Clinical trial results:
A Phase 3, Randomized, Double-Blind Study Comparing Upadacitinib (ABT-494) Once Daily Monotherapy to Methotrexate (MTX) Monotherapy in MTX-Naïve Subjects with Moderately to Severely Active Rheumatoid Arthritis

Summary

EudraCT number	2015-003334-27
Trial protocol	SK SI ES GR LT BE CZ IE LV PL GB PT HU FI RO HR BG IT
Global end of trial date	11 November 2022
Results information	
Result version number	v1 (current)
This version publication date	07 July 2023
First version publication date	07 July 2023

Trial information

Trial identification	
Sponsor protocol code	M13-545
Additional study identifiers	
ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02706873
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
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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	11 November 2022
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	11 November 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The objectives of Period 1 were the following:
● To compare the safety and efficacy of upadacitinib 7.5 mg once daily (QD) monotherapy (for participants in Japan only), 15 mg QD monotherapy, and 30 mg QD monotherapy versus weekly methotrexate monotherapy for the treatment of signs and symptoms of RA in methotrexate-naïve adults with moderately to severely active RA;
● To compare the efficacy of upadacitinib 15 mg QD monotherapy and upadacitinib 30 mg QD monotherapy versus weekly methotrexate monotherapy for prevention of structural progression in methotrexate-naïve adults with moderately to severely active RA.
The objective of Period 2 is to evaluate the long-term safety, tolerability, and efficacy of upadacitinib 7.5 mg QD (for participants in Japan only), 15 mg QD, and 30 mg QD in adults with RA who have completed Period 1.

Protection of trial subjects:

Subject read and understood the information provided about the study and gave written permission.

Background therapy:

Subjects should continue on their stable doses of NSAIDs, paracetamol, oral corticosteroids (equivalent to prednisone ≤ 10 mg/day), or inhaled corticosteroids with no change in dose or frequency. If not taking any of the above at Baseline, these must not be initiated except where permitted by protocol-defined rescue therapy.
Those who do not achieve ≥ 20% improvement in both TJC and SJC compared with Baseline at two consecutive visits from Week 12 to 24 were offered rescue therapy with background RA medications: NSAIDs, corticosteroids and/or low-potency analgesics.
Rescue therapy for participants who do not achieve clinical remission (CR) based on Clinical Disease Activity Index (CDAI) (CDAI score ≤ 2.8) at Week 26 includes:
● If ≥ 20% improvement in both TJC and SJC compared with Baseline was achieved the Investigator will optimize (initiate or increase) background RA medications: NSAIDs, corticosteroids (oral ≤ 10 mg/day prednisone equivalent and up to 2 local injections), low-potency analgesics and conventional synthetic disease-modifying anti-rheumatic drug(s) (csDMARDs) (only 1 of the following: sulfasalazine, hydroxychloroquine or chloroquine).
● If ≥ 20% improvement in both TJC and SJC compared with baseline was not achieved subjects originally assigned to methotrexate will be re-randomized in a 1:1 ratio to receive blinded upadacitinib 15 mg or 30 mg QD (participants in Japan will be randomized 1:1:1 to receive upadacitinib 7.5 mg, 15 mg, or 30 mg QD) while continuing methotrexate treatment. Participants originally assigned to upadacitinib will add methotrexate 10 mg/week (7.5 mg for Japan) to upadacitinib.
From Week 36 to Week 40 subjects who do not achieve ≥ 20% improvement in both TJC and SJC compared with Baseline at two consecutive visits starting at Week 36 will be rescued with optimizing background RA medications: NSAIDs, corticosteroids, low-potency analgesics and csDMARDs (1 of the following: sulfasalazine, hydroxychloroquine or chloroquine).

Evidence for comparator: -

Actual start date of recruitment	23 February 2016
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Argentina: 45
Country: Number of subjects enrolled	Australia: 19
Country: Number of subjects enrolled	Belarus: 5
Country: Number of subjects enrolled	Belgium: 15
Country: Number of subjects enrolled	Bosnia and Herzegovina: 17
Country: Number of subjects enrolled	Brazil: 43
Country: Number of subjects enrolled	Bulgaria: 36
Country: Number of subjects enrolled	Canada: 13
Country: Number of subjects enrolled	Chile: 38
Country: Number of subjects enrolled	China: 3
Country: Number of subjects enrolled	Colombia: 12
Country: Number of subjects enrolled	Croatia: 2
Country: Number of subjects enrolled	Czechia: 19
Country: Number of subjects enrolled	Estonia: 4
Country: Number of subjects enrolled	Germany: 24
Country: Number of subjects enrolled	Guatemala: 56
Country: Number of subjects enrolled	Hong Kong: 2
Country: Number of subjects enrolled	Hungary: 18
Country: Number of subjects enrolled	Ireland: 2
Country: Number of subjects enrolled	Israel: 10
Country: Number of subjects enrolled	Italy: 7
Country: Number of subjects enrolled	Japan: 138
Country: Number of subjects enrolled	Kazakhstan: 7
Country: Number of subjects enrolled	Latvia: 3
Country: Number of subjects enrolled	Lithuania: 7
Country: Number of subjects enrolled	Mexico: 78
Country: Number of subjects enrolled	New Zealand: 16
Country: Number of subjects enrolled	Poland: 20
Country: Number of subjects enrolled	Portugal: 11
Country: Number of subjects enrolled	Puerto Rico: 3
Country: Number of subjects enrolled	Romania: 2
Country: Number of subjects enrolled	Russian Federation: 38
Country: Number of subjects enrolled	Slovakia: 19
Country: Number of subjects enrolled	Slovenia: 4
Country: Number of subjects enrolled	South Africa: 16
Country: Number of subjects enrolled	Spain: 38
Country: Number of subjects enrolled	Switzerland: 4
Country: Number of subjects enrolled	Taiwan: 7
Country: Number of subjects enrolled	Tunisia: 9
Country: Number of subjects enrolled	Turkey: 10
Country: Number of subjects enrolled	Ukraine: 49
Country: Number of subjects enrolled	United Kingdom: 9

Country: Number of subjects enrolled	United States: 124
Worldwide total number of subjects	1002
EEA total number of subjects	231

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)	798
From 65 to 84 years	203
85 years and over	1

Subject disposition

Recruitment

Recruitment details:

Participants were randomized at 236 sites in 43 countries. The study included 2 periods and a Japan sub-study. The global study analysis included participants from Japan, but excluded the upadacitinib 7.5 mg group. The Japan sub-study included all participants from Japan, including the upadacitinib 7.5 mg treatment group.

Pre-assignment

Screening details:

Participants were randomized in a 1:1:1 ratio to Groups 1, 3, and 4 below, except for participants in Japan who were randomized in a 1:2:1:1 ratio to Groups 1, 2, 3, and 4. Randomization was stratified by geographic region.
Efficacy analyses were conducted separately for the Japan sub-study.

Period 1

Period 1 title	Period 1 (Week 1 to Week 48)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Blinding implementation details:

Sponsor personnel with direct oversight conduct and management of the trial, the Investigator, study site personnel, and the subject were blinded to each subject's treatment throughout Period 1. When the last subject completed the last visit of Period 1 (Week 48), study drug assignment in both periods was unblinded to the Sponsor and 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	Methotrexate

Arm description:

Group 1 participants received up to 20 mg methotrexate orally per week (15 mg/week in China and Japan) and placebo to upadacitinib once a day (QD) for 48 weeks during Period 1.
Participants who did not achieve Clinical Remission (CR) based on clinical disease activity index (CDAI) score (CDAI ≤ 2.8) and did not achieve a ≥ 20% improvement from Baseline in both tender joint count (TJC) and swollen joint count (SJC) at Week 26 were re-randomized in a 1:1 ratio to receive rescue therapy with upadacitinib 15 mg or 30 mg QD (or in a 1:1:1 ratio to receive upadacitinib 7.5 mg, 15 mg, or 30 mg QD for participants in Japan) in addition to methotrexate.

Arm type	Active comparator
Investigational medicinal product name	Methotrexate
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, Tablet
Routes of administration	Oral use

Dosage and administration details:

Methotrexate starting at 10 mg/week [7.5 mg/week for patients in China and Japan] and titrated up to a maximum of 20 mg/week [15 mg/week for patients in Japan] through week 8, as tolerated).
Methotrexate dose increment was 5 mg/4 weeks with a minimum of 15 mg/week as the final dose, if intolerance of 20 mg/week was documented.

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

Dosage and administration details:

Taken orally once a day

Arm title	Upadacitinib 7.5 mg

Arm description:

Group 2 participants (Japan only) received 7.5 mg upadacitinib orally once a day and placebo to methotrexate once a week for 48 weeks in Period 1.
Participants who did not achieve CR based on CDAI and did not achieve a ≥ 20% improvement from Baseline in both TJC and SJC at Week 26 received rescue treatment with methotrexate 7.5 mg/week in addition to continuing to receive upadacitinib 7.5 mg QD through Week 48.

Arm type	Experimental
Investigational medicinal product name	Placebo to methotrexate
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, Tablet
Routes of administration	Oral use

Dosage and administration details:

Placebo to methotrexate taken orally once a week.

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

Dosage and administration details:

Upadacitinib 7.5 mg taken orally once a day.

Arm title	Upadacitinib 15 mg

Arm description:

Group 3 participants received 15 mg upadacitinib orally once a day and placebo to methotrexate once a week for 48 weeks in Period 1.
Participants who did not achieve CR based on CDAI and did not achieve a ≥ 20% improvement from Baseline in both TJC and SJC at Week 26 received rescue treatment with methotrexate 10 mg/week (7.5 mg for China and Japan) in addition to continuing to receive upadacitinib 15 mg QD through Week 48.

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

Dosage and administration details:

Upadacitinib 15 mg taken orally once a day.

Investigational medicinal product name	Placebo to methotrexate
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, Tablet
Routes of administration	Oral use

Dosage and administration details:

Placebo to methotrexate taken orally once a week.

Arm title	Upadacitinib 30 mg

Arm description:

Group 4 participants received 30 mg upadacitinib orally once a day and placebo to methotrexate once a week for 48 weeks in Period 1.

Participants who did not achieve CR by CDAI and did not achieve a ≥ 20% improvement from Baseline in both TJC and SJC at Week 26 received rescue treatment with methotrexate 10 mg/week (7.5 mg for China and Japan) in addition to continuing to receive upadacitinib 30 mg QD through Week 48.

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

Dosage and administration details:

Upadacitinib 30 mg taken orally once a day.

Investigational medicinal product name	Placebo to methotrexate
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, Tablet
Routes of administration	Oral use

Dosage and administration details:

Placebo to methotrexate taken orally once a week.

Number of subjects in period 1	Methotrexate	Upadacitinib 7.5 mg	Upadacitinib 15 mg
Started	315	55	317
Received Study Drug	314	55	317
Global Analysis Population	314	0 [1]	317
Japan Sub-study	28 [2]	55	27 [3]
Completed Week 24 Study Drug	268	51	290
Received Rescue Therapy at Week 26	37 [4]	3 [5]	19 [6]
Completed	256	51	277
Not completed	59	4	40
Consent withdrawn by subject	22	-	12
Other	5	1	2
Adverse event	15	3	18
Lost to follow-up	4	-	6
Lack of efficacy	12	-	2
Not dosed	1	-	-

Number of subjects in period 1	Upadacitinib 30 mg
Started	315
Received Study Drug	314
Global Analysis Population	314
Japan Sub-study	28 [7]
Completed Week 24 Study Drug	282
Received Rescue Therapy at Week 26	9 [8]

Completed	271
Not completed	44
Consent withdrawn by subject	20
Other	3
Adverse event	11
Lost to follow-up	5
Lack of efficacy	4
Not dosed	1

Notes:

[1] - 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: Participants in the upadacitinib 7.5 mg treatment group were not included in the Global Analysis Population.

[2] - 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 methotrexate treatment group included 28 subjects from Japan.

[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 upadacitinib 15 mg treatment group included 27 subjects from Japan.

[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: Rescue therapy at Week 26 was offered to subjects who did not achieve CR based on CDAI and who did not achieve a ≥ 20% improvement in both TJC and SJC compared with Baseline.

[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: Rescue therapy at Week 26 was offered to subjects who did not achieve CR based on CDAI and who did not achieve a ≥ 20% improvement in both TJC and SJC compared with Baseline.

[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: Rescue therapy at Week 26 was offered to subjects who did not achieve CR based on CDAI and who did not achieve a ≥ 20% improvement in both TJC and SJC compared with Baseline.

[7] - 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 upadacitinib 30 mg treatment group included 28 subjects from Japan.

[8] - 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: Rescue therapy was offered to subjects who did not achieve CR based on CDAI and who did not achieve a ≥ 20% improvement in both TJC and SJC compared with Baseline.

Period 2

Period 2 title	Period 2 (Week 48 to Week 260)
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes

Arm title	Methotrexate

Arm description:

Participants received up to 20 mg methotrexate orally per week (15 mg/week in China and Japan) and placebo to upadacitinib QD for 48 weeks during Period 1.
Participants who did not achieve CR based on CDAI score (CDAI ≤ 2.8) and did not achieve a ≥ 20% improvement from Baseline in both TJC and SJC at Week 26 were re-randomized in a 1:1 ratio to receive rescue therapy with upadacitinib 15 mg or 30 mg QD (or in a 1:1:1 ratio to receive upadacitinib 7.5 mg, 15 mg, or 30 mg QD for participants in Japan) in addition to methotrexate.
In Period 2 (Weeks 48 to 260) participants continued to receive the treatment they were assigned at the end of Period 1.

Arm type	Active comparator
Investigational medicinal product name	Methotrexate
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, Tablet
Routes of administration	Oral use

Dosage and administration details:

Methotrexate starting at 10 mg/week [7.5 mg/week for patients in China and Japan] and titrated up to a maximum of 20 mg/week [15 mg/week for patients in Japan] through week 8, as tolerated).
Methotrexate dose increment was 5 mg/4 weeks with a minimum of 15 mg/week as the final dose, if intolerance of 20 mg/week was documented.

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

Dosage and administration details:

Taken orally once a day

Arm title	Upadacitinib 7.5 mg

Arm description:

Participants received 7.5 mg upadacitinib orally once a day and placebo to methotrexate once a week for 48 weeks in Period 1.
Participants who did not achieve CR based on CDAI and did not achieve a ≥ 20% improvement from Baseline in both TJC and SJC at Week 26 received rescue treatment with methotrexate 7.5 mg/week in addition to continuing to receive upadacitinib 7.5 mg QD.
In Period 2 participants continued to receive the treatment they were assigned at the end of Period 1.

Arm type	Experimental
Investigational medicinal product name	Placebo to methotrexate
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, Tablet
Routes of administration	Oral use

Dosage and administration details:

Placebo to methotrexate taken orally once a week.

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

Dosage and administration details:

Upadacitinib 7.5 mg taken orally once a day.

Arm title	Upadacitinib 15 mg

Arm description:

Participants received 15 mg upadacitinib orally once a day and placebo to methotrexate once a week for 48 weeks in Period 1.

Participants who did not achieve CR based on CDAI and did not achieve a ≥ 20% improvement from Baseline in both TJC and SJC at Week 26 received rescue treatment with methotrexate 10 mg/week (7.5 mg for China and Japan) in addition to continuing to receive upadacitinib 15 mg QD.
In Period 2 participants continued to receive the treatment they were assigned at the end of Period 1.

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

Dosage and administration details:

Upadacitinib 15 mg taken orally once a day.

Investigational medicinal product name	Placebo to methotrexate
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, Tablet
Routes of administration	Oral use

Dosage and administration details:

Placebo to methotrexate taken orally once a week.

Arm title	Upadacitinib 30 mg

Arm description:

Participants received 30 mg upadacitinib orally once a day and placebo to methotrexate once a week for 48 weeks in Period 1.
Participants who did not achieve CR by CDAI and did not achieve a ≥ 20% improvement from Baseline in both TJC and SJC at Week 26 received rescue treatment with methotrexate 10 mg/week (7.5 mg for China and Japan) in addition to continuing to receive upadacitinib 30 mg QD.
In Period 2 participants continued to receive the treatment they were assigned at the end of Period 1.
Starting with Protocol Amendment 6 participants were switched to receive open-label upadacitinib 15 mg QD.

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

Dosage and administration details:

Upadacitinib 30 mg taken orally once a day.

Investigational medicinal product name	Placebo to methotrexate
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, Tablet
Routes of administration	Oral use

Dosage and administration details:

Placebo to methotrexate taken orally once a week.

Number of subjects in period 2[9]	Methotrexate	Upadacitinib 7.5 mg	Upadacitinib 15 mg
Started	253	50	275
Received Study Drug	242	48	273
Completed	163	40	217
Not completed	90	10	58
Consent withdrawn by subject	32	5	23
Coronavirus Disease of 2019 (COVID-19) Infection	-	-	-
Other	14	1	11
Adverse event	16	4	11
COVID-19 Logistic Restrictions	-	-	2
Lost to follow-up	17	-	10
Lack of efficacy	11	-	1

Number of subjects in period 2[9]	Upadacitinib 30 mg
Started	268
Received Study Drug	260
Completed	187
Not completed	81
Consent withdrawn by subject	27
Coronavirus Disease of 2019 (COVID-19) Infection	3
Other	17
Adverse event	26
COVID-19 Logistic Restrictions	1
Lost to follow-up	6
Lack of efficacy	1

Notes:

[9] - 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: Nine participants who completed Period 1 opted not to enter Period 2.

Baseline characteristics

Reporting groups	
Reporting group title	Methotrexate
Reporting group description:	
Group 1 participants received up to 20 mg methotrexate orally per week (15 mg/week in China and Japan) and placebo to upadacitinib once a day (QD) for 48 weeks during Period 1. Participants who did not achieve Clinical Remission (CR) based on clinical disease activity index (CDAI) score (CDAI ≤ 2.8) and did not achieve a ≥ 20% improvement from Baseline in both tender joint count (TJC) and swollen joint count (SJC) at Week 26 were re-randomized in a 1:1 ratio to receive rescue therapy with upadacitinib 15 mg or 30 mg QD (or in a 1:1:1 ratio to receive upadacitinib 7.5 mg, 15 mg, or 30 mg QD for participants in Japan) in addition to methotrexate.	
Reporting group title	Upadacitinib 7.5 mg
Reporting group description:	
Group 2 participants (Japan only) received 7.5 mg upadacitinib orally once a day and placebo to methotrexate once a week for 48 weeks in Period 1. Participants who did not achieve CR based on CDAI and did not achieve a ≥ 20% improvement from Baseline in both TJC and SJC at Week 26 received rescue treatment with methotrexate 7.5 mg/week in addition to continuing to receive upadacitinib 7.5 mg QD through Week 48.	
Reporting group title	Upadacitinib 15 mg
Reporting group description:	
Group 3 participants received 15 mg upadacitinib orally once a day and placebo to methotrexate once a week for 48 weeks in Period 1. Participants who did not achieve CR based on CDAI and did not achieve a ≥ 20% improvement from Baseline in both TJC and SJC at Week 26 received rescue treatment with methotrexate 10 mg/week (7.5 mg for China and Japan) in addition to continuing to receive upadacitinib 15 mg QD through Week 48.	
Reporting group title	Upadacitinib 30 mg
Reporting group description:	
Group 4 participants received 30 mg upadacitinib orally once a day and placebo to methotrexate once a week for 48 weeks in Period 1. Participants who did not achieve CR by CDAI and did not achieve a ≥ 20% improvement from Baseline in both TJC and SJC at Week 26 received rescue treatment with methotrexate 10 mg/week (7.5 mg for China and Japan) in addition to continuing to receive upadacitinib 30 mg QD through Week 48.	

Reporting group values	Methotrexate	Upadacitinib 7.5 mg	Upadacitinib 15 mg
Number of subjects	315	55	317
Age categorical Units: Subjects			
< 40 years	51	5	60
40 – 65 years	206	25	204
≥ 65 years	58	25	53
Age continuous Units: years			
arithmetic mean	53.3	59.7	51.9
standard deviation	± 12.89	± 13.8	± 12.58
Gender categorical Units: Subjects			
Female	241	36	241
Male	74	19	76
Ethnicity Units: Subjects			
Hispanic or Latino	102	0	107
Not Hispanic or Latino	213	55	210
Race			

Units: Subjects			
White	257	0	256
Black or African American	12	0	8
American Indian/Alaska Native	2	0	8
Native Hawaiian or other Pacific Islander	2	0	3
Asian	37	55	35
Multiple	5	0	7
Geographic Region Units: Subjects			
North America	46	0	48
South/Central America	90	0	91
Western Europe	37	0	36
Eastern Europe	86	0	87
Asia-Japan	28	55	27
Asia - China	1	0	1
Asia - Other	3	0	4
Other	24	0	23
Duration of Rheumatoid Arthritis Diagnosis			
Data are reported for the full analysis set (FAS; N = 314, 55, 317, and 314 participants in each treatment group respectively).			
Units: years			
arithmetic mean	2.6	2.3	2.9
standard deviation	± 5.14	± 5.77	± 5.38
Tender Joint Count			
A total of 68 joints were assessed for the presence or absence of tenderness. Data are reported for the full analysis set (N = 314, 55, 317, and 314 participants in each treatment group respectively).			
Units: joints			
arithmetic mean	26.4	18.0	25.4
standard deviation	± 16.15	± 11.75	± 14.42
Swollen Joint Count			
A total of 66 joints were assessed for the presence or absence of swelling. Data are reported for the full analysis set (N = 314, 55, 317, and 314 participants in each treatment group respectively).			
Units: joints			
arithmetic mean	16.9	14.7	16.9
standard deviation	± 10.58	± 8.24	± 10.35
Patient's Assessment of Pain			
Participants were asked to indicate the severity of their arthritis pain within the previous week on a visual analog scale (VAS) from 0 to 100 mm. A score of 0 mm indicates "no pain" and a score of 100 mm indicates "worst possible pain." Data are reported for the full analysis set with available data (N = 314, 55, 317, and 311 participants in each treatment group respectively).			
Units: mm			
arithmetic mean	65.7	64.1	68.4
standard deviation	± 21.46	± 21.20	± 20.60
Patient's Global Assessment of Disease Activity			
The participant was asked to rate their current RA disease activity over the past 24 hours on a 100 mm VAS, where 0 mm indicates very low disease activity and 100 mm indicates very high disease activity. Data are reported for the full analysis set with available data (N = 314, 55, 317, and 311 participants in each treatment group respectively).			
Units: mm			

arithmetic mean	65.8	64.1	66.6
standard deviation	± 21.45	± 21.36	± 22.01
Physician's Global Assessment of Disease Activity			
The physician rated the participant's current global RA disease activity (independently from the participant's assessment) on a VAS scale from 0 to 100 mm, where 0 mm indicates very low disease activity and 100 mm indicates very high disease activity. Data are reported for the full analysis set with available data; N = 299, 54, 301, and 304 participants in each treatment group respectively).			
Units: mm			
arithmetic mean	68.7	63.3	67.1
standard deviation	± 16.45	± 19.34	± 17.00
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 (no disability) to 3 (very severe disability). Data are reported for the FAS with available data (N = 314, 55, 317, and 311 participants in each groop respectively).			
Units: units on a scale			
arithmetic mean	1.6	1.3	1.6
standard deviation	± 0.67	± 0.62	± 0.67
High-sensitivity C-reactive Protein (hsCRP)			
Data are reported for the full analysis set (N = 314, 55, 317, and 314 participants in each groop respectively).			
Units: g/L			
arithmetic mean	21.2	18.5	23.0
standard deviation	± 22.05	± 17.55	± 27.37
Disease Activity Score 28 Based on CRP (DAS28[CRP])			
The DAS28(CRP) is a composite index used to assess RA disease activity, calculated based on the tender joint count (out of 28 evaluated joints), swollen joint count (out of 28 evaluated joints), Patient's Global Assessment of Disease Activity (0-100 mm), and hsCRP (in mg/L). Scores on the DAS28 range from 0 to approximately 10, where higher scores indicate more disease activity. Data are reported for the FAS with available data (N = 314, 55, 317, and 311 participants in each groop respectively).			
Units: units on a scale			
arithmetic mean	5.9	5.5	5.9
standard deviation	± 0.97	± 0.90	± 0.97
Modified Total Sharp Score (mTSS)			
The mTSS measures the level of joint damage from radiographs of the hands and feet, calculated as the sum of the total joint erosion score and total joint space narrowing (JSN) score and ranges from 0 (normal) to 448 (worst). Data are reported for the FAS with available data (N = 309, 55, 309, and 309 participants in each groop respectively).			
Units: units on a scale			
arithmetic mean	13.3	15.9	18.1
standard deviation	± 30.55	± 39.10	± 38.15

Reporting group values	Upadacitinib 30 mg	Total	
Number of subjects	315	1002	
Age categorical Units: Subjects			
< 40 years	34	150	
40 – 65 years	213	648	

≥ 65 years	68	204	

Age continuous			
Units: years			
arithmetic mean	54.9		
standard deviation	± 12.58	-	
Gender categorical			
Units: Subjects			
Female	241	759	
Male	74	243	
Ethnicity			
Units: Subjects			
Hispanic or Latino	107	316	
Not Hispanic or Latino	208	686	
Race			
Units: Subjects			
White	255	768	
Black or African American	13	33	
American Indian/Alaska Native	7	17	
Native Hawaiian or other Pacific Islander	1	6	
Asian	34	161	
Multiple	5	17	
Geographic Region			
Units: Subjects			
North America	46	140	
South/Central America	91	272	
Western Europe	37	110	
Eastern Europe	87	260	
Asia-Japan	28	138	
Asia - China	1	3	
Asia - Other	2	9	
Other	23	70	
Duration of Rheumatoid Arthritis Diagnosis			
Data are reported for the full analysis set (FAS; N = 314, 55, 317, and 314 participants in each treatment group respectively).			
Units: years			
arithmetic mean	2.8		
standard deviation	± 5.63	-	
Tender Joint Count			
A total of 68 joints were assessed for the presence or absence of tenderness. Data are reported for the full analysis set (N = 314, 55, 317, and 314 participants in each treatment group respectively).			
Units: joints			
arithmetic mean	25.2		
standard deviation	± 14.99	-	
Swollen Joint Count			
A total of 66 joints were assessed for the presence or absence of swelling. Data are reported for the full analysis set (N = 314, 55, 317, and 314 participants in each treatment group respectively).			
Units: joints			

arithmetic mean	15.7		
standard deviation	± 9.71	-	
Patient's Assessment of Pain			
Participants were asked to indicate the severity of their arthritis pain within the previous week on a visual analog scale (VAS) from 0 to 100 mm. A score of 0 mm indicates "no pain" and a score of 100 mm indicates "worst possible pain." Data are reported for the full analysis set with available data (N = 314, 55, 317, and 311 participants in each treatment group respectively).			
Units: mm			
arithmetic mean	65.3		
standard deviation	± 25.51	-	
Patient's Global Assessment of Disease Activity			
The participant was asked to rate their current RA disease activity over the past 24 hours on a 100 mm VAS, where 0 mm indicates very low disease activity and 100 mm indicates very high disease activity. Data are reported for the full analysis set with available data (N = 314, 55, 317, and 311 participants in each treatment group respectively).			
Units: mm			
arithmetic mean	64.9		
standard deviation	± 21.63	-	
Physician's Global Assessment of Disease Activity			
The physician rated the participant's current global RA disease activity (independently from the participant's assessment) on a VAS scale from 0 to 100 mm, where 0 mm indicates very low disease activity and 100 mm indicates very high disease activity. Data are reported for the full analysis set with available data; N = 299, 54, 301, and 304 participants in each treatment group respectively).			
Units: mm			
arithmetic mean	65.3		
standard deviation	± 16.60	-	
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 (no disability) to 3 (very severe disability). Data are reported for the FAS with available data (N = 314, 55, 317, and 311 participants in each groop respectively).			
Units: units on a scale			
arithmetic mean	1.5		
standard deviation	± 0.66	-	
High-sensitivity C-reactive Protein (hsCRP)			
Data are reported for the full analysis set (N = 314, 55, 317, and 314 participants in each groop respectively).			
Units: g/L			
arithmetic mean	19.4		
standard deviation	± 22.59	-	
Disease Activity Score 28 Based on CRP (DAS28[CRP])			
The DAS28(CRP) is a composite index used to assess RA disease activity, calculated based on the tender joint count (out of 28 evaluated joints), swollen joint count (out of 28 evaluated joints), Patient's Global Assessment of Disease Activity (0-100 mm), and hsCRP (in mg/L). Scores on the DAS28 range from 0 to approximately 10, where higher scores indicate more disease activity. Data are reported for the FAS with available data (N = 314, 55, 317, and 311 participants in each groop respectively).			
Units: units on a scale			

arithmetic mean	5.8		
standard deviation	± 1.02	-	
Modified Total Sharp Score (mTSS)			
The mTSS measures the level of joint damage from radiographs of the hands and feet, calculated as the sum of the total joint erosion score and total joint space narrowing (JSN) score and ranges from 0 (normal) to 448 (worst). Data are reported for the FAS with available data (N = 309, 55, 309, and 309 participants in each groop respectively).			
Units: units on a scale			
arithmetic mean	17.2		
standard deviation	± 38.25	-	

End points

End points reporting groups

Reporting group title	Methotrexate

Reporting group description:

Group 1 participants received up to 20 mg methotrexate orally per week (15 mg/week in China and Japan) and placebo to upadacitinib once a day (QD) for 48 weeks during Period 1.
Participants who did not achieve Clinical Remission (CR) based on clinical disease activity index (CDAI) score (CDAI ≤ 2.8) and did not achieve a ≥ 20% improvement from Baseline in both tender joint count (TJC) and swollen joint count (SJC) at Week 26 were re-randomized in a 1:1 ratio to receive rescue therapy with upadacitinib 15 mg or 30 mg QD (or in a 1:1:1 ratio to receive upadacitinib 7.5 mg, 15 mg, or 30 mg QD for participants in Japan) in addition to methotrexate.

Reporting group title	Upadacitinib 7.5 mg

Reporting group description:

Group 2 participants (Japan only) received 7.5 mg upadacitinib orally once a day and placebo to methotrexate once a week for 48 weeks in Period 1.
Participants who did not achieve CR based on CDAI and did not achieve a ≥ 20% improvement from Baseline in both TJC and SJC at Week 26 received rescue treatment with methotrexate 7.5 mg/week in addition to continuing to receive upadacitinib 7.5 mg QD through Week 48.

Reporting group title	Upadacitinib 15 mg

Reporting group description:

Group 3 participants received 15 mg upadacitinib orally once a day and placebo to methotrexate once a week for 48 weeks in Period 1.
Participants who did not achieve CR based on CDAI and did not achieve a ≥ 20% improvement from Baseline in both TJC and SJC at Week 26 received rescue treatment with methotrexate 10 mg/week (7.5 mg for China and Japan) in addition to continuing to receive upadacitinib 15 mg QD through Week 48.

Reporting group title	Upadacitinib 30 mg

Reporting group description:

Group 4 participants received 30 mg upadacitinib orally once a day and placebo to methotrexate once a week for 48 weeks in Period 1.
Participants who did not achieve CR by CDAI and did not achieve a ≥ 20% improvement from Baseline in both TJC and SJC at Week 26 received rescue treatment with methotrexate 10 mg/week (7.5 mg for China and Japan) in addition to continuing to receive upadacitinib 30 mg QD through Week 48.

Reporting group title	Methotrexate

Reporting group description:

Participants received up to 20 mg methotrexate orally per week (15 mg/week in China and Japan) and placebo to upadacitinib QD for 48 weeks during Period 1.
Participants who did not achieve CR based on CDAI score (CDAI ≤ 2.8) and did not achieve a ≥ 20% improvement from Baseline in both TJC and SJC at Week 26 were re-randomized in a 1:1 ratio to receive rescue therapy with upadacitinib 15 mg or 30 mg QD (or in a 1:1:1 ratio to receive upadacitinib 7.5 mg, 15 mg, or 30 mg QD for participants in Japan) in addition to methotrexate.
In Period 2 (Weeks 48 to 260) participants continued to receive the treatment they were assigned at the end of Period 1.

Reporting group title	Upadacitinib 7.5 mg

Reporting group description:

Participants received 7.5 mg upadacitinib orally once a day and placebo to methotrexate once a week for 48 weeks in Period 1.
Participants who did not achieve CR based on CDAI and did not achieve a ≥ 20% improvement from Baseline in both TJC and SJC at Week 26 received rescue treatment with methotrexate 7.5 mg/week in addition to continuing to receive upadacitinib 7.5 mg QD.
In Period 2 participants continued to receive the treatment they were assigned at the end of Period 1.

Reporting group title	Upadacitinib 15 mg

Reporting group description:

Participants received 15 mg upadacitinib orally once a day and placebo to methotrexate once a week for 48 weeks in Period 1.
Participants who did not achieve CR based on CDAI and did not achieve a ≥ 20% improvement from Baseline in both TJC and SJC at Week 26 received rescue treatment with methotrexate 10 mg/week (7.5 mg for China and Japan) in addition to continuing to receive upadacitinib 15 mg QD.
In Period 2 participants continued to receive the treatment they were assigned at the end of Period 1.

Reporting group title	Upadacitinib 30 mg

Reporting group description:

Participants received 30 mg upadacitinib orally once a day and placebo to methotrexate once a week for 48 weeks in Period 1.
Participants who did not achieve CR by CDAI and did not achieve a ≥ 20% improvement from Baseline in both TJC and SJC at Week 26 received rescue treatment with methotrexate 10 mg/week (7.5 mg for China and Japan) in addition to continuing to receive upadacitinib 30 mg QD.
In Period 2 participants continued to receive the treatment they were assigned at the end of Period 1. Starting with Protocol Amendment 6 participants were switched to receive open-label upadacitinib 15 mg QD.

Primary: Percentage of Participants Achieving Clinical Remission (CR) Based on DAS28(CRP) at Week 24 - Global Analysis

End point title	Percentage of Participants Achieving Clinical Remission (CR) Based on DAS28(CRP) at Week 24 - Global Analysis[1]

End point description:

The primary endpoint for European Union (EU)/European Medicines Agency (EMA) regulatory purposes was clinical remission, based on a Disease Activity Score 28 (DAS28)-CRP score of < 2.6 at Week 24.
The DAS28 is a composite index used to assess rheumatoid arthritis disease activity, calculated based on the tender joint count (out of 28 evaluated joints), swollen joint count (out of 28 evaluated joints), Patient's Global Assessment of Disease Activity (0-100 mm), and hsCRP (in mg/L). Scores on the DAS28 range from 0 to approximately 10, where higher scores indicate more disease activity.
A DAS28 score less than 2.6 indicates clinical remission.
Participants who prematurely discontinued from study drug prior to Week 24 or for whom DAS28 data were missing at Week 24 were considered non-responders.

End point type	Primary

End point timeframe:

Week 24

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: The global analysis includes participants enrolled under the methotrexate and upadacitinib 15 mg and 30 mg treatment groups.

End point values	Methotrexate	Upadacitinib 15 mg	Upadacitinib 30 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	314[2]	317[3]	314[4]	
Units: percentage of participants				
number (confidence interval 95%)	18.5 (14.2 to 22.8)	48.3 (42.8 to 53.8)	50.0 (44.5 to 55.5)	

Notes:

[2] - Full analysis set

[3] - Full analysis set

[4] - Full analysis set

Statistical analyses

Statistical analysis title	Analysis of DAS28(CRP) Clinical Remisison

Statistical analysis description:

For the global analysis, comparisons of the primary and key secondary efficacy endpoints were made between the upadacitinib 15 mg and 30 mg groups versus the methotrexate group.

Comparison groups	Upadacitinib 15 mg v Methotrexate

Number of subjects included in analysis	631
Analysis specification	Pre-specified
Analysis type	superiority[5]
P-value	< 0.001 [6]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Response Rate Difference
Point estimate	29.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	22.8
upper limit	36.8

Notes:

[5] - The overall type I error rate of the primary and ranked key secondary endpoints for the two upadacitinib doses (15 mg and 30 mg) was controlled using a graphical multiple testing procedure defined separately for United States (US)/Food and Drug Administration (FDA), EU/EMA and Japan/Pharmaceuticals and Medical Devices Agency regulatory purposes.
The adjusted p-value under multiplicity control is reported, with significance achieved if the adjusted p-value is less than 0.05.
[6] - Cochran-Mantel-Haenszel test adjusting for geographic region (North America, South/central America, Western Europe, Eastern Europe, Asia/other).

Statistical analysis title	Analysis of DAS28(CRP) Clinical Remisison

Statistical analysis description:

For the global analysis, comparisons of the primary and key secondary efficacy endpoints were made between the upadacitinib 15 mg and 30 mg groups versus the methotrexate group.

Comparison groups	Upadacitinib 30 mg v Methotrexate
Number of subjects included in analysis	628
Analysis specification	Pre-specified
Analysis type	superiority[7]
P-value	< 0.001 [8]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Response Rate Difference
Point estimate	31.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	24.5
upper limit	38.5

Notes:

[7] - The overall type I error rate of the primary and ranked key secondary endpoints for the two upadacitinib doses (15 mg and 30 mg) was controlled using a graphical multiple testing procedure defined separately for United States (US)/Food and Drug Administration (FDA), EU/EMA and Japan/Pharmaceuticals and Medical Devices Agency regulatory purposes.
The adjusted p-value under multiplicity control is reported, with significance achieved if the adjusted p-value is less than 0.05.
[8] - Cochran-Mantel-Haenszel test adjusting for geographic region (North America, South/central America, Western Europe, Eastern Europe, Asia/other).

Primary: Percentage of Participants With an American College of Rheumatology 50% (ACR50) Response at Week 12 - Global Analysis

End point title	Percentage of Participants With an American College of Rheumatology 50% (ACR50) Response at Week 12 - Global Analysis[9]

End point description:

The primary endpoint for United States (US)/Food and Drug Administration (FDA) regulatory purposes was ACR 50% response (ACR50) at Week 12. Participants who met the following 3 conditions for

improvement from Baseline were classified as meeting the ACR50 response criteria:
1. ≥ 50% improvement in 68-tender joint count;
2. ≥ 50% improvement in 66-swollen joint count; and
3. ≥ 50% improvement in at least 3 of the 5 following parameters:
• Physician global assessment of disease activity (PhGA);
• Patient global assessment of disease activity;
• Patient assessment of pain;
• Health Assessment Questionnaire - Disability Index (HAQ-DI);
• High-sensitivity C-reactive protein (hsCRP).
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	Primary

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: The global analysis includes participants enrolled under the methotrexate and upadacitinib 15 mg and 30 mg treatment groups.

End point values	Methotrexate	Upadacitinib 15 mg	Upadacitinib 30 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	314[10]	317[11]	314[12]	
Units: percentage of participants				
number (confidence interval 95%)	28.3 (23.4 to 33.3)	52.1 (46.6 to 57.5)	56.4 (50.9 to 61.9)	

Notes:

[10] - Full analysis set

[11] - Full analysis set

[12] - Full analysis set

Statistical analyses

Statistical analysis title	Analysis of ACR50 Response at Week 12

Statistical analysis description:

For the global analysis, comparisons of the primary and key secondary efficacy endpoints were made between the upadacitinib 15 mg and 30 mg groups versus the methotrexate group.

Comparison groups	Upadacitinib 15 mg v Methotrexate
Number of subjects included in analysis	631
Analysis specification	Pre-specified
Analysis type	superiority[13]
P-value	< 0.001 [14]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Response Rate Difference
Point estimate	23.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	16.3
upper limit	31.1

Notes:

[13] - The overall type I error rate of the primary and ranked key secondary endpoints for the two upadacitinib doses (15 mg and 30 mg) was controlled using a graphical multiple testing procedure defined separately for US/FDA, EU/EMA and Japan/Pharmaceuticals and Medical Devices Agency regulatory purposes.
The adjusted p-value under multiplicity control is reported, with significance achieved if the adjusted p-value is less than 0.05.

[14] - Cochran-Mantel-Haenszel test adjusting for geographic region (North America, South/central America, Western Europe, Eastern Europe, Asia/other).

Statistical analysis title	Analysis of ACR50 Response at Week 12

Statistical analysis description:

For the global analysis, comparisons of the primary and key secondary efficacy endpoints were made between the upadacitinib 15 mg and 30 mg groups versus the methotrexate group.

Comparison groups	Upadacitinib 30 mg v Methotrexate
Number of subjects included in analysis	628
Analysis specification	Pre-specified
Analysis type	superiority[15]
P-value	< 0.001 [16]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Response Rate Difference
Point estimate	28
Confidence interval	
level	95 %
sides	2-sided
lower limit	20.6
upper limit	35.4

Notes:

[15] - The overall type I error rate of the primary and ranked key secondary endpoints for the two upadacitinib doses (15 mg and 30 mg) was controlled using a graphical multiple testing procedure defined separately for US/FDA, EU/EMA and Japan/Pharmaceuticals and Medical Devices Agency regulatory purposes.
The adjusted p-value under multiplicity control is reported, with significance achieved if the adjusted p-value is less than 0.05.
[16] - Cochran-Mantel-Haenszel test adjusting for geographic region (North America, South/central America, Western Europe, Eastern Europe, Asia/other).

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

End point title	Percentage of Participants With an American College of Rheumatology 20% (ACR20) Response at Week 12 - Global Analysis[17]

End point description:

The primary endpoint for Japan/Pharmaceuticals and Medical Devices Agency (PMDA) regulatory purposes was ACR 20% response (ACR20) at Week 12. Participants who met the following 3 conditions for improvement from Baseline were classified as meeting the ACR20 response criteria:
1. ≥ 20% improvement in 68-tender joint count;
2. ≥ 20% improvement in 66-swollen joint count; and
3. ≥ 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).

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	Primary

End point timeframe:

Baseline and Week 12

Notes:

[17] - 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: The global analysis includes participants enrolled under the methotrexate and upadacitinib 15 mg and 30 mg treatment groups.

End point values	Methotrexate	Upadacitinib 15 mg	Upadacitinib 30 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	314[18]	317[19]	314[20]	
Units: percentage of participants				
number (confidence interval 95%)	54.1 (48.6 to 59.7)	75.7 (71.0 to 80.4)	77.1 (72.4 to 81.7)	

Notes:

[18] - Full analysis set

[19] - Full analysis set

[20] - Full analysis set

Statistical analyses

Statistical analysis title	Analysis of ACR20 Response At Week 12

Statistical analysis description:

For the global analysis, comparisons of the primary and key secondary efficacy endpoints were made between the upadacitinib 15 mg and 30 mg groups versus the methotrexate group.

Comparison groups	Upadacitinib 15 mg v Methotrexate
Number of subjects included in analysis	631
Analysis specification	Pre-specified
Analysis type	superiority[21]
P-value	< 0.001 [22]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Response Rate Difference
Point estimate	21.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	14.3
upper limit	28.8

Notes:

[21] - The overall type I error rate of the primary and ranked key secondary endpoints for the two upadacitinib doses (15 mg and 30 mg) was controlled using a graphical multiple testing procedure defined separately for US/FDA, EU/EMA and Japan/Pharmaceuticals and Medical Devices Agency regulatory purposes.
The adjusted p-value under multiplicity control is reported, with significance achieved if the adjusted p-value is less than 0.05.

[22] - Cochran-Mantel-Haenszel test adjusting for geographic region (North America, South/central America, Western Europe, Eastern Europe, Asia/other).

Statistical analysis title	Analysis of ACR20 Response at Week 12

Statistical analysis description:

For the global analysis, comparisons of the primary and key secondary efficacy endpoints were made between the upadacitinib 15 mg and 30 mg groups versus the methotrexate group.

Comparison groups	Upadacitinib 30 mg v Methotrexate
Number of subjects included in analysis	628
Analysis specification	Pre-specified
Analysis type	superiority[23]
P-value	< 0.001 [24]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Response Rate Difference
Point estimate	22.9

Confidence interval	
level	95 %
sides	2-sided
lower limit	15.7
upper limit	30.1

Notes:

[23] - The overall type I error rate of the primary and ranked key secondary endpoints for the two upadacitinib doses (15 mg and 30 mg) was controlled using a graphical multiple testing procedure defined separately for US/FDA, EU/EMA and Japan/Pharmaceuticals and Medical Devices Agency regulatory purposes.
The adjusted p-value under multiplicity control is reported, with significance achieved if the adjusted p-value is less than 0.05.
[24] - Cochran-Mantel-Haenszel test adjusting for geographic region (North America, South/central America, Western Europe, Eastern Europe, Asia/other).

Primary: Change From Baseline in Modified Total Sharp Score (mTSS) at Week 24 - Global Analysis

End point title	Change From Baseline in Modified Total Sharp Score (mTSS) at Week 24 - Global Analysis[25]

End point description:

The second primary endpoint for Japan/PMDA was change from baseline in mTSS at Week 24. The mTSS measures the level of joint damage from radiographs of the hands and feet and was assessed by two independent, blinded readers.
Joint erosion was assessed in 16 joints in each hand/wrist and 6 joints in each foot. Each joint was scored from 0 (no erosion) to 5 for hands/wrists or to 10 for feet (complete collapse). The total erosion score ranges from 0 to 280 (worst).
JSN was assessed in 15 joints of each hand and wrist, and 6 joints of each foot, including subluxation, from 0 (normal) to 4 (complete loss of joint space, bony ankylosis, or luxation). The total JSN score ranges from 0 to 168 (worst).
The mTSS is the sum of the joint erosion and JSN scores and ranges from 0 (normal) to 448 (worst). A change from Baseline greater than 0 indicates progression.
Linear extrapolation was used for participants who discontinued prior to Week 24 or for whom x-ray data were missing.

End point type	Primary

End point timeframe:

Baseline to Week 24

Notes:

[25] - 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: The global analysis includes participants enrolled under the methotrexate and upadacitinib 15 mg and 30 mg treatment groups.

End point values	Methotrexate	Upadacitinib 15 mg	Upadacitinib 30 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	264[26]	279[27]	270[28]	
Units: units on a scale				
least squares mean (confidence interval 95%)	0.67 (0.43 to 0.90)	0.14 (-0.09 to 0.37)	0.07 (-0.16 to 0.31)	

Notes:

[26] - Full analysis set participants with available data at Baseline

[27] - Full analysis set participants with available data at Baseline

[28] - Full analysis set participants with available data at Baseline

Statistical analyses

Statistical analysis title	Analysis of Change in mTSS at Week 24

Statistical analysis description:

For the global analysis, comparisons of the primary and key secondary efficacy endpoints were made

between the upadacitinib 15 mg and 30 mg groups versus the methotrexate group.

Comparison groups	Upadacitinib 15 mg v Methotrexate
Number of subjects included in analysis	543
Analysis specification	Pre-specified
Analysis type	superiority[29]
P-value	= 0.001 [30]
Method	ANCOVA
Parameter estimate	Least Squares (LS) Mean Difference
Point estimate	-0.53
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.85
upper limit	-0.2

Notes:

[29] - The overall type I error rate of the primary and ranked key secondary endpoints for the two upadacitinib doses (15 mg and 30 mg) was controlled using a graphical multiple testing procedure defined separately for US/FDA, European Union/European Medicines Agency and Japan/Pharmaceuticals and Medical Devices Agency regulatory purposes.
The adjusted p-value under multiplicity control is reported, with significance achieved if the adjusted p-value is less than 0.05.
[30] - Analysis of covariance (ANCOVA) model with treatment, geographic region as fixed factors and baseline value as the covariate.

Statistical analysis title	Analysis of Change in mTSS at Week 24

Statistical analysis description:

For the global analysis, comparisons of the primary and key secondary efficacy endpoints were made between the upadacitinib 15 mg and 30 mg groups versus the methotrexate group.

Comparison groups	Upadacitinib 30 mg v Methotrexate
Number of subjects included in analysis	534
Analysis specification	Pre-specified
Analysis type	superiority[31]
P-value	< 0.001 [32]
Method	ANCOVA
Parameter estimate	Least Squares (LS) Mean Difference
Point estimate	-0.59
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.91
upper limit	-0.27

Notes:

[31] - The overall type I error rate of the primary and ranked key secondary endpoints for the two upadacitinib doses (15 mg and 30 mg) was controlled using a graphical multiple testing procedure defined separately for US/FDA, European Union/European Medicines Agency and Japan/Pharmaceuticals and Medical Devices Agency regulatory purposes.
The adjusted p-value under multiplicity control is reported, with significance achieved if the adjusted p-value is less than 0.05.
[32] - Analysis of covariance (ANCOVA) model with treatment, geographic region as fixed factors and baseline value as the covariate.

Secondary: Change From Baseline in DAS28 (CRP) at Week 24 - Global Analysis

End point title	Change From Baseline in DAS28 (CRP) at Week 24 - Global Analysis[33]

End point description:

The DAS28 is a composite index used to assess rheumatoid arthritis disease activity, calculated based on the tender joint count (out of 28 evaluated joints), swollen joint count (out of 28 evaluated joints),

Patient's Global Assessment of Disease Activity (0-100 mm), and hsCRP (in mg/L). Scores on the DAS28 range from 0 to approximately 10, where higher scores indicate more disease activity. A negative change from Baseline in DAS28 (CRP) indicates improvement in disease activity.
Multiple imputation was used for missing post-baseline data.

End point type	Secondary

End point timeframe:

Baseline to Week 24

Notes:

[33] - 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: The global analysis includes participants enrolled under the methotrexate and upadacitinib 15 mg and 30 mg treatment groups.

End point values	Methotrexate	Upadacitinib 15 mg	Upadacitinib 30 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	312[34]	317[35]	310[36]	
Units: score on a scale				
least squares mean (confidence interval 95%)	-2.15 (-2.31 to -1.99)	-3.07 (-3.21 to -2.92)	-3.34 (-3.49 to -3.19)	

Notes:

[34] - Full analysis set participants with available data at Baseline

[35] - Full analysis set participants with available data at Baseline

[36] - Full analysis set participants with available data at Baseline

Statistical analyses

Statistical analysis title	Analysis of Change in DAS28(CRP) at Week 24
Comparison groups	Upadacitinib 15 mg v Methotrexate
Number of subjects included in analysis	629
Analysis specification	Pre-specified
Analysis type	superiority[37]
P-value	< 0.001 [38]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.92
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.12
upper limit	-0.71

Notes:

[37] - The overall type I error rate of the primary and ranked key secondary endpoints for the two doses was controlled using a graphical multiple testing procedure. This endpoint was a ranked key secondary endpoint for EU/EMA regulatory purposes.
The nominal p-value is reported.
[38] - ANCOVA model with treatment and geographic region as fixed factors and Baseline value as the covariate.

Statistical analysis title	Analysis of Change in DAS28(CRP) at Week 24
Comparison groups	Upadacitinib 30 mg v Methotrexate

Number of subjects included in analysis	622
Analysis specification	Pre-specified
Analysis type	superiority[39]
P-value	< 0.001 [40]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-1.19
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.4
upper limit	-0.99

Notes:

[39] - TThe overall type I error rate of the primary and ranked key secondary endpoints for the two doses was controlled using a graphical multiple testing procedure. This endpoint was a ranked key secondary endpoint for EU/EMA regulatory purposes.
The nominal p-value is reported.

[40] - ANCOVA model with treatment and geographic region as fixed factors and Baseline value as the covariate.

Secondary: Change From Baseline in Health Assessment Questionnaire Disability Index (HAQ-DI) at Week 24 - Global Analysis

End point title	Change From Baseline in Health Assessment Questionnaire Disability Index (HAQ-DI) at Week 24 - Global Analysis[41]

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.
Multiple imputation was used for missing data.

End point type	Secondary

End point timeframe:

Baseline and Week 24

Notes:

[41] - 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: The global analysis includes participants enrolled under the methotrexate and upadacitinib 15 mg and 30 mg treatment groups.

End point values	Methotrexate	Upadacitinib 15 mg	Upadacitinib 30 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	313[42]	317[43]	310[44]	
Units: score on a scale				
least squares mean (confidence interval 95%)	-0.60 (-0.67 to -0.52)	-0.87 (-0.94 to -0.80)	-0.91 (-0.98 to -0.84)	

Notes:

[42] - Full analysis set participants with available data at Baseline

[43] - Full analysis set participants with available data at Baseline

[44] - Full analysis set participants with available data at Baseline

Statistical analyses

Statistical analysis title	Analysis of Change in HAQ-DI at Week 24
Comparison groups	Upadacitinib 15 mg v Methotrexate
Number of subjects included in analysis	630
Analysis specification	Pre-specified
Analysis type	superiority[45]
P-value	< 0.001 [46]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.27
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.37
upper limit	-0.17

Notes:

[45] - The overall type I error rate of the primary and ranked key secondary endpoints for the two doses was controlled using a graphical multiple testing procedure. This endpoint was a ranked key secondary endpoint for EU/EMA regulatory purposes.
The nominal p-value is reported.
[46] - ANCOVA model with treatment and geographic region as fixed factors and Baseline value as the covariate.

Statistical analysis title	Analysis of Change in HAQ-DI at Week 24
Comparison groups	Upadacitinib 30 mg v Methotrexate
Number of subjects included in analysis	623
Analysis specification	Pre-specified
Analysis type	superiority[47]
P-value	< 0.001 [48]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.31
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.41
upper limit	-0.21

Notes:

[47] - The overall type I error rate of the primary and ranked key secondary endpoints for the two doses was controlled using a graphical multiple testing procedure. This endpoint was a ranked key secondary endpoint for EU/EMA regulatory purposes.
The nominal p-value is reported.
[48] - ANCOVA model with treatment and geographic region as fixed factors and Baseline value as the covariate.

Secondary: Percentage of Participants With an ACR50 Response at Week 24 - Global Analysis

End point title	Percentage of Participants With an ACR50 Response at Week 24 - Global Analysis[49]

End point description:

Participants who met the following 3 conditions for improvement from Baseline were classified as meeting the ACR50 response criteria:
1. ≥ 50% improvement in 68-tender joint count;
2. ≥ 50% improvement in 66-swollen joint count; and
3. ≥ 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).
Participants who prematurely discontinued from study drug prior to Week 24 or for whom ACR data were missing at Week 24 were considered non-responders.

End point type	Secondary

End point timeframe:

Baseline and Week 24

Notes:

[49] - 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: The global analysis includes participants enrolled under the methotrexate and upadacitinib 15 mg and 30 mg treatment groups.

End point values	Methotrexate	Upadacitinib 15 mg	Upadacitinib 30 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	314[50]	317[51]	314[52]	
Units: percentage of participants				
number (confidence interval 95%)	33.4 (28.2 to 38.7)	60.3 (54.9 to 65.6)	65.6 (60.4 to 70.9)	

Notes:

[50] - Full analysis set

[51] - Full analysis set

[52] - Full analysis set

Statistical analyses

Statistical analysis title	Analysis of ACR50 Response at Week 24
Comparison groups	Upadacitinib 15 mg v Methotrexate
Number of subjects included in analysis	631
Analysis specification	Pre-specified
Analysis type	superiority[53]
P-value	< 0.001 [54]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Response Rate Difference
Point estimate	26.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	19.3
upper limit	34.3

Notes:

[53] - The overall type I error rate of the primary and ranked key secondary endpoints for the two doses was controlled using a graphical multiple testing procedure. This endpoint was a ranked key secondary endpoint for EU/EMA regulatory purposes.
The nominal p-value is reported.
[54] - Cochran-Mantel-Haenszel test adjusting for geographic region (North America, South/central America, Western Europe, Eastern Europe, Asia/other).

Statistical analysis title	Analysis of ACR50 Response at Week 24
Comparison groups	Upadacitinib 30 mg v Methotrexate

Number of subjects included in analysis	628
Analysis specification	Pre-specified
Analysis type	superiority[55]
P-value	< 0.001 [56]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Response Rate Difference
Point estimate	32.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	24.8
upper limit	39.6

Notes:

[55] - The overall type I error rate of the primary and ranked key secondary endpoints for the two doses was controlled using a graphical multiple testing procedure. This endpoint was a ranked key secondary endpoint for EU/EMA regulatory purposes.
The nominal p-value is reported.

[56] - Cochran-Mantel-Haenszel test adjusting for geographic region (North America, South/central America, Western Europe, Eastern Europe, Asia/other).

Secondary: Percentage of Participants Achieving Low Disease Activity (LDA) Based on DAS28(CRP) at Week 24 - Global Analysis

End point title	Percentage of Participants Achieving Low Disease Activity (LDA) Based on DAS28(CRP) at Week 24 - Global Analysis[57]

End point description:

The DAS28(CRP) is a composite index used to assess rheumatoid arthritis disease activity, calculated based on the tender joint count (out of 28 evaluated joints), swollen joint count (out of 28 evaluated joints), Patient's Global Assessment of Disease Activity (0-100 mm), and hsCRP (in mg/L). Scores on the DAS28 range from 0 to approximately 10, where higher scores indicate more disease activity.
A DAS28(CRP) score less than or equal to 3.2 indicates low disease activity.
Participants who prematurely discontinued from study drug prior to Week 24 or for whom DAS28 data were missing at Week 24 were considered non-responders.

End point type	Secondary

End point timeframe:

Week 24

Notes:

[57] - 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: The global analysis includes participants enrolled under the methotrexate and upadacitinib 15 mg and 30 mg treatment groups.

End point values	Methotrexate	Upadacitinib 15 mg	Upadacitinib 30 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	314[58]	317[59]	314[60]	
Units: percentage of participants				
number (confidence interval 95%)	32.2 (27.0 to 37.3)	59.9 (54.5 to 65.3)	65.0 (59.7 to 70.2)	

Notes:

[58] - Full analysis set

[59] - Full analysis set

[60] - Full analysis set

Statistical analyses

Statistical analysis title	Analysis of LDA at Week 24
Comparison groups	Upadacitinib 15 mg v Methotrexate
Number of subjects included in analysis	631
Analysis specification	Pre-specified
Analysis type	superiority[61]
P-value	< 0.001 [62]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Response Rate Difference
Point estimate	27.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	20.3
upper limit	35.2

Notes:

[61] - The overall type I error rate of the primary and ranked key secondary endpoints for the two doses was controlled using a graphical multiple testing procedure. This endpoint was a ranked key secondary endpoint for EU/EMA regulatory purposes.
The nominal p-value is reported.
[62] - Cochran-Mantel-Haenszel test adjusting for geographic region (North America, South/central America, Western Europe, Eastern Europe, Asia/other).

Statistical analysis title	Analysis of LDA at Week 24
Comparison groups	Upadacitinib 30 mg v Methotrexate
Number of subjects included in analysis	628
Analysis specification	Pre-specified
Analysis type	superiority[63]
P-value	< 0.001 [64]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Response Rate Difference
Point estimate	32.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	25.4
upper limit	40.2

Notes:

[63] - The overall type I error rate of the primary and ranked key secondary endpoints for the two doses was controlled using a graphical multiple testing procedure. This endpoint was a ranked key secondary endpoint for EU/EMA regulatory purposes.
The nominal p-value is reported.
[64] - Cochran-Mantel-Haenszel test adjusting for geographic region (North America, South/central America, Western Europe, Eastern Europe, Asia/other).

Secondary: Change From Baseline in Short-Form 36 (SF-36) Physical Component Score (PCS) at Week 24 - Global Analysis

End point title	Change From Baseline in Short-Form 36 (SF-36) Physical Component Score (PCS) at Week 24 - Global Analysis[65]

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.
Multiple imputation was used for missing data.

End point type	Secondary

End point timeframe:

Baseline to Week 24

Notes:

[65] - 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: The global analysis includes participants enrolled under the methotrexate and upadacitinib 15 mg and 30 mg treatment groups.

End point values	Methotrexate	Upadacitinib 15 mg	Upadacitinib 30 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	313[66]	315[67]	312[68]	
Units: score on a scale				
least squares mean (confidence interval 95%)	6.97 (6.03 to 7.91)	10.70 (9.76 to 11.63)	11.39 (10.42 to 12.36)	

Notes:

[66] - Full analysis set participants with available data at Baseline

[67] - Full analysis set participants with available data at Baseline

[68] - Full analysis set participants with available data at Baseline

Statistical analyses

Statistical analysis title	Analysis of Change in SF-36 PCS at Week 24
Comparison groups	Upadacitinib 15 mg v Methotrexate
Number of subjects included in analysis	628
Analysis specification	Pre-specified
Analysis type	superiority[69]
P-value	< 0.001 [70]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	3.72
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.42
upper limit	5.03

Notes:

[69] - The overall type I error rate of the primary and ranked key secondary endpoints for the two doses was controlled using a graphical multiple testing procedure. This endpoint was a ranked key secondary endpoint for EU/EMA regulatory purposes.
The nominal p-value is reported.

[70] - ANCOVA model with treatment and geographic region as fixed factors and Baseline value as the covariate.

Statistical analysis title	Analysis of Change in SF-36 PCS at Week 24
Comparison groups	Upadacitinib 30 mg v Methotrexate

Number of subjects included in analysis	625
Analysis specification	Pre-specified
Analysis type	superiority[71]
P-value	< 0.001 [72]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	4.42
Confidence interval	
level	95 %
sides	2-sided
lower limit	3.12
upper limit	5.72

Notes:

[71] - The overall type I error rate of the primary and ranked key secondary endpoints for the two doses was controlled using a graphical multiple testing procedure. This endpoint was a ranked key secondary endpoint for EU/EMA regulatory purposes.
The nominal p-value is reported.

[72] - ANCOVA model with treatment and geographic region as fixed factors and Baseline value as the covariate.

Secondary: Percentage of Participants With No Radiographic Progression at Week 24 - Global Analysis

End point title	Percentage of Participants With No Radiographic Progression at Week 24 - Global Analysis[73]

End point description:

No radiographic progression is defined as a change from Baseline in mTSS ≤ 0. The mTSS measures the level of joint damage from radiographs of the hands and feet. Joint erosion and joint space narrowing (JSN) were assessed by two independent, blinded readers.
Joint erosion severity was assessed in 16 joints in each hand and wrist and 6 joints in each foot. Each joint was scored from 0 (no erosion) to 5 for hands/wrists or to 10 for feet (complete collapse). The total erosion score ranges from 0 to 280 (worst).
Joint space narrowing (JSN) was assessed in 15 joints of each hand and wrist, and 6 joints of each foot, including subluxation, from 0 (normal) to 4 (complete loss of joint space, bony ankylosis, or luxation). The total JSN score ranges from 0 to 168 (worst).
The mTSS is the sum of the joint erosion and JSN scores and ranges from 0 (normal) to 448 (worst).
Linear extrapolation was used for participants who discontinued prior to Week 24 or for whom x-ray data were missing.

End point type	Secondary

End point timeframe:

Week 24

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: The global analysis includes participants enrolled under the methotrexate and upadacitinib 15 mg and 30 mg treatment groups.

End point values	Methotrexate	Upadacitinib 15 mg	Upadacitinib 30 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	264[74]	279[75]	270[76]	
Units: percentage of participants				
number (confidence interval 95%)	77.7 (72.6 to 82.7)	87.5 (83.6 to 91.3)	89.3 (85.6 to 93.0)	

Notes:

[74] - Full analysis set participants with available data at Baseline

[75] - Full analysis set participants with available data at Baseline

[76] - Full analysis set participants with available data at Baseline

Statistical analyses

Statistical analysis title	Analysis of No Radiographic Progression at Week 24
Comparison groups	Upadacitinib 15 mg v Methotrexate
Number of subjects included in analysis	543
Analysis specification	Pre-specified
Analysis type	superiority[77]
P-value	= 0.002 [78]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Response Rate Difference
Point estimate	9.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	3.5
upper limit	16.2

Notes:

[77] - The overall type I error rate of the primary and ranked key secondary endpoints for the two doses was controlled using a graphical multiple testing procedure. This endpoint was a ranked key secondary endpoint for EU/EMA regulatory purposes.
The nominal p-value is reported.
[78] - Cochran-Mantel-Haenszel test adjusting for geographic region (North America, South/central America, Western Europe, Eastern Europe, Asia/other).

Statistical analysis title	Analysis of No Radiographic Progression at Week 24
Comparison groups	Upadacitinib 30 mg v Methotrexate
Number of subjects included in analysis	534
Analysis specification	Pre-specified
Analysis type	superiority[79]
P-value	< 0.001 [80]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Response Rate Difference
Point estimate	11.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	5.4
upper limit	17.8

Notes:

[79] - The overall type I error rate of the primary and ranked key secondary endpoints for the two doses was controlled using a graphical multiple testing procedure. This endpoint was a ranked key secondary endpoint for EU/EMA regulatory purposes.
The nominal p-value is reported.
[80] - Cochran-Mantel-Haenszel test adjusting for geographic region (North America, South/central America, Western Europe, Eastern Europe, Asia/other).

Secondary: Change From Baseline in DAS28 (CRP) at Week 12 - Global Analysis

End point title	Change From Baseline in DAS28 (CRP) at Week 12 - Global Analysis[81]

End point description:

The DAS28 is a composite index used to assess rheumatoid arthritis disease activity, calculated based on the tender joint count (out of 28 evaluated joints), swollen joint count (out of 28 evaluated joints), Patient's Global Assessment of Disease Activity (0-100 mm), and hsCRP (in mg/L). Scores on the DAS28 range from 0 to approximately 10, where higher scores indicate more disease activity. A negative change from Baseline in DAS28 (CRP) indicates improvement in disease activity.
Multiple imputation was used for missing post-baseline data.

End point type	Secondary

End point timeframe:

Baseline to Week 12

Notes:

[81] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The global analysis includes participants enrolled under the methotrexate and upadacitinib 15 mg and 30 mg treatment groups.

End point values	Methotrexate	Upadacitinib 15 mg	Upadacitinib 30 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	312[82]	317[83]	310[84]	
Units: score on a scale				
least squares mean (confidence interval 95%)	-1.85 (-2.00 to -1.69)	-2.73 (-2.87 to -2.58)	-2.85 (-3.00 to -2.70)	

Notes:

[82] - Full analysis set participants with available data at Baseline

[83] - Full analysis set participants with available data at Baseline

[84] - Full analysis set participants with available data at Baseline

Statistical analyses

Statistical analysis title	Analysis of Change in DAS28 (CRP) at Week 12
Comparison groups	Upadacitinib 15 mg v Methotrexate
Number of subjects included in analysis	629
Analysis specification	Pre-specified
Analysis type	superiority[85]
P-value	< 0.001 [86]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.88
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.09
upper limit	-0.67

Notes:

[85] - The overall type I error rate of the primary and ranked key secondary endpoints for the two doses was controlled using a graphical multiple testing procedure. This endpoint was a ranked key secondary endpoint for US/FDA and Japan/PMDA regulatory purposes.
The nominal p-value is reported.
[86] - ANCOVA model with treatment and geographic region as fixed factors and Baseline value as the covariate.

Statistical analysis title	Analysis of Change in DAS28 (CRP) at Week 12
Comparison groups	Upadacitinib 30 mg v Methotrexate

Number of subjects included in analysis	622
Analysis specification	Pre-specified
Analysis type	superiority[87]
P-value	< 0.001 [88]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-1.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.21
upper limit	-0.8

Notes:

[87] - The overall type I error rate of the primary and ranked key secondary endpoints for the two doses was controlled using a graphical multiple testing procedure. This endpoint was a ranked key secondary endpoint for US/FDA and Japan/PMDA regulatory purposes.
The nominal p-value is reported.

[88] - ANCOVA model with treatment and geographic region as fixed factors and Baseline value as the covariate.

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

End point title	Change From Baseline in Health Assessment Questionnaire Disability Index (HAQ-DI) at Week 12 - Global Analysis[89]

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.
Multiple imputation was used for missing data.

End point type	Secondary

End point timeframe:

Baseline to Week 12

Notes:

[89] - 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: The global analysis includes participants enrolled under the methotrexate and upadacitinib 15 mg and 30 mg treatment groups.

End point values	Methotrexate	Upadacitinib 15 mg	Upadacitinib 30 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	313[90]	317[91]	310[92]	
Units: score on a scale				
least squares mean (confidence interval 95%)	-0.49 (-0.55 to -0.42)	-0.83 (-0.90 to -0.76)	-0.86 (-0.93 to -0.79)	

Notes:

[90] - Full analysis set participants with available data at Baseline

[91] - Full analysis set participants with available data at Baseline

[92] - Full analysis set participants with available data at Baseline

Statistical analyses

Statistical analysis title	Analysis of Change in HAQ-DI at Week 12
Comparison groups	Upadacitinib 15 mg v Methotrexate
Number of subjects included in analysis	630
Analysis specification	Pre-specified
Analysis type	superiority[93]
P-value	< 0.001 [94]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.34
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.44
upper limit	-0.25

Notes:

[93] - The overall type I error rate of the primary and ranked key secondary endpoints for the two doses was controlled using a graphical multiple testing procedure. This endpoint was a ranked key secondary endpoint for US/FDA and Japan/PMDA regulatory purposes.
The nominal p-value is reported.
[94] - ANCOVA model with treatment and geographic region as fixed factors and Baseline value as the covariate.

Statistical analysis title	Analysis of Change in HAQ-DI at Week 12
Comparison groups	Upadacitinib 30 mg v Methotrexate
Number of subjects included in analysis	623
Analysis specification	Pre-specified
Analysis type	superiority[95]
P-value	< 0.001 [96]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.37
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.47
upper limit	-0.28

Notes:

[95] - The overall type I error rate of the primary and ranked key secondary endpoints for the two doses was controlled using a graphical multiple testing procedure. This endpoint was a ranked key secondary endpoint for US/FDA and Japan/PMDA regulatory purposes.
The nominal p-value is reported.
[96] - ANCOVA model with treatment and geographic region as fixed factors and Baseline value as the covariate.

Secondary: Percentage of Participants Achieving Low Disease Activity (LDA) Based on DAS28(CRP) at Week 12 - Global Analysis

End point title	Percentage of Participants Achieving Low Disease Activity (LDA) Based on DAS28(CRP) at Week 12 - Global Analysis[97]

End point description:

The DAS28(CRP) is a composite index used to assess rheumatoid arthritis disease activity, calculated based on the tender joint count (out of 28 evaluated joints), swollen joint count (out of 28 evaluated joints), Patient's Global Assessment of Disease Activity (0-100 mm), and hsCRP (in mg/L). Scores on the DAS28 range from 0 to approximately 10, where higher scores indicate more disease activity.
A DAS28(CRP) score less than or equal to 3.2 indicates low disease activity.
Participants who prematurely discontinued from study drug prior to Week 12 or for whom DAS28 data were missing at Week 12 were considered non-responders.

End point type	Secondary

End point timeframe:

Week 12

Notes:

[97] - 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: The global analysis includes participants enrolled under the methotrexate and upadacitinib 15 mg and 30 mg treatment groups.

End point values	Methotrexate	Upadacitinib 15 mg	Upadacitinib 30 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	314[98]	317[99]	314[100]	
Units: percentage of participants				
number (confidence interval 95%)	28.3 (23.4 to 33.3)	53.3 (47.8 to 58.8)	54.8 (49.3 to 60.3)	

Notes:

[98] - Full analysis set

[99] - Full analysis set

[100] - Full analysis set

Statistical analyses

Statistical analysis title	Analysis of LDA at Week 12
Comparison groups	Upadacitinib 15 mg v Methotrexate
Number of subjects included in analysis	631
Analysis specification	Pre-specified
Analysis type	superiority[101]
P-value	< 0.001 [102]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Response Rate Difference
Point estimate	25
Confidence interval	
level	95 %
sides	2-sided
lower limit	17.6
upper limit	32.4

Notes:

[101] - The overall type I error rate of the primary and ranked key secondary endpoints for the two doses was controlled using a graphical multiple testing procedure. This endpoint was a ranked key secondary endpoint for US/FDA and Japan/PMDA regulatory purposes.
The nominal p-value is reported.
[102] - Cochran-Mantel-Haenszel test adjusting for geographic region (North America, South/central America, Western Europe, Eastern Europe, Asia/other).

Statistical analysis title	Analysis of LDA at Week 12
Comparison groups	Upadacitinib 30 mg v Methotrexate
Number of subjects included in analysis	628
Analysis specification	Pre-specified
Analysis type	superiority[103]
P-value	< 0.001 [104]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Response Rate Difference
Point estimate	26.4

Confidence interval	
level	95 %
sides	2-sided
lower limit	19
upper limit	33.9

Notes:

[103] - The overall type I error rate of the primary and ranked key secondary endpoints for the two doses was controlled using a graphical multiple testing procedure. This endpoint was a ranked key secondary endpoint for US/FDA and Japan/PMDA regulatory purposes.
The nominal p-value is reported.
[104] - Cochran-Mantel-Haenszel test adjusting for geographic region (North America, South/central America, Western Europe, Eastern Europe, Asia/other).

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

End point title	Change From Baseline in Short-Form 36 (SF-36) Physical Component Score (PCS) at Week 12 - Global Analysis[105]

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.
Multiple imputation was used for missing data.

End point type	Secondary

End point timeframe:

Baseline to Week 12

Notes:

[105] - 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: The global analysis includes participants enrolled under the methotrexate and upadacitinib 15 mg and 30 mg treatment groups.

End point values	Methotrexate	Upadacitinib 15 mg	Upadacitinib 30 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	311[106]	315[107]	311[108]	
Units: score on a scale				
least squares mean (confidence interval 95%)	5.74 (4.84 to 6.64)	9.99 (9.11 to 10.88)	10.08 (9.19 to 10.98)	

Notes:

[106] - Full analysis set participants with available data at Baseline

[107] - Full analysis set participants with available data at Baseline

[108] - Full analysis set participants with available data at Baseline

Statistical analyses

Statistical analysis title	Analysis of Change in SF-36 PCS at Week 12
Comparison groups	Upadacitinib 15 mg v Methotrexate

Number of subjects included in analysis	626
Analysis specification	Pre-specified
Analysis type	superiority[109]
P-value	< 0.001 [110]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	4.25
Confidence interval	
level	95 %
sides	2-sided
lower limit	3
upper limit	5.5

Notes:

[109] - The overall type I error rate of the primary and ranked key secondary endpoints for the two doses was controlled using a graphical multiple testing procedure. This endpoint was a ranked key secondary endpoint for US/FDA and Japan/PMDA regulatory purposes.
The nominal p-value is reported.
[110] - ANCOVA model with treatment and geographic region as fixed factors and Baseline value as the covariate.

Statistical analysis title	Analysis of Change in SF-36 PCS at Week 12
Comparison groups	Upadacitinib 30 mg v Methotrexate
Number of subjects included in analysis	622
Analysis specification	Pre-specified
Analysis type	superiority[111]
P-value	< 0.001 [112]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	4.34
Confidence interval	
level	95 %
sides	2-sided
lower limit	3.09
upper limit	5.59

Notes:

[111] - The overall type I error rate of the primary and ranked key secondary endpoints for the two doses was controlled using a graphical multiple testing procedure. This endpoint was a ranked key secondary endpoint for US/FDA and Japan/PMDA regulatory purposes.
The nominal p-value is reported.
[112] - ANCOVA model with treatment and geographic region as fixed factors and Baseline value as the covariate.

Secondary: Percentage of Participants With an American College of Rheumatology 20% (ACR20) Response at Week 24 - Global Analysis

End point title	Percentage of Participants With an American College of Rheumatology 20% (ACR20) Response at Week 24 - Global Analysis[113]

End point description:

Participants who met the following 3 conditions for improvement from baseline were classified as meeting the ACR20 response criteria:
1. ≥ 20% improvement in 68-tender joint count;
2. ≥ 20% improvement in 66-swollen joint count; and
3. ≥ 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).

Participants who prematurely discontinued from study drug prior to Week 24 or for whom ACR data were missing at Week 24 were considered non-responders.

End point type	Secondary

End point timeframe:

Baseline and Week 24

Notes:

[113] - 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: The global analysis includes participants enrolled under the methotrexate and upadacitinib 15 mg and 30 mg treatment groups.

End point values	Methotrexate	Upadacitinib 15 mg	Upadacitinib 30 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	314[114]	317[115]	314[116]	
Units: percentage of participants				
number (confidence interval 95%)	58.6 (53.2 to 64.0)	78.9 (74.4 to 83.4)	78.0 (73.4 to 82.6)	

Notes:

[114] - Full analysis set

[115] - Full analysis set

[116] - Full analysis set

Statistical analyses

Statistical analysis title	Analysis of ACR20 Response at Week 24
Comparison groups	Upadacitinib 15 mg v Methotrexate
Number of subjects included in analysis	631
Analysis specification	Pre-specified
Analysis type	superiority[117]
P-value	< 0.001 [118]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Response Rate Difference
Point estimate	20.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	13.2
upper limit	27.3

Notes:

[117] - The nominal p-value is reported.

[118] - Cochran-Mantel-Haenszel test adjusting for geographic region (North America, South/central America, Western Europe, Eastern Europe, Asia/other).

Statistical analysis title	Analysis of ACR20 Response at Week 24
Comparison groups	Upadacitinib 30 mg v Methotrexate
Number of subjects included in analysis	628
Analysis specification	Pre-specified
Analysis type	superiority[119]
P-value	< 0.001 [120]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Response Rate Difference
Point estimate	19.4

Confidence interval	
level	95 %
sides	2-sided
lower limit	12.3
upper limit	26.5

Notes:

[119] - The nominal p-value is reported.

[120] - Cochran-Mantel-Haenszel test adjusting for geographic region (North America, South/central America, Western Europe, Eastern Europe, Asia/other).

Secondary: Percentage of Participants With an ACR70 Response at Week 24 - Global Analysis

End point title	Percentage of Participants With an ACR70 Response at Week 24 - Global Analysis[121]

End point description:

Participants who met the following 3 conditions for improvement from baseline were classified as meeting the ACR70 response criteria:
1. ≥ 70% improvement in 68-tender joint count;
2. ≥ 70% improvement in 66-swollen joint count; and
3. ≥ 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).

Participants who prematurely discontinued from study drug prior to Week 24 or for whom ACR data were missing at Week 24 were considered non-responders.

End point type	Secondary

End point timeframe:

Baseline and Week 24

Notes:

[121] - 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: The global analysis includes participants enrolled under the methotrexate and upadacitinib 15 mg and 30 mg treatment groups.

End point values	Methotrexate	Upadacitinib 15 mg	Upadacitinib 30 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	314[122]	317[123]	314[124]	
Units: percentage of participants				
number (confidence interval 95%)	18.5 (14.2 to 22.8)	44.5 (39.0 to 49.9)	49.7 (44.2 to 55.2)	

Notes:

[122] - Full analysis set

[123] - Full analysis set

[124] - Full analysis set

Statistical analyses

Statistical analysis title	Analysis of ACR70 Response at Week 24
Comparison groups	Upadacitinib 15 mg v Methotrexate

Number of subjects included in analysis	631
Analysis specification	Pre-specified
Analysis type	superiority[125]
P-value	< 0.001 [126]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Response Rate Difference
Point estimate	26
Confidence interval	
level	95 %
sides	2-sided
lower limit	19.1
upper limit	33

Notes:

[125] - The nominal p-value is reported.

[126] - Cochran-Mantel-Haenszel test adjusting for geographic region (North America, South/central America, Western Europe, Eastern Europe, Asia/other).

Statistical analysis title	Analysis of ACR70 Response at Week 24
Comparison groups	Upadacitinib 15 mg v Methotrexate
Number of subjects included in analysis	631
Analysis specification	Pre-specified
Analysis type	superiority[127]
P-value	< 0.001 [128]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Response Rate Difference
Point estimate	31.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	24.2
upper limit	38.2

Notes:

[127] - The nominal p-value is reported.

[128] - Cochran-Mantel-Haenszel test adjusting for geographic region (North America, South/central America, Western Europe, Eastern Europe, Asia/other).

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

End point title	Percentage of Participants With an American College of Rheumatology 70% (ACR70) Response at Week 12 - Global Analysis[129]

End point description:

Participants who met the following 3 conditions for improvement from Baseline were classified as meeting the ACR70 response criteria:
1. ≥ 70% improvement in 68-tender joint count;
2. ≥ 70% improvement in 66-swollen joint count; and
3. ≥ 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).

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:

[129] - 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: The global analysis includes participants enrolled under the methotrexate and upadacitinib 15 mg and 30 mg treatment groups.

End point values	Methotrexate	Upadacitinib 15 mg	Upadacitinib 30 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	314[130]	317[131]	314[132]	
Units: percentage of participants				
number (confidence interval 95%)	14.0 (10.2 to 17.9)	32.5 (27.3 to 37.6)	36.9 (31.6 to 42.3)	

Notes:

[130] - Full analysis set

[131] - Full analysis set

[132] - Full analysis set

Statistical analyses

Statistical analysis title	Analysis of ACR70 Response at Week 12
Comparison groups	Upadacitinib 15 mg v Methotrexate
Number of subjects included in analysis	631
Analysis specification	Pre-specified
Analysis type	superiority[133]
P-value	< 0.001 [134]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Response Rate Difference
Point estimate	18.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	12.1
upper limit	24.9

Notes:

[133] - The nominal p-value is reported.

[134] - Cochran-Mantel-Haenszel test adjusting for geographic region (North America, South/central America, Western Europe, Eastern Europe, Asia/other).

Statistical analysis title	Analysis of ACR70 Response at Week 12
Comparison groups	Upadacitinib 30 mg v Methotrexate
Number of subjects included in analysis	628
Analysis specification	Pre-specified
Analysis type	superiority[135]
P-value	< 0.001 [136]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Response Rate Difference
Point estimate	22.9

Confidence interval	
level	95 %
sides	2-sided
lower limit	16.4
upper limit	29.5

Notes:

[135] - The nominal p-value is reported.

[136] - Cochran-Mantel-Haenszel test adjusting for geographic region (North America, South/central America, Western Europe, Eastern Europe, Asia/other).

Secondary: Percentage of Participants With an ACR20 Response at Week 12 - Japan Sub-study

End point title	Percentage of Participants With an ACR20 Response at Week 12 - Japan Sub-study

End point description:

Participants who met the following 3 conditions for improvement from baseline were classified as meeting the ACR20 response criteria:
1. ≥ 20% improvement in 68-tender joint count;
2. ≥ 20% improvement in 66-swollen joint count; and
3. ≥ 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).

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

End point values	Methotrexate	Upadacitinib 7.5 mg	Upadacitinib 15 mg	Upadacitinib 30 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	28[137]	55	27[138]	28[139]
Units: percentage of participants				
number (confidence interval 95%)	57.1 (38.8 to 75.5)	85.5 (76.1 to 94.8)	85.2 (71.8 to 98.6)	78.6 (63.4 to 93.8)

Notes:

[137] - Japan sub-study full analysis set

[138] - Japan sub-study full analysis set

[139] - Japan sub-study full analysis set

Statistical analyses

Statistical analysis title	Analysis of ACR20 Response at Week 12
Comparison groups	Upadacitinib 7.5 mg v Methotrexate
Number of subjects included in analysis	83
Analysis specification	Pre-specified
Analysis type	superiority[140]
P-value	= 0.004
Method	Chi-squared
Parameter estimate	Response Rate Difference
Point estimate	28.3

Confidence interval	
level	95 %
sides	2-sided
lower limit	7.7
upper limit	48.9

Notes:

[140] - For the Japan sub-study, no multiplicity adjustments were applied and only nominal p-values were provided for all efficacy analyses.

Statistical analysis title	Analysis of ACR20 Response at Week 12
Comparison groups	Upadacitinib 15 mg v Methotrexate
Number of subjects included in analysis	55
Analysis specification	Pre-specified
Analysis type	superiority[141]
P-value	= 0.022
Method	Chi-squared
Parameter estimate	Response Rate Difference
Point estimate	28
Confidence interval	
level	95 %
sides	2-sided
lower limit	5.3
upper limit	50.7

Notes:

[141] - For the Japan sub-study, no multiplicity adjustments were applied and only nominal p-values were provided for all efficacy analyses.

Statistical analysis title	Analysis of ACR20 Response at Week 12
Comparison groups	Upadacitinib 30 mg v Methotrexate
Number of subjects included in analysis	56
Analysis specification	Pre-specified
Analysis type	superiority[142]
P-value	= 0.086
Method	Chi-squared
Parameter estimate	Response Rate Difference
Point estimate	21.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.4
upper limit	45.2

Notes:

[142] - For the Japan sub-study, no multiplicity adjustments were applied and only nominal p-values were provided for all efficacy analyses.

Secondary: Percentage of Participants With an ACR50 Response at Week 12 - Japan Sub-study

End point title	Percentage of Participants With an ACR50 Response at Week 12 - Japan Sub-study

End point description:

Participants who met the following 3 conditions for improvement from baseline were classified as meeting the ACR50 response criteria:
1. ≥ 50% improvement in 68-tender joint count;
2. ≥ 50% improvement in 66-swollen joint count; and

3. ≥ 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).
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

End point values	Methotrexate	Upadacitinib 7.5 mg	Upadacitinib 15 mg	Upadacitinib 30 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	28[143]	55[144]	27[145]	28[146]
Units: percentage of participants				
number (confidence interval 95%)	21.4 (6.2 to 36.6)	60.0 (47.1 to 72.9)	66.7 (48.9 to 84.4)	71.4 (54.7 to 88.2)

Notes:

[143] - Japan sub-study full analysis set

[144] - Japan sub-study full analysis set

[145] - Japan sub-study full analysis set

[146] - Japan sub-study full analysis set

Statistical analyses

Statistical analysis title	Analysis of ACR50 Response at Week 12
Comparison groups	Upadacitinib 7.5 mg v Methotrexate
Number of subjects included in analysis	83
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Chi-squared
Parameter estimate	Response Rate Difference
Point estimate	38.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	18.6
upper limit	58.5

Statistical analysis title	Analysis of ACR50 Response at Week 12
Comparison groups	Upadacitinib 15 mg v Methotrexate

Number of subjects included in analysis	55
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Chi-squared
Parameter estimate	Response Rate Difference
Point estimate	45.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	21.8
upper limit	68.6

Statistical analysis title	Analysis of ACR50 Response at Week 12
Comparison groups	Upadacitinib 30 mg v Methotrexate
Number of subjects included in analysis	56
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Chi-squared
Parameter estimate	Response Rate Difference
Point estimate	50
Confidence interval	
level	95 %
sides	2-sided
lower limit	27.4
upper limit	72.6

Secondary: Percentage of Participants With an ACR70 Response at Week 12 - Japan Sub-study

End point title	Percentage of Participants With an ACR70 Response at Week 12 - Japan Sub-study

End point description:

Participants who met the following 3 conditions for improvement from Baseline were classified as meeting the ACR70 response criteria:
1. ≥ 70% improvement in 68-tender joint count;
2. ≥ 70% improvement in 66-swollen joint count; and
3. ≥ 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).

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

End point values	Methotrexate	Upadacitinib 7.5 mg	Upadacitinib 15 mg	Upadacitinib 30 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	28[147]	55[148]	27[149]	28[150]
Units: percentage of participants				
number (confidence interval 95%)	0.0 (0.0 to 0.0)	34.5 (22.0 to 47.1)	51.9 (33.0 to 70.7)	64.3 (46.5 to 82.0)

Notes:

[147] - Japan sub-study full analysis set

[148] - Japan sub-study full analysis set

[149] - Japan sub-study full analysis set

[150] - Japan sub-study full analysis set

Statistical analyses

Statistical analysis title	Analysis of ACR70 Response at Week 12
Comparison groups	Upadacitinib 7.5 mg v Methotrexate
Number of subjects included in analysis	83
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Chi-squared
Parameter estimate	Response Rate Difference
Point estimate	34.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	22
upper limit	47.1

Statistical analysis title	Analysis of ACR70 Response at Week 12
Comparison groups	Upadacitinib 15 mg v Methotrexate
Number of subjects included in analysis	55
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Chi-squared
Parameter estimate	Response Rate Difference
Point estimate	51.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	33
upper limit	70.7

Statistical analysis title	Analysis of ACR70 Response at Week 12
Comparison groups	Upadacitinib 30 mg v Methotrexate
Number of subjects included in analysis	56
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Chi-squared
Parameter estimate	Response Rate Difference
Point estimate	64.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	46.5
upper limit	82

Secondary: Change From Baseline in DAS28 (CRP) at Week 12 - Japan Sub-study

End point title	Change From Baseline in DAS28 (CRP) at Week 12 - Japan Sub-study

End point description:

The DAS28 is a composite index used to assess rheumatoid arthritis disease activity, calculated based on the tender joint count (out of 28 evaluated joints), swollen joint count (out of 28 evaluated joints), Patient's Global Assessment of Disease Activity (0-100 mm), and hsCRP (in mg/L). Scores on the DAS28 range from 0 to approximately 10, where higher scores indicate more disease activity. A negative change from Baseline in DAS28 (CRP) indicates improvement in disease activity.
Multiple imputation was used for missing post-baseline data.

End point type	Secondary

End point timeframe:

Baseline to Week 12

End point values	Methotrexate	Upadacitinib 7.5 mg	Upadacitinib 15 mg	Upadacitinib 30 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	28[151]	55[152]	27[153]	28[154]
Units: score on a scale				
least squares mean (confidence interval 95%)	-1.42 (-1.82 to -1.03)	-2.86 (-3.14 to -2.58)	-3.28 (-3.68 to -2.89)	-3.34 (-3.74 to -2.95)

Notes:

[151] - Japan sub-study full analysis set participants with available data at Baseline

[152] - Japan sub-study full analysis set participants with available data at Baseline

[153] - Japan sub-study full analysis set participants with available data at Baseline

[154] - Japan sub-study full analysis set participants with available data at Baseline

Statistical analyses

Statistical analysis title	Analysis of Change in DAS28 (CRP) at Week 12
Comparison groups	Upadacitinib 7.5 mg v Methotrexate
Number of subjects included in analysis	83
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [155]
Method	ANOVA
Parameter estimate	LS Mean Difference
Point estimate	-1.43
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.92
upper limit	-0.95

Notes:

[155] - ANOVA model with Baseline value as covariate.

Statistical analysis title	Analysis of Change in DAS28 (CRP) at Week 12
Comparison groups	Upadacitinib 15 mg v Methotrexate
Number of subjects included in analysis	55
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [156]
Method	ANOVA
Parameter estimate	LS Mean Difference
Point estimate	-1.86
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.42
upper limit	-1.3

Notes:

[156] - ANOVA model with Baseline value as covariate.

Statistical analysis title	Analysis of Change in DAS28 (CRP) at Week 12
Comparison groups	Upadacitinib 30 mg v Methotrexate
Number of subjects included in analysis	56
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [157]
Method	ANOVA
Parameter estimate	LS Mean Difference
Point estimate	-1.92
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.48
upper limit	-1.36

Notes:

[157] - ANOVA model with Baseline value as covariate.

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

End point title	Change From Baseline in Health Assessment Questionnaire Disability Index (HAQ-DI) at Week 12 - Japan Sub-study

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.
Multiple imputation was used for missing data.

End point type	Secondary

End point timeframe:

Baseline to Week 12

End point values	Methotrexate	Upadacitinib 7.5 mg	Upadacitinib 15 mg	Upadacitinib 30 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	28[158]	55[159]	27[160]	28[161]
Units: score on a scale				
least squares mean (confidence interval 95%)	-0.20 (-0.37 to -0.04)	-0.75 (-0.86 to -0.63)	-0.95 (-1.12 to -0.78)	-0.95 (-1.12 to -0.79)

Notes:

[158] - Japan sub-study full analysis set participants with available data at baseline

[159] - Japan sub-study full analysis set participants with available data at baseline

[160] - Japan sub-study full analysis set participants with available data at baseline

[161] - Japan sub-study full analysis set participants with available data at baseline

Statistical analyses

Statistical analysis title	Analysis of Change in HAQ-DI at Week 12
Comparison groups	Upadacitinib 7.5 mg v Methotrexate
Number of subjects included in analysis	83
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [162]
Method	ANOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.54
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.75
upper limit	-0.34

Notes:
[162] - ANOVA model with Baseline value as covariate.

Statistical analysis title	Analysis of Change in HAQ-DI at Week 12
Comparison groups	Upadacitinib 15 mg v Methotrexate
Number of subjects included in analysis	55
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [163]
Method	ANOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.75
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.99
upper limit	-0.51

Notes:
[163] - ANOVA model with Baseline value as covariate.

Statistical analysis title	Analysis of Change in HAQ-DI at Week 12
Comparison groups	Upadacitinib 30 mg v Methotrexate
Number of subjects included in analysis	56
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [164]
Method	ANOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.75
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.99
upper limit	-0.51

Notes:
[164] - ANOVA model with Baseline value as covariate.

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

End point title	Change From Baseline in Short-Form 36 (SF-36) Physical Component Score (PCS) at Week 12 - Japan Sub-study

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.
Multiple imputation was used for missing data.

End point type	Secondary

End point timeframe:
Baseline to Week 12

End point values	Methotrexate	Upadacitinib 7.5 mg	Upadacitinib 15 mg	Upadacitinib 30 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	28[165]	55[166]	27[167]	28[168]
Units: score on a scale				
least squares mean (confidence interval 95%)	2.87 (0.56 to 5.18)	8.84 (7.18 to 10.50)	10.79 (8.48 to 13.09)	9.63 (7.13 to 12.13)

Notes:
[165] - Japan sub-study full analysis set participants with available data at baseline
[166] - Japan sub-study full analysis set participants with available data at baseline
[167] - Japan sub-study full analysis set participants with available data at baseline
[168] - Japan sub-study full analysis set participants with available data at baseline

Statistical analyses

Statistical analysis title	Analysis of Change in SF-36 PCS at Week 12
Comparison groups	Upadacitinib 7.5 mg v Methotrexate
Number of subjects included in analysis	83
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [169]
Method	ANOVA
Parameter estimate	LS Mean Difference
Point estimate	5.97
Confidence interval	
level	95 %
sides	2-sided
lower limit	3.15
upper limit	8.8

Notes:
[169] - ANOVA model with Baseline value as covariate.

Statistical analysis title	Analysis of Change in SF-36 PCS at Week 12
Comparison groups	Upadacitinib 15 mg v Methotrexate
Number of subjects included in analysis	55
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [170]
Method	ANOVA
Parameter estimate	LS Mean Difference
Point estimate	7.92
Confidence interval	
level	95 %
sides	2-sided
lower limit	4.66
upper limit	11.19

Notes:

[170] - ANOVA model with Baseline value as covariate.

Statistical analysis title	Analysis of Change in SF-36 PCS at Week 12
Comparison groups	Upadacitinib 30 mg v Methotrexate
Number of subjects included in analysis	56
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [171]
Method	ANOVA
Parameter estimate	LS Mean Difference
Point estimate	6.76
Confidence interval	
level	95 %
sides	2-sided
lower limit	3.33
upper limit	10.2

Notes:

[171] - ANOVA model with Baseline value as covariate.

Secondary: Percentage of Participants Achieving Low Disease Activity (LDA) Based on DAS28(CRP) at Week 12 - Japan Sub-study

End point title	Percentage of Participants Achieving Low Disease Activity (LDA) Based on DAS28(CRP) at Week 12 - Japan Sub-study

End point description:

The DAS28(CRP) is a composite index used to assess rheumatoid arthritis disease activity, calculated based on the tender joint count (out of 28 evaluated joints), swollen joint count (out of 28 evaluated joints), Patient's Global Assessment of Disease Activity (0-100 mm), and hsCRP (in mg/L). Scores on the DAS28 range from 0 to approximately 10, where higher scores indicate more disease activity.
A DAS28(CRP) score less than or equal to 3.2 indicates low disease activity.
Participants who prematurely discontinued from study drug prior to Week 12 or for whom DAS28 data were missing at Week 12 were considered non-responders.

End point type	Secondary

End point timeframe:

Week 12

End point values	Methotrexate	Upadacitinib 7.5 mg	Upadacitinib 15 mg	Upadacitinib 30 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	28[172]	55[173]	27[174]	28[175]
Units: percentage of participants				
number (confidence interval 95%)	17.9 (3.7 to 32.0)	69.1 (56.9 to 81.3)	77.8 (62.1 to 93.5)	78.6 (63.4 to 93.8)

Notes:

[172] - Japan sub-study full analysis set

[173] - Japan sub-study full analysis set

[174] - Japan sub-study full analysis set

[175] - Japan sub-study full analysis set

Statistical analyses

Statistical analysis title	Analysis of LDA at Week 12
Comparison groups	Upadacitinib 7.5 mg v Methotrexate
Number of subjects included in analysis	83
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Chi-squared
Parameter estimate	Response Rate Difference
Point estimate	51.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	32.5
upper limit	70

Statistical analysis title	Analysis of LDA at Week 12
Comparison groups	Upadacitinib 15 mg v Methotrexate
Number of subjects included in analysis	55
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Chi-squared
Parameter estimate	Response Rate Difference
Point estimate	59.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	38.8
upper limit	81.1

Statistical analysis title	Analysis of LDA at Week 12
Comparison groups	Upadacitinib 30 mg v Methotrexate
Number of subjects included in analysis	56
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Chi-squared
Parameter estimate	Response Rate Difference
Point estimate	60.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	39.9
upper limit	81.5

Secondary: Percentage of Participants Achieving Clinical Remission (CR) Based on DAS28(CRP) at Week 24 - Japan Sub-study

End point title	Percentage of Participants Achieving Clinical Remission (CR) Based on DAS28(CRP) at Week 24 - Japan Sub-study

End point description:

The DAS28(CRP) is a composite index used to assess rheumatoid arthritis disease activity, calculated based on the tender joint count (out of 28 evaluated joints), swollen joint count (out of 28 evaluated joints), Patient's Global Assessment of Disease Activity (0-100 mm), and hsCRP (in mg/L). Scores on the DAS28 range from 0 to approximately 10, where higher scores indicate more disease activity. Participants who prematurely discontinued from study drug prior to Week 12 or for whom DAS28 data were missing at Week 12 were considered non-responders.

End point type	Secondary

End point timeframe:

Week 24

End point values	Methotrexate	Upadacitinib 7.5 mg	Upadacitinib 15 mg	Upadacitinib 30 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	28[176]	55[177]	27[178]	28[179]
Units: percentage of participants				
number (confidence interval 95%)	17.9 (3.7 to 32.0)	67.3 (54.9 to 79.7)	70.4 (53.1 to 87.6)	82.1 (68.0 to 96.3)

Notes:

[176] - Japan sub-study full analysis set

[177] - Japan sub-study full analysis set

[178] - Japan sub-study full analysis set

[179] - Japan sub-study full analysis set

Statistical analyses

Statistical analysis title	Analysis of CR at Week 24
Comparison groups	Upadacitinib 7.5 mg v Methotrexate
Number of subjects included in analysis	83
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Chi-squared
Parameter estimate	Response Rate Difference
Point estimate	49.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	30.6
upper limit	68.3

Statistical analysis title	Analysis of CR at Week 24
Comparison groups	Upadacitinib 15 mg v Methotrexate
Number of subjects included in analysis	55
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Chi-squared
Parameter estimate	Response Rate Difference
Point estimate	52.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	30.2
upper limit	74.8

Statistical analysis title	Analysis of CR at Week 24
Comparison groups	Upadacitinib 30 mg v Methotrexate
Number of subjects included in analysis	56
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Chi-squared
Parameter estimate	Response Rate Difference
Point estimate	64.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	44.2
upper limit	84.3

Secondary: Change From Baseline in Modified Total Sharp Score (mTSS) at Week 24 - Japan Sub-study

End point title	Change From Baseline in Modified Total Sharp Score (mTSS) at Week 24 - Japan Sub-study

End point description:

The mTSS measures the level of joint damage from radiographs of the hands and feet. Joint erosion and joint space narrowing (JSN) were assessed by two independent, blinded readers.
Joint erosion was assessed in 16 joints in each hand/wrist and 6 joints in each foot. Each joint was scored from 0 (no erosion) to 5 for hands/wrists or to 10 for feet (complete collapse). The total erosion score ranges from 0 to 280 (worst).
JSN was assessed in 15 joints of each hand and wrist, and 6 joints of each foot, including subluxation, from 0 (normal) to 4 (complete loss of joint space, bony ankylosis, or luxation). The total JSN score ranges from 0 to 168 (worst).
The mTSS is the sum of the joint erosion and JSN scores and ranges from 0 (normal) to 448 (worst). A change from Baseline greater than 0 indicates progression.
Linear extrapolation was used for participants who discontinued prior to Week 24 or for whom x-ray data were missing at Week 24.

End point type	Secondary

End point timeframe:
Baseline to Week 24

End point values	Methotrexate	Upadacitinib 7.5 mg	Upadacitinib 15 mg	Upadacitinib 30 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	26[180]	51[181]	26[182]	24[183]
Units: score on a scale				
least squares mean (confidence interval 95%)	2.64 (1.19 to 4.09)	0.95 (-0.09 to 1.98)	0.24 (-1.21 to 1.69)	0.19 (-1.31 to 1.70)

Notes:

[180] - Japan sub-study full analysis set participants with available data at Baseline

[181] - Japan sub-study full analysis set participants with available data at Baseline

[182] - Japan sub-study full analysis set participants with available data at Baseline

[183] - Japan sub-study full analysis set participants with available data at Baseline

Statistical analyses

Statistical analysis title	Analysis of Change in mTSS at Week 24
Comparison groups	Upadacitinib 7.5 mg v Methotrexate
Number of subjects included in analysis	77
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.063 [184]
Method	ANOVA
Parameter estimate	LS Mean Difference
Point estimate	-1.69
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.47
upper limit	0.09

Notes:

[184] - ANOVA model with Baseline value as covariate.

Statistical analysis title	Analysis of Change in mTSS at Week 24
Comparison groups	Upadacitinib 15 mg v Methotrexate
Number of subjects included in analysis	52
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.022 [185]
Method	ANOVA
Parameter estimate	LS Mean Difference
Point estimate	-2.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.45
upper limit	-0.35

Notes:

[185] - ANOVA model with Baseline value as covariate.

Statistical analysis title	Analysis of Change in mTSS at Week 24
Comparison groups	Upadacitinib 30 mg v Methotrexate
Number of subjects included in analysis	50
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.022 [186]
Method	ANOVA
Parameter estimate	LS Mean Difference
Point estimate	-2.45
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.54
upper limit	-0.35

Notes:

[186] - ANOVA model with Baseline value as covariate.

Secondary: Percentage of Participants With No Radiographic Progression at Week 24 - Japan Sub-study

End point title	Percentage of Participants With No Radiographic Progression at Week 24 - Japan Sub-study

End point description:

No radiographic progression is defined as a change from Baseline in mTSS ≤ 0. The mTSS measures the level of joint damage from radiographs of the hands and feet. Joint erosion and joint space narrowing (JSN) were assessed by two independent, blinded readers.
Joint erosion severity was assessed in 16 joints in each hand and wrist and 6 joints in each foot. Each joint was scored from 0 (no erosion) to 5 for hands/wrists or to 10 for feet (complete collapse). The total erosion score ranges from 0 to 280 (worst).
Joint space narrowing (JSN) was assessed in 15 joints of each hand and wrist, and 6 joints of each foot, including subluxation, from 0 (normal) to 4 (complete loss of joint space, bony ankylosis, or luxation). The total JSN score ranges from 0 to 168 (worst).
The mTSS is the sum of the joint erosion and JSN scores and ranges from 0 (normal) to 448 (worst).
Linear extrapolation was used for participants who discontinued prior to Week 24 or for whom x-ray data were missing.

End point type	Secondary

End point timeframe:

Week 24

End point values	Methotrexate	Upadacitinib 7.5 mg	Upadacitinib 15 mg	Upadacitinib 30 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	26[187]	51[188]	26[189]	24[190]
Units: percentage of participants				
number (confidence interval 95%)	46.2 (27.0 to 65.3)	82.4 (71.9 to 92.8)	80.8 (65.6 to 95.9)	79.2 (62.9 to 95.4)

Notes:

[187] - Japan sub-study full analysis set participants with available data at Baseline

[188] - Japan sub-study full analysis set participants with available data at Baseline

[189] - Japan sub-study full analysis set participants with available data at Baseline
[190] - Japan sub-study full analysis set participants with available data at Baseline

Statistical analyses

Statistical analysis title	Analysis of No Radiographic Progression at Week 24
Comparison groups	Upadacitinib 7.5 mg v Methotrexate
Number of subjects included in analysis	77
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.001
Method	Chi-squared
Parameter estimate	Response Rate Difference
Point estimate	36.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	14.4
upper limit	58

Statistical analysis title	Analysis of No Radiographic Progression at Week 24
Comparison groups	Upadacitinib 15 mg v Methotrexate
Number of subjects included in analysis	52
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.01
Method	Chi-squared
Parameter estimate	Response Rate Difference
Point estimate	34.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	10.2
upper limit	59

Statistical analysis title	Analysis of No Radiographic Progression at Week 24
Comparison groups	Upadacitinib 30 mg v Methotrexate

Number of subjects included in analysis	50
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.016
Method	Chi-squared
Parameter estimate	Response Rate Difference
Point estimate	33
Confidence interval	
level	95 %
sides	2-sided
lower limit	7.9
upper limit	58.1

Adverse events information

Timeframe for reporting adverse events:

From first dose of study drug to 30 days after last dose, up to 264 weeks; AEs are reported for Weeks 1 to 24, Weeks 1 to 260, and After Switch for participants switched from upadacitinib 30 mg QD to 15 mg QD after implementation of Protocol Amendment 6.

Adverse event reporting additional description:

In Weeks 1 to 24 all participants received monotherapy. For Weeks 1 to 260 and After Switch, AEs are reported for the following:
Monotherapy: includes events through the end of study or until rescue treatment was initiated.
All upadacitinib: includes any exposure to upadacitinib, alone or in addition to methotrexate or csDMARD after rescue.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	25.0

Reporting groups

Reporting group title	Weeks 1-24: Methotrexate Monotherapy

Reporting group description:

Participants received up to 20 mg methotrexate orally per week (15 mg/week in China and Japan) and placebo to upadacitinib QD for 24 weeks during Period 1.

Reporting group title	Weeks 1-24: Upadacitinib 7.5 mg Monotherapy

Reporting group description:

Participants received 7.5 mg upadacitinib orally once a day and placebo to methotrexate once a week for 24 weeks in Period 1.

Reporting group title	Weeks 1-24: Upadacitinib 15 mg Monotherapy

Reporting group description:

Participants received 15 mg upadacitinib orally once a day and placebo to methotrexate once a week for 24 weeks in Period 1.

Reporting group title	Weeks 1-24: Upadacitinib 30 mg Monotherapy

Reporting group description:

Participants received 30 mg upadacitinib orally once a day and placebo to methotrexate once a week for 24 weeks in Period 1.

Reporting group title	Weeks 1-260: Methotrexate Monotherapy

Reporting group description:

Participants received up to 20 mg methotrexate orally per week (15 mg/week in China and Japan) for 260 weeks. Includes events up until the addition of upadacitinib for participants who were rescued at Week 26.

Reporting group title	Weeks 1-260: Upadacitinib 7.5 mg Monotherapy

Reporting group description:

Participants received 7.5 mg upadacitinib monotherapy once a day for 260 weeks. Includes events up until the addition of methotrexate or addition of background csDMARD for participants who received rescue.

Reporting group title	Weeks 1-260: Upadacitinib 15 mg Monotherapy

Reporting group description:

Participants received 15 mg upadacitinib monotherapy once a day for 260 weeks. Includes events up until the addition of methotrexate or addition of background csDMARD for participants who received rescue.

Reporting group title	Weeks 1-260/Switch: Upadacitinib 30 mg Monotherapy

Reporting group description:

Participants received 30 mg upadacitinib monotherapy once a day for 260 weeks or until implementation of Protocol Amendment 6 (December 2019) when they were switched to upadacitinib 15 mg. Includes events up until the addition of methotrexate or addition of background csDMARD for participants who received rescue, or up until the switch to upadacitinib 15 mg.

Reporting group title	Weeks 1-260: Any Upadacitinib 7.5 mg

Reporting group description:

Participants originally randomized to upadacitinib 7.5 mg received upadacitinib 7.5 mg QD for up to 260 weeks, including events after the addition of rescue therapy. Participants originally randomized to methotrexate and rescued at Week 26 to methotrexate plus upadacitinib 7.5 mg received upadacitinib 7.5 mg QD from Week 26 to Week 260.

Reporting group title	Weeks 1-260: Any Upadacitinib 15 mg

Reporting group description:

Participants originally randomized to upadacitinib 15 mg received upadacitinib 15 mg QD for up to 260 weeks, including events after the addition of rescue therapy. Participants originally randomized to methotrexate and rescued at Week 26 to methotrexate plus upadacitinib 15 mg received upadacitinib 15 mg QD from Week 26 to Week 260.

Reporting group title	Weeks 1-260/Switch: Any Upadacitinib 30 mg

Reporting group description:

Participants originally randomized to upadacitinib 30 mg received upadacitinib 30 mg QD for up to 260 weeks or until implementation of Protocol Amendment 6 (December 2019)when they were switched to upadacitinib 15 mg, including events after the addition of rescue therapy. Participants originally randomized to methotrexate and rescued at Week 26 to methotrexate plus upadacitinib 30 mg received upadacitinib 30 mg QD from Week 26 to Week 260 or until implementation of Protocol Amendment 6 when they were switched to methotrexate plus upadacitinib 15 mg. Includes events up until the switch to upadacitinib 15 mg.

Reporting group title	After Switch: Upadacitinib 15 mg Monotherapy

Reporting group description:

Participants who were receiving upadacitinib 30 mg QD monotherapy in Period 2 were switched to upadacitinib 15 mg QD monotherapy after implementation of Protocol Amendment 6 (December 2019) up to Week 260.

Reporting group title	After Switch: Any Upadacitinib 15 mg

Reporting group description:

Participants who were receiving any upadacitinib 30 mg QD (monotherapy or in combination with methotrexate or csDMARD after rescue) in Period 2 were switched to upadacitinib 15 mg QD (monotherapy or in combination with methotrexate or csDMARD if rescued) after implementation of Protocol Amendment 6 (December 2019) up to Week 260.

Serious adverse events	Weeks 1-24: Methotrexate Monotherapy	Weeks 1-24: Upadacitinib 7.5 mg Monotherapy	Weeks 1-24: Upadacitinib 15 mg Monotherapy
Total subjects affected by serious adverse events			
subjects affected / exposed	13 / 314 (4.14%)	5 / 55 (9.09%)	16 / 317 (5.05%)
number of deaths (all causes)	1	0	2
number of deaths resulting from adverse events	0	0	1
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
ADENOCARCINOMA GASTRIC			
subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ADENOCARCINOMA OF COLON			
subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

ADENOCARCINOMA METASTATIC			
subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ANGIOFIBROMA			
subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
B-CELL LYMPHOMA			
subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BASAL CELL CARCINOMA			
subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
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 OVARIAN TUMOUR			
subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BLADDER CANCER			
subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BLADDER NEOPLASM			
subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BOWEN'S DISEASE			
subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BREAST CANCER METASTATIC			

subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CERVIX CARCINOMA STAGE 0			
subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BREAST CANCER			
subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ENDOMETRIAL ADENOCARCINOMA			
subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
FIBROMA			
subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
GASTRIC CANCER			
subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
LUNG ADENOCARCINOMA			
subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
LIPOMA			
subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
LEIOMYOMA			

subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
LUNG SQUAMOUS CELL CARCINOMA METASTATIC			
subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
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 PALATE NEOPLASM			
subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
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			
subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	1 / 317 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
METASTATIC NEOPLASM			
subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
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 TUMOUR			
subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
METASTASES TO BONE			
subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
NON-SMALL CELL LUNG CANCER METASTATIC			
subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
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 GERM CELL TERATOMA			

subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
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	1 / 314 (0.32%)	0 / 55 (0.00%)	0 / 317 (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
PAPILLARY THYROID CANCER			
subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
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 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
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 CANCER			
subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
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 CELL CARCINOMA STAGE I			
subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SEBACEOUS CARCINOMA			
subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SQUAMOUS CELL CARCINOMA OF LUNG			
subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	1 / 317 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SQUAMOUS CELL CARCINOMA OF SKIN			

subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SQUAMOUS CELL CARCINOMA OF THE TONGUE			
subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
TONGUE NEOPLASM MALIGNANT STAGE UNSPECIFIED			
subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
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 CANCER			
subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
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 CARCINOMA IN SITU			
subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	1 / 317 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
DEEP VEIN THROMBOSIS			
subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
EMBOLISM ARTERIAL			
subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HYPERTENSION			
subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PERIPHERAL ARTERIAL OCCLUSIVE			

DISEASE			
subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PERIPHERAL ARTERY STENOSIS			
subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PERIPHERAL ISCHAEMIA			
subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SHOCK HAEMORRHAGIC			
subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
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 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
CHEST DISCOMFORT			
subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
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 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
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 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
MULTIPLE ORGAN DYSFUNCTION SYNDROME			
subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SUDDEN DEATH			
subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
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			
BENIGN PROSTATIC HYPERPLASIA			
subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BREAST HYPOPLASIA			
subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CERVIX HAEMORRHAGE UTERINE			
subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CERVICAL DYSPLASIA			
subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ENDOMETRIAL HYPERPLASIA			
subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
MENOMETRORRHAGIA			

subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
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 CYST			
subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PROSTATITIS			
subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
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 CYST RUPTURED			
subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
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 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ASTHMATIC CRISIS			
subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
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 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
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 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PLEURAL EFFUSION			

subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PLEURISY			
subjects affected / exposed	1 / 314 (0.32%)	0 / 55 (0.00%)	0 / 317 (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
PNEUMOTHORAX			
subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
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 SPONTANEOUS			
subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
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 / 314 (0.32%)	0 / 55 (0.00%)	0 / 317 (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
PULMONARY FIBROSIS			
subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	1 / 317 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
RESPIRATORY FAILURE			
subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
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			
DEPRESSION			
subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
MENTAL DISORDER DUE TO A GENERAL MEDICAL CONDITION			

subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
BLOOD CREATINE PHOSPHOKINASE INCREASED			
subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HEPATIC ENZYME INCREASED			
subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
TRANSAMINASES INCREASED			
subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
WHITE BLOOD CELL COUNT INCREASED			
subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
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			
ANKLE FRACTURE			
subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CONTUSION			
subjects affected / exposed	0 / 314 (0.00%)	1 / 55 (1.82%)	0 / 317 (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
CORNEAL LACERATION			

subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CONCUSSION			
subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
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 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
FEMUR FRACTURE			
subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
FOOT FRACTURE			
subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HIP FRACTURE			
subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HUMERUS FRACTURE			
subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
JOINT DISLOCATION			
subjects affected / exposed	1 / 314 (0.32%)	0 / 55 (0.00%)	0 / 317 (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
LIMB CRUSHING INJURY			

subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
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 LIMB FRACTURE			
subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
MENISCUS INJURY			
subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PATELLA FRACTURE			
subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
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 LUMBAR PUNCTURE SYNDROME			
subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
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 FISTULA			
subjects affected / exposed	1 / 314 (0.32%)	0 / 55 (0.00%)	0 / 317 (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
RADIUS FRACTURE			
subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
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	1 / 314 (0.32%)	0 / 55 (0.00%)	0 / 317 (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 HAEMATOMA			

subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
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 / 314 (0.00%)	0 / 55 (0.00%)	1 / 317 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
THORACIC VERTEBRAL FRACTURE			
subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
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 LIMB FRACTURE			
subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
WRIST FRACTURE			
subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Congenital, familial and genetic disorders			
HAEMORRHAGIC ARTERIOVENOUS MALFORMATION			
subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
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 CORONARY SYNDROME			
subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
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 PECTORIS			
subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

ACUTE MYOCARDIAL INFARCTION			
subjects affected / exposed	2 / 314 (0.64%)	0 / 55 (0.00%)	0 / 317 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
ARTERIOSPASM CORONARY			
subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
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	1 / 314 (0.32%)	0 / 55 (0.00%)	0 / 317 (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 ARREST			
subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
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 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
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 CONGESTIVE			
subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
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 TAMPONADE			
subjects affected / exposed	0 / 314 (0.00%)	1 / 55 (1.82%)	0 / 317 (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
CARDIO-RESPIRATORY ARREST			
subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CARDIOVASCULAR DISORDER			

subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
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 CARDIOMYOPATHY			
subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
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 / 314 (0.00%)	0 / 55 (0.00%)	1 / 317 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
MYOCARDIAL FIBROSIS			
subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
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 ISCHAEMIA			
subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SINUS NODE DYSFUNCTION			
subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PERICARDITIS			
subjects affected / exposed	0 / 314 (0.00%)	1 / 55 (1.82%)	0 / 317 (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
SUPRAVENTRICULAR TACHYCARDIA			
subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
TACHYCARDIA			

subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
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			
CAROTID ARTERIOSCLEROSIS			
subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HYPOXIC-ISCHAEMIC ENCEPHALOPATHY			
subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	1 / 317 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 1
MONOPARESIS			
subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
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 DISEASE			
subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SCIATICA			
subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SPONDYLITIC MYELOPATHY			
subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
MYELOPATHY			
subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
VERTEBROBASILAR INSUFFICIENCY			

subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
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 ISCHAEMIC ATTACK			
subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	1 / 317 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SYNCOPE			
subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
ANAEMIA			
subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
IRON DEFICIENCY ANAEMIA			
subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
CATARACT			
subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CATARACT DIABETIC			
subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
IRIDOCYCLITIS			
subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
MACULAR HOLE			

subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
VITREOUS HAEMORRHAGE			
subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
VITREORETINAL TRACTION SYNDROME			
subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
ABDOMINAL PAIN			
subjects affected / exposed	1 / 314 (0.32%)	0 / 55 (0.00%)	0 / 317 (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
ABDOMINAL WALL HAEMATOMA			
subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ANAL FISTULA			
subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ASCITES			
subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COLITIS			
subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CONSTIPATION			

subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
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 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DIVERTICULAR PERFORATION			
subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
FOOD POISONING			
subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
GASTRIC ULCER			
subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
GASTRIC ULCER HAEMORRHAGE			
subjects affected / exposed	0 / 314 (0.00%)	1 / 55 (1.82%)	0 / 317 (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
GASTRIC ULCER PERFORATION			
subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
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 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
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 HAEMORRHAGE			

subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
GINGIVAL RECESSION			
subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
INCARCERATED INGUINAL HERNIA			
subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HIATUS HERNIA			
subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
LARGE INTESTINE PERFORATION			
subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
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 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
LARGE INTESTINE POLYP			
subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PANCREATIC DISORDER			
subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PANCREATITIS			

subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
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 HAEMORRHAGE			
subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SALIVARY GLAND CALCULUS			
subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
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 POLYP			
subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
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			
BILE DUCT STONE			
subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
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 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CHOLANGITIS			
subjects affected / exposed	1 / 314 (0.32%)	0 / 55 (0.00%)	0 / 317 (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
CHOLELITHIASIS			
subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
GALLBLADDER RUPTURE			

subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
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			
ANGIOEDEMA			
subjects affected / exposed	1 / 314 (0.32%)	0 / 55 (0.00%)	1 / 317 (0.32%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DIABETIC FOOT			
subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
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 ERUPTION			
subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SKIN ULCER			
subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
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			
NEPHROLITHIASIS			
subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ACUTE KIDNEY INJURY			
subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
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 COLIC			
subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
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 CYST			

subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
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 FAILURE			
subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
URETEROLITHIASIS			
subjects affected / exposed	0 / 314 (0.00%)	1 / 55 (1.82%)	0 / 317 (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			
ACQUIRED CLAW TOE			
subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
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			
subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
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 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
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 SPINAL STENOSIS			
subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
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 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
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 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
OSTEONECROSIS			
subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	1 / 317 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PAIN IN EXTREMITY			
subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PATHOLOGICAL FRACTURE			
subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ROTATOR CUFF SYNDROME			
subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SPONDYLOLISTHESIS			
subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SUBCHONDRAL INSUFFICIENCY FRACTURE			
subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SYMPATHETIC POSTERIOR CERVICAL SYNDROME			
subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
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 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
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			
ACTINOMYCOTIC PULMONARY INFECTION			
subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
APPENDICITIS			
subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BACTERIAL PYELONEPHRITIS			
subjects affected / exposed	1 / 314 (0.32%)	0 / 55 (0.00%)	0 / 317 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BRONCHITIS			
subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BRONCHOPULMONARY ASPERGILLOSIS			
subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
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 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
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 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CORONAVIRUS PNEUMONIA			

subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
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	1 / 314 (0.32%)	0 / 55 (0.00%)	1 / 317 (0.32%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DIVERTICULITIS			
subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	1 / 317 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
EMPYEMA			
subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ENDOCARDITIS			
subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ERYSIPELAS			
subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ESCHERICHIA INFECTION			
subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
FEMALE GENITAL TRACT TUBERCULOSIS			
subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	1 / 317 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
GALLBLADDER ABSCESS			

subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
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 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
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 DISSEMINATED			
subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
GENITAL HERPES SIMPLEX			
subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
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 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HERPES ZOSTER MENINGITIS			
subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
INFECTIVE SPONDYLITIS			
subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
INFLUENZA			
subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
KERATITIS BACTERIAL			

subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
LUNG ABSCESS			
subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
NECROTISING FASCIITIS			
subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
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 BACTERIAL			
subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
OPHTHALMIC HERPES ZOSTER			
subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PERITONEAL TUBERCULOSIS			
subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	1 / 317 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
OSTEOMYELITIS			
subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PARAINFLUENZAE VIRUS INFECTION			
subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PERITONITIS			

subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
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	2 / 314 (0.64%)	0 / 55 (0.00%)	2 / 317 (0.63%)
occurrences causally related to treatment / all	1 / 2	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PNEUMONIA BACTERIAL			
subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PNEUMONIA CRYPTOCOCCAL			
subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	1 / 317 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PNEUMONIA ESCHERICHIA			
subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
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 KLEBSIELLA			
subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PROSTATITIS ESCHERICHIA COLI			
subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PNEUMONIA PNEUMOCOCCAL			
subjects affected / exposed	0 / 314 (0.00%)	1 / 55 (1.82%)	0 / 317 (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
PYELONEPHRITIS ACUTE			

subjects affected / exposed	0 / 314 (0.00%)	1 / 55 (1.82%)	0 / 317 (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
PYELONEPHRITIS			
subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PYELONEPHRITIS CHRONIC			
subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
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 VIRAL			
subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
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 / 314 (0.00%)	1 / 55 (1.82%)	0 / 317 (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
Q FEVER			
subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
STAPHYLOCOCCAL INFECTION			
subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SEPTIC SHOCK			
subjects affected / exposed	0 / 314 (0.00%)	1 / 55 (1.82%)	0 / 317 (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
SINOBRONCHITIS			

subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
TOOTH ABSCESS			
subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
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 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
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 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
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 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
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			
ABNORMAL WEIGHT GAIN			
subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	1 / 317 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CENTRAL OBESITY			
subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DEHYDRATION			
subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
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 / 314 (0.00%)	0 / 55 (0.00%)	1 / 317 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HYPOKALAEMIA			
subjects affected / exposed	1 / 314 (0.32%)	0 / 55 (0.00%)	0 / 317 (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
OBESITY			
subjects affected / exposed	1 / 314 (0.32%)	0 / 55 (0.00%)	0 / 317 (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

Serious adverse events	Weeks 1-24: Upadacitinib 30 mg Monotherapy	Weeks 1-260: Methotrexate Monotherapy	Weeks 1-260: Upadacitinib 7.5 mg Monotherapy
Total subjects affected by serious adverse events			
subjects affected / exposed	20 / 314 (6.37%)	49 / 314 (15.61%)	13 / 55 (23.64%)
number of deaths (all causes)	3	8	1
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
ADENOCARCINOMA GASTRIC			
subjects affected / exposed	0 / 314 (0.00%)	0 / 314 (0.00%)	0 / 55 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ADENOCARCINOMA OF COLON			
subjects affected / exposed	0 / 314 (0.00%)	1 / 314 (0.32%)	0 / 55 (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
ADENOCARCINOMA METASTATIC			
subjects affected / exposed	0 / 314 (0.00%)	0 / 314 (0.00%)	0 / 55 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ANGIOFIBROMA			

subjects affected / exposed	0 / 314 (0.00%)	0 / 314 (0.00%)	0 / 55 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
B-CELL LYMPHOMA			
subjects affected / exposed	0 / 314 (0.00%)	0 / 314 (0.00%)	0 / 55 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BASAL CELL CARCINOMA			
subjects affected / exposed	0 / 314 (0.00%)	0 / 314 (0.00%)	0 / 55 (0.00%)
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 OVARIAN TUMOUR			
subjects affected / exposed	0 / 314 (0.00%)	0 / 314 (0.00%)	0 / 55 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BLADDER CANCER			
subjects affected / exposed	0 / 314 (0.00%)	0 / 314 (0.00%)	0 / 55 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BLADDER NEOPLASM			
subjects affected / exposed	0 / 314 (0.00%)	0 / 314 (0.00%)	1 / 55 (1.82%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BOWEN'S DISEASE			
subjects affected / exposed	0 / 314 (0.00%)	0 / 314 (0.00%)	0 / 55 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BREAST CANCER METASTATIC			
subjects affected / exposed	0 / 314 (0.00%)	0 / 314 (0.00%)	0 / 55 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CERVIX CARCINOMA STAGE 0			

subjects affected / exposed	0 / 314 (0.00%)	0 / 314 (0.00%)	0 / 55 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BREAST CANCER			
subjects affected / exposed	0 / 314 (0.00%)	0 / 314 (0.00%)	0 / 55 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ENDOMETRIAL ADENOCARCINOMA			
subjects affected / exposed	0 / 314 (0.00%)	1 / 314 (0.32%)	0 / 55 (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
FIBROMA			
subjects affected / exposed	0 / 314 (0.00%)	1 / 314 (0.32%)	0 / 55 (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
GASTRIC CANCER			
subjects affected / exposed	0 / 314 (0.00%)	0 / 314 (0.00%)	0 / 55 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
LUNG ADENOCARCINOMA			
subjects affected / exposed	0 / 314 (0.00%)	1 / 314 (0.32%)	0 / 55 (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
LIPOMA			
subjects affected / exposed	0 / 314 (0.00%)	0 / 314 (0.00%)	0 / 55 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
LEIOMYOMA			
subjects affected / exposed	0 / 314 (0.00%)	1 / 314 (0.32%)	0 / 55 (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
LUNG SQUAMOUS CELL CARCINOMA METASTATIC			

subjects affected / exposed	0 / 314 (0.00%)	0 / 314 (0.00%)	0 / 55 (0.00%)
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 PALATE NEOPLASM			
subjects affected / exposed	0 / 314 (0.00%)	0 / 314 (0.00%)	0 / 55 (0.00%)
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			
subjects affected / exposed	0 / 314 (0.00%)	0 / 314 (0.00%)	0 / 55 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
METASTATIC NEOPLASM			
subjects affected / exposed	0 / 314 (0.00%)	1 / 314 (0.32%)	0 / 55 (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
NEUROENDOCRINE TUMOUR			
subjects affected / exposed	0 / 314 (0.00%)	0 / 314 (0.00%)	0 / 55 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
METASTASES TO BONE			
subjects affected / exposed	0 / 314 (0.00%)	0 / 314 (0.00%)	0 / 55 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
NON-SMALL CELL LUNG CANCER METASTATIC			
subjects affected / exposed	0 / 314 (0.00%)	0 / 314 (0.00%)	0 / 55 (0.00%)
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 GERM CELL TERATOMA			
subjects affected / exposed	0 / 314 (0.00%)	0 / 314 (0.00%)	0 / 55 (0.00%)
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 / 314 (0.00%)	1 / 314 (0.32%)	0 / 55 (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
PAPILLARY THYROID CANCER			
subjects affected / exposed	0 / 314 (0.00%)	0 / 314 (0.00%)	0 / 55 (0.00%)
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 / 314 (0.00%)	0 / 314 (0.00%)	1 / 55 (1.82%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
RENAL CANCER			
subjects affected / exposed	0 / 314 (0.00%)	0 / 314 (0.00%)	0 / 55 (0.00%)
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 CELL CARCINOMA STAGE I			
subjects affected / exposed	0 / 314 (0.00%)	1 / 314 (0.32%)	0 / 55 (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
SEBACEOUS CARCINOMA			
subjects affected / exposed	0 / 314 (0.00%)	0 / 314 (0.00%)	0 / 55 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SQUAMOUS CELL CARCINOMA OF LUNG			
subjects affected / exposed	0 / 314 (0.00%)	0 / 314 (0.00%)	0 / 55 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SQUAMOUS CELL CARCINOMA OF SKIN			
subjects affected / exposed	0 / 314 (0.00%)	0 / 314 (0.00%)	0 / 55 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SQUAMOUS CELL CARCINOMA OF THE TONGUE			

subjects affected / exposed	0 / 314 (0.00%)	0 / 314 (0.00%)	0 / 55 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
TONGUE NEOPLASM MALIGNANT STAGE UNSPECIFIED			
subjects affected / exposed	0 / 314 (0.00%)	1 / 314 (0.32%)	0 / 55 (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
UTERINE CANCER			
subjects affected / exposed	0 / 314 (0.00%)	0 / 314 (0.00%)	0 / 55 (0.00%)
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 CARCINOMA IN SITU			
subjects affected / exposed	0 / 314 (0.00%)	0 / 314 (0.00%)	0 / 55 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
DEEP VEIN THROMBOSIS			
subjects affected / exposed	0 / 314 (0.00%)	2 / 314 (0.64%)	0 / 55 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
EMBOLISM ARTERIAL			
subjects affected / exposed	0 / 314 (0.00%)	0 / 314 (0.00%)	0 / 55 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HYPERTENSION			
subjects affected / exposed	0 / 314 (0.00%)	1 / 314 (0.32%)	0 / 55 (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
PERIPHERAL ARTERIAL OCCLUSIVE DISEASE			
subjects affected / exposed	1 / 314 (0.32%)	0 / 314 (0.00%)	0 / 55 (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
PERIPHERAL ARTERY STENOSIS			

subjects affected / exposed	0 / 314 (0.00%)	1 / 314 (0.32%)	0 / 55 (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
PERIPHERAL ISCHAEMIA			
subjects affected / exposed	0 / 314 (0.00%)	1 / 314 (0.32%)	0 / 55 (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
SHOCK HAEMORRHAGIC			
subjects affected / exposed	0 / 314 (0.00%)	0 / 314 (0.00%)	0 / 55 (0.00%)
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 / 314 (0.00%)	1 / 314 (0.32%)	0 / 55 (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			
CHEST DISCOMFORT			
subjects affected / exposed	0 / 314 (0.00%)	0 / 314 (0.00%)	0 / 55 (0.00%)
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 / 314 (0.00%)	0 / 314 (0.00%)	0 / 55 (0.00%)
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 / 314 (0.00%)	0 / 314 (0.00%)	0 / 55 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
MULTIPLE ORGAN DYSFUNCTION SYNDROME			

subjects affected / exposed	0 / 314 (0.00%)	0 / 314 (0.00%)	0 / 55 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SUDDEN DEATH			
subjects affected / exposed	1 / 314 (0.32%)	0 / 314 (0.00%)	0 / 55 (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
Reproductive system and breast disorders			
BENIGN PROSTATIC HYPERPLASIA			
subjects affected / exposed	0 / 314 (0.00%)	0 / 314 (0.00%)	0 / 55 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BREAST HYPOPLASIA			
subjects affected / exposed	0 / 314 (0.00%)	0 / 314 (0.00%)	0 / 55 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CERVIX HAEMORRHAGE UTERINE			
subjects affected / exposed	0 / 314 (0.00%)	0 / 314 (0.00%)	0 / 55 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CERVICAL DYSPLASIA			
subjects affected / exposed	0 / 314 (0.00%)	0 / 314 (0.00%)	0 / 55 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ENDOMETRIAL HYPERPLASIA			
subjects affected / exposed	0 / 314 (0.00%)	1 / 314 (0.32%)	0 / 55 (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
MENOMETRORRHAGIA			
subjects affected / exposed	0 / 314 (0.00%)	1 / 314 (0.32%)	0 / 55 (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 CYST			

subjects affected / exposed	0 / 314 (0.00%)	1 / 314 (0.32%)	0 / 55 (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
PROSTATITIS			
subjects affected / exposed	1 / 314 (0.32%)	0 / 314 (0.00%)	0 / 55 (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
OVARIAN CYST RUPTURED			
subjects affected / exposed	1 / 314 (0.32%)	0 / 314 (0.00%)	0 / 55 (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
Respiratory, thoracic and mediastinal disorders			
ACUTE RESPIRATORY FAILURE			
subjects affected / exposed	0 / 314 (0.00%)	0 / 314 (0.00%)	0 / 55 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ASTHMATIC CRISIS			
subjects affected / exposed	0 / 314 (0.00%)	0 / 314 (0.00%)	0 / 55 (0.00%)
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	1 / 314 (0.32%)	0 / 314 (0.00%)	0 / 55 (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
CHRONIC OBSTRUCTIVE PULMONARY DISEASE			
subjects affected / exposed	0 / 314 (0.00%)	0 / 314 (0.00%)	0 / 55 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PLEURAL EFFUSION			
subjects affected / exposed	0 / 314 (0.00%)	0 / 314 (0.00%)	0 / 55 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PLEURISY			

subjects affected / exposed	0 / 314 (0.00%)	1 / 314 (0.32%)	0 / 55 (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
PNEUMOTHORAX			
subjects affected / exposed	0 / 314 (0.00%)	0 / 314 (0.00%)	0 / 55 (0.00%)
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 SPONTANEOUS			
subjects affected / exposed	0 / 314 (0.00%)	0 / 314 (0.00%)	0 / 55 (0.00%)
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 / 314 (0.00%)	3 / 314 (0.96%)	0 / 55 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PULMONARY FIBROSIS			
subjects affected / exposed	0 / 314 (0.00%)	1 / 314 (0.32%)	0 / 55 (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 FAILURE			
subjects affected / exposed	1 / 314 (0.32%)	0 / 314 (0.00%)	0 / 55 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
DEPRESSION			
subjects affected / exposed	0 / 314 (0.00%)	0 / 314 (0.00%)	0 / 55 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
MENTAL DISORDER DUE TO A GENERAL MEDICAL CONDITION			
subjects affected / exposed	0 / 314 (0.00%)	0 / 314 (0.00%)	0 / 55 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			

BLOOD CREATINE PHOSPHOKINASE INCREASED			
subjects affected / exposed	0 / 314 (0.00%)	0 / 314 (0.00%)	0 / 55 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HEPATIC ENZYME INCREASED			
subjects affected / exposed	0 / 314 (0.00%)	0 / 314 (0.00%)	0 / 55 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
TRANSAMINASES INCREASED			
subjects affected / exposed	0 / 314 (0.00%)	0 / 314 (0.00%)	0 / 55 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
WHITE BLOOD CELL COUNT INCREASED			
subjects affected / exposed	0 / 314 (0.00%)	0 / 314 (0.00%)	0 / 55 (0.00%)
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			
ANKLE FRACTURE			
subjects affected / exposed	0 / 314 (0.00%)	0 / 314 (0.00%)	0 / 55 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CONTUSION			
subjects affected / exposed	0 / 314 (0.00%)	0 / 314 (0.00%)	1 / 55 (1.82%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CORNEAL LACERATION			
subjects affected / exposed	0 / 314 (0.00%)	0 / 314 (0.00%)	0 / 55 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CONCUSSION			

subjects affected / exposed	0 / 314 (0.00%)	1 / 314 (0.32%)	0 / 55 (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
FEMORAL NECK FRACTURE			
subjects affected / exposed	0 / 314 (0.00%)	0 / 314 (0.00%)	0 / 55 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
FEMUR FRACTURE			
subjects affected / exposed	0 / 314 (0.00%)	1 / 314 (0.32%)	1 / 55 (1.82%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
FOOT FRACTURE			
subjects affected / exposed	0 / 314 (0.00%)	1 / 314 (0.32%)	0 / 55 (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
HIP FRACTURE			
subjects affected / exposed	1 / 314 (0.32%)	1 / 314 (0.32%)	0 / 55 (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
HUMERUS FRACTURE			
subjects affected / exposed	0 / 314 (0.00%)	0 / 314 (0.00%)	0 / 55 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
JOINT DISLOCATION			
subjects affected / exposed	0 / 314 (0.00%)	2 / 314 (0.64%)	0 / 55 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
LIMB CRUSHING INJURY			
subjects affected / exposed	0 / 314 (0.00%)	0 / 314 (0.00%)	0 / 55 (0.00%)
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 LIMB FRACTURE			

subjects affected / exposed	0 / 314 (0.00%)	1 / 314 (0.32%)	0 / 55 (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
MENISCUS INJURY			
subjects affected / exposed	0 / 314 (0.00%)	0 / 314 (0.00%)	0 / 55 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PATELLA FRACTURE			
subjects affected / exposed	0 / 314 (0.00%)	0 / 314 (0.00%)	0 / 55 (0.00%)
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 LUMBAR PUNCTURE SYNDROME			
subjects affected / exposed	0 / 314 (0.00%)	0 / 314 (0.00%)	0 / 55 (0.00%)
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 FISTULA			
subjects affected / exposed	0 / 314 (0.00%)	1 / 314 (0.32%)	0 / 55 (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
RADIUS FRACTURE			
subjects affected / exposed	1 / 314 (0.32%)	0 / 314 (0.00%)	0 / 55 (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	0 / 314 (0.00%)	1 / 314 (0.32%)	0 / 55 (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
SUBDURAL HAEMATOMA			
subjects affected / exposed	0 / 314 (0.00%)	0 / 314 (0.00%)	1 / 55 (1.82%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
TENDON RUPTURE			

subjects affected / exposed	0 / 314 (0.00%)	1 / 314 (0.32%)	0 / 55 (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
THORACIC VERTEBRAL FRACTURE			
subjects affected / exposed	0 / 314 (0.00%)	0 / 314 (0.00%)	0 / 55 (0.00%)
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 LIMB FRACTURE			
subjects affected / exposed	0 / 314 (0.00%)	0 / 314 (0.00%)	0 / 55 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
WRIST FRACTURE			
subjects affected / exposed	1 / 314 (0.32%)	0 / 314 (0.00%)	0 / 55 (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
Congenital, familial and genetic disorders			
HAEMORRHAGIC ARTERIOVENOUS MALFORMATION			
subjects affected / exposed	0 / 314 (0.00%)	0 / 314 (0.00%)	0 / 55 (0.00%)
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 CORONARY SYNDROME			
subjects affected / exposed	0 / 314 (0.00%)	0 / 314 (0.00%)	0 / 55 (0.00%)
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 PECTORIS			
subjects affected / exposed	0 / 314 (0.00%)	0 / 314 (0.00%)	0 / 55 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ACUTE MYOCARDIAL INFARCTION			
subjects affected / exposed	1 / 314 (0.32%)	2 / 314 (0.64%)	0 / 55 (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

ARTERIOSPASM CORONARY			
subjects affected / exposed	0 / 314 (0.00%)	1 / 314 (0.32%)	0 / 55 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ATRIAL FIBRILLATION			
subjects affected / exposed	0 / 314 (0.00%)	2 / 314 (0.64%)	0 / 55 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CARDIAC ARREST			
subjects affected / exposed	0 / 314 (0.00%)	0 / 314 (0.00%)	0 / 55 (0.00%)
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 / 314 (0.00%)	0 / 314 (0.00%)	0 / 55 (0.00%)
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 CONGESTIVE			
subjects affected / exposed	0 / 314 (0.00%)	0 / 314 (0.00%)	0 / 55 (0.00%)
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 TAMPONADE			
subjects affected / exposed	0 / 314 (0.00%)	0 / 314 (0.00%)	1 / 55 (1.82%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CARDIO-RESPIRATORY ARREST			
subjects affected / exposed	0 / 314 (0.00%)	0 / 314 (0.00%)	0 / 55 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CARDIOVASCULAR DISORDER			
subjects affected / exposed	0 / 314 (0.00%)	0 / 314 (0.00%)	0 / 55 (0.00%)
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 CARDIOMYOPATHY			

subjects affected / exposed	0 / 314 (0.00%)	0 / 314 (0.00%)	0 / 55 (0.00%)
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 / 314 (0.00%)	2 / 314 (0.64%)	0 / 55 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
MYOCARDIAL FIBROSIS			
subjects affected / exposed	0 / 314 (0.00%)	0 / 314 (0.00%)	0 / 55 (0.00%)
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 ISCHAEMIA			
subjects affected / exposed	1 / 314 (0.32%)	1 / 314 (0.32%)	0 / 55 (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
SINUS NODE DYSFUNCTION			
subjects affected / exposed	0 / 314 (0.00%)	1 / 314 (0.32%)	0 / 55 (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
PERICARDITIS			
subjects affected / exposed	0 / 314 (0.00%)	0 / 314 (0.00%)	1 / 55 (1.82%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SUPRAVENTRICULAR TACHYCARDIA			
subjects affected / exposed	0 / 314 (0.00%)	0 / 314 (0.00%)	0 / 55 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
TACHYCARDIA			
subjects affected / exposed	0 / 314 (0.00%)	0 / 314 (0.00%)	0 / 55 (0.00%)
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			
CAROTID ARTERIOSCLEROSIS			

subjects affected / exposed	0 / 314 (0.00%)	0 / 314 (0.00%)	0 / 55 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HYPOXIC-ISCHAEMIC ENCEPHALOPATHY			
subjects affected / exposed	0 / 314 (0.00%)	0 / 314 (0.00%)	0 / 55 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
MONOPARESIS			
subjects affected / exposed	0 / 314 (0.00%)	1 / 314 (0.32%)	0 / 55 (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
CAROTID ARTERY DISEASE			
subjects affected / exposed	0 / 314 (0.00%)	0 / 314 (0.00%)	0 / 55 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SCIATICA			
subjects affected / exposed	0 / 314 (0.00%)	0 / 314 (0.00%)	0 / 55 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SPONDYLITIC MYELOPATHY			
subjects affected / exposed	0 / 314 (0.00%)	0 / 314 (0.00%)	0 / 55 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
MYELOPATHY			
subjects affected / exposed	0 / 314 (0.00%)	0 / 314 (0.00%)	0 / 55 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
VERTEBROBASILAR INSUFFICIENCY			
subjects affected / exposed	0 / 314 (0.00%)	0 / 314 (0.00%)	0 / 55 (0.00%)
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 ISCHAEMIC ATTACK			

subjects affected / exposed	0 / 314 (0.00%)	1 / 314 (0.32%)	1 / 55 (1.82%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SYNCOPE			
subjects affected / exposed	0 / 314 (0.00%)	1 / 314 (0.32%)	0 / 55 (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
Blood and lymphatic system disorders			
ANAEMIA			
subjects affected / exposed	0 / 314 (0.00%)	0 / 314 (0.00%)	0 / 55 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
IRON DEFICIENCY ANAEMIA			
subjects affected / exposed	0 / 314 (0.00%)	0 / 314 (0.00%)	0 / 55 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
CATARACT			
subjects affected / exposed	0 / 314 (0.00%)	0 / 314 (0.00%)	0 / 55 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CATARACT DIABETIC			
subjects affected / exposed	0 / 314 (0.00%)	1 / 314 (0.32%)	0 / 55 (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
IRIDOCYCLITIS			
subjects affected / exposed	0 / 314 (0.00%)	0 / 314 (0.00%)	0 / 55 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
MACULAR HOLE			
subjects affected / exposed	0 / 314 (0.00%)	0 / 314 (0.00%)	0 / 55 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
VITREOUS HAEMORRHAGE			

subjects affected / exposed	0 / 314 (0.00%)	1 / 314 (0.32%)	0 / 55 (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
VITREORETINAL TRACTION SYNDROME			
subjects affected / exposed	0 / 314 (0.00%)	0 / 314 (0.00%)	0 / 55 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
ABDOMINAL PAIN			
subjects affected / exposed	0 / 314 (0.00%)	1 / 314 (0.32%)	0 / 55 (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
ABDOMINAL WALL HAEMATOMA			
subjects affected / exposed	0 / 314 (0.00%)	0 / 314 (0.00%)	0 / 55 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ANAL FISTULA			
subjects affected / exposed	0 / 314 (0.00%)	0 / 314 (0.00%)	0 / 55 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ASCITES			
subjects affected / exposed	1 / 314 (0.32%)	0 / 314 (0.00%)	0 / 55 (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
COLITIS			
subjects affected / exposed	0 / 314 (0.00%)	0 / 314 (0.00%)	0 / 55 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CONSTIPATION			
subjects affected / exposed	0 / 314 (0.00%)	0 / 314 (0.00%)	0 / 55 (0.00%)
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 / 314 (0.00%)	0 / 314 (0.00%)	0 / 55 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DIVERTICULAR PERFORATION			
subjects affected / exposed	0 / 314 (0.00%)	0 / 314 (0.00%)	0 / 55 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
FOOD POISONING			
subjects affected / exposed	1 / 314 (0.32%)	0 / 314 (0.00%)	0 / 55 (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
GASTRIC ULCER			
subjects affected / exposed	0 / 314 (0.00%)	0 / 314 (0.00%)	0 / 55 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
GASTRIC ULCER HAEMORRHAGE			
subjects affected / exposed	0 / 314 (0.00%)	0 / 314 (0.00%)	1 / 55 (1.82%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
GASTRIC ULCER PERFORATION			
subjects affected / exposed	1 / 314 (0.32%)	0 / 314 (0.00%)	0 / 55 (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
GASTRITIS			
subjects affected / exposed	0 / 314 (0.00%)	0 / 314 (0.00%)	1 / 55 (1.82%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
GASTROINTESTINAL HAEMORRHAGE			
subjects affected / exposed	0 / 314 (0.00%)	1 / 314 (0.32%)	0 / 55 (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
GINGIVAL RECESSION			

subjects affected / exposed	0 / 314 (0.00%)	1 / 314 (0.32%)	0 / 55 (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
INCARCERATED INGUINAL HERNIA			
subjects affected / exposed	0 / 314 (0.00%)	0 / 314 (0.00%)	0 / 55 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HIATUS HERNIA			
subjects affected / exposed	0 / 314 (0.00%)	0 / 314 (0.00%)	0 / 55 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
LARGE INTESTINE PERFORATION			
subjects affected / exposed	1 / 314 (0.32%)	0 / 314 (0.00%)	0 / 55 (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	1 / 314 (0.32%)	0 / 314 (0.00%)	0 / 55 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
LARGE INTESTINE POLYP			
subjects affected / exposed	1 / 314 (0.32%)	0 / 314 (0.00%)	0 / 55 (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
PANCREATIC DISORDER			
subjects affected / exposed	0 / 314 (0.00%)	0 / 314 (0.00%)	0 / 55 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PANCREATITIS			
subjects affected / exposed	0 / 314 (0.00%)	0 / 314 (0.00%)	0 / 55 (0.00%)
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 HAEMORRHAGE			

subjects affected / exposed	0 / 314 (0.00%)	0 / 314 (0.00%)	0 / 55 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SALIVARY GLAND CALCULUS			
subjects affected / exposed	0 / 314 (0.00%)	0 / 314 (0.00%)	1 / 55 (1.82%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
RECTAL POLYP			
subjects affected / exposed	0 / 314 (0.00%)	0 / 314 (0.00%)	0 / 55 (0.00%)
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			
BILE DUCT STONE			
subjects affected / exposed	0 / 314 (0.00%)	0 / 314 (0.00%)	0 / 55 (0.00%)
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 / 314 (0.00%)	1 / 314 (0.32%)	0 / 55 (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
CHOLANGITIS			
subjects affected / exposed	0 / 314 (0.00%)	1 / 314 (0.32%)	0 / 55 (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
CHOLELITHIASIS			
subjects affected / exposed	0 / 314 (0.00%)	0 / 314 (0.00%)	0 / 55 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
GALLBLADDER RUPTURE			
subjects affected / exposed	0 / 314 (0.00%)	0 / 314 (0.00%)	0 / 55 (0.00%)
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			

ANGIOEDEMA			
subjects affected / exposed	0 / 314 (0.00%)	1 / 314 (0.32%)	0 / 55 (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
DIABETIC FOOT			
subjects affected / exposed	0 / 314 (0.00%)	1 / 314 (0.32%)	0 / 55 (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
DRUG ERUPTION			
subjects affected / exposed	0 / 314 (0.00%)	0 / 314 (0.00%)	0 / 55 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SKIN ULCER			
subjects affected / exposed	0 / 314 (0.00%)	0 / 314 (0.00%)	0 / 55 (0.00%)
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			
NEPHROLITHIASIS			
subjects affected / exposed	0 / 314 (0.00%)	0 / 314 (0.00%)	0 / 55 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ACUTE KIDNEY INJURY			
subjects affected / exposed	0 / 314 (0.00%)	1 / 314 (0.32%)	0 / 55 (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
RENAL COLIC			
subjects affected / exposed	0 / 314 (0.00%)	0 / 314 (0.00%)	0 / 55 (0.00%)
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 CYST			
subjects affected / exposed	0 / 314 (0.00%)	0 / 314 (0.00%)	0 / 55 (0.00%)
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 FAILURE			

subjects affected / exposed	1 / 314 (0.32%)	0 / 314 (0.00%)	0 / 55 (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
URETEROLITHIASIS			
subjects affected / exposed	0 / 314 (0.00%)	0 / 314 (0.00%)	1 / 55 (1.82%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
ACQUIRED CLAW TOE			
subjects affected / exposed	0 / 314 (0.00%)	0 / 314 (0.00%)	0 / 55 (0.00%)
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			
subjects affected / exposed	0 / 314 (0.00%)	1 / 314 (0.32%)	0 / 55 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
INTERVERTEBRAL DISC PROTRUSION			
subjects affected / exposed	0 / 314 (0.00%)	0 / 314 (0.00%)	0 / 55 (0.00%)
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 SPINAL STENOSIS			
subjects affected / exposed	0 / 314 (0.00%)	0 / 314 (0.00%)	0 / 55 (0.00%)
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 / 314 (0.00%)	0 / 314 (0.00%)	0 / 55 (0.00%)
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	2 / 314 (0.64%)	0 / 314 (0.00%)	0 / 55 (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
OSTEONECROSIS			

subjects affected / exposed	0 / 314 (0.00%)	0 / 314 (0.00%)	0 / 55 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PAIN IN EXTREMITY			
subjects affected / exposed	0 / 314 (0.00%)	0 / 314 (0.00%)	0 / 55 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PATHOLOGICAL FRACTURE			
subjects affected / exposed	0 / 314 (0.00%)	0 / 314 (0.00%)	0 / 55 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ROTATOR CUFF SYNDROME			
subjects affected / exposed	0 / 314 (0.00%)	0 / 314 (0.00%)	0 / 55 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SPONDYLOLISTHESIS			
subjects affected / exposed	0 / 314 (0.00%)	1 / 314 (0.32%)	0 / 55 (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
SUBCHONDRAL INSUFFICIENCY FRACTURE			
subjects affected / exposed	0 / 314 (0.00%)	0 / 314 (0.00%)	1 / 55 (1.82%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SYMPATHETIC POSTERIOR CERVICAL SYNDROME			
subjects affected / exposed	0 / 314 (0.00%)	1 / 314 (0.32%)	0 / 55 (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
SYSTEMIC LUPUS ERYTHEMATOSUS			
subjects affected / exposed	0 / 314 (0.00%)	0 / 314 (0.00%)	0 / 55 (0.00%)
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			

ACTINOMYCOTIC PULMONARY INFECTION			
subjects affected / exposed	0 / 314 (0.00%)	0 / 314 (0.00%)	0 / 55 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
APPENDICITIS			
subjects affected / exposed	0 / 314 (0.00%)	0 / 314 (0.00%)	0 / 55 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BACTERIAL PYELONEPHRITIS			
subjects affected / exposed	0 / 314 (0.00%)	1 / 314 (0.32%)	0 / 55 (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 / 314 (0.00%)	1 / 314 (0.32%)	0 / 55 (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
BRONCHOPULMONARY ASPERGILLOSIS			
subjects affected / exposed	0 / 314 (0.00%)	0 / 314 (0.00%)	0 / 55 (0.00%)
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 / 314 (0.00%)	1 / 314 (0.32%)	0 / 55 (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 / 314 (0.00%)	0 / 314 (0.00%)	1 / 55 (1.82%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CORONAVIRUS PNEUMONIA			
subjects affected / exposed	0 / 314 (0.00%)	0 / 314 (0.00%)	0 / 55 (0.00%)
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	1 / 314 (0.32%)	2 / 314 (0.64%)	0 / 55 (0.00%)
occurrences causally related to treatment / all	0 / 1	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DIVERTICULITIS			
subjects affected / exposed	1 / 314 (0.32%)	0 / 314 (0.00%)	0 / 55 (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
EMPYEMA			
subjects affected / exposed	0 / 314 (0.00%)	0 / 314 (0.00%)	0 / 55 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ENDOCARDITIS			
subjects affected / exposed	0 / 314 (0.00%)	1 / 314 (0.32%)	0 / 55 (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
ERYSIPELAS			
subjects affected / exposed	0 / 314 (0.00%)	0 / 314 (0.00%)	0 / 55 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ESCHERICHIA INFECTION			
subjects affected / exposed	0 / 314 (0.00%)	0 / 314 (0.00%)	0 / 55 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
FEMALE GENITAL TRACT TUBERCULOSIS			
subjects affected / exposed	0 / 314 (0.00%)	0 / 314 (0.00%)	0 / 55 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
GALLBLADDER ABSCESS			
subjects affected / exposed	0 / 314 (0.00%)	1 / 314 (0.32%)	0 / 55 (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 / 314 (0.00%)	0 / 314 (0.00%)	0 / 55 (0.00%)
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 DISSEMINATED			
subjects affected / exposed	0 / 314 (0.00%)	0 / 314 (0.00%)	0 / 55 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
GENITAL HERPES SIMPLEX			
subjects affected / exposed	0 / 314 (0.00%)	0 / 314 (0.00%)	0 / 55 (0.00%)
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 / 314 (0.00%)	0 / 314 (0.00%)	0 / 55 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HERPES ZOSTER MENINGITIS			
subjects affected / exposed	0 / 314 (0.00%)	0 / 314 (0.00%)	0 / 55 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
INFECTIVE SPONDYLITIS			
subjects affected / exposed	0 / 314 (0.00%)	0 / 314 (0.00%)	0 / 55 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
INFLUENZA			
subjects affected / exposed	0 / 314 (0.00%)	0 / 314 (0.00%)	0 / 55 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
KERATITIS BACTERIAL			
subjects affected / exposed	0 / 314 (0.00%)	0 / 314 (0.00%)	1 / 55 (1.82%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
LUNG ABSCESS			

subjects affected / exposed	0 / 314 (0.00%)	0 / 314 (0.00%)	0 / 55 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
NECROTISING FASCIITIS			
subjects affected / exposed	0 / 314 (0.00%)	0 / 314 (0.00%)	0 / 55 (0.00%)
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 BACTERIAL			
subjects affected / exposed	0 / 314 (0.00%)	0 / 314 (0.00%)	0 / 55 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
OPHTHALMIC HERPES ZOSTER			
subjects affected / exposed	0 / 314 (0.00%)	0 / 314 (0.00%)	0 / 55 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PERITONEAL TUBERCULOSIS			
subjects affected / exposed	0 / 314 (0.00%)	0 / 314 (0.00%)	0 / 55 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
OSTEOMYELITIS			
subjects affected / exposed	0 / 314 (0.00%)	1 / 314 (0.32%)	0 / 55 (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
PARAINFLUENZAE VIRUS INFECTION			
subjects affected / exposed	0 / 314 (0.00%)	0 / 314 (0.00%)	0 / 55 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PERITONITIS			
subjects affected / exposed	1 / 314 (0.32%)	0 / 314 (0.00%)	0 / 55 (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
PNEUMONIA			

subjects affected / exposed	2 / 314 (0.64%)	3 / 314 (0.96%)	1 / 55 (1.82%)
occurrences causally related to treatment / all	1 / 2	2 / 3	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PNEUMONIA BACTERIAL			
subjects affected / exposed	0 / 314 (0.00%)	0 / 314 (0.00%)	0 / 55 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PNEUMONIA CRYPTOCOCCAL			
subjects affected / exposed	0 / 314 (0.00%)	1 / 314 (0.32%)	0 / 55 (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 ESCHERICHIA			
subjects affected / exposed	0 / 314 (0.00%)	0 / 314 (0.00%)	0 / 55 (0.00%)
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 KLEBSIELLA			
subjects affected / exposed	1 / 314 (0.32%)	0 / 314 (0.00%)	0 / 55 (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
PROSTATITIS ESCHERICHIA COLI			
subjects affected / exposed	0 / 314 (0.00%)	0 / 314 (0.00%)	0 / 55 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PNEUMONIA PNEUMOCOCCAL			
subjects affected / exposed	0 / 314 (0.00%)	0 / 314 (0.00%)	1 / 55 (1.82%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PYELONEPHRITIS ACUTE			
subjects affected / exposed	0 / 314 (0.00%)	0 / 314 (0.00%)	2 / 55 (3.64%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PYELONEPHRITIS			

subjects affected / exposed	0 / 314 (0.00%)	2 / 314 (0.64%)	0 / 55 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PYELONEPHRITIS CHRONIC			
subjects affected / exposed	0 / 314 (0.00%)	0 / 314 (0.00%)	0 / 55 (0.00%)
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 VIRAL			
subjects affected / exposed	0 / 314 (0.00%)	0 / 314 (0.00%)	0 / 55 (0.00%)
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 / 314 (0.00%)	0 / 314 (0.00%)	1 / 55 (1.82%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Q FEVER			
subjects affected / exposed	0 / 314 (0.00%)	0 / 314 (0.00%)	0 / 55 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
STAPHYLOCOCCAL INFECTION			
subjects affected / exposed	0 / 314 (0.00%)	0 / 314 (0.00%)	0 / 55 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SEPTIC SHOCK			
subjects affected / exposed	1 / 314 (0.32%)	0 / 314 (0.00%)	1 / 55 (1.82%)
occurrences causally related to treatment / all	0 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
SINOBRONCHITIS			
subjects affected / exposed	0 / 314 (0.00%)	0 / 314 (0.00%)	0 / 55 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
TOOTH ABSCESS			

subjects affected / exposed	0 / 314 (0.00%)	1 / 314 (0.32%)	0 / 55 (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 / 314 (0.00%)	1 / 314 (0.32%)	0 / 55 (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 / 314 (0.00%)	0 / 314 (0.00%)	0 / 55 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
URINARY TRACT INFECTION			
subjects affected / exposed	1 / 314 (0.32%)	0 / 314 (0.00%)	0 / 55 (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
Metabolism and nutrition disorders			
ABNORMAL WEIGHT GAIN			
subjects affected / exposed	0 / 314 (0.00%)	0 / 314 (0.00%)	0 / 55 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CENTRAL OBESITY			
subjects affected / exposed	0 / 314 (0.00%)	0 / 314 (0.00%)	0 / 55 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DEHYDRATION			
subjects affected / exposed	0 / 314 (0.00%)	1 / 314 (0.32%)	0 / 55 (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
DIABETIC KETOACIDOSIS			
subjects affected / exposed	0 / 314 (0.00%)	0 / 314 (0.00%)	0 / 55 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HYPOKALAEMIA			

subjects affected / exposed	0 / 314 (0.00%)	1 / 314 (0.32%)	0 / 55 (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
OBESITY			
subjects affected / exposed	0 / 314 (0.00%)	1 / 314 (0.32%)	0 / 55 (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

Serious adverse events	Weeks 1-260: Upadacitinib 15 mg Monotherapy	Weeks 1-260/Switch: Upadacitinib 30 mg Monotherapy	Weeks 1-260: Any Upadacitinib 7.5 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	68 / 317 (21.45%)	71 / 314 (22.61%)	15 / 56 (26.79%)
number of deaths (all causes)	6	9	1
number of deaths resulting from adverse events	1	1	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
ADENOCARCINOMA GASTRIC			
subjects affected / exposed	0 / 317 (0.00%)	0 / 314 (0.00%)	0 / 56 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ADENOCARCINOMA OF COLON			
subjects affected / exposed	0 / 317 (0.00%)	0 / 314 (0.00%)	0 / 56 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ADENOCARCINOMA METASTATIC			
subjects affected / exposed	0 / 317 (0.00%)	0 / 314 (0.00%)	0 / 56 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ANGIOFIBROMA			
subjects affected / exposed	0 / 317 (0.00%)	0 / 314 (0.00%)	0 / 56 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
B-CELL LYMPHOMA			

subjects affected / exposed	0 / 317 (0.00%)	0 / 314 (0.00%)	0 / 56 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BASAL CELL CARCINOMA			
subjects affected / exposed	0 / 317 (0.00%)	1 / 314 (0.32%)	0 / 56 (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
BENIGN OVARIAN TUMOUR			
subjects affected / exposed	0 / 317 (0.00%)	1 / 314 (0.32%)	0 / 56 (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
BLADDER CANCER			
subjects affected / exposed	0 / 317 (0.00%)	1 / 314 (0.32%)	0 / 56 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
BLADDER NEOPLASM			
subjects affected / exposed	0 / 317 (0.00%)	0 / 314 (0.00%)	1 / 56 (1.79%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BOWEN'S DISEASE			
subjects affected / exposed	0 / 317 (0.00%)	1 / 314 (0.32%)	0 / 56 (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
BREAST CANCER METASTATIC			
subjects affected / exposed	0 / 317 (0.00%)	0 / 314 (0.00%)	0 / 56 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CERVIX CARCINOMA STAGE 0			
subjects affected / exposed	0 / 317 (0.00%)	1 / 314 (0.32%)	0 / 56 (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
BREAST CANCER			

subjects affected / exposed	1 / 317 (0.32%)	0 / 314 (0.00%)	0 / 56 (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
ENDOMETRIAL ADENOCARCINOMA			
subjects affected / exposed	0 / 317 (0.00%)	0 / 314 (0.00%)	0 / 56 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
FIBROMA			
subjects affected / exposed	0 / 317 (0.00%)	0 / 314 (0.00%)	0 / 56 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
GASTRIC CANCER			
subjects affected / exposed	0 / 317 (0.00%)	1 / 314 (0.32%)	0 / 56 (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
LUNG ADENOCARCINOMA			
subjects affected / exposed	0 / 317 (0.00%)	0 / 314 (0.00%)	0 / 56 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
LIPOMA			
subjects affected / exposed	0 / 317 (0.00%)	0 / 314 (0.00%)	0 / 56 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
LEIOMYOMA			
subjects affected / exposed	0 / 317 (0.00%)	0 / 314 (0.00%)	0 / 56 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
LUNG SQUAMOUS CELL CARCINOMA METASTATIC			
subjects affected / exposed	0 / 317 (0.00%)	1 / 314 (0.32%)	0 / 56 (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
MALIGNANT PALATE NEOPLASM			

subjects affected / exposed	0 / 317 (0.00%)	0 / 314 (0.00%)	0 / 56 (0.00%)
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			
subjects affected / exposed	1 / 317 (0.32%)	0 / 314 (0.00%)	0 / 56 (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
METASTATIC NEOPLASM			
subjects affected / exposed	0 / 317 (0.00%)	0 / 314 (0.00%)	0 / 56 (0.00%)
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 TUMOUR			
subjects affected / exposed	1 / 317 (0.32%)	0 / 314 (0.00%)	0 / 56 (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
METASTASES TO BONE			
subjects affected / exposed	0 / 317 (0.00%)	0 / 314 (0.00%)	0 / 56 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
NON-SMALL CELL LUNG CANCER METASTATIC			
subjects affected / exposed	0 / 317 (0.00%)	0 / 314 (0.00%)	0 / 56 (0.00%)
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 GERM CELL TERATOMA			
subjects affected / exposed	0 / 317 (0.00%)	1 / 314 (0.32%)	0 / 56 (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
OVARIAN CANCER			
subjects affected / exposed	0 / 317 (0.00%)	0 / 314 (0.00%)	0 / 56 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PAPILLARY THYROID CANCER			

subjects affected / exposed	1 / 317 (0.32%)	0 / 314 (0.00%)	0 / 56 (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	0 / 317 (0.00%)	0 / 314 (0.00%)	1 / 56 (1.79%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
RENAL CANCER			
subjects affected / exposed	0 / 317 (0.00%)	1 / 314 (0.32%)	0 / 56 (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 CELL CARCINOMA STAGE I			
subjects affected / exposed	0 / 317 (0.00%)	0 / 314 (0.00%)	0 / 56 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SEBACEOUS CARCINOMA			
subjects affected / exposed	1 / 317 (0.32%)	0 / 314 (0.00%)	0 / 56 (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
SQUAMOUS CELL CARCINOMA OF LUNG			
subjects affected / exposed	1 / 317 (0.32%)	0 / 314 (0.00%)	0 / 56 (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
SQUAMOUS CELL CARCINOMA OF SKIN			
subjects affected / exposed	0 / 317 (0.00%)	1 / 314 (0.32%)	0 / 56 (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
SQUAMOUS CELL CARCINOMA OF THE TONGUE			
subjects affected / exposed	0 / 317 (0.00%)	0 / 314 (0.00%)	0 / 56 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
TONGUE NEOPLASM MALIGNANT			

STAGE UNSPECIFIED			
subjects affected / exposed	0 / 317 (0.00%)	0 / 314 (0.00%)	0 / 56 (0.00%)
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 CANCER			
subjects affected / exposed	0 / 317 (0.00%)	1 / 314 (0.32%)	0 / 56 (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
UTERINE CARCINOMA IN SITU			
subjects affected / exposed	1 / 317 (0.32%)	0 / 314 (0.00%)	0 / 56 (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
Vascular disorders			
DEEP VEIN THROMBOSIS			
subjects affected / exposed	0 / 317 (0.00%)	1 / 314 (0.32%)	0 / 56 (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
EMBOLISM ARTERIAL			
subjects affected / exposed	0 / 317 (0.00%)	1 / 314 (0.32%)	0 / 56 (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
HYPERTENSION			
subjects affected / exposed	0 / 317 (0.00%)	0 / 314 (0.00%)	0 / 56 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PERIPHERAL ARTERIAL OCCLUSIVE DISEASE			
subjects affected / exposed	0 / 317 (0.00%)	1 / 314 (0.32%)	0 / 56 (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
PERIPHERAL ARTERY STENOSIS			
subjects affected / exposed	0 / 317 (0.00%)	0 / 314 (0.00%)	0 / 56 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

PERIPHERAL ISCHAEMIA			
subjects affected / exposed	0 / 317 (0.00%)	0 / 314 (0.00%)	0 / 56 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SHOCK HAEMORRHAGIC			
subjects affected / exposed	1 / 317 (0.32%)	0 / 314 (0.00%)	0 / 56 (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
Pregnancy, puerperium and perinatal conditions			
ABORTION SPONTANEOUS			
subjects affected / exposed	0 / 317 (0.00%)	1 / 314 (0.32%)	0 / 56 (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			
CHEST DISCOMFORT			
subjects affected / exposed	0 / 317 (0.00%)	0 / 314 (0.00%)	0 / 56 (0.00%)
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	1 / 317 (0.32%)	0 / 314 (0.00%)	0 / 56 (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
DEATH			
subjects affected / exposed	1 / 317 (0.32%)	0 / 314 (0.00%)	0 / 56 (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
MULTIPLE ORGAN DYSFUNCTION SYNDROME			
subjects affected / exposed	1 / 317 (0.32%)	0 / 314 (0.00%)	0 / 56 (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
SUDDEN DEATH			

subjects affected / exposed	0 / 317 (0.00%)	1 / 314 (0.32%)	0 / 56 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Reproductive system and breast disorders			
BENIGN PROSTATIC HYPERPLASIA			
subjects affected / exposed	1 / 317 (0.32%)	0 / 314 (0.00%)	0 / 56 (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
BREAST HYPOPLASIA			
subjects affected / exposed	0 / 317 (0.00%)	0 / 314 (0.00%)	0 / 56 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CERVIX HAEMORRHAGE UTERINE			
subjects affected / exposed	1 / 317 (0.32%)	0 / 314 (0.00%)	0 / 56 (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
CERVICAL DYSPLASIA			
subjects affected / exposed	2 / 317 (0.63%)	0 / 314 (0.00%)	0 / 56 (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
ENDOMETRIAL HYPERPLASIA			
subjects affected / exposed	0 / 317 (0.00%)	0 / 314 (0.00%)	0 / 56 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
MENOMETRORRHAGIA			
subjects affected / exposed	0 / 317 (0.00%)	0 / 314 (0.00%)	0 / 56 (0.00%)
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 CYST			
subjects affected / exposed	1 / 317 (0.32%)	0 / 314 (0.00%)	0 / 56 (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
PROSTATITIS			

subjects affected / exposed	0 / 317 (0.00%)	1 / 314 (0.32%)	0 / 56 (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
OVARIAN CYST RUPTURED			
subjects affected / exposed	0 / 317 (0.00%)	1 / 314 (0.32%)	0 / 56 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
ACUTE RESPIRATORY FAILURE			
subjects affected / exposed	0 / 317 (0.00%)	2 / 314 (0.64%)	0 / 56 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
ASTHMATIC CRISIS			
subjects affected / exposed	0 / 317 (0.00%)	1 / 314 (0.32%)	0 / 56 (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
ASTHMA			
subjects affected / exposed	1 / 317 (0.32%)	1 / 314 (0.32%)	0 / 56 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CHRONIC OBSTRUCTIVE PULMONARY DISEASE			
subjects affected / exposed	1 / 317 (0.32%)	2 / 314 (0.64%)	0 / 56 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PLEURAL EFFUSION			
subjects affected / exposed	0 / 317 (0.00%)	0 / 314 (0.00%)	0 / 56 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PLEURISY			
subjects affected / exposed	0 / 317 (0.00%)	0 / 314 (0.00%)	0 / 56 (0.00%)
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 / 317 (0.00%)	1 / 314 (0.32%)	0 / 56 (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
PNEUMOTHORAX SPONTANEOUS			
subjects affected / exposed	1 / 317 (0.32%)	0 / 314 (0.00%)	0 / 56 (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
PULMONARY EMBOLISM			
subjects affected / exposed	2 / 317 (0.63%)	3 / 314 (0.96%)	0 / 56 (0.00%)
occurrences causally related to treatment / all	2 / 2	1 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PULMONARY FIBROSIS			
subjects affected / exposed	1 / 317 (0.32%)	0 / 314 (0.00%)	0 / 56 (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
RESPIRATORY FAILURE			
subjects affected / exposed	0 / 317 (0.00%)	1 / 314 (0.32%)	0 / 56 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
DEPRESSION			
subjects affected / exposed	0 / 317 (0.00%)	1 / 314 (0.32%)	0 / 56 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
MENTAL DISORDER DUE TO A GENERAL MEDICAL CONDITION			
subjects affected / exposed	0 / 317 (0.00%)	1 / 314 (0.32%)	0 / 56 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
BLOOD CREATINE PHOSPHOKINASE INCREASED			
subjects affected / exposed	0 / 317 (0.00%)	0 / 314 (0.00%)	0 / 56 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

HEPATIC ENZYME INCREASED			
subjects affected / exposed	1 / 317 (0.32%)	0 / 314 (0.00%)	0 / 56 (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
TRANSAMINASES INCREASED			
subjects affected / exposed	1 / 317 (0.32%)	0 / 314 (0.00%)	0 / 56 (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
WHITE BLOOD CELL COUNT INCREASED			
subjects affected / exposed	1 / 317 (0.32%)	0 / 314 (0.00%)	0 / 56 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
ANKLE FRACTURE			
subjects affected / exposed	1 / 317 (0.32%)	0 / 314 (0.00%)	0 / 56 (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
CONTUSION			
subjects affected / exposed	0 / 317 (0.00%)	0 / 314 (0.00%)	1 / 56 (1.79%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CORNEAL LACERATION			
subjects affected / exposed	0 / 317 (0.00%)	0 / 314 (0.00%)	0 / 56 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CONCUSSION			
subjects affected / exposed	0 / 317 (0.00%)	0 / 314 (0.00%)	0 / 56 (0.00%)
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 / 317 (0.00%)	0 / 314 (0.00%)	0 / 56 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

FEMUR FRACTURE			
subjects affected / exposed	1 / 317 (0.32%)	0 / 314 (0.00%)	1 / 56 (1.79%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
FOOT FRACTURE			
subjects affected / exposed	0 / 317 (0.00%)	0 / 314 (0.00%)	0 / 56 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HIP FRACTURE			
subjects affected / exposed	0 / 317 (0.00%)	1 / 314 (0.32%)	0 / 56 (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
HUMERUS FRACTURE			
subjects affected / exposed	0 / 317 (0.00%)	1 / 314 (0.32%)	0 / 56 (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
JOINT DISLOCATION			
subjects affected / exposed	0 / 317 (0.00%)	0 / 314 (0.00%)	0 / 56 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
LIMB CRUSHING INJURY			
subjects affected / exposed	0 / 317 (0.00%)	1 / 314 (0.32%)	0 / 56 (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
LOWER LIMB FRACTURE			
subjects affected / exposed	0 / 317 (0.00%)	1 / 314 (0.32%)	0 / 56 (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
MENISCUS INJURY			
subjects affected / exposed	0 / 317 (0.00%)	0 / 314 (0.00%)	0 / 56 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PATELLA FRACTURE			

subjects affected / exposed	0 / 317 (0.00%)	0 / 314 (0.00%)	1 / 56 (1.79%)
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 LUMBAR PUNCTURE SYNDROME			
subjects affected / exposed	1 / 317 (0.32%)	0 / 314 (0.00%)	0 / 56 (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
POST PROCEDURAL FISTULA			
subjects affected / exposed	0 / 317 (0.00%)	0 / 314 (0.00%)	0 / 56 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
RADIUS FRACTURE			
subjects affected / exposed	0 / 317 (0.00%)	2 / 314 (0.64%)	0 / 56 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ROAD TRAFFIC ACCIDENT			
subjects affected / exposed	1 / 317 (0.32%)	0 / 314 (0.00%)	0 / 56 (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 HAEMATOMA			
subjects affected / exposed	0 / 317 (0.00%)	0 / 314 (0.00%)	1 / 56 (1.79%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
TENDON RUPTURE			
subjects affected / exposed	1 / 317 (0.32%)	0 / 314 (0.00%)	0 / 56 (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
THORACIC VERTEBRAL FRACTURE			
subjects affected / exposed	1 / 317 (0.32%)	0 / 314 (0.00%)	0 / 56 (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
UPPER LIMB FRACTURE			

subjects affected / exposed	0 / 317 (0.00%)	0 / 314 (0.00%)	0 / 56 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
WRIST FRACTURE			
subjects affected / exposed	0 / 317 (0.00%)	1 / 314 (0.32%)	0 / 56 (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
Congenital, familial and genetic disorders			
HAEMORRHAGIC ARTERIOVENOUS MALFORMATION			
subjects affected / exposed	1 / 317 (0.32%)	0 / 314 (0.00%)	0 / 56 (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
Cardiac disorders			
ACUTE CORONARY SYNDROME			
subjects affected / exposed	1 / 317 (0.32%)	0 / 314 (0.00%)	0 / 56 (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
ANGINA PECTORIS			
subjects affected / exposed	0 / 317 (0.00%)	2 / 314 (0.64%)	0 / 56 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ACUTE MYOCARDIAL INFARCTION			
subjects affected / exposed	0 / 317 (0.00%)	2 / 314 (0.64%)	0 / 56 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ARTERIOSPASM CORONARY			
subjects affected / exposed	0 / 317 (0.00%)	0 / 314 (0.00%)	0 / 56 (0.00%)
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 / 317 (0.00%)	0 / 314 (0.00%)	0 / 56 (0.00%)
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 ARREST			
subjects affected / exposed	1 / 317 (0.32%)	0 / 314 (0.00%)	0 / 56 (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
CARDIAC FAILURE			
subjects affected / exposed	0 / 317 (0.00%)	1 / 314 (0.32%)	0 / 56 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
CARDIAC FAILURE CONGESTIVE			
subjects affected / exposed	2 / 317 (0.63%)	0 / 314 (0.00%)	0 / 56 (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
CARDIAC TAMPONADE			
subjects affected / exposed	0 / 317 (0.00%)	0 / 314 (0.00%)	1 / 56 (1.79%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CARDIO-RESPIRATORY ARREST			
subjects affected / exposed	0 / 317 (0.00%)	0 / 314 (0.00%)	0 / 56 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CARDIOVASCULAR DISORDER			
subjects affected / exposed	0 / 317 (0.00%)	1 / 314 (0.32%)	0 / 56 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
METABOLIC CARDIOMYOPATHY			
subjects affected / exposed	0 / 317 (0.00%)	0 / 314 (0.00%)	0 / 56 (0.00%)
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	2 / 317 (0.63%)	1 / 314 (0.32%)	0 / 56 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
MYOCARDIAL FIBROSIS			

subjects affected / exposed	0 / 317 (0.00%)	0 / 314 (0.00%)	0 / 56 (0.00%)
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 ISCHAEMIA			
subjects affected / exposed	0 / 317 (0.00%)	2 / 314 (0.64%)	0 / 56 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SINUS NODE DYSFUNCTION			
subjects affected / exposed	0 / 317 (0.00%)	0 / 314 (0.00%)	0 / 56 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PERICARDITIS			
subjects affected / exposed	0 / 317 (0.00%)	0 / 314 (0.00%)	1 / 56 (1.79%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SUPRAVENTRICULAR TACHYCARDIA			
subjects affected / exposed	0 / 317 (0.00%)	0 / 314 (0.00%)	0 / 56 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
TACHYCARDIA			
subjects affected / exposed	1 / 317 (0.32%)	0 / 314 (0.00%)	0 / 56 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
CAROTID ARTERIOSCLEROSIS			
subjects affected / exposed	1 / 317 (0.32%)	0 / 314 (0.00%)	0 / 56 (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
HYPOXIC-ISCHAEMIC ENCEPHALOPATHY			
subjects affected / exposed	1 / 317 (0.32%)	0 / 314 (0.00%)	0 / 56 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 0
MONOPARESIS			

subjects affected / exposed	0 / 317 (0.00%)	0 / 314 (0.00%)	0 / 56 (0.00%)
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 DISEASE			
subjects affected / exposed	1 / 317 (0.32%)	0 / 314 (0.00%)	0 / 56 (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
SCIATICA			
subjects affected / exposed	0 / 317 (0.00%)	1 / 314 (0.32%)	0 / 56 (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
SPONDYLITIC MYELOPATHY			
subjects affected / exposed	0 / 317 (0.00%)	0 / 314 (0.00%)	0 / 56 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
MYELOPATHY			
subjects affected / exposed	0 / 317 (0.00%)	0 / 314 (0.00%)	0 / 56 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
VERTEBROBASILAR INSUFFICIENCY			
subjects affected / exposed	0 / 317 (0.00%)	1 / 314 (0.32%)	0 / 56 (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
TRANSIENT ISCHAEMIC ATTACK			
subjects affected / exposed	3 / 317 (0.95%)	1 / 314 (0.32%)	1 / 56 (1.79%)
occurrences causally related to treatment / all	1 / 3	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SYNCOPE			
subjects affected / exposed	0 / 317 (0.00%)	0 / 314 (0.00%)	0 / 56 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
ANAEMIA			

subjects affected / exposed	1 / 317 (0.32%)	0 / 314 (0.00%)	0 / 56 (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
IRON DEFICIENCY ANAEMIA			
subjects affected / exposed	1 / 317 (0.32%)	0 / 314 (0.00%)	0 / 56 (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
Eye disorders			
CATARACT			
subjects affected / exposed	1 / 317 (0.32%)	1 / 314 (0.32%)	0 / 56 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CATARACT DIABETIC			
subjects affected / exposed	0 / 317 (0.00%)	0 / 314 (0.00%)	0 / 56 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
IRIDOCYCLITIS			
subjects affected / exposed	1 / 317 (0.32%)	0 / 314 (0.00%)	0 / 56 (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
MACULAR HOLE			
subjects affected / exposed	0 / 317 (0.00%)	1 / 314 (0.32%)	0 / 56 (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
VITREOUS HAEMORRHAGE			
subjects affected / exposed	0 / 317 (0.00%)	0 / 314 (0.00%)	0 / 56 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
VITREORETINAL TRACTION SYNDROME			
subjects affected / exposed	0 / 317 (0.00%)	0 / 314 (0.00%)	0 / 56 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			

ABDOMINAL PAIN			
subjects affected / exposed	0 / 317 (0.00%)	1 / 314 (0.32%)	0 / 56 (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
ABDOMINAL WALL HAEMATOMA			
subjects affected / exposed	1 / 317 (0.32%)	0 / 314 (0.00%)	0 / 56 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ANAL FISTULA			
subjects affected / exposed	1 / 317 (0.32%)	0 / 314 (0.00%)	0 / 56 (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
ASCITES			
subjects affected / exposed	0 / 317 (0.00%)	1 / 314 (0.32%)	0 / 56 (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
COLITIS			
subjects affected / exposed	1 / 317 (0.32%)	0 / 314 (0.00%)	0 / 56 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CONSTIPATION			
subjects affected / exposed	0 / 317 (0.00%)	0 / 314 (0.00%)	0 / 56 (0.00%)
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 / 317 (0.00%)	1 / 314 (0.32%)	0 / 56 (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
DIVERTICULAR PERFORATION			
subjects affected / exposed	0 / 317 (0.00%)	1 / 314 (0.32%)	0 / 56 (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
FOOD POISONING			

subjects affected / exposed	0 / 317 (0.00%)	1 / 314 (0.32%)	0 / 56 (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
GASTRIC ULCER			
subjects affected / exposed	0 / 317 (0.00%)	1 / 314 (0.32%)	0 / 56 (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
GASTRIC ULCER HAEMORRHAGE			
subjects affected / exposed	0 / 317 (0.00%)	0 / 314 (0.00%)	1 / 56 (1.79%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
GASTRIC ULCER PERFORATION			
subjects affected / exposed	0 / 317 (0.00%)	1 / 314 (0.32%)	0 / 56 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
GASTRITIS			
subjects affected / exposed	0 / 317 (0.00%)	0 / 314 (0.00%)	1 / 56 (1.79%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
GASTROINTESTINAL HAEMORRHAGE			
subjects affected / exposed	1 / 317 (0.32%)	0 / 314 (0.00%)	0 / 56 (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
GINGIVAL RECESSION			
subjects affected / exposed	0 / 317 (0.00%)	0 / 314 (0.00%)	0 / 56 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
INCARCERATED INGUINAL HERNIA			
subjects affected / exposed	0 / 317 (0.00%)	0 / 314 (0.00%)	0 / 56 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HIATUS HERNIA			

subjects affected / exposed	0 / 317 (0.00%)	0 / 314 (0.00%)	0 / 56 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
LARGE INTESTINE PERFORATION			
subjects affected / exposed	0 / 317 (0.00%)	1 / 314 (0.32%)	0 / 56 (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
INGUINAL HERNIA			
subjects affected / exposed	0 / 317 (0.00%)	1 / 314 (0.32%)	0 / 56 (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
LARGE INTESTINE POLYP			
subjects affected / exposed	0 / 317 (0.00%)	2 / 314 (0.64%)	0 / 56 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PANCREATIC DISORDER			
subjects affected / exposed	1 / 317 (0.32%)	0 / 314 (0.00%)	0 / 56 (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
PANCREATITIS			
subjects affected / exposed	0 / 317 (0.00%)	0 / 314 (0.00%)	0 / 56 (0.00%)
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 HAEMORRHAGE			
subjects affected / exposed	0 / 317 (0.00%)	0 / 314 (0.00%)	0 / 56 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SALIVARY GLAND CALCULUS			
subjects affected / exposed	0 / 317 (0.00%)	0 / 314 (0.00%)	1 / 56 (1.79%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
RECTAL POLYP			

subjects affected / exposed	0 / 317 (0.00%)	1 / 314 (0.32%)	0 / 56 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
BILE DUCT STONE			
subjects affected / exposed	0 / 317 (0.00%)	1 / 314 (0.32%)	0 / 56 (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
CHOLECYSTITIS ACUTE			
subjects affected / exposed	0 / 317 (0.00%)	1 / 314 (0.32%)	0 / 56 (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
CHOLANGITIS			
subjects affected / exposed	0 / 317 (0.00%)	0 / 314 (0.00%)	0 / 56 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CHOLELITHIASIS			
subjects affected / exposed	0 / 317 (0.00%)	4 / 314 (1.27%)	0 / 56 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
GALLBLADDER RUPTURE			
subjects affected / exposed	1 / 317 (0.32%)	0 / 314 (0.00%)	0 / 56 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
ANGIOEDEMA			
subjects affected / exposed	1 / 317 (0.32%)	0 / 314 (0.00%)	0 / 56 (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 FOOT			
subjects affected / exposed	0 / 317 (0.00%)	0 / 314 (0.00%)	0 / 56 (0.00%)
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 ERUPTION			

subjects affected / exposed	1 / 317 (0.32%)	0 / 314 (0.00%)	0 / 56 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SKIN ULCER			
subjects affected / exposed	0 / 317 (0.00%)	1 / 314 (0.32%)	0 / 56 (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			
NEPHROLITHIASIS			
subjects affected / exposed	0 / 317 (0.00%)	1 / 314 (0.32%)	0 / 56 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ACUTE KIDNEY INJURY			
subjects affected / exposed	2 / 317 (0.63%)	0 / 314 (0.00%)	0 / 56 (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
RENAL COLIC			
subjects affected / exposed	1 / 317 (0.32%)	1 / 314 (0.32%)	0 / 56 (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
RENAL CYST			
subjects affected / exposed	0 / 317 (0.00%)	1 / 314 (0.32%)	0 / 56 (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
RENAL FAILURE			
subjects affected / exposed	0 / 317 (0.00%)	1 / 314 (0.32%)	0 / 56 (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
URETEROLITHIASIS			
subjects affected / exposed	0 / 317 (0.00%)	0 / 314 (0.00%)	1 / 56 (1.79%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			

ACQUIRED CLAW TOE			
subjects affected / exposed	0 / 317 (0.00%)	1 / 314 (0.32%)	0 / 56 (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
BURSITIS			
subjects affected / exposed	0 / 317 (0.00%)	0 / 314 (0.00%)	0 / 56 (0.00%)
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	1 / 317 (0.32%)	1 / 314 (0.32%)	0 / 56 (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
LUMBAR SPINAL STENOSIS			
subjects affected / exposed	1 / 317 (0.32%)	0 / 314 (0.00%)	0 / 56 (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	1 / 317 (0.32%)	0 / 314 (0.00%)	0 / 56 (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	3 / 317 (0.95%)	3 / 314 (0.96%)	0 / 56 (0.00%)
occurrences causally related to treatment / all	0 / 4	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
OSTEONECROSIS			
subjects affected / exposed	1 / 317 (0.32%)	0 / 314 (0.00%)	1 / 56 (1.79%)
occurrences causally related to treatment / all	0 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PAIN IN EXTREMITY			
subjects affected / exposed	0 / 317 (0.00%)	0 / 314 (0.00%)	0 / 56 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PATHOLOGICAL FRACTURE			

subjects affected / exposed	1 / 317 (0.32%)	0 / 314 (0.00%)	0 / 56 (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
ROTATOR CUFF SYNDROME			
subjects affected / exposed	0 / 317 (0.00%)	0 / 314 (0.00%)	0 / 56 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SPONDYLOLISTHESIS			
subjects affected / exposed	1 / 317 (0.32%)	0 / 314 (0.00%)	0 / 56 (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
SUBCHONDRAL INSUFFICIENCY FRACTURE			
subjects affected / exposed	0 / 317 (0.00%)	0 / 314 (0.00%)	1 / 56 (1.79%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SYMPATHETIC POSTERIOR CERVICAL SYNDROME			
subjects affected / exposed	0 / 317 (0.00%)	0 / 314 (0.00%)	0 / 56 (0.00%)
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 / 317 (0.00%)	0 / 314 (0.00%)	0 / 56 (0.00%)
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			
ACTINOMYCOTIC PULMONARY INFECTION			
subjects affected / exposed	0 / 317 (0.00%)	0 / 314 (0.00%)	0 / 56 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
APPENDICITIS			
subjects affected / exposed	1 / 317 (0.32%)	0 / 314 (0.00%)	0 / 56 (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

BACTERIAL PYELONEPHRITIS			
subjects affected / exposed	0 / 317 (0.00%)	0 / 314 (0.00%)	0 / 56 (0.00%)
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	1 / 317 (0.32%)	1 / 314 (0.32%)	0 / 56 (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
BRONCHOPULMONARY ASPERGILLOSIS			
subjects affected / exposed	1 / 317 (0.32%)	0 / 314 (0.00%)	0 / 56 (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
COVID-19 PNEUMONIA			
subjects affected / exposed	2 / 317 (0.63%)	2 / 314 (0.64%)	0 / 56 (0.00%)
occurrences causally related to treatment / all	0 / 2	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	1 / 2	0 / 0
COVID-19			
subjects affected / exposed	0 / 317 (0.00%)	1 / 314 (0.32%)	1 / 56 (1.79%)
occurrences causally related to treatment / all	0 / 0	0 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CORONAVIRUS PNEUMONIA			
subjects affected / exposed	1 / 317 (0.32%)	0 / 314 (0.00%)	0 / 56 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CELLULITIS			
subjects affected / exposed	2 / 317 (0.63%)	2 / 314 (0.64%)	0 / 56 (0.00%)
occurrences causally related to treatment / all	0 / 2	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DIVERTICULITIS			
subjects affected / exposed	1 / 317 (0.32%)	2 / 314 (0.64%)	0 / 56 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
EMPYEMA			

subjects affected / exposed	1 / 317 (0.32%)	0 / 314 (0.00%)	0 / 56 (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
ENDOCARDITIS			
subjects affected / exposed	0 / 317 (0.00%)	0 / 314 (0.00%)	0 / 56 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ERYSIPELAS			
subjects affected / exposed	1 / 317 (0.32%)	0 / 314 (0.00%)	0 / 56 (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
ESCHERICHIA INFECTION			
subjects affected / exposed	1 / 317 (0.32%)	0 / 314 (0.00%)	0 / 56 (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
FEMALE GENITAL TRACT TUBERCULOSIS			
subjects affected / exposed	1 / 317 (0.32%)	0 / 314 (0.00%)	0 / 56 (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
GALLBLADDER ABSCESS			
subjects affected / exposed	0 / 317 (0.00%)	0 / 314 (0.00%)	0 / 56 (0.00%)
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 / 317 (0.00%)	1 / 314 (0.32%)	0 / 56 (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
HERPES ZOSTER DISSEMINATED			
subjects affected / exposed	0 / 317 (0.00%)	1 / 314 (0.32%)	0 / 56 (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
GENITAL HERPES SIMPLEX			

subjects affected / exposed	1 / 317 (0.32%)	0 / 314 (0.00%)	0 / 56 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HERPES ZOSTER			
subjects affected / exposed	0 / 317 (0.00%)	3 / 314 (0.96%)	0 / 56 (0.00%)
occurrences causally related to treatment / all	0 / 0	3 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HERPES ZOSTER MENINGITIS			
subjects affected / exposed	0 / 317 (0.00%)	0 / 314 (0.00%)	0 / 56 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
INFECTIVE SPONDYLITIS			
subjects affected / exposed	1 / 317 (0.32%)	0 / 314 (0.00%)	0 / 56 (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
INFLUENZA			
subjects affected / exposed	0 / 317 (0.00%)	2 / 314 (0.64%)	0 / 56 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
KERATITIS BACTERIAL			
subjects affected / exposed	0 / 317 (0.00%)	0 / 314 (0.00%)	1 / 56 (1.79%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
LUNG ABSCESS			
subjects affected / exposed	0 / 317 (0.00%)	0 / 314 (0.00%)	0 / 56 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
NECROTISING FASCIITIS			
subjects affected / exposed	0 / 317 (0.00%)	0 / 314 (0.00%)	0 / 56 (0.00%)
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 BACTERIAL			

subjects affected / exposed	0 / 317 (0.00%)	0 / 314 (0.00%)	0 / 56 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
OPHTHALMIC HERPES ZOSTER			
subjects affected / exposed	1 / 317 (0.32%)	1 / 314 (0.32%)	0 / 56 (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
PERITONEAL TUBERCULOSIS			
subjects affected / exposed	1 / 317 (0.32%)	0 / 314 (0.00%)	0 / 56 (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
OSTEOMYELITIS			
subjects affected / exposed	0 / 317 (0.00%)	0 / 314 (0.00%)	0 / 56 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PARAINFLUENZAE VIRUS INFECTION			
subjects affected / exposed	1 / 317 (0.32%)	0 / 314 (0.00%)	0 / 56 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PERITONITIS			
subjects affected / exposed	0 / 317 (0.00%)	1 / 314 (0.32%)	0 / 56 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
PNEUMONIA			
subjects affected / exposed	8 / 317 (2.52%)	5 / 314 (1.59%)	1 / 56 (1.79%)
occurrences causally related to treatment / all	7 / 8	3 / 5	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PNEUMONIA BACTERIAL			
subjects affected / exposed	1 / 317 (0.32%)	0 / 314 (0.00%)	0 / 56 (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
PNEUMONIA CRYPTOCOCCAL			

subjects affected / exposed	1 / 317 (0.32%)	0 / 314 (0.00%)	0 / 56 (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
PNEUMONIA ESCHERICHIA			
subjects affected / exposed	1 / 317 (0.32%)	0 / 314 (0.00%)	0 / 56 (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
PNEUMONIA KLEBSIELLA			
subjects affected / exposed	0 / 317 (0.00%)	1 / 314 (0.32%)	0 / 56 (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
PROSTATITIS ESCHERICHIA COLI			
subjects affected / exposed	0 / 317 (0.00%)	0 / 314 (0.00%)	0 / 56 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PNEUMONIA PNEUMOCOCCAL			
subjects affected / exposed	0 / 317 (0.00%)	0 / 314 (0.00%)	1 / 56 (1.79%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PYELONEPHRITIS ACUTE			
subjects affected / exposed	0 / 317 (0.00%)	0 / 314 (0.00%)	2 / 56 (3.57%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PYELONEPHRITIS			
subjects affected / exposed	0 / 317 (0.00%)	1 / 314 (0.32%)	0 / 56 (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
PYELONEPHRITIS CHRONIC			
subjects affected / exposed	0 / 317 (0.00%)	1 / 314 (0.32%)	0 / 56 (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 VIRAL			

subjects affected / exposed	1 / 317 (0.32%)	0 / 314 (0.00%)	0 / 56 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SEPSIS			
subjects affected / exposed	2 / 317 (0.63%)	0 / 314 (0.00%)	1 / 56 (1.79%)
occurrences causally related to treatment / all	1 / 2	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Q FEVER			
subjects affected / exposed	0 / 317 (0.00%)	1 / 314 (0.32%)	0 / 56 (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
STAPHYLOCOCCAL INFECTION			
subjects affected / exposed	1 / 317 (0.32%)	0 / 314 (0.00%)	0 / 56 (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
SEPTIC SHOCK			
subjects affected / exposed	0 / 317 (0.00%)	1 / 314 (0.32%)	1 / 56 (1.79%)
occurrences causally related to treatment / all	0 / 0	0 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
SINOBRONCHITIS			
subjects affected / exposed	0 / 317 (0.00%)	1 / 314 (0.32%)	0 / 56 (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
TOOTH ABSCESS			
subjects affected / exposed	0 / 317 (0.00%)	0 / 314 (0.00%)	0 / 56 (0.00%)
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 / 317 (0.00%)	0 / 314 (0.00%)	0 / 56 (0.00%)
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 / 317 (0.00%)	1 / 314 (0.32%)	0 / 56 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
URINARY TRACT INFECTION			
subjects affected / exposed	0 / 317 (0.00%)	1 / 314 (0.32%)	0 / 56 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
ABNORMAL WEIGHT GAIN			
subjects affected / exposed	2 / 317 (0.63%)	2 / 314 (0.64%)	0 / 56 (0.00%)
occurrences causally related to treatment / all	2 / 2	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CENTRAL OBESITY			
subjects affected / exposed	0 / 317 (0.00%)	0 / 314 (0.00%)	0 / 56 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DEHYDRATION			
subjects affected / exposed	1 / 317 (0.32%)	0 / 314 (0.00%)	0 / 56 (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	1 / 317 (0.32%)	0 / 314 (0.00%)	0 / 56 (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
HYPOKALAEMIA			
subjects affected / exposed	0 / 317 (0.00%)	0 / 314 (0.00%)	0 / 56 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
OBESITY			
subjects affected / exposed	0 / 317 (0.00%)	0 / 314 (0.00%)	0 / 56 (0.00%)
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	Weeks 1-260: Any	Weeks 1-	After Switch:

	Upadacitinib 15 mg	260/Switch: Any Upadacitinib 30 mg	Upadacitinib 15 mg Monotherapy
Total subjects affected by serious adverse events			
subjects affected / exposed	88 / 335 (26.27%)	79 / 332 (23.80%)	28 / 181 (15.47%)
number of deaths (all causes)	6	10	5
number of deaths resulting from adverse events	1	1	2
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
ADENOCARCINOMA GASTRIC			
subjects affected / exposed	0 / 335 (0.00%)	0 / 332 (0.00%)	1 / 181 (0.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 1
ADENOCARCINOMA OF COLON			
subjects affected / exposed	0 / 335 (0.00%)	0 / 332 (0.00%)	0 / 181 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ADENOCARCINOMA METASTATIC			
subjects affected / exposed	0 / 335 (0.00%)	0 / 332 (0.00%)	1 / 181 (0.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ANGIOFIBROMA			
subjects affected / exposed	0 / 335 (0.00%)	0 / 332 (0.00%)	1 / 181 (0.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
B-CELL LYMPHOMA			
subjects affected / exposed	0 / 335 (0.00%)	1 / 332 (0.30%)	0 / 181 (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
BASAL CELL CARCINOMA			
subjects affected / exposed	1 / 335 (0.30%)	1 / 332 (0.30%)	0 / 181 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BENIGN OVARIAN TUMOUR			
subjects affected / exposed	0 / 335 (0.00%)	1 / 332 (0.30%)	0 / 181 (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

BLADDER CANCER			
subjects affected / exposed	0 / 335 (0.00%)	1 / 332 (0.30%)	0 / 181 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
BLADDER NEOPLASM			
subjects affected / exposed	0 / 335 (0.00%)	0 / 332 (0.00%)	0 / 181 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BOWEN'S DISEASE			
subjects affected / exposed	0 / 335 (0.00%)	1 / 332 (0.30%)	0 / 181 (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
BREAST CANCER METASTATIC			
subjects affected / exposed	0 / 335 (0.00%)	1 / 332 (0.30%)	0 / 181 (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
CERVIX CARCINOMA STAGE 0			
subjects affected / exposed	0 / 335 (0.00%)	1 / 332 (0.30%)	0 / 181 (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
BREAST CANCER			
subjects affected / exposed	1 / 335 (0.30%)	0 / 332 (0.00%)	0 / 181 (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
ENDOMETRIAL ADENOCARCINOMA			
subjects affected / exposed	0 / 335 (0.00%)	0 / 332 (0.00%)	0 / 181 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
FIBROMA			
subjects affected / exposed	0 / 335 (0.00%)	0 / 332 (0.00%)	0 / 181 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
GASTRIC CANCER			

subjects affected / exposed	0 / 335 (0.00%)	1 / 332 (0.30%)	0 / 181 (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
LUNG ADENOCARCINOMA			
subjects affected / exposed	0 / 335 (0.00%)	0 / 332 (0.00%)	0 / 181 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
LIPOMA			
subjects affected / exposed	0 / 335 (0.00%)	0 / 332 (0.00%)	1 / 181 (0.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
LEIOMYOMA			
subjects affected / exposed	0 / 335 (0.00%)	0 / 332 (0.00%)	0 / 181 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
LUNG SQUAMOUS CELL CARCINOMA METASTATIC			
subjects affected / exposed	0 / 335 (0.00%)	1 / 332 (0.30%)	0 / 181 (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
MALIGNANT PALATE NEOPLASM			
subjects affected / exposed	1 / 335 (0.30%)	0 / 332 (0.00%)	0 / 181 (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
MALIGNANT MELANOMA			
subjects affected / exposed	1 / 335 (0.30%)	0 / 332 (0.00%)	0 / 181 (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
METASTATIC NEOPLASM			
subjects affected / exposed	0 / 335 (0.00%)	0 / 332 (0.00%)	0 / 181 (0.00%)
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 TUMOUR			

subjects affected / exposed	1 / 335 (0.30%)	0 / 332 (0.00%)	0 / 181 (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
METASTASES TO BONE			
subjects affected / exposed	0 / 335 (0.00%)	0 / 332 (0.00%)	1 / 181 (0.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
NON-SMALL CELL LUNG CANCER METASTATIC			
subjects affected / exposed	0 / 335 (0.00%)	0 / 332 (0.00%)	0 / 181 (0.00%)
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 GERM CELL TERATOMA			
subjects affected / exposed	0 / 335 (0.00%)	1 / 332 (0.30%)	0 / 181 (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
OVARIAN CANCER			
subjects affected / exposed	0 / 335 (0.00%)	0 / 332 (0.00%)	0 / 181 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PAPILLARY THYROID CANCER			
subjects affected / exposed	1 / 335 (0.30%)	0 / 332 (0.00%)	0 / 181 (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	0 / 335 (0.00%)	0 / 332 (0.00%)	0 / 181 (0.00%)
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 CANCER			
subjects affected / exposed	0 / 335 (0.00%)	1 / 332 (0.30%)	0 / 181 (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 CELL CARCINOMA STAGE I			

subjects affected / exposed	0 / 335 (0.00%)	0 / 332 (0.00%)	0 / 181 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SEBACEOUS CARCINOMA			
subjects affected / exposed	1 / 335 (0.30%)	0 / 332 (0.00%)	0 / 181 (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
SQUAMOUS CELL CARCINOMA OF LUNG			
subjects affected / exposed	1 / 335 (0.30%)	0 / 332 (0.00%)	0 / 181 (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
SQUAMOUS CELL CARCINOMA OF SKIN			
subjects affected / exposed	0 / 335 (0.00%)	1 / 332 (0.30%)	0 / 181 (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
SQUAMOUS CELL CARCINOMA OF THE TONGUE			
subjects affected / exposed	0 / 335 (0.00%)	0 / 332 (0.00%)	1 / 181 (0.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
TONGUE NEOPLASM MALIGNANT STAGE UNSPECIFIED			
subjects affected / exposed	0 / 335 (0.00%)	0 / 332 (0.00%)	0 / 181 (0.00%)
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 CANCER			
subjects affected / exposed	0 / 335 (0.00%)	1 / 332 (0.30%)	0 / 181 (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
UTERINE CARCINOMA IN SITU			
subjects affected / exposed	1 / 335 (0.30%)	0 / 332 (0.00%)	0 / 181 (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

Vascular disorders			
DEEP VEIN THROMBOSIS			
subjects affected / exposed	0 / 335 (0.00%)	1 / 332 (0.30%)	1 / 181 (0.55%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
EMBOLISM ARTERIAL			
subjects affected / exposed	0 / 335 (0.00%)	1 / 332 (0.30%)	0 / 181 (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
HYPERTENSION			
subjects affected / exposed	0 / 335 (0.00%)	0 / 332 (0.00%)	0 / 181 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PERIPHERAL ARTERIAL OCCLUSIVE DISEASE			
subjects affected / exposed	0 / 335 (0.00%)	1 / 332 (0.30%)	0 / 181 (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
PERIPHERAL ARTERY STENOSIS			
subjects affected / exposed	0 / 335 (0.00%)	0 / 332 (0.00%)	0 / 181 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PERIPHERAL ISCHAEMIA			
subjects affected / exposed	0 / 335 (0.00%)	0 / 332 (0.00%)	0 / 181 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SHOCK HAEMORRHAGIC			
subjects affected / exposed	1 / 335 (0.30%)	0 / 332 (0.00%)	0 / 181 (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
Pregnancy, puerperium and perinatal conditions			
ABORTION SPONTANEOUS			

subjects affected / exposed	0 / 335 (0.00%)	1 / 332 (0.30%)	0 / 181 (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			
CHEST DISCOMFORT			
subjects affected / exposed	0 / 335 (0.00%)	0 / 332 (0.00%)	1 / 181 (0.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CHEST PAIN			
subjects affected / exposed	2 / 335 (0.60%)	0 / 332 (0.00%)	0 / 181 (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
DEATH			
subjects affected / exposed	1 / 335 (0.30%)	0 / 332 (0.00%)	0 / 181 (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
MULTIPLE ORGAN DYSFUNCTION SYNDROME			
subjects affected / exposed	1 / 335 (0.30%)	0 / 332 (0.00%)	0 / 181 (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
SUDDEN DEATH			
subjects affected / exposed	0 / 335 (0.00%)	1 / 332 (0.30%)	0 / 181 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Reproductive system and breast disorders			
BENIGN PROSTATIC HYPERPLASIA			
subjects affected / exposed	1 / 335 (0.30%)	0 / 332 (0.00%)	0 / 181 (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
BREAST HYPOPLASIA			

subjects affected / exposed	0 / 335 (0.00%)	1 / 332 (0.30%)	0 / 181 (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
CERVIX HAEMORRHAGE UTERINE			
subjects affected / exposed	1 / 335 (0.30%)	0 / 332 (0.00%)	0 / 181 (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
CERVICAL DYSPLASIA			
subjects affected / exposed	2 / 335 (0.60%)	0 / 332 (0.00%)	0 / 181 (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
ENDOMETRIAL HYPERPLASIA			
subjects affected / exposed	0 / 335 (0.00%)	0 / 332 (0.00%)	0 / 181 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
MENOMETRORRHAGIA			
subjects affected / exposed	0 / 335 (0.00%)	0 / 332 (0.00%)	0 / 181 (0.00%)
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 CYST			
subjects affected / exposed	1 / 335 (0.30%)	0 / 332 (0.00%)	0 / 181 (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
PROSTATITIS			
subjects affected / exposed	0 / 335 (0.00%)	1 / 332 (0.30%)	0 / 181 (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
OVARIAN CYST RUPTURED			
subjects affected / exposed	0 / 335 (0.00%)	1 / 332 (0.30%)	0 / 181 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
ACUTE RESPIRATORY FAILURE			

subjects affected / exposed	0 / 335 (0.00%)	2 / 332 (0.60%)	0 / 181 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
ASTHMATIC CRISIS			
subjects affected / exposed	0 / 335 (0.00%)	1 / 332 (0.30%)	0 / 181 (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
ASTHMA			
subjects affected / exposed	1 / 335 (0.30%)	1 / 332 (0.30%)	1 / 181 (0.55%)
occurrences causally related to treatment / all	1 / 1	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CHRONIC OBSTRUCTIVE PULMONARY DISEASE			
subjects affected / exposed	1 / 335 (0.30%)	2 / 332 (0.60%)	1 / 181 (0.55%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PLEURAL EFFUSION			
subjects affected / exposed	0 / 335 (0.00%)	0 / 332 (0.00%)	1 / 181 (0.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PLEURISY			
subjects affected / exposed	0 / 335 (0.00%)	0 / 332 (0.00%)	0 / 181 (0.00%)
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 / 335 (0.00%)	1 / 332 (0.30%)	1 / 181 (0.55%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PNEUMOTHORAX SPONTANEOUS			
subjects affected / exposed	1 / 335 (0.30%)	0 / 332 (0.00%)	0 / 181 (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
PULMONARY EMBOLISM			

subjects affected / exposed	2 / 335 (0.60%)	3 / 332 (0.90%)	0 / 181 (0.00%)
occurrences causally related to treatment / all	2 / 2	1 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PULMONARY FIBROSIS			
subjects affected / exposed	1 / 335 (0.30%)	0 / 332 (0.00%)	0 / 181 (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
RESPIRATORY FAILURE			
subjects affected / exposed	0 / 335 (0.00%)	1 / 332 (0.30%)	0 / 181 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
DEPRESSION			
subjects affected / exposed	0 / 335 (0.00%)	1 / 332 (0.30%)	0 / 181 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
MENTAL DISORDER DUE TO A GENERAL MEDICAL CONDITION			
subjects affected / exposed	0 / 335 (0.00%)	1 / 332 (0.30%)	0 / 181 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
BLOOD CREATINE PHOSPHOKINASE INCREASED			
subjects affected / exposed	1 / 335 (0.30%)	1 / 332 (0.30%)	0 / 181 (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
HEPATIC ENZYME INCREASED			
subjects affected / exposed	1 / 335 (0.30%)	0 / 332 (0.00%)	0 / 181 (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
TRANSAMINASES INCREASED			
subjects affected / exposed	1 / 335 (0.30%)	0 / 332 (0.00%)	0 / 181 (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

WHITE BLOOD CELL COUNT INCREASED			
subjects affected / exposed	1 / 335 (0.30%)	0 / 332 (0.00%)	0 / 181 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
ANKLE FRACTURE			
subjects affected / exposed	1 / 335 (0.30%)	0 / 332 (0.00%)	0 / 181 (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
CONTUSION			
subjects affected / exposed	0 / 335 (0.00%)	0 / 332 (0.00%)	0 / 181 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CORNEAL LACERATION			
subjects affected / exposed	1 / 335 (0.30%)	0 / 332 (0.00%)	0 / 181 (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
CONCUSSION			
subjects affected / exposed	0 / 335 (0.00%)	0 / 332 (0.00%)	0 / 181 (0.00%)
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 / 335 (0.00%)	0 / 332 (0.00%)	1 / 181 (0.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
FEMUR FRACTURE			
subjects affected / exposed	2 / 335 (0.60%)	0 / 332 (0.00%)	0 / 181 (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
FOOT FRACTURE			
subjects affected / exposed	0 / 335 (0.00%)	0 / 332 (0.00%)	0 / 181 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

HIP FRACTURE			
subjects affected / exposed	0 / 335 (0.00%)	1 / 332 (0.30%)	1 / 181 (0.55%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HUMERUS FRACTURE			
subjects affected / exposed	0 / 335 (0.00%)	1 / 332 (0.30%)	0 / 181 (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
JOINT DISLOCATION			
subjects affected / exposed	0 / 335 (0.00%)	0 / 332 (0.00%)	0 / 181 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
LIMB CRUSHING INJURY			
subjects affected / exposed	0 / 335 (0.00%)	1 / 332 (0.30%)	0 / 181 (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
LOWER LIMB FRACTURE			
subjects affected / exposed	0 / 335 (0.00%)	1 / 332 (0.30%)	0 / 181 (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
MENISCUS INJURY			
subjects affected / exposed	0 / 335 (0.00%)	0 / 332 (0.00%)	1 / 181 (0.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PATELLA FRACTURE			
subjects affected / exposed	0 / 335 (0.00%)	0 / 332 (0.00%)	0 / 181 (0.00%)
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 LUMBAR PUNCTURE SYNDROME			
subjects affected / exposed	1 / 335 (0.30%)	0 / 332 (0.00%)	0 / 181 (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
POST PROCEDURAL FISTULA			

subjects affected / exposed	0 / 335 (0.00%)	0 / 332 (0.00%)	0 / 181 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
RADIUS FRACTURE			
subjects affected / exposed	0 / 335 (0.00%)	2 / 332 (0.60%)	0 / 181 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ROAD TRAFFIC ACCIDENT			
subjects affected / exposed	1 / 335 (0.30%)	0 / 332 (0.00%)	0 / 181 (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 HAEMATOMA			
subjects affected / exposed	0 / 335 (0.00%)	0 / 332 (0.00%)	0 / 181 (0.00%)
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 / 335 (0.30%)	0 / 332 (0.00%)	0 / 181 (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
THORACIC VERTEBRAL FRACTURE			
subjects affected / exposed	1 / 335 (0.30%)	0 / 332 (0.00%)	0 / 181 (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
UPPER LIMB FRACTURE			
subjects affected / exposed	1 / 335 (0.30%)	0 / 332 (0.00%)	0 / 181 (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
WRIST FRACTURE			
subjects affected / exposed	0 / 335 (0.00%)	1 / 332 (0.30%)	0 / 181 (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
Congenital, familial and genetic disorders			
HAEMORRHAGIC ARTERIOVENOUS MALFORMATION			

subjects affected / exposed	1 / 335 (0.30%)	0 / 332 (0.00%)	0 / 181 (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
Cardiac disorders			
ACUTE CORONARY SYNDROME			
subjects affected / exposed	1 / 335 (0.30%)	0 / 332 (0.00%)	0 / 181 (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
ANGINA PECTORIS			
subjects affected / exposed	0 / 335 (0.00%)	2 / 332 (0.60%)	0 / 181 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ACUTE MYOCARDIAL INFARCTION			
subjects affected / exposed	0 / 335 (0.00%)	2 / 332 (0.60%)	1 / 181 (0.55%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ARTERIOSPASM CORONARY			
subjects affected / exposed	0 / 335 (0.00%)	0 / 332 (0.00%)	0 / 181 (0.00%)
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 / 335 (0.00%)	0 / 332 (0.00%)	1 / 181 (0.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CARDIAC ARREST			
subjects affected / exposed	1 / 335 (0.30%)	0 / 332 (0.00%)	0 / 181 (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
CARDIAC FAILURE			
subjects affected / exposed	0 / 335 (0.00%)	1 / 332 (0.30%)	1 / 181 (0.55%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
CARDIAC FAILURE CONGESTIVE			

subjects affected / exposed	2 / 335 (0.60%)	0 / 332 (0.00%)	0 / 181 (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
CARDIAC TAMPONADE			
subjects affected / exposed	0 / 335 (0.00%)	0 / 332 (0.00%)	0 / 181 (0.00%)
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	0 / 335 (0.00%)	0 / 332 (0.00%)	1 / 181 (0.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
CARDIOVASCULAR DISORDER			
subjects affected / exposed	0 / 335 (0.00%)	1 / 332 (0.30%)	0 / 181 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
METABOLIC CARDIOMYOPATHY			
subjects affected / exposed	0 / 335 (0.00%)	0 / 332 (0.00%)	1 / 181 (0.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
MYOCARDIAL INFARCTION			
subjects affected / exposed	2 / 335 (0.60%)	1 / 332 (0.30%)	0 / 181 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
MYOCARDIAL FIBROSIS			
subjects affected / exposed	0 / 335 (0.00%)	0 / 332 (0.00%)	1 / 181 (0.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
MYOCARDIAL ISCHAEMIA			
subjects affected / exposed	0 / 335 (0.00%)	2 / 332 (0.60%)	0 / 181 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SINUS NODE DYSFUNCTION			

subjects affected / exposed	0 / 335 (0.00%)	0 / 332 (0.00%)	0 / 181 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PERICARDITIS			
subjects affected / exposed	0 / 335 (0.00%)	0 / 332 (0.00%)	0 / 181 (0.00%)
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 / 335 (0.00%)	0 / 332 (0.00%)	1 / 181 (0.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
TACHYCARDIA			
subjects affected / exposed	1 / 335 (0.30%)	0 / 332 (0.00%)	0 / 181 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
CAROTID ARTERIOSCLEROSIS			
subjects affected / exposed	1 / 335 (0.30%)	0 / 332 (0.00%)	0 / 181 (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
HYPOXIC-ISCHAEMIC ENCEPHALOPATHY			
subjects affected / exposed	1 / 335 (0.30%)	0 / 332 (0.00%)	0 / 181 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 0
MONOPARESIS			
subjects affected / exposed	0 / 335 (0.00%)	0 / 332 (0.00%)	0 / 181 (0.00%)
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 DISEASE			
subjects affected / exposed	1 / 335 (0.30%)	0 / 332 (0.00%)	0 / 181 (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
SCIATICA			

subjects affected / exposed	0 / 335 (0.00%)	1 / 332 (0.30%)	0 / 181 (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
SPONDYLITIC MYELOPATHY			
subjects affected / exposed	1 / 335 (0.30%)	0 / 332 (0.00%)	0 / 181 (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
MYELOPATHY			
subjects affected / exposed	0 / 335 (0.00%)	1 / 332 (0.30%)	0 / 181 (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
VERTEBROBASILAR INSUFFICIENCY			
subjects affected / exposed	0 / 335 (0.00%)	1 / 332 (0.30%)	0 / 181 (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
TRANSIENT ISCHAEMIC ATTACK			
subjects affected / exposed	3 / 335 (0.90%)	1 / 332 (0.30%)	0 / 181 (0.00%)
occurrences causally related to treatment / all	1 / 3	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SYNCOPE			
subjects affected / exposed	1 / 335 (0.30%)	0 / 332 (0.00%)	0 / 181 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
ANAEMIA			
subjects affected / exposed	1 / 335 (0.30%)	1 / 332 (0.30%)	0 / 181 (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
IRON DEFICIENCY ANAEMIA			
subjects affected / exposed	1 / 335 (0.30%)	0 / 332 (0.00%)	0 / 181 (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
Eye disorders			

CATARACT			
subjects affected / exposed	1 / 335 (0.30%)	1 / 332 (0.30%)	0 / 181 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CATARACT DIABETIC			
subjects affected / exposed	0 / 335 (0.00%)	0 / 332 (0.00%)	0 / 181 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
IRIDOCYCLITIS			
subjects affected / exposed	1 / 335 (0.30%)	0 / 332 (0.00%)	0 / 181 (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
MACULAR HOLE			
subjects affected / exposed	0 / 335 (0.00%)	1 / 332 (0.30%)	0 / 181 (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
VITREOUS HAEMORRHAGE			
subjects affected / exposed	0 / 335 (0.00%)	0 / 332 (0.00%)	0 / 181 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
VITREORETINAL TRACTION SYNDROME			
subjects affected / exposed	0 / 335 (0.00%)	0 / 332 (0.00%)	1 / 181 (0.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
ABDOMINAL PAIN			
subjects affected / exposed	1 / 335 (0.30%)	1 / 332 (0.30%)	0 / 181 (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
ABDOMINAL WALL HAEMATOMA			
subjects affected / exposed	1 / 335 (0.30%)	0 / 332 (0.00%)	0 / 181 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

ANAL FISTULA			
subjects affected / exposed	1 / 335 (0.30%)	0 / 332 (0.00%)	0 / 181 (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
ASCITES			
subjects affected / exposed	0 / 335 (0.00%)	1 / 332 (0.30%)	0 / 181 (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
COLITIS			
subjects affected / exposed	1 / 335 (0.30%)	0 / 332 (0.00%)	0 / 181 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CONSTIPATION			
subjects affected / exposed	1 / 335 (0.30%)	0 / 332 (0.00%)	0 / 181 (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
DUODENAL ULCER			
subjects affected / exposed	0 / 335 (0.00%)	1 / 332 (0.30%)	0 / 181 (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
DIVERTICULAR PERFORATION			
subjects affected / exposed	0 / 335 (0.00%)	1 / 332 (0.30%)	0 / 181 (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
FOOD POISONING			
subjects affected / exposed	0 / 335 (0.00%)	1 / 332 (0.30%)	0 / 181 (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
GASTRIC ULCER			
subjects affected / exposed	0 / 335 (0.00%)	1 / 332 (0.30%)	0 / 181 (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
GASTRIC ULCER HAEMORRHAGE			

subjects affected / exposed	0 / 335 (0.00%)	0 / 332 (0.00%)	0 / 181 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
GASTRIC ULCER PERFORATION			
subjects affected / exposed	0 / 335 (0.00%)	1 / 332 (0.30%)	0 / 181 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
GASTRITIS			
subjects affected / exposed	0 / 335 (0.00%)	0 / 332 (0.00%)	0 / 181 (0.00%)
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 HAEMORRHAGE			
subjects affected / exposed	1 / 335 (0.30%)	0 / 332 (0.00%)	0 / 181 (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
GINGIVAL RECESSION			
subjects affected / exposed	0 / 335 (0.00%)	0 / 332 (0.00%)	0 / 181 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
INCARCERATED INGUINAL HERNIA			
subjects affected / exposed	0 / 335 (0.00%)	1 / 332 (0.30%)	0 / 181 (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
HIATUS HERNIA			
subjects affected / exposed	1 / 335 (0.30%)	0 / 332 (0.00%)	0 / 181 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
LARGE INTESTINE PERFORATION			
subjects affected / exposed	0 / 335 (0.00%)	1 / 332 (0.30%)	0 / 181 (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
INGUINAL HERNIA			

subjects affected / exposed	0 / 335 (0.00%)	1 / 332 (0.30%)	1 / 181 (0.55%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
LARGE INTESTINE POLYP			
subjects affected / exposed	0 / 335 (0.00%)	2 / 332 (0.60%)	0 / 181 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PANCREATIC DISORDER			
subjects affected / exposed	1 / 335 (0.30%)	0 / 332 (0.00%)	0 / 181 (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
PANCREATITIS			
subjects affected / exposed	0 / 335 (0.00%)	0 / 332 (0.00%)	1 / 181 (0.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
RECTAL HAEMORRHAGE			
subjects affected / exposed	0 / 335 (0.00%)	0 / 332 (0.00%)	1 / 181 (0.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SALIVARY GLAND CALCULUS			
subjects affected / exposed	0 / 335 (0.00%)	0 / 332 (0.00%)	0 / 181 (0.00%)
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 POLYP			
subjects affected / exposed	0 / 335 (0.00%)	1 / 332 (0.30%)	0 / 181 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
BILE DUCT STONE			
subjects affected / exposed	0 / 335 (0.00%)	1 / 332 (0.30%)	0 / 181 (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
CHOLECYSTITIS ACUTE			

subjects affected / exposed	0 / 335 (0.00%)	1 / 332 (0.30%)	0 / 181 (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
CHOLANGITIS			
subjects affected / exposed	0 / 335 (0.00%)	0 / 332 (0.00%)	0 / 181 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CHOLELITHIASIS			
subjects affected / exposed	0 / 335 (0.00%)	4 / 332 (1.20%)	0 / 181 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
GALLBLADDER RUPTURE			
subjects affected / exposed	1 / 335 (0.30%)	0 / 332 (0.00%)	0 / 181 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
ANGIOEDEMA			
subjects affected / exposed	1 / 335 (0.30%)	0 / 332 (0.00%)	0 / 181 (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 FOOT			
subjects affected / exposed	0 / 335 (0.00%)	0 / 332 (0.00%)	0 / 181 (0.00%)
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 ERUPTION			
subjects affected / exposed	1 / 335 (0.30%)	0 / 332 (0.00%)	0 / 181 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SKIN ULCER			
subjects affected / exposed	0 / 335 (0.00%)	1 / 332 (0.30%)	0 / 181 (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			

NEPHROLITHIASIS			
subjects affected / exposed	0 / 335 (0.00%)	1 / 332 (0.30%)	0 / 181 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ACUTE KIDNEY INJURY			
subjects affected / exposed	2 / 335 (0.60%)	0 / 332 (0.00%)	0 / 181 (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
RENAL COLIC			
subjects affected / exposed	1 / 335 (0.30%)	1 / 332 (0.30%)	0 / 181 (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
RENAL CYST			
subjects affected / exposed	0 / 335 (0.00%)	1 / 332 (0.30%)	0 / 181 (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
RENAL FAILURE			
subjects affected / exposed	0 / 335 (0.00%)	1 / 332 (0.30%)	0 / 181 (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
URETEROLITHIASIS			
subjects affected / exposed	0 / 335 (0.00%)	0 / 332 (0.00%)	0 / 181 (0.00%)
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			
ACQUIRED CLAW TOE			
subjects affected / exposed	0 / 335 (0.00%)	1 / 332 (0.30%)	0 / 181 (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
BURSITIS			
subjects affected / exposed	0 / 335 (0.00%)	0 / 332 (0.00%)	0 / 181 (0.00%)
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	1 / 335 (0.30%)	2 / 332 (0.60%)	0 / 181 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
LUMBAR SPINAL STENOSIS			
subjects affected / exposed	2 / 335 (0.60%)	0 / 332 (0.00%)	1 / 181 (0.55%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
NECK PAIN			
subjects affected / exposed	1 / 335 (0.30%)	0 / 332 (0.00%)	0 / 181 (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	4 / 335 (1.19%)	3 / 332 (0.90%)	0 / 181 (0.00%)
occurrences causally related to treatment / all	0 / 5	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
OSTEONECROSIS			
subjects affected / exposed	1 / 335 (0.30%)	0 / 332 (0.00%)	1 / 181 (0.55%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PAIN IN EXTREMITY			
subjects affected / exposed	0 / 335 (0.00%)	1 / 332 (0.30%)	0 / 181 (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
PATHOLOGICAL FRACTURE			
subjects affected / exposed	1 / 335 (0.30%)	0 / 332 (0.00%)	0 / 181 (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
ROTATOR CUFF SYNDROME			
subjects affected / exposed	1 / 335 (0.30%)	0 / 332 (0.00%)	0 / 181 (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
SPONDYLOLISTHESIS			

subjects affected / exposed	1 / 335 (0.30%)	0 / 332 (0.00%)	0 / 181 (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
SUBCHONDRAL INSUFFICIENCY FRACTURE			
subjects affected / exposed	0 / 335 (0.00%)	0 / 332 (0.00%)	0 / 181 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SYMPATHETIC POSTERIOR CERVICAL SYNDROME			
subjects affected / exposed	0 / 335 (0.00%)	0 / 332 (0.00%)	0 / 181 (0.00%)
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 / 335 (0.30%)	0 / 332 (0.00%)	0 / 181 (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
Infections and infestations			
ACTINOMYCOTIC PULMONARY INFECTION			
subjects affected / exposed	1 / 335 (0.30%)	0 / 332 (0.00%)	0 / 181 (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
APPENDICITIS			
subjects affected / exposed	1 / 335 (0.30%)	0 / 332 (0.00%)	0 / 181 (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
BACTERIAL PYELONEPHRITIS			
subjects affected / exposed	0 / 335 (0.00%)	0 / 332 (0.00%)	0 / 181 (0.00%)
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	1 / 335 (0.30%)	1 / 332 (0.30%)	0 / 181 (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

BRONCHOPULMONARY ASPERGILLOSIS			
subjects affected / exposed	1 / 335 (0.30%)	0 / 332 (0.00%)	0 / 181 (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
COVID-19 PNEUMONIA			
subjects affected / exposed	3 / 335 (0.90%)	2 / 332 (0.60%)	8 / 181 (4.42%)
occurrences causally related to treatment / all	0 / 3	1 / 2	2 / 8
deaths causally related to treatment / all	0 / 0	1 / 2	1 / 2
COVID-19			
subjects affected / exposed	2 / 335 (0.60%)	1 / 332 (0.30%)	2 / 181 (1.10%)
occurrences causally related to treatment / all	0 / 3	0 / 1	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CORONAVIRUS PNEUMONIA			
subjects affected / exposed	1 / 335 (0.30%)	0 / 332 (0.00%)	0 / 181 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CELLULITIS			
subjects affected / exposed	2 / 335 (0.60%)	2 / 332 (0.60%)	0 / 181 (0.00%)
occurrences causally related to treatment / all	0 / 2	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DIVERTICULITIS			
subjects affected / exposed	1 / 335 (0.30%)	2 / 332 (0.60%)	0 / 181 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
EMPYEMA			
subjects affected / exposed	1 / 335 (0.30%)	0 / 332 (0.00%)	0 / 181 (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
ENDOCARDITIS			
subjects affected / exposed	0 / 335 (0.00%)	0 / 332 (0.00%)	0 / 181 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ERYSIPELAS			

subjects affected / exposed	1 / 335 (0.30%)	0 / 332 (0.00%)	0 / 181 (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
ESCHERICHIA INFECTION			
subjects affected / exposed	1 / 335 (0.30%)	0 / 332 (0.00%)	0 / 181 (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
FEMALE GENITAL TRACT TUBERCULOSIS			
subjects affected / exposed	1 / 335 (0.30%)	0 / 332 (0.00%)	0 / 181 (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
GALLBLADDER ABSCESS			
subjects affected / exposed	0 / 335 (0.00%)	0 / 332 (0.00%)	0 / 181 (0.00%)
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 / 335 (0.00%)	1 / 332 (0.30%)	0 / 181 (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
HERPES ZOSTER DISSEMINATED			
subjects affected / exposed	0 / 335 (0.00%)	1 / 332 (0.30%)	0 / 181 (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
GENITAL HERPES SIMPLEX			
subjects affected / exposed	1 / 335 (0.30%)	0 / 332 (0.00%)	0 / 181 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HERPES ZOSTER			
subjects affected / exposed	1 / 335 (0.30%)	3 / 332 (0.90%)	0 / 181 (0.00%)
occurrences causally related to treatment / all	1 / 1	3 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HERPES ZOSTER MENINGITIS			

subjects affected / exposed	0 / 335 (0.00%)	1 / 332 (0.30%)	0 / 181 (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
INFECTIVE SPONDYLITIS			
subjects affected / exposed	1 / 335 (0.30%)	0 / 332 (0.00%)	0 / 181 (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
INFLUENZA			
subjects affected / exposed	1 / 335 (0.30%)	2 / 332 (0.60%)	0 / 181 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
KERATITIS BACTERIAL			
subjects affected / exposed	0 / 335 (0.00%)	0 / 332 (0.00%)	0 / 181 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
LUNG ABSCESS			
subjects affected / exposed	0 / 335 (0.00%)	0 / 332 (0.00%)	1 / 181 (0.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
NECROTISING FASCIITIS			
subjects affected / exposed	1 / 335 (0.30%)	0 / 332 (0.00%)	0 / 181 (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
MENINGITIS BACTERIAL			
subjects affected / exposed	0 / 335 (0.00%)	1 / 332 (0.30%)	0 / 181 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
OPHTHALMIC HERPES ZOSTER			
subjects affected / exposed	1 / 335 (0.30%)	1 / 332 (0.30%)	1 / 181 (0.55%)
occurrences causally related to treatment / all	0 / 1	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PERITONEAL TUBERCULOSIS			

subjects affected / exposed	1 / 335 (0.30%)	0 / 332 (0.00%)	0 / 181 (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
OSTEOMYELITIS			
subjects affected / exposed	0 / 335 (0.00%)	0 / 332 (0.00%)	0 / 181 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PARAINFLUENZAE VIRUS INFECTION			
subjects affected / exposed	1 / 335 (0.30%)	0 / 332 (0.00%)	0 / 181 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PERITONITIS			
subjects affected / exposed	0 / 335 (0.00%)	1 / 332 (0.30%)	0 / 181 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
PNEUMONIA			
subjects affected / exposed	9 / 335 (2.69%)	5 / 332 (1.51%)	1 / 181 (0.55%)
occurrences causally related to treatment / all	8 / 9	3 / 5	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PNEUMONIA BACTERIAL			
subjects affected / exposed	1 / 335 (0.30%)	0 / 332 (0.00%)	0 / 181 (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
PNEUMONIA CRYPTOCOCCAL			
subjects affected / exposed	1 / 335 (0.30%)	0 / 332 (0.00%)	0 / 181 (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
PNEUMONIA ESCHERICHIA			
subjects affected / exposed	1 / 335 (0.30%)	0 / 332 (0.00%)	0 / 181 (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
PNEUMONIA KLEBSIELLA			

subjects affected / exposed	0 / 335 (0.00%)	1 / 332 (0.30%)	0 / 181 (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
PROSTATITIS ESCHERICHIA COLI			
subjects affected / exposed	0 / 335 (0.00%)	0 / 332 (0.00%)	1 / 181 (0.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PNEUMONIA PNEUMOCOCCAL			
subjects affected / exposed	0 / 335 (0.00%)	0 / 332 (0.00%)	0 / 181 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PYELONEPHRITIS ACUTE			
subjects affected / exposed	0 / 335 (0.00%)	0 / 332 (0.00%)	0 / 181 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PYELONEPHRITIS			
subjects affected / exposed	0 / 335 (0.00%)	1 / 332 (0.30%)	0 / 181 (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
PYELONEPHRITIS CHRONIC			
subjects affected / exposed	0 / 335 (0.00%)	1 / 332 (0.30%)	0 / 181 (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 VIRAL			
subjects affected / exposed	1 / 335 (0.30%)	0 / 332 (0.00%)	0 / 181 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SEPSIS			
subjects affected / exposed	2 / 335 (0.60%)	0 / 332 (0.00%)	0 / 181 (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
Q FEVER			

subjects affected / exposed	0 / 335 (0.00%)	1 / 332 (0.30%)	0 / 181 (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
STAPHYLOCOCCAL INFECTION			
subjects affected / exposed	1 / 335 (0.30%)	0 / 332 (0.00%)	0 / 181 (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
SEPTIC SHOCK			
subjects affected / exposed	0 / 335 (0.00%)	1 / 332 (0.30%)	0 / 181 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
SINOBRONCHITIS			
subjects affected / exposed	0 / 335 (0.00%)	1 / 332 (0.30%)	0 / 181 (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
TOOTH ABSCESS			
subjects affected / exposed	0 / 335 (0.00%)	0 / 332 (0.00%)	0 / 181 (0.00%)
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 / 335 (0.00%)	0 / 332 (0.00%)	0 / 181 (0.00%)
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 / 335 (0.00%)	1 / 332 (0.30%)	0 / 181 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
URINARY TRACT INFECTION			
subjects affected / exposed	0 / 335 (0.00%)	1 / 332 (0.30%)	1 / 181 (0.55%)
occurrences causally related to treatment / all	0 / 0	0 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
ABNORMAL WEIGHT GAIN			

subjects affected / exposed	2 / 335 (0.60%)	2 / 332 (0.60%)	0 / 181 (0.00%)
occurrences causally related to treatment / all	2 / 2	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CENTRAL OBESITY			
subjects affected / exposed	0 / 335 (0.00%)	1 / 332 (0.30%)	0 / 181 (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
DEHYDRATION			
subjects affected / exposed	1 / 335 (0.30%)	0 / 332 (0.00%)	0 / 181 (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	1 / 335 (0.30%)	0 / 332 (0.00%)	0 / 181 (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
HYPOKALAEMIA			
subjects affected / exposed	0 / 335 (0.00%)	0 / 332 (0.00%)	0 / 181 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
OBESITY			
subjects affected / exposed	0 / 335 (0.00%)	0 / 332 (0.00%)	0 / 181 (0.00%)
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	After Switch: Any Upadacitinib 15 mg		
Total subjects affected by serious adverse events			
subjects affected / exposed	35 / 218 (16.06%)		
number of deaths (all causes)	7		
number of deaths resulting from adverse events	2		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
ADENOCARCINOMA GASTRIC			
subjects affected / exposed	1 / 218 (0.46%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	1 / 1		

ADENOCARCINOMA OF COLON			
subjects affected / exposed	0 / 218 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
ADENOCARCINOMA METASTATIC			
subjects affected / exposed	1 / 218 (0.46%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
ANGIOFIBROMA			
subjects affected / exposed	1 / 218 (0.46%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
B-CELL LYMPHOMA			
subjects affected / exposed	0 / 218 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
BASAL CELL CARCINOMA			
subjects affected / exposed	0 / 218 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
BENIGN OVARIAN TUMOUR			
subjects affected / exposed	0 / 218 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
BLADDER CANCER			
subjects affected / exposed	0 / 218 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
BLADDER NEOPLASM			
subjects affected / exposed	0 / 218 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
BOWEN'S DISEASE			

subjects affected / exposed	0 / 218 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
BREAST CANCER METASTATIC				
subjects affected / exposed	0 / 218 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
CERVIX CARCINOMA STAGE 0				
subjects affected / exposed	0 / 218 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
BREAST CANCER				
subjects affected / exposed	0 / 218 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
ENDOMETRIAL ADENOCARCINOMA				
subjects affected / exposed	0 / 218 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
FIBROMA				
subjects affected / exposed	0 / 218 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
GASTRIC CANCER				
subjects affected / exposed	0 / 218 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
LUNG ADENOCARCINOMA				
subjects affected / exposed	1 / 218 (0.46%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
LIPOMA				

subjects affected / exposed	1 / 218 (0.46%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
LEIOMYOMA				
subjects affected / exposed	0 / 218 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
LUNG SQUAMOUS CELL CARCINOMA METASTATIC				
subjects affected / exposed	0 / 218 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
MALIGNANT PALATE NEOPLASM				
subjects affected / exposed	0 / 218 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
MALIGNANT MELANOMA				
subjects affected / exposed	0 / 218 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
METASTATIC NEOPLASM				
subjects affected / exposed	0 / 218 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
NEUROENDOCRINE TUMOUR				
subjects affected / exposed	0 / 218 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
METASTASES TO BONE				
subjects affected / exposed	1 / 218 (0.46%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
NON-SMALL CELL LUNG CANCER METASTATIC				

subjects affected / exposed	1 / 218 (0.46%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
OVARIAN GERM CELL TERATOMA				
subjects affected / exposed	0 / 218 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
OVARIAN CANCER				
subjects affected / exposed	0 / 218 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
PAPILLARY THYROID CANCER				
subjects affected / exposed	0 / 218 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
PROSTATE CANCER				
subjects affected / exposed	0 / 218 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
RENAL CANCER				
subjects affected / exposed	0 / 218 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
RENAL CELL CARCINOMA STAGE I				
subjects affected / exposed	0 / 218 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
SEBACEOUS CARCINOMA				
subjects affected / exposed	0 / 218 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
SQUAMOUS CELL CARCINOMA OF LUNG				

subjects affected / exposed	0 / 218 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
SQUAMOUS CELL CARCINOMA OF SKIN				
subjects affected / exposed	0 / 218 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
SQUAMOUS CELL CARCINOMA OF THE TONGUE				
subjects affected / exposed	1 / 218 (0.46%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
TONGUE NEOPLASM MALIGNANT STAGE UNSPECIFIED				
subjects affected / exposed	0 / 218 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
UTERINE CANCER				
subjects affected / exposed	0 / 218 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
UTERINE CARCINOMA IN SITU				
subjects affected / exposed	0 / 218 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Vascular disorders				
DEEP VEIN THROMBOSIS				
subjects affected / exposed	1 / 218 (0.46%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
EMBOLISM ARTERIAL				
subjects affected / exposed	0 / 218 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			

HYPERTENSION				
subjects affected / exposed	0 / 218 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
PERIPHERAL ARTERIAL OCCLUSIVE DISEASE				
subjects affected / exposed	0 / 218 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
PERIPHERAL ARTERY STENOSIS				
subjects affected / exposed	0 / 218 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
PERIPHERAL ISCHAEMIA				
subjects affected / exposed	0 / 218 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
SHOCK HAEMORRHAGIC				
subjects affected / exposed	0 / 218 (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 / 218 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
General disorders and administration site conditions				
CHEST DISCOMFORT				
subjects affected / exposed	1 / 218 (0.46%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
CHEST PAIN				

subjects affected / exposed	0 / 218 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
DEATH				
subjects affected / exposed	0 / 218 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
MULTIPLE ORGAN DYSFUNCTION SYNDROME				
subjects affected / exposed	0 / 218 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
SUDDEN DEATH				
subjects affected / exposed	0 / 218 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Reproductive system and breast disorders				
BENIGN PROSTATIC HYPERPLASIA				
subjects affected / exposed	0 / 218 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
BREAST HYPOPLASIA				
subjects affected / exposed	0 / 218 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
CERVIX HAEMORRHAGE UTERINE				
subjects affected / exposed	0 / 218 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
CERVICAL DYSPLASIA				
subjects affected / exposed	0 / 218 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
ENDOMETRIAL HYPERPLASIA				

subjects affected / exposed	0 / 218 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
MENOMETRORRHAGIA				
subjects affected / exposed	0 / 218 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
OVARIAN CYST				
subjects affected / exposed	0 / 218 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
PROSTATITIS				
subjects affected / exposed	0 / 218 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
OVARIAN CYST RUPTURED				
subjects affected / exposed	0 / 218 (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 / 218 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
ASTHMATIC CRISIS				
subjects affected / exposed	0 / 218 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
ASTHMA				
subjects affected / exposed	1 / 218 (0.46%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
CHRONIC OBSTRUCTIVE PULMONARY DISEASE				

subjects affected / exposed	1 / 218 (0.46%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
PLEURAL EFFUSION				
subjects affected / exposed	1 / 218 (0.46%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
PLEURISY				
subjects affected / exposed	0 / 218 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
PNEUMOTHORAX				
subjects affected / exposed	1 / 218 (0.46%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
PNEUMOTHORAX SPONTANEOUS				
subjects affected / exposed	0 / 218 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
PULMONARY EMBOLISM				
subjects affected / exposed	0 / 218 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
PULMONARY FIBROSIS				
subjects affected / exposed	0 / 218 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
RESPIRATORY FAILURE				
subjects affected / exposed	0 / 218 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Psychiatric disorders				
DEPRESSION				

subjects affected / exposed	0 / 218 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
MENTAL DISORDER DUE TO A GENERAL MEDICAL CONDITION				
subjects affected / exposed	0 / 218 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Investigations				
BLOOD CREATINE PHOSPHOKINASE INCREASED				
subjects affected / exposed	0 / 218 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
HEPATIC ENZYME INCREASED				
subjects affected / exposed	0 / 218 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
TRANSAMINASES INCREASED				
subjects affected / exposed	0 / 218 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
WHITE BLOOD CELL COUNT INCREASED				
subjects affected / exposed	0 / 218 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Injury, poisoning and procedural complications				
ANKLE FRACTURE				
subjects affected / exposed	0 / 218 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
CONTUSION				

subjects affected / exposed	0 / 218 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
CORNEAL LACERATION				
subjects affected / exposed	0 / 218 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
CONCUSSION				
subjects affected / exposed	0 / 218 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
FEMORAL NECK FRACTURE				
subjects affected / exposed	1 / 218 (0.46%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
FEMUR FRACTURE				
subjects affected / exposed	0 / 218 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
FOOT FRACTURE				
subjects affected / exposed	0 / 218 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
HIP FRACTURE				
subjects affected / exposed	1 / 218 (0.46%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
HUMERUS FRACTURE				
subjects affected / exposed	0 / 218 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
JOINT DISLOCATION				

subjects affected / exposed	0 / 218 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
LIMB CRUSHING INJURY				
subjects affected / exposed	0 / 218 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
LOWER LIMB FRACTURE				
subjects affected / exposed	0 / 218 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
MENISCUS INJURY				
subjects affected / exposed	1 / 218 (0.46%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
PATELLA FRACTURE				
subjects affected / exposed	0 / 218 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
POST LUMBAR PUNCTURE SYNDROME				
subjects affected / exposed	0 / 218 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
POST PROCEDURAL FISTULA				
subjects affected / exposed	0 / 218 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
RADIUS FRACTURE				
subjects affected / exposed	0 / 218 (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 / 218 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
SUBDURAL HAEMATOMA				
subjects affected / exposed	0 / 218 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
TENDON RUPTURE				
subjects affected / exposed	0 / 218 (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 / 218 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
UPPER LIMB FRACTURE				
subjects affected / exposed	0 / 218 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
WRIST FRACTURE				
subjects affected / exposed	0 / 218 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Congenital, familial and genetic disorders				
HAEMORRHAGIC ARTERIOVENOUS MALFORMATION				
subjects affected / exposed	0 / 218 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardiac disorders				
ACUTE CORONARY SYNDROME				
subjects affected / exposed	0 / 218 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			

ANGINA PECTORIS			
subjects affected / exposed	0 / 218 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
ACUTE MYOCARDIAL INFARCTION			
subjects affected / exposed	1 / 218 (0.46%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
ARTERIOSPASM CORONARY			
subjects affected / exposed	0 / 218 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
ATRIAL FIBRILLATION			
subjects affected / exposed	1 / 218 (0.46%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
CARDIAC ARREST			
subjects affected / exposed	0 / 218 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
CARDIAC FAILURE			
subjects affected / exposed	1 / 218 (0.46%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
CARDIAC FAILURE CONGESTIVE			
subjects affected / exposed	0 / 218 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
CARDIAC TAMPONADE			
subjects affected / exposed	0 / 218 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
CARDIO-RESPIRATORY ARREST			

subjects affected / exposed	1 / 218 (0.46%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
CARDIOVASCULAR DISORDER				
subjects affected / exposed	0 / 218 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
METABOLIC CARDIOMYOPATHY				
subjects affected / exposed	1 / 218 (0.46%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
MYOCARDIAL INFARCTION				
subjects affected / exposed	0 / 218 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
MYOCARDIAL FIBROSIS				
subjects affected / exposed	1 / 218 (0.46%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
MYOCARDIAL ISCHAEMIA				
subjects affected / exposed	0 / 218 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
SINUS NODE DYSFUNCTION				
subjects affected / exposed	0 / 218 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
PERICARDITIS				
subjects affected / exposed	0 / 218 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
SUPRAVENTRICULAR TACHYCARDIA				

subjects affected / exposed	1 / 218 (0.46%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
TACHYCARDIA				
subjects affected / exposed	0 / 218 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Nervous system disorders				
CAROTID ARTERIOSCLEROSIS				
subjects affected / exposed	0 / 218 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
HYPOXIC-ISCHAEMIC ENCEPHALOPATHY				
subjects affected / exposed	0 / 218 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
MONOPARESIS				
subjects affected / exposed	0 / 218 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
CAROTID ARTERY DISEASE				
subjects affected / exposed	0 / 218 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
SCIATICA				
subjects affected / exposed	0 / 218 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
SPONDYLITIC MYELOPATHY				
subjects affected / exposed	0 / 218 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
MYELOPATHY				

subjects affected / exposed	0 / 218 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
VERTEBROBASILAR INSUFFICIENCY				
subjects affected / exposed	0 / 218 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
TRANSIENT ISCHAEMIC ATTACK				
subjects affected / exposed	0 / 218 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
SYNCOPE				
subjects affected / exposed	0 / 218 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Blood and lymphatic system disorders				
ANAEMIA				
subjects affected / exposed	0 / 218 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
IRON DEFICIENCY ANAEMIA				
subjects affected / exposed	0 / 218 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Eye disorders				
CATARACT				
subjects affected / exposed	0 / 218 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
CATARACT DIABETIC				
subjects affected / exposed	0 / 218 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
IRIDOCYCLITIS				

subjects affected / exposed	0 / 218 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
MACULAR HOLE				
subjects affected / exposed	0 / 218 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
VITREOUS HAEMORRHAGE				
subjects affected / exposed	0 / 218 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
VITREORETINAL TRACTION SYNDROME				
subjects affected / exposed	1 / 218 (0.46%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal disorders				
ABDOMINAL PAIN				
subjects affected / exposed	0 / 218 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
ABDOMINAL WALL HAEMATOMA				
subjects affected / exposed	0 / 218 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
ANAL FISTULA				
subjects affected / exposed	0 / 218 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
ASCITES				
subjects affected / exposed	0 / 218 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
COLITIS				

subjects affected / exposed	0 / 218 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
CONSTIPATION			
subjects affected / exposed	0 / 218 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
DUODENAL ULCER			
subjects affected / exposed	0 / 218 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
DIVERTICULAR PERFORATION			
subjects affected / exposed	0 / 218 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
FOOD POISONING			
subjects affected / exposed	0 / 218 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
GASTRIC ULCER			
subjects affected / exposed	0 / 218 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
GASTRIC ULCER HAEMORRHAGE			
subjects affected / exposed	0 / 218 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
GASTRIC ULCER PERFORATION			
subjects affected / exposed	0 / 218 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
GASTRITIS			

subjects affected / exposed	0 / 218 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
GASTROINTESTINAL HAEMORRHAGE				
subjects affected / exposed	0 / 218 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
GINGIVAL RECESSION				
subjects affected / exposed	0 / 218 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
INCARCERATED INGUINAL HERNIA				
subjects affected / exposed	0 / 218 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
HIATUS HERNIA				
subjects affected / exposed	0 / 218 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
LARGE INTESTINE PERFORATION				
subjects affected / exposed	0 / 218 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
INGUINAL HERNIA				
subjects affected / exposed	1 / 218 (0.46%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
LARGE INTESTINE POLYP				
subjects affected / exposed	0 / 218 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
PANCREATIC DISORDER				

subjects affected / exposed	0 / 218 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
PANCREATITIS				
subjects affected / exposed	1 / 218 (0.46%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
RECTAL HAEMORRHAGE				
subjects affected / exposed	1 / 218 (0.46%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
SALIVARY GLAND CALCULUS				
subjects affected / exposed	0 / 218 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
RECTAL POLYP				
subjects affected / exposed	0 / 218 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hepatobiliary disorders				
BILE DUCT STONE				
subjects affected / exposed	0 / 218 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
CHOLECYSTITIS ACUTE				
subjects affected / exposed	0 / 218 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
CHOLANGITIS				
subjects affected / exposed	0 / 218 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
CHOLELITHIASIS				

subjects affected / exposed	0 / 218 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
GALLBLADDER RUPTURE				
subjects affected / exposed	0 / 218 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Skin and subcutaneous tissue disorders				
ANGIOEDEMA				
subjects affected / exposed	0 / 218 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
DIABETIC FOOT				
subjects affected / exposed	0 / 218 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
DRUG ERUPTION				
subjects affected / exposed	0 / 218 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
SKIN ULCER				
subjects affected / exposed	0 / 218 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Renal and urinary disorders				
NEPHROLITHIASIS				
subjects affected / exposed	0 / 218 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
ACUTE KIDNEY INJURY				
subjects affected / exposed	0 / 218 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
RENAL COLIC				

subjects affected / exposed	0 / 218 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
RENAL CYST				
subjects affected / exposed	0 / 218 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
RENAL FAILURE				
subjects affected / exposed	0 / 218 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
URETEROLITHIASIS				
subjects affected / exposed	0 / 218 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Musculoskeletal and connective tissue disorders				
ACQUIRED CLAW TOE				
subjects affected / exposed	0 / 218 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
BURSITIS				
subjects affected / exposed	0 / 218 (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 / 218 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
LUMBAR SPINAL STENOSIS				
subjects affected / exposed	1 / 218 (0.46%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
NECK PAIN				

subjects affected / exposed	0 / 218 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
OSTEOARTHRITIS			
subjects affected / exposed	0 / 218 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
OSTEONECROSIS			
subjects affected / exposed	1 / 218 (0.46%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
PAIN IN EXTREMITY			
subjects affected / exposed	0 / 218 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
PATHOLOGICAL FRACTURE			
subjects affected / exposed	0 / 218 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
ROTATOR CUFF SYNDROME			
subjects affected / exposed	0 / 218 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
SPONDYLOLISTHESIS			
subjects affected / exposed	0 / 218 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
SUBCHONDRAL INSUFFICIENCY FRACTURE			
subjects affected / exposed	0 / 218 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
SYMPATHETIC POSTERIOR CERVICAL SYNDROME			

subjects affected / exposed	0 / 218 (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 / 218 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Infections and infestations				
ACTINOMYCOTIC PULMONARY INFECTION				
subjects affected / exposed	0 / 218 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
APPENDICITIS				
subjects affected / exposed	0 / 218 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
BACTERIAL PYELONEPHRITIS				
subjects affected / exposed	0 / 218 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
BRONCHITIS				
subjects affected / exposed	0 / 218 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
BRONCHOPULMONARY ASPERGILLOSIS				
subjects affected / exposed	0 / 218 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
COVID-19 PNEUMONIA				
subjects affected / exposed	12 / 218 (5.50%)			
occurrences causally related to treatment / all	2 / 12			
deaths causally related to treatment / all	1 / 4			
COVID-19				

subjects affected / exposed	3 / 218 (1.38%)			
occurrences causally related to treatment / all	2 / 3			
deaths causally related to treatment / all	0 / 0			
CORONAVIRUS PNEUMONIA				
subjects affected / exposed	0 / 218 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
CELLULITIS				
subjects affected / exposed	0 / 218 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
DIVERTICULITIS				
subjects affected / exposed	0 / 218 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
EMPYEMA				
subjects affected / exposed	0 / 218 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
ENDOCARDITIS				
subjects affected / exposed	0 / 218 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
ERYSIPELAS				
subjects affected / exposed	0 / 218 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
ESCHERICHIA INFECTION				
subjects affected / exposed	0 / 218 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
FEMALE GENITAL TRACT TUBERCULOSIS				

subjects affected / exposed	0 / 218 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
GALLBLADDER ABSCESS				
subjects affected / exposed	0 / 218 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
GASTROENTERITIS				
subjects affected / exposed	0 / 218 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
HERPES ZOSTER DISSEMINATED				
subjects affected / exposed	0 / 218 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
GENITAL HERPES SIMPLEX				
subjects affected / exposed	0 / 218 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
HERPES ZOSTER				
subjects affected / exposed	0 / 218 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
HERPES ZOSTER MENINGITIS				
subjects affected / exposed	0 / 218 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
INFECTIVE SPONDYLITIS				
subjects affected / exposed	0 / 218 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
INFLUENZA				

subjects affected / exposed	0 / 218 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
KERATITIS BACTERIAL			
subjects affected / exposed	0 / 218 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
LUNG ABSCESS			
subjects affected / exposed	1 / 218 (0.46%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
NECROTISING FASCIITIS			
subjects affected / exposed	0 / 218 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
MENINGITIS BACTERIAL			
subjects affected / exposed	0 / 218 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
OPHTHALMIC HERPES ZOSTER			
subjects affected / exposed	1 / 218 (0.46%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
PERITONEAL TUBERCULOSIS			
subjects affected / exposed	0 / 218 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
OSTEOMYELITIS			
subjects affected / exposed	0 / 218 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
PARAINFLUENZAE VIRUS INFECTION			

subjects affected / exposed	0 / 218 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
PERITONITIS				
subjects affected / exposed	0 / 218 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
PNEUMONIA				
subjects affected / exposed	2 / 218 (0.92%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 0			
PNEUMONIA BACTERIAL				
subjects affected / exposed	0 / 218 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
PNEUMONIA CRYPTOCOCCAL				
subjects affected / exposed	0 / 218 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
PNEUMONIA ESCHERICHIA				
subjects affected / exposed	0 / 218 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
PNEUMONIA KLEBSIELLA				
subjects affected / exposed	0 / 218 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
PROSTATITIS ESCHERICHIA COLI				
subjects affected / exposed	1 / 218 (0.46%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
PNEUMONIA PNEUMOCOCCAL				

subjects affected / exposed	0 / 218 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
PYELONEPHRITIS ACUTE			
subjects affected / exposed	0 / 218 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
PYELONEPHRITIS			
subjects affected / exposed	0 / 218 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
PYELONEPHRITIS CHRONIC			
subjects affected / exposed	0 / 218 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
RESPIRATORY TRACT INFECTION VIRAL			
subjects affected / exposed	0 / 218 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
SEPSIS			
subjects affected / exposed	0 / 218 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Q FEVER			
subjects affected / exposed	0 / 218 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
STAPHYLOCOCCAL INFECTION			
subjects affected / exposed	0 / 218 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
SEPTIC SHOCK			

subjects affected / exposed	0 / 218 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
SINOBRONCHITIS				
subjects affected / exposed	0 / 218 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
TOOTH ABSCESS				
subjects affected / exposed	0 / 218 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
SUBCUTANEOUS ABSCESS				
subjects affected / exposed	0 / 218 (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 / 218 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
URINARY TRACT INFECTION				
subjects affected / exposed	1 / 218 (0.46%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Metabolism and nutrition disorders				
ABNORMAL WEIGHT GAIN				
subjects affected / exposed	0 / 218 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
CENTRAL OBESITY				
subjects affected / exposed	0 / 218 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
DEHYDRATION				

subjects affected / exposed	0 / 218 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
DIABETIC KETOACIDOSIS			
subjects affected / exposed	0 / 218 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
HYPOKALAEMIA			
subjects affected / exposed	0 / 218 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
OBESITY			
subjects affected / exposed	0 / 218 (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	Weeks 1-24: Methotrexate Monotherapy	Weeks 1-24: Upadacitinib 7.5 mg Monotherapy	Weeks 1-24: Upadacitinib 15 mg Monotherapy
Total subjects affected by non-serious adverse events			
subjects affected / exposed	159 / 314 (50.64%)	38 / 55 (69.09%)	169 / 317 (53.31%)
Vascular disorders			
HYPERTENSION			
subjects affected / exposed	8 / 314 (2.55%)	3 / 55 (5.45%)	12 / 317 (3.79%)
occurrences (all)	9	3	12
General disorders and administration site conditions			
FATIGUE			
subjects affected / exposed	1 / 314 (0.32%)	0 / 55 (0.00%)	7 / 317 (2.21%)
occurrences (all)	1	0	8
INFLUENZA LIKE ILLNESS			
subjects affected / exposed	8 / 314 (2.55%)	0 / 55 (0.00%)	7 / 317 (2.21%)
occurrences (all)	8	0	8
PYREXIA			

subjects affected / exposed	1 / 314 (0.32%)	0 / 55 (0.00%)	1 / 317 (0.32%)
occurrences (all)	1	0	1
Respiratory, thoracic and mediastinal disorders			
ASTHMA			
subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
occurrences (all)	0	0	0
COUGH			
subjects affected / exposed	5 / 314 (1.59%)	0 / 55 (0.00%)	10 / 317 (3.15%)
occurrences (all)	5	0	12
RHINITIS ALLERGIC			
subjects affected / exposed	1 / 314 (0.32%)	0 / 55 (0.00%)	0 / 317 (0.00%)
occurrences (all)	1	0	0
Psychiatric disorders			
INSOMNIA			
subjects affected / exposed	4 / 314 (1.27%)	0 / 55 (0.00%)	3 / 317 (0.95%)
occurrences (all)	4	0	3
Investigations			
ALANINE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	12 / 314 (3.82%)	2 / 55 (3.64%)	16 / 317 (5.05%)
occurrences (all)	12	2	21
ASPARTATE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	8 / 314 (2.55%)	0 / 55 (0.00%)	10 / 317 (3.15%)
occurrences (all)	8	0	14
BLOOD CREATINE PHOSPHOKINASE INCREASED			
subjects affected / exposed	2 / 314 (0.64%)	2 / 55 (3.64%)	9 / 317 (2.84%)
occurrences (all)	3	2	10
BLOOD CREATININE INCREASED			
subjects affected / exposed	2 / 314 (0.64%)	1 / 55 (1.82%)	1 / 317 (0.32%)
occurrences (all)	2	1	1
LIVER FUNCTION TEST INCREASED			
subjects affected / exposed	2 / 314 (0.64%)	1 / 55 (1.82%)	0 / 317 (0.00%)
occurrences (all)	2	1	0
LYMPHOCYTE COUNT DECREASED			

subjects affected / exposed	2 / 314 (0.64%)	0 / 55 (0.00%)	0 / 317 (0.00%)
occurrences (all)	2	0	0
NEUTROPHIL COUNT DECREASED			
subjects affected / exposed	0 / 314 (0.00%)	1 / 55 (1.82%)	3 / 317 (0.95%)
occurrences (all)	0	1	3
WEIGHT INCREASED			
subjects affected / exposed	2 / 314 (0.64%)	0 / 55 (0.00%)	8 / 317 (2.52%)
occurrences (all)	2	0	8
WHITE BLOOD CELL COUNT DECREASED			
subjects affected / exposed	0 / 314 (0.00%)	1 / 55 (1.82%)	0 / 317 (0.00%)
occurrences (all)	0	1	0
Injury, poisoning and procedural complications			
CONTUSION			
subjects affected / exposed	2 / 314 (0.64%)	1 / 55 (1.82%)	2 / 317 (0.63%)
occurrences (all)	2	1	2
SPINAL COMPRESSION FRACTURE			
subjects affected / exposed	1 / 314 (0.32%)	0 / 55 (0.00%)	0 / 317 (0.00%)
occurrences (all)	1	0	0
Nervous system disorders			
DIZZINESS			
subjects affected / exposed	4 / 314 (1.27%)	0 / 55 (0.00%)	5 / 317 (1.58%)
occurrences (all)	4	0	5
HEADACHE			
subjects affected / exposed	6 / 314 (1.91%)	2 / 55 (3.64%)	7 / 317 (2.21%)
occurrences (all)	6	2	7
POST HERPETIC NEURALGIA			
subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
ANAEMIA			
subjects affected / exposed	5 / 314 (1.59%)	3 / 55 (5.45%)	6 / 317 (1.89%)
occurrences (all)	5	3	8
LEUKOPENIA			
subjects affected / exposed	4 / 314 (1.27%)	1 / 55 (1.82%)	6 / 317 (1.89%)
occurrences (all)	5	1	6
NEUTROPENIA			

subjects affected / exposed	2 / 314 (0.64%)	1 / 55 (1.82%)	7 / 317 (2.21%)
occurrences (all)	3	1	7
Eye disorders			
CATARACT			
subjects affected / exposed	2 / 314 (0.64%)	0 / 55 (0.00%)	1 / 317 (0.32%)
occurrences (all)	2	0	1
DRY EYE			
subjects affected / exposed	3 / 314 (0.96%)	0 / 55 (0.00%)	0 / 317 (0.00%)
occurrences (all)	3	0	0
Gastrointestinal disorders			
CHRONIC GASTRITIS			
subjects affected / exposed	0 / 314 (0.00%)	1 / 55 (1.82%)	0 / 317 (0.00%)
occurrences (all)	0	1	0
CONSTIPATION			
subjects affected / exposed	2 / 314 (0.64%)	3 / 55 (5.45%)	0 / 317 (0.00%)
occurrences (all)	2	3	0
DENTAL CARIES			
subjects affected / exposed	1 / 314 (0.32%)	2 / 55 (3.64%)	1 / 317 (0.32%)
occurrences (all)	1	2	1
GASTROOESOPHAGEAL REFLUX DISEASE			
subjects affected / exposed	2 / 314 (0.64%)	0 / 55 (0.00%)	4 / 317 (1.26%)
occurrences (all)	2	0	4
DYSPEPSIA			
subjects affected / exposed	12 / 314 (3.82%)	0 / 55 (0.00%)	8 / 317 (2.52%)
occurrences (all)	13	0	8
DIARRHOEA			
subjects affected / exposed	10 / 314 (3.18%)	0 / 55 (0.00%)	11 / 317 (3.47%)
occurrences (all)	10	0	12
HAEMORRHOIDS			
subjects affected / exposed	0 / 314 (0.00%)	1 / 55 (1.82%)	0 / 317 (0.00%)
occurrences (all)	0	1	0
STOMATITIS			
subjects affected / exposed	2 / 314 (0.64%)	4 / 55 (7.27%)	1 / 317 (0.32%)
occurrences (all)	2	5	2
NAUSEA			

subjects affected / exposed	17 / 314 (5.41%)	1 / 55 (1.82%)	18 / 317 (5.68%)
occurrences (all)	29	2	20
Hepatobiliary disorders			
HEPATIC STEATOSIS			
subjects affected / exposed	1 / 314 (0.32%)	0 / 55 (0.00%)	0 / 317 (0.00%)
occurrences (all)	1	0	0
Skin and subcutaneous tissue disorders			
DRY SKIN			
subjects affected / exposed	0 / 314 (0.00%)	1 / 55 (1.82%)	1 / 317 (0.32%)
occurrences (all)	0	1	1
ECZEMA			
subjects affected / exposed	1 / 314 (0.32%)	2 / 55 (3.64%)	1 / 317 (0.32%)
occurrences (all)	1	2	1
DERMATITIS			
subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	1 / 317 (0.32%)
occurrences (all)	0	0	1
RASH			
subjects affected / exposed	5 / 314 (1.59%)	1 / 55 (1.82%)	5 / 317 (1.58%)
occurrences (all)	5	1	6
PRURITUS			
subjects affected / exposed	3 / 314 (0.96%)	0 / 55 (0.00%)	3 / 317 (0.95%)
occurrences (all)	3	0	3
Renal and urinary disorders			
POLLAKIURIA			
subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
BACK PAIN			
subjects affected / exposed	3 / 314 (0.96%)	1 / 55 (1.82%)	4 / 317 (1.26%)
occurrences (all)	3	1	4
ARTHRALGIA			
subjects affected / exposed	3 / 314 (0.96%)	0 / 55 (0.00%)	6 / 317 (1.89%)
occurrences (all)	3	0	6
INTERVERTEBRAL DISC PROTRUSION			
subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	1 / 317 (0.32%)
occurrences (all)	0	0	1

MYALGIA			
subjects affected / exposed	3 / 314 (0.96%)	1 / 55 (1.82%)	3 / 317 (0.95%)
occurrences (all)	3	1	3
RHEUMATOID ARTHRITIS			
subjects affected / exposed	19 / 314 (6.05%)	0 / 55 (0.00%)	6 / 317 (1.89%)
occurrences (all)	20	0	7
PERIARTHRITIS			
subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
occurrences (all)	0	0	0
OSTEOPOROSIS			
subjects affected / exposed	0 / 314 (0.00%)	1 / 55 (1.82%)	1 / 317 (0.32%)
occurrences (all)	0	1	1
Infections and infestations			
CONJUNCTIVITIS			
subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
occurrences (all)	0	0	0
COVID-19			
subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
occurrences (all)	0	0	0
BRONCHITIS			
subjects affected / exposed	6 / 314 (1.91%)	0 / 55 (0.00%)	7 / 317 (2.21%)
occurrences (all)	6	0	8
GASTROENTERITIS			
subjects affected / exposed	7 / 314 (2.23%)	2 / 55 (3.64%)	5 / 317 (1.58%)
occurrences (all)	7	2	5
CYSTITIS			
subjects affected / exposed	2 / 314 (0.64%)	1 / 55 (1.82%)	2 / 317 (0.63%)
occurrences (all)	2	1	2
HERPES ZOSTER			
subjects affected / exposed	1 / 314 (0.32%)	2 / 55 (3.64%)	7 / 317 (2.21%)
occurrences (all)	1	2	8
INFLUENZA			
subjects affected / exposed	1 / 314 (0.32%)	2 / 55 (3.64%)	1 / 317 (0.32%)
occurrences (all)	1	2	1
NASOPHARYNGITIS			

subjects affected / exposed	13 / 314 (4.14%)	5 / 55 (9.09%)	18 / 317 (5.68%)
occurrences (all)	15	10	22
LATENT TUBERCULOSIS			
subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
occurrences (all)	0	0	0
ORAL CANDIDIASIS			
subjects affected / exposed	0 / 314 (0.00%)	2 / 55 (3.64%)	0 / 317 (0.00%)
occurrences (all)	0	2	0
PERIODONTITIS			
subjects affected / exposed	1 / 314 (0.32%)	1 / 55 (1.82%)	1 / 317 (0.32%)
occurrences (all)	1	1	1
ORAL HERPES			
subjects affected / exposed	2 / 314 (0.64%)	3 / 55 (5.45%)	4 / 317 (1.26%)
occurrences (all)	2	3	4
SINUSITIS			
subjects affected / exposed	6 / 314 (1.91%)	1 / 55 (1.82%)	5 / 317 (1.58%)
occurrences (all)	6	1	7
TINEA PEDIS			
subjects affected / exposed	0 / 314 (0.00%)	0 / 55 (0.00%)	0 / 317 (0.00%)
occurrences (all)	0	0	0
PHARYNGITIS			
subjects affected / exposed	6 / 314 (1.91%)	5 / 55 (9.09%)	4 / 317 (1.26%)
occurrences (all)	6	7	4
UPPER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	14 / 314 (4.46%)	3 / 55 (5.45%)	20 / 317 (6.31%)
occurrences (all)	17	3	23
URINARY TRACT INFECTION			
subjects affected / exposed	20 / 314 (6.37%)	1 / 55 (1.82%)	17 / 317 (5.36%)
occurrences (all)	24	1	19
Metabolism and nutrition disorders			
DYSLIPIDAEMIA			
subjects affected / exposed	0 / 314 (0.00%)	3 / 55 (5.45%)	3 / 317 (0.95%)
occurrences (all)	0	3	3
HYPERCHOLESTEROLAEMIA			

subjects affected / exposed	0 / 314 (0.00%)	1 / 55 (1.82%)	7 / 317 (2.21%)
occurrences (all)	0	1	7
HYPERLIPIDAEMIA			
subjects affected / exposed	1 / 314 (0.32%)	1 / 55 (1.82%)	4 / 317 (1.26%)
occurrences (all)	1	1	4
HYPERTRIGLYCERIDAEMIA			
subjects affected / exposed	8 / 314 (2.55%)	0 / 55 (0.00%)	11 / 317 (3.47%)
occurrences (all)	8	0	12

Non-serious adverse events	Weeks 1-24: Upadacitinib 30 mg Monotherapy	Weeks 1-260: Methotrexate Monotherapy	Weeks 1-260: Upadacitinib 7.5 mg Monotherapy
Total subjects affected by non-serious adverse events			
subjects affected / exposed	174 / 314 (55.41%)	234 / 314 (74.52%)	52 / 55 (94.55%)
Vascular disorders			
HYPERTENSION			
subjects affected / exposed	14 / 314 (4.46%)	31 / 314 (9.87%)	8 / 55 (14.55%)
occurrences (all)	14	34	9
General disorders and administration site conditions			
FATIGUE			
subjects affected / exposed	2 / 314 (0.64%)	3 / 314 (0.96%)	1 / 55 (1.82%)
occurrences (all)	2	3	1
INFLUENZA LIKE ILLNESS			
subjects affected / exposed	2 / 314 (0.64%)	15 / 314 (4.78%)	1 / 55 (1.82%)
occurrences (all)	3	20	1
PYREXIA			
subjects affected / exposed	5 / 314 (1.59%)	6 / 314 (1.91%)	5 / 55 (9.09%)
occurrences (all)	5	6	5
Respiratory, thoracic and mediastinal disorders			
ASTHMA			
subjects affected / exposed	0 / 314 (0.00%)	4 / 314 (1.27%)	3 / 55 (5.45%)
occurrences (all)	0	4	4
COUGH			
subjects affected / exposed	10 / 314 (3.18%)	15 / 314 (4.78%)	2 / 55 (3.64%)
occurrences (all)	11	15	2
RHINITIS ALLERGIC			

subjects affected / exposed	0 / 314 (0.00%)	3 / 314 (0.96%)	3 / 55 (5.45%)
occurrences (all)	0	4	3
Psychiatric disorders			
INSOMNIA			
subjects affected / exposed	3 / 314 (0.96%)	9 / 314 (2.87%)	1 / 55 (1.82%)
occurrences (all)	4	9	1
Investigations			
ALANINE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	8 / 314 (2.55%)	28 / 314 (8.92%)	3 / 55 (5.45%)
occurrences (all)	9	34	3
ASPARTATE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	7 / 314 (2.23%)	23 / 314 (7.32%)	1 / 55 (1.82%)
occurrences (all)	8	27	1
BLOOD CREATINE PHOSPHOKINASE INCREASED			
subjects affected / exposed	34 / 314 (10.83%)	10 / 314 (3.18%)	3 / 55 (5.45%)
occurrences (all)	39	12	4
BLOOD CREATININE INCREASED			
subjects affected / exposed	2 / 314 (0.64%)	6 / 314 (1.91%)	3 / 55 (5.45%)
occurrences (all)	4	8	3
LIVER FUNCTION TEST INCREASED			
subjects affected / exposed	0 / 314 (0.00%)	3 / 314 (0.96%)	3 / 55 (5.45%)
occurrences (all)	0	3	5
LYMPHOCYTE COUNT DECREASED			
subjects affected / exposed	0 / 314 (0.00%)	2 / 314 (0.64%)	3 / 55 (5.45%)
occurrences (all)	0	2	5
NEUTROPHIL COUNT DECREASED			
subjects affected / exposed	2 / 314 (0.64%)	0 / 314 (0.00%)	3 / 55 (5.45%)
occurrences (all)	2	0	3
WEIGHT INCREASED			
subjects affected / exposed	2 / 314 (0.64%)	6 / 314 (1.91%)	3 / 55 (5.45%)
occurrences (all)	2	7	3
WHITE BLOOD CELL COUNT DECREASED			
subjects affected / exposed	1 / 314 (0.32%)	0 / 314 (0.00%)	3 / 55 (5.45%)
occurrences (all)	1	0	5

Injury, poisoning and procedural complications			
CONTUSION			
subjects affected / exposed	2 / 314 (0.64%)	8 / 314 (2.55%)	8 / 55 (14.55%)
occurrences (all)	2	8	10
SPINAL COMPRESSION FRACTURE			
subjects affected / exposed	0 / 314 (0.00%)	1 / 314 (0.32%)	2 / 55 (3.64%)
occurrences (all)	0	1	2
Nervous system disorders			
DIZZINESS			
subjects affected / exposed	2 / 314 (0.64%)	8 / 314 (2.55%)	4 / 55 (7.27%)
occurrences (all)	2	9	4
HEADACHE			
subjects affected / exposed	14 / 314 (4.46%)	17 / 314 (5.41%)	4 / 55 (7.27%)
occurrences (all)	16	19	4
POST HERPETIC NEURALGIA			
subjects affected / exposed	0 / 314 (0.00%)	0 / 314 (0.00%)	4 / 55 (7.27%)
occurrences (all)	0	0	4
Blood and lymphatic system disorders			
ANAEMIA			
subjects affected / exposed	9 / 314 (2.87%)	17 / 314 (5.41%)	4 / 55 (7.27%)
occurrences (all)	10	19	4
LEUKOPENIA			
subjects affected / exposed	4 / 314 (1.27%)	13 / 314 (4.14%)	2 / 55 (3.64%)
occurrences (all)	4	23	2
NEUTROPENIA			
subjects affected / exposed	9 / 314 (2.87%)	11 / 314 (3.50%)	1 / 55 (1.82%)
occurrences (all)	11	15	1
Eye disorders			
CATARACT			
subjects affected / exposed	0 / 314 (0.00%)	4 / 314 (1.27%)	3 / 55 (5.45%)
occurrences (all)	0	4	4
DRY EYE			
subjects affected / exposed	0 / 314 (0.00%)	4 / 314 (1.27%)	3 / 55 (5.45%)
occurrences (all)	0	4	3
Gastrointestinal disorders			

CHRONIC GASTRITIS			
subjects affected / exposed	1 / 314 (0.32%)	1 / 314 (0.32%)	4 / 55 (7.27%)
occurrences (all)	1	1	4
CONSTIPATION			
subjects affected / exposed	13 / 314 (4.14%)	6 / 314 (1.91%)	4 / 55 (7.27%)
occurrences (all)	13	6	4
DENTAL CARIES			
subjects affected / exposed	1 / 314 (0.32%)	4 / 314 (1.27%)	4 / 55 (7.27%)
occurrences (all)	1	4	5
GASTROOESOPHAGEAL REFLUX DISEASE			
subjects affected / exposed	3 / 314 (0.96%)	9 / 314 (2.87%)	4 / 55 (7.27%)
occurrences (all)	3	9	5
DYSPEPSIA			
subjects affected / exposed	4 / 314 (1.27%)	20 / 314 (6.37%)	1 / 55 (1.82%)
occurrences (all)	4	29	1
DIARRHOEA			
subjects affected / exposed	6 / 314 (1.91%)	16 / 314 (5.10%)	3 / 55 (5.45%)
occurrences (all)	6	16	3
HAEMORRHOIDS			
subjects affected / exposed	1 / 314 (0.32%)	1 / 314 (0.32%)	3 / 55 (5.45%)
occurrences (all)	1	1	3
STOMATITIS			
subjects affected / exposed	3 / 314 (0.96%)	4 / 314 (1.27%)	8 / 55 (14.55%)
occurrences (all)	3	5	10
NAUSEA			
subjects affected / exposed	12 / 314 (3.82%)	29 / 314 (9.24%)	4 / 55 (7.27%)
occurrences (all)	13	47	5
Hepatobiliary disorders			
HEPATIC STEATOSIS			
subjects affected / exposed	0 / 314 (0.00%)	5 / 314 (1.59%)	3 / 55 (5.45%)
occurrences (all)	0	5	3
Skin and subcutaneous tissue disorders			
DRY SKIN			
subjects affected / exposed	1 / 314 (0.32%)	0 / 314 (0.00%)	3 / 55 (5.45%)
occurrences (all)	1	0	3
ECZEMA			

subjects affected / exposed	2 / 314 (0.64%)	3 / 314 (0.96%)	5 / 55 (9.09%)
occurrences (all)	2	4	5
DERMATITIS			
subjects affected / exposed	0 / 314 (0.00%)	2 / 314 (0.64%)	3 / 55 (5.45%)
occurrences (all)	0	2	3
RASH			
subjects affected / exposed	4 / 314 (1.27%)	9 / 314 (2.87%)	5 / 55 (9.09%)
occurrences (all)	4	12	5
PRURITUS			
subjects affected / exposed	2 / 314 (0.64%)	5 / 314 (1.59%)	3 / 55 (5.45%)
occurrences (all)	3	6	4
Renal and urinary disorders			
POLLAKIURIA			
subjects affected / exposed	0 / 314 (0.00%)	0 / 314 (0.00%)	2 / 55 (3.64%)
occurrences (all)	0	0	2
Musculoskeletal and connective tissue disorders			
BACK PAIN			
subjects affected / exposed	4 / 314 (1.27%)	10 / 314 (3.18%)	6 / 55 (10.91%)
occurrences (all)	4	12	7
ARTHRALGIA			
subjects affected / exposed	6 / 314 (1.91%)	13 / 314 (4.14%)	3 / 55 (5.45%)
occurrences (all)	6	14	3
INTERVERTEBRAL DISC PROTRUSION			
subjects affected / exposed	1 / 314 (0.32%)	0 / 314 (0.00%)	2 / 55 (3.64%)
occurrences (all)	1	0	2
MYALGIA			
subjects affected / exposed	2 / 314 (0.64%)	5 / 314 (1.59%)	4 / 55 (7.27%)
occurrences (all)	2	5	5
RHEUMATOID ARTHRITIS			
subjects affected / exposed	1 / 314 (0.32%)	44 / 314 (14.01%)	4 / 55 (7.27%)
occurrences (all)	1	65	4
PERIARTHRITIS			
subjects affected / exposed	0 / 314 (0.00%)	1 / 314 (0.32%)	3 / 55 (5.45%)
occurrences (all)	0	1	3
OSTEOPOROSIS			

subjects affected / exposed	1 / 314 (0.32%)	6 / 314 (1.91%)	3 / 55 (5.45%)
occurrences (all)	1	6	3
Infections and infestations			
CONJUNCTIVITIS			
subjects affected / exposed	2 / 314 (0.64%)	6 / 314 (1.91%)	3 / 55 (5.45%)
occurrences (all)	2	6	3
COVID-19			
subjects affected / exposed	0 / 314 (0.00%)	18 / 314 (5.73%)	4 / 55 (7.27%)
occurrences (all)	0	20	4
BRONCHITIS			
subjects affected / exposed	5 / 314 (1.59%)	24 / 314 (7.64%)	7 / 55 (12.73%)
occurrences (all)	6	27	9
GASTROENTERITIS			
subjects affected / exposed	5 / 314 (1.59%)	12 / 314 (3.82%)	8 / 55 (14.55%)
occurrences (all)	5	12	9
CYSTITIS			
subjects affected / exposed	2 / 314 (0.64%)	4 / 314 (1.27%)	5 / 55 (9.09%)
occurrences (all)	2	4	6
HERPES ZOSTER			
subjects affected / exposed	7 / 314 (2.23%)	7 / 314 (2.23%)	12 / 55 (21.82%)
occurrences (all)	7	7	12
INFLUENZA			
subjects affected / exposed	3 / 314 (0.96%)	7 / 314 (2.23%)	8 / 55 (14.55%)
occurrences (all)	3	7	8
NASOPHARYNGITIS			
subjects affected / exposed	17 / 314 (5.41%)	43 / 314 (13.69%)	22 / 55 (40.00%)
occurrences (all)	18	70	49
LATENT TUBERCULOSIS			
subjects affected / exposed	0 / 314 (0.00%)	14 / 314 (4.46%)	0 / 55 (0.00%)
occurrences (all)	0	14	0
ORAL CANDIDIASIS			
subjects affected / exposed	0 / 314 (0.00%)	0 / 314 (0.00%)	4 / 55 (7.27%)
occurrences (all)	0	0	5
PERIODONTITIS			
subjects affected / exposed	2 / 314 (0.64%)	4 / 314 (1.27%)	4 / 55 (7.27%)
occurrences (all)	2	7	4

ORAL HERPES			
subjects affected / exposed	4 / 314 (1.27%)	8 / 314 (2.55%)	7 / 55 (12.73%)
occurrences (all)	4	10	9
SINUSITIS			
subjects affected / exposed	4 / 314 (1.27%)	11 / 314 (3.50%)	3 / 55 (5.45%)
occurrences (all)	4	19	3
TINEA PEDIS			
subjects affected / exposed	0 / 314 (0.00%)	2 / 314 (0.64%)	3 / 55 (5.45%)
occurrences (all)	0	3	3
PHARYNGITIS			
subjects affected / exposed	8 / 314 (2.55%)	16 / 314 (5.10%)	12 / 55 (21.82%)
occurrences (all)	9	20	22
UPPER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	23 / 314 (7.32%)	31 / 314 (9.87%)	9 / 55 (16.36%)
occurrences (all)	28	45	14
URINARY TRACT INFECTION			
subjects affected / exposed	18 / 314 (5.73%)	41 / 314 (13.06%)	1 / 55 (1.82%)
occurrences (all)	21	59	3
Metabolism and nutrition disorders			
DYSLIPIDAEMIA			
subjects affected / exposed	6 / 314 (1.91%)	3 / 314 (0.96%)	5 / 55 (9.09%)
occurrences (all)	6	4	5
HYPERCHOLESTEROLAEMIA			
subjects affected / exposed	8 / 314 (2.55%)	2 / 314 (0.64%)	2 / 55 (3.64%)
occurrences (all)	9	2	2
HYPERLIPIDAEMIA			
subjects affected / exposed	3 / 314 (0.96%)	2 / 314 (0.64%)	4 / 55 (7.27%)
occurrences (all)	3	2	4
HYPERTRIGLYCERIDAEMIA			
subjects affected / exposed	8 / 314 (2.55%)	10 / 314 (3.18%)	0 / 55 (0.00%)
occurrences (all)	10	12	0

Non-serious adverse events	Weeks 1-260: Upadacitinib 15 mg Monotherapy	Weeks 1-260/Switch: Upadacitinib 30 mg Monotherapy	Weeks 1-260: Any Upadacitinib 7.5 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	242 / 317 (76.34%)	256 / 314 (81.53%)	55 / 56 (98.21%)

Vascular disorders			
HYPERTENSION			
subjects affected / exposed	36 / 317 (11.36%)	44 / 314 (14.01%)	9 / 56 (16.07%)
occurrences (all)	40	46	10
General disorders and administration site conditions			
FATIGUE			
subjects affected / exposed	16 / 317 (5.05%)	3 / 314 (0.96%)	1 / 56 (1.79%)
occurrences (all)	20	3	1
INFLUENZA LIKE ILLNESS			
subjects affected / exposed	17 / 317 (5.36%)	14 / 314 (4.46%)	1 / 56 (1.79%)
occurrences (all)	19	15	1
PYREXIA			
subjects affected / exposed	9 / 317 (2.84%)	9 / 314 (2.87%)	7 / 56 (12.50%)
occurrences (all)	10	9	8
Respiratory, thoracic and mediastinal disorders			
ASTHMA			
subjects affected / exposed	1 / 317 (0.32%)	1 / 314 (0.32%)	3 / 56 (5.36%)
occurrences (all)	1	1	4
COUGH			
subjects affected / exposed	24 / 317 (7.57%)	19 / 314 (6.05%)	2 / 56 (3.57%)
occurrences (all)	28	23	2
RHINITIS ALLERGIC			
subjects affected / exposed	2 / 317 (0.63%)	3 / 314 (0.96%)	3 / 56 (5.36%)
occurrences (all)	2	3	3
Psychiatric disorders			
INSOMNIA			
subjects affected / exposed	16 / 317 (5.05%)	5 / 314 (1.59%)	2 / 56 (3.57%)
occurrences (all)	18	6	2
Investigations			
ALANINE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	27 / 317 (8.52%)	28 / 314 (8.92%)	4 / 56 (7.14%)
occurrences (all)	49	48	4
ASPARTATE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	21 / 317 (6.62%)	24 / 314 (7.64%)	2 / 56 (3.57%)
occurrences (all)	31	33	2
BLOOD CREATINE PHOSPHOKINASE			

INCREASED			
subjects affected / exposed	37 / 317 (11.67%)	51 / 314 (16.24%)	5 / 56 (8.93%)
occurrences (all)	68	106	6
BLOOD CREATININE INCREASED			
subjects affected / exposed	6 / 317 (1.89%)	8 / 314 (2.55%)	3 / 56 (5.36%)
occurrences (all)	10	13	3
LIVER FUNCTION TEST INCREASED			
subjects affected / exposed	0 / 317 (0.00%)	1 / 314 (0.32%)	3 / 56 (5.36%)
occurrences (all)	0	2	5
LYMPHOCYTE COUNT DECREASED			
subjects affected / exposed	2 / 317 (0.63%)	3 / 314 (0.96%)	3 / 56 (5.36%)
occurrences (all)	2	3	5
NEUTROPHIL COUNT DECREASED			
subjects affected / exposed	5 / 317 (1.58%)	3 / 314 (0.96%)	3 / 56 (5.36%)
occurrences (all)	8	4	3
WEIGHT INCREASED			
subjects affected / exposed	15 / 317 (4.73%)	7 / 314 (2.23%)	3 / 56 (5.36%)
occurrences (all)	17	8	3
WHITE BLOOD CELL COUNT DECREASED			
subjects affected / exposed	2 / 317 (0.63%)	5 / 314 (1.59%)	3 / 56 (5.36%)
occurrences (all)	2	7	5
Injury, poisoning and procedural complications			
CONTUSION			
subjects affected / exposed	10 / 317 (3.15%)	5 / 314 (1.59%)	10 / 56 (17.86%)
occurrences (all)	10	6	12
SPINAL COMPRESSION FRACTURE			
subjects affected / exposed	3 / 317 (0.95%)	0 / 314 (0.00%)	3 / 56 (5.36%)
occurrences (all)	3	0	4
Nervous system disorders			
DIZZINESS			
subjects affected / exposed	8 / 317 (2.52%)	8 / 314 (2.55%)	4 / 56 (7.14%)
occurrences (all)	11	8	4
HEADACHE			
subjects affected / exposed	12 / 317 (3.79%)	21 / 314 (6.69%)	4 / 56 (7.14%)
occurrences (all)	13	26	4
POST HERPETIC NEURALGIA			

subjects affected / exposed	2 / 317 (0.63%)	2 / 314 (0.64%)	5 / 56 (8.93%)
occurrences (all)	2	2	5
Blood and lymphatic system disorders			
ANAEMIA			
subjects affected / exposed	20 / 317 (6.31%)	16 / 314 (5.10%)	5 / 56 (8.93%)
occurrences (all)	31	21	5
LEUKOPENIA			
subjects affected / exposed	9 / 317 (2.84%)	15 / 314 (4.78%)	2 / 56 (3.57%)
occurrences (all)	19	25	2
NEUTROPENIA			
subjects affected / exposed	13 / 317 (4.10%)	25 / 314 (7.96%)	1 / 56 (1.79%)
occurrences (all)	26	37	1
Eye disorders			
CATARACT			
subjects affected / exposed	3 / 317 (0.95%)	2 / 314 (0.64%)	3 / 56 (5.36%)
occurrences (all)	3	3	4
DRY EYE			
subjects affected / exposed	1 / 317 (0.32%)	3 / 314 (0.96%)	3 / 56 (5.36%)
occurrences (all)	1	3	3
Gastrointestinal disorders			
CHRONIC GASTRITIS			
subjects affected / exposed	2 / 317 (0.63%)	3 / 314 (0.96%)	5 / 56 (8.93%)
occurrences (all)	2	3	5
CONSTIPATION			
subjects affected / exposed	12 / 317 (3.79%)	18 / 314 (5.73%)	6 / 56 (10.71%)
occurrences (all)	13	21	6
DENTAL CARIES			
subjects affected / exposed	5 / 317 (1.58%)	3 / 314 (0.96%)	4 / 56 (7.14%)
occurrences (all)	5	3	5
GASTROOESOPHAGEAL REFLUX DISEASE			
subjects affected / exposed	7 / 317 (2.21%)	9 / 314 (2.87%)	5 / 56 (8.93%)
occurrences (all)	7	9	6
DYSPEPSIA			
subjects affected / exposed	12 / 317 (3.79%)	6 / 314 (1.91%)	1 / 56 (1.79%)
occurrences (all)	12	6	1
DIARRHOEA			

subjects affected / exposed	25 / 317 (7.89%)	19 / 314 (6.05%)	3 / 56 (5.36%)
occurrences (all)	33	26	3
HAEMORRHOIDS			
subjects affected / exposed	4 / 317 (1.26%)	4 / 314 (1.27%)	3 / 56 (5.36%)
occurrences (all)	4	4	3
STOMATITIS			
subjects affected / exposed	4 / 317 (1.26%)	3 / 314 (0.96%)	8 / 56 (14.29%)
occurrences (all)	6	3	10
NAUSEA			
subjects affected / exposed	25 / 317 (7.89%)	17 / 314 (5.41%)	4 / 56 (7.14%)
occurrences (all)	28	19	5
Hepatobiliary disorders			
HEPATIC STEATOSIS			
subjects affected / exposed	6 / 317 (1.89%)	6 / 314 (1.91%)	3 / 56 (5.36%)
occurrences (all)	6	6	3
Skin and subcutaneous tissue disorders			
DRY SKIN			
subjects affected / exposed	1 / 317 (0.32%)	1 / 314 (0.32%)	3 / 56 (5.36%)
occurrences (all)	1	1	3
ECZEMA			
subjects affected / exposed	6 / 317 (1.89%)	6 / 314 (1.91%)	5 / 56 (8.93%)
occurrences (all)	7	7	5
DERMATITIS			
subjects affected / exposed	4 / 317 (1.26%)	1 / 314 (0.32%)	3 / 56 (5.36%)
occurrences (all)	4	1	3
RASH			
subjects affected / exposed	8 / 317 (2.52%)	11 / 314 (3.50%)	5 / 56 (8.93%)
occurrences (all)	9	13	5
PRURITUS			
subjects affected / exposed	6 / 317 (1.89%)	5 / 314 (1.59%)	3 / 56 (5.36%)
occurrences (all)	7	6	4
Renal and urinary disorders			
POLLAKIURIA			
subjects affected / exposed	1 / 317 (0.32%)	0 / 314 (0.00%)	3 / 56 (5.36%)
occurrences (all)	1	0	3
Musculoskeletal and connective tissue disorders			

BACK PAIN			
subjects affected / exposed	20 / 317 (6.31%)	20 / 314 (6.37%)	6 / 56 (10.71%)
occurrences (all)	20	27	7
ARTHRALGIA			
subjects affected / exposed	20 / 317 (6.31%)	16 / 314 (5.10%)	3 / 56 (5.36%)
occurrences (all)	31	19	3
INTERVERTEBRAL DISC PROTRUSION			
subjects affected / exposed	5 / 317 (1.58%)	1 / 314 (0.32%)	3 / 56 (5.36%)
occurrences (all)	7	1	3
MYALGIA			
subjects affected / exposed	6 / 317 (1.89%)	3 / 314 (0.96%)	4 / 56 (7.14%)
occurrences (all)	6	3	5
RHEUMATOID ARTHRITIS			
subjects affected / exposed	29 / 317 (9.15%)	11 / 314 (3.50%)	5 / 56 (8.93%)
occurrences (all)	37	12	5
PERIARTHRITIS			
subjects affected / exposed	1 / 317 (0.32%)	1 / 314 (0.32%)	3 / 56 (5.36%)
occurrences (all)	1	1	3
OSTEOPOROSIS			
subjects affected / exposed	4 / 317 (1.26%)	8 / 314 (2.55%)	3 / 56 (5.36%)
occurrences (all)	4	8	3
Infections and infestations			
CONJUNCTIVITIS			
subjects affected / exposed	7 / 317 (2.21%)	4 / 314 (1.27%)	4 / 56 (7.14%)
occurrences (all)	7	4	4
COVID-19			
subjects affected / exposed	28 / 317 (8.83%)	3 / 314 (0.96%)	4 / 56 (7.14%)
occurrences (all)	28	3	4
BRONCHITIS			
subjects affected / exposed	22 / 317 (6.94%)	27 / 314 (8.60%)	9 / 56 (16.07%)
occurrences (all)	26	38	11
GASTROENTERITIS			
subjects affected / exposed	11 / 317 (3.47%)	10 / 314 (3.18%)	9 / 56 (16.07%)
occurrences (all)	14	11	10
CYSTITIS			

subjects affected / exposed	8 / 317 (2.52%)	9 / 314 (2.87%)	6 / 56 (10.71%)
occurrences (all)	10	9	9
HERPES ZOSTER			
subjects affected / exposed	32 / 317 (10.09%)	24 / 314 (7.64%)	13 / 56 (23.21%)
occurrences (all)	38	26	13
INFLUENZA			
subjects affected / exposed	5 / 317 (1.58%)	9 / 314 (2.87%)	10 / 56 (17.86%)
occurrences (all)	5	10	10
NASOPHARYNGITIS			
subjects affected / exposed	48 / 317 (15.14%)	51 / 314 (16.24%)	25 / 56 (44.64%)
occurrences (all)	87	72	59
LATENT TUBERCULOSIS			
subjects affected / exposed	11 / 317 (3.47%)	15 / 314 (4.78%)	0 / 56 (0.00%)
occurrences (all)	11	15	0
ORAL CANDIDIASIS			
subjects affected / exposed	5 / 317 (1.58%)	1 / 314 (0.32%)	4 / 56 (7.14%)
occurrences (all)	9	1	5
PERIODONTITIS			
subjects affected / exposed	4 / 317 (1.26%)	3 / 314 (0.96%)	5 / 56 (8.93%)
occurrences (all)	6	3	5
ORAL HERPES			
subjects affected / exposed	16 / 317 (5.05%)	11 / 314 (3.50%)	8 / 56 (14.29%)
occurrences (all)	21	13	10
SINUSITIS			
subjects affected / exposed	14 / 317 (4.42%)	6 / 314 (1.91%)	3 / 56 (5.36%)
occurrences (all)	27	7	3
TINEA PEDIS			
subjects affected / exposed	4 / 317 (1.26%)	3 / 314 (0.96%)	3 / 56 (5.36%)
occurrences (all)	4	4	3
PHARYNGITIS			
subjects affected / exposed	12 / 317 (3.79%)	17 / 314 (5.41%)	13 / 56 (23.21%)
occurrences (all)	14	22	24
UPPER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	49 / 317 (15.46%)	43 / 314 (13.69%)	9 / 56 (16.07%)
occurrences (all)	88	72	14

URINARY TRACT INFECTION			
subjects affected / exposed	43 / 317 (13.56%)	38 / 314 (12.10%)	1 / 56 (1.79%)
occurrences (all)	93	64	3
Metabolism and nutrition disorders			
DYSLIPIDAEMIA			
subjects affected / exposed	15 / 317 (4.73%)	15 / 314 (4.78%)	5 / 56 (8.93%)
occurrences (all)	17	17	5
HYPERCHOLESTEROLAEMIA			
subjects affected / exposed	17 / 317 (5.36%)	14 / 314 (4.46%)	2 / 56 (3.57%)
occurrences (all)	23	19	2
HYPERLIPIDAEMIA			
subjects affected / exposed	7 / 317 (2.21%)	6 / 314 (1.91%)	4 / 56 (7.14%)
occurrences (all)	8	6	4
HYPERTRIGLYCERIDAEMIA			
subjects affected / exposed	21 / 317 (6.62%)	19 / 314 (6.05%)	0 / 56 (0.00%)
occurrences (all)	31	31	0

Non-serious adverse events	Weeks 1-260: Any Upadacitinib 15 mg	Weeks 1-260/Switch: Any Upadacitinib 30 mg	After Switch: Upadacitinib 15 mg Monotherapy
Total subjects affected by non-serious adverse events			
subjects affected / exposed	272 / 335 (81.19%)	277 / 332 (83.43%)	100 / 181 (55.25%)
Vascular disorders			
HYPERTENSION			
subjects affected / exposed	43 / 335 (12.84%)	47 / 332 (14.16%)	8 / 181 (4.42%)
occurrences (all)	48	51	8
General disorders and administration site conditions			
FATIGUE			
subjects affected / exposed	16 / 335 (4.78%)	3 / 332 (0.90%)	1 / 181 (0.55%)
occurrences (all)	21	3	1
INFLUENZA LIKE ILLNESS			
subjects affected / exposed	21 / 335 (6.27%)	18 / 332 (5.42%)	1 / 181 (0.55%)
occurrences (all)	24	21	1
PYREXIA			
subjects affected / exposed	11 / 335 (3.28%)	9 / 332 (2.71%)	2 / 181 (1.10%)
occurrences (all)	12	9	2
Respiratory, thoracic and mediastinal disorders			

ASTHMA			
subjects affected / exposed	3 / 335 (0.90%)	1 / 332 (0.30%)	0 / 181 (0.00%)
occurrences (all)	3	1	0
COUGH			
subjects affected / exposed	29 / 335 (8.66%)	22 / 332 (6.63%)	3 / 181 (1.66%)
occurrences (all)	35	26	3
RHINITIS ALLERGIC			
subjects affected / exposed	4 / 335 (1.19%)	3 / 332 (0.90%)	1 / 181 (0.55%)
occurrences (all)	4	3	1
Psychiatric disorders			
INSOMNIA			
subjects affected / exposed	17 / 335 (5.07%)	5 / 332 (1.51%)	1 / 181 (0.55%)
occurrences (all)	19	7	1
Investigations			
ALANINE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	32 / 335 (9.55%)	32 / 332 (9.64%)	3 / 181 (1.66%)
occurrences (all)	58	52	4
ASPARTATE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	24 / 335 (7.16%)	27 / 332 (8.13%)	2 / 181 (1.10%)
occurrences (all)	35	36	2
BLOOD CREATINE PHOSPHOKINASE INCREASED			
subjects affected / exposed	46 / 335 (13.73%)	54 / 332 (16.27%)	10 / 181 (5.52%)
occurrences (all)	79	110	14
BLOOD CREATININE INCREASED			
subjects affected / exposed	9 / 335 (2.69%)	9 / 332 (2.71%)	0 / 181 (0.00%)
occurrences (all)	14	15	0
LIVER FUNCTION TEST INCREASED			
subjects affected / exposed	0 / 335 (0.00%)	1 / 332 (0.30%)	0 / 181 (0.00%)
occurrences (all)	0	2	0
LYMPHOCYTE COUNT DECREASED			
subjects affected / exposed	2 / 335 (0.60%)	3 / 332 (0.90%)	1 / 181 (0.55%)
occurrences (all)	2	3	1
NEUTROPHIL COUNT DECREASED			
subjects affected / exposed	5 / 335 (1.49%)	4 / 332 (1.20%)	2 / 181 (1.10%)
occurrences (all)	8	5	2

WEIGHT INCREASED			
subjects affected / exposed	17 / 335 (5.07%)	7 / 332 (2.11%)	1 / 181 (0.55%)
occurrences (all)	19	8	1
WHITE BLOOD CELL COUNT DECREASED			
subjects affected / exposed	2 / 335 (0.60%)	7 / 332 (2.11%)	1 / 181 (0.55%)
occurrences (all)	2	9	1
Injury, poisoning and procedural complications			
CONTUSION			
subjects affected / exposed	11 / 335 (3.28%)	5 / 332 (1.51%)	3 / 181 (1.66%)
occurrences (all)	11	6	4
SPINAL COMPRESSION FRACTURE			
subjects affected / exposed	3 / 335 (0.90%)	0 / 332 (0.00%)	0 / 181 (0.00%)
occurrences (all)	3	0	0
Nervous system disorders			
DIZZINESS			
subjects affected / exposed	9 / 335 (2.69%)	8 / 332 (2.41%)	1 / 181 (0.55%)
occurrences (all)	13	8	1
HEADACHE			
subjects affected / exposed	18 / 335 (5.37%)	28 / 332 (8.43%)	2 / 181 (1.10%)
occurrences (all)	20	33	2
POST HERPETIC NEURALGIA			
subjects affected / exposed	4 / 335 (1.19%)	2 / 332 (0.60%)	0 / 181 (0.00%)
occurrences (all)	4	2	0
Blood and lymphatic system disorders			
ANAEMIA			
subjects affected / exposed	22 / 335 (6.57%)	18 / 332 (5.42%)	4 / 181 (2.21%)
occurrences (all)	34	24	4
LEUKOPENIA			
subjects affected / exposed	11 / 335 (3.28%)	18 / 332 (5.42%)	10 / 181 (5.52%)
occurrences (all)	24	39	14
NEUTROPENIA			
subjects affected / exposed	15 / 335 (4.48%)	27 / 332 (8.13%)	8 / 181 (4.42%)
occurrences (all)	32	56	9
Eye disorders			
CATARACT			

subjects affected / exposed	5 / 335 (1.49%)	3 / 332 (0.90%)	2 / 181 (1.10%)
occurrences (all)	5	4	3
DRY EYE			
subjects affected / exposed	3 / 335 (0.90%)	3 / 332 (0.90%)	1 / 181 (0.55%)
occurrences (all)	3	3	1
Gastrointestinal disorders			
CHRONIC GASTRITIS			
subjects affected / exposed	2 / 335 (0.60%)	3 / 332 (0.90%)	1 / 181 (0.55%)
occurrences (all)	2	3	1
CONSTIPATION			
subjects affected / exposed	13 / 335 (3.88%)	20 / 332 (6.02%)	1 / 181 (0.55%)
occurrences (all)	14	23	1
DENTAL CARIES			
subjects affected / exposed	5 / 335 (1.49%)	4 / 332 (1.20%)	1 / 181 (0.55%)
occurrences (all)	5	4	1
GASTROOESOPHAGEAL REFLUX DISEASE			
subjects affected / exposed	8 / 335 (2.39%)	10 / 332 (3.01%)	0 / 181 (0.00%)
occurrences (all)	8	10	0
DYSPEPSIA			
subjects affected / exposed	13 / 335 (3.88%)	6 / 332 (1.81%)	1 / 181 (0.55%)
occurrences (all)	14	6	1
DIARRHOEA			
subjects affected / exposed	27 / 335 (8.06%)	21 / 332 (6.33%)	3 / 181 (1.66%)
occurrences (all)	36	28	3
HAEMORRHOIDS			
subjects affected / exposed	4 / 335 (1.19%)	4 / 332 (1.20%)	0 / 181 (0.00%)
occurrences (all)	4	4	0
STOMATITIS			
subjects affected / exposed	4 / 335 (1.19%)	3 / 332 (0.90%)	0 / 181 (0.00%)
occurrences (all)	6	4	0
NAUSEA			
subjects affected / exposed	25 / 335 (7.46%)	19 / 332 (5.72%)	1 / 181 (0.55%)
occurrences (all)	30	22	1
Hepatobiliary disorders			

HEPATIC STEATOSIS			
subjects affected / exposed	8 / 335 (2.39%)	7 / 332 (2.11%)	5 / 181 (2.76%)
occurrences (all)	8	7	6
Skin and subcutaneous tissue disorders			
DRY SKIN			
subjects affected / exposed	1 / 335 (0.30%)	1 / 332 (0.30%)	0 / 181 (0.00%)
occurrences (all)	1	1	0
ECZEMA			
subjects affected / exposed	8 / 335 (2.39%)	6 / 332 (1.81%)	3 / 181 (1.66%)
occurrences (all)	9	7	3
DERMATITIS			
subjects affected / exposed	4 / 335 (1.19%)	2 / 332 (0.60%)	0 / 181 (0.00%)
occurrences (all)	4	2	0
RASH			
subjects affected / exposed	9 / 335 (2.69%)	13 / 332 (3.92%)	2 / 181 (1.10%)
occurrences (all)	10	17	2
PRURITUS			
subjects affected / exposed	6 / 335 (1.79%)	5 / 332 (1.51%)	1 / 181 (0.55%)
occurrences (all)	7	6	1
Renal and urinary disorders			
POLLAKIURIA			
subjects affected / exposed	1 / 335 (0.30%)	0 / 332 (0.00%)	0 / 181 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal and connective tissue disorders			
BACK PAIN			
subjects affected / exposed	25 / 335 (7.46%)	23 / 332 (6.93%)	6 / 181 (3.31%)
occurrences (all)	27	30	6
ARTHRALGIA			
subjects affected / exposed	26 / 335 (7.76%)	17 / 332 (5.12%)	3 / 181 (1.66%)
occurrences (all)	40	22	3
INTERVERTEBRAL DISC PROTRUSION			
subjects affected / exposed	6 / 335 (1.79%)	1 / 332 (0.30%)	1 / 181 (0.55%)
occurrences (all)	8	1	1
MYALGIA			
subjects affected / exposed	7 / 335 (2.09%)	5 / 332 (1.51%)	0 / 181 (0.00%)
occurrences (all)	7	5	0

RHEUMATOID ARTHRITIS			
subjects affected / exposed	39 / 335 (11.64%)	12 / 332 (3.61%)	17 / 181 (9.39%)
occurrences (all)	57	14	19
PERIARTHRITIS			
subjects affected / exposed	2 / 335 (0.60%)	1 / 332 (0.30%)	0 / 181 (0.00%)
occurrences (all)	2	1	0
OSTEOPOROSIS			
subjects affected / exposed	6 / 335 (1.79%)	8 / 332 (2.41%)	1 / 181 (0.55%)
occurrences (all)	6	8	1
Infections and infestations			
CONJUNCTIVITIS			
subjects affected / exposed	9 / 335 (2.69%)	4 / 332 (1.20%)	1 / 181 (0.55%)
occurrences (all)	9	4	1
COVID-19			
subjects affected / exposed	37 / 335 (11.04%)	4 / 332 (1.20%)	19 / 181 (10.50%)
occurrences (all)	38	4	20
BRONCHITIS			
subjects affected / exposed	33 / 335 (9.85%)	29 / 332 (8.73%)	5 / 181 (2.76%)
occurrences (all)	37	40	9
GASTROENTERITIS			
subjects affected / exposed	13 / 335 (3.88%)	10 / 332 (3.01%)	1 / 181 (0.55%)
occurrences (all)	17	11	1
CYSTITIS			
subjects affected / exposed	8 / 335 (2.39%)	11 / 332 (3.31%)	5 / 181 (2.76%)
occurrences (all)	10	11	5
HERPES ZOSTER			
subjects affected / exposed	34 / 335 (10.15%)	27 / 332 (8.13%)	7 / 181 (3.87%)
occurrences (all)	42	29	8
INFLUENZA			
subjects affected / exposed	9 / 335 (2.69%)	11 / 332 (3.31%)	2 / 181 (1.10%)
occurrences (all)	9	12	2
NASOPHARYNGITIS			
subjects affected / exposed	57 / 335 (17.01%)	58 / 332 (17.47%)	8 / 181 (4.42%)
occurrences (all)	99	79	10
LATENT TUBERCULOSIS			

subjects affected / exposed	14 / 335 (4.18%)	18 / 332 (5.42%)	2 / 181 (1.10%)
occurrences (all)	14	18	2
ORAL CANDIDIASIS			
subjects affected / exposed	5 / 335 (1.49%)	2 / 332 (0.60%)	0 / 181 (0.00%)
occurrences (all)	9	2	0
PERIODONTITIS			
subjects affected / exposed	4 / 335 (1.19%)	3 / 332 (0.90%)	0 / 181 (0.00%)
occurrences (all)	6	3	0
ORAL HERPES			
subjects affected / exposed	17 / 335 (5.07%)	13 / 332 (3.92%)	1 / 181 (0.55%)
occurrences (all)	22	16	1
SINUSITIS			
subjects affected / exposed	16 / 335 (4.78%)	8 / 332 (2.41%)	2 / 181 (1.10%)
occurrences (all)	29	10	2
TINEA PEDIS			
subjects affected / exposed	6 / 335 (1.79%)	3 / 332 (0.90%)	2 / 181 (1.10%)
occurrences (all)	6	4	2
PHARYNGITIS			
subjects affected / exposed	14 / 335 (4.18%)	18 / 332 (5.42%)	3 / 181 (1.66%)
occurrences (all)	18	23	3
UPPER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	59 / 335 (17.61%)	51 / 332 (15.36%)	5 / 181 (2.76%)
occurrences (all)	102	87	7
URINARY TRACT INFECTION			
subjects affected / exposed	51 / 335 (15.22%)	45 / 332 (13.55%)	13 / 181 (7.18%)
occurrences (all)	107	76	14
Metabolism and nutrition disorders			
DYSLIPIDAEMIA			
subjects affected / exposed	17 / 335 (5.07%)	15 / 332 (4.52%)	2 / 181 (1.10%)
occurrences (all)	22	18	2
HYPERCHOLESTEROLAEMIA			
subjects affected / exposed	19 / 335 (5.67%)	16 / 332 (4.82%)	3 / 181 (1.66%)
occurrences (all)	27	21	3
HYPERLIPIDAEMIA			

subjects affected / exposed	8 / 335 (2.39%)	8 / 332 (2.41%)	1 / 181 (0.55%)
occurrences (all)	9	9	1
HYPERTRIGLYCERIDAEMIA			
subjects affected / exposed	22 / 335 (6.57%)	21 / 332 (6.33%)	4 / 181 (2.21%)
occurrences (all)	33	33	4

Non-serious adverse events	After Switch: Any Upadacitinib 15 mg		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	126 / 218 (57.80%)		
Vascular disorders			
HYPERTENSION			
subjects affected / exposed	10 / 218 (4.59%)		
occurrences (all)	10		
General disorders and administration site conditions			
FATIGUE			
subjects affected / exposed	1 / 218 (0.46%)		
occurrences (all)	1		
INFLUENZA LIKE ILLNESS			
subjects affected / exposed	1 / 218 (0.46%)		
occurrences (all)	1		
PYREXIA			
subjects affected / exposed	3 / 218 (1.38%)		
occurrences (all)	3		
Respiratory, thoracic and mediastinal disorders			
ASTHMA			
subjects affected / exposed	0 / 218 (0.00%)		
occurrences (all)	0		
COUGH			
subjects affected / exposed	3 / 218 (1.38%)		
occurrences (all)	3		
RHINITIS ALLERGIC			
subjects affected / exposed	1 / 218 (0.46%)		
occurrences (all)	1		
Psychiatric disorders			
INSOMNIA			

subjects affected / exposed	1 / 218 (0.46%)		
occurrences (all)	1		
Investigations			
ALANINE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	4 / 218 (1.83%)		
occurrences (all)	5		
ASPARTATE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	3 / 218 (1.38%)		
occurrences (all)	3		
BLOOD CREATINE PHOSPHOKINASE INCREASED			
subjects affected / exposed	12 / 218 (5.50%)		
occurrences (all)	17		
BLOOD CREATININE INCREASED			
subjects affected / exposed	0 / 218 (0.00%)		
occurrences (all)	0		
LIVER FUNCTION TEST INCREASED			
subjects affected / exposed	0 / 218 (0.00%)		
occurrences (all)	0		
LYMPHOCYTE COUNT DECREASED			
subjects affected / exposed	1 / 218 (0.46%)		
occurrences (all)	1		
NEUTROPHIL COUNT DECREASED			
subjects affected / exposed	3 / 218 (1.38%)		
occurrences (all)	3		
WEIGHT INCREASED			
subjects affected / exposed	1 / 218 (0.46%)		
occurrences (all)	1		
WHITE BLOOD CELL COUNT DECREASED			
subjects affected / exposed	1 / 218 (0.46%)		
occurrences (all)	1		
Injury, poisoning and procedural complications			
CONTUSION			
subjects affected / exposed	5 / 218 (2.29%)		
occurrences (all)	6		

SPINAL COMPRESSION FRACTURE subjects affected / exposed occurrences (all)	1 / 218 (0.46%) 1		
Nervous system disorders DIZZINESS subjects affected / exposed occurrences (all) HEADACHE subjects affected / exposed occurrences (all) POST HERPETIC NEURALGIA subjects affected / exposed occurrences (all)	 2 / 218 (0.92%) 2 4 / 218 (1.83%) 4 0 / 218 (0.00%) 0		
Blood and lymphatic system disorders ANAEMIA subjects affected / exposed occurrences (all) LEUKOPENIA subjects affected / exposed occurrences (all) NEUTROPENIA subjects affected / exposed occurrences (all)	 7 / 218 (3.21%) 8 10 / 218 (4.59%) 14 9 / 218 (4.13%) 11		
Eye disorders CATARACT subjects affected / exposed occurrences (all) DRY EYE subjects affected / exposed occurrences (all)	 2 / 218 (0.92%) 3 1 / 218 (0.46%) 1		
Gastrointestinal disorders CHRONIC GASTRITIS subjects affected / exposed occurrences (all) CONSTIPATION subjects affected / exposed occurrences (all)	 1 / 218 (0.46%) 1 1 / 218 (0.46%) 1		

DENTAL CARIES			
subjects affected / exposed	1 / 218 (0.46%)		
occurrences (all)	1		
GASTROOESOPHAGEAL REFLUX DISEASE			
subjects affected / exposed	0 / 218 (0.00%)		
occurrences (all)	0		
DYSPEPSIA			
subjects affected / exposed	1 / 218 (0.46%)		
occurrences (all)	1		
DIARRHOEA			
subjects affected / exposed	3 / 218 (1.38%)		
occurrences (all)	3		
HAEMORRHOIDS			
subjects affected / exposed	0 / 218 (0.00%)		
occurrences (all)	0		
STOMATITIS			
subjects affected / exposed	0 / 218 (0.00%)		
occurrences (all)	0		
NAUSEA			
subjects affected / exposed	3 / 218 (1.38%)		
occurrences (all)	7		
Hepatobiliary disorders			
HEPATIC STEATOSIS			
subjects affected / exposed	5 / 218 (2.29%)		
occurrences (all)	6		
Skin and subcutaneous tissue disorders			
DRY SKIN			
subjects affected / exposed	0 / 218 (0.00%)		
occurrences (all)	0		
ECZEMA			
subjects affected / exposed	3 / 218 (1.38%)		
occurrences (all)	3		
DERMATITIS			
subjects affected / exposed	0 / 218 (0.00%)		
occurrences (all)	0		
RASH			

subjects affected / exposed	2 / 218 (0.92%)		
occurrences (all)	2		
PRURITUS			
subjects affected / exposed	1 / 218 (0.46%)		
occurrences (all)	1		
Renal and urinary disorders			
POLLAKIURIA			
subjects affected / exposed	0 / 218 (0.00%)		
occurrences (all)	0		
Musculoskeletal and connective tissue disorders			
BACK PAIN			
subjects affected / exposed	7 / 218 (3.21%)		
occurrences (all)	7		
ARTHRALGIA			
subjects affected / exposed	6 / 218 (2.75%)		
occurrences (all)	7		
INTERVERTEBRAL DISC PROTRUSION			
subjects affected / exposed	1 / 218 (0.46%)		
occurrences (all)	1		
MYALGIA			
subjects affected / exposed	1 / 218 (0.46%)		
occurrences (all)	1		
RHEUMATOID ARTHRITIS			
subjects affected / exposed	25 / 218 (11.47%)		
occurrences (all)	31		
PERIARTHRITIS			
subjects affected / exposed	0 / 218 (0.00%)		
occurrences (all)	0		
OSTEOPOROSIS			
subjects affected / exposed	3 / 218 (1.38%)		
occurrences (all)	3		
Infections and infestations			
CONJUNCTIVITIS			
subjects affected / exposed	1 / 218 (0.46%)		
occurrences (all)	1		
COVID-19			

subjects affected / exposed	22 / 218 (10.09%)			
occurrences (all)	23			
BRONCHITIS				
subjects affected / exposed	7 / 218 (3.21%)			
occurrences (all)	11			
GASTROENTERITIS				
subjects affected / exposed	1 / 218 (0.46%)			
occurrences (all)	1			
CYSTITIS				
subjects affected / exposed	5 / 218 (2.29%)			
occurrences (all)	5			
HERPES ZOSTER				
subjects affected / exposed	8 / 218 (3.67%)			
occurrences (all)	9			
INFLUENZA				
subjects affected / exposed	2 / 218 (0.92%)			
occurrences (all)	2			
NASOPHARYNGITIS				
subjects affected / exposed	10 / 218 (4.59%)			
occurrences (all)	12			
LATENT TUBERCULOSIS				
subjects affected / exposed	3 / 218 (1.38%)			
occurrences (all)	3			
ORAL CANDIDIASIS				
subjects affected / exposed	0 / 218 (0.00%)			
occurrences (all)	0			
PERIODONTITIS				
subjects affected / exposed	0 / 218 (0.00%)			
occurrences (all)	0			
ORAL HERPES				
subjects affected / exposed	1 / 218 (0.46%)			
occurrences (all)	1			
SINUSITIS				
subjects affected / exposed	3 / 218 (1.38%)			
occurrences (all)	3			
TINEA PEDIS				

subjects affected / exposed	2 / 218 (0.92%)		
occurrences (all)	2		
PHARYNGITIS			
subjects affected / exposed	4 / 218 (1.83%)		
occurrences (all)	4		
UPPER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	7 / 218 (3.21%)		
occurrences (all)	9		
URINARY TRACT INFECTION			
subjects affected / exposed	19 / 218 (8.72%)		
occurrences (all)	21		
Metabolism and nutrition disorders			
DYSLIPIDAEMIA			
subjects affected / exposed	2 / 218 (0.92%)		
occurrences (all)	2		
HYPERCHOLESTEROLAEMIA			
subjects affected / exposed	3 / 218 (1.38%)		
occurrences (all)	3		
HYPERLIPIDAEMIA			
subjects affected / exposed	2 / 218 (0.92%)		
occurrences (all)	2		
HYPERTRIGLYCERIDAEMIA			
subjects affected / exposed	5 / 218 (2.29%)		
occurrences (all)	5		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
15 January 2016	Added Period 2 study objectives. Added 7.5 mg treatment group for subjects in Japan and increased the number of subjects to be enrolled accordingly. Added frequency of methotrexate (MTX) administration. Updated study duration and study design to include a 48-week randomized, double-blind treatment period (Period 1), and to add a long-term extension (Period 2). Clarify the double-blind details and how the blind will be maintained and the Week 24 interim analysis. Added language regarding study drug dose reduction and background RA medication(s). Added the following exclusion criteria: females who are considering becoming pregnant or males considering fathering a child or donating sperm during the study or for up to 180 days after last dose of study drug; subjects with a history of gastrointestinal (GI) perforation or a history of associated GI diseases, with conditions that could interfere with drug absorption, who have been the recipient of an organ transplant, who had significant electrocardiogram (ECG) abnormalities and with a positive result of beta-D-glucan (Japan only). Updated permitted RA therapies. Updated durations of prohibited therapies. Added criteria for rescue therapy at Week 26. Clarified informed consent details. Clarified tuberculosis (TB) testing. Added requirement in Japan that a positive result for hepatitis B surface (HBs) antibody (Ab)/anti-HBs requires hepatitis B virus (HBV) DNA polymerase chain reaction testing and added testing for varicella zoster virus. Updated PK sampling visits. Added efficacy assessments for Period 2; Primary, secondary, and other variables updated to reflect current rationale and planned analyses. Updated discontinuation procedures. Updated rules regarding study drug interruption; clarified that administration of both daily and weekly study drug must be stopped if study drug is interrupted or withdrawn. Updated the AST or ALT specific toxicity management guidelines.
29 February 2016	Updated text to provide clarification for discontinuation criteria. Updated Inclusion Criterion 2 text to avoid ambiguity regarding RA classification criteria. Updated Inclusion Criterion 9 text to clarify pregnancy testing and women of childbearing potential. Updated text to clarify RA optimization therapies. Added criteria for adjusting or adding background medication at Week 26 if subjects do not achieve LDA as defined by CDAI or do not achieve > 20% improvement from baseline in both TJC and SJC. Updated text to clarify Independent Joint Assessor. Updated text to clarify tuberculosis (TB) assessment and testing. Added text that all subjects to have electrocardiogram (ECG) performed at screening and every 48 weeks.
31 May 2016	Added criteria for rescue therapy between Weeks 12 and 24 and between Weeks 36 and 40 if subjects do not achieve ≥ 20% improvement from baseline in both TJC and SJC. Updated text to clarify exceptions for rescue therapy. Added text to follow MTX local label for concomitant treatment contraindications.

18 August 2016	Updated Inclusion Criterion 2 text to select subject population based on duration of symptoms consistent with RA. Updated text to clarify when to administer live vaccines and to provide examples of inactivated vaccines. Added text to describe the addition of MTX for Week 26 rescue therapy. Added requirement to perform pregnancy testing if follicle-stimulating hormone results are consistent with premenopausal status. Updated text to account for local contraception requirements. Added text to clarify different primary efficacy variable for different regulatory purposes. Updated time points for key secondary variables to allow for rescue therapy at Week 12. Added text for local country requirements for Colombia.
26 December 2017	Included approved International Nonproprietary Name. Clarified Period 1 blinding and additional unblinded analyses. Clarified that study drug dose changes are not permitted in unblinded Period 2. Clarified 30-day follow-up visit and premature discontinuation requirements. Added text on oral traditional Chinese medicines. Clarified use of grapefruit; updated list of commonly used strong cytochrome 3A inhibitors and inducers. Clarified that live vaccines may not be administered up to 30 days after last dose of study drug. Added injectable hormonal contraception; clarified contraception requirements for females if childbearing potential status changes. Clarified TB testing and prophylaxis requirements; Added rifapentine as excluded medication. Allowed a pulmonologist to perform chest x-ray assessments. Clarified QT interval calculation. Updated x-ray time points for subjects who prematurely discontinue study drug but continue in the study. Clarified that serum samples may be used to assay study drugs. Updated efficacy variables for different regulatory purposes and to align with the Statistical Analysis Plan. Reduced malignancy and lymphoproliferative disorders to malignancy (all types). Removed hemoglobin effects. Included embolic and thrombotic events as AEs of special interest. Updated text for assessing the relationship of AEs to use of study drug and Suspected Unexpected Serious Adverse Reaction reporting text per sponsor guidelines. Clarified discontinuation criteria for ECG abnormalities. Clarified that all abnormal lab tests considered clinically significant should be followed to resolution. Clarified toxicity management for ALT, AST, international normalized ratio (INR) and for serum creatinine levels within normal reference range. Added text for management of subjects with laboratory values that may indicate active hepatitis. Clarified procedures for elevated creatine phosphokinase without clinical signs and symtoms.

16 December 2019	Changed length of study from 240 weeks to 260 weeks. Changed dosing for subjects from blinded upadacitinib 15 mg and 30 mg QD to upadacitinib 15 mg QD open-label throughout protocol. Specified throughout protocol that subjects receiving MTX will continue receiving MTX open-label. Clarified that restart of study drug after an interruption of > 30 consecutive days is at the discretion of the Investigator. Removed the limit for only two corticosteroid injections. Clarified concurrent use of JAK inhibitors is prohibited during the study. Added excluded biologic therapies to be consistent with current available biologic therapies in RA. Added allowance of systemic use of known strong CYP3A inhibitors or strong CYP3A inducers for subjects not receiving upadacitinib. Added allowance of high potency opiates for analgesic care related to AEs or serious AEs (SAEs) as there is no expected effect on major efficacy outcomes now that the study is in long-term extension. Added guidance for use of live vaccines administration during Period 2 to align with guidelines on live vaccine administration in the setting of immunosuppressive. Removed male contraception requirements for subject receiving upadacitinib, as based on the calculated safety margins for human fetal exposure with seminal fluid transfer, risks to a fetus from a male taking the study drug are not anticipated. Clarified that all cardiac, embolic and thrombotic events will be adjudicated. Added an additional safety precaution for subjects, given the recent concerns raised for the JAK inhibitor class regarding risk of VTE.
01 July 2020	Added allowance for administration of live vaccines during Period 2.
03 December 2020	Clarified that the state of emergency and pandemic-related restrictions may allow mitigation strategies to ensure subject safety and continuity of care as an alternative to discontinuation and AbbVie TA MD role in reviewing cases. Modified study visits and procedures impacted by COVID-19 as follows ●Revised benefit-risk section. ●Verbal consent may be obtained in addition to study informed consent per local regulations. ●Added provisions for virtual or alternative location for study visits; added home healthcare visits and remote monitoring as options. ●Clarified study activities that can be performed by phone/video conference or at local clinic/hospital/laboratory or through the optional home healthcare service, including pregnancy and laboratory testing, and allowed study drug dispensation in such cases. ●Specified that Questionnaires and PhGA cannot be completed virtually and will be completed at the next earliest feasible visit. ●Specified tests that can be performed at the next earliest feasible visit, unless required to ensure safety of continuing study drug, including x-rays, ECG, physical exam, TJC, SJC. ●Added provision allowing Direct-to Patient shipment of study drug and study ancillaries. ●Added guidance for investigators on management of subjects with COVID-19 infection. ●Added supplemental COVID-19 case report forms for missed or virtual visits, study drug interruptions or discontinuations, or AEs and instructions to collect safety data related to COVID-19. ●Added provision for modifications due to protocol deviations that may be due to pandemic to guide investigators to notify IRB/EC when deviations occur. Updated Synopsis to be consistent with Amendment 7. Updated list of commonly used strong cytochrome 3A inducers. Clarified that subjects should discontinue study drug immediately if they develop a GI perforation except for appendicitis or mechanical injury. Clarified and updated the list of the AEs of special interest.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported