Clinical trial results:
A Phase 3, Randomized, Active-Controlled, Double-Blind Study Comparing Upadacitinib (ABT-494) to Abatacept in Subjects With Moderately to Severely Active Rheumatoid Arthritis With Inadequate Response or Intolerance to Biologic DMARDs (bDMARDs) on Stable Conventional Synthetic Disease Modifying Anti-Rheumatic Drugs (csDMARDs)

Summary

EudraCT number	2016-000933-37
Trial protocol	HU DE LV PT SE ES CZ BE NL SK BG IT
Global end of trial date	06 June 2023

Results information

Result version number	v1 (current)
This version publication date	15 June 2024
First version publication date	15 June 2024

Trial information

Trial identification

Sponsor protocol code	M15-925

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03086343
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	AbbVie Deutschland GmbH & Co. KG
Sponsor organisation address	AbbVie House, Vanwall Business Park, Vanwall Road, Maidenhead, Berkshire, United Kingdom, SL6 4UB
Public contact	Global Medical Services, AbbVie, 001 8006339110, abbvieclinicaltrials@abbvie.com
Scientific contact	Global Medical Services, AbbVie, 001 8006339110, abbvieclinicaltrials@abbvie.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	06 June 2023
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	06 June 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The study objective of Period 1 was to compare the safety and efficacy of upadacitinib 15 mg once daily (QD) to abatacept on a background of conventional synthetic disease-modifying antirheumatic drugs (csDMARDs) for the treatment of signs and symptoms of rheumatoid arthritis (RA) in biologic disease-modifying antirheumatic drug (bDMARD)-inadequate response or bDMARD-intolerant participants with moderately to severely active RA. The study objective of Period 2 is to evaluate the long term safety, tolerability, and efficacy of upadacitinib 15 mg QD in participants with RA who had completed Period 1.

Protection of trial subjects:

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

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	09 May 2017
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Argentina: 76
Country: Number of subjects enrolled	Australia: 5
Country: Number of subjects enrolled	Belgium: 1
Country: Number of subjects enrolled	Brazil: 59
Country: Number of subjects enrolled	Bulgaria: 47
Country: Number of subjects enrolled	Canada: 2
Country: Number of subjects enrolled	Czechia: 24
Country: Number of subjects enrolled	Germany: 27
Country: Number of subjects enrolled	Greece: 4
Country: Number of subjects enrolled	Hungary: 20
Country: Number of subjects enrolled	Israel: 13
Country: Number of subjects enrolled	Italy: 2
Country: Number of subjects enrolled	Korea, Republic of: 8
Country: Number of subjects enrolled	Latvia: 4
Country: Number of subjects enrolled	Mexico: 62
Country: Number of subjects enrolled	Netherlands: 9
Country: Number of subjects enrolled	New Zealand: 2
Country: Number of subjects enrolled	Poland: 42

Country: Number of subjects enrolled	Portugal: 23
Country: Number of subjects enrolled	Puerto Rico: 8
Country: Number of subjects enrolled	Romania: 2
Country: Number of subjects enrolled	Russian Federation: 24
Country: Number of subjects enrolled	Spain: 16
Country: Number of subjects enrolled	Sweden: 1
Country: Number of subjects enrolled	Switzerland: 5
Country: Number of subjects enrolled	Türkiye: 3
Country: Number of subjects enrolled	United Kingdom: 3
Country: Number of subjects enrolled	United States: 165
Worldwide total number of subjects	657
EEA total number of subjects	222

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)	512
From 65 to 84 years	143
85 years and over	2

Subject disposition

Recruitment

Recruitment details:

The study had a 24-week, randomized, double-blind, parallel-group, active-controlled period (Period 1) and an open-label long-term extension study (Period 2).
Primary Cohort: Participants enrolled under Amendment 4 or 3.01, randomized to upadacitinib 15 mg QD or abatacept IV/upadacitinib 15 mg QD.

Pre-assignment

Screening details:

30 mg Cohort: Participants enrolled under Amendment 3, randomized to upadacitinib 30 mg QD or abatacept IV/upadacitinib 30 mg QD. Starting with Amendment 5, all participants received open-label upadacitinib 15 mg QD, including those currently on upadacitinib 30 mg QD.

Period 1

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

Blinding implementation details:

All AbbVie personnel with direct oversight of the conduct and management of the trial (with the exception of AbbVie Drug Supply Management Team and unblinded monitors conducting study drug accountability), the Investigator, study site personnel, and the subject will remain blinded to each subject's treatment throughout the study.

Arms

Are arms mutually exclusive?	Yes
Arm title	Primary Cohort: Upadacitinib 15 mg QD

Arm description:

Period 1: One 15 mg upadacitinib oral tablet taken once per day (QD) for 24 weeks.

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

Dosage and administration details:

One 15 mg tablet taken once per day by mouth

Investigational medicinal product name	Placebo for abatacept (0.9% Sodium Chloride Injection or Solution for Infusion)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

IV infusion: Day 1, Weeks 2, 4, 8, 12, 16, and 20

Arm title	Primary Cohort: Abatacept

Arm description:

Period 1: 500 mg (for body weight <60 kg); 750 mg (for body weight 60-100 kg); and 1000 mg (for body weight >100 kg) intravenous (IV) infusion at Baseline, Week 2, Week 4, Week 8, Week 12, Week 16 and Week 20.

Arm type	Experimental

Investigational medicinal product name	Abatacept
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

500 mg (for body weight <60 kg); 750 mg (for body weight 60-100 kg); and 1000 mg (for body weight >100 kg) intravenous (IV) infusion at Baseline, Week 2, Week 4, Week 8, Week 12, Week 16 and Week 20.

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

Dosage and administration details:

matching placebo taken orally QD

Arm title	30 mg Cohort: Upadacitinib 30 mg QD

Arm description:

Period 1: One upadacitinib 30 mg oral tablet QD for 24 weeks.

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

Dosage and administration details:

One 30 mg tablet taken once per day by mouth for 24 weeks

Investigational medicinal product name	Placebo for abatacept (0.9% Sodium Chloride Injection or Solution for Infusion)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

IV infusion: Day 1, Weeks 2, 4, 8, 12, 16, and 20

Arm title	30 mg Cohort: Abatacept

Arm description:

Period 1: 500 mg (for body weight <60 kg); 750 mg (for body weight 60-100 kg); and 1000 mg (for body weight >100 kg) IV infusion at Baseline, Week 2, Week 4, Week 8, Week 12, Week 16 and Week 20.

Arm type	Experimental
Investigational medicinal product name	Abatacept
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

500 mg (for body weight <60 kg); 750 mg (for body weight 60-100 kg); and 1000 mg (for body weight >100 kg) intravenous (IV) infusion at Baseline, Week 2, Week 4, Week 8, Week 12, Week 16 and Week 20

Investigational medicinal product name	Placebo for upadacitinib
Investigational medicinal product code	
Other name	

Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

matching placebo taken orally QD

Number of subjects in period 1[1]	Primary Cohort: Upadacitinib 15 mg QD	Primary Cohort: Abatacept	30 mg Cohort: Upadacitinib 30 mg QD
Started	303	309	21
Completed	278	277	18
Not completed	25	32	3
Consent withdrawn by subject	6	10	-
Adverse Event	7	7	-
Lost to follow-up	1	3	1
Missing	1	-	-
Other, Not Specified	10	12	2

Number of subjects in period 1[1]	30 mg Cohort: Abatacept
Started	23
Completed	21
Not completed	2
Consent withdrawn by subject	-
Adverse Event	1
Lost to follow-up	-
Missing	-
Other, Not Specified	1

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: One participant who was a screen failure was randomized in error and did not receive study drug.

Period 2

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

Arms

Are arms mutually exclusive?	Yes

Arm title	Primary Cohort: Upadacitinib 15 mg QD/Upadacitinib 15 mg QD

Arm description:

Period 1: One 15 mg upadacitinib oral tablet QD for 24 weeks. Period 2: open label upadacitinib 15 mg QD for 192 weeks.

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

Dosage and administration details:

One 15 mg tablet taken once per day by mouth

Arm title	Primary Cohort: Abatacept/Upadacitinib 15 mg QD

Arm description:

Period 1: 500 mg (for body weight <60 kg); 750 mg (for body weight 60-100 kg); and 1000 mg (for body weight >100 kg) IV infusion at Baseline, Week 2, Week 4, Week 8, Week 12, Week 16 and Week 20. Period 2: open label upadacitinib 15 mg QD for 192 weeks.

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

Dosage and administration details:

One 15 mg tablet taken once per day by mouth

Arm title	30 mg Cohort: Upadacitinib 30 mg QD/Upadacitinib 30 mg QD

Arm description:

Period 1: One upadacitinib 30 mg oral tablet QD for 24 weeks. Period 2: open label upadacitinib 30 mg (reduced to 15 mg per Amendment 5) QD for 192 weeks.

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

Dosage and administration details:

One 30 mg tablet taken once per day by mouth

Arm title	30 mg Cohort: Abatacept/Upadacitinib 30 mg QD

Arm description:

Period 1: 500 mg (for body weight <60 kg); 750 mg (for body weight 60-100 kg); and 1000 mg (for body weight >100 kg) IV infusion at Baseline, Week 2, Week 4, Week 8, Week 12, Week 16 and Week 20. Period 2: open label upadacitinib 30 mg (reduced to 15 mg per Amendment 5) QD for 192 weeks.

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

Dosage and administration details:

One 30 mg tablet taken once per day by mouth

Number of subjects in period 2[2]	Primary Cohort: Upadacitinib 15 mg QD/Upadacitinib 15 mg QD	Primary Cohort: Abatacept/Upadacitinib 15 mg QD	30 mg Cohort: Upadacitinib 30 mg QD/Upadacitinib 30 mg QD
Started	277	277	17
Entered Period 2 on Study Drug	271	276	17
Upa Dose Switch From 30 mg to 15 mg QD	0 [3]	0 [4]	12
No Upadacitinib Dose Switch	0 [5]	0 [6]	5 [7]
Completed	207	208	11
Not completed	70	69	6
Consent withdrawn by subject	15	25	2
Adverse Event	20	11	1
COVID-19 Logistical Restrictions	1	-	-
COVID-19 Infection	5	-	-
Lost to follow-up	6	11	1
Other, Not Specified	23	22	2

Number of subjects in period 2[2]	30 mg Cohort: Abatacept/Upadacitinib 30 mg QD
Started	20
Entered Period 2 on Study Drug	19
Upa Dose Switch From 30 mg to 15 mg QD	12
No Upadacitinib Dose Switch	7 [8]
Completed	12
Not completed	8
Consent withdrawn by subject	2
Adverse Event	2
COVID-19 Logistical Restrictions	-
COVID-19 Infection	-
Lost to follow-up	-
Other, Not Specified	4

Notes:

[2] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: Only participants continuing on to Period 2 are included in this table.

[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: Milestone data are presented correctly in this table.

[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: Milestone data are presented correctly in this table.

[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: Milestone data are presented correctly in this table.

[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: Milestone data are presented correctly in this table.

[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: Milestone data are presented correctly in this table.

[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: Milestone data are presented correctly in this table.

Baseline characteristics

Reporting groups	
Reporting group title	Primary Cohort: Upadacitinib 15 mg QD
Reporting group description:	
Period 1: One 15 mg upadacitinib oral tablet taken once per day (QD) for 24 weeks.	
Reporting group title	Primary Cohort: Abatacept
Reporting group description:	
Period 1: 500 mg (for body weight <60 kg); 750 mg (for body weight 60-100 kg); and 1000 mg (for body weight >100 kg) intravenous (IV) infusion at Baseline, Week 2, Week 4, Week 8, Week 12, Week 16 and Week 20.	
Reporting group title	30 mg Cohort: Upadacitinib 30 mg QD
Reporting group description:	
Period 1: One upadacitinib 30 mg oral tablet QD for 24 weeks.	
Reporting group title	30 mg Cohort: Abatacept
Reporting group description:	
Period 1: 500 mg (for body weight <60 kg); 750 mg (for body weight 60-100 kg); and 1000 mg (for body weight >100 kg) IV infusion at Baseline, Week 2, Week 4, Week 8, Week 12, Week 16 and Week 20.	

Reporting group values	Primary Cohort: Upadacitinib 15 mg QD	Primary Cohort: Abatacept	30 mg Cohort: Upadacitinib 30 mg QD
Number of subjects	303	309	21
Age categorical Units: Subjects			
< 40 years	30	31	5
40 - 64 years	209	207	10
≥ 65 years	64	71	6
Gender categorical Units: Subjects			
Female	249	253	16
Male	54	56	5
Race Units: Subjects			
White	288	285	19
Black or African American	7	14	2
American Indian or Alaska Native	1	2	0
Native Hawaiian or other Pacific Islander	0	0	0
Asian	5	6	0
Multiple	2	2	0
Other	0	0	0
Ethnicity Units: Subjects			
Hispanic or Latino	112	117	4
Not Hispanic or Latino	191	192	17
Geographic Region Units: Subjects			
North America	72	73	14
South/Central America	98	99	0

Western Europe	43	45	1
Eastern Europe	77	77	6
Asia	4	4	0
Other	9	11	0
Disease Activity Score Based on C-reactive protein (CRP; DAS28 [CRP])			
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), 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 > 5.1 indicates high disease activity, a DAS28 score ≤ 3.2 indicates low disease activity, and a DAS28 score < 2.6 indicates clinical remission.			
Units: Subjects			
Score > 5.1	224	241	15
Score ≤ 5.1	79	67	4
Score Missing	0	1	2

Reporting group values	30 mg Cohort: Abatacept	Total	
Number of subjects	23	656	
Age categorical Units: Subjects			
< 40 years	2	68	
40 - 64 years	17	443	
≥ 65 years	4	145	
Gender categorical Units: Subjects			
Female	20	538	
Male	3	118	
Race Units: Subjects			
White	20	612	
Black or African American	3	26	
American Indian or Alaska Native	0	3	
Native Hawaiian or other Pacific Islander	0	0	
Asian	0	11	
Multiple	0	4	
Other	0	0	
Ethnicity Units: Subjects			
Hispanic or Latino	5	238	
Not Hispanic or Latino	18	418	
Geographic Region Units: Subjects			
North America	16	175	
South/Central America	0	197	
Western Europe	1	90	
Eastern Europe	6	166	
Asia	0	8	
Other	0	20	
Disease Activity Score Based on C-reactive protein (CRP; DAS28 [CRP])			
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), 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 > 5.1 indicates high disease activity, a DAS28 score ≤ 3.2 indicates low disease activity, and a DAS28 score < 2.6 indicates clinical remission.			
Units: Subjects			
Score > 5.1	19	499	
Score ≤ 5.1	3	153	
Score Missing	1	4	

End points

End points reporting groups

Reporting group title	Primary Cohort: Upadacitinib 15 mg QD
Reporting group description:	
Period 1: One 15 mg upadacitinib oral tablet taken once per day (QD) for 24 weeks.	
Reporting group title	Primary Cohort: Abatacept
Reporting group description:	
Period 1: 500 mg (for body weight <60 kg); 750 mg (for body weight 60-100 kg); and 1000 mg (for body weight >100 kg) intravenous (IV) infusion at Baseline, Week 2, Week 4, Week 8, Week 12, Week 16 and Week 20.	
Reporting group title	30 mg Cohort: Upadacitinib 30 mg QD
Reporting group description:	
Period 1: One upadacitinib 30 mg oral tablet QD for 24 weeks.	
Reporting group title	30 mg Cohort: Abatacept
Reporting group description:	
Period 1: 500 mg (for body weight <60 kg); 750 mg (for body weight 60-100 kg); and 1000 mg (for body weight >100 kg) IV infusion at Baseline, Week 2, Week 4, Week 8, Week 12, Week 16 and Week 20.	
Reporting group title	Primary Cohort: Upadacitinib 15 mg QD/Upadacitinib 15 mg QD
Reporting group description:	
Period 1: One 15 mg upadacitinib oral tablet QD for 24 weeks. Period 2: open label upadacitinib 15 mg QD for 192 weeks.	
Reporting group title	Primary Cohort: Abatacept/Upadacitinib 15 mg QD
Reporting group description:	
Period 1: 500 mg (for body weight <60 kg); 750 mg (for body weight 60-100 kg); and 1000 mg (for body weight >100 kg) IV infusion at Baseline, Week 2, Week 4, Week 8, Week 12, Week 16 and Week 20. Period 2: open label upadacitinib 15 mg QD for 192 weeks.	
Reporting group title	30 mg Cohort: Upadacitinib 30 mg QD/Upadacitinib 30 mg QD
Reporting group description:	
Period 1: One upadacitinib 30 mg oral tablet QD for 24 weeks. Period 2: open label upadacitinib 30 mg (reduced to 15 mg per Amendment 5) QD for 192 weeks.	
Reporting group title	30 mg Cohort: Abatacept/Upadacitinib 30 mg QD
Reporting group description:	
Period 1: 500 mg (for body weight <60 kg); 750 mg (for body weight 60-100 kg); and 1000 mg (for body weight >100 kg) IV infusion at Baseline, Week 2, Week 4, Week 8, Week 12, Week 16 and Week 20. Period 2: open label upadacitinib 30 mg (reduced to 15 mg per Amendment 5) QD for 192 weeks.	

Primary: Change From Baseline in Disease Activity Score (DAS) 28 C-Reactive Protein (CRP) at Week 12 (Non-inferiority)

End point title	Change From Baseline in Disease Activity Score (DAS) 28 C-Reactive Protein (CRP) at Week 12 (Non-inferiority)[1]
End point description:	
The Disease Activity Score (DAS) 28 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 high-sensitivity C-reactive protein (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 indicates improvement in disease activity. Full Analysis Set: all randomized participants who received at least one dose of study drug; multiple imputation was used for missing data.	
End point type	Primary

End point timeframe:

Baseline and Week 12

Notes:

[1] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Primary and Secondary endpoints were analyzed in the Primary Cohorts only.

End point values	Primary Cohort: Upadacitinib 15 mg QD	Primary Cohort: Abatacept		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	303	309		
Units: units on a scale				
least squares mean (confidence interval 95%)	-2.52 (-2.66 to -2.37)	-2.00 (-2.14 to -1.85)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

In order to preserve Type I error, a step-down approach was used to test the primary and ranked secondary endpoints in a pre-specified order where statistical significance at the 0.05 level could be claimed for a lower ranked endpoint only if the previous endpoint in the sequence met the requirements of significance.

Treatment Difference = Upadacitinib 15 mg - Abatacept

Comparison groups	Primary Cohort: Upadacitinib 15 mg QD v Primary Cohort: Abatacept
Number of subjects included in analysis	612
Analysis specification	Pre-specified
Analysis type	non-inferiority[2]
P-value	< 0.001 [3]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.52
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.69
upper limit	-0.35

Notes:

[2] - The non-inferiority of upadacitinib 15 mg versus abatacept was tested using the 95% confidence interval (CI) of treatment difference against a non-inferiority margin of 0.6.
[3] - The ANCOVA model included treatment as the fixed factor; corresponding baseline value and the stratification factor of prior bDMARD used as covariates.

Secondary: Change From Baseline in Disease Activity Score (DAS) 28 C-Reactive Protein (CRP) at Week 12 (Superiority)

End point title	Change From Baseline in Disease Activity Score (DAS) 28 C-Reactive Protein (CRP) at Week 12 (Superiority)[4]

End point description:

The Disease Activity Score (DAS) 28 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 high-

sensitivity C-reactive protein (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 indicates improvement in disease activity.

End point type	Secondary

End point timeframe:

Baseline and Week 12

Notes:

[4] - 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: Primary and Secondary endpoints were analyzed in the Primary Cohorts only.

End point values	Primary Cohort: Upadacitinib 15 mg QD	Primary Cohort: Abatacept		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	303	309		
Units: units on a scale				
least squares mean (confidence interval 95%)	-2.52 (-2.66 to -2.37)	-2.00 (-2.14 to -1.85)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

In order to preserve Type I error, a step-down approach was used to test the primary and ranked secondary endpoints in a pre specified order where statistical significance at the 0.05 level could be claimed for a lower ranked endpoint only if the previous endpoint in the sequence met the requirements of significance.

Treatment Difference = Upadacitinib 15 mg - Abatacept

Comparison groups	Primary Cohort: Upadacitinib 15 mg QD v Primary Cohort: Abatacept
Number of subjects included in analysis	612
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [5]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.52
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.69
upper limit	-0.35

Notes:

[5] - This comparison was a ranked secondary endpoint in the pre-specified multiplicity testing sequence. The ANCOVA model included treatment as the fixed factor; corresponding baseline value and the stratification factor of prior bDMARD used as covariates

Secondary: Percentage of Participants Achieving Clinical Remission (CR) Based on Disease Activity Score (DAS) 28 C-Reactive Protein (CRP) at Week 12 (Superiority)

End point title	Percentage of Participants Achieving Clinical Remission (CR) Based on Disease Activity Score (DAS) 28 C-Reactive Protein (CRP) at Week 12 (Superiority)[6]

End point description:

The Disease Activity Score (DAS) 28 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 high-sensitivity C-reactive protein (hsCRP; in mg/L). Scores on the DAS28 range from 0 to approximately 10, where higher scores indicate more disease activity. A DAS 28 score less than 2.6 indicates clinical remission.

Full Analysis Set: all randomized participants who received at least one dose of study drug; participants who prematurely discontinued study drug were considered non-responders after discontinuation.

End point type	Secondary

End point timeframe:

At Week 12

Notes:

[6] - 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: Primary and Secondary endpoints were analyzed in the Primary Cohorts only.

End point values	Primary Cohort: Upadacitinib 15 mg QD	Primary Cohort: Abatacept		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	303	309		
Units: percentage of participants				
number (confidence interval 95%)	30.0 (24.9 to 35.2)	13.3 (9.5 to 17.1)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

In order to preserve Type I error, a step-down approach was used to test the primary and ranked secondary endpoints in a pre-specified order where statistical significance at the 0.05 level could be claimed for a lower ranked endpoint only if the previous endpoint in the sequence met the requirements of significance.

Treatment Difference = Upadacitinib 15 mg - Abatacept

Comparison groups	Primary Cohort: Upadacitinib 15 mg QD v Primary Cohort: Abatacept
Number of subjects included in analysis	612
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [7]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Mean Difference
Point estimate	16.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	10.4
upper limit	23.2

Notes:

[7] - This comparison was a ranked secondary endpoint in the pre-specified multiplicity testing sequence.

The stratification factor of prior failed bDMARD was used.

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From informed consent until discontinuation of study drug administration (up to 24 weeks for Period 1 and up to 192 weeks for Period 2), plus 70 days.

Adverse event reporting additional description:

Per protocol, for analysis of Period 1 safety data, the Primary and 30 mg Cohorts receiving abatacept were combined.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	22.0

Reporting groups

Reporting group title	Period 2, Primary Cohort:Abatacept/Upadacitinib (Upa) 15 mg QD

Reporting group description:

Period 1: 500 mg (for body weight <60 kg); 750 mg (for body weight 60-100 kg); and 1000 mg (for body weight >100 kg) IV infusion at Baseline, Week 2, Week 4, Week 8, Week 12, Week 16 and Week 20. Period 2: open label upadacitinib 15 mg QD for 192 weeks.

Reporting group title	Period 1, 30 mg Cohort: Upa 30 mg QD

Reporting group description:

Period 1: One upadacitinib 30 mg oral tablet QD for 24 weeks.

Reporting group title	Period 1, Primary Cohort: Upa 15 mg QD

Reporting group description:

Period 1: One 15 mg upadacitinib oral tablet QD for 24 weeks.

Reporting group title	Period 1, Primary and 30 mg Cohorts: Abatacept

Reporting group description:

Period 1: 500 mg (for body weight <60 kg); 750 mg (for body weight 60-100 kg); and 1000 mg (for body weight >100 kg) IV infusion at Baseline, Week 2, Week 4, Week 8, Week 12, Week 16 and Week 20.

Reporting group title	Period 2, 30 mg Cohort: Abatacept/Upa 30 mg QD/Upa 15 mg QD

Reporting group description:

Period 1: 500 mg (for body weight <60 kg); 750 mg (for body weight 60-100 kg); and 1000 mg (for body weight >100 kg) IV infusion at Baseline, Week 2, Week 4, Week 8, Week 12, Week 16 and Week 20. Period 2: open label upadacitinib 30 mg QD followed by upadacitinib 15 mg QD for a total of 192 weeks.

Reporting group title	Period 2, 30mg Cohort: Upa 30 mg QD/Upa 30 mg QD

Reporting group description:

Period 1: One upadacitinib 30 mg oral tablet taken once per day (QD) for 24 weeks. Period 2: open label upadacitinib 30 mg QD for 192 weeks.

Reporting group title	Period 2, 30 mg Cohort: Abatacept/Upa 30 mg QD

Reporting group description:

Period 1: 500 mg (for body weight <60 kg); 750 mg (for body weight 60-100 kg); and 1000 mg (for body weight >100 kg) IV infusion at Baseline, Week 2, Week 4, Week 8, Week 12, Week 16 and Week 20. Period 2: open label upadacitinib 30 mg QD for 192 weeks.

Reporting group title	Period 2, 30 mg Cohort: Upa 30 mg QD/Upa 30 mg QD/Upa 15 mg QD

Reporting group description:

Period 1: One upadacitinib 30 mg oral tablet QD for 24 weeks. Period 2: open label upadacitinib 30 mg QD followed by upadacitinib 15 mg QD for a total of 192 weeks.

Reporting group title	Period 2, Primary Cohort: Upa 15 mg QD/Upa 15 mg QD

Reporting group description:

Period 1: One 15 mg upadacitinib oral tablet QD for 24 weeks. Period 2: open label upadacitinib 15 mg QD for 192 weeks.

Serious adverse events	Period 2, Primary Cohort:Abatacept/Upadacitinib (Upa) 15 mg QD	Period 1, 30 mg Cohort: Upa 30 mg QD	Period 1, Primary Cohort: Upa 15 mg QD
Total subjects affected by serious adverse events			
subjects affected / exposed	68 / 276 (24.64%)	4 / 21 (19.05%)	12 / 303 (3.96%)
number of deaths (all causes)	7	0	2
number of deaths resulting from adverse events	1	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
COLORECTAL ADENOMA			
subjects affected / exposed	1 / 276 (0.36%)	0 / 21 (0.00%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
INTESTINAL METASTASIS			
subjects affected / exposed	0 / 276 (0.00%)	0 / 21 (0.00%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
INVASIVE DUCTAL BREAST CARCINOMA			
subjects affected / exposed	1 / 276 (0.36%)	0 / 21 (0.00%)	0 / 303 (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
INVASIVE BREAST CARCINOMA			
subjects affected / exposed	1 / 276 (0.36%)	0 / 21 (0.00%)	0 / 303 (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
KAPOSI'S SARCOMA			
subjects affected / exposed	0 / 276 (0.00%)	0 / 21 (0.00%)	0 / 303 (0.00%)
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 STAGE IV			

subjects affected / exposed	0 / 276 (0.00%)	0 / 21 (0.00%)	0 / 303 (0.00%)
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 CARCINOMA CELL TYPE UNSPECIFIED STAGE IV			
subjects affected / exposed	0 / 276 (0.00%)	0 / 21 (0.00%)	0 / 303 (0.00%)
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 / 276 (0.00%)	0 / 21 (0.00%)	0 / 303 (0.00%)
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 NEOPLASM MALIGNANT			
subjects affected / exposed	0 / 276 (0.00%)	0 / 21 (0.00%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
RECTAL CANCER			
subjects affected / exposed	0 / 276 (0.00%)	0 / 21 (0.00%)	0 / 303 (0.00%)
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 EPITHELIAL CANCER METASTATIC			
subjects affected / exposed	0 / 276 (0.00%)	0 / 21 (0.00%)	0 / 303 (0.00%)
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-SECRETORY ADENOMA OF PITUITARY			
subjects affected / exposed	1 / 276 (0.36%)	0 / 21 (0.00%)	0 / 303 (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 LIVER			
subjects affected / exposed	0 / 276 (0.00%)	0 / 21 (0.00%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
MANTLE CELL LYMPHOMA			

subjects affected / exposed	1 / 276 (0.36%)	0 / 21 (0.00%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
UTERINE LEIOMYOMA			
subjects affected / exposed	1 / 276 (0.36%)	0 / 21 (0.00%)	0 / 303 (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
UTERINE CANCER			
subjects affected / exposed	0 / 276 (0.00%)	0 / 21 (0.00%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SMALL CELL LUNG CANCER			
subjects affected / exposed	1 / 276 (0.36%)	0 / 21 (0.00%)	0 / 303 (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			
AORTIC INTRAMURAL HAEMATOMA			
subjects affected / exposed	0 / 276 (0.00%)	0 / 21 (0.00%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DEEP VEIN THROMBOSIS			
subjects affected / exposed	1 / 276 (0.36%)	0 / 21 (0.00%)	0 / 303 (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
HYPERTENSION			
subjects affected / exposed	0 / 276 (0.00%)	0 / 21 (0.00%)	1 / 303 (0.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PERIPHERAL ARTERY OCCLUSION			
subjects affected / exposed	1 / 276 (0.36%)	0 / 21 (0.00%)	0 / 303 (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
Surgical and medical procedures			

ARTHRODESIS			
subjects affected / exposed	1 / 276 (0.36%)	0 / 21 (0.00%)	0 / 303 (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
KNEE ARTHROPLASTY			
subjects affected / exposed	0 / 276 (0.00%)	0 / 21 (0.00%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
WOUND DRAINAGE			
subjects affected / exposed	0 / 276 (0.00%)	0 / 21 (0.00%)	0 / 303 (0.00%)
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	1 / 276 (0.36%)	0 / 21 (0.00%)	1 / 303 (0.33%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
CHEST PAIN			
subjects affected / exposed	0 / 276 (0.00%)	0 / 21 (0.00%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DEATH			
subjects affected / exposed	1 / 276 (0.36%)	0 / 21 (0.00%)	0 / 303 (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
FAT NECROSIS			
subjects affected / exposed	0 / 276 (0.00%)	0 / 21 (0.00%)	0 / 303 (0.00%)
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 / 276 (0.00%)	0 / 21 (0.00%)	0 / 303 (0.00%)
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			
subjects affected / exposed	0 / 276 (0.00%)	0 / 21 (0.00%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
CERVICAL DYSPLASIA			
subjects affected / exposed	1 / 276 (0.36%)	0 / 21 (0.00%)	0 / 303 (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
ADNEXA UTERI CYST			
subjects affected / exposed	1 / 276 (0.36%)	0 / 21 (0.00%)	0 / 303 (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
ENDOMETRIOSIS			
subjects affected / exposed	0 / 276 (0.00%)	0 / 21 (0.00%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
INTERMENSTRUAL BLEEDING			
subjects affected / exposed	1 / 276 (0.36%)	0 / 21 (0.00%)	0 / 303 (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
MENOMETRORRHAGIA			
subjects affected / exposed	0 / 276 (0.00%)	0 / 21 (0.00%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PELVIC ORGAN PROLAPSE			
subjects affected / exposed	0 / 276 (0.00%)	0 / 21 (0.00%)	0 / 303 (0.00%)
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 HAEMORRHAGE			

subjects affected / exposed	0 / 276 (0.00%)	0 / 21 (0.00%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
VAGINAL PROLAPSE			
subjects affected / exposed	0 / 276 (0.00%)	0 / 21 (0.00%)	0 / 303 (0.00%)
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 DISTRESS SYNDROME			
subjects affected / exposed	0 / 276 (0.00%)	0 / 21 (0.00%)	0 / 303 (0.00%)
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 RESPIRATORY FAILURE			
subjects affected / exposed	1 / 276 (0.36%)	0 / 21 (0.00%)	0 / 303 (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 / 276 (0.00%)	0 / 21 (0.00%)	0 / 303 (0.00%)
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 / 276 (0.00%)	0 / 21 (0.00%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DYSPHONIA			
subjects affected / exposed	0 / 276 (0.00%)	0 / 21 (0.00%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
EPISTAXIS			
subjects affected / exposed	0 / 276 (0.00%)	0 / 21 (0.00%)	1 / 303 (0.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

PLEURAL EFFUSION			
subjects affected / exposed	0 / 276 (0.00%)	0 / 21 (0.00%)	1 / 303 (0.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PNEUMONITIS			
subjects affected / exposed	1 / 276 (0.36%)	0 / 21 (0.00%)	0 / 303 (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
PULMONARY EMBOLISM			
subjects affected / exposed	2 / 276 (0.72%)	0 / 21 (0.00%)	1 / 303 (0.33%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
UPPER-AIRWAY COUGH SYNDROME			
subjects affected / exposed	0 / 276 (0.00%)	0 / 21 (0.00%)	0 / 303 (0.00%)
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			
ACUTE PSYCHOSIS			
subjects affected / exposed	0 / 276 (0.00%)	0 / 21 (0.00%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ALCOHOL WITHDRAWAL SYNDROME			
subjects affected / exposed	1 / 276 (0.36%)	0 / 21 (0.00%)	0 / 303 (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
ALCOHOL ABUSE			
subjects affected / exposed	1 / 276 (0.36%)	0 / 21 (0.00%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
ARTHROPOD BITE			
subjects affected / exposed	0 / 276 (0.00%)	1 / 21 (4.76%)	0 / 303 (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

COMMINUTED FRACTURE			
subjects affected / exposed	0 / 276 (0.00%)	0 / 21 (0.00%)	0 / 303 (0.00%)
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	2 / 276 (0.72%)	0 / 21 (0.00%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
FEMUR FRACTURE			
subjects affected / exposed	0 / 276 (0.00%)	0 / 21 (0.00%)	0 / 303 (0.00%)
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 / 276 (0.00%)	0 / 21 (0.00%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
FOREARM FRACTURE			
subjects affected / exposed	1 / 276 (0.36%)	0 / 21 (0.00%)	0 / 303 (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
FIBULA FRACTURE			
subjects affected / exposed	1 / 276 (0.36%)	0 / 21 (0.00%)	0 / 303 (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
JOINT DISLOCATION			
subjects affected / exposed	0 / 276 (0.00%)	0 / 21 (0.00%)	0 / 303 (0.00%)
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	1 / 276 (0.36%)	0 / 21 (0.00%)	0 / 303 (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
MENISCUS INJURY			

subjects affected / exposed	1 / 276 (0.36%)	0 / 21 (0.00%)	0 / 303 (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
PATELLA FRACTURE			
subjects affected / exposed	1 / 276 (0.36%)	1 / 21 (4.76%)	0 / 303 (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
PELVIC FRACTURE			
subjects affected / exposed	0 / 276 (0.00%)	0 / 21 (0.00%)	1 / 303 (0.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
RADIUS FRACTURE			
subjects affected / exposed	1 / 276 (0.36%)	0 / 21 (0.00%)	0 / 303 (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	2 / 276 (0.72%)	0 / 21 (0.00%)	0 / 303 (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
TIBIA FRACTURE			
subjects affected / exposed	1 / 276 (0.36%)	0 / 21 (0.00%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
TENDON RUPTURE			
subjects affected / exposed	0 / 276 (0.00%)	0 / 21 (0.00%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SPINAL COMPRESSION FRACTURE			
subjects affected / exposed	0 / 276 (0.00%)	0 / 21 (0.00%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SYNOVIAL RUPTURE			

subjects affected / exposed	0 / 276 (0.00%)	0 / 21 (0.00%)	0 / 303 (0.00%)
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 / 276 (0.36%)	0 / 21 (0.00%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
ATRIAL FIBRILLATION			
subjects affected / exposed	1 / 276 (0.36%)	0 / 21 (0.00%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ANGINA UNSTABLE			
subjects affected / exposed	0 / 276 (0.00%)	0 / 21 (0.00%)	0 / 303 (0.00%)
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 / 276 (0.00%)	0 / 21 (0.00%)	0 / 303 (0.00%)
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 / 276 (0.00%)	0 / 21 (0.00%)	1 / 303 (0.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CARDIAC FAILURE			
subjects affected / exposed	0 / 276 (0.00%)	0 / 21 (0.00%)	0 / 303 (0.00%)
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	0 / 276 (0.00%)	0 / 21 (0.00%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ATRIOVENTRICULAR BLOCK COMPLETE			

subjects affected / exposed	1 / 276 (0.36%)	0 / 21 (0.00%)	1 / 303 (0.33%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Nervous system disorders			
CAUDA EQUINA SYNDROME			
subjects affected / exposed	1 / 276 (0.36%)	0 / 21 (0.00%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CAROTID ARTERY STENOSIS			
subjects affected / exposed	1 / 276 (0.36%)	0 / 21 (0.00%)	0 / 303 (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
CEREBROVASCULAR ACCIDENT			
subjects affected / exposed	2 / 276 (0.72%)	0 / 21 (0.00%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 2	0 / 0	0 / 0
DIZZINESS			
subjects affected / exposed	1 / 276 (0.36%)	0 / 21 (0.00%)	0 / 303 (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
HEADACHE			
subjects affected / exposed	0 / 276 (0.00%)	0 / 21 (0.00%)	0 / 303 (0.00%)
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 RADICULOPATHY			
subjects affected / exposed	1 / 276 (0.36%)	0 / 21 (0.00%)	0 / 303 (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
ISCHAEMIC STROKE			
subjects affected / exposed	0 / 276 (0.00%)	0 / 21 (0.00%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HEMIPARESIS			

subjects affected / exposed	0 / 276 (0.00%)	0 / 21 (0.00%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
MIGRAINE			
subjects affected / exposed	0 / 276 (0.00%)	1 / 21 (4.76%)	0 / 303 (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
SPONDYLITIC MYELOPATHY			
subjects affected / exposed	0 / 276 (0.00%)	0 / 21 (0.00%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
OCCIPITAL NEURALGIA			
subjects affected / exposed	0 / 276 (0.00%)	0 / 21 (0.00%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
MOTOR NEURONE DISEASE			
subjects affected / exposed	0 / 276 (0.00%)	0 / 21 (0.00%)	1 / 303 (0.33%)
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 / 276 (0.00%)	0 / 21 (0.00%)	0 / 303 (0.00%)
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 / 276 (0.00%)	0 / 21 (0.00%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
NEUTROPENIA			
subjects affected / exposed	1 / 276 (0.36%)	0 / 21 (0.00%)	0 / 303 (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
Ear and labyrinth disorders			

VERTIGO POSITIONAL			
subjects affected / exposed	0 / 276 (0.00%)	0 / 21 (0.00%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
RETINAL DETACHMENT			
subjects affected / exposed	0 / 276 (0.00%)	0 / 21 (0.00%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DACRYOSTENOSIS ACQUIRED			
subjects affected / exposed	0 / 276 (0.00%)	0 / 21 (0.00%)	0 / 303 (0.00%)
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			
subjects affected / exposed	0 / 276 (0.00%)	1 / 21 (4.76%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
ABDOMINAL PAIN			
subjects affected / exposed	0 / 276 (0.00%)	1 / 21 (4.76%)	0 / 303 (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
ENTERITIS			
subjects affected / exposed	0 / 276 (0.00%)	0 / 21 (0.00%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DYSPHAGIA			
subjects affected / exposed	0 / 276 (0.00%)	0 / 21 (0.00%)	0 / 303 (0.00%)
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 / 276 (0.00%)	0 / 21 (0.00%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

DIARRHOEA			
subjects affected / exposed	0 / 276 (0.00%)	0 / 21 (0.00%)	0 / 303 (0.00%)
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 DISORDER			
subjects affected / exposed	0 / 276 (0.00%)	0 / 21 (0.00%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
INTRA-ABDOMINAL HAEMORRHAGE			
subjects affected / exposed	0 / 276 (0.00%)	0 / 21 (0.00%)	0 / 303 (0.00%)
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	2 / 276 (0.72%)	0 / 21 (0.00%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ILEUS			
subjects affected / exposed	1 / 276 (0.36%)	0 / 21 (0.00%)	0 / 303 (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
HAEMORRHOIDS			
subjects affected / exposed	0 / 276 (0.00%)	0 / 21 (0.00%)	1 / 303 (0.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
LARGE INTESTINE POLYP			
subjects affected / exposed	1 / 276 (0.36%)	0 / 21 (0.00%)	0 / 303 (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
NAUSEA			
subjects affected / exposed	0 / 276 (0.00%)	1 / 21 (4.76%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PANCREATITIS			

subjects affected / exposed	1 / 276 (0.36%)	0 / 21 (0.00%)	0 / 303 (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
PANCREATITIS ACUTE			
subjects affected / exposed	1 / 276 (0.36%)	0 / 21 (0.00%)	0 / 303 (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
VOLVULUS OF SMALL BOWEL			
subjects affected / exposed	0 / 276 (0.00%)	0 / 21 (0.00%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
VOMITING			
subjects affected / exposed	0 / 276 (0.00%)	1 / 21 (4.76%)	0 / 303 (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			
BILIARY COLIC			
subjects affected / exposed	0 / 276 (0.00%)	0 / 21 (0.00%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BILIARY OBSTRUCTION			
subjects affected / exposed	0 / 276 (0.00%)	0 / 21 (0.00%)	0 / 303 (0.00%)
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			
subjects affected / exposed	0 / 276 (0.00%)	0 / 21 (0.00%)	0 / 303 (0.00%)
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	2 / 276 (0.72%)	0 / 21 (0.00%)	0 / 303 (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
Renal and urinary disorders			

ACUTE KIDNEY INJURY			
subjects affected / exposed	1 / 276 (0.36%)	0 / 21 (0.00%)	0 / 303 (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
Endocrine disorders			
GOITRE			
subjects affected / exposed	1 / 276 (0.36%)	0 / 21 (0.00%)	0 / 303 (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
HYPERPARATHYROIDISM			
subjects affected / exposed	1 / 276 (0.36%)	0 / 21 (0.00%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
ARTHRALGIA			
subjects affected / exposed	0 / 276 (0.00%)	0 / 21 (0.00%)	0 / 303 (0.00%)
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 DEFORMITY			
subjects affected / exposed	1 / 276 (0.36%)	0 / 21 (0.00%)	0 / 303 (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 SPINAL STENOSIS			
subjects affected / exposed	0 / 276 (0.00%)	0 / 21 (0.00%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
FRACTURE PAIN			
subjects affected / exposed	0 / 276 (0.00%)	0 / 21 (0.00%)	0 / 303 (0.00%)
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	3 / 276 (1.09%)	0 / 21 (0.00%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 5	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
INTERVERTEBRAL DISC DEGENERATION			
subjects affected / exposed	1 / 276 (0.36%)	0 / 21 (0.00%)	0 / 303 (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	5 / 276 (1.81%)	0 / 21 (0.00%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 5	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
RHEUMATOID ARTHRITIS			
subjects affected / exposed	0 / 276 (0.00%)	0 / 21 (0.00%)	0 / 303 (0.00%)
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 / 276 (0.00%)	0 / 21 (0.00%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SPINAL OSTEOARTHRITIS			
subjects affected / exposed	1 / 276 (0.36%)	0 / 21 (0.00%)	0 / 303 (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
SPINAL STENOSIS			
subjects affected / exposed	1 / 276 (0.36%)	0 / 21 (0.00%)	0 / 303 (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
SYNOVIAL CYST			
subjects affected / exposed	0 / 276 (0.00%)	0 / 21 (0.00%)	1 / 303 (0.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
BACTERIAL SEPSIS			

subjects affected / exposed	0 / 276 (0.00%)	0 / 21 (0.00%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ARTHRITIS BACTERIAL			
subjects affected / exposed	0 / 276 (0.00%)	0 / 21 (0.00%)	1 / 303 (0.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ABSCESS SOFT TISSUE			
subjects affected / exposed	1 / 276 (0.36%)	0 / 21 (0.00%)	0 / 303 (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
COVID-19			
subjects affected / exposed	4 / 276 (1.45%)	0 / 21 (0.00%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	1 / 4	0 / 0	0 / 0
deaths causally related to treatment / all	1 / 2	0 / 0	0 / 0
BURSITIS INFECTIVE			
subjects affected / exposed	0 / 276 (0.00%)	0 / 21 (0.00%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BRONCHITIS			
subjects affected / exposed	0 / 276 (0.00%)	0 / 21 (0.00%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BONE ABSCESS			
subjects affected / exposed	1 / 276 (0.36%)	0 / 21 (0.00%)	0 / 303 (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
COVID-19 PNEUMONIA			
subjects affected / exposed	6 / 276 (2.17%)	0 / 21 (0.00%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	1 / 6	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
CELLULITIS STAPHYLOCOCCAL			

subjects affected / exposed	0 / 276 (0.00%)	1 / 21 (4.76%)	0 / 303 (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
DEVICE RELATED INFECTION			
subjects affected / exposed	0 / 276 (0.00%)	0 / 21 (0.00%)	0 / 303 (0.00%)
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 URINARY TRACT INFECTION			
subjects affected / exposed	1 / 276 (0.36%)	0 / 21 (0.00%)	0 / 303 (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
DIVERTICULITIS			
subjects affected / exposed	1 / 276 (0.36%)	0 / 21 (0.00%)	0 / 303 (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
GASTROENTERITIS VIRAL			
subjects affected / exposed	1 / 276 (0.36%)	0 / 21 (0.00%)	0 / 303 (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
INFECTIOUS PLEURAL EFFUSION			
subjects affected / exposed	0 / 276 (0.00%)	0 / 21 (0.00%)	0 / 303 (0.00%)
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	1 / 276 (0.36%)	0 / 21 (0.00%)	0 / 303 (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
MEDICAL DEVICE SITE ABSCESS			
subjects affected / exposed	1 / 276 (0.36%)	0 / 21 (0.00%)	0 / 303 (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
OPHTHALMIC HERPES ZOSTER			

subjects affected / exposed	0 / 276 (0.00%)	0 / 21 (0.00%)	0 / 303 (0.00%)
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 / 276 (0.00%)	0 / 21 (0.00%)	0 / 303 (0.00%)
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	3 / 276 (1.09%)	0 / 21 (0.00%)	1 / 303 (0.33%)
occurrences causally related to treatment / all	3 / 3	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PNEUMONIA BACTERIAL			
subjects affected / exposed	1 / 276 (0.36%)	0 / 21 (0.00%)	0 / 303 (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 VIRAL			
subjects affected / exposed	0 / 276 (0.00%)	0 / 21 (0.00%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
POSTOPERATIVE WOUND INFECTION			
subjects affected / exposed	1 / 276 (0.36%)	0 / 21 (0.00%)	0 / 303 (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
PYELONEPHRITIS			
subjects affected / exposed	1 / 276 (0.36%)	0 / 21 (0.00%)	1 / 303 (0.33%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PYELONEPHRITIS CHRONIC			
subjects affected / exposed	1 / 276 (0.36%)	0 / 21 (0.00%)	0 / 303 (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 TRACT INFECTION			

subjects affected / exposed	1 / 276 (0.36%)	0 / 21 (0.00%)	0 / 303 (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 / 276 (0.72%)	0 / 21 (0.00%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SOFT TISSUE INFECTION			
subjects affected / exposed	0 / 276 (0.00%)	1 / 21 (4.76%)	0 / 303 (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
SKIN INFECTION			
subjects affected / exposed	0 / 276 (0.00%)	1 / 21 (4.76%)	0 / 303 (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
SEPTIC SHOCK			
subjects affected / exposed	0 / 276 (0.00%)	0 / 21 (0.00%)	0 / 303 (0.00%)
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 BACTERAEMIA			
subjects affected / exposed	0 / 276 (0.00%)	0 / 21 (0.00%)	0 / 303 (0.00%)
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	1 / 276 (0.36%)	0 / 21 (0.00%)	0 / 303 (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
URINARY TRACT INFECTION			
subjects affected / exposed	4 / 276 (1.45%)	0 / 21 (0.00%)	0 / 303 (0.00%)
occurrences causally related to treatment / all	3 / 5	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
HYPONATRAEMIA			

subjects affected / exposed	0 / 276 (0.00%)	0 / 21 (0.00%)	0 / 303 (0.00%)
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	1 / 276 (0.36%)	0 / 21 (0.00%)	0 / 303 (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
DEHYDRATION			
subjects affected / exposed	1 / 276 (0.36%)	0 / 21 (0.00%)	1 / 303 (0.33%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CENTRAL OBESITY			
subjects affected / exposed	1 / 276 (0.36%)	0 / 21 (0.00%)	0 / 303 (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	Period 1, Primary and 30 mg Cohorts: Abatacept	Period 2, 30 mg Cohort: Abatacept/Upa 30 mg QD/Upa 15 mg QD	Period 2, 30mg Cohort: Upa 30 mg QD/Upa 30 mg QD
Total subjects affected by serious adverse events			
subjects affected / exposed	7 / 332 (2.11%)	3 / 12 (25.00%)	6 / 17 (35.29%)
number of deaths (all causes)	1	1	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
COLORECTAL ADENOMA			
subjects affected / exposed	0 / 332 (0.00%)	0 / 12 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
INTESTINAL METASTASIS			
subjects affected / exposed	0 / 332 (0.00%)	0 / 12 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
INVASIVE DUCTAL BREAST CARCINOMA			

subjects affected / exposed	0 / 332 (0.00%)	0 / 12 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
INVASIVE BREAST CARCINOMA			
subjects affected / exposed	0 / 332 (0.00%)	0 / 12 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
KAPOSI'S SARCOMA			
subjects affected / exposed	0 / 332 (0.00%)	0 / 12 (0.00%)	0 / 17 (0.00%)
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 STAGE IV			
subjects affected / exposed	0 / 332 (0.00%)	0 / 12 (0.00%)	0 / 17 (0.00%)
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 CARCINOMA CELL TYPE UNSPECIFIED STAGE IV			
subjects affected / exposed	0 / 332 (0.00%)	0 / 12 (0.00%)	0 / 17 (0.00%)
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 / 332 (0.00%)	0 / 12 (0.00%)	0 / 17 (0.00%)
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 NEOPLASM MALIGNANT			
subjects affected / exposed	0 / 332 (0.00%)	0 / 12 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
RECTAL CANCER			
subjects affected / exposed	0 / 332 (0.00%)	0 / 12 (0.00%)	0 / 17 (0.00%)
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 EPITHELIAL CANCER METASTATIC			

subjects affected / exposed	0 / 332 (0.00%)	0 / 12 (0.00%)	0 / 17 (0.00%)
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-SECRETORY ADENOMA OF PITUITARY			
subjects affected / exposed	0 / 332 (0.00%)	0 / 12 (0.00%)	0 / 17 (0.00%)
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 LIVER			
subjects affected / exposed	0 / 332 (0.00%)	0 / 12 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
MANTLE CELL LYMPHOMA			
subjects affected / exposed	0 / 332 (0.00%)	0 / 12 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
UTERINE LEIOMYOMA			
subjects affected / exposed	0 / 332 (0.00%)	0 / 12 (0.00%)	0 / 17 (0.00%)
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 / 332 (0.00%)	0 / 12 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SMALL CELL LUNG CANCER			
subjects affected / exposed	0 / 332 (0.00%)	0 / 12 (0.00%)	0 / 17 (0.00%)
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			
AORTIC INTRAMURAL HAEMATOMA			
subjects affected / exposed	0 / 332 (0.00%)	0 / 12 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DEEP VEIN THROMBOSIS			

subjects affected / exposed	0 / 332 (0.00%)	0 / 12 (0.00%)	0 / 17 (0.00%)
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 / 332 (0.00%)	0 / 12 (0.00%)	0 / 17 (0.00%)
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 OCCLUSION			
subjects affected / exposed	0 / 332 (0.00%)	0 / 12 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Surgical and medical procedures			
ARTHRODESIS			
subjects affected / exposed	0 / 332 (0.00%)	0 / 12 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
KNEE ARTHROPLASTY			
subjects affected / exposed	0 / 332 (0.00%)	0 / 12 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
WOUND DRAINAGE			
subjects affected / exposed	0 / 332 (0.00%)	0 / 12 (0.00%)	0 / 17 (0.00%)
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 / 332 (0.00%)	0 / 12 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
CHEST PAIN			

subjects affected / exposed	0 / 332 (0.00%)	0 / 12 (0.00%)	0 / 17 (0.00%)
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 / 332 (0.00%)	0 / 12 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
FAT NECROSIS			
subjects affected / exposed	0 / 332 (0.00%)	0 / 12 (0.00%)	0 / 17 (0.00%)
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 / 332 (0.00%)	0 / 12 (0.00%)	0 / 17 (0.00%)
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			
subjects affected / exposed	0 / 332 (0.00%)	0 / 12 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
CERVICAL DYSPLASIA			
subjects affected / exposed	0 / 332 (0.00%)	0 / 12 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ADNEXA UTERI CYST			
subjects affected / exposed	0 / 332 (0.00%)	0 / 12 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ENDOMETRIOSIS			
subjects affected / exposed	0 / 332 (0.00%)	0 / 12 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
INTERMENSTRUAL BLEEDING			

subjects affected / exposed	0 / 332 (0.00%)	0 / 12 (0.00%)	0 / 17 (0.00%)
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 / 332 (0.00%)	0 / 12 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PELVIC ORGAN PROLAPSE			
subjects affected / exposed	0 / 332 (0.00%)	0 / 12 (0.00%)	0 / 17 (0.00%)
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 HAEMORRHAGE			
subjects affected / exposed	0 / 332 (0.00%)	0 / 12 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
VAGINAL PROLAPSE			
subjects affected / exposed	0 / 332 (0.00%)	0 / 12 (0.00%)	0 / 17 (0.00%)
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 DISTRESS SYNDROME			
subjects affected / exposed	0 / 332 (0.00%)	0 / 12 (0.00%)	0 / 17 (0.00%)
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 RESPIRATORY FAILURE			
subjects affected / exposed	0 / 332 (0.00%)	0 / 12 (0.00%)	2 / 17 (11.76%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CHRONIC OBSTRUCTIVE PULMONARY DISEASE			
subjects affected / exposed	0 / 332 (0.00%)	0 / 12 (0.00%)	1 / 17 (5.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

ASTHMA			
subjects affected / exposed	1 / 332 (0.30%)	0 / 12 (0.00%)	1 / 17 (5.88%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DYSPHONIA			
subjects affected / exposed	0 / 332 (0.00%)	0 / 12 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
EPISTAXIS			
subjects affected / exposed	0 / 332 (0.00%)	0 / 12 (0.00%)	0 / 17 (0.00%)
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 / 332 (0.00%)	0 / 12 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PNEUMONITIS			
subjects affected / exposed	0 / 332 (0.00%)	0 / 12 (0.00%)	0 / 17 (0.00%)
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 / 332 (0.00%)	0 / 12 (0.00%)	1 / 17 (5.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
UPPER-AIRWAY COUGH SYNDROME			
subjects affected / exposed	1 / 332 (0.30%)	0 / 12 (0.00%)	0 / 17 (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			
ACUTE PSYCHOSIS			
subjects affected / exposed	0 / 332 (0.00%)	0 / 12 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ALCOHOL WITHDRAWAL SYNDROME			

subjects affected / exposed	0 / 332 (0.00%)	0 / 12 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ALCOHOL ABUSE			
subjects affected / exposed	0 / 332 (0.00%)	0 / 12 (0.00%)	0 / 17 (0.00%)
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			
ARTHROPOD BITE			
subjects affected / exposed	0 / 332 (0.00%)	0 / 12 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COMMINUTED FRACTURE			
subjects affected / exposed	0 / 332 (0.00%)	0 / 12 (0.00%)	0 / 17 (0.00%)
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 / 332 (0.00%)	0 / 12 (0.00%)	0 / 17 (0.00%)
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 / 332 (0.00%)	0 / 12 (0.00%)	1 / 17 (5.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HIP FRACTURE			
subjects affected / exposed	0 / 332 (0.00%)	0 / 12 (0.00%)	1 / 17 (5.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
FOREARM FRACTURE			
subjects affected / exposed	0 / 332 (0.00%)	0 / 12 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
FIBULA FRACTURE			

subjects affected / exposed	0 / 332 (0.00%)	0 / 12 (0.00%)	0 / 17 (0.00%)
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 / 332 (0.00%)	0 / 12 (0.00%)	0 / 17 (0.00%)
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 / 332 (0.00%)	0 / 12 (0.00%)	0 / 17 (0.00%)
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 / 332 (0.00%)	0 / 12 (0.00%)	0 / 17 (0.00%)
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 / 332 (0.00%)	0 / 12 (0.00%)	1 / 17 (5.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PELVIC FRACTURE			
subjects affected / exposed	0 / 332 (0.00%)	0 / 12 (0.00%)	0 / 17 (0.00%)
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 / 332 (0.00%)	0 / 12 (0.00%)	0 / 17 (0.00%)
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 / 332 (0.00%)	0 / 12 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
TIBIA FRACTURE			

subjects affected / exposed	0 / 332 (0.00%)	0 / 12 (0.00%)	0 / 17 (0.00%)
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 / 332 (0.00%)	0 / 12 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SPINAL COMPRESSION FRACTURE			
subjects affected / exposed	1 / 332 (0.30%)	0 / 12 (0.00%)	0 / 17 (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
SYNOVIAL RUPTURE			
subjects affected / exposed	0 / 332 (0.00%)	0 / 12 (0.00%)	0 / 17 (0.00%)
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 / 332 (0.00%)	0 / 12 (0.00%)	0 / 17 (0.00%)
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			
ATRIAL FIBRILLATION			
subjects affected / exposed	0 / 332 (0.00%)	0 / 12 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ANGINA UNSTABLE			
subjects affected / exposed	0 / 332 (0.00%)	0 / 12 (0.00%)	0 / 17 (0.00%)
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 / 332 (0.00%)	0 / 12 (0.00%)	0 / 17 (0.00%)
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 / 332 (0.00%)	0 / 12 (0.00%)	0 / 17 (0.00%)
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 / 332 (0.00%)	1 / 12 (8.33%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CARDIAC ARREST			
subjects affected / exposed	0 / 332 (0.00%)	1 / 12 (8.33%)	0 / 17 (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
ATRIOVENTRICULAR BLOCK COMPLETE			
subjects affected / exposed	0 / 332 (0.00%)	0 / 12 (0.00%)	0 / 17 (0.00%)
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			
CAUDA EQUINA SYNDROME			
subjects affected / exposed	0 / 332 (0.00%)	0 / 12 (0.00%)	0 / 17 (0.00%)
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 STENOSIS			
subjects affected / exposed	0 / 332 (0.00%)	0 / 12 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CEREBROVASCULAR ACCIDENT			
subjects affected / exposed	0 / 332 (0.00%)	0 / 12 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DIZZINESS			
subjects affected / exposed	0 / 332 (0.00%)	0 / 12 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HEADACHE			

subjects affected / exposed	0 / 332 (0.00%)	0 / 12 (0.00%)	0 / 17 (0.00%)
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 RADICULOPATHY			
subjects affected / exposed	0 / 332 (0.00%)	0 / 12 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ISCHAEMIC STROKE			
subjects affected / exposed	0 / 332 (0.00%)	0 / 12 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HEMIPARESIS			
subjects affected / exposed	0 / 332 (0.00%)	0 / 12 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
MIGRAINE			
subjects affected / exposed	0 / 332 (0.00%)	0 / 12 (0.00%)	0 / 17 (0.00%)
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 / 332 (0.00%)	0 / 12 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
OCCIPITAL NEURALGIA			
subjects affected / exposed	0 / 332 (0.00%)	0 / 12 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
MOTOR NEURONE DISEASE			
subjects affected / exposed	0 / 332 (0.00%)	0 / 12 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SYNCOPE			

subjects affected / exposed	1 / 332 (0.30%)	0 / 12 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
ANAEMIA			
subjects affected / exposed	0 / 332 (0.00%)	0 / 12 (0.00%)	1 / 17 (5.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
NEUTROPENIA			
subjects affected / exposed	0 / 332 (0.00%)	0 / 12 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ear and labyrinth disorders			
VERTIGO POSITIONAL			
subjects affected / exposed	0 / 332 (0.00%)	0 / 12 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
RETINAL DETACHMENT			
subjects affected / exposed	0 / 332 (0.00%)	0 / 12 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DACRYOSTENOSIS ACQUIRED			
subjects affected / exposed	0 / 332 (0.00%)	0 / 12 (0.00%)	0 / 17 (0.00%)
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			
subjects affected / exposed	0 / 332 (0.00%)	0 / 12 (0.00%)	0 / 17 (0.00%)
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 / 332 (0.00%)	0 / 12 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ENTERITIS			
subjects affected / exposed	0 / 332 (0.00%)	0 / 12 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DYSPHAGIA			
subjects affected / exposed	0 / 332 (0.00%)	0 / 12 (0.00%)	1 / 17 (5.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DIVERTICULAR PERFORATION			
subjects affected / exposed	0 / 332 (0.00%)	0 / 12 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DIARRHOEA			
subjects affected / exposed	0 / 332 (0.00%)	0 / 12 (0.00%)	0 / 17 (0.00%)
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 DISORDER			
subjects affected / exposed	0 / 332 (0.00%)	0 / 12 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
INTRA-ABDOMINAL HAEMORRHAGE			
subjects affected / exposed	0 / 332 (0.00%)	0 / 12 (0.00%)	0 / 17 (0.00%)
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 / 332 (0.00%)	0 / 12 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ILEUS			

subjects affected / exposed	0 / 332 (0.00%)	0 / 12 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HAEMORRHOIDS			
subjects affected / exposed	0 / 332 (0.00%)	0 / 12 (0.00%)	0 / 17 (0.00%)
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 / 332 (0.00%)	0 / 12 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
NAUSEA			
subjects affected / exposed	0 / 332 (0.00%)	0 / 12 (0.00%)	0 / 17 (0.00%)
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 / 332 (0.00%)	0 / 12 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PANCREATITIS ACUTE			
subjects affected / exposed	0 / 332 (0.00%)	0 / 12 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
VOLVULUS OF SMALL BOWEL			
subjects affected / exposed	0 / 332 (0.00%)	0 / 12 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
VOMITING			
subjects affected / exposed	0 / 332 (0.00%)	0 / 12 (0.00%)	0 / 17 (0.00%)
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			
BILIARY COLIC			

subjects affected / exposed	0 / 332 (0.00%)	0 / 12 (0.00%)	1 / 17 (5.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BILIARY OBSTRUCTION			
subjects affected / exposed	0 / 332 (0.00%)	0 / 12 (0.00%)	0 / 17 (0.00%)
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			
subjects affected / exposed	0 / 332 (0.00%)	0 / 12 (0.00%)	0 / 17 (0.00%)
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 / 332 (0.00%)	0 / 12 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
ACUTE KIDNEY INJURY			
subjects affected / exposed	0 / 332 (0.00%)	0 / 12 (0.00%)	1 / 17 (5.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endocrine disorders			
GOITRE			
subjects affected / exposed	0 / 332 (0.00%)	0 / 12 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HYPERPARATHYROIDISM			
subjects affected / exposed	0 / 332 (0.00%)	0 / 12 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
ARTHRALGIA			
subjects affected / exposed	0 / 332 (0.00%)	0 / 12 (0.00%)	2 / 17 (11.76%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

FOOT DEFORMITY			
subjects affected / exposed	0 / 332 (0.00%)	0 / 12 (0.00%)	0 / 17 (0.00%)
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 SPINAL STENOSIS			
subjects affected / exposed	0 / 332 (0.00%)	0 / 12 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
FRACTURE PAIN			
subjects affected / exposed	0 / 332 (0.00%)	0 / 12 (0.00%)	0 / 17 (0.00%)
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 / 332 (0.00%)	0 / 12 (0.00%)	0 / 17 (0.00%)
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 DEGENERATION			
subjects affected / exposed	0 / 332 (0.00%)	0 / 12 (0.00%)	0 / 17 (0.00%)
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 / 332 (0.60%)	0 / 12 (0.00%)	1 / 17 (5.88%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
RHEUMATOID ARTHRITIS			
subjects affected / exposed	0 / 332 (0.00%)	0 / 12 (0.00%)	0 / 17 (0.00%)
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 / 332 (0.00%)	0 / 12 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SPINAL OSTEOARTHRITIS			

subjects affected / exposed	0 / 332 (0.00%)	0 / 12 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SPINAL STENOSIS			
subjects affected / exposed	0 / 332 (0.00%)	0 / 12 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SYNOVIAL CYST			
subjects affected / exposed	0 / 332 (0.00%)	0 / 12 (0.00%)	0 / 17 (0.00%)
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			
BACTERIAL SEPSIS			
subjects affected / exposed	0 / 332 (0.00%)	0 / 12 (0.00%)	1 / 17 (5.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ARTHRITIS BACTERIAL			
subjects affected / exposed	0 / 332 (0.00%)	0 / 12 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ABSCESS SOFT TISSUE			
subjects affected / exposed	0 / 332 (0.00%)	0 / 12 (0.00%)	0 / 17 (0.00%)
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 / 332 (0.00%)	0 / 12 (0.00%)	1 / 17 (5.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BURSITIS INFECTIVE			
subjects affected / exposed	0 / 332 (0.00%)	0 / 12 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BRONCHITIS			

subjects affected / exposed	0 / 332 (0.00%)	0 / 12 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BONE ABSCESS			
subjects affected / exposed	0 / 332 (0.00%)	0 / 12 (0.00%)	0 / 17 (0.00%)
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 / 332 (0.00%)	0 / 12 (0.00%)	0 / 17 (0.00%)
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 STAPHYLOCOCCAL			
subjects affected / exposed	0 / 332 (0.00%)	0 / 12 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DEVICE RELATED INFECTION			
subjects affected / exposed	0 / 332 (0.00%)	0 / 12 (0.00%)	0 / 17 (0.00%)
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 URINARY TRACT INFECTION			
subjects affected / exposed	0 / 332 (0.00%)	0 / 12 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DIVERTICULITIS			
subjects affected / exposed	0 / 332 (0.00%)	0 / 12 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
GASTROENTERITIS VIRAL			
subjects affected / exposed	0 / 332 (0.00%)	0 / 12 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
INFECTIOUS PLEURAL EFFUSION			

subjects affected / exposed	0 / 332 (0.00%)	0 / 12 (0.00%)	1 / 17 (5.88%)
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 / 332 (0.00%)	0 / 12 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
MEDICAL DEVICE SITE ABSCESS			
subjects affected / exposed	0 / 332 (0.00%)	0 / 12 (0.00%)	0 / 17 (0.00%)
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 / 332 (0.00%)	0 / 12 (0.00%)	0 / 17 (0.00%)
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 / 332 (0.00%)	0 / 12 (0.00%)	0 / 17 (0.00%)
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 / 332 (0.60%)	1 / 12 (8.33%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PNEUMONIA BACTERIAL			
subjects affected / exposed	0 / 332 (0.00%)	0 / 12 (0.00%)	1 / 17 (5.88%)
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 VIRAL			
subjects affected / exposed	0 / 332 (0.00%)	0 / 12 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
POSTOPERATIVE WOUND INFECTION			

subjects affected / exposed	0 / 332 (0.00%)	0 / 12 (0.00%)	0 / 17 (0.00%)
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 / 332 (0.00%)	0 / 12 (0.00%)	0 / 17 (0.00%)
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 / 332 (0.00%)	0 / 12 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
RESPIRATORY TRACT INFECTION			
subjects affected / exposed	0 / 332 (0.00%)	0 / 12 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SEPSIS			
subjects affected / exposed	1 / 332 (0.30%)	0 / 12 (0.00%)	0 / 17 (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
SOFT TISSUE INFECTION			
subjects affected / exposed	0 / 332 (0.00%)	0 / 12 (0.00%)	0 / 17 (0.00%)
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 INFECTION			
subjects affected / exposed	0 / 332 (0.00%)	0 / 12 (0.00%)	0 / 17 (0.00%)
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 / 332 (0.00%)	0 / 12 (0.00%)	0 / 17 (0.00%)
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 BACTERAEMIA			

subjects affected / exposed	0 / 332 (0.00%)	0 / 12 (0.00%)	0 / 17 (0.00%)
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 / 332 (0.00%)	0 / 12 (0.00%)	0 / 17 (0.00%)
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 / 332 (0.00%)	0 / 12 (0.00%)	1 / 17 (5.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
HYPONATRAEMIA			
subjects affected / exposed	0 / 332 (0.00%)	0 / 12 (0.00%)	1 / 17 (5.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DIABETIC KETOACIDOSIS			
subjects affected / exposed	0 / 332 (0.00%)	0 / 12 (0.00%)	0 / 17 (0.00%)
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 / 332 (0.00%)	0 / 12 (0.00%)	0 / 17 (0.00%)
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 / 332 (0.00%)	0 / 12 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Period 2, 30 mg Cohort: Abatacept/Upa 30 mg QD	Period 2, 30 mg Cohort: Upa 30 mg QD/Upa 30 mg QD/Upa 15 mg QD	Period 2, Primary Cohort: Upa 15 mg QD/Upa 15 mg QD
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 19 (21.05%)	2 / 12 (16.67%)	64 / 271 (23.62%)
number of deaths (all causes)	0	0	16

number of deaths resulting from adverse events	0	0	1
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
COLORECTAL ADENOMA			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	0 / 271 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
INTESTINAL METASTASIS			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	1 / 271 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
INVASIVE DUCTAL BREAST CARCINOMA			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	0 / 271 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
INVASIVE BREAST CARCINOMA			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	0 / 271 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
KAPOSI'S SARCOMA			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	1 / 271 (0.37%)
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 ADENOCARCINOMA STAGE IV			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	1 / 271 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
LUNG CARCINOMA CELL TYPE UNSPECIFIED STAGE IV			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	1 / 271 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
MALIGNANT MELANOMA			

subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	1 / 271 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
LUNG NEOPLASM MALIGNANT			
subjects affected / exposed	1 / 19 (5.26%)	0 / 12 (0.00%)	0 / 271 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
RECTAL CANCER			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	1 / 271 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
OVARIAN EPITHELIAL CANCER METASTATIC			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	1 / 271 (0.37%)
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-SECRETORY ADENOMA OF PITUITARY			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	0 / 271 (0.00%)
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 LIVER			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	1 / 271 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
MANTLE CELL LYMPHOMA			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	0 / 271 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
UTERINE LEIOMYOMA			
subjects affected / exposed	1 / 19 (5.26%)	0 / 12 (0.00%)	1 / 271 (0.37%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
UTERINE CANCER			

subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	1 / 271 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SMALL CELL LUNG CANCER			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	0 / 271 (0.00%)
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			
AORTIC INTRAMURAL HAEMATOMA			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	1 / 271 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DEEP VEIN THROMBOSIS			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	1 / 271 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HYPERTENSION			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	0 / 271 (0.00%)
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 OCCLUSION			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	0 / 271 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Surgical and medical procedures			
ARTHRODESIS			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	0 / 271 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
KNEE ARTHROPLASTY			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	1 / 271 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
WOUND DRAINAGE			

subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	1 / 271 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pregnancy, puerperium and perinatal conditions			
ABORTION SPONTANEOUS			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	0 / 271 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
CHEST PAIN			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	1 / 271 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DEATH			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	1 / 271 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
FAT NECROSIS			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	1 / 271 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
MULTIPLE ORGAN DYSFUNCTION SYNDROME			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	1 / 271 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
PAIN			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	1 / 271 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
CERVICAL DYSPLASIA			

subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	0 / 271 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ADNEXA UTERI CYST			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	0 / 271 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ENDOMETRIOSIS			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	1 / 271 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
INTERMENSTRUAL BLEEDING			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	0 / 271 (0.00%)
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 / 19 (0.00%)	0 / 12 (0.00%)	1 / 271 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PELVIC ORGAN PROLAPSE			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	1 / 271 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
UTERINE HAEMORRHAGE			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	1 / 271 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
VAGINAL PROLAPSE			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	1 / 271 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
ACUTE RESPIRATORY DISTRESS SYNDROME			

subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	1 / 271 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
ACUTE RESPIRATORY FAILURE			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	1 / 271 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CHRONIC OBSTRUCTIVE PULMONARY DISEASE			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	0 / 271 (0.00%)
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 / 19 (0.00%)	0 / 12 (0.00%)	0 / 271 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DYSPHONIA			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	1 / 271 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
EPISTAXIS			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	0 / 271 (0.00%)
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 / 19 (0.00%)	0 / 12 (0.00%)	2 / 271 (0.74%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PNEUMONITIS			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	1 / 271 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
PULMONARY EMBOLISM			

subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	2 / 271 (0.74%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
UPPER-AIRWAY COUGH SYNDROME			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	0 / 271 (0.00%)
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			
ACUTE PSYCHOSIS			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	1 / 271 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ALCOHOL WITHDRAWAL SYNDROME			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	0 / 271 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ALCOHOL ABUSE			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	0 / 271 (0.00%)
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			
ARTHROPOD BITE			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	0 / 271 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COMMINUTED FRACTURE			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	1 / 271 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
FEMORAL NECK FRACTURE			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	0 / 271 (0.00%)
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 / 19 (0.00%)	0 / 12 (0.00%)	1 / 271 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HIP FRACTURE			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	2 / 271 (0.74%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
FOREARM FRACTURE			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	0 / 271 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
FIBULA FRACTURE			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	0 / 271 (0.00%)
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 / 19 (0.00%)	0 / 12 (0.00%)	1 / 271 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
LOWER LIMB FRACTURE			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	0 / 271 (0.00%)
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 / 19 (0.00%)	0 / 12 (0.00%)	0 / 271 (0.00%)
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 / 19 (0.00%)	0 / 12 (0.00%)	0 / 271 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PELVIC FRACTURE			

subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	1 / 271 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
RADIUS FRACTURE			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	1 / 271 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
UPPER LIMB FRACTURE			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	0 / 271 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
TIBIA FRACTURE			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	1 / 271 (0.37%)
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 / 19 (0.00%)	0 / 12 (0.00%)	1 / 271 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SPINAL COMPRESSION FRACTURE			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	0 / 271 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SYNOVIAL RUPTURE			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	1 / 271 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
WRIST FRACTURE			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	0 / 271 (0.00%)
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			
ATRIAL FIBRILLATION			

subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	2 / 271 (0.74%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ANGINA UNSTABLE			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	1 / 271 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SUPRAVENTRICULAR TACHYCARDIA			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	1 / 271 (0.37%)
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 / 19 (0.00%)	0 / 12 (0.00%)	0 / 271 (0.00%)
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 / 19 (0.00%)	0 / 12 (0.00%)	1 / 271 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
CARDIAC ARREST			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	1 / 271 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
ATRIOVENTRICULAR BLOCK COMPLETE			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	0 / 271 (0.00%)
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			
CAUDA EQUINA SYNDROME			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	0 / 271 (0.00%)
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 STENOSIS			

subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	0 / 271 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CEREBROVASCULAR ACCIDENT			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	0 / 271 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DIZZINESS			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	0 / 271 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HEADACHE			
subjects affected / exposed	0 / 19 (0.00%)	1 / 12 (8.33%)	0 / 271 (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
LUMBAR RADICULOPATHY			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	0 / 271 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ISCHAEMIC STROKE			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	1 / 271 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HEMIPARESIS			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	1 / 271 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
MIGRAINE			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	0 / 271 (0.00%)
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 / 19 (0.00%)	0 / 12 (0.00%)	1 / 271 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
OCCIPITAL NEURALGIA			
subjects affected / exposed	0 / 19 (0.00%)	1 / 12 (8.33%)	0 / 271 (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
MOTOR NEURONE DISEASE			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	0 / 271 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SYNCOPE			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	0 / 271 (0.00%)
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 / 19 (0.00%)	0 / 12 (0.00%)	2 / 271 (0.74%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
NEUTROPENIA			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	0 / 271 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ear and labyrinth disorders			
VERTIGO POSITIONAL			
subjects affected / exposed	0 / 19 (0.00%)	1 / 12 (8.33%)	0 / 271 (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
Eye disorders			
RETINAL DETACHMENT			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	1 / 271 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

DACRYOSTENOSIS ACQUIRED			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	1 / 271 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CATARACT			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	0 / 271 (0.00%)
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 / 19 (0.00%)	0 / 12 (0.00%)	1 / 271 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ENTERITIS			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	1 / 271 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DYSPHAGIA			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	0 / 271 (0.00%)
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 / 19 (0.00%)	0 / 12 (0.00%)	1 / 271 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DIARRHOEA			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	1 / 271 (0.37%)
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 DISORDER			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	1 / 271 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
INTRA-ABDOMINAL HAEMORRHAGE			

subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	1 / 271 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
INGUINAL HERNIA			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	0 / 271 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ILEUS			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	0 / 271 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HAEMORRHOIDS			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	0 / 271 (0.00%)
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 / 19 (0.00%)	0 / 12 (0.00%)	0 / 271 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
NAUSEA			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	0 / 271 (0.00%)
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 / 19 (0.00%)	0 / 12 (0.00%)	0 / 271 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PANCREATITIS ACUTE			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	0 / 271 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
VOLVULUS OF SMALL BOWEL			

subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	1 / 271 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
VOMITING			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	0 / 271 (0.00%)
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			
BILIARY COLIC			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	0 / 271 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BILIARY OBSTRUCTION			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	1 / 271 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CHOLECYSTITIS			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	1 / 271 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CHOLELITHIASIS			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	1 / 271 (0.37%)
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 and urinary disorders			
ACUTE KIDNEY INJURY			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	0 / 271 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endocrine disorders			
GOITRE			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	0 / 271 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

HYPERPARATHYROIDISM			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	0 / 271 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
ARTHRALGIA			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	2 / 271 (0.74%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
FOOT DEFORMITY			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	1 / 271 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CERVICAL SPINAL STENOSIS			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	1 / 271 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
FRACTURE PAIN			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	1 / 271 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
INTERVERTEBRAL DISC PROTRUSION			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	0 / 271 (0.00%)
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 DEGENERATION			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	0 / 271 (0.00%)
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 / 19 (0.00%)	0 / 12 (0.00%)	3 / 271 (1.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
RHEUMATOID ARTHRITIS			
subjects affected / exposed	0 / 19 (0.00%)	1 / 12 (8.33%)	1 / 271 (0.37%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ROTATOR CUFF SYNDROME			
subjects affected / exposed	1 / 19 (5.26%)	0 / 12 (0.00%)	0 / 271 (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
SPINAL OSTEOARTHRITIS			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	1 / 271 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SPINAL STENOSIS			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	1 / 271 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SYNOVIAL CYST			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	0 / 271 (0.00%)
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			
BACTERIAL SEPSIS			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	0 / 271 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ARTHRITIS BACTERIAL			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	0 / 271 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ABSCESS SOFT TISSUE			

subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	0 / 271 (0.00%)
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 / 19 (0.00%)	0 / 12 (0.00%)	6 / 271 (2.21%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 6
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 4
BURSITIS INFECTIVE			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	1 / 271 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BRONCHITIS			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	1 / 271 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BONE ABSCESS			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	0 / 271 (0.00%)
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 / 19 (0.00%)	0 / 12 (0.00%)	9 / 271 (3.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 9
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 3
CELLULITIS STAPHYLOCOCCAL			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	0 / 271 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DEVICE RELATED INFECTION			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	1 / 271 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ESCHERICHIA URINARY TRACT INFECTION			

subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	0 / 271 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DIVERTICULITIS			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	0 / 271 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
GASTROENTERITIS VIRAL			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	0 / 271 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
INFECTIOUS PLEURAL EFFUSION			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	0 / 271 (0.00%)
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 / 19 (0.00%)	0 / 12 (0.00%)	1 / 271 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
MEDICAL DEVICE SITE ABSCESS			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	0 / 271 (0.00%)
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 / 19 (0.00%)	0 / 12 (0.00%)	1 / 271 (0.37%)
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	1 / 19 (5.26%)	0 / 12 (0.00%)	0 / 271 (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			

subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	3 / 271 (1.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	3 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PNEUMONIA BACTERIAL			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	0 / 271 (0.00%)
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 VIRAL			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	1 / 271 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
POSTOPERATIVE WOUND INFECTION			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	0 / 271 (0.00%)
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 / 19 (0.00%)	0 / 12 (0.00%)	0 / 271 (0.00%)
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 / 19 (0.00%)	0 / 12 (0.00%)	0 / 271 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
RESPIRATORY TRACT INFECTION			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	0 / 271 (0.00%)
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 / 19 (0.00%)	0 / 12 (0.00%)	1 / 271 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SOFT TISSUE INFECTION			

subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	0 / 271 (0.00%)
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 INFECTION			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	0 / 271 (0.00%)
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 / 19 (0.00%)	0 / 12 (0.00%)	2 / 271 (0.74%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 2
STAPHYLOCOCCAL BACTERAEMIA			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	1 / 271 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
STAPHYLOCOCCAL INFECTION			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	0 / 271 (0.00%)
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 / 19 (0.00%)	0 / 12 (0.00%)	1 / 271 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
HYPONATRAEMIA			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	1 / 271 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DIABETIC KETOACIDOSIS			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	0 / 271 (0.00%)
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 / 19 (0.00%)	0 / 12 (0.00%)	1 / 271 (0.37%)
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 / 19 (0.00%)	0 / 12 (0.00%)	0 / 271 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	Period 2, Primary Cohort:Abatacept/Upadacitinib (Upa) 15 mg QD	Period 1, 30 mg Cohort: Upa 30 mg QD	Period 1, Primary Cohort: Upa 15 mg QD
Total subjects affected by non-serious adverse events			
subjects affected / exposed	221 / 276 (80.07%)	13 / 21 (61.90%)	174 / 303 (57.43%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
SKIN PAPILLOMA			
subjects affected / exposed	1 / 276 (0.36%)	0 / 21 (0.00%)	2 / 303 (0.66%)
occurrences (all)	1	0	2
SEBORRHOEIC KERATOSIS			
subjects affected / exposed	2 / 276 (0.72%)	0 / 21 (0.00%)	0 / 303 (0.00%)
occurrences (all)	2	0	0
HAEMANGIOMA OF SPLEEN			
subjects affected / exposed	0 / 276 (0.00%)	0 / 21 (0.00%)	0 / 303 (0.00%)
occurrences (all)	0	0	0
UTERINE LEIOMYOMA			
subjects affected / exposed	4 / 276 (1.45%)	0 / 21 (0.00%)	0 / 303 (0.00%)
occurrences (all)	4	0	0
Vascular disorders			
HYPERTENSION			
subjects affected / exposed	25 / 276 (9.06%)	0 / 21 (0.00%)	16 / 303 (5.28%)
occurrences (all)	27	0	16
General disorders and administration site conditions			
NON-CARDIAC CHEST PAIN			
subjects affected / exposed	0 / 276 (0.00%)	0 / 21 (0.00%)	1 / 303 (0.33%)
occurrences (all)	0	0	1

CHEST PAIN			
subjects affected / exposed	3 / 276 (1.09%)	0 / 21 (0.00%)	1 / 303 (0.33%)
occurrences (all)	3	0	1
FATIGUE			
subjects affected / exposed	7 / 276 (2.54%)	0 / 21 (0.00%)	3 / 303 (0.99%)
occurrences (all)	8	0	3
FEELING HOT			
subjects affected / exposed	0 / 276 (0.00%)	0 / 21 (0.00%)	0 / 303 (0.00%)
occurrences (all)	0	0	0
PERIPHERAL SWELLING			
subjects affected / exposed	1 / 276 (0.36%)	0 / 21 (0.00%)	1 / 303 (0.33%)
occurrences (all)	1	0	1
PYREXIA			
subjects affected / exposed	6 / 276 (2.17%)	2 / 21 (9.52%)	2 / 303 (0.66%)
occurrences (all)	9	2	2
SWELLING			
subjects affected / exposed	0 / 276 (0.00%)	0 / 21 (0.00%)	0 / 303 (0.00%)
occurrences (all)	0	0	0
Immune system disorders			
DRUG HYPERSENSITIVITY			
subjects affected / exposed	1 / 276 (0.36%)	0 / 21 (0.00%)	0 / 303 (0.00%)
occurrences (all)	1	0	0
Reproductive system and breast disorders			
CYSTOCELE			
subjects affected / exposed	1 / 276 (0.36%)	0 / 21 (0.00%)	0 / 303 (0.00%)
occurrences (all)	1	0	0
Respiratory, thoracic and mediastinal disorders			
ASTHMA			
subjects affected / exposed	0 / 276 (0.00%)	1 / 21 (4.76%)	0 / 303 (0.00%)
occurrences (all)	0	1	0
OROPHARYNGEAL PAIN			
subjects affected / exposed	2 / 276 (0.72%)	0 / 21 (0.00%)	1 / 303 (0.33%)
occurrences (all)	2	0	1
INTERSTITIAL LUNG DISEASE			
subjects affected / exposed	1 / 276 (0.36%)	0 / 21 (0.00%)	0 / 303 (0.00%)
occurrences (all)	1	0	0

DYSPHONIA			
subjects affected / exposed	1 / 276 (0.36%)	0 / 21 (0.00%)	0 / 303 (0.00%)
occurrences (all)	1	0	0
COUGH			
subjects affected / exposed	12 / 276 (4.35%)	2 / 21 (9.52%)	7 / 303 (2.31%)
occurrences (all)	13	2	7
BRONCHIECTASIS			
subjects affected / exposed	1 / 276 (0.36%)	0 / 21 (0.00%)	0 / 303 (0.00%)
occurrences (all)	1	0	0
NASAL CONGESTION			
subjects affected / exposed	0 / 276 (0.00%)	0 / 21 (0.00%)	0 / 303 (0.00%)
occurrences (all)	0	0	0
PLEURAL EFFUSION			
subjects affected / exposed	0 / 276 (0.00%)	0 / 21 (0.00%)	0 / 303 (0.00%)
occurrences (all)	0	0	0
PULMONARY MASS			
subjects affected / exposed	2 / 276 (0.72%)	0 / 21 (0.00%)	0 / 303 (0.00%)
occurrences (all)	2	0	0
RHINORRHOEA			
subjects affected / exposed	1 / 276 (0.36%)	0 / 21 (0.00%)	0 / 303 (0.00%)
occurrences (all)	1	0	0
Psychiatric disorders			
ANXIETY			
subjects affected / exposed	2 / 276 (0.72%)	0 / 21 (0.00%)	1 / 303 (0.33%)
occurrences (all)	2	0	1
AFFECT LABILITY			
subjects affected / exposed	0 / 276 (0.00%)	0 / 21 (0.00%)	0 / 303 (0.00%)
occurrences (all)	0	0	0
DEPRESSION			
subjects affected / exposed	6 / 276 (2.17%)	0 / 21 (0.00%)	0 / 303 (0.00%)
occurrences (all)	6	0	0
PANIC ATTACK			
subjects affected / exposed	1 / 276 (0.36%)	0 / 21 (0.00%)	0 / 303 (0.00%)
occurrences (all)	1	0	0
INSOMNIA			

subjects affected / exposed	2 / 276 (0.72%)	0 / 21 (0.00%)	1 / 303 (0.33%)
occurrences (all)	3	0	1
DEPRESSION SUICIDAL			
subjects affected / exposed	0 / 276 (0.00%)	0 / 21 (0.00%)	0 / 303 (0.00%)
occurrences (all)	0	0	0
Investigations			
ALANINE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	13 / 276 (4.71%)	0 / 21 (0.00%)	14 / 303 (4.62%)
occurrences (all)	24	0	20
ASPARTATE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	13 / 276 (4.71%)	0 / 21 (0.00%)	12 / 303 (3.96%)
occurrences (all)	22	0	18
BLOOD CREATINE PHOSPHOKINASE INCREASED			
subjects affected / exposed	31 / 276 (11.23%)	0 / 21 (0.00%)	9 / 303 (2.97%)
occurrences (all)	48	0	10
BLOOD CREATININE INCREASED			
subjects affected / exposed	3 / 276 (1.09%)	0 / 21 (0.00%)	1 / 303 (0.33%)
occurrences (all)	3	0	1
WEIGHT INCREASED			
subjects affected / exposed	14 / 276 (5.07%)	0 / 21 (0.00%)	6 / 303 (1.98%)
occurrences (all)	19	0	7
SCAN ADRENAL GLAND ABNORMAL			
subjects affected / exposed	0 / 276 (0.00%)	0 / 21 (0.00%)	0 / 303 (0.00%)
occurrences (all)	0	0	0
WHITE BLOOD CELLS URINE POSITIVE			
subjects affected / exposed	0 / 276 (0.00%)	1 / 21 (4.76%)	0 / 303 (0.00%)
occurrences (all)	0	1	0
BLOOD PRESSURE INCREASED			
subjects affected / exposed	2 / 276 (0.72%)	0 / 21 (0.00%)	0 / 303 (0.00%)
occurrences (all)	2	0	0
BLOOD TRIGLYCERIDES INCREASED			
subjects affected / exposed	1 / 276 (0.36%)	0 / 21 (0.00%)	2 / 303 (0.66%)
occurrences (all)	1	0	2
ELECTROCARDIOGRAM ABNORMAL			

subjects affected / exposed	0 / 276 (0.00%)	0 / 21 (0.00%)	0 / 303 (0.00%)
occurrences (all)	0	0	0
HAEMOGLOBIN DECREASED			
subjects affected / exposed	2 / 276 (0.72%)	0 / 21 (0.00%)	0 / 303 (0.00%)
occurrences (all)	5	0	0
HEPATIC ENZYME INCREASED			
subjects affected / exposed	2 / 276 (0.72%)	0 / 21 (0.00%)	0 / 303 (0.00%)
occurrences (all)	2	0	0
HIGH DENSITY LIPOPROTEIN DECREASED			
subjects affected / exposed	0 / 276 (0.00%)	0 / 21 (0.00%)	0 / 303 (0.00%)
occurrences (all)	0	0	0
LIVER FUNCTION TEST INCREASED			
subjects affected / exposed	1 / 276 (0.36%)	1 / 21 (4.76%)	0 / 303 (0.00%)
occurrences (all)	1	1	0
Injury, poisoning and procedural complications			
CONTUSION			
subjects affected / exposed	0 / 276 (0.00%)	1 / 21 (4.76%)	1 / 303 (0.33%)
occurrences (all)	0	1	1
BONE CONTUSION			
subjects affected / exposed	0 / 276 (0.00%)	0 / 21 (0.00%)	1 / 303 (0.33%)
occurrences (all)	0	0	1
BURNS SECOND DEGREE			
subjects affected / exposed	0 / 276 (0.00%)	0 / 21 (0.00%)	0 / 303 (0.00%)
occurrences (all)	0	0	0
CORNEAL ABRASION			
subjects affected / exposed	0 / 276 (0.00%)	0 / 21 (0.00%)	0 / 303 (0.00%)
occurrences (all)	0	0	0
FALL			
subjects affected / exposed	14 / 276 (5.07%)	0 / 21 (0.00%)	2 / 303 (0.66%)
occurrences (all)	15	0	2
LIGAMENT RUPTURE			
subjects affected / exposed	0 / 276 (0.00%)	0 / 21 (0.00%)	1 / 303 (0.33%)
occurrences (all)	0	0	1
SCRATCH			

subjects affected / exposed	0 / 276 (0.00%)	0 / 21 (0.00%)	0 / 303 (0.00%)
occurrences (all)	0	0	0
SKIN LACERATION			
subjects affected / exposed	2 / 276 (0.72%)	0 / 21 (0.00%)	1 / 303 (0.33%)
occurrences (all)	2	0	1
TOOTH FRACTURE			
subjects affected / exposed	0 / 276 (0.00%)	0 / 21 (0.00%)	0 / 303 (0.00%)
occurrences (all)	0	0	0
Congenital, familial and genetic disorders			
TYPE V HYPERLIPIDAEMIA			
subjects affected / exposed	0 / 276 (0.00%)	0 / 21 (0.00%)	0 / 303 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
ATRIOVENTRICULAR BLOCK FIRST DEGREE			
subjects affected / exposed	2 / 276 (0.72%)	0 / 21 (0.00%)	0 / 303 (0.00%)
occurrences (all)	2	0	0
ATRIAL FIBRILLATION			
subjects affected / exposed	4 / 276 (1.45%)	0 / 21 (0.00%)	1 / 303 (0.33%)
occurrences (all)	5	0	1
CARDIOMYOPATHY			
subjects affected / exposed	0 / 276 (0.00%)	0 / 21 (0.00%)	0 / 303 (0.00%)
occurrences (all)	0	0	0
MITRAL VALVE INCOMPETENCE			
subjects affected / exposed	3 / 276 (1.09%)	0 / 21 (0.00%)	1 / 303 (0.33%)
occurrences (all)	3	0	1
SUPRAVENTRICULAR TACHYCARDIA			
subjects affected / exposed	0 / 276 (0.00%)	0 / 21 (0.00%)	0 / 303 (0.00%)
occurrences (all)	0	0	0
TACHYCARDIA			
subjects affected / exposed	1 / 276 (0.36%)	0 / 21 (0.00%)	0 / 303 (0.00%)
occurrences (all)	1	0	0
TRICUSPID VALVE INCOMPETENCE			
subjects affected / exposed	4 / 276 (1.45%)	0 / 21 (0.00%)	0 / 303 (0.00%)
occurrences (all)	4	0	0
Nervous system disorders			

SCIATICA			
subjects affected / exposed	8 / 276 (2.90%)	0 / 21 (0.00%)	2 / 303 (0.66%)
occurrences (all)	10	0	2
CARPAL TUNNEL SYNDROME			
subjects affected / exposed	5 / 276 (1.81%)	0 / 21 (0.00%)	0 / 303 (0.00%)
occurrences (all)	5	0	0
DIZZINESS			
subjects affected / exposed	2 / 276 (0.72%)	1 / 21 (4.76%)	2 / 303 (0.66%)
occurrences (all)	2	1	3
HEADACHE			
subjects affected / exposed	12 / 276 (4.35%)	0 / 21 (0.00%)	10 / 303 (3.30%)
occurrences (all)	17	0	10
PARAESTHESIA			
subjects affected / exposed	3 / 276 (1.09%)	0 / 21 (0.00%)	1 / 303 (0.33%)
occurrences (all)	3	0	1
TREMOR			
subjects affected / exposed	1 / 276 (0.36%)	0 / 21 (0.00%)	0 / 303 (0.00%)
occurrences (all)	1	0	0
SYNCOPE			
subjects affected / exposed	2 / 276 (0.72%)	0 / 21 (0.00%)	2 / 303 (0.66%)
occurrences (all)	2	0	2
Blood and lymphatic system disorders			
ANAEMIA			
subjects affected / exposed	15 / 276 (5.43%)	1 / 21 (4.76%)	3 / 303 (0.99%)
occurrences (all)	15	1	4
IRON DEFICIENCY ANAEMIA			
subjects affected / exposed	2 / 276 (0.72%)	0 / 21 (0.00%)	0 / 303 (0.00%)
occurrences (all)	2	0	0
NEUTROPENIA			
subjects affected / exposed	14 / 276 (5.07%)	0 / 21 (0.00%)	5 / 303 (1.65%)
occurrences (all)	26	0	5
LEUKOCYTOSIS			
subjects affected / exposed	0 / 276 (0.00%)	0 / 21 (0.00%)	0 / 303 (0.00%)
occurrences (all)	0	0	0
Ear and labyrinth disorders			

TINNITUS			
subjects affected / exposed	0 / 276 (0.00%)	0 / 21 (0.00%)	0 / 303 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
EYELID PTOSIS			
subjects affected / exposed	0 / 276 (0.00%)	0 / 21 (0.00%)	0 / 303 (0.00%)
occurrences (all)	0	0	0
CATARACT			
subjects affected / exposed	6 / 276 (2.17%)	0 / 21 (0.00%)	0 / 303 (0.00%)
occurrences (all)	8	0	0
EYE HAEMATOMA			
subjects affected / exposed	0 / 276 (0.00%)	0 / 21 (0.00%)	0 / 303 (0.00%)
occurrences (all)	0	0	0
GLAUCOMA			
subjects affected / exposed	1 / 276 (0.36%)	0 / 21 (0.00%)	1 / 303 (0.33%)
occurrences (all)	1	0	1
Gastrointestinal disorders			
ABDOMINAL PAIN			
subjects affected / exposed	3 / 276 (1.09%)	0 / 21 (0.00%)	3 / 303 (0.99%)
occurrences (all)	3	0	3
CONSTIPATION			
subjects affected / exposed	3 / 276 (1.09%)	0 / 21 (0.00%)	3 / 303 (0.99%)
occurrences (all)	5	0	4
DIARRHOEA			
subjects affected / exposed	14 / 276 (5.07%)	1 / 21 (4.76%)	8 / 303 (2.64%)
occurrences (all)	17	2	9
HAEMORRHOIDS			
subjects affected / exposed	3 / 276 (1.09%)	0 / 21 (0.00%)	2 / 303 (0.66%)
occurrences (all)	3	0	2
DUODENOGASTRIC REFLUX			
subjects affected / exposed	2 / 276 (0.72%)	0 / 21 (0.00%)	0 / 303 (0.00%)
occurrences (all)	2	0	0
DYSPEPSIA			
subjects affected / exposed	3 / 276 (1.09%)	1 / 21 (4.76%)	4 / 303 (1.32%)
occurrences (all)	3	1	4
GASTRITIS			

subjects affected / exposed	11 / 276 (3.99%)	1 / 21 (4.76%)	3 / 303 (0.99%)
occurrences (all)	14	1	4
DIVERTICULUM INTESTINAL			
subjects affected / exposed	1 / 276 (0.36%)	0 / 21 (0.00%)	1 / 303 (0.33%)
occurrences (all)	1	0	1
LARGE INTESTINE POLYP			
subjects affected / exposed	2 / 276 (0.72%)	0 / 21 (0.00%)	1 / 303 (0.33%)
occurrences (all)	2	0	1
NAUSEA			
subjects affected / exposed	8 / 276 (2.90%)	2 / 21 (9.52%)	11 / 303 (3.63%)
occurrences (all)	8	2	11
PANCREATIC CYST			
subjects affected / exposed	0 / 276 (0.00%)	0 / 21 (0.00%)	0 / 303 (0.00%)
occurrences (all)	0	0	0
STOMATITIS			
subjects affected / exposed	0 / 276 (0.00%)	0 / 21 (0.00%)	1 / 303 (0.33%)
occurrences (all)	0	0	1
VOMITING			
subjects affected / exposed	4 / 276 (1.45%)	2 / 21 (9.52%)	3 / 303 (0.99%)
occurrences (all)	5	2	3
Hepatobiliary disorders			
CHOLELITHIASIS			
subjects affected / exposed	3 / 276 (1.09%)	0 / 21 (0.00%)	1 / 303 (0.33%)
occurrences (all)	3	0	1
HEPATIC STEATOSIS			
subjects affected / exposed	11 / 276 (3.99%)	0 / 21 (0.00%)	4 / 303 (1.32%)
occurrences (all)	11	0	4
Skin and subcutaneous tissue disorders			
DERMATITIS ALLERGIC			
subjects affected / exposed	5 / 276 (1.81%)	0 / 21 (0.00%)	0 / 303 (0.00%)
occurrences (all)	5	0	0
DERMATITIS CONTACT			
subjects affected / exposed	0 / 276 (0.00%)	0 / 21 (0.00%)	1 / 303 (0.33%)
occurrences (all)	0	0	1
ERYTHEMA			

subjects affected / exposed	1 / 276 (0.36%)	0 / 21 (0.00%)	0 / 303 (0.00%)
occurrences (all)	1	0	0
NIGHT SWEATS			
subjects affected / exposed	0 / 276 (0.00%)	0 / 21 (0.00%)	1 / 303 (0.33%)
occurrences (all)	0	0	1
PHOTODERMATOSIS			
subjects affected / exposed	0 / 276 (0.00%)	0 / 21 (0.00%)	0 / 303 (0.00%)
occurrences (all)	0	0	0
PRURITUS			
subjects affected / exposed	2 / 276 (0.72%)	1 / 21 (4.76%)	1 / 303 (0.33%)
occurrences (all)	2	1	1
ACTINIC KERATOSIS			
subjects affected / exposed	0 / 276 (0.00%)	0 / 21 (0.00%)	0 / 303 (0.00%)
occurrences (all)	0	0	0
RASH			
subjects affected / exposed	4 / 276 (1.45%)	2 / 21 (9.52%)	2 / 303 (0.66%)
occurrences (all)	4	2	2
ROSACEA			
subjects affected / exposed	3 / 276 (1.09%)	0 / 21 (0.00%)	0 / 303 (0.00%)
occurrences (all)	3	0	0
Renal and urinary disorders			
CYSTITIS NONINFECTIVE			
subjects affected / exposed	0 / 276 (0.00%)	0 / 21 (0.00%)	0 / 303 (0.00%)
occurrences (all)	0	0	0
BLADDER HYPERTROPHY			
subjects affected / exposed	0 / 276 (0.00%)	0 / 21 (0.00%)	0 / 303 (0.00%)
occurrences (all)	0	0	0
RENAL CYST			
subjects affected / exposed	4 / 276 (1.45%)	0 / 21 (0.00%)	0 / 303 (0.00%)
occurrences (all)	4	0	0
URETHRAL STENOSIS			
subjects affected / exposed	0 / 276 (0.00%)	0 / 21 (0.00%)	0 / 303 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			

COSTOCHONDRITIS			
subjects affected / exposed	0 / 276 (0.00%)	0 / 21 (0.00%)	1 / 303 (0.33%)
occurrences (all)	0	0	1
BACK PAIN			
subjects affected / exposed	20 / 276 (7.25%)	0 / 21 (0.00%)	6 / 303 (1.98%)
occurrences (all)	25	0	6
ARTHRALGIA			
subjects affected / exposed	15 / 276 (5.43%)	2 / 21 (9.52%)	3 / 303 (0.99%)
occurrences (all)	15	2	3
FLANK PAIN			
subjects affected / exposed	0 / 276 (0.00%)	0 / 21 (0.00%)	0 / 303 (0.00%)
occurrences (all)	0	0	0
SPINAL OSTEOARTHRITIS			
subjects affected / exposed	5 / 276 (1.81%)	0 / 21 (0.00%)	3 / 303 (0.99%)
occurrences (all)	5	0	3
SJOGREN'S SYNDROME			
subjects affected / exposed	2 / 276 (0.72%)	0 / 21 (0.00%)	0 / 303 (0.00%)
occurrences (all)	2	0	0
RHEUMATOID ARTHRITIS			
subjects affected / exposed	32 / 276 (11.59%)	3 / 21 (14.29%)	11 / 303 (3.63%)
occurrences (all)	57	4	13
OSTEOPOROSIS			
subjects affected / exposed	6 / 276 (2.17%)	0 / 21 (0.00%)	1 / 303 (0.33%)
occurrences (all)	6	0	1
OSTEOPENIA			
subjects affected / exposed	5 / 276 (1.81%)	0 / 21 (0.00%)	0 / 303 (0.00%)
occurrences (all)	5	0	0
OSTEOARTHRITIS			
subjects affected / exposed	18 / 276 (6.52%)	0 / 21 (0.00%)	2 / 303 (0.66%)
occurrences (all)	21	0	2
MUSCULOSKELETAL CHEST PAIN			
subjects affected / exposed	0 / 276 (0.00%)	0 / 21 (0.00%)	1 / 303 (0.33%)
occurrences (all)	0	0	1
MUSCLE SPASMS			
subjects affected / exposed	2 / 276 (0.72%)	0 / 21 (0.00%)	4 / 303 (1.32%)
occurrences (all)	2	0	4

GREATER TROCHANTERIC PAIN SYNDROME			
subjects affected / exposed	6 / 276 (2.17%)	0 / 21 (0.00%)	1 / 303 (0.33%)
occurrences (all)	6	0	1
SPONDYLOLISTHESIS			
subjects affected / exposed	1 / 276 (0.36%)	0 / 21 (0.00%)	0 / 303 (0.00%)
occurrences (all)	1	0	0
TRIGGER FINGER			
subjects affected / exposed	0 / 276 (0.00%)	0 / 21 (0.00%)	1 / 303 (0.33%)
occurrences (all)	0	0	1
Infections and infestations			
CANDIDA INFECTION			
subjects affected / exposed	0 / 276 (0.00%)	0 / 21 (0.00%)	0 / 303 (0.00%)
occurrences (all)	0	0	0
ASYMPTOMATIC COVID-19			
subjects affected / exposed	7 / 276 (2.54%)	0 / 21 (0.00%)	0 / 303 (0.00%)
occurrences (all)	7	0	0
BRONCHITIS			
subjects affected / exposed	26 / 276 (9.42%)	1 / 21 (4.76%)	8 / 303 (2.64%)
occurrences (all)	33	1	8
COVID-19			
subjects affected / exposed	47 / 276 (17.03%)	0 / 21 (0.00%)	0 / 303 (0.00%)
occurrences (all)	53	0	0
CYSTITIS			
subjects affected / exposed	10 / 276 (3.62%)	0 / 21 (0.00%)	4 / 303 (1.32%)
occurrences (all)	16	0	5
EAR INFECTION			
subjects affected / exposed	7 / 276 (2.54%)	0 / 21 (0.00%)	0 / 303 (0.00%)
occurrences (all)	7	0	0
GASTROENTERITIS			
subjects affected / exposed	12 / 276 (4.35%)	0 / 21 (0.00%)	12 / 303 (3.96%)
occurrences (all)	13	0	14
HERPES SIMPLEX			
subjects affected / exposed	2 / 276 (0.72%)	0 / 21 (0.00%)	3 / 303 (0.99%)
occurrences (all)	4	0	3
NASOPHARYNGITIS			

subjects affected / exposed	28 / 276 (10.14%)	1 / 21 (4.76%)	22 / 303 (7.26%)
occurrences (all)	39	1	22
INFLUENZA			
subjects affected / exposed	10 / 276 (3.62%)	0 / 21 (0.00%)	4 / 303 (1.32%)
occurrences (all)	14	0	5
LATENT TUBERCULOSIS			
subjects affected / exposed	14 / 276 (5.07%)	0 / 21 (0.00%)	0 / 303 (0.00%)
occurrences (all)	14	0	0
LOCALISED INFECTION			
subjects affected / exposed	0 / 276 (0.00%)	0 / 21 (0.00%)	1 / 303 (0.33%)
occurrences (all)	0	0	1
HERPES ZOSTER			
subjects affected / exposed	35 / 276 (12.68%)	0 / 21 (0.00%)	3 / 303 (0.99%)
occurrences (all)	35	0	3
ONYCHOMYCOSIS			
subjects affected / exposed	4 / 276 (1.45%)	0 / 21 (0.00%)	2 / 303 (0.66%)
occurrences (all)	4	0	2
OPHTHALMIC HERPES ZOSTER			
subjects affected / exposed	0 / 276 (0.00%)	0 / 21 (0.00%)	1 / 303 (0.33%)
occurrences (all)	0	0	1
ORAL CANDIDIASIS			
subjects affected / exposed	1 / 276 (0.36%)	1 / 21 (4.76%)	3 / 303 (0.99%)
occurrences (all)	2	1	3
PERIODONTITIS			
subjects affected / exposed	3 / 276 (1.09%)	0 / 21 (0.00%)	0 / 303 (0.00%)
occurrences (all)	3	0	0
RHINITIS			
subjects affected / exposed	4 / 276 (1.45%)	0 / 21 (0.00%)	0 / 303 (0.00%)
occurrences (all)	5	0	0
PHARYNGITIS STREPTOCOCCAL			
subjects affected / exposed	1 / 276 (0.36%)	0 / 21 (0.00%)	1 / 303 (0.33%)
occurrences (all)	1	0	1
PNEUMONIA			
subjects affected / exposed	3 / 276 (1.09%)	0 / 21 (0.00%)	3 / 303 (0.99%)
occurrences (all)	3	0	3
POST PROCEDURAL CELLULITIS			

subjects affected / exposed	0 / 276 (0.00%)	0 / 21 (0.00%)	0 / 303 (0.00%)
occurrences (all)	0	0	0
RESPIRATORY TRACT INFECTION			
subjects affected / exposed	10 / 276 (3.62%)	0 / 21 (0.00%)	1 / 303 (0.33%)
occurrences (all)	11	0	1
PHARYNGITIS			
subjects affected / exposed	8 / 276 (2.90%)	0 / 21 (0.00%)	4 / 303 (1.32%)
occurrences (all)	9	0	4
SINUSITIS			
subjects affected / exposed	10 / 276 (3.62%)	2 / 21 (9.52%)	5 / 303 (1.65%)
occurrences (all)	10	2	6
STAPHYLOCOCCAL INFECTION			
subjects affected / exposed	0 / 276 (0.00%)	0 / 21 (0.00%)	0 / 303 (0.00%)
occurrences (all)	0	0	0
TOOTH INFECTION			
subjects affected / exposed	6 / 276 (2.17%)	0 / 21 (0.00%)	2 / 303 (0.66%)
occurrences (all)	6	0	2
UPPER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	32 / 276 (11.59%)	0 / 21 (0.00%)	26 / 303 (8.58%)
occurrences (all)	49	0	31
VIRAL UPPER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	4 / 276 (1.45%)	0 / 21 (0.00%)	0 / 303 (0.00%)
occurrences (all)	4	0	0
VULVOVAGINAL MYCOTIC INFECTION			
subjects affected / exposed	1 / 276 (0.36%)	0 / 21 (0.00%)	0 / 303 (0.00%)
occurrences (all)	1	0	0
URINARY TRACT INFECTION			
subjects affected / exposed	40 / 276 (14.49%)	1 / 21 (4.76%)	20 / 303 (6.60%)
occurrences (all)	75	1	27
Metabolism and nutrition disorders			
DECREASED APPETITE			
subjects affected / exposed	1 / 276 (0.36%)	0 / 21 (0.00%)	2 / 303 (0.66%)
occurrences (all)	1	0	2
HYPOKALAEMIA			

subjects affected / exposed	1 / 276 (0.36%)	0 / 21 (0.00%)	0 / 303 (0.00%)
occurrences (all)	1	0	0
HYPERCHOLESTEROLAEMIA			
subjects affected / exposed	8 / 276 (2.90%)	0 / 21 (0.00%)	3 / 303 (0.99%)
occurrences (all)	8	0	3
DIABETES MELLITUS			
subjects affected / exposed	5 / 276 (1.81%)	0 / 21 (0.00%)	2 / 303 (0.66%)
occurrences (all)	6	0	2
DEHYDRATION			
subjects affected / exposed	0 / 276 (0.00%)	0 / 21 (0.00%)	0 / 303 (0.00%)
occurrences (all)	0	0	0
VITAMIN D DEFICIENCY			
subjects affected / exposed	8 / 276 (2.90%)	0 / 21 (0.00%)	2 / 303 (0.66%)
occurrences (all)	8	0	2

Non-serious adverse events	Period 1, Primary and 30 mg Cohorts: Abatacept	Period 2, 30 mg Cohort: Abatacept/Upa 30 mg QD/Upa 15 mg QD	Period 2, 30mg Cohort: Upa 30 mg QD/Upa 30 mg QD
Total subjects affected by non-serious adverse events			
subjects affected / exposed	149 / 332 (44.88%)	9 / 12 (75.00%)	15 / 17 (88.24%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
SKIN PAPILLOMA			
subjects affected / exposed	0 / 332 (0.00%)	0 / 12 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
SEBORRHOEIC KERATOSIS			
subjects affected / exposed	0 / 332 (0.00%)	0 / 12 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
HAEMANGIOMA OF SPLEEN			
subjects affected / exposed	0 / 332 (0.00%)	1 / 12 (8.33%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
UTERINE LEIOMYOMA			
subjects affected / exposed	0 / 332 (0.00%)	0 / 12 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Vascular disorders			
HYPERTENSION			

subjects affected / exposed	11 / 332 (3.31%)	0 / 12 (0.00%)	4 / 17 (23.53%)
occurrences (all)	11	0	4
General disorders and administration site conditions			
NON-CARDIAC CHEST PAIN			
subjects affected / exposed	0 / 332 (0.00%)	0 / 12 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
CHEST PAIN			
subjects affected / exposed	2 / 332 (0.60%)	0 / 12 (0.00%)	1 / 17 (5.88%)
occurrences (all)	2	0	1
FATIGUE			
subjects affected / exposed	2 / 332 (0.60%)	0 / 12 (0.00%)	1 / 17 (5.88%)
occurrences (all)	2	0	1
FEELING HOT			
subjects affected / exposed	0 / 332 (0.00%)	0 / 12 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
PERIPHERAL SWELLING			
subjects affected / exposed	1 / 332 (0.30%)	0 / 12 (0.00%)	1 / 17 (5.88%)
occurrences (all)	1	0	1
PYREXIA			
subjects affected / exposed	3 / 332 (0.90%)	0 / 12 (0.00%)	0 / 17 (0.00%)
occurrences (all)	3	0	0
SWELLING			
subjects affected / exposed	1 / 332 (0.30%)	0 / 12 (0.00%)	1 / 17 (5.88%)
occurrences (all)	1	0	1
Immune system disorders			
DRUG HYPERSENSITIVITY			
subjects affected / exposed	0 / 332 (0.00%)	0 / 12 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	2
Reproductive system and breast disorders			
CYSTOCELE			
subjects affected / exposed	0 / 332 (0.00%)	1 / 12 (8.33%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
Respiratory, thoracic and mediastinal disorders			
ASTHMA			

subjects affected / exposed	1 / 332 (0.30%)	0 / 12 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
OROPHARYNGEAL PAIN			
subjects affected / exposed	1 / 332 (0.30%)	0 / 12 (0.00%)	2 / 17 (11.76%)
occurrences (all)	1	0	2
INTERSTITIAL LUNG DISEASE			
subjects affected / exposed	0 / 332 (0.00%)	1 / 12 (8.33%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
DYSPHONIA			
subjects affected / exposed	0 / 332 (0.00%)	0 / 12 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
COUGH			
subjects affected / exposed	8 / 332 (2.41%)	0 / 12 (0.00%)	1 / 17 (5.88%)
occurrences (all)	8	0	1
BRONCHIECTASIS			
subjects affected / exposed	0 / 332 (0.00%)	0 / 12 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
NASAL CONGESTION			
subjects affected / exposed	2 / 332 (0.60%)	0 / 12 (0.00%)	1 / 17 (5.88%)
occurrences (all)	2	0	1
PLEURAL EFFUSION			
subjects affected / exposed	0 / 332 (0.00%)	1 / 12 (8.33%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
PULMONARY MASS			
subjects affected / exposed	0 / 332 (0.00%)	0 / 12 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
RHINORRHOEA			
subjects affected / exposed	1 / 332 (0.30%)	0 / 12 (0.00%)	1 / 17 (5.88%)
occurrences (all)	1	0	1
Psychiatric disorders			
ANXIETY			
subjects affected / exposed	3 / 332 (0.90%)	0 / 12 (0.00%)	0 / 17 (0.00%)
occurrences (all)	3	0	0
AFFECT LABILITY			
subjects affected / exposed	0 / 332 (0.00%)	1 / 12 (8.33%)	0 / 17 (0.00%)
occurrences (all)	0	1	0

DEPRESSION			
subjects affected / exposed	2 / 332 (0.60%)	1 / 12 (8.33%)	0 / 17 (0.00%)
occurrences (all)	2	1	0
PANIC ATTACK			
subjects affected / exposed	0 / 332 (0.00%)	0 / 12 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
INSOMNIA			
subjects affected / exposed	0 / 332 (0.00%)	0 / 12 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
DEPRESSION SUICIDAL			
subjects affected / exposed	0 / 332 (0.00%)	0 / 12 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Investigations			
ALANINE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	3 / 332 (0.90%)	0 / 12 (0.00%)	0 / 17 (0.00%)
occurrences (all)	3	0	0
ASPARTATE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	1 / 332 (0.30%)	0 / 12 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
BLOOD CREATINE PHOSPHOKINASE INCREASED			
subjects affected / exposed	6 / 332 (1.81%)	0 / 12 (0.00%)	1 / 17 (5.88%)
occurrences (all)	7	0	1
BLOOD CREATININE INCREASED			
subjects affected / exposed	0 / 332 (0.00%)	0 / 12 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
WEIGHT INCREASED			
subjects affected / exposed	3 / 332 (0.90%)	0 / 12 (0.00%)	2 / 17 (11.76%)
occurrences (all)	3	0	2
SCAN ADRENAL GLAND ABNORMAL			
subjects affected / exposed	0 / 332 (0.00%)	1 / 12 (8.33%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
WHITE BLOOD CELLS URINE POSITIVE			
subjects affected / exposed	0 / 332 (0.00%)	0 / 12 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0

BLOOD PRESSURE INCREASED			
subjects affected / exposed	0 / 332 (0.00%)	0 / 12 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
BLOOD TRIGLYCERIDES INCREASED			
subjects affected / exposed	0 / 332 (0.00%)	0 / 12 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
ELECTROCARDIOGRAM ABNORMAL			
subjects affected / exposed	0 / 332 (0.00%)	0 / 12 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
HAEMOGLOBIN DECREASED			
subjects affected / exposed	0 / 332 (0.00%)	0 / 12 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
HEPATIC ENZYME INCREASED			
subjects affected / exposed	0 / 332 (0.00%)	0 / 12 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
HIGH DENSITY LIPOPROTEIN DECREASED			
subjects affected / exposed	0 / 332 (0.00%)	0 / 12 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
LIVER FUNCTION TEST INCREASED			
subjects affected / exposed	1 / 332 (0.30%)	0 / 12 (0.00%)	2 / 17 (11.76%)
occurrences (all)	1	0	2
Injury, poisoning and procedural complications			
CONTUSION			
subjects affected / exposed	0 / 332 (0.00%)	1 / 12 (8.33%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
BONE CONTUSION			
subjects affected / exposed	0 / 332 (0.00%)	0 / 12 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
BURNS SECOND DEGREE			
subjects affected / exposed	0 / 332 (0.00%)	0 / 12 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
CORNEAL ABRASION			
subjects affected / exposed	0 / 332 (0.00%)	0 / 12 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
FALL			

subjects affected / exposed	2 / 332 (0.60%)	0 / 12 (0.00%)	2 / 17 (11.76%)
occurrences (all)	2	0	2
LIGAMENT RUPTURE			
subjects affected / exposed	0 / 332 (0.00%)	0 / 12 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
SCRATCH			
subjects affected / exposed	0 / 332 (0.00%)	0 / 12 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
SKIN LACERATION			
subjects affected / exposed	1 / 332 (0.30%)	0 / 12 (0.00%)	1 / 17 (5.88%)
occurrences (all)	1	0	1
TOOTH FRACTURE			
subjects affected / exposed	0 / 332 (0.00%)	0 / 12 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Congenital, familial and genetic disorders			
TYPE V HYPERLIPIDAEMIA			
subjects affected / exposed	0 / 332 (0.00%)	0 / 12 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
ATRIOVENTRICULAR BLOCK FIRST DEGREE			
subjects affected / exposed	0 / 332 (0.00%)	0 / 12 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
ATRIAL FIBRILLATION			
subjects affected / exposed	0 / 332 (0.00%)	1 / 12 (8.33%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
CARDIOMYOPATHY			
subjects affected / exposed	1 / 332 (0.30%)	1 / 12 (8.33%)	0 / 17 (0.00%)
occurrences (all)	1	1	0
MITRAL VALVE INCOMPETENCE			
subjects affected / exposed	0 / 332 (0.00%)	1 / 12 (8.33%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
SUPRAVENTRICULAR TACHYCARDIA			
subjects affected / exposed	0 / 332 (0.00%)	0 / 12 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
TACHYCARDIA			

subjects affected / exposed	0 / 332 (0.00%)	0 / 12 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
TRICUSPID VALVE INCOMPETENCE			
subjects affected / exposed	0 / 332 (0.00%)	1 / 12 (8.33%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
Nervous system disorders			
SCIATICA			
subjects affected / exposed	1 / 332 (0.30%)	0 / 12 (0.00%)	1 / 17 (5.88%)
occurrences (all)	1	0	1
CARPAL TUNNEL SYNDROME			
subjects affected / exposed	3 / 332 (0.90%)	0 / 12 (0.00%)	0 / 17 (0.00%)
occurrences (all)	4	0	0
DIZZINESS			
subjects affected / exposed	2 / 332 (0.60%)	0 / 12 (0.00%)	1 / 17 (5.88%)
occurrences (all)	2	0	1
HEADACHE			
subjects affected / exposed	10 / 332 (3.01%)	0 / 12 (0.00%)	1 / 17 (5.88%)
occurrences (all)	11	0	1
PARAESTHESIA			
subjects affected / exposed	1 / 332 (0.30%)	0 / 12 (0.00%)	1 / 17 (5.88%)
occurrences (all)	1	0	1
TREMOR			
subjects affected / exposed	0 / 332 (0.00%)	1 / 12 (8.33%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
SYNCOPE			
subjects affected / exposed	0 / 332 (0.00%)	0 / 12 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
ANAEMIA			
subjects affected / exposed	3 / 332 (0.90%)	0 / 12 (0.00%)	0 / 17 (0.00%)
occurrences (all)	3	0	0
IRON DEFICIENCY ANAEMIA			
subjects affected / exposed	0 / 332 (0.00%)	0 / 12 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
NEUTROPENIA			

subjects affected / exposed	2 / 332 (0.60%)	0 / 12 (0.00%)	0 / 17 (0.00%)
occurrences (all)	2	0	0
LEUKOCYTOSIS			
subjects affected / exposed	1 / 332 (0.30%)	0 / 12 (0.00%)	1 / 17 (5.88%)
occurrences (all)	1	0	1
Ear and labyrinth disorders			
TINNITUS			
subjects affected / exposed	1 / 332 (0.30%)	0 / 12 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
Eye disorders			
EYELID PTOSIS			
subjects affected / exposed	0 / 332 (0.00%)	0 / 12 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
CATARACT			
subjects affected / exposed	0 / 332 (0.00%)	0 / 12 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
EYE HAEMATOMA			
subjects affected / exposed	0 / 332 (0.00%)	0 / 12 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
GLAUCOMA			
subjects affected / exposed	0 / 332 (0.00%)	0 / 12 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Gastrointestinal disorders			
ABDOMINAL PAIN			
subjects affected / exposed	4 / 332 (1.20%)	0 / 12 (0.00%)	0 / 17 (0.00%)
occurrences (all)	4	0	0
CONSTIPATION			
subjects affected / exposed	4 / 332 (1.20%)	0 / 12 (0.00%)	1 / 17 (5.88%)
occurrences (all)	4	0	1
DIARRHOEA			
subjects affected / exposed	13 / 332 (3.92%)	0 / 12 (0.00%)	0 / 17 (0.00%)
occurrences (all)	13	0	0
HAEMORRHOIDS			
subjects affected / exposed	2 / 332 (0.60%)	1 / 12 (8.33%)	0 / 17 (0.00%)
occurrences (all)	2	1	0
DUODENOGASTRIC REFLUX			

subjects affected / exposed	0 / 332 (0.00%)	1 / 12 (8.33%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
DYSPEPSIA			
subjects affected / exposed	1 / 332 (0.30%)	0 / 12 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
GASTRITIS			
subjects affected / exposed	2 / 332 (0.60%)	1 / 12 (8.33%)	0 / 17 (0.00%)
occurrences (all)	2	1	0
DIVERTICULUM INTESTINAL			
subjects affected / exposed	0 / 332 (0.00%)	1 / 12 (8.33%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
LARGE INTESTINE POLYP			
subjects affected / exposed	0 / 332 (0.00%)	1 / 12 (8.33%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
NAUSEA			
subjects affected / exposed	8 / 332 (2.41%)	0 / 12 (0.00%)	1 / 17 (5.88%)
occurrences (all)	13	0	1
PANCREATIC CYST			
subjects affected / exposed	0 / 332 (0.00%)	1 / 12 (8.33%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
STOMATITIS			
subjects affected / exposed	3 / 332 (0.90%)	0 / 12 (0.00%)	1 / 17 (5.88%)
occurrences (all)	3	0	1
VOMITING			
subjects affected / exposed	1 / 332 (0.30%)	0 / 12 (0.00%)	1 / 17 (5.88%)
occurrences (all)	1	0	1
Hepatobiliary disorders			
CHOLELITHIASIS			
subjects affected / exposed	0 / 332 (0.00%)	0 / 12 (0.00%)	2 / 17 (11.76%)
occurrences (all)	0	0	3
HEPATIC STEATOSIS			
subjects affected / exposed	0 / 332 (0.00%)	1 / 12 (8.33%)	1 / 17 (5.88%)
occurrences (all)	0	1	1
Skin and subcutaneous tissue disorders			
DERMATITIS ALLERGIC			

subjects affected / exposed	0 / 332 (0.00%)	0 / 12 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
DERMATITIS CONTACT			
subjects affected / exposed	1 / 332 (0.30%)	0 / 12 (0.00%)	1 / 17 (5.88%)
occurrences (all)	1	0	1
ERYTHEMA			
subjects affected / exposed	0 / 332 (0.00%)	0 / 12 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
NIGHT SWEATS			
subjects affected / exposed	0 / 332 (0.00%)	0 / 12 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
PHOTODERMATOSIS			
subjects affected / exposed	0 / 332 (0.00%)	0 / 12 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
PRURITUS			
subjects affected / exposed	5 / 332 (1.51%)	0 / 12 (0.00%)	1 / 17 (5.88%)
occurrences (all)	6	0	1
ACTINIC KERATOSIS			
subjects affected / exposed	0 / 332 (0.00%)	0 / 12 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
RASH			
subjects affected / exposed	1 / 332 (0.30%)	0 / 12 (0.00%)	2 / 17 (11.76%)
occurrences (all)	1	0	2
ROSACEA			
subjects affected / exposed	1 / 332 (0.30%)	0 / 12 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
Renal and urinary disorders			
CYSTITIS NONINFECTIVE			
subjects affected / exposed	0 / 332 (0.00%)	0 / 12 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
BLADDER HYPERTROPHY			
subjects affected / exposed	0 / 332 (0.00%)	0 / 12 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
RENAL CYST			
subjects affected / exposed	0 / 332 (0.00%)	1 / 12 (8.33%)	0 / 17 (0.00%)
occurrences (all)	0	1	0

URETHRAL STENOSIS			
subjects affected / exposed	0 / 332 (0.00%)	0 / 12 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
COSTOCHONDRITIS			
subjects affected / exposed	1 / 332 (0.30%)	0 / 12 (0.00%)	1 / 17 (5.88%)
occurrences (all)	1	0	1
BACK PAIN			
subjects affected / exposed	10 / 332 (3.01%)	0 / 12 (0.00%)	1 / 17 (5.88%)
occurrences (all)	10	0	1
ARTHRALGIA			
subjects affected / exposed	6 / 332 (1.81%)	0 / 12 (0.00%)	1 / 17 (5.88%)
occurrences (all)	7	0	1
FLANK PAIN			
subjects affected / exposed	0 / 332 (0.00%)	0 / 12 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
SPINAL OSTEOARTHRITIS			
subjects affected / exposed	0 / 332 (0.00%)	0 / 12 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
SJOGREN'S SYNDROME			
subjects affected / exposed	0 / 332 (0.00%)	0 / 12 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
RHEUMATOID ARTHRITIS			
subjects affected / exposed	15 / 332 (4.52%)	1 / 12 (8.33%)	1 / 17 (5.88%)
occurrences (all)	15	1	1
OSTEOPOROSIS			
subjects affected / exposed	0 / 332 (0.00%)	0 / 12 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
OSTEOPENIA			
subjects affected / exposed	1 / 332 (0.30%)	0 / 12 (0.00%)	1 / 17 (5.88%)
occurrences (all)	1	0	1
OSTEOARTHRITIS			
subjects affected / exposed	3 / 332 (0.90%)	1 / 12 (8.33%)	0 / 17 (0.00%)
occurrences (all)	3	1	0
MUSCULOSKELETAL CHEST PAIN			

subjects affected / exposed	2 / 332 (0.60%)	0 / 12 (0.00%)	0 / 17 (0.00%)
occurrences (all)	2	0	0
MUSCLE SPASMS			
subjects affected / exposed	6 / 332 (1.81%)	0 / 12 (0.00%)	2 / 17 (11.76%)
occurrences (all)	6	0	2
GREATER TROCHANTERIC PAIN SYNDROME			
subjects affected / exposed	2 / 332 (0.60%)	0 / 12 (0.00%)	0 / 17 (0.00%)
occurrences (all)	2	0	0
SPONDYLOLISTHESIS			
subjects affected / exposed	0 / 332 (0.00%)	0 / 12 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
TRIGGER FINGER			
subjects affected / exposed	0 / 332 (0.00%)	0 / 12 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
CANDIDA INFECTION			
subjects affected / exposed	0 / 332 (0.00%)	0 / 12 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
ASYMPTOMATIC COVID-19			
subjects affected / exposed	0 / 332 (0.00%)	0 / 12 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
BRONCHITIS			
subjects affected / exposed	13 / 332 (3.92%)	0 / 12 (0.00%)	3 / 17 (17.65%)
occurrences (all)	13	0	3
COVID-19			
subjects affected / exposed	0 / 332 (0.00%)	5 / 12 (41.67%)	0 / 17 (0.00%)
occurrences (all)	0	5	0
CYSTITIS			
subjects affected / exposed	3 / 332 (0.90%)	0 / 12 (0.00%)	0 / 17 (0.00%)
occurrences (all)	3	0	0
EAR INFECTION			
subjects affected / exposed	1 / 332 (0.30%)	1 / 12 (8.33%)	0 / 17 (0.00%)
occurrences (all)	1	1	0
GASTROENTERITIS			

subjects affected / exposed	4 / 332 (1.20%)	0 / 12 (0.00%)	0 / 17 (0.00%)
occurrences (all)	4	0	0
HERPES SIMPLEX			
subjects affected / exposed	1 / 332 (0.30%)	0 / 12 (0.00%)	1 / 17 (5.88%)
occurrences (all)	1	0	1
NASOPHARYNGITIS			
subjects affected / exposed	14 / 332 (4.22%)	1 / 12 (8.33%)	2 / 17 (11.76%)
occurrences (all)	15	1	2
INFLUENZA			
subjects affected / exposed	2 / 332 (0.60%)	0 / 12 (0.00%)	2 / 17 (11.76%)
occurrences (all)	2	0	2
LATENT TUBERCULOSIS			
subjects affected / exposed	0 / 332 (0.00%)	0 / 12 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
LOCALISED INFECTION			
subjects affected / exposed	0 / 332 (0.00%)	0 / 12 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
HERPES ZOSTER			
subjects affected / exposed	4 / 332 (1.20%)	0 / 12 (0.00%)	1 / 17 (5.88%)
occurrences (all)	4	0	1
ONYCHOMYCOSIS			
subjects affected / exposed	0 / 332 (0.00%)	0 / 12 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
OPHTHALMIC HERPES ZOSTER			
subjects affected / exposed	0 / 332 (0.00%)	0 / 12 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
ORAL CANDIDIASIS			
subjects affected / exposed	1 / 332 (0.30%)	0 / 12 (0.00%)	1 / 17 (5.88%)
occurrences (all)	1	0	1
PERIODONTITIS			
subjects affected / exposed	0 / 332 (0.00%)	0 / 12 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
RHINITIS			
subjects affected / exposed	1 / 332 (0.30%)	0 / 12 (0.00%)	1 / 17 (5.88%)
occurrences (all)	1	0	1
PHARYNGITIS STREPTOCOCCAL			

subjects affected / exposed	0 / 332 (0.00%)	0 / 12 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
PNEUMONIA			
subjects affected / exposed	3 / 332 (0.90%)	0 / 12 (0.00%)	1 / 17 (5.88%)
occurrences (all)	3	0	1
POST PROCEDURAL CELLULITIS			
subjects affected / exposed	0 / 332 (0.00%)	0 / 12 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
RESPIRATORY TRACT INFECTION			
subjects affected / exposed	2 / 332 (0.60%)	0 / 12 (0.00%)	0 / 17 (0.00%)
occurrences (all)	2	0	0
PHARYNGITIS			
subjects affected / exposed	3 / 332 (0.90%)	0 / 12 (0.00%)	1 / 17 (5.88%)
occurrences (all)	3	0	1
SINUSITIS			
subjects affected / exposed	5 / 332 (1.51%)	0 / 12 (0.00%)	2 / 17 (11.76%)
occurrences (all)	5	0	2
STAPHYLOCOCCAL INFECTION			
subjects affected / exposed	0 / 332 (0.00%)	0 / 12 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
TOOTH INFECTION			
subjects affected / exposed	1 / 332 (0.30%)	1 / 12 (8.33%)	0 / 17 (0.00%)
occurrences (all)	2	1	0
UPPER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	15 / 332 (4.52%)	2 / 12 (16.67%)	4 / 17 (23.53%)
occurrences (all)	18	2	4
VIRAL UPPER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	0 / 332 (0.00%)	0 / 12 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
VULVOVAGINAL MYCOTIC INFECTION			
subjects affected / exposed	3 / 332 (0.90%)	0 / 12 (0.00%)	1 / 17 (5.88%)
occurrences (all)	3	0	1
URINARY TRACT INFECTION			

subjects affected / exposed	22 / 332 (6.63%)	1 / 12 (8.33%)	2 / 17 (11.76%)
occurrences (all)	28	1	3
Metabolism and nutrition disorders			
DECREASED APPETITE			
subjects affected / exposed	1 / 332 (0.30%)	1 / 12 (8.33%)	0 / 17 (0.00%)
occurrences (all)	1	1	0
HYPOKALAEMIA			
subjects affected / exposed	1 / 332 (0.30%)	0 / 12 (0.00%)	1 / 17 (5.88%)
occurrences (all)	1	0	1
HYPERCHOLESTEROLAEMIA			
subjects affected / exposed	0 / 332 (0.00%)	0 / 12 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
DIABETES MELLITUS			
subjects affected / exposed	4 / 332 (1.20%)	0 / 12 (0.00%)	1 / 17 (5.88%)
occurrences (all)	4	0	1
DEHYDRATION			
subjects affected / exposed	1 / 332 (0.30%)	0 / 12 (0.00%)	1 / 17 (5.88%)
occurrences (all)	1	0	1
VITAMIN D DEFICIENCY			
subjects affected / exposed	0 / 332 (0.00%)	0 / 12 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1

Non-serious adverse events	Period 2, 30 mg Cohort: Abatacept/Upa 30 mg QD	Period 2, 30 mg Cohort: Upa 30 mg QD/Upa 30 mg QD/Upa 15 mg QD	Period 2, Primary Cohort: Upa 15 mg QD/Upa 15 mg QD
Total subjects affected by non-serious adverse events			
subjects affected / exposed	17 / 19 (89.47%)	7 / 12 (58.33%)	221 / 271 (81.55%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
SKIN PAPILLOMA			
subjects affected / exposed	1 / 19 (5.26%)	0 / 12 (0.00%)	1 / 271 (0.37%)
occurrences (all)	1	0	1
SEBORRHOEIC KERATOSIS			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	0 / 271 (0.00%)
occurrences (all)	0	0	0
HAEMANGIOMA OF SPLEEN			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	0 / 271 (0.00%)
occurrences (all)	0	0	0

UTERINE LEIOMYOMA			
subjects affected / exposed	1 / 19 (5.26%)	0 / 12 (0.00%)	0 / 271 (0.00%)
occurrences (all)	1	0	0
Vascular disorders			
HYPERTENSION			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	24 / 271 (8.86%)
occurrences (all)	0	0	26
General disorders and administration site conditions			
NON-CARDIAC CHEST PAIN			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	0 / 271 (0.00%)
occurrences (all)	0	0	0
CHEST PAIN			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	1 / 271 (0.37%)
occurrences (all)	0	0	1
FATIGUE			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	7 / 271 (2.58%)
occurrences (all)	0	0	7
FEELING HOT			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	0 / 271 (0.00%)
occurrences (all)	0	0	0
PERIPHERAL SWELLING			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	3 / 271 (1.11%)
occurrences (all)	0	0	3
PYREXIA			
subjects affected / exposed	1 / 19 (5.26%)	0 / 12 (0.00%)	7 / 271 (2.58%)
occurrences (all)	1	0	7
SWELLING			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	0 / 271 (0.00%)
occurrences (all)	0	0	0
Immune system disorders			
DRUG HYPERSENSITIVITY			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	1 / 271 (0.37%)
occurrences (all)	0	0	1
Reproductive system and breast disorders			
CYSTOCELE			

subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	0 / 271 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
ASTHMA			
subjects affected / exposed	1 / 19 (5.26%)	0 / 12 (0.00%)	2 / 271 (0.74%)
occurrences (all)	1	0	2
OROPHARYNGEAL PAIN			
subjects affected / exposed	1 / 19 (5.26%)	0 / 12 (0.00%)	1 / 271 (0.37%)
occurrences (all)	1	0	1
INTERSTITIAL LUNG DISEASE			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	0 / 271 (0.00%)
occurrences (all)	0	0	0
DYSPHONIA			
subjects affected / exposed	1 / 19 (5.26%)	0 / 12 (0.00%)	2 / 271 (0.74%)
occurrences (all)	2	0	2
COUGH			
subjects affected / exposed	1 / 19 (5.26%)	0 / 12 (0.00%)	17 / 271 (6.27%)
occurrences (all)	1	0	20
BRONCHIECTASIS			
subjects affected / exposed	0 / 19 (0.00%)	1 / 12 (8.33%)	1 / 271 (0.37%)
occurrences (all)	0	1	1
NASAL CONGESTION			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	3 / 271 (1.11%)
occurrences (all)	0	0	3
PLEURAL EFFUSION			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	0 / 271 (0.00%)
occurrences (all)	0	0	0
PULMONARY MASS			
subjects affected / exposed	0 / 19 (0.00%)	1 / 12 (8.33%)	3 / 271 (1.11%)
occurrences (all)	0	1	3
RHINORRHOEA			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	2 / 271 (0.74%)
occurrences (all)	0	0	2
Psychiatric disorders			

ANXIETY			
subjects affected / exposed	1 / 19 (5.26%)	0 / 12 (0.00%)	6 / 271 (2.21%)
occurrences (all)	1	0	8
AFFECT LABILITY			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	0 / 271 (0.00%)
occurrences (all)	0	0	0
DEPRESSION			
subjects affected / exposed	1 / 19 (5.26%)	0 / 12 (0.00%)	10 / 271 (3.69%)
occurrences (all)	1	0	14
PANIC ATTACK			
subjects affected / exposed	1 / 19 (5.26%)	0 / 12 (0.00%)	0 / 271 (0.00%)
occurrences (all)	1	0	0
INSOMNIA			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	5 / 271 (1.85%)
occurrences (all)	0	0	5
DEPRESSION SUICIDAL			
subjects affected / exposed	1 / 19 (5.26%)	0 / 12 (0.00%)	0 / 271 (0.00%)
occurrences (all)	1	0	0
Investigations			
ALANINE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	1 / 19 (5.26%)	0 / 12 (0.00%)	15 / 271 (5.54%)
occurrences (all)	1	0	20
ASPARTATE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	17 / 271 (6.27%)
occurrences (all)	0	0	28
BLOOD CREATINE PHOSPHOKINASE INCREASED			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	16 / 271 (5.90%)
occurrences (all)	0	0	25
BLOOD CREATININE INCREASED			
subjects affected / exposed	1 / 19 (5.26%)	0 / 12 (0.00%)	3 / 271 (1.11%)
occurrences (all)	1	0	5
WEIGHT INCREASED			
subjects affected / exposed	1 / 19 (5.26%)	0 / 12 (0.00%)	13 / 271 (4.80%)
occurrences (all)	1	0	18
SCAN ADRENAL GLAND ABNORMAL			

subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	0 / 271 (0.00%)
occurrences (all)	0	0	0
WHITE BLOOD CELLS URINE POSITIVE			
subjects affected / exposed	1 / 19 (5.26%)	0 / 12 (0.00%)	0 / 271 (0.00%)
occurrences (all)	1	0	0
BLOOD PRESSURE INCREASED			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	4 / 271 (1.48%)
occurrences (all)	0	0	6
BLOOD TRIGLYCERIDES INCREASED			
subjects affected / exposed	2 / 19 (10.53%)	0 / 12 (0.00%)	2 / 271 (0.74%)
occurrences (all)	2	0	2
ELECTROCARDIOGRAM ABNORMAL			
subjects affected / exposed	1 / 19 (5.26%)	0 / 12 (0.00%)	1 / 271 (0.37%)
occurrences (all)	1	0	1
HAEMOGLOBIN DECREASED			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	2 / 271 (0.74%)
occurrences (all)	0	0	3
HEPATIC ENZYME INCREASED			
subjects affected / exposed	1 / 19 (5.26%)	0 / 12 (0.00%)	3 / 271 (1.11%)
occurrences (all)	1	0	3
HIGH DENSITY LIPOPROTEIN DECREASED			
subjects affected / exposed	1 / 19 (5.26%)	0 / 12 (0.00%)	0 / 271 (0.00%)
occurrences (all)	1	0	0
LIVER FUNCTION TEST INCREASED			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	3 / 271 (1.11%)
occurrences (all)	0	0	3
Injury, poisoning and procedural complications			
CONTUSION			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	4 / 271 (1.48%)
occurrences (all)	0	0	4
BONE CONTUSION			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	1 / 271 (0.37%)
occurrences (all)	0	0	2
BURNS SECOND DEGREE			

subjects affected / exposed	1 / 19 (5.26%)	0 / 12 (0.00%)	1 / 271 (0.37%)
occurrences (all)	1	0	1
CORNEAL ABRASION			
subjects affected / exposed	1 / 19 (5.26%)	0 / 12 (0.00%)	0 / 271 (0.00%)
occurrences (all)	1	0	0
FALL			
subjects affected / exposed	1 / 19 (5.26%)	0 / 12 (0.00%)	12 / 271 (4.43%)
occurrences (all)	1	0	13
LIGAMENT RUPTURE			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	1 / 271 (0.37%)
occurrences (all)	0	0	1
SCRATCH			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	0 / 271 (0.00%)
occurrences (all)	0	0	0
SKIN LACERATION			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	1 / 271 (0.37%)
occurrences (all)	0	0	1
TOOTH FRACTURE			
subjects affected / exposed	1 / 19 (5.26%)	0 / 12 (0.00%)	4 / 271 (1.48%)
occurrences (all)	1	0	4
Congenital, familial and genetic disorders			
TYPE V HYPERLIPIDAEMIA			
subjects affected / exposed	1 / 19 (5.26%)	0 / 12 (0.00%)	0 / 271 (0.00%)
occurrences (all)	1	0	0
Cardiac disorders			
ATRIOVENTRICULAR BLOCK FIRST DEGREE			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	1 / 271 (0.37%)
occurrences (all)	0	0	1
ATRIAL FIBRILLATION			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	1 / 271 (0.37%)
occurrences (all)	0	0	1
CARDIOMYOPATHY			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	0 / 271 (0.00%)
occurrences (all)	0	0	0
MITRAL VALVE INCOMPETENCE			

subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	2 / 271 (0.74%)
occurrences (all)	0	0	2
SUPRAVENTRICULAR TACHYCARDIA			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	0 / 271 (0.00%)
occurrences (all)	0	0	0
TACHYCARDIA			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	3 / 271 (1.11%)
occurrences (all)	0	0	4
TRICUSPID VALVE INCOMPETENCE			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	2 / 271 (0.74%)
occurrences (all)	0	0	2
Nervous system disorders			
SCIATICA			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	6 / 271 (2.21%)
occurrences (all)	0	0	10
CARPAL TUNNEL SYNDROME			
subjects affected / exposed	1 / 19 (5.26%)	0 / 12 (0.00%)	2 / 271 (0.74%)
occurrences (all)	1	0	2
DIZZINESS			
subjects affected / exposed	1 / 19 (5.26%)	0 / 12 (0.00%)	2 / 271 (0.74%)
occurrences (all)	2	0	2
HEADACHE			
subjects affected / exposed	1 / 19 (5.26%)	0 / 12 (0.00%)	11 / 271 (4.06%)
occurrences (all)	1	0	11
PARAESTHESIA			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	3 / 271 (1.11%)
occurrences (all)	0	0	3
TREMOR			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	0 / 271 (0.00%)
occurrences (all)	0	0	0
SYNCOPE			
subjects affected / exposed	1 / 19 (5.26%)	0 / 12 (0.00%)	2 / 271 (0.74%)
occurrences (all)	1	0	2
Blood and lymphatic system disorders			
ANAEMIA			

subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	10 / 271 (3.69%)
occurrences (all)	0	0	13
IRON DEFICIENCY ANAEMIA			
subjects affected / exposed	1 / 19 (5.26%)	0 / 12 (0.00%)	3 / 271 (1.11%)
occurrences (all)	1	0	3
NEUTROPENIA			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	9 / 271 (3.32%)
occurrences (all)	0	0	13
LEUKOCYTOSIS			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	0 / 271 (0.00%)
occurrences (all)	0	0	0
Ear and labyrinth disorders			
TINNITUS			
subjects affected / exposed	0 / 19 (0.00%)	1 / 12 (8.33%)	2 / 271 (0.74%)
occurrences (all)	0	1	2
Eye disorders			
EYELID PTOSIS			
subjects affected / exposed	1 / 19 (5.26%)	0 / 12 (0.00%)	0 / 271 (0.00%)
occurrences (all)	1	0	0
CATARACT			
subjects affected / exposed	1 / 19 (5.26%)	0 / 12 (0.00%)	3 / 271 (1.11%)
occurrences (all)	1	0	4
EYE HAEMATOMA			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	0 / 271 (0.00%)
occurrences (all)	0	0	0
GLAUCOMA			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	2 / 271 (0.74%)
occurrences (all)	0	0	2
Gastrointestinal disorders			
ABDOMINAL PAIN			
subjects affected / exposed	1 / 19 (5.26%)	0 / 12 (0.00%)	3 / 271 (1.11%)
occurrences (all)	1	0	3
CONSTIPATION			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	3 / 271 (1.11%)
occurrences (all)	0	0	3
DIARRHOEA			

subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	9 / 271 (3.32%)
occurrences (all)	0	0	9
HAEMORRHOIDS			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	1 / 271 (0.37%)
occurrences (all)	0	0	1
DUODENOGASTRIC REFLUX			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	1 / 271 (0.37%)
occurrences (all)	0	0	1
DYSPEPSIA			
subjects affected / exposed	1 / 19 (5.26%)	0 / 12 (0.00%)	5 / 271 (1.85%)
occurrences (all)	1	0	6
GASTRITIS			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	6 / 271 (2.21%)
occurrences (all)	0	0	8
DIVERTICULUM INTESTINAL			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	0 / 271 (0.00%)
occurrences (all)	0	0	0
LARGE INTESTINE POLYP			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	0 / 271 (0.00%)
occurrences (all)	0	0	0
NAUSEA			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	15 / 271 (5.54%)
occurrences (all)	0	0	16
PANCREATIC CYST			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	0 / 271 (0.00%)
occurrences (all)	0	0	0
STOMATITIS			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	0 / 271 (0.00%)
occurrences (all)	0	0	0
VOMITING			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	7 / 271 (2.58%)
occurrences (all)	0	0	8
Hepatobiliary disorders			
CHOLELITHIASIS			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	3 / 271 (1.11%)
occurrences (all)	0	0	3

HEPATIC STEATOSIS			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	8 / 271 (2.95%)
occurrences (all)	0	0	8
Skin and subcutaneous tissue disorders			
DERMATITIS ALLERGIC			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	2 / 271 (0.74%)
occurrences (all)	0	0	2
DERMATITIS CONTACT			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	1 / 271 (0.37%)
occurrences (all)	0	0	2
ERYTHEMA			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	1 / 271 (0.37%)
occurrences (all)	0	0	1
NIGHT SWEATS			
subjects affected / exposed	1 / 19 (5.26%)	0 / 12 (0.00%)	1 / 271 (0.37%)
occurrences (all)	1	0	1
PHOTODERMATOSIS			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	0 / 271 (0.00%)
occurrences (all)	0	0	0
PRURITUS			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	2 / 271 (0.74%)
occurrences (all)	0	0	2
ACTINIC KERATOSIS			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	0 / 271 (0.00%)
occurrences (all)	0	0	0
RASH			
subjects affected / exposed	2 / 19 (10.53%)	0 / 12 (0.00%)	1 / 271 (0.37%)
occurrences (all)	2	0	1
ROSACEA			
subjects affected / exposed	1 / 19 (5.26%)	0 / 12 (0.00%)	1 / 271 (0.37%)
occurrences (all)	1	0	1
Renal and urinary disorders			
CYSTITIS NONINFECTIVE			
subjects affected / exposed	0 / 19 (0.00%)	1 / 12 (8.33%)	0 / 271 (0.00%)
occurrences (all)	0	1	0
BLADDER HYPERTROPHY			

subjects affected / exposed	1 / 19 (5.26%)	0 / 12 (0.00%)	0 / 271 (0.00%)
occurrences (all)	1	0	0
RENAL CYST			
subjects affected / exposed	0 / 19 (0.00%)	1 / 12 (8.33%)	2 / 271 (0.74%)
occurrences (all)	0	1	2
URETHRAL STENOSIS			
subjects affected / exposed	1 / 19 (5.26%)	0 / 12 (0.00%)	0 / 271 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal and connective tissue disorders			
COSTOCHONDRITIS			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	3 / 271 (1.11%)
occurrences (all)	0	0	3
BACK PAIN			
subjects affected / exposed	1 / 19 (5.26%)	0 / 12 (0.00%)	18 / 271 (6.64%)
occurrences (all)	1	0	20
ARTHRALGIA			
subjects affected / exposed	1 / 19 (5.26%)	0 / 12 (0.00%)	15 / 271 (5.54%)
occurrences (all)	1	0	16
FLANK PAIN			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	1 / 271 (0.37%)
occurrences (all)	0	0	1
SPINAL OSTEOARTHRITIS			
subjects affected / exposed	1 / 19 (5.26%)	0 / 12 (0.00%)	9 / 271 (3.32%)
occurrences (all)	1	0	9
SJOGREN'S SYNDROME			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	0 / 271 (0.00%)
occurrences (all)	0	0	0
RHEUMATOID ARTHRITIS			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	27 / 271 (9.96%)
occurrences (all)	0	0	43
OSTEOPOROSIS			
subjects affected / exposed	1 / 19 (5.26%)	0 / 12 (0.00%)	4 / 271 (1.48%)
occurrences (all)	1	0	4
OSTEOPENIA			

subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	4 / 271 (1.48%)
occurrences (all)	0	0	4
OSTEOARTHRITIS			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	11 / 271 (4.06%)
occurrences (all)	0	0	13
MUSCULOSKELETAL CHEST PAIN			
subjects affected / exposed	1 / 19 (5.26%)	0 / 12 (0.00%)	2 / 271 (0.74%)
occurrences (all)	1	0	2
MUSCLE SPASMS			
subjects affected / exposed	1 / 19 (5.26%)	0 / 12 (0.00%)	2 / 271 (0.74%)
occurrences (all)	1	0	2
GREATER TROCHANTERIC PAIN SYNDROME			
subjects affected / exposed	2 / 19 (10.53%)	0 / 12 (0.00%)	7 / 271 (2.58%)
occurrences (all)	2	0	7
SPONDYLOLISTHESIS			
subjects affected / exposed	1 / 19 (5.26%)	0 / 12 (0.00%)	1 / 271 (0.37%)
occurrences (all)	1	0	1
TRIGGER FINGER			
subjects affected / exposed	1 / 19 (5.26%)	0 / 12 (0.00%)	1 / 271 (0.37%)
occurrences (all)	1	0	1
Infections and infestations			
CANDIDA INFECTION			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	0 / 271 (0.00%)
occurrences (all)	0	0	0
ASYMPTOMATIC COVID-19			
subjects affected / exposed	1 / 19 (5.26%)	0 / 12 (0.00%)	4 / 271 (1.48%)
occurrences (all)	1	0	4
BRONCHITIS			
subjects affected / exposed	1 / 19 (5.26%)	0 / 12 (0.00%)	16 / 271 (5.90%)
occurrences (all)	1	0	18
COVID-19			
subjects affected / exposed	0 / 19 (0.00%)	1 / 12 (8.33%)	64 / 271 (23.62%)
occurrences (all)	0	1	69
CYSTITIS			

subjects affected / exposed	2 / 19 (10.53%)	0 / 12 (0.00%)	9 / 271 (3.32%)
occurrences (all)	2	0	10
EAR INFECTION			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	7 / 271 (2.58%)
occurrences (all)	0	0	7
GASTROENTERITIS			
subjects affected / exposed	1 / 19 (5.26%)	0 / 12 (0.00%)	9 / 271 (3.32%)
occurrences (all)	1	0	9
HERPES SIMPLEX			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	2 / 271 (0.74%)
occurrences (all)	0	0	3
NASOPHARYNGITIS			
subjects affected / exposed	4 / 19 (21.05%)	0 / 12 (0.00%)	37 / 271 (13.65%)
occurrences (all)	5	0	57
INFLUENZA			
subjects affected / exposed	2 / 19 (10.53%)	0 / 12 (0.00%)	12 / 271 (4.43%)
occurrences (all)	2	0	12
LATENT TUBERCULOSIS			
subjects affected / exposed	0 / 19 (0.00%)	1 / 12 (8.33%)	6 / 271 (2.21%)
occurrences (all)	0	1	6
LOCALISED INFECTION			
subjects affected / exposed	1 / 19 (5.26%)	0 / 12 (0.00%)	2 / 271 (0.74%)
occurrences (all)	1	0	4
HERPES ZOSTER			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	24 / 271 (8.86%)
occurrences (all)	0	0	27
ONYCHOMYCOSIS			
subjects affected / exposed	1 / 19 (5.26%)	0 / 12 (0.00%)	4 / 271 (1.48%)
occurrences (all)	1	0	4
OPHTHALMIC HERPES ZOSTER			
subjects affected / exposed	1 / 19 (5.26%)	0 / 12 (0.00%)	0 / 271 (0.00%)
occurrences (all)	2	0	0
ORAL CANDIDIASIS			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	4 / 271 (1.48%)
occurrences (all)	0	0	9
PERIODONTITIS			

subjects affected / exposed	1 / 19 (5.26%)	0 / 12 (0.00%)	2 / 271 (0.74%)
occurrences (all)	1	0	2
RHINITIS			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	1 / 271 (0.37%)
occurrences (all)	0	0	4
PHARYNGITIS STREPTOCOCCAL			
subjects affected / exposed	1 / 19 (5.26%)	0 / 12 (0.00%)	2 / 271 (0.74%)
occurrences (all)	1	0	2
PNEUMONIA			
subjects affected / exposed	2 / 19 (10.53%)	0 / 12 (0.00%)	6 / 271 (2.21%)
occurrences (all)	2	0	6
POST PROCEDURAL CELLULITIS			
subjects affected / exposed	1 / 19 (5.26%)	0 / 12 (0.00%)	0 / 271 (0.00%)
occurrences (all)	1	0	0
RESPIRATORY TRACT INFECTION			
subjects affected / exposed	1 / 19 (5.26%)	0 / 12 (0.00%)	7 / 271 (2.58%)
occurrences (all)	1	0	8
PHARYNGITIS			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	9 / 271 (3.32%)
occurrences (all)	0	0	9
SINUSITIS			
subjects affected / exposed	1 / 19 (5.26%)	0 / 12 (0.00%)	7 / 271 (2.58%)
occurrences (all)	3	0	9
STAPHYLOCOCCAL INFECTION			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	1 / 271 (0.37%)
occurrences (all)	0	0	1
TOOTH INFECTION			
subjects affected / exposed	1 / 19 (5.26%)	0 / 12 (0.00%)	4 / 271 (1.48%)
occurrences (all)	2	0	4
UPPER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	5 / 19 (26.32%)	1 / 12 (8.33%)	30 / 271 (11.07%)
occurrences (all)	5	1	46
VIRAL UPPER RESPIRATORY TRACT INFECTION			

subjects affected / exposed	1 / 19 (5.26%)	0 / 12 (0.00%)	2 / 271 (0.74%)
occurrences (all)	1	0	2
VULVOVAGINAL MYCOTIC INFECTION			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	0 / 271 (0.00%)
occurrences (all)	0	0	0
URINARY TRACT INFECTION			
subjects affected / exposed	3 / 19 (15.79%)	1 / 12 (8.33%)	40 / 271 (14.76%)
occurrences (all)	8	1	67
Metabolism and nutrition disorders			
DECREASED APPETITE			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	3 / 271 (1.11%)
occurrences (all)	0	0	3
HYPOKALAEMIA			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	0 / 271 (0.00%)
occurrences (all)	0	0	0
HYPERCHOLESTEROLAEMIA			
subjects affected / exposed	1 / 19 (5.26%)	0 / 12 (0.00%)	13 / 271 (4.80%)
occurrences (all)	1	0	15
DIABETES MELLITUS			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	4 / 271 (1.48%)
occurrences (all)	0	0	4
DEHYDRATION			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	1 / 271 (0.37%)
occurrences (all)	0	0	1
VITAMIN D DEFICIENCY			
subjects affected / exposed	0 / 19 (0.00%)	0 / 12 (0.00%)	7 / 271 (2.58%)
occurrences (all)	0	0	7

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
31 August 2016	The study design was updated from a 24-week randomized, double-blind, parallel group active-controlled treatment period to 12-weeks in Period 1. Exclusion criteria were updated to include human immunodeficiency virus (HIV) testing at screening and extended timeline for receipt of live vaccines to comply with abatacept product label on live vaccination. Toxicity management guides was updated to include infusion reaction guidance and the protocol introduction was updated to include results of in-vitro drug interactions.
25 January 2017	The design was updated from 12-weeks to 24-weeks in Period 1 and provided limit on the number of methotrexate (MTX) inadequate responders. Subject rescue criteria, discontinuation criteria along with primary, secondary and additional study endpoints were updated. Sample size increased from 300 to 500 subjects with approximately 200 sites. Period 2 was extended up to 5 years. Other text was updated to provide clarity and improve readability.
28 March 2017	Permitted the addition or increase in doses of up to 2 conventional synthetic disease-modifying antirheumatic drugs (csDMARDs; except the combination of MTX and leflunomide) after Week 12 for those not achieving 20% improvement in both tender and swollen join counts. Added the additional endpoint of cumulative corticosteroid exposure at 24-weeks.
12 October 2017	Changes consistent with Amendment 3.01 for VHP countries. In addition, it allowed (at the discretion of the investigator) laboratory abnormalities to be recorded as AEs. Also this amendment replaced the dose of upadacitinib being studied for the primary analysis. The current dose of upadacitinib 30 mg QD was amended to 15 mg QD for patients not yet enrolled.
12 March 2020	(continued) The study drug accountability requirements were updated according to the revised sponsor guidelines. Text was added in Adverse Events of Special Interest to clarify that all cardiac, embolic, and thrombotic events will be adjudicated. In Toxicity Management herpes zoster and a recommendation for skin examination were added, the aspartate aminotransferase (AST) or alanine aminotransferase (ALT) parameters for management were updated, and study drug interruption prior to elective surgery in Period 2 was updated to 1 week.”

12 March 2020	Included an update to clarify guidance for the use of live vaccine administration during Period 2 such that if a live vaccine must be administered during study participation, study drug must be held for at least 30 days prior to the vaccination and at least 30 days after the vaccination (or longer if required locally). The removal of male contraception requirements for upadacitinib were clarified, 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. References to pregnancy of partners of male subjects were removed for consistency with the removal of male contraception requirements. Clarified permitted changes in background therapy and clarified background medication(s) optimization criteria in Period 2. Clarified concurrent use of JAK inhibitors is prohibited during the study. Added excluded biologic therapies to be consistent with current available biologic therapies in rheumatoid arthritis. Added allowance of high potency opiates for analgesic care related to AEs or SAEs. Provided guidance for interpretation of positive TB testing results in low risk subjects and added the ability to retest locally to confirm central laboratory result as a false-positive result is more likely in low risk subjects. Added use of Interferon Gamma Release Assay as a substitute for local TB testing since it is an equivalent assay to the QuantiFERON-TB Gold Plus. Specified that only subjects with newly identified TB risks are subject to chest x-rays to limit unnecessary procedures. Added discontinuation criteria concerning VTE. Included update that the DMC concluded its oversight of the study after the end of Period 1.
04 December 2020	Included changes in response to COVID-19 (or any state of emergency). An evaluation of the benefit and risk to subjects participating in the study relative to COVID-19 was added. Provisions for virtual or alternative locations for study visits due to the pandemic or any state of emergency were added. Clarifications were added regarding study activities that can be performed by phone/video conference or at local clinic/hospital/laboratory or through the optional home healthcare service in the event study visits are impacted by any state of emergency or pandemic situation. Study Procedures, including questionnaires, TB testing, chest X-rays, ECG, physical exam, efficacy assessments, laboratory tests, and pregnancy tests were updated to include provisions if an onsite visit cannot be performed due to the pandemic. Discontinuation criteria were revised regarding GI perforation and mitigation strategies related to the pandemic. Provision of study drug through direct-to-patient shipment was added. Language was added to include provision for modifications due to protocol deviations that may be due to the pandemic. Provisions allowing verbal consent in addition to the study informed consent in accordance with local regulations were added. Supplemental COVID-19 case report forms were added. Text was added to define pregnancy and product complaint reporting timeline as 24 hours from site staff awareness. Guidance was added for investigators on the management of subjects with suspected or confirmed COVID-19 infection. A clarification was added that the Investigator should also contact the AbbVie TA MD for confirmed ALT or AST > 8 x ULN in addition to immediate study drug interruption. The list of examples of commonly used strong cytochrome 3A inducers and the list of the adverse events of special interest was updated. Added language that remote monitoring may be employed as needed, due to COVID-19 or any pandemic/state of emergency. Updated the Ethical Conduct of the Study Se

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported