICIENCY			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
29 September 2016	Global Amendment 1 ● Corrected the definition of clinical response per Adapted Mayo score ● Further clarified the timeframe of providing written informed consent as it relates to screening procedures ● Excluded subjects who received traditional Chinese medicines within 28 days prior to Baseline and during the study ● Added birth control requirements for US and Colombian women of childbearing potential and updated effective birth control methods ● Updated text regarding 30 day follow up pregnancy testing ● Updated requirements and acceptable procedures for chest x-ray and computed tomography (CT) scan ● Added the Ulcerative Colitis Symptoms Questionnaire (UC-SQ) ● Clarified that local testing for C-reactive protein was not allowed ● Removed proportion of subjects with stool frequency subscore (SFS) ≤ 1 and proportion of subjects with RBS of 0 as multiplicity-controlled secondary endpoints and included them as non-multiplicity-controlled secondary endpoints ● Added the justification of the assumption of 60% average induction response rates for upadacitinib doses in the sample size determination
10 October 2017	Global Amendment 2 ● Updated the percentage of subjects with a history of inadequate response or intolerance to biologic therapies expected to enroll in Substudy 1 from 50% to 75% ● Made several administrative changes
03 July 2018	Global Amendment 3 ● Updated the protocol to reflect the selected Phase 3 Substudy 2 induction dose of upadacitinib 45 mg and updated the study design for both induction and maintenance studies ● Added the Patient Global Impression of Change (PGIC) and Patient Global Impression of Severity (PGIS), added Cohort 3 in Substudy 3 for subjects treated with upadacitinib 45 mg for 16 weeks who achieved clinical response at the end of the Extended Treatment Period at Week 16 (Study M14-234 Substudy 2 Part 2 and Study M14-675 Part 2) ● Added the Extended Treatment Period in Substudy 2 to offer upadacitinib induction treatment to placebo clinical non-responders from 8-week induction therapy and evaluate the delayed clinical response in upadacitinib clinical non-responders from 8-week induction therapy ● Updated the sample size based on Phase 2b results ● Clarified that serious and disease-related events that are at least possibly related to study drug should also be reported in an expedited manner ● Reduced the number of pharmacokinetic samples ● Increased the duration of the maintenance period from 44 to 52 weeks ● Updated sample size calculations to reflect study design changes ● Added concomitant medication and rescue therapy wording ● Updated vaccine wording, removed requirement for male contraception ● Updated pregnancy test wording ● Updated the primary and secondary endpoints based on Food and Drug Administration guidance ● Modified the stratification factors ● Set maximum enrollment at 50% for non-bio-IR subjects, 30% for Bio-IR subjects who failed 3 or more biologics, and 20% non-bio-IR subjects who had exposure to biologics

24 April 2019	Global Amendment 4 Aligned Study M14-234 and Study M14-675 protocols by: • Updating the study objective to include the secondary objectives • Updating the benefit risk language, modifying Exclusion Criterion #14 to allow for undetectable biologic levels to be measured via a commercially available assay as an alternative to the washout period, based on regulatory feedback • Adding the country-specific requirements in the inclusion/exclusion criteria (included 16- and 17-year-old subjects, where locally permitted) • Adding, amending, and clarifying the study procedures • Adding justification for the use of placebo and further elaborating on the details of the DMC
29 April 2020	Global Amendment 5 • Updated wording about re-testing of exclusionary laboratory values during the screening period • Clarified intervals for testing biologic drug levels • Updated the criteria of clinical response for entering extended treatment period for subjects with missing Week 8 endoscopy when endoscopies cannot be performed due to the COVID-19 pandemic • Moved non-multiplicity-controlled secondary efficacy variables to additional efficacy variables • Added criteria for failure of ustekinumab treatment, added wording to define borderline serum pregnancy test results, clarified that live vaccines should not be administered for at least 30 days prior to or after study drug administration • Excluded subjects with a history of gastrointestinal (GI) perforation (perforation due to mechanical injury should not exclude a subject from participation) • Prohibited cytapheresis treatment for 60 days prior to screening • Excluded subjects with prior history of thrombotic events including deep vein thrombosis (DVT) and pulmonary embolism (PE) or known inherited conditions that predispose to hypercoagulability • Added wording about gastric banding/segmentation to make clear that it is not an exclusion • Added wording to the washout requirements for all biologic therapies • Removed wording about women classified as non-childbearing potential • Updated ECG review requirements • Updated the type of QuantiFERON TB test used • Updated toxicity management for aspartate aminotransferase (AST) and alanine aminotransferase (ALT), thrombosis events, and herpes zoster • Revised the Statistical and Analytical Plans in Protocol Section 8.1
31 July 2020	Global Amendment 6 • Updated information on the re-evaluation of the benefit and risk to subjects participating in the study • Updated wording to allow for changes in visits and procedures affected by the COVID-19 pandemic and associated changes in global/local regulations • Updated the wording on enrollment to note that enrollment is closed for Substudy 2
10 May 2021	Global Amendment 7 • Removed UC-related hospitalizations and UC-related surgeries from the multiplicity-controlled secondary endpoints • Clarified the primary ITT and Substudy 3 ITT populations • Added non-responder imputation (NRI) while incorporating multiple imputation to handle missing data due to COVID-19 (NRI-C) and mixed-effect model repeated measurement (MMRM) methods to ensure clarity of statistical analysis; clarified rescue handling approaches used • Added a subgroup analysis of the primary endpoint: Baseline aminosalicylate use (yes, no) • Clarified the analysis for continuous laboratory and vital sign parameters

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported