Clinical trial results:
A Phase 3, Randomized, Double-Blind, Study Comparing Upadacitinib (ABT-494) to Placebo in Subjects With Active Psoriatic Arthritis Who Have a History of Inadequate Response to at Least One Biologic Disease Modifying Anti-Rheumatic Drug (bDMARD)

Summary

EudraCT number	2016-004152-30
Trial protocol	BE CZ GB NL FR GR PT HU ES IT
Global end of trial date	30 September 2024

Results information

Result version number	v1 (current)
This version publication date	23 October 2025
First version publication date	23 October 2025

Trial information

Trial identification

Sponsor protocol code	M15-554

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03104374
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?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	30 September 2024
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	30 September 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

This was a Phase 3 multicenter study that included two periods. Period 1 was designed to compare the safety, tolerability, and efficacy of upadacitinib 15 mg once daily (QD) and 30 mg QD versus placebo in subjects with moderately to severely active Psoriatic Arthritis (PsA) who have an inadequate response to Biological Disease Modifying Anti-Rheumatic Drug (bDMARDs). Period 2 evaluated the safety, tolerability and efficacy of upadacitinib 15 mg QD and 30 mg QD in subjects with PsA who have completed Period 1.

Upon approval of protocol amendment 8, subjects receiving upadacitinib 30 mg QD in Period 2 were switched to upadacitinib 15 mg QD for the remainder of the study.

Protection of trial subjects:

Prior to the initiation of any screening or study-specific procedures, the investigator or his or her representative explained the nature of the study to the subject or his or her representative and answered all questions regarding this study. The informed consent statement was reviewed and signed and dated by the subject and/or the subject's legal guardian and the person who administered the informed consent. For subjects in Japan
only: if a subject is under 20 years of age, then the subject and their parent or legal guardian must voluntarily sign and date an informed consent.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 May 2017
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Belgium: 5
Country: Number of subjects enrolled	Brazil: 21
Country: Number of subjects enrolled	Canada: 17
Country: Number of subjects enrolled	Chile: 49
Country: Number of subjects enrolled	Czechia: 32
Country: Number of subjects enrolled	France: 8
Country: Number of subjects enrolled	Greece: 4
Country: Number of subjects enrolled	Hungary: 41
Country: Number of subjects enrolled	Italy: 10
Country: Number of subjects enrolled	Japan: 39
Country: Number of subjects enrolled	Netherlands: 1
Country: Number of subjects enrolled	New Zealand: 14

Country: Number of subjects enrolled	Portugal: 8
Country: Number of subjects enrolled	Puerto Rico: 30
Country: Number of subjects enrolled	Spain: 6
Country: Number of subjects enrolled	United Kingdom: 3
Country: Number of subjects enrolled	United States: 354
Worldwide total number of subjects	642
EEA total number of subjects	115

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	518
From 65 to 84 years	124
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Randomization was stratified by extent of psoriasis (≥ 3% body surface area [BSA] or < 3% BSA), current use of at least 1 DMARD, and number of prior failed biologic DMARDs (1 vs > 1), except for participants from Japan, for whom randomization was stratified by extent of psoriasis (≥ 3% BSA or < 3% BSA) only.

Pre-assignment

Screening details:

For assessment of the primary and secondary endpoints, all subjects from Period 1 who received Placebo for the first 24 weeks were pooled for data analysis.

Period 1

Period 1 title	Period 1 (Week 1 to Week 56)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Blinding implementation details:

When the last subject completed the last visit of Period 1 (Week 56), study drug assignment in both periods was unblinded to the sites, and subjects were dispensed study drug in an open-label fashion until the completion of Period 2.

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo / Upadacitinib 15 mg

Arm description:

Participants were randomized to receive placebo once daily up to Week 24 followed by Upadacitinib 15 mg once daily for Week 25 to Week 56.

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

Dosage and administration details:

It is administered once daily.

Investigational medicinal product name	Upadacitinib 15 mg
Investigational medicinal product code	
Other name	ABT-494
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

15 mg administered once daily.

Arm title	Placebo / Upadacitinib 30 mg

Arm description:

Participants were randomized to receive placebo once daily up to Week 24 followed by Upadacitinib 30 mg once daily for Week 25 to Week 56.

Arm type	Placebo

Investigational medicinal product name	Upadacitinib 30 mg
Investigational medicinal product code	
Other name	ABT-494
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

30 mg administered once daily.

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

Dosage and administration details:

It is administered once daily.

Arm title	Upadacitinib 15 mg

Arm description:

Participants randomized to receive Upadacitinib 15 mg once daily from Week 1 to Week 56 in Period 1.

Arm type	Experimental
Investigational medicinal product name	Upadacitinib 15 mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

It is administered once daily.

Arm title	Upadacitinib 30 mg

Arm description:

Subjects were randomized to receive Upadacitinib 30 mg once daily from Week 1 to Week 56 in Period 1. One randomized subject did not qualify per inclusion/exclusion criteria and discontinued prior to treatment. This subject is not included in the disposition table.

Arm type	Experimental
Investigational medicinal product name	Upadacitinib 30 mg
Investigational medicinal product code	
Other name	ABT-494
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

It is administered once daily.

Number of subjects in period 1[1]	Placebo / Upadacitinib 15 mg	Placebo / Upadacitinib 30 mg	Upadacitinib 15 mg
Started	106	106	211
Received Study Drug	106	106	211
Completed Week 24	81	92	192
Completed	69	77	167
Not completed	37	29	44

Consent withdrawn by subject	18	9	10
Adverse event, non-fatal	7	7	12
Not Specified	2	2	4
Lost to follow-up	4	4	6
Lack of efficacy	6	7	12

Number of subjects in period 1[1]	Upadacitinib 30 mg
Started	218
Received Study Drug	218
Completed Week 24	195
Completed	166
Not completed	52
Consent withdrawn by subject	17
Adverse event, non-fatal	14
Not Specified	7
Lost to follow-up	8
Lack of efficacy	6

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: One randomized subject did not qualify per inclusion/exclusion criteria and discontinued prior to treatment.

Period 2

Period 2 title	Period 2 (Week 56 to End-of-Study)
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Not blinded

Blinding implementation details:

In order to maintain the blind, the upadacitinib/placebo tablets provided for the study will be identical in appearance. The Interactive Response Technology (IRT) will provide access to unblinded subject treatment information in the case of medical emergency. When the last subject completed the last visit of Period 1 (Week 56), study drug assignment in both periods was unblinded to the sites, and subjects were dispensed study drug in an open-label fashion until the completion of Period 2.

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo / Upadacitinib 15 mg

Arm description:

In Period 1, participants who were randomized to receive placebo once daily up to Week 24 followed by Upadacitinib 15 mg once daily for Week 25 to Week 56. In Period 2, participants received Upadacitinib 15 mg from Week 56 to EOS.

Arm type	Experimental
Investigational medicinal product name	Upadacitinib 15 mg
Investigational medicinal product code	
Other name	ABT-494
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

15 mg by mouth once daily.

Arm title	Placebo / Upadacitinib 30 mg

Arm description:

In Period 1, participants who were randomized to receive placebo once daily up to Week 24 followed by Upadacitinib 30 mg once daily for Week 25 to Week 56. In Period 2, participants received Upadacitinib 30 mg from Week 56 to EOS. Participants in this group were switched to upadacitinib 15mg QD during Period 2 after week 116, following a protocol amendment

Arm type	Experimental
Investigational medicinal product name	Upadacitinib 30 mg
Investigational medicinal product code	
Other name	ABT-494
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

30 mg by mouth once daily.

Arm title	Upadacitinib 15 mg

Arm description:

In Period 2, participants in this arm continued to receive Upadacitinib 15 mg once daily from Week 56 to EOS.

Arm type	Experimental
Investigational medicinal product name	Upadacitinib 15 mg
Investigational medicinal product code	
Other name	ABT-494
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

15 mg by mouth once daily.

Arm title	Upadacitinib 30 mg

Arm description:

In Period 2, participants in this arm continued to receive Upadacitinib 30 mg once daily from Week 56 to EOS. Participants in this group were switched to upadacitinib 15mg QD during Period 2 after week 116, following a protocol amendment

Arm type	Experimental
Investigational medicinal product name	Upadacitinib 30 mg
Investigational medicinal product code	
Other name	ABT-494
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

30 mg by mouth once daily.

Number of subjects in period 2[2]	Placebo / Upadacitinib 15 mg	Placebo / Upadacitinib 30 mg	Upadacitinib 15 mg
Started	69	77	167
Switched to 15mg QD Upa Dosing in Per 2	0 [3]	28 [4]	0 [5]
Completed	55	55	131
Not completed	14	22	36
Consent withdrawn by subject	3	7	13
Adverse event, non-fatal	4	7	10
Not Specified	3	2	2
COVID-19 Infection	-	-	1
Lost to follow-up	2	2	3
Lack of efficacy	2	4	7

Number of subjects in period 2[2]	Upadacitinib 30 mg
Started	165
Switched to 15mg QD Upa Dosing in Per 2	59 [6]
Completed	126
Not completed	39
Consent withdrawn by subject	16
Adverse event, non-fatal	10
Not Specified	4
COVID-19 Infection	-
Lost to follow-up	5
Lack of efficacy	4

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: One participant who completed Period 1 did not enter Period 2.

[3] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: The milestone indicates the number of subjects who switched from 30mg QD to 15mg QD Upa Dosing in Period 2. This milestone is not applicable to this arm.

[4] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: The milestone indicates the number of subjects who switched from 30mg QD to 15mg QD Upa Dosing in Period 2.

[5] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: The milestone indicates the number of subjects who switched from 30mg QD to 15mg QD Upa Dosing in Period 2. This milestone is not applicable to this arm.

[6] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: The milestone indicates the number of subjects who switched from 30mg QD to 15mg QD

Upa Dosing in Period 2.

Baseline characteristics

Reporting groups	
Reporting group title	Placebo / Upadacitinib 15 mg
Reporting group description:	
Participants were randomized to receive placebo once daily up to Week 24 followed by Upadacitinib 15 mg once daily for Week 25 to Week 56.	
Reporting group title	Placebo / Upadacitinib 30 mg
Reporting group description:	
Participants were randomized to receive placebo once daily up to Week 24 followed by Upadacitinib 30 mg once daily for Week 25 to Week 56.	
Reporting group title	Upadacitinib 15 mg
Reporting group description:	
Participants randomized to receive Upadacitinib 15 mg once daily from Week 1 to Week 56 in Period 1.	
Reporting group title	Upadacitinib 30 mg
Reporting group description:	
Subjects were randomized to receive Upadacitinib 30 mg once daily from Week 1 to Week 56 in Period 1. One randomized subject did not qualify per inclusion/exclusion criteria and discontinued prior to treatment. This subject is not included in the disposition table.	

Reporting group values	Placebo / Upadacitinib 15 mg	Placebo / Upadacitinib 30 mg	Upadacitinib 15 mg
Number of subjects	106	106	211
Age categorical			
Units: Subjects			
In utero			
Preterm newborn infants (gestational age < 37 wks)			
Newborns (0-27 days)			
Infants and toddlers (28 days-23 months)			
Children (2-11 years)			
Adolescents (12-17 years)			
Adults (18-64 years)			
From 65-84 years			
85 years and over			
Age continuous			
Units: years			
arithmetic mean	52.3	56.0	53.0
standard deviation	± 11.65	± 11.16	± 12.02
Gender categorical			
Units: Subjects			
Female	57	63	113
Male	49	43	98
Extent of Psoriasis			
The extent of psoriasis was measured by the physician as the total body surface area (BSA) involved with psoriasis. For purposes of clinical estimation, the total surface of the participant's palm and five digits was assumed to be approximately equivalent to 1% of BSA.			
Units: Subjects			
< 3% BSA	41	40	81
≥ 3% BSA	65	66	130

Number of Prior Failed Biologic DMARDs			
Failed treatment with prior biologic DMARD is defined as lack of efficacy after a minimum 12 week duration of therapy. The zero category includes participants with intolerance but not inadequate response to a biologic DMARD.			
Units: Subjects			
bDMARDS (0)	12	6	16
bDMARD (1)	65	70	126
bDMARDS (2)	18	17	35
bDMARDS (≥ 3)	11	13	34
Duration of Psoriatic Arthritis Symptoms			
Units: years			
arithmetic mean	13.8	15.3	12.2
standard deviation	± 11.65	± 11.75	± 8.81
Duration of PsA Diagnosis			
Units: years			
arithmetic mean	10.3	11.6	9.6
standard deviation	± 9.97	± 10.68	± 8.36
Tender Joint Count			
A total of 68 joints were assessed for the presence or absence of tenderness.			
Units: joints			
arithmetic mean	26.1	24.4	24.9
standard deviation	± 18.01	± 17.27	± 17.27
Swollen Joint Count			
A total of 66 joints were assessed for the presence or absence of swelling.			
Units: joints			
arithmetic mean	11.8	12.3	11.3
standard deviation	± 9.04	± 8.70	± 8.19
Patient's Assessment of Pain			
Participants were asked to indicate the severity of their arthritis pain within the previous week on a numeric rating scale (NRS) from 0 to 10. A score of 0 indicates "no pain" and a score of 10 indicates "worst possible pain." Measure Analysis Population Description: Participants with available data			
Units: units on a scale			
arithmetic mean	6.6	6.5	6.4
standard deviation	± 2.06	± 2.20	± 2.13
Patient's Global Assessment of Disease Activity			
The participant was asked to rate their current psoriatic arthritis disease activity on a 0 to 10 NRS, where 0 indicates no disease activity and 10 indicates severe disease activity. Measure Analysis Population Description: Participants with available data			
Units: units on a scale			
arithmetic mean	7.0	6.7	6.8
standard deviation	± 1.84	± 2.23	± 1.91
Physician's Global Assessment of Disease Activity			
The physician rated the participant's current global psoriatic arthritis disease activity (independently from the participant's assessment) on a 0 to 10 NRS where 0 indicates no disease activity and 10 indicates severe disease activity.			
Units: units on a scale			
arithmetic mean	6.5	6.5	6.5
standard deviation	± 1.91	± 1.61	± 1.80
Health Assessment Questionnaire - Disability Index (HAQ-DI)			
The HAQ-DI is a patient-reported questionnaire that measures the degree of difficulty a person has in			

accomplishing tasks in 8 functional areas (dressing, arising, eating, walking, hygiene, reaching, gripping, and errands and chores) over the past week. Participants assessed their ability to do each task on a scale from 0 (without any difficulty) to 3 (unable to do). Scores were averaged to provide an overall score ranging from 0 to 3, where 0 represents no disability and 3 represents very severe, high-dependency disability. Analysis Population Description: Participants with available data.			
Units: units on a scale			
arithmetic mean	1.26	1.19	1.10
standard deviation	± 0.721	± 0.661	± 0.61
High-sensitivity Creactive Protein (hsCRP)			
Units: mg/L			
arithmetic mean	11.83	8.98	11.16
standard deviation	± 22.06	± 13.929	± 18.55

Reporting group values	Upadacitinib 30 mg	Total	
Number of subjects	218	641	
Age categorical			
Units: Subjects			
In utero		0	
Preterm newborn infants (gestational age < 37 wks)		0	
Newborns (0-27 days)		0	
Infants and toddlers (28 days-23 months)		0	
Children (2-11 years)		0	
Adolescents (12-17 years)		0	
Adults (18-64 years)		0	
From 65-84 years		0	
85 years and over		0	
Age continuous			
Units: years			
arithmetic mean	53.0		
standard deviation	± 11.94	-	
Gender categorical			
Units: Subjects			
Female	115	348	
Male	103	293	
Extent of Psoriasis			
The extent of psoriasis was measured by the physician as the total body surface area (BSA) involved with psoriasis. For purposes of clinical estimation, the total surface of the participant's palm and five digits was assumed to be approximately equivalent to 1% of BSA.			
Units: Subjects			
< 3% BSA	87	249	
≥ 3% BSA	131	392	
Number of Prior Failed Biologic DMARDs			
Failed treatment with prior biologic DMARD is defined as lack of efficacy after a minimum 12 week duration of therapy. The zero category includes participants with intolerance but not inadequate response to a biologic DMARD.			
Units: Subjects			
bDMARDS (0)	17	51	
bDMARD (1)	130	391	
bDMARDS (2)	46	116	
bDMARDS (≥ 3)	25	83	

Duration of Psoriatic Arthritis Symptoms			
Units: years			
arithmetic mean	13.3		
standard deviation	± 10.84	-	
Duration of PsA Diagnosis			
Units: years			
arithmetic mean	9.7		
standard deviation	± 8.71	-	
Tender Joint Count			
A total of 68 joints were assessed for the presence or absence of tenderness.			
Units: joints			
arithmetic mean	24.2		
standard deviation	± 15.87	-	
Swollen Joint Count			
A total of 66 joints were assessed for the presence or absence of swelling.			
Units: joints			
arithmetic mean	12.9		
standard deviation	± 9.41	-	
Patient's Assessment of Pain			
Participants were asked to indicate the severity of their arthritis pain within the previous week on a numeric rating scale (NRS) from 0 to 10. A score of 0 indicates "no pain" and a score of 10 indicates "worst possible pain." Measure Analysis Population Description: Participants with available data			
Units: units on a scale			
arithmetic mean	6.2		
standard deviation	± 2.21	-	
Patient's Global Assessment of Disease Activity			
The participant was asked to rate their current psoriatic arthritis disease activity on a 0 to 10 NRS, where 0 indicates no disease activity and 10 indicates severe disease activity. Measure Analysis Population Description: Participants with available data			
Units: units on a scale			
arithmetic mean	6.7		
standard deviation	± 2.15	-	
Physician's Global Assessment of Disease Activity			
The physician rated the participant's current global psoriatic arthritis disease activity (independently from the participant's assessment) on a 0 to 10 NRS where 0 indicates no disease activity and 10 indicates severe disease activity.			
Units: units on a scale			
arithmetic mean	6.6		
standard deviation	± 1.73	-	
Health Assessment Questionnaire - Disability Index (HAQ-DI)			
The HAQ-DI is a patient-reported questionnaire that measures the degree of difficulty a person has in accomplishing tasks in 8 functional areas (dressing, arising, eating, walking, hygiene, reaching, gripping, and errands and chores) over the past week. Participants assessed their ability to do each task on a scale from 0 (without any difficulty) to 3 (unable to do). Scores were averaged to provide an overall score ranging from 0 to 3, where 0 represents no disability and 3 represents very severe, high-dependency disability. Analysis Population Description: Participants with available data.			
Units: units on a scale			
arithmetic mean	1.19		
standard deviation	± 0.662	-	
High-sensitivity Creactive Protein (hsCRP)			

Units: mg/L			
arithmetic mean	10.53		
standard deviation	± 17.21	-	

Subject analysis sets

Subject analysis set title	Placebo (Pooled Week 1 - Week 24)
Subject analysis set type	Full analysis

Subject analysis set description:

Full analysis set; participants who prematurely discontinued from study drug prior to Week 12 or for whom ACR data were missing at Week 12 were considered non-responders. Participants received placebo once daily for 24 weeks.

Reporting group values	Placebo (Pooled Week 1 - Week 24)		
Number of subjects	212		
Age categorical Units: Subjects			
In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			
Age continuous Units: years			
arithmetic mean	54.1		
standard deviation	± 11.53		
Gender categorical Units: Subjects			
Female	120		
Male	92		
Extent of Psoriasis			
The extent of psoriasis was measured by the physician as the total body surface area (BSA) involved with psoriasis. For purposes of clinical estimation, the total surface of the participant's palm and five digits was assumed to be approximately equivalent to 1% of BSA.			
Units: Subjects			
< 3% BSA	81		
≥ 3% BSA	131		
Number of Prior Failed Biologic DMARDs			
Failed treatment with prior biologic DMARD is defined as lack of efficacy after a minimum 12 week duration of therapy. The zero category includes participants with intolerance but not inadequate response to a biologic DMARD.			
Units: Subjects			
bDMARDS (0)	18		
bDMARD (1)	135		
bDMARDS (2)	35		
bDMARDS (≥ 3)	24		

Duration of Psoriatic Arthritis Symptoms Units: years arithmetic mean standard deviation	 14.6 ± 11.70		
Duration of PsA Diagnosis Units: years arithmetic mean standard deviation	 11.0 ± 10.33		
Tender Joint Count			
A total of 68 joints were assessed for the presence or absence of tenderness.			
Units: joints arithmetic mean standard deviation	 25.3 ± 17.62		
Swollen Joint Count			
A total of 66 joints were assessed for the presence or absence of swelling.			
Units: joints arithmetic mean standard deviation	 12.0 ± 8.85		
Patient's Assessment of Pain			
Participants were asked to indicate the severity of their arthritis pain within the previous week on a numeric rating scale (NRS) from 0 to 10. A score of 0 indicates "no pain" and a score of 10 indicates "worst possible pain." Measure Analysis Population Description: Participants with available data			
Units: units on a scale arithmetic mean standard deviation	 6.6 ± 2.12		
Patient's Global Assessment of Disease Activity			
The participant was asked to rate their current psoriatic arthritis disease activity on a 0 to 10 NRS, where 0 indicates no disease activity and 10 indicates severe disease activity. Measure Analysis Population Description: Participants with available data			
Units: units on a scale arithmetic mean standard deviation	 6.8 ± 2.04		
Physician's Global Assessment of Disease Activity			
The physician rated the participant's current global psoriatic arthritis disease activity (independently from the participant's assessment) on a 0 to 10 NRS where 0 indicates no disease activity and 10 indicates severe disease activity.			
Units: units on a scale arithmetic mean standard deviation	 6.5 ± 1.76		
Health Assessment Questionnaire - Disability Index (HAQ-DI)			
The HAQ-DI is a patient-reported questionnaire that measures the degree of difficulty a person has in accomplishing tasks in 8 functional areas (dressing, arising, eating, walking, hygiene, reaching, gripping, and errands and chores) over the past week. Participants assessed their ability to do each task on a scale from 0 (without any difficulty) to 3 (unable to do). Scores were averaged to provide an overall score ranging from 0 to 3, where 0 represents no disability and 3 represents very severe, high-dependency disability. Analysis Population Description: Participants with available data.			
Units: units on a scale arithmetic mean standard deviation	 1.23 ± 0.691		
High-sensitivity Creactive Protein (hsCRP)			

Units: mg/L			
arithmetic mean	10.40		
standard deviation	± 18.46		

End points

End points reporting groups

Reporting group title	Placebo / Upadacitinib 15 mg

Reporting group description:

Participants were randomized to receive placebo once daily up to Week 24 followed by Upadacitinib 15 mg once daily for Week 25 to Week 56.

Reporting group title	Placebo / Upadacitinib 30 mg

Reporting group description:

Participants were randomized to receive placebo once daily up to Week 24 followed by Upadacitinib 30 mg once daily for Week 25 to Week 56.

Reporting group title	Upadacitinib 15 mg

Reporting group description:

Participants randomized to receive Upadacitinib 15 mg once daily from Week 1 to Week 56 in Period 1.

Reporting group title	Upadacitinib 30 mg

Reporting group description:

Subjects were randomized to receive Upadacitinib 30 mg once daily from Week 1 to Week 56 in Period 1. One randomized subject did not qualify per inclusion/exclusion criteria and discontinued prior to treatment. This subject is not included in the disposition table.

Reporting group title	Placebo / Upadacitinib 15 mg

Reporting group description:

In Period 1, participants who were randomized to receive placebo once daily up to Week 24 followed by Upadacitinib 15 mg once daily for Week 25 to Week 56. In Period 2, participants received Upadacitinib 15 mg from Week 56 to EOS.

Reporting group title	Placebo / Upadacitinib 30 mg

Reporting group description:

In Period 1, participants who were randomized to receive placebo once daily up to Week 24 followed by Upadacitinib 30 mg once daily for Week 25 to Week 56. In Period 2, participants received Upadacitinib 30 mg from Week 56 to EOS. Participants in this group were switched to upadacitinib 15mg QD during Period 2 after week 116, following a protocol amendment

Reporting group title	Upadacitinib 15 mg

Reporting group description:

In Period 2, participants in this arm continued to receive Upadacitinib 15 mg once daily from Week 56 to EOS.

Reporting group title	Upadacitinib 30 mg

Reporting group description:

In Period 2, participants in this arm continued to receive Upadacitinib 30 mg once daily from Week 56 to EOS. Participants in this group were switched to upadacitinib 15mg QD during Period 2 after week 116, following a protocol amendment

Subject analysis set title	Placebo (Pooled Week 1 - Week 24)
Subject analysis set type	Full analysis

Subject analysis set description:

Full analysis set; participants who prematurely discontinued from study drug prior to Week 12 or for whom ACR data were missing at Week 12 were considered non-responders. Participants received placebo once daily for 24 weeks.

Primary: Percentage of Participants With an American College of Rheumatology 20% (ACR20) Response at Week 12

End point title	Percentage of Participants With an American College of Rheumatology 20% (ACR20) Response at Week 12[1]

End point description:

Participants who met the following 3 conditions for improvement from Baseline were classified as meeting the ACR20 response criteria:
- ≥ 20% improvement in 68-tender joint count;
- ≥ 20% improvement in 66-swollen joint count; and

- ≥ 20% improvement in at least 3 of the 5 following parameters:
  -Physician global assessment of disease activity
  -Patient global assessment of disease activity
  -Patient assessment of pain
  -Health Assessment Questionnaire - Disability Index (HAQ-DI)
  -High-sensitivity C-reactive protein (hsCRP).

End point type	Primary

End point timeframe:

Baseline and Week 12

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: Statistical analyses are reported as planned in the protocol/SAP.

End point values	Upadacitinib 15 mg	Upadacitinib 30 mg	Placebo (Pooled Week 1 - Week 24)	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	211[2]	218[3]	212[4]	
Units: percentage				
number (confidence interval 95%)	56.9 (50.2 to 63.6)	63.8 (57.4 to 70.1)	24.1 (18.3 to 29.8)	

Notes:

[2] - Full analysis set

[3] - Full analysis set

[4] - Full analysis set

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Upadacitinib 15 mg v Placebo (Pooled Week 1 - Week 24)
Number of subjects included in analysis	423
Analysis specification	Pre-specified
Analysis type	superiority[5]
P-value	< 0.0001 [6]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Response Rate Difference
Point estimate	32.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	24
upper limit	41.6

Notes:

[5] - The overall type I error rate of primary and ranked key secondary endpoints was strongly controlled using a graphical multiple testing procedure starting with the primary endpoint using α/2 for each dose followed by a prespecified α transfer path.

[6] - Cochran-Mantel-Haenszel (CMH) test adjusted for the main stratification factor of current DMARD use (yes/no).

Statistical analysis title	Statistical Analysis 2
Comparison groups	Upadacitinib 30 mg v Placebo (Pooled Week 1 - Week 24)

Number of subjects included in analysis	430
Analysis specification	Pre-specified
Analysis type	superiority[7]
P-value	< 0.0001 [8]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Response Rate Difference
Point estimate	39.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	31.1
upper limit	48.3

Notes:

[7] - The overall type I error rate of primary and ranked key secondary endpoints was strongly controlled using a graphical multiple testing procedure starting with the primary endpoint using α/2 for each dose followed by a prespecified α transfer path.

[8] - Cochran-Mantel-Haenszel (CMH) test adjusted for the main stratification factor of current DMARD use (yes/no).

Secondary: Change From Baseline in Health Assessment Questionnaire Disability Index (HAQ-DI) at Week 12

End point title	Change From Baseline in Health Assessment Questionnaire Disability Index (HAQ-DI) at Week 12[9]

End point description:

The Health Assessment Questionnaire - Disability Index is a patient-reported questionnaire that measures the degree of difficulty a person has in accomplishing tasks in 8 functional areas (dressing, arising, eating, walking, hygiene, reaching, gripping, and errands and chores) over the past week. Participants assessed their ability to do each task on a scale from 0 (without any difficulty) to 3 (unable to do). Scores were averaged to provide an overall score ranging from 0 to 3, where 0 represents no disability and 3 represents very severe, high-dependency disability.
A negative change from Baseline in the overall score indicates improvement.
Full analysis set participants with available data; a mixed effect model repeat measurement (MMRM) analysis with longitudinal data from observed cases up to Week 12 was used.

End point type	Secondary

End point timeframe:

Baseline and Week 12

Notes:

[9] - 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: Statistical analyses are reported as planned in the protocol/SAP.

End point values	Upadacitinib 15 mg	Upadacitinib 30 mg	Placebo (Pooled Week 1 - Week 24)	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	199[10]	204[11]	180[12]	
Units: score on a scale				
least squares mean (confidence interval 95%)	-0.30 (-0.37 to -0.24)	-0.41 (-0.47 to -0.35)	-0.10 (-0.16 to -0.03)	

Notes:

[10] - Full analysis set participants with available data

[11] - Full analysis set participants with available data

[12] - Full analysis set participants with available data

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

The overall type I error rate of primary and ranked key secondary endpoints was strongly controlled using a graphical multiple testing procedure starting with the primary endpoint using α/2 for each dose followed by a prespecified α transfer path.

Comparison groups	Upadacitinib 15 mg v Placebo (Pooled Week 1 - Week 24)
Number of subjects included in analysis	379
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [13]
Method	Mixed Effect Model Repeated Measurement
Parameter estimate	Response Rate Difference
Point estimate	-0.21
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.3
upper limit	-0.12

Notes:

[13] - Mixed Effect Model Repeated Measurement test adjusted for the main stratification factor of current DMARD use (yes/no).

Statistical analysis title	Statistical Analysis 2

Statistical analysis description:

The overall type I error rate of primary and ranked key secondary endpoints was strongly controlled using a graphical multiple testing procedure starting with the primary endpoint using α/2 for each dose followed by a prespecified α transfer path.

Comparison groups	Upadacitinib 30 mg v Placebo (Pooled Week 1 - Week 24)
Number of subjects included in analysis	384
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [14]
Method	Mixed Effect Model Repeated Measurement
Parameter estimate	Response Rate Difference
Point estimate	-0.31
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.4
upper limit	-0.22

Notes:

[14] - [Mixed Effect Model Repeated Measurement test adjusted for the main stratification factor of current DMARD use (yes/no).

Secondary: Percentage of Participants Achieving a Static Investigator Global Assessment (sIGA) of Psoriasis of 0 or 1 and at Least a 2-point Improvement From Baseline (sIGA 0/1) at Week 16

End point title	Percentage of Participants Achieving a Static Investigator Global Assessment (sIGA) of Psoriasis of 0 or 1 and at Least a 2-point Improvement From Baseline (sIGA 0/1) at Week 16[15]

End point description:

The sIGA is a 5 point scale ranging from 0 to 4, based on the investigator's assessment of the average elevation, erythema, and scaling of all psoriatic lesions at the current visit. A lower score indicates less severe psoriasis (0 = clear, 1 = almost clear, 2 = mild, 3 = moderate and 4 = severe).

Analysis Population Description: Full analysis set participants with a Baseline sIGA score ≥ 2; participants who prematurely discontinued from study drug prior to Week 16 or for whom sIGA data were missing at Week 16 were considered non-responders.

End point type	Secondary

End point timeframe:

Baseline and Week 16

Notes:

[15] - 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: Statistical analyses are reported as planned in the protocol/SAP.

End point values	Upadacitinib 15 mg	Upadacitinib 30 mg	Placebo (Pooled Week 1 - Week 24)	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	171[16]	164[17]	163[18]	
Units: percentage of participants				
number (confidence interval 95%)	36.8 (29.6 to 44.1)	40.2 (32.7 to 47.7)	9.2 (4.8 to 13.6)	

Notes:

[16] - Full analysis set participants with a Baseline sIGA score ≥ 2

[17] - Full analysis set participants with a Baseline sIGA score ≥ 2

[18] - Full analysis set participants with a Baseline sIGA score ≥ 2

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Upadacitinib 15 mg v Placebo (Pooled Week 1 - Week 24)
Number of subjects included in analysis	334
Analysis specification	Pre-specified
Analysis type	superiority[19]
P-value	< 0.0001 [20]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Response Rate Difference
Point estimate	27.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	19.2
upper limit	36.1

Notes:

[19] - The overall type I error rate of primary and ranked key secondary endpoints was strongly controlled using a graphical multiple testing procedure starting with the primary endpoint using α/2 for each dose followed by a prespecified α transfer path
[20] - Cochran-Mantel-Haenszel (CMH) test adjusted for the main stratification factor of current DMARD use (yes/no).

Statistical analysis title	Statistical Analysis 2
Comparison groups	Upadacitinib 30 mg v Placebo (Pooled Week 1 - Week 24)

Number of subjects included in analysis	327
Analysis specification	Pre-specified
Analysis type	superiority[21]
P-value	< 0.0001 [22]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Response Rate Difference
Point estimate	31
Confidence interval	
level	95 %
sides	2-sided
lower limit	22.3
upper limit	39.8

Notes:

[21] - The overall type I error rate of primary and ranked key secondary endpoints was strongly controlled using a graphical multiple testing procedure starting with the primary endpoint using α/2 for each dose followed by a prespecified α transfer path.

[22] - Cochran-Mantel-Haenszel (CMH) test adjusted for the main stratification factor of current DMARD use (yes/no).

Secondary: Change From Baseline in Short-Form 36 (SF-36) Physical Component Score (PCS) at Week 12

End point title	Change From Baseline in Short-Form 36 (SF-36) Physical Component Score (PCS) at Week 12[23]

End point description:

The Short Form 36-Item Health Survey (SF-36) Version 2 is a self-administered questionnaire that measures the impact of disease on overall quality of life during the past 4 weeks. The SF-36 consists of 36 questions in eight domains (physical function, pain, general and mental health, vitality, social function, physical and emotional health).
The physical component score is a weighted combination of the 8 subscales with positive weighting for physical functioning, role-physical, bodily pain, and general health. The PCS was calculated using norm-based scoring so that 50 is the average score and the standard deviation equals 10. Higher scores are associated with better functioning/quality of life; a positive change from Baseline score indicates an improvement.

Analysis Population Description: Full analysis set participants with available data; a mixed effect model repeat measurement (MMRM) analysis with longitudinal data from observed cases up to Week 12 was used.

End point type	Secondary

End point timeframe:

Baseline and Week 12

Notes:

[23] - 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: Statistical analyses are reported as planned in the protocol/SAP.

End point values	Upadacitinib 15 mg	Upadacitinib 30 mg	Placebo (Pooled Week 1 - Week 24)	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	201[24]	206[25]	185[26]	
Units: score on a scale				
least squares mean (confidence interval 95%)	5.15 (4.14 to 6.15)	7.06 (6.07 to 8.06)	1.62 (0.58 to 2.67)	

Notes:

[24] - Full analysis set participants with available data

[25] - Full analysis set participants with available data

[26] - Full analysis set participants with available data

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Upadacitinib 15 mg v Placebo (Pooled Week 1 - Week 24)
Number of subjects included in analysis	386
Analysis specification	Pre-specified
Analysis type	superiority[27]
P-value	< 0.0001 [28]
Method	Mixed models analysis
Parameter estimate	Least Squares (LS) Mean Difference
Point estimate	3.52
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.07
upper limit	4.98

Notes:

[27] - The overall type I error rate of primary and ranked key secondary endpoints was strongly controlled using a graphical multiple testing procedure starting with the primary endpoint using α/2 for each dose followed by a prespecified α transfer path.
[28] - MMRM analysis including treatment, visit, treatment-by-visit interaction, current DMARD use (yes/no) as fixed factors and Baseline value as covariate.

Statistical analysis title	Statistical Analysis 2
Comparison groups	Upadacitinib 30 mg v Placebo (Pooled Week 1 - Week 24)
Number of subjects included in analysis	391
Analysis specification	Pre-specified
Analysis type	superiority[29]
P-value	< 0.0001 [30]
Method	Mixed models analysis
Parameter estimate	Least Squares (LS) Mean Difference
Point estimate	5.44
Confidence interval	
level	95 %
sides	2-sided
lower limit	3.99
upper limit	6.88

Notes:

[29] - The overall type I error rate of primary and ranked key secondary endpoints was strongly controlled using a graphical multiple testing procedure starting with the primary endpoint using α/2 for each dose followed by a prespecified α transfer path.
[30] - MMRM analysis including treatment, visit, treatment-by-visit interaction, current DMARD use (yes/no) as fixed factors and Baseline value as covariate.

Secondary: Percentage of Participants Achieving Psoriasis Area Severity Index (PASI) 75 Response at Week 16

End point title	Percentage of Participants Achieving Psoriasis Area Severity Index (PASI) 75 Response at Week 16[31]

End point description:

PASI is a composite score based on the percentage of the body surface area (BSA) affected by psoriasis and the intensity of erythema (reddening), induration (thickening or hardening of the skin), and desquamation (peeling of the skin) of lesions assessed at 4 anatomic sites (head, upper extremities, trunk, and lower extremities). At each location, the percentage of BSA involvement is assigned a score from 0 (no involvement) to 6 (90% to 100% involvement), and erythema, induration, and desquamation are scored on a scale from 0 (no symptoms) to 4 (very marked).
The PASI score ranges from 0 (no psoriasis) to 72 (very severe psoriasis). A PASI-75 response is the percentage of participants who achieved at least a 75% reduction (improvement) from Baseline in PASI score.

Analysis Population Description: Full analysis set participants with Baseline psoriasis BSA involvement ≥ 3%; participants who prematurely discontinued from study drug prior to Week 16 or for whom PASI data were missing

End point type	Secondary

End point timeframe:

Baseline and Week 16

Notes:

[31] - 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: Statistical analyses are reported as planned in the protocol/SAP.

End point values	Upadacitinib 15 mg	Upadacitinib 30 mg	Placebo (Pooled Week 1 - Week 24)	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	130[32]	131[33]	131[34]	
Units: percentage of participants				
number (confidence interval 95%)	52.3 (43.7 to 60.9)	56.5 (48.0 to 65.0)	16.0 (9.7 to 22.3)	

Notes:

[32] - Full analysis set participants with Baseline psoriasis BSA involvement ≥ 3%

[33] - Full analysis set participants with Baseline psoriasis BSA involvement ≥ 3%

[34] - Full analysis set participants with Baseline psoriasis BSA involvement ≥ 3%

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Upadacitinib 15 mg v Placebo (Pooled Week 1 - Week 24)
Number of subjects included in analysis	261
Analysis specification	Pre-specified
Analysis type	superiority[35]
P-value	< 0.0001 [36]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Response Rate Difference
Point estimate	36.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	25.6
upper limit	46.9

Notes:

[35] - The overall type I error rate of primary and ranked key secondary endpoints was strongly controlled using a graphical multiple testing procedure starting with the primary endpoint using α/2 for each dose followed by a prespecified α transfer path.
[36] - Cochran-Mantel-Haenszel (CMH) test adjusted for the main stratification factor of current DMARD

use (yes/no).

Statistical analysis title	Statistical Analysis 2
Comparison groups	Upadacitinib 30 mg v Placebo (Pooled Week 1 - Week 24)
Number of subjects included in analysis	262
Analysis specification	Pre-specified
Analysis type	superiority[37]
P-value	< 0.0001 [38]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Response Rate Difference
Point estimate	40.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	29.9
upper limit	51

Notes:

[37] - The overall type I error rate of primary and ranked key secondary endpoints was strongly controlled using a graphical multiple testing procedure starting with the primary endpoint using α/2 for each dose followed by a prespecified α transfer path.
[38] - Cochran-Mantel-Haenszel (CMH) test adjusted for the main stratification factor of current DMARD use (yes/no).

Secondary: Change From Baseline in Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F) Score at Week 12

End point title	Change From Baseline in Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F) Score at Week 12[39]

End point description:

The FACIT-Fatigue questionnaire is a self-administered patient questionnaire that consists of 13 questions designed to measure the degree of fatigue experienced by participants in the previous 7 days, including physical fatigue (e.g., I feel tired), functional fatigue (e.g., trouble finishing things), emotional fatigue (e.g., frustration), and social consequences of fatigue (e.g., limits social activity). Participants respond to the questions on a scale from 0 'not at all' to 4 'very much'. The FACIT Fatigue score is computed by summing the item scores, after reversing those items that are worded in the negative direction. The FACIT-Fatigue subscale score ranges from 0 to 52, where higher scores represent less fatigue. A positive change from Baseline indicates improvement.

Analysis Population Description: Full analysis set participants with available data; a mixed effect model repeat measurement (MMRM) analysis with longitudinal data from observed cases up to Week 12 was used.

End point type	Secondary

End point timeframe:

Baseline and Week 12

Notes:

[39] - 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: Statistical analyses are reported as planned in the protocol/SAP.

End point values	Upadacitinib 15 mg	Upadacitinib 30 mg	Placebo (Pooled Week 1 - Week 24)	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	201[40]	206[41]	184[42]	
Units: score on a scale				
least squares mean (confidence interval	5.0 (3.8 to 6.1)	6.1 (4.9 to 7.2)	1.3 (0.1 to 2.5)	

95%)

Notes:

[40] - Full analysis set participants with available data

[41] - Full analysis set participants with available data

[42] - Full analysis set participants with available data

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Upadacitinib 15 mg v Placebo (Pooled Week 1 - Week 24)
Number of subjects included in analysis	385
Analysis specification	Pre-specified
Analysis type	superiority[43]
P-value	< 0.0001 [44]
Method	Mixed models analysis
Parameter estimate	Least Squares (LS) Mean Difference
Point estimate	3.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	2
upper limit	5.4

Notes:

[43] - The overall type I error rate of primary and ranked key secondary endpoints was strongly controlled using a graphical multiple testing procedure starting with the primary endpoint using α/2 for each dose followed by a prespecified α transfer path.

[44] - MMRM analysis including treatment, visit, treatment-by-visit interaction, current DMARD use (yes/no) as fixed factors and Baseline value as covariate.

Statistical analysis title	Statistical Analysis 2
Comparison groups	Upadacitinib 30 mg v Placebo (Pooled Week 1 - Week 24)
Number of subjects included in analysis	390
Analysis specification	Pre-specified
Analysis type	superiority[45]
P-value	< 0.0001 [46]
Method	Mixed models analysis
Parameter estimate	Least Squares (LS) Mean Difference
Point estimate	4.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	3.1
upper limit	6.4

Notes:

[45] - The overall type I error rate of primary and ranked key secondary endpoints was strongly controlled using a graphical multiple testing procedure starting with the primary endpoint using α/2 for each dose followed by a prespecified α transfer path.

[46] - MMRM analysis including treatment, visit, treatment-by-visit interaction, current DMARD use (yes/no) as fixed factors and Baseline value as covariate.

Secondary: Percentage of Participants Achieving Minimal Disease Activity (MDA) at Week 24

End point title	Percentage of Participants Achieving Minimal Disease Activity (MDA) at Week 24[47]

End point description:

A participant was classified as achieving MDA if 5 of the following 7 criteria were met:
- Tender joint count (out of 68 joints) ≤ 1
- Swollen joint count (out of 66 joints) ≤ 1
- PASI score ≤ 1 (score ranges from 0 - 72) or percent BSA involved with psoriasis ≤ 3%
- Patient's assessment of pain ≤ 1.5 (NRS from 0 to 10)
- Patient's Global Assessment of disease activity ≤ 2 (NRS from 0 to 10)
- HAQ-DI score ≤ 0.5 (index score ranges from 0 to 3)

Analysis Population Description: Full analysis set; participants who prematurely discontinued from study drug prior to Week 24 or for whom data were missing at Week 24, or who met rescue criteria at Week 16 were considered non-responders.
- Leeds Enthesitis Index ≤ 1 (assesses the presence or absence of enthesitis at 3 bilateral sites, with an overall score range from 0 to 6)

End point type	Secondary

End point timeframe:

Week 24

Notes:

[47] - 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: Statistical analyses are reported as planned in the protocol/SAP.

End point values	Upadacitinib 15 mg	Upadacitinib 30 mg	Placebo (Pooled Week 1 - Week 24)	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	211[48]	218[49]	212[50]	
Units: percentage of participants				
number (confidence interval 95%)	25.1 (19.3 to 31.0)	28.9 (22.9 to 34.9)	2.8 (0.6 to 5.1)	

Notes:

[48] - Full analysis set

[49] - Full analysis set

[50] - Full analysis set

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Upadacitinib 15 mg v Placebo (Pooled Week 1 - Week 24)
Number of subjects included in analysis	423
Analysis specification	Pre-specified
Analysis type	superiority[51]
P-value	< 0.0001 [52]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Response Rate Difference
Point estimate	22.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	16
upper limit	28.6

Notes:

[51] - The overall type I error rate of primary and ranked key secondary endpoints was strongly controlled using a graphical multiple testing procedure starting with the primary endpoint using α/2 for each dose followed by a prespecified α transfer path.
[52] - Cochran-Mantel-Haenszel (CMH) test adjusted for the main stratification factor of current DMARD

use (yes/no).

Statistical analysis title	Statistical Analysis 2
Comparison groups	Upadacitinib 30 mg v Placebo (Pooled Week 1 - Week 24)
Number of subjects included in analysis	430
Analysis specification	Pre-specified
Analysis type	superiority[53]
P-value	< 0.0001 [54]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Response Rate Difference
Point estimate	26.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	19.7
upper limit	32.5

Notes:

[53] - The overall type I error rate of primary and ranked key secondary endpoints was strongly controlled using a graphical multiple testing procedure starting with the primary endpoint using α/2 for each dose followed by a prespecified α transfer path.
[54] - Cochran-Mantel-Haenszel (CMH) test adjusted for the main stratification factor of current DMARD use (yes/no

Secondary: Change From Baseline in Self-Assessment of Psoriasis Symptoms (SAPS) Score at Week 16

End point title	Change From Baseline in Self-Assessment of Psoriasis Symptoms (SAPS) Score at Week 16[55]

End point description:

The SAPS is an 11-item self-assessment of psoriasis symptoms that includes questions on: pain, itching, redness, scaling, flaking, bleeding, burning, stinging, tenderness, pain due to skin cracking, and joint pain. Each item is scored from 0 to 10, with 0 being least severe and 10 being most severe. The total score is generated by summing the 11 items and ranges from 0 to 110 (worst). A negative change from Baseline in the total score indicates improvement.

Analysis Population Description: Full analysis set participants with available data; a mixed effect model repeat measurement (MMRM) analysis with longitudinal data from observed cases up to Week 16 was used.

End point type	Secondary

End point timeframe:

Baseline and Week 16

Notes:

[55] - 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: Statistical analyses are reported as planned in the protocol/SAP.

End point values	Upadacitinib 15 mg	Upadacitinib 30 mg	Placebo (Pooled Week 1 - Week 24)	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	191[56]	200[57]	182[58]	
Units: score on a scale				
least squares mean (confidence interval 95%)	-24.4 (-27.5 to -21.2)	-29.7 (-32.8 to -26.6)	-1.5 (-4.7 to 1.8)	

Notes:

[56] - Full analysis set participants with available data

[57] - Full analysis set participants with available data

[58] - Full analysis set participants with available data

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Upadacitinib 15 mg v Placebo (Pooled Week 1 - Week 24)
Number of subjects included in analysis	373
Analysis specification	Pre-specified
Analysis type	superiority[59]
P-value	< 0.0001 [60]
Method	Mixed models analysis
Parameter estimate	Response Rate Difference
Point estimate	-22.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-27.4
upper limit	-18.4

Notes:

[59] - The overall type I error rate of primary and ranked key secondary endpoints was strongly controlled using a graphical multiple testing procedure starting with the primary endpoint using α/2 for each dose followed by a prespecified α transfer path.

[60] - MMRM analysis including treatment, visit, treatment-by-visit interaction, current DMARD use (yes/no) as fixed factors and Baseline value as covariate.

Secondary: Percentage of Participants With an American College of Rheumatology 50% (ACR50) Response at Week 12

End point title	Percentage of Participants With an American College of Rheumatology 50% (ACR50) Response at Week 12[61]

End point description:

Participants who met the following 3 conditions for improvement from Baseline were classified as meeting the ACR50 response criteria:
- ≥ 50% improvement in 68-tender joint count;
- ≥ 50% improvement in 66-swollen joint count; and
- ≥ 50% improvement in at least 3 of the 5 following parameters:
    - Physician global assessment of disease activity
    - Patient global assessment of disease activity
    - Patient assessment of pain
    - Health Assessment Questionnaire - Disability Index (HAQ-DI)
    - High-sensitivity C-reactive protein (hsCRP).

Analysis Population Description: Full analysis set; participants who prematurely discontinued from study drug prior to Week 12 or for whom ACR data were missing at Week 12 were considered non-responders.

End point type	Secondary

End point timeframe:

Baseline and Week 12

Notes:

[61] - 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: Statistical analyses are reported as planned in the protocol/SAP.

End point values	Upadacitinib 15 mg	Upadacitinib 30 mg	Placebo (Pooled Week 1 - Week 24)	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	211[62]	218[63]	212[64]	
Units: percentage of participants				
number (confidence interval 95%)	31.8 (25.5 to 38.0)	37.6 (31.2 to 44.0)	4.7 (1.9 to 7.6)	

Notes:

[62] - Full analysis set

[63] - Full analysis set

[64] - Full analysis set

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Upadacitinib 15 mg v Placebo (Pooled Week 1 - Week 24)
Number of subjects included in analysis	423
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [65]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Response Rate Difference
Point estimate	27
Confidence interval	
level	95 %
sides	2-sided
lower limit	20.1
upper limit	33.9

Notes:

[65] - Cochran-Mantel-Haenszel (CMH) test adjusted for the main stratification factor of current DMARD use (yes/no).

Statistical analysis title	Statistical Analysis 2
Comparison groups	Upadacitinib 30 mg v Placebo (Pooled Week 1 - Week 24)
Number of subjects included in analysis	430
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [66]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Response Rate Difference
Point estimate	32.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	25.9
upper limit	39.9

Notes:

[66] - Cochran-Mantel-Haenszel (CMH) test adjusted for the main stratification factor of current DMARD use (yes/no).

Secondary: Percentage of Participants With an American College of Rheumatology 70% (ACR70) Response at Week 12

End point title	Percentage of Participants With an American College of

	Rheumatology 70% (ACR70) Response at Week 12[67]

End point description:

Participants who met the following 3 conditions for improvement from Baseline were classified as meeting the ACR70 response criteria:
- ≥ 70% improvement in 68-tender joint count;
- ≥ 70% improvement in 66-swollen joint count; and
- ≥ 70% improvement in at least 3 of the 5 following parameters:
    - Physician global assessment of disease activity
    - Patient global assessment of disease activity
    - Patient assessment of pain
    - Health Assessment Questionnaire - Disability Index (HAQ-DI)
    - High-sensitivity C-reactive protein (hsCRP).

Analysis Population Description: Full analysis set; participants who prematurely discontinued from study drug prior to Week 12 or for whom ACR data were missing at Week 12 were considered non-responders.

End point type	Secondary

End point timeframe:

Baseline and Week 12

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: Statistical analyses are reported as planned in the protocol/SAP.

End point values	Upadacitinib 15 mg	Upadacitinib 30 mg	Placebo (Pooled Week 1 - Week 24)	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	211[68]	218[69]	212[70]	
Units: percentage of participants				
number (confidence interval 95%)	8.5 (4.8 to 12.3)	16.5 (11.6 to 21.4)	0.5 (0.0 to 1.4)	

Notes:

[68] - Full analysis set

[69] - Full analysis set

[70] - Full analysis set

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Upadacitinib 15 mg v Placebo (Pooled Week 1 - Week 24)
Number of subjects included in analysis	423
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [71]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Response Rate Difference
Point estimate	8.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	4.2
upper limit	11.9

Notes:

[71] - Cochran-Mantel-Haenszel (CMH) test adjusted for the main stratification factor of current DMARD use (yes/no).

Statistical analysis title	Statistical Analysis 2
Comparison groups	Upadacitinib 30 mg v Placebo (Pooled Week 1 - Week 24)
Number of subjects included in analysis	430
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [72]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Response Rate Difference
Point estimate	16
Confidence interval	
level	95 %
sides	2-sided
lower limit	11
upper limit	21.1

Notes:

[72] - Cochran-Mantel-Haenszel (CMH) test adjusted for the main stratification factor of current DMARD use (yes/no).

Secondary: Percentage of Participants With an American College of Rheumatology 20% (ACR20) Response at Week 2

End point title	Percentage of Participants With an American College of Rheumatology 20% (ACR20) Response at Week 2[73]

End point description:

Participants who met the following 3 conditions for improvement from Baseline were classified as meeting the ACR20 response criteria:
- ≥ 20% improvement in 68-tender joint count;
- ≥ 20% improvement in 66-swollen joint count; and
- ≥ 20% improvement in at least 3 of the 5 following parameters:
    - Physician global assessment of disease activity
    - Patient global assessment of disease activity
    - Patient assessment of pain
    - Health Assessment Questionnaire - Disability Index (HAQ-DI)
    - High-sensitivity C-reactive protein (hsCRP).

Analysis Population Description: Full analysis set; participants who prematurely discontinued from study drug prior to Week 2 or for whom ACR data were missing at Week 2 were considered non-responders.

End point type	Secondary

End point timeframe:

Baseline and Week 2

Notes:

[73] - 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: Statistical analyses are reported as planned in the protocol/SAP.

End point values	Upadacitinib 15 mg	Upadacitinib 30 mg	Placebo (Pooled Week 1 - Week 24)	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	211[74]	218[75]	212[76]	
Units: percentage of participants				
number (confidence interval 95%)	32.7 (26.4 to 39.0)	33.5 (27.2 to 39.8)	10.8 (6.7 to 15.0)	

Notes:

[74] - Full analysis set

[75] - Full analysis set

[76] - Full analysis set

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Upadacitinib 15 mg v Placebo (Pooled Week 1 - Week 24)
Number of subjects included in analysis	423
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [77]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Response Rate Difference
Point estimate	21.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	14.3
upper limit	29.4

Notes:

[77] - Cochran-Mantel-Haenszel test adjusting for the main stratification factor of current DMARD use (yes/no).

Statistical analysis title	Statistical Analysis 2
Comparison groups	Upadacitinib 30 mg v Placebo (Pooled Week 1 - Week 24)
Number of subjects included in analysis	430
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [78]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Response Rate Difference
Point estimate	22.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	15.1
upper limit	30.2

Notes:

[78] - Cochran-Mantel-Haenszel (CMH) test adjusted for the main stratification factor of current DMARD use (yes/no).

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All-cause mortality and adverse event tables include events reported from enrollment to the end of the study (EOS).

Adverse event reporting additional description:

The median time subjects were followed ranged from 190 to 415 days (Period 1) and 672 to 712 days (Period 2). Subjects receiving Upadacitinib 30 mg once daily (QD) were switched to Upadacitinib 15 mg QD during Period 2. Following the switch, adverse events for these subjects were pooled to EOS (median follow-up = 223 days).

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	27.0

Reporting groups

Reporting group title	Period 1: Upadacitinib 15mg (ICF to Week 56)

Reporting group description:

Participants randomized to receive Upadacitinib 15 mg once daily to Week 56.

Reporting group title	Period 1: Upadacitinib 30mg (ICF to Week 56)

Reporting group description:

Participants randomized to receive Upadacitinib 30 mg once daily to Week 56.

Reporting group title	Period 1: Pooled Placebo (ICF to Week 24)

Reporting group description:

This group includes all participants in Period 1 who were randomized to receive Placebo to Week 24.

Reporting group title	Period 1: Placebo / Upadacitinib 15mg (Week 24 to Week 56)

Reporting group description:

Participants were randomized to receive placebo once daily for 24 weeks followed by Upadacitinib 15 mg once daily to Week 56. AEs in this group were reported while participants received 15 mg Upadacitinib between Week 24 to Week 56.

Reporting group title	Period 1: Placebo / Upadacitinib 30mg (Week 24 to Week 56)

Reporting group description:

Participants weree randomized to receive placebo once daily for 24 weeks followed by Upadacitinib 30 mg once daily to Week 56. AEs in this group were reported while participants received 30 mg Upadacitinib between Week 24 to Week 56.

Reporting group title	Period 2: Upadacitinib 30mg (Week 56 to EOS)

Reporting group description:

Participants randomized to receive Upadacitinib 30 mg once daily in Period 2 from Week 56 to EOS. Participants in this group were switched to upadacitinib 15mg QD during Period 2 after week 116, following a protocol amendment.

Reporting group title	Period 2: Upadacitinib 15mg (Week 56 to EOS)

Reporting group description:

Participants randomized to receive Upadacitinib 15 mg once daily in Period 2 from Week 56 to EOS.

Reporting group title	Period 2: Placebo / Upadacitinib 30mg (Week 56 to Week EOS)

Reporting group description:

Participants from the Period 1 Placebo / Upadacitinib 30 mg group received 30 mg upadacitinib from Week 56 to EOS. Participants in this group were switched to upadacitinib 15mg QD during Period 2 after week 116, following a protocol amendment.

Reporting group title	Period 2: Placebo / Upadacitinib 15mg (Week 56 to Week EOS)

Reporting group description:

Participants from the Period 1 Placebo / Upadacitinib 15 mg group received 15 mg upadacitinib from Week 56 to EOS.

Reporting group title	Period 2: Pooled Upadacitinib (Switched From 30mg to 15mg P2)

Reporting group description:

All participants in Period 2 who switched from 30 mg to 15 mg Upadacitinib to EOS during Period 2. This group includes all participants who received any upadacitinib 30 mg in Period 2 and switched dose to upadacitinib 15 mg once daily during Period 2 (following a protocol amendment, after week 116). The AEs in this group were reported while participants received 15 mg upadacitinib once daily.

Serious adverse events	Period 1: Upadacitinib 15mg (ICF to Week 56)	Period 1: Upadacitinib 30mg (ICF to Week 56)	Period 1: Pooled Placebo (ICF to Week 24)
Total subjects affected by serious adverse events			
subjects affected / exposed	22 / 211 (10.43%)	25 / 219 (11.42%)	5 / 212 (2.36%)
number of deaths (all causes)	0	0	1
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 / 211 (0.00%)	0 / 219 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ANOGENITAL WARTS			
subjects affected / exposed	0 / 211 (0.00%)	1 / 219 (0.46%)	0 / 212 (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
GASTROINTESTINAL CANCER METASTATIC			
subjects affected / exposed	0 / 211 (0.00%)	0 / 219 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
INTRADUCTAL PAPILLARY BREAST NEOPLASM			
subjects affected / exposed	0 / 211 (0.00%)	0 / 219 (0.00%)	0 / 212 (0.00%)
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 CARCINOMA			
subjects affected / exposed	0 / 211 (0.00%)	0 / 219 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
MALIGNANT MELANOMA STAGE III			

subjects affected / exposed	1 / 211 (0.47%)	0 / 219 (0.00%)	0 / 212 (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
NEUROENDOCRINE CARCINOMA OF THE SKIN			
subjects affected / exposed	1 / 211 (0.47%)	0 / 219 (0.00%)	0 / 212 (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
NEOPLASM MALIGNANT			
subjects affected / exposed	0 / 211 (0.00%)	0 / 219 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
OVARIAN CANCER			
subjects affected / exposed	0 / 211 (0.00%)	1 / 219 (0.46%)	0 / 212 (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
OROPHARYNGEAL SQUAMOUS CELL CARCINOMA			
subjects affected / exposed	0 / 211 (0.00%)	1 / 219 (0.46%)	0 / 212 (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
OVARIAN THECA CELL TUMOUR			
subjects affected / exposed	0 / 211 (0.00%)	0 / 219 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PARATHYROID TUMOUR BENIGN			
subjects affected / exposed	1 / 211 (0.47%)	0 / 219 (0.00%)	0 / 212 (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
PROSTATE CANCER			
subjects affected / exposed	1 / 211 (0.47%)	0 / 219 (0.00%)	0 / 212 (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
RECTAL ADENOCARCINOMA			

subjects affected / exposed	0 / 211 (0.00%)	1 / 219 (0.46%)	0 / 212 (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
RECTAL CANCER			
subjects affected / exposed	1 / 211 (0.47%)	0 / 219 (0.00%)	0 / 212 (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
UTERINE LEIOMYOMA			
subjects affected / exposed	0 / 211 (0.00%)	0 / 219 (0.00%)	1 / 212 (0.47%)
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			
CIRCULATORY COLLAPSE			
subjects affected / exposed	0 / 211 (0.00%)	0 / 219 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pregnancy, puerperium and perinatal conditions			
ABORTION SPONTANEOUS			
subjects affected / exposed	0 / 211 (0.00%)	0 / 219 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ECTOPIC PREGNANCY			
subjects affected / exposed	0 / 211 (0.00%)	1 / 219 (0.46%)	0 / 212 (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
General disorders and administration site conditions			
PYREXIA			
subjects affected / exposed	0 / 211 (0.00%)	0 / 219 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DEATH			

subjects affected / exposed	0 / 211 (0.00%)	0 / 219 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CHEST PAIN			
subjects affected / exposed	0 / 211 (0.00%)	0 / 219 (0.00%)	1 / 212 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SYSTEMIC INFLAMMATORY RESPONSE SYNDROME			
subjects affected / exposed	0 / 211 (0.00%)	1 / 219 (0.46%)	0 / 212 (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	1 / 211 (0.47%)	0 / 219 (0.00%)	0 / 212 (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
BENIGN PROSTATIC HYPERPLASIA			
subjects affected / exposed	0 / 211 (0.00%)	1 / 219 (0.46%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
ACUTE RESPIRATORY FAILURE			
subjects affected / exposed	1 / 211 (0.47%)	1 / 219 (0.46%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ASTHMA			
subjects affected / exposed	0 / 211 (0.00%)	0 / 219 (0.00%)	0 / 212 (0.00%)
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 / 211 (0.00%)	0 / 219 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HAEMOTHORAX			
subjects affected / exposed	0 / 211 (0.00%)	0 / 219 (0.00%)	1 / 212 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
INTERSTITIAL LUNG DISEASE			
subjects affected / exposed	0 / 211 (0.00%)	0 / 219 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PNEUMOTHORAX			
subjects affected / exposed	0 / 211 (0.00%)	0 / 219 (0.00%)	0 / 212 (0.00%)
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	1 / 211 (0.47%)	0 / 219 (0.00%)	0 / 212 (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
Psychiatric disorders			
DISORIENTATION			
subjects affected / exposed	1 / 211 (0.47%)	0 / 219 (0.00%)	0 / 212 (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
MENTAL STATUS CHANGES			
subjects affected / exposed	0 / 211 (0.00%)	0 / 219 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SUICIDE ATTEMPT			
subjects affected / exposed	0 / 211 (0.00%)	0 / 219 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Product issues			

DEVICE DISLOCATION			
subjects affected / exposed	0 / 211 (0.00%)	0 / 219 (0.00%)	0 / 212 (0.00%)
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			
CERVICAL VERTEBRAL FRACTURE			
subjects affected / exposed	0 / 211 (0.00%)	0 / 219 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
FALL			
subjects affected / exposed	1 / 211 (0.47%)	0 / 219 (0.00%)	0 / 212 (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
FEMORAL NECK FRACTURE			
subjects affected / exposed	0 / 211 (0.00%)	1 / 219 (0.46%)	0 / 212 (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
FIBULA FRACTURE			
subjects affected / exposed	0 / 211 (0.00%)	0 / 219 (0.00%)	1 / 212 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
LUMBAR VERTEBRAL FRACTURE			
subjects affected / exposed	0 / 211 (0.00%)	0 / 219 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SUBDURAL HAEMORRHAGE			
subjects affected / exposed	0 / 211 (0.00%)	0 / 219 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SKULL FRACTURED BASE			
subjects affected / exposed	0 / 211 (0.00%)	0 / 219 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

ROAD TRAFFIC ACCIDENT			
subjects affected / exposed	0 / 211 (0.00%)	0 / 219 (0.00%)	1 / 212 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
RIB FRACTURE			
subjects affected / exposed	0 / 211 (0.00%)	0 / 219 (0.00%)	1 / 212 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
POST PROCEDURAL BILE LEAK			
subjects affected / exposed	0 / 211 (0.00%)	0 / 219 (0.00%)	0 / 212 (0.00%)
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 PSEUDOANEURYSM			
subjects affected / exposed	0 / 211 (0.00%)	0 / 219 (0.00%)	1 / 212 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
TRAUMATIC HAEMOTHORAX			
subjects affected / exposed	0 / 211 (0.00%)	0 / 219 (0.00%)	0 / 212 (0.00%)
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 / 211 (0.00%)	0 / 219 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
TENDON RUPTURE			
subjects affected / exposed	1 / 211 (0.47%)	0 / 219 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
ACUTE MYOCARDIAL INFARCTION			
subjects affected / exposed	1 / 211 (0.47%)	0 / 219 (0.00%)	0 / 212 (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
ANGINA PECTORIS			

subjects affected / exposed	0 / 211 (0.00%)	0 / 219 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ANGINA UNSTABLE			
subjects affected / exposed	0 / 211 (0.00%)	1 / 219 (0.46%)	1 / 212 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
AORTIC VALVE STENOSIS			
subjects affected / exposed	0 / 211 (0.00%)	0 / 219 (0.00%)	0 / 212 (0.00%)
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 / 211 (0.00%)	1 / 219 (0.46%)	0 / 212 (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
BRADYCARDIA			
subjects affected / exposed	0 / 211 (0.00%)	1 / 219 (0.46%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CARDIAC FAILURE			
subjects affected / exposed	0 / 211 (0.00%)	0 / 219 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CARDIO-RESPIRATORY ARREST			
subjects affected / exposed	1 / 211 (0.47%)	0 / 219 (0.00%)	0 / 212 (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
CORONARY ARTERY STENOSIS			
subjects affected / exposed	0 / 211 (0.00%)	1 / 219 (0.46%)	0 / 212 (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
MYOCARDIAL INFARCTION			

subjects affected / exposed	1 / 211 (0.47%)	0 / 219 (0.00%)	0 / 212 (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
SUPRAVENTRICULAR TACHYCARDIA			
subjects affected / exposed	0 / 211 (0.00%)	0 / 219 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
VENTRICULAR FIBRILLATION			
subjects affected / exposed	1 / 211 (0.47%)	0 / 219 (0.00%)	0 / 212 (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
Nervous system disorders			
BRAIN OEDEMA			
subjects affected / exposed	0 / 211 (0.00%)	0 / 219 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CAROTID ARTERY INSUFFICIENCY			
subjects affected / exposed	0 / 211 (0.00%)	0 / 219 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DIZZINESS			
subjects affected / exposed	1 / 211 (0.47%)	0 / 219 (0.00%)	0 / 212 (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
GENERALISED TONIC-CLONIC SEIZURE			
subjects affected / exposed	0 / 211 (0.00%)	0 / 219 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
FACIAL PARALYSIS			
subjects affected / exposed	0 / 211 (0.00%)	0 / 219 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SPEECH DISORDER			

subjects affected / exposed	1 / 211 (0.47%)	0 / 219 (0.00%)	0 / 212 (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
TRANSIENT GLOBAL AMNESIA			
subjects affected / exposed	0 / 211 (0.00%)	1 / 219 (0.46%)	0 / 212 (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
SUBARACHNOID HAEMORRHAGE			
subjects affected / exposed	0 / 211 (0.00%)	0 / 219 (0.00%)	0 / 212 (0.00%)
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			
BLOOD LOSS ANAEMIA			
subjects affected / exposed	1 / 211 (0.47%)	0 / 219 (0.00%)	0 / 212 (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
PANCYTOPENIA			
subjects affected / exposed	0 / 211 (0.00%)	0 / 219 (0.00%)	0 / 212 (0.00%)
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			
RETINAL DETACHMENT			
subjects affected / exposed	0 / 211 (0.00%)	0 / 219 (0.00%)	0 / 212 (0.00%)
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			
DUODENAL ULCER HAEMORRHAGE			
subjects affected / exposed	1 / 211 (0.47%)	0 / 219 (0.00%)	0 / 212 (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
DIARRHOEA			
subjects affected / exposed	0 / 211 (0.00%)	1 / 219 (0.46%)	0 / 212 (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	0 / 211 (0.00%)	0 / 219 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DUODENAL ULCER			
subjects affected / exposed	0 / 211 (0.00%)	0 / 219 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ABDOMINAL PAIN			
subjects affected / exposed	0 / 211 (0.00%)	1 / 219 (0.46%)	0 / 212 (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
GASTRITIS			
subjects affected / exposed	0 / 211 (0.00%)	0 / 219 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
GASTRITIS EROSIVE			
subjects affected / exposed	1 / 211 (0.47%)	0 / 219 (0.00%)	0 / 212 (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
INGUINAL HERNIA			
subjects affected / exposed	0 / 211 (0.00%)	0 / 219 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HAEMATEMESIS			
subjects affected / exposed	0 / 211 (0.00%)	0 / 219 (0.00%)	0 / 212 (0.00%)
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 INTESTINE ULCER			
subjects affected / exposed	0 / 211 (0.00%)	1 / 219 (0.46%)	0 / 212 (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
PANCREATITIS ACUTE			

subjects affected / exposed	0 / 211 (0.00%)	0 / 219 (0.00%)	0 / 212 (0.00%)
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			
CHOLELITHIASIS			
subjects affected / exposed	0 / 211 (0.00%)	0 / 219 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CHOLECYSTITIS ACUTE			
subjects affected / exposed	0 / 211 (0.00%)	0 / 219 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DRUG-INDUCED LIVER INJURY			
subjects affected / exposed	0 / 211 (0.00%)	0 / 219 (0.00%)	0 / 212 (0.00%)
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			
SUBCUTANEOUS EMPHYSEMA			
subjects affected / exposed	0 / 211 (0.00%)	0 / 219 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
ACUTE KIDNEY INJURY			
subjects affected / exposed	0 / 211 (0.00%)	1 / 219 (0.46%)	0 / 212 (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
NEPHROLITHIASIS			
subjects affected / exposed	2 / 211 (0.95%)	1 / 219 (0.46%)	0 / 212 (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
Endocrine disorders			
GOITRE			

subjects affected / exposed	0 / 211 (0.00%)	1 / 219 (0.46%)	0 / 212 (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
ADRENAL INSUFFICIENCY			
subjects affected / exposed	0 / 211 (0.00%)	0 / 219 (0.00%)	0 / 212 (0.00%)
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			
ARTHRALGIA			
subjects affected / exposed	0 / 211 (0.00%)	0 / 219 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
OSTEOARTHRITIS			
subjects affected / exposed	1 / 211 (0.47%)	0 / 219 (0.00%)	0 / 212 (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
NECK PAIN			
subjects affected / exposed	0 / 211 (0.00%)	0 / 219 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
INTERVERTEBRAL DISC PROTRUSION			
subjects affected / exposed	0 / 211 (0.00%)	0 / 219 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
FLANK PAIN			
subjects affected / exposed	1 / 211 (0.47%)	0 / 219 (0.00%)	0 / 212 (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
BACK PAIN			
subjects affected / exposed	0 / 211 (0.00%)	0 / 219 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SYSTEMIC LUPUS ERYTHEMATOSUS			

subjects affected / exposed	1 / 211 (0.47%)	0 / 219 (0.00%)	0 / 212 (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
RAPIDLY PROGRESSIVE OSTEOARTHRITIS			
subjects affected / exposed	1 / 211 (0.47%)	0 / 219 (0.00%)	0 / 212 (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
PSORIATIC ARTHROPATHY			
subjects affected / exposed	2 / 211 (0.95%)	0 / 219 (0.00%)	0 / 212 (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
Infections and infestations			
ABSCESS			
subjects affected / exposed	0 / 211 (0.00%)	0 / 219 (0.00%)	0 / 212 (0.00%)
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 / 211 (0.00%)	0 / 219 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BRONCHIOLITIS			
subjects affected / exposed	0 / 211 (0.00%)	0 / 219 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BACTERAEMIA			
subjects affected / exposed	0 / 211 (0.00%)	1 / 219 (0.46%)	0 / 212 (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
BRONCHITIS			
subjects affected / exposed	0 / 211 (0.00%)	1 / 219 (0.46%)	0 / 212 (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
COVID-19			

subjects affected / exposed	0 / 211 (0.00%)	0 / 219 (0.00%)	0 / 212 (0.00%)
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 STAPHYLOCOCCAL			
subjects affected / exposed	0 / 211 (0.00%)	0 / 219 (0.00%)	1 / 212 (0.47%)
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 / 211 (0.00%)	0 / 219 (0.00%)	0 / 212 (0.00%)
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 / 211 (0.00%)	1 / 219 (0.46%)	0 / 212 (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
DIVERTICULITIS			
subjects affected / exposed	0 / 211 (0.00%)	1 / 219 (0.46%)	0 / 212 (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
CYTOMEGALOVIRUS INFECTION			
subjects affected / exposed	0 / 211 (0.00%)	0 / 219 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
EXTRADURAL ABSCESS			
subjects affected / exposed	0 / 211 (0.00%)	1 / 219 (0.46%)	0 / 212 (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
GASTROENTERITIS			
subjects affected / exposed	0 / 211 (0.00%)	0 / 219 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
LOWER RESPIRATORY TRACT INFECTION BACTERIAL			

subjects affected / exposed	0 / 211 (0.00%)	0 / 219 (0.00%)	0 / 212 (0.00%)
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 ABSCESS			
subjects affected / exposed	0 / 211 (0.00%)	0 / 219 (0.00%)	0 / 212 (0.00%)
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 / 211 (0.00%)	0 / 219 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HIV INFECTION			
subjects affected / exposed	0 / 211 (0.00%)	0 / 219 (0.00%)	0 / 212 (0.00%)
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 VIRAL			
subjects affected / exposed	1 / 211 (0.47%)	1 / 219 (0.46%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PNEUMONIA INFLUENZAL			
subjects affected / exposed	0 / 211 (0.00%)	1 / 219 (0.46%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PNEUMONIA			
subjects affected / exposed	3 / 211 (1.42%)	3 / 219 (1.37%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	3 / 3	2 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PNEUMOCYSTIS JIROVECII PNEUMONIA			
subjects affected / exposed	0 / 211 (0.00%)	0 / 219 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PHARYNGITIS			

subjects affected / exposed	0 / 211 (0.00%)	0 / 219 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
MENINGITIS			
subjects affected / exposed	0 / 211 (0.00%)	0 / 219 (0.00%)	0 / 212 (0.00%)
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 TRACT INFECTION			
subjects affected / exposed	0 / 211 (0.00%)	0 / 219 (0.00%)	0 / 212 (0.00%)
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 / 211 (0.00%)	1 / 219 (0.46%)	0 / 212 (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
SUBCUTANEOUS ABSCESS			
subjects affected / exposed	0 / 211 (0.00%)	0 / 219 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
URINARY TRACT INFECTION			
subjects affected / exposed	0 / 211 (0.00%)	1 / 219 (0.46%)	0 / 212 (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
UPPER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	0 / 211 (0.00%)	0 / 219 (0.00%)	0 / 212 (0.00%)
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 UPPER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	0 / 211 (0.00%)	0 / 219 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			

DEHYDRATION			
subjects affected / exposed	0 / 211 (0.00%)	0 / 219 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DIABETES MELLITUS			
subjects affected / exposed	0 / 211 (0.00%)	0 / 219 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HYPONATRAEMIA			
subjects affected / exposed	0 / 211 (0.00%)	0 / 219 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DIABETIC KETOACIDOSIS			
subjects affected / exposed	0 / 211 (0.00%)	0 / 219 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
METABOLIC ACIDOSIS			
subjects affected / exposed	0 / 211 (0.00%)	0 / 219 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
TYPE 1 DIABETES MELLITUS			
subjects affected / exposed	0 / 211 (0.00%)	0 / 219 (0.00%)	0 / 212 (0.00%)
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	Period 1: Placebo / Upadacitinib 15mg (Week 24 to Week 56)	Period 1: Placebo / Upadacitinib 30mg (Week 24 to Week 56)	Period 2: Upadacitinib 30mg (Week 56 to EOS)
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 79 (3.80%)	6 / 90 (6.67%)	18 / 165 (10.91%)
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 / 79 (0.00%)	0 / 90 (0.00%)	0 / 165 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ANOGENITAL WARTS			
subjects affected / exposed	0 / 79 (0.00%)	0 / 90 (0.00%)	0 / 165 (0.00%)
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 CANCER METASTATIC			
subjects affected / exposed	0 / 79 (0.00%)	0 / 90 (0.00%)	0 / 165 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
INTRADUCTAL PAPILLARY BREAST NEOPLASM			
subjects affected / exposed	0 / 79 (0.00%)	0 / 90 (0.00%)	1 / 165 (0.61%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
GASTROINTESTINAL CARCINOMA			
subjects affected / exposed	0 / 79 (0.00%)	0 / 90 (0.00%)	0 / 165 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
MALIGNANT MELANOMA STAGE III			
subjects affected / exposed	0 / 79 (0.00%)	0 / 90 (0.00%)	0 / 165 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
NEUROENDOCRINE CARCINOMA OF THE SKIN			
subjects affected / exposed	0 / 79 (0.00%)	0 / 90 (0.00%)	0 / 165 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
NEOPLASM MALIGNANT			
subjects affected / exposed	0 / 79 (0.00%)	0 / 90 (0.00%)	0 / 165 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
OVARIAN CANCER			

subjects affected / exposed	0 / 79 (0.00%)	0 / 90 (0.00%)	0 / 165 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
OROPHARYNGEAL SQUAMOUS CELL CARCINOMA			
subjects affected / exposed	0 / 79 (0.00%)	0 / 90 (0.00%)	0 / 165 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
OVARIAN THECA CELL TUMOUR			
subjects affected / exposed	0 / 79 (0.00%)	0 / 90 (0.00%)	1 / 165 (0.61%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PARATHYROID TUMOUR BENIGN			
subjects affected / exposed	0 / 79 (0.00%)	0 / 90 (0.00%)	0 / 165 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PROSTATE CANCER			
subjects affected / exposed	0 / 79 (0.00%)	0 / 90 (0.00%)	0 / 165 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
RECTAL ADENOCARCINOMA			
subjects affected / exposed	0 / 79 (0.00%)	0 / 90 (0.00%)	0 / 165 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
RECTAL CANCER			
subjects affected / exposed	0 / 79 (0.00%)	0 / 90 (0.00%)	0 / 165 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
UTERINE LEIOMYOMA			
subjects affected / exposed	0 / 79 (0.00%)	0 / 90 (0.00%)	0 / 165 (0.00%)
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			
CIRCULATORY COLLAPSE			

subjects affected / exposed	0 / 79 (0.00%)	0 / 90 (0.00%)	0 / 165 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pregnancy, puerperium and perinatal conditions			
ABORTION SPONTANEOUS			
subjects affected / exposed	0 / 79 (0.00%)	0 / 90 (0.00%)	1 / 165 (0.61%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ECTOPIC PREGNANCY			
subjects affected / exposed	0 / 79 (0.00%)	0 / 90 (0.00%)	0 / 165 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
PYREXIA			
subjects affected / exposed	0 / 79 (0.00%)	1 / 90 (1.11%)	0 / 165 (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
DEATH			
subjects affected / exposed	0 / 79 (0.00%)	0 / 90 (0.00%)	0 / 165 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CHEST PAIN			
subjects affected / exposed	0 / 79 (0.00%)	0 / 90 (0.00%)	0 / 165 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SYSTEMIC INFLAMMATORY RESPONSE SYNDROME			
subjects affected / exposed	0 / 79 (0.00%)	0 / 90 (0.00%)	0 / 165 (0.00%)
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 / 79 (0.00%)	0 / 90 (0.00%)	0 / 165 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BENIGN PROSTATIC HYPERPLASIA			
subjects affected / exposed	0 / 79 (0.00%)	0 / 90 (0.00%)	0 / 165 (0.00%)
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 / 79 (0.00%)	0 / 90 (0.00%)	0 / 165 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ASTHMA			
subjects affected / exposed	0 / 79 (0.00%)	0 / 90 (0.00%)	0 / 165 (0.00%)
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 / 79 (0.00%)	1 / 90 (1.11%)	0 / 165 (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
HAEMOTHORAX			
subjects affected / exposed	0 / 79 (0.00%)	0 / 90 (0.00%)	0 / 165 (0.00%)
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 / 79 (0.00%)	0 / 90 (0.00%)	0 / 165 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PNEUMOTHORAX			
subjects affected / exposed	0 / 79 (0.00%)	0 / 90 (0.00%)	0 / 165 (0.00%)
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 / 79 (0.00%)	0 / 90 (0.00%)	0 / 165 (0.00%)
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			
DISORIENTATION			
subjects affected / exposed	0 / 79 (0.00%)	0 / 90 (0.00%)	0 / 165 (0.00%)
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 STATUS CHANGES			
subjects affected / exposed	0 / 79 (0.00%)	1 / 90 (1.11%)	0 / 165 (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
SUICIDE ATTEMPT			
subjects affected / exposed	0 / 79 (0.00%)	0 / 90 (0.00%)	0 / 165 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Product issues			
DEVICE DISLOCATION			
subjects affected / exposed	0 / 79 (0.00%)	0 / 90 (0.00%)	0 / 165 (0.00%)
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			
CERVICAL VERTEBRAL FRACTURE			
subjects affected / exposed	0 / 79 (0.00%)	0 / 90 (0.00%)	0 / 165 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
FALL			
subjects affected / exposed	0 / 79 (0.00%)	0 / 90 (0.00%)	0 / 165 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
FEMORAL NECK FRACTURE			
subjects affected / exposed	0 / 79 (0.00%)	0 / 90 (0.00%)	0 / 165 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

FIBULA FRACTURE			
subjects affected / exposed	0 / 79 (0.00%)	0 / 90 (0.00%)	0 / 165 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
LUMBAR VERTEBRAL FRACTURE			
subjects affected / exposed	0 / 79 (0.00%)	0 / 90 (0.00%)	0 / 165 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SUBDURAL HAEMORRHAGE			
subjects affected / exposed	0 / 79 (0.00%)	0 / 90 (0.00%)	0 / 165 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SKULL FRACTURED BASE			
subjects affected / exposed	0 / 79 (0.00%)	0 / 90 (0.00%)	0 / 165 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ROAD TRAFFIC ACCIDENT			
subjects affected / exposed	0 / 79 (0.00%)	0 / 90 (0.00%)	0 / 165 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
RIB FRACTURE			
subjects affected / exposed	0 / 79 (0.00%)	0 / 90 (0.00%)	0 / 165 (0.00%)
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 BILE LEAK			
subjects affected / exposed	0 / 79 (0.00%)	0 / 90 (0.00%)	0 / 165 (0.00%)
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 PSEUDOANEURYSM			
subjects affected / exposed	0 / 79 (0.00%)	0 / 90 (0.00%)	0 / 165 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
TRAUMATIC HAEMOTHORAX			

subjects affected / exposed	0 / 79 (0.00%)	0 / 90 (0.00%)	0 / 165 (0.00%)
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 / 79 (0.00%)	0 / 90 (0.00%)	0 / 165 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
TENDON RUPTURE			
subjects affected / exposed	0 / 79 (0.00%)	0 / 90 (0.00%)	0 / 165 (0.00%)
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 / 79 (0.00%)	0 / 90 (0.00%)	1 / 165 (0.61%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ANGINA PECTORIS			
subjects affected / exposed	0 / 79 (0.00%)	0 / 90 (0.00%)	0 / 165 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ANGINA UNSTABLE			
subjects affected / exposed	0 / 79 (0.00%)	0 / 90 (0.00%)	0 / 165 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
AORTIC VALVE STENOSIS			
subjects affected / exposed	0 / 79 (0.00%)	0 / 90 (0.00%)	0 / 165 (0.00%)
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 / 79 (0.00%)	1 / 90 (1.11%)	0 / 165 (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
BRADYCARDIA			

subjects affected / exposed	0 / 79 (0.00%)	0 / 90 (0.00%)	0 / 165 (0.00%)
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 FAILURE			
subjects affected / exposed	1 / 79 (1.27%)	0 / 90 (0.00%)	0 / 165 (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
CARDIO-RESPIRATORY ARREST			
subjects affected / exposed	0 / 79 (0.00%)	0 / 90 (0.00%)	0 / 165 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CORONARY ARTERY STENOSIS			
subjects affected / exposed	0 / 79 (0.00%)	0 / 90 (0.00%)	0 / 165 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
MYOCARDIAL INFARCTION			
subjects affected / exposed	0 / 79 (0.00%)	0 / 90 (0.00%)	0 / 165 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SUPRAVENTRICULAR TACHYCARDIA			
subjects affected / exposed	0 / 79 (0.00%)	0 / 90 (0.00%)	1 / 165 (0.61%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
VENTRICULAR FIBRILLATION			
subjects affected / exposed	0 / 79 (0.00%)	0 / 90 (0.00%)	0 / 165 (0.00%)
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			
BRAIN OEDEMA			
subjects affected / exposed	0 / 79 (0.00%)	0 / 90 (0.00%)	0 / 165 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CAROTID ARTERY INSUFFICIENCY			

subjects affected / exposed	0 / 79 (0.00%)	0 / 90 (0.00%)	1 / 165 (0.61%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DIZZINESS			
subjects affected / exposed	0 / 79 (0.00%)	0 / 90 (0.00%)	0 / 165 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
GENERALISED TONIC-CLONIC SEIZURE			
subjects affected / exposed	0 / 79 (0.00%)	0 / 90 (0.00%)	0 / 165 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
FACIAL PARALYSIS			
subjects affected / exposed	0 / 79 (0.00%)	0 / 90 (0.00%)	0 / 165 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SPEECH DISORDER			
subjects affected / exposed	0 / 79 (0.00%)	0 / 90 (0.00%)	0 / 165 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
TRANSIENT GLOBAL AMNESIA			
subjects affected / exposed	0 / 79 (0.00%)	0 / 90 (0.00%)	0 / 165 (0.00%)
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 / 79 (0.00%)	0 / 90 (0.00%)	0 / 165 (0.00%)
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			
BLOOD LOSS ANAEMIA			
subjects affected / exposed	0 / 79 (0.00%)	0 / 90 (0.00%)	1 / 165 (0.61%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PANCYTOPENIA			

subjects affected / exposed	0 / 79 (0.00%)	0 / 90 (0.00%)	0 / 165 (0.00%)
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			
RETINAL DETACHMENT			
subjects affected / exposed	0 / 79 (0.00%)	0 / 90 (0.00%)	0 / 165 (0.00%)
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			
DUODENAL ULCER HAEMORRHAGE			
subjects affected / exposed	0 / 79 (0.00%)	0 / 90 (0.00%)	1 / 165 (0.61%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DIARRHOEA			
subjects affected / exposed	0 / 79 (0.00%)	0 / 90 (0.00%)	0 / 165 (0.00%)
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 / 79 (0.00%)	0 / 90 (0.00%)	0 / 165 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DUODENAL ULCER			
subjects affected / exposed	0 / 79 (0.00%)	0 / 90 (0.00%)	0 / 165 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ABDOMINAL PAIN			
subjects affected / exposed	0 / 79 (0.00%)	0 / 90 (0.00%)	0 / 165 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
GASTRITIS			
subjects affected / exposed	0 / 79 (0.00%)	0 / 90 (0.00%)	0 / 165 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
GASTRITIS EROSIVE			

subjects affected / exposed	0 / 79 (0.00%)	0 / 90 (0.00%)	0 / 165 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
INGUINAL HERNIA			
subjects affected / exposed	0 / 79 (0.00%)	1 / 90 (1.11%)	0 / 165 (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
HAEMATEMESIS			
subjects affected / exposed	0 / 79 (0.00%)	0 / 90 (0.00%)	1 / 165 (0.61%)
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 INTESTINE ULCER			
subjects affected / exposed	0 / 79 (0.00%)	0 / 90 (0.00%)	0 / 165 (0.00%)
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 ACUTE			
subjects affected / exposed	0 / 79 (0.00%)	0 / 90 (0.00%)	0 / 165 (0.00%)
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			
CHOLELITHIASIS			
subjects affected / exposed	0 / 79 (0.00%)	0 / 90 (0.00%)	0 / 165 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CHOLECYSTITIS ACUTE			
subjects affected / exposed	0 / 79 (0.00%)	0 / 90 (0.00%)	0 / 165 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DRUG-INDUCED LIVER INJURY			
subjects affected / exposed	0 / 79 (0.00%)	0 / 90 (0.00%)	1 / 165 (0.61%)
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			

SUBCUTANEOUS EMPHYSEMA			
subjects affected / exposed	0 / 79 (0.00%)	0 / 90 (0.00%)	0 / 165 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
ACUTE KIDNEY INJURY			
subjects affected / exposed	0 / 79 (0.00%)	0 / 90 (0.00%)	0 / 165 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
NEPHROLITHIASIS			
subjects affected / exposed	0 / 79 (0.00%)	0 / 90 (0.00%)	0 / 165 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endocrine disorders			
GOITRE			
subjects affected / exposed	0 / 79 (0.00%)	0 / 90 (0.00%)	0 / 165 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ADRENAL INSUFFICIENCY			
subjects affected / exposed	0 / 79 (0.00%)	0 / 90 (0.00%)	0 / 165 (0.00%)
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			
ARTHRALGIA			
subjects affected / exposed	0 / 79 (0.00%)	0 / 90 (0.00%)	0 / 165 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
OSTEOARTHRITIS			
subjects affected / exposed	0 / 79 (0.00%)	1 / 90 (1.11%)	0 / 165 (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
NECK PAIN			

subjects affected / exposed	0 / 79 (0.00%)	0 / 90 (0.00%)	1 / 165 (0.61%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
INTERVERTEBRAL DISC PROTRUSION			
subjects affected / exposed	0 / 79 (0.00%)	0 / 90 (0.00%)	1 / 165 (0.61%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
FLANK PAIN			
subjects affected / exposed	0 / 79 (0.00%)	0 / 90 (0.00%)	0 / 165 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BACK PAIN			
subjects affected / exposed	0 / 79 (0.00%)	0 / 90 (0.00%)	0 / 165 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SYSTEMIC LUPUS ERYTHEMATOSUS			
subjects affected / exposed	0 / 79 (0.00%)	0 / 90 (0.00%)	0 / 165 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
RAPIDLY PROGRESSIVE OSTEOARTHRITIS			
subjects affected / exposed	0 / 79 (0.00%)	0 / 90 (0.00%)	0 / 165 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PSORIATIC ARTHROPATHY			
subjects affected / exposed	0 / 79 (0.00%)	0 / 90 (0.00%)	0 / 165 (0.00%)
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			
ABSCESS			
subjects affected / exposed	0 / 79 (0.00%)	0 / 90 (0.00%)	0 / 165 (0.00%)
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 / 79 (0.00%)	0 / 90 (0.00%)	1 / 165 (0.61%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BRONCHIOLITIS			
subjects affected / exposed	1 / 79 (1.27%)	0 / 90 (0.00%)	0 / 165 (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
BACTERAEMIA			
subjects affected / exposed	0 / 79 (0.00%)	0 / 90 (0.00%)	0 / 165 (0.00%)
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 / 79 (0.00%)	0 / 90 (0.00%)	0 / 165 (0.00%)
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 / 79 (0.00%)	0 / 90 (0.00%)	0 / 165 (0.00%)
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 STAPHYLOCOCCAL			
subjects affected / exposed	0 / 79 (0.00%)	0 / 90 (0.00%)	0 / 165 (0.00%)
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 / 79 (0.00%)	0 / 90 (0.00%)	2 / 165 (1.21%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CELLULITIS			
subjects affected / exposed	0 / 79 (0.00%)	0 / 90 (0.00%)	0 / 165 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DIVERTICULITIS			

subjects affected / exposed	0 / 79 (0.00%)	0 / 90 (0.00%)	0 / 165 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CYTOMEGALOVIRUS INFECTION			
subjects affected / exposed	0 / 79 (0.00%)	0 / 90 (0.00%)	0 / 165 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
EXTRADURAL ABSCESS			
subjects affected / exposed	0 / 79 (0.00%)	0 / 90 (0.00%)	0 / 165 (0.00%)
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			
subjects affected / exposed	0 / 79 (0.00%)	0 / 90 (0.00%)	1 / 165 (0.61%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
LOWER RESPIRATORY TRACT INFECTION BACTERIAL			
subjects affected / exposed	0 / 79 (0.00%)	0 / 90 (0.00%)	0 / 165 (0.00%)
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 ABSCESS			
subjects affected / exposed	0 / 79 (0.00%)	0 / 90 (0.00%)	0 / 165 (0.00%)
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 / 79 (0.00%)	0 / 90 (0.00%)	1 / 165 (0.61%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HIV INFECTION			
subjects affected / exposed	0 / 79 (0.00%)	0 / 90 (0.00%)	0 / 165 (0.00%)
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 VIRAL			

subjects affected / exposed	0 / 79 (0.00%)	0 / 90 (0.00%)	0 / 165 (0.00%)
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 INFLUENZAL			
subjects affected / exposed	0 / 79 (0.00%)	0 / 90 (0.00%)	0 / 165 (0.00%)
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 / 79 (1.27%)	0 / 90 (0.00%)	2 / 165 (1.21%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PNEUMOCYSTIS JIROVECII PNEUMONIA			
subjects affected / exposed	0 / 79 (0.00%)	0 / 90 (0.00%)	0 / 165 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PHARYNGITIS			
subjects affected / exposed	0 / 79 (0.00%)	0 / 90 (0.00%)	0 / 165 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
MENINGITIS			
subjects affected / exposed	0 / 79 (0.00%)	0 / 90 (0.00%)	0 / 165 (0.00%)
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 TRACT INFECTION			
subjects affected / exposed	0 / 79 (0.00%)	0 / 90 (0.00%)	0 / 165 (0.00%)
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 / 79 (0.00%)	0 / 90 (0.00%)	0 / 165 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SUBCUTANEOUS ABSCESS			

subjects affected / exposed	0 / 79 (0.00%)	0 / 90 (0.00%)	0 / 165 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
URINARY TRACT INFECTION			
subjects affected / exposed	0 / 79 (0.00%)	0 / 90 (0.00%)	0 / 165 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
UPPER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	0 / 79 (0.00%)	0 / 90 (0.00%)	1 / 165 (0.61%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
VIRAL UPPER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	0 / 79 (0.00%)	1 / 90 (1.11%)	0 / 165 (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
Metabolism and nutrition disorders			
DEHYDRATION			
subjects affected / exposed	0 / 79 (0.00%)	0 / 90 (0.00%)	0 / 165 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DIABETES MELLITUS			
subjects affected / exposed	1 / 79 (1.27%)	0 / 90 (0.00%)	0 / 165 (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
HYPONATRAEMIA			
subjects affected / exposed	0 / 79 (0.00%)	0 / 90 (0.00%)	0 / 165 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DIABETIC KETOACIDOSIS			
subjects affected / exposed	0 / 79 (0.00%)	0 / 90 (0.00%)	0 / 165 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
METABOLIC ACIDOSIS			

subjects affected / exposed	0 / 79 (0.00%)	0 / 90 (0.00%)	0 / 165 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
TYPE 1 DIABETES MELLITUS			
subjects affected / exposed	0 / 79 (0.00%)	0 / 90 (0.00%)	1 / 165 (0.61%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Period 2: Upadacitinib 15mg (Week 56 to EOS)	Period 2: Placebo / Upadacitinib 30mg (Week 56 to Week EOS)	Period 2: Placebo / Upadacitinib 15mg (Week 56 to Week EOS)
Total subjects affected by serious adverse events			
subjects affected / exposed	24 / 167 (14.37%)	12 / 77 (15.58%)	7 / 69 (10.14%)
number of deaths (all causes)	5	2	0
number of deaths resulting from adverse events	1	1	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
ADENOCARCINOMA OF COLON			
subjects affected / exposed	1 / 167 (0.60%)	0 / 77 (0.00%)	0 / 69 (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
ANOGENITAL WARTS			
subjects affected / exposed	0 / 167 (0.00%)	0 / 77 (0.00%)	0 / 69 (0.00%)
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 CANCER METASTATIC			
subjects affected / exposed	0 / 167 (0.00%)	0 / 77 (0.00%)	0 / 69 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
INTRADUCTAL PAPILLARY BREAST NEOPLASM			
subjects affected / exposed	0 / 167 (0.00%)	0 / 77 (0.00%)	0 / 69 (0.00%)
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 CARCINOMA			

subjects affected / exposed	0 / 167 (0.00%)	0 / 77 (0.00%)	0 / 69 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
MALIGNANT MELANOMA STAGE III			
subjects affected / exposed	0 / 167 (0.00%)	0 / 77 (0.00%)	0 / 69 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
NEUROENDOCRINE CARCINOMA OF THE SKIN			
subjects affected / exposed	0 / 167 (0.00%)	0 / 77 (0.00%)	0 / 69 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
NEOPLASM MALIGNANT			
subjects affected / exposed	1 / 167 (0.60%)	0 / 77 (0.00%)	0 / 69 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
OVARIAN CANCER			
subjects affected / exposed	1 / 167 (0.60%)	0 / 77 (0.00%)	0 / 69 (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
OROPHARYNGEAL SQUAMOUS CELL CARCINOMA			
subjects affected / exposed	0 / 167 (0.00%)	0 / 77 (0.00%)	0 / 69 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
OVARIAN THECA CELL TUMOUR			
subjects affected / exposed	0 / 167 (0.00%)	0 / 77 (0.00%)	0 / 69 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PARATHYROID TUMOUR BENIGN			
subjects affected / exposed	0 / 167 (0.00%)	0 / 77 (0.00%)	0 / 69 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PROSTATE CANCER			

subjects affected / exposed	0 / 167 (0.00%)	0 / 77 (0.00%)	0 / 69 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
RECTAL ADENOCARCINOMA			
subjects affected / exposed	0 / 167 (0.00%)	0 / 77 (0.00%)	0 / 69 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
RECTAL CANCER			
subjects affected / exposed	0 / 167 (0.00%)	0 / 77 (0.00%)	0 / 69 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
UTERINE LEIOMYOMA			
subjects affected / exposed	0 / 167 (0.00%)	0 / 77 (0.00%)	0 / 69 (0.00%)
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			
CIRCULATORY COLLAPSE			
subjects affected / exposed	1 / 167 (0.60%)	0 / 77 (0.00%)	0 / 69 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Pregnancy, puerperium and perinatal conditions			
ABORTION SPONTANEOUS			
subjects affected / exposed	0 / 167 (0.00%)	0 / 77 (0.00%)	0 / 69 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ECTOPIC PREGNANCY			
subjects affected / exposed	0 / 167 (0.00%)	0 / 77 (0.00%)	0 / 69 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
PYREXIA			

subjects affected / exposed	0 / 167 (0.00%)	0 / 77 (0.00%)	0 / 69 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DEATH			
subjects affected / exposed	1 / 167 (0.60%)	0 / 77 (0.00%)	0 / 69 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
CHEST PAIN			
subjects affected / exposed	0 / 167 (0.00%)	0 / 77 (0.00%)	0 / 69 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SYSTEMIC INFLAMMATORY RESPONSE SYNDROME			
subjects affected / exposed	0 / 167 (0.00%)	0 / 77 (0.00%)	0 / 69 (0.00%)
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 / 167 (0.00%)	0 / 77 (0.00%)	0 / 69 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BENIGN PROSTATIC HYPERPLASIA			
subjects affected / exposed	0 / 167 (0.00%)	0 / 77 (0.00%)	0 / 69 (0.00%)
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 / 167 (0.00%)	0 / 77 (0.00%)	0 / 69 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ASTHMA			

subjects affected / exposed	0 / 167 (0.00%)	1 / 77 (1.30%)	0 / 69 (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	0 / 167 (0.00%)	0 / 77 (0.00%)	0 / 69 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HAEMOTHORAX			
subjects affected / exposed	0 / 167 (0.00%)	0 / 77 (0.00%)	0 / 69 (0.00%)
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 / 167 (0.00%)	1 / 77 (1.30%)	0 / 69 (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
PNEUMOTHORAX			
subjects affected / exposed	0 / 167 (0.00%)	1 / 77 (1.30%)	0 / 69 (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 EMBOLISM			
subjects affected / exposed	0 / 167 (0.00%)	1 / 77 (1.30%)	0 / 69 (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			
DISORIENTATION			
subjects affected / exposed	0 / 167 (0.00%)	0 / 77 (0.00%)	0 / 69 (0.00%)
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 STATUS CHANGES			
subjects affected / exposed	0 / 167 (0.00%)	0 / 77 (0.00%)	0 / 69 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SUICIDE ATTEMPT			

subjects affected / exposed	0 / 167 (0.00%)	1 / 77 (1.30%)	0 / 69 (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
Product issues			
DEVICE DISLOCATION			
subjects affected / exposed	1 / 167 (0.60%)	0 / 77 (0.00%)	0 / 69 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
CERVICAL VERTEBRAL FRACTURE			
subjects affected / exposed	1 / 167 (0.60%)	0 / 77 (0.00%)	0 / 69 (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
FALL			
subjects affected / exposed	0 / 167 (0.00%)	0 / 77 (0.00%)	0 / 69 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
FEMORAL NECK FRACTURE			
subjects affected / exposed	0 / 167 (0.00%)	0 / 77 (0.00%)	0 / 69 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
FIBULA FRACTURE			
subjects affected / exposed	0 / 167 (0.00%)	0 / 77 (0.00%)	0 / 69 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
LUMBAR VERTEBRAL FRACTURE			
subjects affected / exposed	1 / 167 (0.60%)	0 / 77 (0.00%)	0 / 69 (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
SUBDURAL HAEMORRHAGE			
subjects affected / exposed	1 / 167 (0.60%)	0 / 77 (0.00%)	0 / 69 (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

SKULL FRACTURED BASE			
subjects affected / exposed	1 / 167 (0.60%)	0 / 77 (0.00%)	0 / 69 (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
ROAD TRAFFIC ACCIDENT			
subjects affected / exposed	1 / 167 (0.60%)	0 / 77 (0.00%)	0 / 69 (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
RIB FRACTURE			
subjects affected / exposed	0 / 167 (0.00%)	0 / 77 (0.00%)	0 / 69 (0.00%)
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 BILE LEAK			
subjects affected / exposed	0 / 167 (0.00%)	0 / 77 (0.00%)	1 / 69 (1.45%)
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 PSEUDOANEURYSM			
subjects affected / exposed	0 / 167 (0.00%)	0 / 77 (0.00%)	0 / 69 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
TRAUMATIC HAEMOTHORAX			
subjects affected / exposed	1 / 167 (0.60%)	0 / 77 (0.00%)	0 / 69 (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 / 167 (0.60%)	0 / 77 (0.00%)	0 / 69 (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
TENDON RUPTURE			
subjects affected / exposed	0 / 167 (0.00%)	0 / 77 (0.00%)	0 / 69 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			

ACUTE MYOCARDIAL INFARCTION			
subjects affected / exposed	1 / 167 (0.60%)	0 / 77 (0.00%)	0 / 69 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
ANGINA PECTORIS			
subjects affected / exposed	1 / 167 (0.60%)	0 / 77 (0.00%)	0 / 69 (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
ANGINA UNSTABLE			
subjects affected / exposed	0 / 167 (0.00%)	0 / 77 (0.00%)	0 / 69 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
AORTIC VALVE STENOSIS			
subjects affected / exposed	2 / 167 (1.20%)	0 / 77 (0.00%)	0 / 69 (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
ATRIAL FIBRILLATION			
subjects affected / exposed	1 / 167 (0.60%)	1 / 77 (1.30%)	0 / 69 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BRADYCARDIA			
subjects affected / exposed	0 / 167 (0.00%)	0 / 77 (0.00%)	0 / 69 (0.00%)
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 FAILURE			
subjects affected / exposed	0 / 167 (0.00%)	1 / 77 (1.30%)	0 / 69 (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
CARDIO-RESPIRATORY ARREST			
subjects affected / exposed	0 / 167 (0.00%)	0 / 77 (0.00%)	0 / 69 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CORONARY ARTERY STENOSIS			

subjects affected / exposed	0 / 167 (0.00%)	0 / 77 (0.00%)	0 / 69 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
MYOCARDIAL INFARCTION			
subjects affected / exposed	0 / 167 (0.00%)	0 / 77 (0.00%)	0 / 69 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SUPRAVENTRICULAR TACHYCARDIA			
subjects affected / exposed	0 / 167 (0.00%)	0 / 77 (0.00%)	0 / 69 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
VENTRICULAR FIBRILLATION			
subjects affected / exposed	0 / 167 (0.00%)	0 / 77 (0.00%)	0 / 69 (0.00%)
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			
BRAIN OEDEMA			
subjects affected / exposed	1 / 167 (0.60%)	0 / 77 (0.00%)	0 / 69 (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
CAROTID ARTERY INSUFFICIENCY			
subjects affected / exposed	0 / 167 (0.00%)	0 / 77 (0.00%)	0 / 69 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DIZZINESS			
subjects affected / exposed	0 / 167 (0.00%)	0 / 77 (0.00%)	1 / 69 (1.45%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
GENERALISED TONIC-CLONIC SEIZURE			
subjects affected / exposed	1 / 167 (0.60%)	0 / 77 (0.00%)	0 / 69 (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
FACIAL PARALYSIS			

subjects affected / exposed	0 / 167 (0.00%)	1 / 77 (1.30%)	0 / 69 (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
SPEECH DISORDER			
subjects affected / exposed	0 / 167 (0.00%)	0 / 77 (0.00%)	0 / 69 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
TRANSIENT GLOBAL AMNESIA			
subjects affected / exposed	0 / 167 (0.00%)	0 / 77 (0.00%)	0 / 69 (0.00%)
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	1 / 167 (0.60%)	0 / 77 (0.00%)	0 / 69 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
BLOOD LOSS ANAEMIA			
subjects affected / exposed	0 / 167 (0.00%)	0 / 77 (0.00%)	0 / 69 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PANCYTOPENIA			
subjects affected / exposed	0 / 167 (0.00%)	1 / 77 (1.30%)	0 / 69 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0
Eye disorders			
RETINAL DETACHMENT			
subjects affected / exposed	0 / 167 (0.00%)	1 / 77 (1.30%)	0 / 69 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
DUODENAL ULCER HAEMORRHAGE			
subjects affected / exposed	0 / 167 (0.00%)	0 / 77 (0.00%)	0 / 69 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

DIARRHOEA			
subjects affected / exposed	0 / 167 (0.00%)	0 / 77 (0.00%)	0 / 69 (0.00%)
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 / 167 (0.00%)	1 / 77 (1.30%)	0 / 69 (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
DUODENAL ULCER			
subjects affected / exposed	0 / 167 (0.00%)	1 / 77 (1.30%)	0 / 69 (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
ABDOMINAL PAIN			
subjects affected / exposed	0 / 167 (0.00%)	0 / 77 (0.00%)	0 / 69 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
GASTRITIS			
subjects affected / exposed	0 / 167 (0.00%)	0 / 77 (0.00%)	1 / 69 (1.45%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
GASTRITIS EROSIVE			
subjects affected / exposed	0 / 167 (0.00%)	0 / 77 (0.00%)	0 / 69 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
INGUINAL HERNIA			
subjects affected / exposed	0 / 167 (0.00%)	0 / 77 (0.00%)	0 / 69 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HAEMATEMESIS			
subjects affected / exposed	0 / 167 (0.00%)	0 / 77 (0.00%)	0 / 69 (0.00%)
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 INTESTINE ULCER			

subjects affected / exposed	0 / 167 (0.00%)	0 / 77 (0.00%)	0 / 69 (0.00%)
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 ACUTE			
subjects affected / exposed	1 / 167 (0.60%)	0 / 77 (0.00%)	0 / 69 (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
Hepatobiliary disorders			
CHOLELITHIASIS			
subjects affected / exposed	1 / 167 (0.60%)	0 / 77 (0.00%)	1 / 69 (1.45%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CHOLECYSTITIS ACUTE			
subjects affected / exposed	1 / 167 (0.60%)	0 / 77 (0.00%)	0 / 69 (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
DRUG-INDUCED LIVER INJURY			
subjects affected / exposed	0 / 167 (0.00%)	0 / 77 (0.00%)	0 / 69 (0.00%)
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			
SUBCUTANEOUS EMPHYSEMA			
subjects affected / exposed	0 / 167 (0.00%)	1 / 77 (1.30%)	0 / 69 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
ACUTE KIDNEY INJURY			
subjects affected / exposed	1 / 167 (0.60%)	0 / 77 (0.00%)	0 / 69 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
NEPHROLITHIASIS			
subjects affected / exposed	0 / 167 (0.00%)	0 / 77 (0.00%)	0 / 69 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Endocrine disorders			
GOITRE			
subjects affected / exposed	0 / 167 (0.00%)	0 / 77 (0.00%)	0 / 69 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ADRENAL INSUFFICIENCY			
subjects affected / exposed	0 / 167 (0.00%)	1 / 77 (1.30%)	0 / 69 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
ARTHRALGIA			
subjects affected / exposed	1 / 167 (0.60%)	0 / 77 (0.00%)	0 / 69 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
OSTEOARTHRITIS			
subjects affected / exposed	0 / 167 (0.00%)	0 / 77 (0.00%)	0 / 69 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
NECK PAIN			
subjects affected / exposed	0 / 167 (0.00%)	0 / 77 (0.00%)	0 / 69 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
INTERVERTEBRAL DISC PROTRUSION			
subjects affected / exposed	0 / 167 (0.00%)	0 / 77 (0.00%)	0 / 69 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
FLANK PAIN			
subjects affected / exposed	0 / 167 (0.00%)	0 / 77 (0.00%)	0 / 69 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BACK PAIN			

subjects affected / exposed	0 / 167 (0.00%)	0 / 77 (0.00%)	1 / 69 (1.45%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SYSTEMIC LUPUS ERYTHEMATOSUS			
subjects affected / exposed	0 / 167 (0.00%)	0 / 77 (0.00%)	0 / 69 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
RAPIDLY PROGRESSIVE OSTEOARTHRITIS			
subjects affected / exposed	0 / 167 (0.00%)	0 / 77 (0.00%)	0 / 69 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PSORIATIC ARTHROPATHY			
subjects affected / exposed	2 / 167 (1.20%)	0 / 77 (0.00%)	0 / 69 (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
Infections and infestations			
ABSCESS			
subjects affected / exposed	0 / 167 (0.00%)	0 / 77 (0.00%)	1 / 69 (1.45%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ANAL ABSCESS			
subjects affected / exposed	0 / 167 (0.00%)	0 / 77 (0.00%)	0 / 69 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BRONCHIOLITIS			
subjects affected / exposed	0 / 167 (0.00%)	0 / 77 (0.00%)	0 / 69 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BACTERAEMIA			
subjects affected / exposed	0 / 167 (0.00%)	0 / 77 (0.00%)	0 / 69 (0.00%)
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 / 167 (0.00%)	0 / 77 (0.00%)	0 / 69 (0.00%)
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	4 / 167 (2.40%)	0 / 77 (0.00%)	1 / 69 (1.45%)
occurrences causally related to treatment / all	2 / 4	0 / 0	0 / 1
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 0
BURSITIS INFECTIVE STAPHYLOCOCCAL			
subjects affected / exposed	0 / 167 (0.00%)	0 / 77 (0.00%)	0 / 69 (0.00%)
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	1 / 167 (0.60%)	2 / 77 (2.60%)	0 / 69 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
CELLULITIS			
subjects affected / exposed	2 / 167 (1.20%)	1 / 77 (1.30%)	0 / 69 (0.00%)
occurrences causally related to treatment / all	1 / 2	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DIVERTICULITIS			
subjects affected / exposed	1 / 167 (0.60%)	1 / 77 (1.30%)	0 / 69 (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
CYTOMEGALOVIRUS INFECTION			
subjects affected / exposed	0 / 167 (0.00%)	1 / 77 (1.30%)	0 / 69 (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
EXTRADURAL ABSCESS			
subjects affected / exposed	0 / 167 (0.00%)	0 / 77 (0.00%)	0 / 69 (0.00%)
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			

subjects affected / exposed	1 / 167 (0.60%)	0 / 77 (0.00%)	0 / 69 (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
LOWER RESPIRATORY TRACT INFECTION BACTERIAL			
subjects affected / exposed	0 / 167 (0.00%)	1 / 77 (1.30%)	0 / 69 (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
LIVER ABSCESS			
subjects affected / exposed	0 / 167 (0.00%)	0 / 77 (0.00%)	1 / 69 (1.45%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HERPES ZOSTER			
subjects affected / exposed	0 / 167 (0.00%)	0 / 77 (0.00%)	0 / 69 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HIV INFECTION			
subjects affected / exposed	1 / 167 (0.60%)	0 / 77 (0.00%)	0 / 69 (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
GASTROENTERITIS VIRAL			
subjects affected / exposed	0 / 167 (0.00%)	1 / 77 (1.30%)	0 / 69 (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 INFLUENZAL			
subjects affected / exposed	0 / 167 (0.00%)	0 / 77 (0.00%)	0 / 69 (0.00%)
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 / 167 (0.00%)	1 / 77 (1.30%)	0 / 69 (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
PNEUMOCYSTIS JIROVECII PNEUMONIA			

subjects affected / exposed	0 / 167 (0.00%)	1 / 77 (1.30%)	0 / 69 (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
PHARYNGITIS			
subjects affected / exposed	0 / 167 (0.00%)	1 / 77 (1.30%)	0 / 69 (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
MENINGITIS			
subjects affected / exposed	0 / 167 (0.00%)	1 / 77 (1.30%)	0 / 69 (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 TRACT INFECTION			
subjects affected / exposed	0 / 167 (0.00%)	1 / 77 (1.30%)	0 / 69 (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
SEPSIS			
subjects affected / exposed	0 / 167 (0.00%)	1 / 77 (1.30%)	0 / 69 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SUBCUTANEOUS ABSCESS			
subjects affected / exposed	0 / 167 (0.00%)	0 / 77 (0.00%)	0 / 69 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
URINARY TRACT INFECTION			
subjects affected / exposed	0 / 167 (0.00%)	0 / 77 (0.00%)	0 / 69 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
UPPER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	0 / 167 (0.00%)	0 / 77 (0.00%)	0 / 69 (0.00%)
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 UPPER RESPIRATORY TRACT INFECTION			

subjects affected / exposed	0 / 167 (0.00%)	0 / 77 (0.00%)	0 / 69 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
DEHYDRATION			
subjects affected / exposed	1 / 167 (0.60%)	0 / 77 (0.00%)	0 / 69 (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
DIABETES MELLITUS			
subjects affected / exposed	0 / 167 (0.00%)	0 / 77 (0.00%)	0 / 69 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HYPONATRAEMIA			
subjects affected / exposed	1 / 167 (0.60%)	0 / 77 (0.00%)	0 / 69 (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
DIABETIC KETOACIDOSIS			
subjects affected / exposed	0 / 167 (0.00%)	0 / 77 (0.00%)	1 / 69 (1.45%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
METABOLIC ACIDOSIS			
subjects affected / exposed	0 / 167 (0.00%)	1 / 77 (1.30%)	0 / 69 (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
TYPE 1 DIABETES MELLITUS			
subjects affected / exposed	0 / 167 (0.00%)	0 / 77 (0.00%)	0 / 69 (0.00%)
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	Period 2: Pooled Upadacitinib (Switched From 30mg to 15mg P2)		
Total subjects affected by serious adverse events			
subjects affected / exposed	5 / 87 (5.75%)		
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 / 87 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
ANOGENITAL WARTS			
subjects affected / exposed	0 / 87 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
GASTROINTESTINAL CANCER METASTATIC			
subjects affected / exposed	1 / 87 (1.15%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
INTRADUCTAL PAPILLARY BREAST NEOPLASM			
subjects affected / exposed	0 / 87 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
GASTROINTESTINAL CARCINOMA			
subjects affected / exposed	1 / 87 (1.15%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
MALIGNANT MELANOMA STAGE III			
subjects affected / exposed	0 / 87 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
NEUROENDOCRINE CARCINOMA OF THE SKIN			
subjects affected / exposed	0 / 87 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
NEOPLASM MALIGNANT			

subjects affected / exposed	0 / 87 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
OVARIAN CANCER				
subjects affected / exposed	0 / 87 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
OROPHARYNGEAL SQUAMOUS CELL CARCINOMA				
subjects affected / exposed	0 / 87 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
OVARIAN THECA CELL TUMOUR				
subjects affected / exposed	0 / 87 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
PARATHYROID TUMOUR BENIGN				
subjects affected / exposed	0 / 87 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
PROSTATE CANCER				
subjects affected / exposed	1 / 87 (1.15%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
RECTAL ADENOCARCINOMA				
subjects affected / exposed	0 / 87 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
RECTAL CANCER				
subjects affected / exposed	0 / 87 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
UTERINE LEIOMYOMA				

subjects affected / exposed	0 / 87 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
CIRCULATORY COLLAPSE			
subjects affected / exposed	0 / 87 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pregnancy, puerperium and perinatal conditions			
ABORTION SPONTANEOUS			
subjects affected / exposed	0 / 87 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
ECTOPIC PREGNANCY			
subjects affected / exposed	0 / 87 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
PYREXIA			
subjects affected / exposed	0 / 87 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
DEATH			
subjects affected / exposed	0 / 87 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
CHEST PAIN			
subjects affected / exposed	0 / 87 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
SYSTEMIC INFLAMMATORY RESPONSE SYNDROME			

subjects affected / exposed	0 / 87 (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 / 87 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
BENIGN PROSTATIC HYPERPLASIA			
subjects affected / exposed	0 / 87 (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 / 87 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
ASTHMA			
subjects affected / exposed	0 / 87 (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 / 87 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
HAEMOTHORAX			
subjects affected / exposed	0 / 87 (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 / 87 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
PNEUMOTHORAX			
subjects affected / exposed	0 / 87 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
PULMONARY EMBOLISM			
subjects affected / exposed	0 / 87 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
DISORIENTATION			
subjects affected / exposed	0 / 87 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
MENTAL STATUS CHANGES			
subjects affected / exposed	0 / 87 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
SUICIDE ATTEMPT			
subjects affected / exposed	0 / 87 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Product issues			
DEVICE DISLOCATION			
subjects affected / exposed	0 / 87 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
CERVICAL VERTEBRAL FRACTURE			
subjects affected / exposed	0 / 87 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

FALL				
subjects affected / exposed	0 / 87 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
FEMORAL NECK FRACTURE				
subjects affected / exposed	0 / 87 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
FIBULA FRACTURE				
subjects affected / exposed	0 / 87 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
LUMBAR VERTEBRAL FRACTURE				
subjects affected / exposed	0 / 87 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
SUBDURAL HAEMORRHAGE				
subjects affected / exposed	0 / 87 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
SKULL FRACTURED BASE				
subjects affected / exposed	0 / 87 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
ROAD TRAFFIC ACCIDENT				
subjects affected / exposed	0 / 87 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
RIB FRACTURE				
subjects affected / exposed	0 / 87 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
POST PROCEDURAL BILE LEAK				

subjects affected / exposed	0 / 87 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
VASCULAR PSEUDOANEURYSM				
subjects affected / exposed	0 / 87 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
TRAUMATIC HAEMOTHORAX				
subjects affected / exposed	0 / 87 (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 / 87 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
TENDON RUPTURE				
subjects affected / exposed	0 / 87 (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 / 87 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
ANGINA PECTORIS				
subjects affected / exposed	0 / 87 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
ANGINA UNSTABLE				
subjects affected / exposed	0 / 87 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
AORTIC VALVE STENOSIS				

subjects affected / exposed	0 / 87 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
ATRIAL FIBRILLATION				
subjects affected / exposed	0 / 87 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
BRADYCARDIA				
subjects affected / exposed	0 / 87 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
CARDIAC FAILURE				
subjects affected / exposed	0 / 87 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
CARDIO-RESPIRATORY ARREST				
subjects affected / exposed	0 / 87 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
CORONARY ARTERY STENOSIS				
subjects affected / exposed	0 / 87 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
MYOCARDIAL INFARCTION				
subjects affected / exposed	0 / 87 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
SUPRAVENTRICULAR TACHYCARDIA				
subjects affected / exposed	0 / 87 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
VENTRICULAR FIBRILLATION				

subjects affected / exposed	0 / 87 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Nervous system disorders				
BRAIN OEDEMA				
subjects affected / exposed	0 / 87 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
CAROTID ARTERY INSUFFICIENCY				
subjects affected / exposed	0 / 87 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
DIZZINESS				
subjects affected / exposed	0 / 87 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
GENERALISED TONIC-CLONIC SEIZURE				
subjects affected / exposed	0 / 87 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
FACIAL PARALYSIS				
subjects affected / exposed	0 / 87 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
SPEECH DISORDER				
subjects affected / exposed	0 / 87 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
TRANSIENT GLOBAL AMNESIA				
subjects affected / exposed	0 / 87 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
SUBARACHNOID HAEMORRHAGE				

subjects affected / exposed	0 / 87 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
BLOOD LOSS ANAEMIA			
subjects affected / exposed	0 / 87 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
PANCYTOPENIA			
subjects affected / exposed	0 / 87 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Eye disorders			
RETINAL DETACHMENT			
subjects affected / exposed	0 / 87 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
DUODENAL ULCER HAEMORRHAGE			
subjects affected / exposed	0 / 87 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
DIARRHOEA			
subjects affected / exposed	0 / 87 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
COLITIS ULCERATIVE			
subjects affected / exposed	0 / 87 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
DUODENAL ULCER			
subjects affected / exposed	0 / 87 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

ABDOMINAL PAIN				
subjects affected / exposed	0 / 87 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
GASTRITIS				
subjects affected / exposed	0 / 87 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
GASTRITIS EROSIVE				
subjects affected / exposed	0 / 87 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
INGUINAL HERNIA				
subjects affected / exposed	0 / 87 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
HAEMATEMESIS				
subjects affected / exposed	0 / 87 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
SMALL INTESTINE ULCER				
subjects affected / exposed	0 / 87 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
PANCREATITIS ACUTE				
subjects affected / exposed	0 / 87 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hepatobiliary disorders				
CHOLELITHIASIS				
subjects affected / exposed	1 / 87 (1.15%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
CHOLECYSTITIS ACUTE				

subjects affected / exposed	0 / 87 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
DRUG-INDUCED LIVER INJURY			
subjects affected / exposed	0 / 87 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
SUBCUTANEOUS EMPHYSEMA			
subjects affected / exposed	0 / 87 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
ACUTE KIDNEY INJURY			
subjects affected / exposed	0 / 87 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
NEPHROLITHIASIS			
subjects affected / exposed	0 / 87 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Endocrine disorders			
GOITRE			
subjects affected / exposed	0 / 87 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
ADRENAL INSUFFICIENCY			
subjects affected / exposed	0 / 87 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
ARTHRALGIA			

subjects affected / exposed	0 / 87 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
OSTEOARTHRITIS				
subjects affected / exposed	0 / 87 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
NECK PAIN				
subjects affected / exposed	0 / 87 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
INTERVERTEBRAL DISC PROTRUSION				
subjects affected / exposed	0 / 87 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
FLANK PAIN				
subjects affected / exposed	0 / 87 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
BACK PAIN				
subjects affected / exposed	0 / 87 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
SYSTEMIC LUPUS ERYTHEMATOSUS				
subjects affected / exposed	0 / 87 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
RAPIDLY PROGRESSIVE OSTEOARTHRITIS				
subjects affected / exposed	0 / 87 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
PSORIATIC ARTHROPATHY				

subjects affected / exposed	0 / 87 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
ABSCESS			
subjects affected / exposed	0 / 87 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
ANAL ABSCESS			
subjects affected / exposed	0 / 87 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
BRONCHIOLITIS			
subjects affected / exposed	0 / 87 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
BACTERAEMIA			
subjects affected / exposed	0 / 87 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
BRONCHITIS			
subjects affected / exposed	0 / 87 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
COVID-19			
subjects affected / exposed	0 / 87 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
BURSITIS INFECTIVE STAPHYLOCOCCAL			
subjects affected / exposed	0 / 87 (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 / 87 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
CELLULITIS				
subjects affected / exposed	0 / 87 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
DIVERTICULITIS				
subjects affected / exposed	0 / 87 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
CYTOMEGALOVIRUS INFECTION				
subjects affected / exposed	0 / 87 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
EXTRADURAL ABSCESS				
subjects affected / exposed	0 / 87 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
GASTROENTERITIS				
subjects affected / exposed	0 / 87 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
LOWER RESPIRATORY TRACT INFECTION BACTERIAL				
subjects affected / exposed	0 / 87 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
LIVER ABSCESS				
subjects affected / exposed	0 / 87 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
HERPES ZOSTER				

subjects affected / exposed	0 / 87 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
HIV INFECTION				
subjects affected / exposed	0 / 87 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
GASTROENTERITIS VIRAL				
subjects affected / exposed	0 / 87 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
PNEUMONIA INFLUENZAL				
subjects affected / exposed	0 / 87 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
PNEUMONIA				
subjects affected / exposed	2 / 87 (2.30%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
PNEUMOCYSTIS JIROVECII PNEUMONIA				
subjects affected / exposed	0 / 87 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
PHARYNGITIS				
subjects affected / exposed	0 / 87 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
MENINGITIS				
subjects affected / exposed	0 / 87 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
RESPIRATORY TRACT INFECTION				

subjects affected / exposed	0 / 87 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
SEPSIS				
subjects affected / exposed	0 / 87 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
SUBCUTANEOUS ABSCESS				
subjects affected / exposed	1 / 87 (1.15%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
URINARY TRACT INFECTION				
subjects affected / exposed	0 / 87 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
UPPER RESPIRATORY TRACT INFECTION				
subjects affected / exposed	0 / 87 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
VIRAL UPPER RESPIRATORY TRACT INFECTION				
subjects affected / exposed	0 / 87 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Metabolism and nutrition disorders				
DEHYDRATION				
subjects affected / exposed	0 / 87 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
DIABETES MELLITUS				
subjects affected / exposed	0 / 87 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
HYPONATRAEMIA				

subjects affected / exposed	0 / 87 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
DIABETIC KETOACIDOSIS			
subjects affected / exposed	0 / 87 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
METABOLIC ACIDOSIS			
subjects affected / exposed	0 / 87 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
TYPE 1 DIABETES MELLITUS			
subjects affected / exposed	0 / 87 (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	Period 1: Upadacitinib 15mg (ICF to Week 56)	Period 1: Upadacitinib 30mg (ICF to Week 56)	Period 1: Pooled Placebo (ICF to Week 24)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	111 / 211 (52.61%)	139 / 219 (63.47%)	87 / 212 (41.04%)
Investigations			
ALANINE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	5 / 211 (2.37%)	11 / 219 (5.02%)	1 / 212 (0.47%)
occurrences (all)	5	13	1
BLOOD CREATINE PHOSPHOKINASE INCREASED			
subjects affected / exposed	9 / 211 (4.27%)	22 / 219 (10.05%)	4 / 212 (1.89%)
occurrences (all)	10	29	4
Vascular disorders			
HYPERTENSION			
subjects affected / exposed	8 / 211 (3.79%)	10 / 219 (4.57%)	10 / 212 (4.72%)
occurrences (all)	9	10	12
Gastrointestinal disorders			

DIARRHOEA			
subjects affected / exposed	8 / 211 (3.79%)	15 / 219 (6.85%)	12 / 212 (5.66%)
occurrences (all)	8	18	13
NAUSEA			
subjects affected / exposed	8 / 211 (3.79%)	12 / 219 (5.48%)	7 / 212 (3.30%)
occurrences (all)	8	12	8
Hepatobiliary disorders			
HEPATIC STEATOSIS			
subjects affected / exposed	1 / 211 (0.47%)	3 / 219 (1.37%)	1 / 212 (0.47%)
occurrences (all)	1	3	1
Musculoskeletal and connective tissue disorders			
PSORIATIC ARTHROPATHY			
subjects affected / exposed	13 / 211 (6.16%)	7 / 219 (3.20%)	11 / 212 (5.19%)
occurrences (all)	14	8	12
Infections and infestations			
BRONCHITIS			
subjects affected / exposed	17 / 211 (8.06%)	15 / 219 (6.85%)	5 / 212 (2.36%)
occurrences (all)	20	16	5
COVID-19			
subjects affected / exposed	0 / 211 (0.00%)	0 / 219 (0.00%)	0 / 212 (0.00%)
occurrences (all)	0	0	0
HERPES ZOSTER			
subjects affected / exposed	8 / 211 (3.79%)	13 / 219 (5.94%)	2 / 212 (0.94%)
occurrences (all)	8	13	2
INFLUENZA			
subjects affected / exposed	14 / 211 (6.64%)	13 / 219 (5.94%)	3 / 212 (1.42%)
occurrences (all)	16	14	3
NASOPHARYNGITIS			
subjects affected / exposed	24 / 211 (11.37%)	29 / 219 (13.24%)	17 / 212 (8.02%)
occurrences (all)	29	34	18
PNEUMONIA			
subjects affected / exposed	1 / 211 (0.47%)	4 / 219 (1.83%)	3 / 212 (1.42%)
occurrences (all)	1	4	3
UPPER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	22 / 211 (10.43%)	29 / 219 (13.24%)	10 / 212 (4.72%)
occurrences (all)	27	34	13

TOOTH INFECTION			
subjects affected / exposed	3 / 211 (1.42%)	3 / 219 (1.37%)	1 / 212 (0.47%)
occurrences (all)	3	4	1
SINUSITIS			
subjects affected / exposed	8 / 211 (3.79%)	9 / 219 (4.11%)	9 / 212 (4.25%)
occurrences (all)	9	10	11
URINARY TRACT INFECTION			
subjects affected / exposed	19 / 211 (9.00%)	16 / 219 (7.31%)	12 / 212 (5.66%)
occurrences (all)	24	18	14
Metabolism and nutrition disorders			
DYSLIPIDAEMIA			
subjects affected / exposed	0 / 211 (0.00%)	1 / 219 (0.46%)	0 / 212 (0.00%)
occurrences (all)	0	1	0

Non-serious adverse events	Period 1: Placebo / Upadacitinib 15mg (Week 24 to Week 56)	Period 1: Placebo / Upadacitinib 30mg (Week 24 to Week 56)	Period 2: Upadacitinib 30mg (Week 56 to EOS)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	32 / 79 (40.51%)	34 / 90 (37.78%)	97 / 165 (58.79%)
Investigations			
ALANINE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	0 / 79 (0.00%)	4 / 90 (4.44%)	6 / 165 (3.64%)
occurrences (all)	0	4	6
BLOOD CREATINE PHOSPHOKINASE INCREASED			
subjects affected / exposed	2 / 79 (2.53%)	4 / 90 (4.44%)	8 / 165 (4.85%)
occurrences (all)	3	5	8
Vascular disorders			
HYPERTENSION			
subjects affected / exposed	4 / 79 (5.06%)	3 / 90 (3.33%)	11 / 165 (6.67%)
occurrences (all)	4	3	11
Gastrointestinal disorders			
DIARRHOEA			
subjects affected / exposed	3 / 79 (3.80%)	3 / 90 (3.33%)	4 / 165 (2.42%)
occurrences (all)	4	3	7
NAUSEA			
subjects affected / exposed	0 / 79 (0.00%)	1 / 90 (1.11%)	10 / 165 (6.06%)
occurrences (all)	0	1	10
Hepatobiliary disorders			

HEPATIC STEATOSIS			
subjects affected / exposed	0 / 79 (0.00%)	0 / 90 (0.00%)	3 / 165 (1.82%)
occurrences (all)	0	0	3
Musculoskeletal and connective tissue disorders			
PSORIATIC ARTHROPATHY			
subjects affected / exposed	2 / 79 (2.53%)	3 / 90 (3.33%)	16 / 165 (9.70%)
occurrences (all)	2	3	18
Infections and infestations			
BRONCHITIS			
subjects affected / exposed	5 / 79 (6.33%)	4 / 90 (4.44%)	8 / 165 (4.85%)
occurrences (all)	7	4	10
COVID-19			
subjects affected / exposed	0 / 79 (0.00%)	0 / 90 (0.00%)	12 / 165 (7.27%)
occurrences (all)	0	0	12
HERPES ZOSTER			
subjects affected / exposed	2 / 79 (2.53%)	5 / 90 (5.56%)	13 / 165 (7.88%)
occurrences (all)	2	5	13
INFLUENZA			
subjects affected / exposed	2 / 79 (2.53%)	2 / 90 (2.22%)	6 / 165 (3.64%)
occurrences (all)	2	3	6
NASOPHARYNGITIS			
subjects affected / exposed	5 / 79 (6.33%)	6 / 90 (6.67%)	11 / 165 (6.67%)
occurrences (all)	5	8	12
PNEUMONIA			
subjects affected / exposed	2 / 79 (2.53%)	0 / 90 (0.00%)	4 / 165 (2.42%)
occurrences (all)	2	0	5
UPPER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	6 / 79 (7.59%)	2 / 90 (2.22%)	9 / 165 (5.45%)
occurrences (all)	7	2	13
TOOTH INFECTION			
subjects affected / exposed	0 / 79 (0.00%)	2 / 90 (2.22%)	4 / 165 (2.42%)
occurrences (all)	0	2	4
SINUSITIS			
subjects affected / exposed	3 / 79 (3.80%)	2 / 90 (2.22%)	7 / 165 (4.24%)
occurrences (all)	4	2	7
URINARY TRACT INFECTION			

subjects affected / exposed	4 / 79 (5.06%)	4 / 90 (4.44%)	14 / 165 (8.48%)
occurrences (all)	4	4	22
Metabolism and nutrition disorders			
DYSLIPIDAEMIA			
subjects affected / exposed	0 / 79 (0.00%)	0 / 90 (0.00%)	4 / 165 (2.42%)
occurrences (all)	0	0	4

Non-serious adverse events	Period 2: Upadacitinib 15mg (Week 56 to EOS)	Period 2: Placebo / Upadacitinib 30mg (Week 56 to Week EOS)	Period 2: Placebo / Upadacitinib 15mg (Week 56 to Week EOS)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	110 / 167 (65.87%)	49 / 77 (63.64%)	40 / 69 (57.97%)
Investigations			
ALANINE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	6 / 167 (3.59%)	2 / 77 (2.60%)	3 / 69 (4.35%)
occurrences (all)	7	2	3
BLOOD CREATINE PHOSPHOKINASE INCREASED			
subjects affected / exposed	13 / 167 (7.78%)	6 / 77 (7.79%)	5 / 69 (7.25%)
occurrences (all)	15	7	5
Vascular disorders			
HYPERTENSION			
subjects affected / exposed	19 / 167 (11.38%)	7 / 77 (9.09%)	5 / 69 (7.25%)
occurrences (all)	20	8	5
Gastrointestinal disorders			
DIARRHOEA			
subjects affected / exposed	5 / 167 (2.99%)	2 / 77 (2.60%)	1 / 69 (1.45%)
occurrences (all)	5	2	1
NAUSEA			
subjects affected / exposed	4 / 167 (2.40%)	0 / 77 (0.00%)	0 / 69 (0.00%)
occurrences (all)	5	0	0
Hepatobiliary disorders			
HEPATIC STEATOSIS			
subjects affected / exposed	5 / 167 (2.99%)	5 / 77 (6.49%)	1 / 69 (1.45%)
occurrences (all)	5	5	1
Musculoskeletal and connective tissue disorders			
PSORIATIC ARTHROPATHY			

subjects affected / exposed	11 / 167 (6.59%)	8 / 77 (10.39%)	9 / 69 (13.04%)
occurrences (all)	14	8	9
Infections and infestations			
BRONCHITIS			
subjects affected / exposed	15 / 167 (8.98%)	4 / 77 (5.19%)	4 / 69 (5.80%)
occurrences (all)	17	5	4
COVID-19			
subjects affected / exposed	22 / 167 (13.17%)	7 / 77 (9.09%)	7 / 69 (10.14%)
occurrences (all)	22	7	7
HERPES ZOSTER			
subjects affected / exposed	10 / 167 (5.99%)	5 / 77 (6.49%)	3 / 69 (4.35%)
occurrences (all)	10	5	3
INFLUENZA			
subjects affected / exposed	3 / 167 (1.80%)	1 / 77 (1.30%)	2 / 69 (2.90%)
occurrences (all)	4	1	2
NASOPHARYNGITIS			
subjects affected / exposed	14 / 167 (8.38%)	6 / 77 (7.79%)	7 / 69 (10.14%)
occurrences (all)	17	6	8
PNEUMONIA			
subjects affected / exposed	2 / 167 (1.20%)	4 / 77 (5.19%)	1 / 69 (1.45%)
occurrences (all)	2	6	1
UPPER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	15 / 167 (8.98%)	6 / 77 (7.79%)	4 / 69 (5.80%)
occurrences (all)	15	7	4
TOOTH INFECTION			
subjects affected / exposed	2 / 167 (1.20%)	0 / 77 (0.00%)	4 / 69 (5.80%)
occurrences (all)	2	0	4
SINUSITIS			
subjects affected / exposed	7 / 167 (4.19%)	6 / 77 (7.79%)	2 / 69 (2.90%)
occurrences (all)	9	8	4
URINARY TRACT INFECTION			
subjects affected / exposed	17 / 167 (10.18%)	9 / 77 (11.69%)	8 / 69 (11.59%)
occurrences (all)	24	12	11
Metabolism and nutrition disorders			

DYSLIPIDAEMIA			
subjects affected / exposed	2 / 167 (1.20%)	4 / 77 (5.19%)	1 / 69 (1.45%)
occurrences (all)	2	4	1

Non-serious adverse events	Period 2: Pooled Upadacitinib (Switched From 30mg to 15mg P2)		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	34 / 87 (39.08%)		
Investigations			
ALANINE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	0 / 87 (0.00%)		
occurrences (all)	0		
BLOOD CREATINE PHOSPHOKINASE INCREASED			
subjects affected / exposed	2 / 87 (2.30%)		
occurrences (all)	2		
Vascular disorders			
HYPERTENSION			
subjects affected / exposed	1 / 87 (1.15%)		
occurrences (all)	1		
Gastrointestinal disorders			
DIARRHOEA			
subjects affected / exposed	4 / 87 (4.60%)		
occurrences (all)	4		
NAUSEA			
subjects affected / exposed	1 / 87 (1.15%)		
occurrences (all)	1		
Hepatobiliary disorders			
HEPATIC STEATOSIS			
subjects affected / exposed	1 / 87 (1.15%)		
occurrences (all)	1		
Musculoskeletal and connective tissue disorders			
PSORIATIC ARTHROPATHY			
subjects affected / exposed	8 / 87 (9.20%)		
occurrences (all)	8		
Infections and infestations			

BRONCHITIS subjects affected / exposed occurrences (all)	2 / 87 (2.30%) 2		
COVID-19 subjects affected / exposed occurrences (all)	14 / 87 (16.09%) 17		
HERPES ZOSTER subjects affected / exposed occurrences (all)	1 / 87 (1.15%) 1		
INFLUENZA subjects affected / exposed occurrences (all)	0 / 87 (0.00%) 0		
NASOPHARYNGITIS subjects affected / exposed occurrences (all)	5 / 87 (5.75%) 6		
PNEUMONIA subjects affected / exposed occurrences (all)	1 / 87 (1.15%) 1		
UPPER RESPIRATORY TRACT INFECTION subjects affected / exposed occurrences (all)	3 / 87 (3.45%) 3		
TOOTH INFECTION subjects affected / exposed occurrences (all)	0 / 87 (0.00%) 0		
SINUSITIS subjects affected / exposed occurrences (all)	0 / 87 (0.00%) 0		
URINARY TRACT INFECTION subjects affected / exposed occurrences (all)	3 / 87 (3.45%) 3		
Metabolism and nutrition disorders DYSLIPIDAEMIA subjects affected / exposed occurrences (all)	0 / 87 (0.00%) 0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
27 February 2017	Amendment 1: The protocol amendment includes various updates focused on enhancing subject safety, ensuring adherence to local guidelines, and improving communication. Key updates are: Contact Information: The Title Page now contains updated Sponsor/Emergency Contact fax numbers with country codes, providing sites with current and complete contact information. Safety Enhancements: The Inclusion Criteria, Exclusion Criteria, and Prohibited Therapies sections are revised to enhance subject safety during the study. Hepatitis Screening Compliance: Updates to relevant sections ensure that subjects in Japan with positive HBs Ab+ and/or HBc Ab+ at Screening undergo required testing per local guidelines. Adverse Event Reporting: The Serious Adverse Event and Malignancy Reporting section is updated to include country codes in the contact numbers for the Immunology Safety Team and Therapeutic Area Medical Director, aiding clear communication during emergencies. Study Activities Table: Appendix C revisions ensure: Correct footnotes for FSH testing; Accurate completion timing for subject questionnaires at Week 2; Annual frequency of activities noted in footnotes; Necessary testing for Japanese subjects with certain hepatitis markers per footnote. These amendments aim to maintain thorough and consistent communication across study sites, enhance participant safety, and adhere to locale-specific guidelines, ensuring efficient and compliant study operation.
03 March 2017	Amendment 2: This protocol amendment includes updates focused on enhancing subject safety, improving clarity, and removing redundant information. Key updates are: Subject Safety Improvements: Section 1.2 (Synopsis), Section 5.1 (Overall Study Design and Plan), and Table 2 (Clinical Laboratory Tests) have been revised to enhance safety measures for participants. The Inclusion Criteria in Section 5.2.1 are updated to further ensure subject safety. Removal of Redundancies: Duplicate information has been removed from the Exclusion Criteria in Section 5.2.2, streamlining the protocol. Clarifications: Footnote "h" in Table 2 and footnote "s" in Appendix C have been updated to clarify the reporting period for protocol deviations. Section 9.3 (Subject Information and Consent) now provides clearer procedures on subject withdrawal concerning optional exploratory samples. Overall, these amendments aim to maintain high safety standards, ensure precise procedural guidance, and create a more efficient and clear protocol for study conduct.

07 July 2017	Amendment 3: The amendment outlines updates focusing on clarifications, error corrections, methodological adjustments, and modifications in criteria. Key changes include: Title Page and Synopsis: Added the generic name of ABT-494 and corrected typos. Clarified the sponsor's role and enrollment criteria. Methodology Changes: Adjustments were made to allow the addition or modification of non-biologic DMARDs and oral corticosteroids. Non-responder criteria for rescue therapy and discontinuation were clarified. Exclusion and Safety Criteria: Added details on HBV testing requirements based on local regulations and updated safety information. Certain medical conditions previously listed as exclusions have been clarified or removed. Therapy and Drug Guidelines: Provided updates to permitted and prohibited therapies, including allowances for the modification of some medications and clarifications on live vaccine prohibition. Contraception Recommendations: Clarified requirements for contraception, particularly concerning surgically sterile or post-menopausal women, and updates regarding vasectomized partners. Study Procedures: Clarified procedures like informed consent, physical exams, pregnancy tests, and TB testing. Adjusted guidelines for ECGs and CXR assessments. Adverse Events and Toxicity Management: Updated classifications and management guidelines for adverse events and toxicity, including the handling of gastrointestinal events and ECG abnormalities. Study Activities and Appendices: Revised the timeframe and details for follow-up visits. Removed an outdated appendix and updated local requirement guidelines. These updates aim to enhance the study's clarity, ensure regulatory compliance, and improve participant safety and protocol adherence.
23 March 2018	Amendment 4: This protocol amendment includes administrative updates to enhance consistency, readability, and clarity. Sponsor information for non-EU countries is updated on the title page, and the emergency contact number is prominently added. Stratification will be based on the number of prior biologics a subject has failed. Inclusion criteria changes include shortening washout periods for certain drugs to reduce flare rates and removing male contraception requirements due to new studies showing upadacitinib poses no reproductive risk for males. Exclusion criteria adjustments permit enrollment in non-interventional studies and refine conditions around organ transplant histories, psoriasis treatments, and pregnancy post-study drug use. Study methodologies for TB testing and hepatitis screening are updated for consistency with safety standards, including specific PCR testing guidelines. Adverse event classifications are revised, removing subtypes of malignancies and adding embolic and thrombotic events. Contraception guidelines for males are updated based on new data showing no reproductive effects from upadacitinib. Sections on therapy options provide clarity: permitted changes in background DMARDs are preferred but not mandatory, responding flexibly to subject safety needs. Randomization methods emphasize stratification based on prior biologics. Adverse event severity grading is specified for investigators, with updated management for AST and ALT abnormalities and HBV testing procedures to manage potential reactivation risks. Further revisions include updated guidelines for protocol signatories, study activities related to TB, requirements for specific testing, and the prohibition of certain therapies. The revisions reflect efforts to align the protocol with current findings and maintain participant safety throughout the study.

14 January 2019	Amendment 5: This amendment to the clinical study protocol includes administrative and methodological updates aimed at enhancing consistency and clarity. Key updates involve defining stratification enrollment limits based on psoriasis involvement and prior biologic DMARD failures. These limits ensure a balanced study population, similar to past studies, and sufficiently power skin-related efficacy endpoints without altering study conduct or analysis. Key sections revised include the overall study design and discontinuation criteria to improve clarity. Male contraception requirements are removed, aligning with previous amendments, thereby eliminating the need to discuss pregnancy avoidance for female partners of male subjects. TB testing procedures are updated to allow retesting of QuantiFERON-TB Gold in low-risk subjects both initially and annually, and IGRA blood tests are now permitted for TB screening. Language across clinical laboratory tests is clarified for consistency with toxicity management guidelines. Randomization and drug assignment updates specify stratification limits, ensuring a comparative and balanced study population. Drug accountability requirements are aligned with revised sponsor guidelines. Serious adverse event reporting is refined to exclude USA-specific SUSAR references, applicable only to EU countries. Table 4 updates specify that ALT/AST toxicity-related symptoms must be new from baseline, with appropriate eCRFs provided for hepatic and renal situations. Protocol deviations include address updates, and Appendix changes reflect updates to protocol signatories and study activities, ensuring alignment across sections. Overall, these amendments streamline protocol management while maintaining focus on study integrity and participant safety.
04 October 2019	Amendment 6: This amendment involves numerous updates to the clinical study protocol, aimed at enhancing clarity, consistency, and accuracy. Key changes include: Administrative Revisions: Improved consistency and readability across the protocol, correcting descriptions of key terms and adding definitions such as PsO. Updates include adjustments in the efficacy section for FACIT-F and PsARC descriptions. Risk and Safety Updates: Updated safety information covers thromboembolic events and embryofetal effects, with toxicity management guidelines adding herpes zoster, skin cancer screening, and thrombosis considerations in line with Rinvoq® labeling. Procedural Adjustments: Changes in study procedures detail the removal of unnecessary ECG monitoring requirements, clarify who needs annual chest X-rays, and refine TB prophylaxis initiation processes. Prohibited therapy terminology is updated to reflect common usage (rifampicin for rifampin). Subjects may request withdrawal from both study drug or the study. Study Design and Variable Clarifications: Adjustments to secondary and additional efficacy variables align with new data, ensuring accurate reflections in sections on key secondary variables. Multiplicity control methods are revised for endpoint evaluations. Adverse Event Criteria: Specifies using the National Cancer Institute Common Terminology Criteria for Adverse Events (CTCAE) version for adverse event severity. Laboratory data analysis now uses CTCAE grades rather than simple categories. Appendices and Signatory Updates: Protocol signatories are updated, and study activities clarify requirements for specific tests and evaluations during follow-ups. Overall, these changes ensure the study protocol is up-to-date with current safety and efficacy standards while providing clear guidelines for subject management and data analysis, maintaining the integrity and reliability of study outcomes.

01 April 2020	Amendment 7: This amendment involves several updates to enhance protocol clarity, subject safety, and consistency: Administrative Updates: Text revisions enhance consistency and readability throughout the protocol. Safety Information: Updated information regarding risk of pregnancy for female partners of male subjects. Permitted Therapy: Section 5.2.3.2 is updated to ensure oral corticosteroid doses do not exceed prednisone ≤ 10 mg/day, per inclusion criteria. Hepatitis Screening: Clarifications in Section 5.3.1.1 allow HBV DNA PCR testing at unscheduled visits where mandated every 12 weeks. Similar updates apply to Figure 2's footnote. Subject Discontinuation and Safety Precautions: Section 5.4.1 clarifies that gastrointestinal perforations from appendicitis or mechanical injury do not require study drug discontinuation. It also adds precautions due to thrombotic risks associated with the JAK inhibitor class. Drug Accountability: Section 5.5.7 notes that drug receipt verification is through IRT systems, eliminating paper records. Toxicity Management: Updates in Section 6.1.7 clarify handling gastrointestinal perforations and add thrombotic risk precautions. It specifies additional eCRFs for certain lab abnormalities. Toxicity Guidelines: Table 4 updates provide clearer guidelines on managing laboratory value abnormalities to ensure subject safety. Cardiovascular Assessment: Section 6.1.9 clarifies that the Cardiovascular Adjudication Committee evaluates embolic and thrombotic adverse events. Protocol Signatories and Activities: Appendix B sees a title update, while Appendix C removes 'X' marks for Week 12 and 24 to clarify Hepatitis B testing applicability for Japan or where required. Footnotes clarify unscheduled HBV DNA PCR testing permissions. These amendments aim to improve the study's procedural clarity and ensure ongoing participant safety in light of new insights and regulatory mandates.
29 January 2021	Amendment 8: The protocol amendment includes administrative changes to improve consistency and clarity, replacing "ABT-494" with "upadacitinib" as the drug's generic name. Subjects on upadacitinib 30 mg daily now shift to 15 mg daily in Period 2 following approval, deemed optimal for active psoriatic arthritis and proposed for global marketing. Updates provide flexibility for study procedures amid emergencies/pandemics, allowing study visits via phone/week and subject/caregiver assessments. Vital signs, weight, physical exams, chest X-rays (CXR), and TB tests adapt to emergencies. If TB test seroconversion occurs without risk factors, CXR should follow ASAP; investigators consult AbbVie TA MD regarding continued drug use. Local labs ensure safety during emergencies. Direct-to-patient drug shipment aids compliance. Patient questionnaires and case report forms include phone interviews to gather patient-reported outcomes (PRO) during emergencies. Gastrointestinal perforation definition changes, with added toxicity management guidelines for COVID-19 suspicions to direct study drug interruption and data collection. AST/ALT guidelines are revised. Dose change impacts are noted in the Statistical Analysis Plan (SAP). Ethical study conduct adapts for protocol-specific hurdles and allows verbal consent for substantial study changes in emergencies. Remote monitoring is enabled; vendors and protocol signatories updated. COVID-19 impacts require supplemental case report forms and specific event data collection. Clarified that subjects should complete a discontinuation visit preferably prior to initiation of another therapy. Overall, these amendments boost protocol consistency, flexibility, safety, and response adaptivity during emergencies/pandemics, ensuring ethical and effective study management.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported