Clinical trial results:
A randomized, double-blind, placebo-controlled, multicenter, two-part, dose ranging and confirmatory study with an operationally seamless design, evaluating efficacy and safety of SAR153191 on top of methotrexate (MTX) in patients with active rheumatoid arthritis who are inadequate responders to MTX therapy

Summary

EudraCT number	2009-016266-90
Trial protocol	ES CZ FI HU EE DE LT PT NL GR RO AT BE
Global end of trial date	08 October 2013

Results information

Result version number	v1 (current)
This version publication date	27 April 2016
First version publication date	07 August 2015

Trial information

Trial identification

Sponsor protocol code	EFC11072

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01061736
WHO universal trial number (UTN)	-
Other trial identifiers	Study name: SARIL-RA-MOBILITY

Notes:

Sponsors

Sponsor organisation name	Sanofi aventis recherche & développement
Sponsor organisation address	1 avenue Pierre Brossolette, Chilly-Mazarin, France, 91380
Public contact	Trial Transparency Team, Sanofi aventis recherche & développement, Contact-US@sanofi.com
Scientific contact	Trial Transparency Team, Sanofi aventis recherche & développement, Contact-US@sanofi.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 November 2013
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	08 October 2013
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

This phase II/III study in subjects with active rheumatoid arthritis used an operationally seamless design. Main objectives were:

Phase II - 12 week dose-ranging study (part A): to evaluate efficacy and safety of 5 dose regimens of sarilumab (SAR153191/REGN88) on top of methotrexate (MTX);

Phase III - 52-week confirmatory study (part B): to confirm the efficacy and safety of the 2 dose regimens selected from part A.

Protection of trial subjects:

Subjects were fully informed of all pertinent aspects of the clinical trial as well as the possibility to discontinue at any time in language and terms appropriate for the subject and considering the local culture. During the course of the trial, subjects were provided with individual subject cards indicating the nature of the trial the subject is participating, contact details and any information needed in the event of a medical emergency.
Collected personal data and human biological samples were processed in compliance with the Sanofi-Aventis Group Personal Data Protection Charter ensuring that the Group abides by the laws governing personal data protection in force in all countries in which it operates.

Background therapy:

All subjects were treated with weekly MTX for the duration of the study and received the same weekly dose as they were receiving prior to enrollment. Subjects were required to be stable for at least 6 weeks prior to the screening visit.

Evidence for comparator: -

Actual start date of recruitment	22 March 2010
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	Norway: 1
Country: Number of subjects enrolled	Poland: 154
Country: Number of subjects enrolled	Portugal: 1
Country: Number of subjects enrolled	Romania: 45
Country: Number of subjects enrolled	Spain: 22
Country: Number of subjects enrolled	Austria: 4
Country: Number of subjects enrolled	Belgium: 1
Country: Number of subjects enrolled	Czech Republic: 12
Country: Number of subjects enrolled	Estonia: 20
Country: Number of subjects enrolled	Finland: 14

Country: Number of subjects enrolled	Germany: 22
Country: Number of subjects enrolled	Greece: 4
Country: Number of subjects enrolled	Hungary: 55
Country: Number of subjects enrolled	Lithuania: 10
Country: Number of subjects enrolled	Argentina: 130
Country: Number of subjects enrolled	Australia: 27
Country: Number of subjects enrolled	Belarus: 14
Country: Number of subjects enrolled	Brazil: 72
Country: Number of subjects enrolled	Canada: 10
Country: Number of subjects enrolled	Chile: 133
Country: Number of subjects enrolled	Colombia: 78
Country: Number of subjects enrolled	India: 24
Country: Number of subjects enrolled	Korea, Republic of: 46
Country: Number of subjects enrolled	Malaysia: 5
Country: Number of subjects enrolled	Mexico: 175
Country: Number of subjects enrolled	New Zealand: 9
Country: Number of subjects enrolled	Philippines: 15
Country: Number of subjects enrolled	Russian Federation: 213
Country: Number of subjects enrolled	South Africa: 97
Country: Number of subjects enrolled	Taiwan: 2
Country: Number of subjects enrolled	Thailand: 3
Country: Number of subjects enrolled	Turkey: 3
Country: Number of subjects enrolled	Ukraine: 67
Country: Number of subjects enrolled	United States: 187
Worldwide total number of subjects	1675
EEA total number of subjects	365

Notes:

Subjects enrolled per age group	
In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	1460
From 65 to 84 years	215
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was conducted at 247 centers in 36 countries. Overall, 3715 subjects were screened between March 2010 and July 2012, 2040 of whom were screen failures. Screen failures were mainly due to failure to meet the inclusion criterion for severity of the disease and/or due to meeting the exclusion criterion.

Pre-assignment

Screening details:

Randomization was performed centrally with allocation generated by Interactive Voice/Web Response System, stratified by geographical region and prior biological use. 306 subjects were randomized in Part A. 1369 subjects were randomized in part B, 172 before dose selection (cohort 1) and 1197 after dose selection (cohort 2).

Period 1

Period 1 title	Overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Assessor

Blinding implementation details:

Investigators were blinded with regard to each subject's CRP and IL-6 levels, except at screening and baseline, with the swollen and tender joint counts performed by a separate qualified assessor. Two readers, blinded with regard to treatment assignment, chronologic order of the radiographs, and subject's clinical status, independently reviewed and scored images using the modified Sharp/van der Heijde scoring (SHS) system.

Arms

Are arms mutually exclusive?	Yes
Arm title	Part A: SAR 100 mg QW

Arm description:

Sarilumab 100 mg weekly (qw) on top of MTX for 12 weeks.

Arm type	Experimental
Investigational medicinal product name	Sarilumab
Investigational medicinal product code	SAR153191
Other name	REGN88
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Single injection in abdomen.

Arm title	Part A: SAR 150 mg QW

Arm description:

Sarilumab 150 mg qw on top of MTX for 12-weeks.

Arm type	Experimental
Investigational medicinal product name	Sarilumab
Investigational medicinal product code	SAR153191
Other name	REGN88
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Single injection in abdomen.

Arm title	Part A: SAR 100 mg Q2W

Arm description:	
Sarilumab 100 mg every other week (q2w) alternating with placebo on top of MTX for 12 weeks.	
Arm type	Experimental
Investigational medicinal product name	Sarilumab
Investigational medicinal product code	SAR153191
Other name	REGN88
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use
Dosage and administration details:	
Single injection in abdomen.	
Investigational medicinal product name	Placebo (for sarilumab)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use
Dosage and administration details:	
Single injection in abdomen.	
Arm title	Part A: SAR 150 mg Q2W
Arm description:	
Sarilumab 150 mg q2w alternating with placebo on top of MTX for 12 weeks.	
Arm type	Experimental
Investigational medicinal product name	Sarilumab
Investigational medicinal product code	SAR153191
Other name	REGN88
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use
Dosage and administration details:	
Single injection in abdomen.	
Investigational medicinal product name	Placebo (for sarilumab)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use
Dosage and administration details:	
Single injection in abdomen.	
Arm title	Part A: SAR 200 mg Q2W
Arm description:	
Sarilumab 200 mg q2w alternating with placebo on top of MTX for 12 weeks.	
Arm type	Experimental
Investigational medicinal product name	Sarilumab
Investigational medicinal product code	SAR153191
Other name	REGN88
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use
Dosage and administration details:	
Single injection in abdomen.	
Investigational medicinal product name	Placebo (for sarilumab)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Single injection in abdomen.

Arm title	Part A: Placebo QW

Arm description:

Placebo (for sarilumab) qw on top of MTX for 12 weeks.

Arm type	Placebo
Investigational medicinal product name	Placebo (for sarilumab)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Single injection in abdomen.

Arm title	Part B cohort 1: Non-selected doses

Arm description:

Sarilumab 100 mg qw, 150 mg qw or 100 mg q2w on top of MTX up to dose selection. After dose selection, subjects were not continued but were allowed to participate in the open-label, long-term, extension study RA-EXTEND (LTS11210). These subjects were not included in any analysis.

Arm type	Experimental
Investigational medicinal product name	Sarilumab
Investigational medicinal product code	SAR153191
Other name	REGN88
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Single injection in abdomen.

Investigational medicinal product name	Placebo (for sarilumab)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Single injection in abdomen.

Arm title	Part B: SAR 150 mg Q2W

Arm description:

Sarilumab 150 mg q2w on top of MTX for a maximum of 52 weeks. Subjects with inadequate response from Week 16 could be rescued with open-label highest dose of sarilumab.

Arm type	Experimental
Investigational medicinal product name	Sarilumab
Investigational medicinal product code	SAR153191
Other name	REGN88
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Single injection in abdomen.

Arm title	Part B: SAR 200 mg Q2W

Arm description:

Sarilumab 200 mg q2w on top of MTX for a maximum of 52 weeks. Subjects with inadequate response

from Week 16 could be rescued with open-label highest dose of sarilumab.

Arm type	Experimental
Investigational medicinal product name	Sarilumab
Investigational medicinal product code	SAR153191
Other name	REGN88
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Single injection in abdomen.

Arm title	Part B: Placebo Q2W

Arm description:

Placebo (for sarilumab) q2w on top of MTX for a maximum of 52 weeks. Subjects with inadequate response from Week 16 could be rescued with open-label highest dose of sarilumab.

Arm type	Placebo
Investigational medicinal product name	Placebo (for sarilumab)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Single injection in abdomen.

Number of subjects in period 1	Part A: SAR 100 mg QW	Part A: SAR 150 mg QW	Part A: SAR 100 mg Q2W
Started	50	50	51
Treated	50	50	51
Completed	37	46	45
Not completed	13	4	6
Dose regimen not selected	-	-	-
Other	-	1	2
Adverse event	13	1	3
Poor compliance to protocol	-	-	-
Lack of efficacy	-	2	1
Not treated	-	-	-

Number of subjects in period 1	Part A: SAR 150 mg Q2W	Part A: SAR 200 mg Q2W	Part A: Placebo QW
Started	51	52	52
Treated	51	51	52
Completed	48	45	49
Not completed	3	7	3
Dose regimen not selected	-	-	-
Other	-	1	-
Adverse event	2	4	1
Poor compliance to protocol	-	-	-

Lack of efficacy	1	1	2
Not treated	-	1	-

Number of subjects in period 1	Part B cohort 1: Non-selected doses	Part B: SAR 150 mg Q2W	Part B: SAR 200 mg Q2W
Started	84	430	427
Treated	84	428	426
Completed	0	336	330
Not completed	84	94	97
Dose regimen not selected	79	-	-
Other	-	18	15
Adverse event	4	63	67
Poor compliance to protocol	-	2	5
Lack of efficacy	1	9	9
Not treated	-	2	1

Number of subjects in period 1	Part B: Placebo Q2W
Started	428
Treated	428
Completed	354
Not completed	74
Dose regimen not selected	-
Other	21
Adverse event	34
Poor compliance to protocol	9
Lack of efficacy	10
Not treated	-

Baseline characteristics

Reporting groups	
Reporting group title	Part A: SAR 100 mg QW
Reporting group description:	
Sarilumab 100 mg weekly (qw) on top of MTX for 12 weeks.	
Reporting group title	Part A: SAR 150 mg QW
Reporting group description:	
Sarilumab 150 mg qw on top of MTX for 12-weeks.	
Reporting group title	Part A: SAR 100 mg Q2W
Reporting group description:	
Sarilumab 100 mg every other week (q2w) alternating with placebo on top of MTX for 12 weeks.	
Reporting group title	Part A: SAR 150 mg Q2W
Reporting group description:	
Sarilumab 150 mg q2w alternating with placebo on top of MTX for 12 weeks.	
Reporting group title	Part A: SAR 200 mg Q2W
Reporting group description:	
Sarilumab 200 mg q2w alternating with placebo on top of MTX for 12 weeks.	
Reporting group title	Part A: Placebo QW
Reporting group description:	
Placebo (for sarilumab) qw on top of MTX for 12 weeks.	
Reporting group title	Part B cohort 1: Non-selected doses
Reporting group description:	
Sarilumab 100 mg qw, 150 mg qw or 100 mg q2w on top of MTX up to dose selection. After dose selection, subjects were not continued but were allowed to participate in the open-label, long-term, extension study RA-EXTEND (LTS11210). These subjects were not included in any analysis.	
Reporting group title	Part B: SAR 150 mg Q2W
Reporting group description:	
Sarilumab 150 mg q2w on top of MTX for a maximum of 52 weeks. Subjects with inadequate response from Week 16 could be rescued with open-label highest dose of sarilumab.	
Reporting group title	Part B: SAR 200 mg Q2W
Reporting group description:	
Sarilumab 200 mg q2w on top of MTX for a maximum of 52 weeks. Subjects with inadequate response from Week 16 could be rescued with open-label highest dose of sarilumab.	
Reporting group title	Part B: Placebo Q2W
Reporting group description:	
Placebo (for sarilumab) q2w on top of MTX for a maximum of 52 weeks. Subjects with inadequate response from Week 16 could be rescued with open-label highest dose of sarilumab.	

Reporting group values	Part A: SAR 100 mg QW	Part A: SAR 150 mg QW	Part A: SAR 100 mg Q2W
Number of subjects	50	50	51
Age categorical			
Units: Subjects			

Age continuous			
Units: years			
arithmetic mean	53.9	50.9	53.5
standard deviation	± 12.3	± 11.1	± 11.8

Gender categorical Units: Subjects			
Female	41	42	38
Male	9	8	13
Recruitment Phase Units: Subjects			
Part A	50	50	51
Part B Cohort 1	0	0	0
Part B Cohort 2	0	0	0
Rescued			
Part B (Cohort 1 selected doses and Cohort 2) subjects with inadequate response from Week 16 could be rescued with open-label highest dose of sarilumab. 'Not applicable' enumerates subjects from Part A or Part B Cohort 1 treated with doses not selected for Part B Cohort 2, and subjects from Cohort 2 who discontinued before or on Week 16.			
Units: Subjects			
Yes	0	0	0
No	0	0	0
Not applicable	50	50	51

Reporting group values	Part A: SAR 150 mg Q2W	Part A: SAR 200 mg Q2W	Part A: Placebo QW
Number of subjects	51	52	52
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	51.2	48.7	55.2
standard deviation	± 12.9	± 12.4	± 12.5
Gender categorical Units: Subjects			
Female	42	42	38
Male	9	10	14
Recruitment Phase Units: Subjects			
Part A	51	52	52
Part B Cohort 1	0	0	0
Part B Cohort 2	0	0	0
Rescued			
Part B (Cohort 1 selected doses and Cohort 2) subjects with inadequate response from Week 16 could be rescued with open-label highest dose of sarilumab. 'Not applicable' enumerates subjects from Part A or Part B Cohort 1 treated with doses not selected for Part B Cohort 2, and subjects from Cohort 2 who discontinued before or on Week 16.			
Units: Subjects			
Yes	0	0	0
No	0	0	0
Not applicable	51	52	52

Reporting group values	Part B cohort 1: Non-selected doses	Part B: SAR 150 mg Q2W	Part B: SAR 200 mg Q2W
Number of subjects	84	430	427

Age categorical Units: Subjects			

Age continuous Units: years			
arithmetic mean	51.1	50.3	50.8
standard deviation	± 11.5	± 11.9	± 12
Gender categorical Units: Subjects			
Female	69	345	359
Male	15	85	68
Recruitment Phase Units: Subjects			
Part A	0	0	0
Part B Cohort 1	84	30	28
Part B Cohort 2	0	400	399
Rescued			
Part B (Cohort 1 selected doses and Cohort 2) subjects with inadequate response from Week 16 could be rescued with open-label highest dose of sarilumab. 'Not applicable' enumerates subjects from Part A or Part B Cohort 1 treated with doses not selected for Part B Cohort 2, and subjects from Cohort 2 who discontinued before or on Week 16.			
Units: Subjects			
Yes	0	61	55
No	0	336	341
Not applicable	84	33	31

Reporting group values	Part B: Placebo Q2W	Total	
Number of subjects	428	1675	
Age categorical Units: Subjects			

Age continuous Units: years			
arithmetic mean	51.1		
standard deviation	± 11.2	-	
Gender categorical Units: Subjects			
Female	346	1362	
Male	82	313	
Recruitment Phase Units: Subjects			
Part A	0	306	
Part B Cohort 1	30	172	
Part B Cohort 2	398	1197	
Rescued			
Part B (Cohort 1 selected doses and Cohort 2) subjects with inadequate response from Week 16 could be rescued with open-label highest dose of sarilumab. 'Not applicable' enumerates subjects from Part A or Part B Cohort 1 treated with doses not selected for Part B Cohort 2, and subjects from Cohort 2 who discontinued before or on Week 16.			
Units: Subjects			

Yes	168	284	
No	243	920	
Not applicable	17	471	

End points

End points reporting groups

Reporting group title	Part A: SAR 100 mg QW
Reporting group description:	
Sarilumab 100 mg weekly (qw) on top of MTX for 12 weeks.	
Reporting group title	Part A: SAR 150 mg QW
Reporting group description:	
Sarilumab 150 mg qw on top of MTX for 12-weeks.	
Reporting group title	Part A: SAR 100 mg Q2W
Reporting group description:	
Sarilumab 100 mg every other week (q2w) alternating with placebo on top of MTX for 12 weeks.	
Reporting group title	Part A: SAR 150 mg Q2W
Reporting group description:	
Sarilumab 150 mg q2w alternating with placebo on top of MTX for 12 weeks.	
Reporting group title	Part A: SAR 200 mg Q2W
Reporting group description:	
Sarilumab 200 mg q2w alternating with placebo on top of MTX for 12 weeks.	
Reporting group title	Part A: Placebo QW
Reporting group description:	
Placebo (for sarilumab) qw on top of MTX for 12 weeks.	
Reporting group title	Part B cohort 1: Non-selected doses
Reporting group description:	
Sarilumab 100 mg qw, 150 mg qw or 100 mg q2w on top of MTX up to dose selection. After dose selection, subjects were not continued but were allowed to participate in the open-label, long-term, extension study RA-EXTEND (LTS11210). These subjects were not included in any analysis.	
Reporting group title	Part B: SAR 150 mg Q2W
Reporting group description:	
Sarilumab 150 mg q2w on top of MTX for a maximum of 52 weeks. Subjects with inadequate response from Week 16 could be rescued with open-label highest dose of sarilumab.	
Reporting group title	Part B: SAR 200 mg Q2W
Reporting group description:	
Sarilumab 200 mg q2w on top of MTX for a maximum of 52 weeks. Subjects with inadequate response from Week 16 could be rescued with open-label highest dose of sarilumab.	
Reporting group title	Part B: Placebo Q2W
Reporting group description:	
Placebo (for sarilumab) q2w on top of MTX for a maximum of 52 weeks. Subjects with inadequate response from Week 16 could be rescued with open-label highest dose of sarilumab.	
Subject analysis set title	Part B cohort 2: SAR 150 mg Q2W
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
Part B subjects randomized to Sarilumab 150 mg q2w after dose selection.	
Subject analysis set title	Part B cohort 2: SAR 200 mg Q2W
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
Part B subjects randomized to Sarilumab 200 mg q2w after dose selection.	
Subject analysis set title	Part B cohort 2: Placebo Q2W
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
Part B subjects randomized to placebo q2w after dose selection.	

Primary: Part A: Percentage of Subjects Achieving American College of Rheumatology 20% (ACR20) Response at Week 12

End point title	Part A: Percentage of Subjects Achieving American College of Rheumatology 20% (ACR20) Response at Week 12[1]

End point description:

ACR20 response is defined, based on guidelines set forth by the American College of Rheumatology (ACR), as ≥20 % improvement in tender joint count and swollen joint count as well as ≥20% improvement in at least 3 of 5 following measures: C-Reactive Protein (CRP), subject assessment of pain; subject global assessment of disease activity; physician global assessment of disease activity; and Health Assessment Question-Disability Index (HAQ-DI).
Analysis was carried out on Part A Intent-to-treat (ITT) population defined as all randomized subjects who received at least 1 dose of study drug.

End point type	Primary

End point timeframe:

Baseline to Week 12 (missing data imputed by Last Observation Carried Forward [LOCF]).

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: Part A and Part B were analyzed separately.

End point values	Part A: SAR 100 mg QW	Part A: SAR 150 mg QW	Part A: SAR 100 mg Q2W	Part A: SAR 150 mg Q2W
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	50	50	51	51
Units: percentage of subjects				
number (not applicable)	62	72	49	66.7

End point values	Part A: SAR 200 mg Q2W	Part A: Placebo QW		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	52	52		
Units: percentage of subjects				
number (not applicable)	65.4	46.2		

Statistical analyses

Statistical analysis title	Sarilumab 100 mg qw vs Placebo

Statistical analysis description:

Analysis was performed using two-sided Cochran-Mantel-Haenszel test. Pairwise comparisons of the response rates between each dose of sarilumab and placebo were derived. The multiplicity issues were addressed by using the Hommel-procedure.

Comparison groups	Part A: SAR 100 mg QW v Part A: Placebo QW
Number of subjects included in analysis	102
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1155 [2]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	1.99

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.85
upper limit	4.64

Notes:

[2] - Threshold for significance = 0.05.

Statistical analysis title	Sarilumab 150 mg qw vs Placebo
Comparison groups	Part A: SAR 150 mg QW v Part A: Placebo QW
Number of subjects included in analysis	102
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0041 [3]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	3.84
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.53
upper limit	9.63

Notes:

[3] - Threshold for significance = 0.05.

Statistical analysis title	Sarilumab 100 mg q2w vs Placebo
Comparison groups	Part A: Placebo QW v Part A: SAR 100 mg Q2W
Number of subjects included in analysis	103
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7119 [4]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	1.17
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.52
upper limit	2.61

Notes:

[4] - Threshold for significance = 0.05.

Statistical analysis title	Sarilumab 150 mg q2w vs Placebo
Comparison groups	Part A: SAR 150 mg Q2W v Part A: Placebo QW

Number of subjects included in analysis	103
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0363 [5]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	2.38
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.06
upper limit	5.35

Notes:

[5] - Threshold for significance = 0.05.

Statistical analysis title	Sarilumab 200 mg q2w vs Placebo
Comparison groups	Part A: SAR 200 mg Q2W v Part A: Placebo QW
Number of subjects included in analysis	104
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0426 [6]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	2.34
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.03
upper limit	5.29

Notes:

[6] - Threshold for significance = 0.05.

Primary: Part B: Percentage of Subjects Achieving ACR20 Response at Week 24

End point title	Part B: Percentage of Subjects Achieving ACR20 Response at Week 24

End point description:

ACR20 improvement responses were determined without imputation of missing post-baseline values. In addition data collected after treatment discontinuation or rescue was set to missing. Analysis was carried out on the ITT population, which included all subjects randomized after dose selection (cohort 2).

End point type	Primary

End point timeframe:

Baseline to Week 24

End point values	Part B cohort 2: SAR 150 mg Q2W	Part B cohort 2: SAR 200 mg Q2W	Part B cohort 2: Placebo Q2W	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	400	399	398	
Units: percentage of subjects				
number (not applicable)	58	66.4	33.4	

Statistical analyses

Statistical analysis title	Sarilumab 150 mg q2w vs. Placebo

Statistical analysis description:

Analysis was performed using two-sided Cochran-Mantel-Haenszel test. Pairwise comparisons of the response rates between each dose of sarilumab and placebo was derived. The multiplicity issues for part B were addressed by using a Bonferroni correction for each dose together with a hierarchical testing procedure across the 3 co-primary and the main secondary endpoints.The hierarchical testing sequence continued only when previous endpoint was statistically significant at 0.025 level.

Comparison groups	Part B cohort 2: SAR 150 mg Q2W v Part B cohort 2: Placebo Q2W
Number of subjects included in analysis	798
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [7]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	2.773
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.077
upper limit	3.703

Notes:

[7] - Threshold for significance = 0.025.

Statistical analysis title	Sarilumab 200 mg q2w vs Placebo
Comparison groups	Part B cohort 2: SAR 200 mg Q2W v Part B cohort 2: Placebo Q2W
Number of subjects included in analysis	797
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [8]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	3.975
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.957
upper limit	5.344

Notes:

[8] - Theshold for significance = 0.025.

Primary: Part B: Change From Baseline in Health Assessment Question-Disability Index (HAQ-DI) at Week 16

End point title	Part B: Change From Baseline in Health Assessment Question-Disability Index (HAQ-DI) at Week 16

End point description:

HAQ-DI is a subject-reported questionnaire that assesses the difficulty of performing daily activities: dress/groom, arise, eat, walk, reach, grip, hygiene and common activities. Overall score range from 0=least difficulty to 3=extreme difficulty. An increase in the score indicates a worsening of physical function while a decrease in the score represents improvement.
Analysis was carried out on the Cohort 2 ITT population only and included subjects with available data of HAQ-DI at baseline and Week 16.

End point type	Primary

End point timeframe:

Baseline, Week 16

End point values	Part B cohort 2: SAR 150 mg Q2W	Part B cohort 2: SAR 200 mg Q2W	Part B cohort 2: Placebo Q2W	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	362	365	378	
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline	1.63 (± 0.63)	1.69 (± 0.63)	1.61 (± 0.65)	
Week 16	1.08 (± 0.67)	1.11 (± 0.7)	1.31 (± 0.67)	
Change From Baseline at Week 16	-0.54 (± 0.55)	-0.58 (± 0.63)	-0.3 (± 0.58)	

Statistical analyses

Statistical analysis title	Sarilumab 150 mg q2w vs Placebo

Statistical analysis description:

Analysis was performed using a mixed model for repeated measures (MMRM). Differences in LS means between each dose of sarilumab and placebo were derived. Testing was performed according to the hierarchical testing procedure (previous endpoint was statistically significant).

Comparison groups	Part B cohort 2: SAR 150 mg Q2W v Part B cohort 2: Placebo Q2W
Number of subjects included in analysis	740
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [9]
Method	Mixed models analysis
Parameter estimate	Least squares mean difference
Point estimate	-0.235

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.312
upper limit	-0.157

Notes:

[9] - Threshold for significance = 0.025.

Statistical analysis title	Sarilumab 200 mg q2w vs Placebo
Comparison groups	Part B cohort 2: SAR 200 mg Q2W v Part B cohort 2: Placebo Q2W
Number of subjects included in analysis	743
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [10]
Method	Mixed models analysis
Parameter estimate	Least squares mean difference
Point estimate	-0.258
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.336
upper limit	-0.181

Notes:

[10] - Threshold for significance = 0.025.

Primary: Part B: Change From Baseline in Van der Heijde Modified Total Sharp Score (mTSS) at Week 52

End point title	Part B: Change From Baseline in Van der Heijde Modified Total Sharp Score (mTSS) at Week 52

End point description:

The Sharp method modified by D. van der Heijde involves separate scores for erosions and joint space narrowing based on radiographs to assess the degree of structural damage. Total score range from 0 (normal) to 448 (worst possible total score). An increase in total score represents progression of structural damage.
Analysis was carried out on the Cohort 2 ITT population and included subjects with available data of mTSS at baseline and Week 52.

End point type	Primary

End point timeframe:

Baseline, Week 52 (missing data imputed by the linear extrapolation method).

End point values	Part B cohort 2: SAR 150 mg Q2W	Part B cohort 2: SAR 200 mg Q2W	Part B cohort 2: Placebo Q2W	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	352	359	352	
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline	54.67 (± 63.42)	46.34 (± 57.43)	48.01 (± 65.23)	

Week 52	55.57 (± 63.73)	46.59 (± 57.63)	50.79 (± 65.82)	
Change From Baseline at Week 52	0.9 (± 4.66)	0.25 (± 4.61)	2.78 (± 7.73)	

Statistical analyses

Statistical analysis title	Sarilumab 150 mg q2w vs Placebo

Statistical analysis description:

Analysis was performed using two-sided rank-based ANCOVA model. Testing was performed according to the hierarchical testing procedure (previous endpoints were statistically significant).

Comparison groups	Part B cohort 2: Placebo Q2W v Part B cohort 2: SAR 150 mg Q2W
Number of subjects included in analysis	704
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [11]
Method	Rank ANCOVA

Notes:

[11] - Threshold for significance = 0.025.

Statistical analysis title	Sarilumab 200 mg q2w vs Placebo
Comparison groups	Part B cohort 2: Placebo Q2W v Part B cohort 2: SAR 200 mg Q2W
Number of subjects included in analysis	711
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [12]
Method	Rank ANCOVA

Notes:

[12] - Threshold for significance = 0.025.

Secondary: Part B: Percentage of Subjects Achieving a Major Clinical Response at Week 52

End point title	Part B: Percentage of Subjects Achieving a Major Clinical Response at Week 52

End point description:

Major clinical response was defined as an ACR70 response maintained for at least 24 consecutive weeks. ACR70 response uses the same criteria as for ACR20 but requires 70% improvement.
Analysis was carried out on Part B Cohort 2 ITT population.

End point type	Secondary

End point timeframe:

Baseline up to Week 52

End point values	Part B cohort 2: SAR 150 mg Q2W	Part B cohort 2: SAR 200 mg Q2W	Part B cohort 2: Placebo Q2W	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	400	399	398	
Units: percentage of subjects				
number (not applicable)	12.8	14.8	3	

Statistical analyses

Statistical analysis title	Sarilumab 150 mg q2w Placebo

Statistical analysis description:

Analysis was performed using two-sided Cochran-Mantel-Haenszel test. Pairwise comparisons of the response rates between each dose of sarilumab and placebo were derived. Testing was performed according to the hierarchical testing procedure (previous endpoints were statistically significant).

Comparison groups	Part B cohort 2: SAR 150 mg Q2W v Part B cohort 2: Placebo Q2W
Number of subjects included in analysis	798
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [13]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	4.661
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.451
upper limit	8.863

Notes:

[13] - Threshold for significance = 0.025.

Statistical analysis title	Sarilumab 200 mg q2w vs Placebo
Comparison groups	Part B cohort 2: SAR 200 mg Q2W v Part B cohort 2: Placebo Q2W
Number of subjects included in analysis	797
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [14]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	5.565
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.946
upper limit	10.515

Notes:

[14] - Threshold for significance = 0.025.

Adverse events information

Timeframe for reporting adverse events:

All Adverse Events (AE) were collected from signature of the informed consent form up to study completion regardless of seriousness or relationship to investigational product.

Adverse event reporting additional description:

Reported AEs and deaths are treatment-emergent that is AEs that developed/worsened and deaths that occurred during the 'treatment-emergent period' (from the first IMP injection up to the end of the study).

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	16.0

Reporting groups

Reporting group title	Part A: Placebo QW

Reporting group description:

Part A subjects exposed to placebo in combination with MTX (mean exposure of 12 weeks). Excluded 1 subject who received an erroneous IMP kit with Sarilumab 150 mg q2w. He/she was considered in the 150 mg q2w treatment group for safety analysis.

Reporting group title	Part A: SAR 100mg Q2W

Reporting group description:

Part A subjects exposed to sarilumab 100 mg q2w in combination with MTX (mean exposure of 11 weeks).

Reporting group title	Part A: SAR 150mg Q2W

Reporting group description:

Part A subjects exposed to sarilumab 150 mg q2w in combination with MTX (mean exposure of 12 weeks). Included the subject randomized to placebo qw who received sarilumab 150 mg q2w in error.

Reporting group title	Part A: SAR 100mg QW

Reporting group description:

Part A subjects exposed to sarilumab 100 mg qw in combination with MTX (mean exposure of 10 weeks).

Reporting group title	Part A: SAR 200mg Q2W

Reporting group description:

Part A subjects exposed to sarilumab 200 mg q2w in combination with (mean exposure of 11 weeks).

Reporting group title	Part A: SAR 150mg QW

Reporting group description:

Part A subjects exposed to sarilumab 150 mg qw in combination with MTX (mean exposure of 12 weeks).

Reporting group title	Part B: Placebo Q2W until rescue

Reporting group description:

Part B subjects exposed to placebo Q2W in combination with MTX until open-label rescue treatment with highest dose (mean exposure of 40 weeks). Excluded 1 subject who received an erroneous IMP kit with Sarilumab 200 mg q2w. He/she was considered in the 200 mg q2w treatment group for safety analysis.

Reporting group title	Part B: SAR 150mg Q2W until rescue

Reporting group description:

Part B subjects exposed to sarilumab 150 mg q2w in combination with MTX until open-label rescue treatment with highest dose (mean exposure of 42 weeks). Included 3 subjects randomized to sarilumab 200 mg q2w who received at least one dose of sarilumab 150 mg q2w in error (lowest dose received).

Reporting group title	Part B: SAR 200mg Q2W until rescue

Reporting group description:

Part B subjects exposed to sarilumab 200 mg q2w in combination with MTX until open-label rescue treatment with highest dose (mean exposure of 42 weeks). Excluded the 3 subjects who received sarilumab 150 mg q2w in error and included the subject randomized to placebo q2w who received

sarilumab 200 mg q2w in error.

Reporting group title	Part B: Rescue SAR 200mg Q2W

Reporting group description:

Part B subjects rescued with sarilumab 200 mg q2w open-label whatever the initial dose received (mean exposure of 28 weeks from beginning of rescue treatment).

Serious adverse events	Part A: Placebo QW	Part A: SAR 100mg Q2W	Part A: SAR 150mg Q2W
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 51 (3.92%)	3 / 51 (5.88%)	0 / 52 (0.00%)
number of deaths (all causes)	0	1	0
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal Cell Carcinoma			
subjects affected / exposed	1 / 51 (1.96%)	0 / 51 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Breast Cancer			
subjects affected / exposed	0 / 51 (0.00%)	0 / 51 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Breast Cancer Metastatic			
subjects affected / exposed	0 / 51 (0.00%)	0 / 51 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ductal Adenocarcinoma Of Pancreas			
subjects affected / exposed	0 / 51 (0.00%)	0 / 51 (0.00%)	0 / 52 (0.00%)
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 Lobular Breast Carcinoma			
subjects affected / exposed	0 / 51 (0.00%)	0 / 51 (0.00%)	0 / 52 (0.00%)
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 / 51 (0.00%)	0 / 51 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Meningioma			
subjects affected / exposed	0 / 51 (0.00%)	0 / 51 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metastatic Bronchial Carcinoma			
subjects affected / exposed	0 / 51 (0.00%)	0 / 51 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neoplasm Of Appendix			
subjects affected / exposed	0 / 51 (0.00%)	0 / 51 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Plasmacytoma			
subjects affected / exposed	0 / 51 (0.00%)	1 / 51 (1.96%)	0 / 52 (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
Squamous Cell Carcinoma Of Skin			
subjects affected / exposed	1 / 51 (1.96%)	0 / 51 (0.00%)	0 / 52 (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 Thrombosis			
subjects affected / exposed	0 / 51 (0.00%)	0 / 51 (0.00%)	0 / 52 (0.00%)
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 / 51 (0.00%)	0 / 51 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Embolism Arterial			

subjects affected / exposed	0 / 51 (0.00%)	0 / 51 (0.00%)	0 / 52 (0.00%)
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 / 51 (0.00%)	0 / 51 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertensive Crisis			
subjects affected / exposed	0 / 51 (0.00%)	0 / 51 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Shock Haemorrhagic			
subjects affected / exposed	0 / 51 (0.00%)	0 / 51 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subgaleal Haematoma			
subjects affected / exposed	0 / 51 (0.00%)	0 / 51 (0.00%)	0 / 52 (0.00%)
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 / 51 (0.00%)	0 / 51 (0.00%)	0 / 52 (0.00%)
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			
Immediate Post-Injection Reaction			
subjects affected / exposed	0 / 51 (0.00%)	0 / 51 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Impaired Healing			
subjects affected / exposed	0 / 51 (0.00%)	0 / 51 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Pyrexia			
subjects affected / exposed	0 / 51 (0.00%)	0 / 51 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	0 / 51 (0.00%)	0 / 51 (0.00%)	0 / 52 (0.00%)
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			
Adenomyosis			
subjects affected / exposed	0 / 51 (0.00%)	0 / 51 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metrorrhagia			
subjects affected / exposed	0 / 51 (0.00%)	0 / 51 (0.00%)	0 / 52 (0.00%)
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 / 51 (0.00%)	1 / 51 (1.96%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0
Acute Respiratory Failure			
subjects affected / exposed	0 / 51 (0.00%)	0 / 51 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchial Secretion Retention			
subjects affected / exposed	0 / 51 (0.00%)	0 / 51 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chronic Obstructive Pulmonary Disease			

subjects affected / exposed	0 / 51 (0.00%)	0 / 51 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspnoea			
subjects affected / exposed	0 / 51 (0.00%)	0 / 51 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Interstitial Lung Disease			
subjects affected / exposed	0 / 51 (0.00%)	0 / 51 (0.00%)	0 / 52 (0.00%)
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 / 51 (0.00%)	0 / 51 (0.00%)	0 / 52 (0.00%)
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 / 51 (0.00%)	0 / 51 (0.00%)	0 / 52 (0.00%)
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 / 51 (0.00%)	0 / 51 (0.00%)	0 / 52 (0.00%)
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 Oedema			
subjects affected / exposed	0 / 51 (0.00%)	0 / 51 (0.00%)	0 / 52 (0.00%)
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 Distress			
subjects affected / exposed	0 / 51 (0.00%)	0 / 51 (0.00%)	0 / 52 (0.00%)
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			
Completed Suicide			

subjects affected / exposed	0 / 51 (0.00%)	0 / 51 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Depression			
subjects affected / exposed	0 / 51 (0.00%)	0 / 51 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychotic Disorder			
subjects affected / exposed	0 / 51 (0.00%)	0 / 51 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Suicide Attempt			
subjects affected / exposed	0 / 51 (0.00%)	0 / 51 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Alanine Aminotransferase Increased			
subjects affected / exposed	0 / 51 (0.00%)	0 / 51 (0.00%)	0 / 52 (0.00%)
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 Alkaline Phosphatase Increased			
subjects affected / exposed	0 / 51 (0.00%)	0 / 51 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic Enzyme Increased			
subjects affected / exposed	0 / 51 (0.00%)	0 / 51 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transaminases Increased			
subjects affected / exposed	0 / 51 (0.00%)	0 / 51 (0.00%)	0 / 52 (0.00%)
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			

Femur Fracture			
subjects affected / exposed	0 / 51 (0.00%)	0 / 51 (0.00%)	0 / 52 (0.00%)
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 / 51 (0.00%)	0 / 51 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Humerus Fracture			
subjects affected / exposed	0 / 51 (0.00%)	0 / 51 (0.00%)	0 / 52 (0.00%)
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 / 51 (0.00%)	0 / 51 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ligament Rupture			
subjects affected / exposed	0 / 51 (0.00%)	0 / 51 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lumbar Vertebral Fracture			
subjects affected / exposed	0 / 51 (0.00%)	0 / 51 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Procedural Pain			
subjects affected / exposed	0 / 51 (0.00%)	0 / 51 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Road Traffic Accident			
subjects affected / exposed	0 / 51 (0.00%)	0 / 51 (0.00%)	0 / 52 (0.00%)
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 Wound			

subjects affected / exposed	0 / 51 (0.00%)	0 / 51 (0.00%)	0 / 52 (0.00%)
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 / 51 (0.00%)	0 / 51 (0.00%)	0 / 52 (0.00%)
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 Haemorrhage			
subjects affected / exposed	0 / 51 (0.00%)	0 / 51 (0.00%)	0 / 52 (0.00%)
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			
Angina Unstable			
subjects affected / exposed	0 / 51 (0.00%)	0 / 51 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial Fibrillation			
subjects affected / exposed	0 / 51 (0.00%)	0 / 51 (0.00%)	0 / 52 (0.00%)
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 / 51 (0.00%)	0 / 51 (0.00%)	0 / 52 (0.00%)
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 / 51 (0.00%)	0 / 51 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiovascular Insufficiency			
subjects affected / exposed	0 / 51 (0.00%)	0 / 51 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial Ischaemia			

subjects affected / exposed	0 / 51 (0.00%)	0 / 51 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pericarditis			
subjects affected / exposed	0 / 51 (0.00%)	0 / 51 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Right Ventricular Failure			
subjects affected / exposed	0 / 51 (0.00%)	0 / 51 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sick Sinus Syndrome			
subjects affected / exposed	0 / 51 (0.00%)	0 / 51 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Brain Oedema			
subjects affected / exposed	0 / 51 (0.00%)	0 / 51 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cauda Equina Syndrome			
subjects affected / exposed	0 / 51 (0.00%)	0 / 51 (0.00%)	0 / 52 (0.00%)
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 / 51 (0.00%)	1 / 51 (1.96%)	0 / 52 (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
Embolic Cerebral Infarction			
subjects affected / exposed	0 / 51 (0.00%)	0 / 51 (0.00%)	0 / 52 (0.00%)
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 / 51 (0.00%)	0 / 51 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myelitis Transverse			
subjects affected / exposed	0 / 51 (0.00%)	0 / 51 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sciatica			
subjects affected / exposed	0 / 51 (0.00%)	0 / 51 (0.00%)	0 / 52 (0.00%)
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 / 51 (0.00%)	0 / 51 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transient Ischaemic Attack			
subjects affected / exposed	0 / 51 (0.00%)	0 / 51 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Viith Nerve Paralysis			
subjects affected / exposed	0 / 51 (0.00%)	0 / 51 (0.00%)	0 / 52 (0.00%)
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			
Iron Deficiency Anaemia			
subjects affected / exposed	0 / 51 (0.00%)	0 / 51 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Leukopenia			
subjects affected / exposed	0 / 51 (0.00%)	0 / 51 (0.00%)	0 / 52 (0.00%)
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	0 / 51 (0.00%)	0 / 51 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Splenic Vein Thrombosis			
subjects affected / exposed	0 / 51 (0.00%)	0 / 51 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombocytopenia			
subjects affected / exposed	0 / 51 (0.00%)	0 / 51 (0.00%)	0 / 52 (0.00%)
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			
Conjunctivitis			
subjects affected / exposed	0 / 51 (0.00%)	0 / 51 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Retinal Vascular Thrombosis			
subjects affected / exposed	0 / 51 (0.00%)	0 / 51 (0.00%)	0 / 52 (0.00%)
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 Discomfort			
subjects affected / exposed	0 / 51 (0.00%)	0 / 51 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal Wall Haematoma			
subjects affected / exposed	0 / 51 (0.00%)	0 / 51 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Alcoholic Pancreatitis			
subjects affected / exposed	0 / 51 (0.00%)	0 / 51 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Constipation			

subjects affected / exposed	0 / 51 (0.00%)	0 / 51 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Duodenal Ulcer			
subjects affected / exposed	0 / 51 (0.00%)	0 / 51 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Duodenal Ulcer Haemorrhage			
subjects affected / exposed	0 / 51 (0.00%)	0 / 51 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Duodenal Ulcer Perforation			
subjects affected / exposed	0 / 51 (0.00%)	0 / 51 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Duodenitis			
subjects affected / exposed	0 / 51 (0.00%)	0 / 51 (0.00%)	0 / 52 (0.00%)
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 Haemorrhage			
subjects affected / exposed	0 / 51 (0.00%)	0 / 51 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastric Ulcer Haemorrhage			
subjects affected / exposed	0 / 51 (0.00%)	0 / 51 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastritis			
subjects affected / exposed	0 / 51 (0.00%)	0 / 51 (0.00%)	0 / 52 (0.00%)
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 / 51 (0.00%)	0 / 51 (0.00%)	0 / 52 (0.00%)
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 / 51 (0.00%)	0 / 51 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Bile Duct Stone			
subjects affected / exposed	0 / 51 (0.00%)	0 / 51 (0.00%)	0 / 52 (0.00%)
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 / 51 (0.00%)	0 / 51 (0.00%)	0 / 52 (0.00%)
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 Chronic			
subjects affected / exposed	0 / 51 (0.00%)	0 / 51 (0.00%)	0 / 52 (0.00%)
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 / 51 (0.00%)	0 / 51 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Drug-Induced Liver Injury			
subjects affected / exposed	0 / 51 (0.00%)	0 / 51 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatitis Toxic			
subjects affected / exposed	0 / 51 (0.00%)	0 / 51 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			

Cutaneous Lupus Erythematosus			
subjects affected / exposed	0 / 51 (0.00%)	0 / 51 (0.00%)	0 / 52 (0.00%)
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			
Calculus Ureteric			
subjects affected / exposed	0 / 51 (0.00%)	0 / 51 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal Failure			
subjects affected / exposed	0 / 51 (0.00%)	0 / 51 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal Failure Acute			
subjects affected / exposed	0 / 51 (0.00%)	0 / 51 (0.00%)	0 / 52 (0.00%)
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	1 / 51 (1.96%)	0 / 51 (0.00%)	0 / 52 (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
Intervertebral Disc Protrusion			
subjects affected / exposed	0 / 51 (0.00%)	0 / 51 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lumbar Spinal Stenosis			
subjects affected / exposed	0 / 51 (0.00%)	0 / 51 (0.00%)	0 / 52 (0.00%)
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 / 51 (0.00%)	0 / 51 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Pathological Fracture			
subjects affected / exposed	0 / 51 (0.00%)	0 / 51 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rheumatoid Arthritis			
subjects affected / exposed	0 / 51 (0.00%)	1 / 51 (1.96%)	0 / 52 (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
Rotator Cuff Syndrome			
subjects affected / exposed	0 / 51 (0.00%)	0 / 51 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Abscess Limb			
subjects affected / exposed	0 / 51 (0.00%)	0 / 51 (0.00%)	0 / 52 (0.00%)
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 Oral			
subjects affected / exposed	0 / 51 (0.00%)	0 / 51 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Appendicitis			
subjects affected / exposed	0 / 51 (0.00%)	0 / 51 (0.00%)	0 / 52 (0.00%)
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 / 51 (0.00%)	0 / 51 (0.00%)	0 / 52 (0.00%)
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 / 51 (0.00%)	0 / 51 (0.00%)	0 / 52 (0.00%)
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 Fungal			

subjects affected / exposed	0 / 51 (0.00%)	0 / 51 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bursitis Infective Staphylococcal			
subjects affected / exposed	0 / 51 (0.00%)	0 / 51 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			
subjects affected / exposed	0 / 51 (0.00%)	0 / 51 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Clostridium Difficile Colitis			
subjects affected / exposed	0 / 51 (0.00%)	0 / 51 (0.00%)	0 / 52 (0.00%)
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 / 51 (0.00%)	0 / 51 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endometritis			
subjects affected / exposed	0 / 51 (0.00%)	0 / 51 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Erysipelas			
subjects affected / exposed	0 / 51 (0.00%)	0 / 51 (0.00%)	0 / 52 (0.00%)
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 / 51 (0.00%)	0 / 51 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			

subjects affected / exposed	0 / 51 (0.00%)	0 / 51 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Herpes Zoster			
subjects affected / exposed	0 / 51 (0.00%)	0 / 51 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Incision Site Infection			
subjects affected / exposed	0 / 51 (0.00%)	0 / 51 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infected Skin Ulcer			
subjects affected / exposed	0 / 51 (0.00%)	0 / 51 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Necrotising Fasciitis			
subjects affected / exposed	0 / 51 (0.00%)	0 / 51 (0.00%)	0 / 52 (0.00%)
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 / 51 (0.00%)	0 / 51 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Otitis Media Acute			
subjects affected / exposed	0 / 51 (0.00%)	0 / 51 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Otitis Media Chronic			
subjects affected / exposed	0 / 51 (0.00%)	0 / 51 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Paronychia			

subjects affected / exposed	0 / 51 (0.00%)	0 / 51 (0.00%)	0 / 52 (0.00%)
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 Abscess			
subjects affected / exposed	0 / 51 (0.00%)	0 / 51 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pharyngitis			
subjects affected / exposed	0 / 51 (0.00%)	0 / 51 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 51 (0.00%)	0 / 51 (0.00%)	0 / 52 (0.00%)
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 Streptococcal			
subjects affected / exposed	0 / 51 (0.00%)	0 / 51 (0.00%)	0 / 52 (0.00%)
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 / 51 (0.00%)	0 / 51 (0.00%)	0 / 52 (0.00%)
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 / 51 (0.00%)	0 / 51 (0.00%)	0 / 52 (0.00%)
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 / 51 (0.00%)	0 / 51 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sinusitis			

subjects affected / exposed	0 / 51 (0.00%)	0 / 51 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subacute Endocarditis			
subjects affected / exposed	0 / 51 (0.00%)	0 / 51 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subcutaneous Abscess			
subjects affected / exposed	0 / 51 (0.00%)	0 / 51 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tinea Cruris			
subjects affected / exposed	0 / 51 (0.00%)	0 / 51 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper Respiratory Tract Infection			
subjects affected / exposed	0 / 51 (0.00%)	0 / 51 (0.00%)	0 / 52 (0.00%)
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 / 51 (0.00%)	0 / 51 (0.00%)	0 / 52 (0.00%)
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 Infection			
subjects affected / exposed	0 / 51 (0.00%)	0 / 51 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 51 (0.00%)	0 / 51 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diabetes Mellitus			

subjects affected / exposed	0 / 51 (0.00%)	0 / 51 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypercalcaemia			
subjects affected / exposed	0 / 51 (0.00%)	0 / 51 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Type 2 Diabetes Mellitus			
subjects affected / exposed	0 / 51 (0.00%)	0 / 51 (0.00%)	0 / 52 (0.00%)
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	Part A: SAR 100mg QW	Part A: SAR 200mg Q2W	Part A: SAR 150mg QW
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 50 (6.00%)	0 / 51 (0.00%)	0 / 50 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal Cell Carcinoma			
subjects affected / exposed	0 / 50 (0.00%)	0 / 51 (0.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Breast Cancer			
subjects affected / exposed	0 / 50 (0.00%)	0 / 51 (0.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Breast Cancer Metastatic			
subjects affected / exposed	0 / 50 (0.00%)	0 / 51 (0.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ductal Adenocarcinoma Of Pancreas			
subjects affected / exposed	0 / 50 (0.00%)	0 / 51 (0.00%)	0 / 50 (0.00%)
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 Lobular Breast Carcinoma			
subjects affected / exposed	0 / 50 (0.00%)	0 / 51 (0.00%)	0 / 50 (0.00%)
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 / 50 (0.00%)	0 / 51 (0.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Meningioma			
subjects affected / exposed	0 / 50 (0.00%)	0 / 51 (0.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metastatic Bronchial Carcinoma			
subjects affected / exposed	0 / 50 (0.00%)	0 / 51 (0.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neoplasm Of Appendix			
subjects affected / exposed	0 / 50 (0.00%)	0 / 51 (0.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Plasmacytoma			
subjects affected / exposed	0 / 50 (0.00%)	0 / 51 (0.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Squamous Cell Carcinoma Of Skin			
subjects affected / exposed	0 / 50 (0.00%)	0 / 51 (0.00%)	0 / 50 (0.00%)
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 Thrombosis			
subjects affected / exposed	0 / 50 (0.00%)	0 / 51 (0.00%)	0 / 50 (0.00%)
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 / 50 (0.00%)	0 / 51 (0.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Embolism Arterial			
subjects affected / exposed	0 / 50 (0.00%)	0 / 51 (0.00%)	0 / 50 (0.00%)
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 / 50 (0.00%)	0 / 51 (0.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertensive Crisis			
subjects affected / exposed	0 / 50 (0.00%)	0 / 51 (0.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Shock Haemorrhagic			
subjects affected / exposed	0 / 50 (0.00%)	0 / 51 (0.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subgaleal Haematoma			
subjects affected / exposed	0 / 50 (0.00%)	0 / 51 (0.00%)	0 / 50 (0.00%)
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 / 50 (0.00%)	0 / 51 (0.00%)	0 / 50 (0.00%)
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			
Immediate Post-Injection Reaction			
subjects affected / exposed	0 / 50 (0.00%)	0 / 51 (0.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Impaired Healing			
subjects affected / exposed	0 / 50 (0.00%)	0 / 51 (0.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia			
subjects affected / exposed	0 / 50 (0.00%)	0 / 51 (0.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	1 / 50 (2.00%)	0 / 51 (0.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Adenomyosis			
subjects affected / exposed	0 / 50 (0.00%)	0 / 51 (0.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metrorrhagia			
subjects affected / exposed	0 / 50 (0.00%)	0 / 51 (0.00%)	0 / 50 (0.00%)
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 / 50 (0.00%)	0 / 51 (0.00%)	0 / 50 (0.00%)
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 / 50 (0.00%)	0 / 51 (0.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchial Secretion Retention			

subjects affected / exposed	0 / 50 (0.00%)	0 / 51 (0.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chronic Obstructive Pulmonary Disease			
subjects affected / exposed	0 / 50 (0.00%)	0 / 51 (0.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspnoea			
subjects affected / exposed	0 / 50 (0.00%)	0 / 51 (0.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Interstitial Lung Disease			
subjects affected / exposed	0 / 50 (0.00%)	0 / 51 (0.00%)	0 / 50 (0.00%)
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 / 50 (0.00%)	0 / 51 (0.00%)	0 / 50 (0.00%)
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 / 50 (0.00%)	0 / 51 (0.00%)	0 / 50 (0.00%)
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 / 50 (0.00%)	0 / 51 (0.00%)	0 / 50 (0.00%)
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 Oedema			
subjects affected / exposed	0 / 50 (0.00%)	0 / 51 (0.00%)	0 / 50 (0.00%)
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 Distress			

subjects affected / exposed	0 / 50 (0.00%)	0 / 51 (0.00%)	0 / 50 (0.00%)
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			
Completed Suicide			
subjects affected / exposed	0 / 50 (0.00%)	0 / 51 (0.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Depression			
subjects affected / exposed	0 / 50 (0.00%)	0 / 51 (0.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychotic Disorder			
subjects affected / exposed	0 / 50 (0.00%)	0 / 51 (0.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Suicide Attempt			
subjects affected / exposed	0 / 50 (0.00%)	0 / 51 (0.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Alanine Aminotransferase Increased			
subjects affected / exposed	0 / 50 (0.00%)	0 / 51 (0.00%)	0 / 50 (0.00%)
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 Alkaline Phosphatase Increased			
subjects affected / exposed	0 / 50 (0.00%)	0 / 51 (0.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic Enzyme Increased			
subjects affected / exposed	0 / 50 (0.00%)	0 / 51 (0.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Transaminases Increased			
subjects affected / exposed	0 / 50 (0.00%)	0 / 51 (0.00%)	0 / 50 (0.00%)
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			
Femur Fracture			
subjects affected / exposed	0 / 50 (0.00%)	0 / 51 (0.00%)	0 / 50 (0.00%)
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 / 50 (0.00%)	0 / 51 (0.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Humerus Fracture			
subjects affected / exposed	0 / 50 (0.00%)	0 / 51 (0.00%)	0 / 50 (0.00%)
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 / 50 (0.00%)	0 / 51 (0.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ligament Rupture			
subjects affected / exposed	0 / 50 (0.00%)	0 / 51 (0.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lumbar Vertebral Fracture			
subjects affected / exposed	0 / 50 (0.00%)	0 / 51 (0.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Procedural Pain			
subjects affected / exposed	0 / 50 (0.00%)	0 / 51 (0.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Road Traffic Accident			
subjects affected / exposed	0 / 50 (0.00%)	0 / 51 (0.00%)	0 / 50 (0.00%)
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 Wound			
subjects affected / exposed	0 / 50 (0.00%)	0 / 51 (0.00%)	0 / 50 (0.00%)
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 / 50 (0.00%)	0 / 51 (0.00%)	0 / 50 (0.00%)
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 Haemorrhage			
subjects affected / exposed	0 / 50 (0.00%)	0 / 51 (0.00%)	0 / 50 (0.00%)
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			
Angina Unstable			
subjects affected / exposed	0 / 50 (0.00%)	0 / 51 (0.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial Fibrillation			
subjects affected / exposed	0 / 50 (0.00%)	0 / 51 (0.00%)	0 / 50 (0.00%)
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 / 50 (0.00%)	0 / 51 (0.00%)	0 / 50 (0.00%)
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 / 50 (0.00%)	0 / 51 (0.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiovascular Insufficiency			

subjects affected / exposed	0 / 50 (0.00%)	0 / 51 (0.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial Ischaemia			
subjects affected / exposed	0 / 50 (0.00%)	0 / 51 (0.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pericarditis			
subjects affected / exposed	0 / 50 (0.00%)	0 / 51 (0.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Right Ventricular Failure			
subjects affected / exposed	0 / 50 (0.00%)	0 / 51 (0.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sick Sinus Syndrome			
subjects affected / exposed	0 / 50 (0.00%)	0 / 51 (0.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Brain Oedema			
subjects affected / exposed	0 / 50 (0.00%)	0 / 51 (0.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cauda Equina Syndrome			
subjects affected / exposed	0 / 50 (0.00%)	0 / 51 (0.00%)	0 / 50 (0.00%)
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 / 50 (0.00%)	0 / 51 (0.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Embolic Cerebral Infarction			

subjects affected / exposed	0 / 50 (0.00%)	0 / 51 (0.00%)	0 / 50 (0.00%)
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 / 50 (0.00%)	0 / 51 (0.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myelitis Transverse			
subjects affected / exposed	0 / 50 (0.00%)	0 / 51 (0.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sciatica			
subjects affected / exposed	0 / 50 (0.00%)	0 / 51 (0.00%)	0 / 50 (0.00%)
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 / 50 (0.00%)	0 / 51 (0.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transient Ischaemic Attack			
subjects affected / exposed	0 / 50 (0.00%)	0 / 51 (0.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Viith Nerve Paralysis			
subjects affected / exposed	0 / 50 (0.00%)	0 / 51 (0.00%)	0 / 50 (0.00%)
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			
Iron Deficiency Anaemia			
subjects affected / exposed	0 / 50 (0.00%)	0 / 51 (0.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Leukopenia			

subjects affected / exposed	0 / 50 (0.00%)	0 / 51 (0.00%)	0 / 50 (0.00%)
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 / 50 (2.00%)	0 / 51 (0.00%)	0 / 50 (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
Splenic Vein Thrombosis			
subjects affected / exposed	0 / 50 (0.00%)	0 / 51 (0.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombocytopenia			
subjects affected / exposed	0 / 50 (0.00%)	0 / 51 (0.00%)	0 / 50 (0.00%)
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			
Conjunctivitis			
subjects affected / exposed	0 / 50 (0.00%)	0 / 51 (0.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Retinal Vascular Thrombosis			
subjects affected / exposed	0 / 50 (0.00%)	0 / 51 (0.00%)	0 / 50 (0.00%)
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 Discomfort			
subjects affected / exposed	0 / 50 (0.00%)	0 / 51 (0.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal Wall Haematoma			
subjects affected / exposed	0 / 50 (0.00%)	0 / 51 (0.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Alcoholic Pancreatitis			

subjects affected / exposed	1 / 50 (2.00%)	0 / 51 (0.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Constipation			
subjects affected / exposed	0 / 50 (0.00%)	0 / 51 (0.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Duodenal Ulcer			
subjects affected / exposed	0 / 50 (0.00%)	0 / 51 (0.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Duodenal Ulcer Haemorrhage			
subjects affected / exposed	0 / 50 (0.00%)	0 / 51 (0.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Duodenal Ulcer Perforation			
subjects affected / exposed	0 / 50 (0.00%)	0 / 51 (0.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Duodenitis			
subjects affected / exposed	0 / 50 (0.00%)	0 / 51 (0.00%)	0 / 50 (0.00%)
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 Haemorrhage			
subjects affected / exposed	0 / 50 (0.00%)	0 / 51 (0.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastric Ulcer Haemorrhage			
subjects affected / exposed	0 / 50 (0.00%)	0 / 51 (0.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastritis			

subjects affected / exposed	0 / 50 (0.00%)	0 / 51 (0.00%)	0 / 50 (0.00%)
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 / 50 (0.00%)	0 / 51 (0.00%)	0 / 50 (0.00%)
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 / 50 (0.00%)	0 / 51 (0.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Bile Duct Stone			
subjects affected / exposed	0 / 50 (0.00%)	0 / 51 (0.00%)	0 / 50 (0.00%)
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 / 50 (0.00%)	0 / 51 (0.00%)	0 / 50 (0.00%)
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 Chronic			
subjects affected / exposed	0 / 50 (0.00%)	0 / 51 (0.00%)	0 / 50 (0.00%)
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 / 50 (0.00%)	0 / 51 (0.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Drug-Induced Liver Injury			
subjects affected / exposed	0 / 50 (0.00%)	0 / 51 (0.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatitis Toxic			

subjects affected / exposed	0 / 50 (0.00%)	0 / 51 (0.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Cutaneous Lupus Erythematosus			
subjects affected / exposed	0 / 50 (0.00%)	0 / 51 (0.00%)	0 / 50 (0.00%)
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			
Calculus Ureteric			
subjects affected / exposed	0 / 50 (0.00%)	0 / 51 (0.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal Failure			
subjects affected / exposed	0 / 50 (0.00%)	0 / 51 (0.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal Failure Acute			
subjects affected / exposed	0 / 50 (0.00%)	0 / 51 (0.00%)	0 / 50 (0.00%)
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 / 50 (0.00%)	0 / 51 (0.00%)	0 / 50 (0.00%)
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 / 50 (0.00%)	0 / 51 (0.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lumbar Spinal Stenosis			
subjects affected / exposed	0 / 50 (0.00%)	0 / 51 (0.00%)	0 / 50 (0.00%)
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 / 50 (0.00%)	0 / 51 (0.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pathological Fracture			
subjects affected / exposed	0 / 50 (0.00%)	0 / 51 (0.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rheumatoid Arthritis			
subjects affected / exposed	0 / 50 (0.00%)	0 / 51 (0.00%)	0 / 50 (0.00%)
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 / 50 (0.00%)	0 / 51 (0.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Abscess Limb			
subjects affected / exposed	0 / 50 (0.00%)	0 / 51 (0.00%)	0 / 50 (0.00%)
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 Oral			
subjects affected / exposed	0 / 50 (0.00%)	0 / 51 (0.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Appendicitis			
subjects affected / exposed	0 / 50 (0.00%)	0 / 51 (0.00%)	0 / 50 (0.00%)
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 / 50 (0.00%)	0 / 51 (0.00%)	0 / 50 (0.00%)
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 / 50 (0.00%)	0 / 51 (0.00%)	0 / 50 (0.00%)
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 Fungal			
subjects affected / exposed	0 / 50 (0.00%)	0 / 51 (0.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bursitis Infective Staphylococcal			
subjects affected / exposed	0 / 50 (0.00%)	0 / 51 (0.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			
subjects affected / exposed	0 / 50 (0.00%)	0 / 51 (0.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Clostridium Difficile Colitis			
subjects affected / exposed	0 / 50 (0.00%)	0 / 51 (0.00%)	0 / 50 (0.00%)
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 / 50 (0.00%)	0 / 51 (0.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endometritis			
subjects affected / exposed	0 / 50 (0.00%)	0 / 51 (0.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Erysipelas			
subjects affected / exposed	0 / 50 (0.00%)	0 / 51 (0.00%)	0 / 50 (0.00%)
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 / 50 (0.00%)	0 / 51 (0.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	0 / 50 (0.00%)	0 / 51 (0.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Herpes Zoster			
subjects affected / exposed	0 / 50 (0.00%)	0 / 51 (0.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Incision Site Infection			
subjects affected / exposed	0 / 50 (0.00%)	0 / 51 (0.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infected Skin Ulcer			
subjects affected / exposed	0 / 50 (0.00%)	0 / 51 (0.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Necrotising Fasciitis			
subjects affected / exposed	0 / 50 (0.00%)	0 / 51 (0.00%)	0 / 50 (0.00%)
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 / 50 (0.00%)	0 / 51 (0.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Otitis Media Acute			
subjects affected / exposed	0 / 50 (0.00%)	0 / 51 (0.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Otitis Media Chronic			

subjects affected / exposed	0 / 50 (0.00%)	0 / 51 (0.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Paronychia			
subjects affected / exposed	0 / 50 (0.00%)	0 / 51 (0.00%)	0 / 50 (0.00%)
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 Abscess			
subjects affected / exposed	0 / 50 (0.00%)	0 / 51 (0.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pharyngitis			
subjects affected / exposed	0 / 50 (0.00%)	0 / 51 (0.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 50 (0.00%)	0 / 51 (0.00%)	0 / 50 (0.00%)
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 Streptococcal			
subjects affected / exposed	0 / 50 (0.00%)	0 / 51 (0.00%)	0 / 50 (0.00%)
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 / 50 (0.00%)	0 / 51 (0.00%)	0 / 50 (0.00%)
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 / 50 (0.00%)	0 / 51 (0.00%)	0 / 50 (0.00%)
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 / 50 (0.00%)	0 / 51 (0.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sinusitis			
subjects affected / exposed	0 / 50 (0.00%)	0 / 51 (0.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subacute Endocarditis			
subjects affected / exposed	0 / 50 (0.00%)	0 / 51 (0.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subcutaneous Abscess			
subjects affected / exposed	0 / 50 (0.00%)	0 / 51 (0.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tinea Cruris			
subjects affected / exposed	0 / 50 (0.00%)	0 / 51 (0.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper Respiratory Tract Infection			
subjects affected / exposed	0 / 50 (0.00%)	0 / 51 (0.00%)	0 / 50 (0.00%)
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 / 50 (0.00%)	0 / 51 (0.00%)	0 / 50 (0.00%)
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 Infection			
subjects affected / exposed	0 / 50 (0.00%)	0 / 51 (0.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Dehydration			

subjects affected / exposed	0 / 50 (0.00%)	0 / 51 (0.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diabetes Mellitus			
subjects affected / exposed	0 / 50 (0.00%)	0 / 51 (0.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypercalcaemia			
subjects affected / exposed	0 / 50 (0.00%)	0 / 51 (0.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Type 2 Diabetes Mellitus			
subjects affected / exposed	0 / 50 (0.00%)	0 / 51 (0.00%)	0 / 50 (0.00%)
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	Part B: Placebo Q2W until rescue	Part B: SAR 150mg Q2W until rescue	Part B: SAR 200mg Q2W until rescue
Total subjects affected by serious adverse events			
subjects affected / exposed	23 / 427 (5.39%)	38 / 431 (8.82%)	48 / 424 (11.32%)
number of deaths (all causes)	2	2	1
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal Cell Carcinoma			
subjects affected / exposed	0 / 427 (0.00%)	0 / 431 (0.00%)	0 / 424 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Breast Cancer			
subjects affected / exposed	0 / 427 (0.00%)	0 / 431 (0.00%)	1 / 424 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Breast Cancer Metastatic			
subjects affected / exposed	0 / 427 (0.00%)	1 / 431 (0.23%)	0 / 424 (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

Ductal Adenocarcinoma Of Pancreas			
subjects affected / exposed	0 / 427 (0.00%)	0 / 431 (0.00%)	0 / 424 (0.00%)
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 Lobular Breast Carcinoma			
subjects affected / exposed	0 / 427 (0.00%)	1 / 431 (0.23%)	0 / 424 (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
Malignant Melanoma			
subjects affected / exposed	0 / 427 (0.00%)	1 / 431 (0.23%)	1 / 424 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Meningioma			
subjects affected / exposed	2 / 427 (0.47%)	0 / 431 (0.00%)	0 / 424 (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
Metastatic Bronchial Carcinoma			
subjects affected / exposed	0 / 427 (0.00%)	0 / 431 (0.00%)	0 / 424 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neoplasm Of Appendix			
subjects affected / exposed	0 / 427 (0.00%)	1 / 431 (0.23%)	0 / 424 (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
Plasmacytoma			
subjects affected / exposed	0 / 427 (0.00%)	0 / 431 (0.00%)	0 / 424 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Squamous Cell Carcinoma Of Skin			
subjects affected / exposed	1 / 427 (0.23%)	0 / 431 (0.00%)	0 / 424 (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 Thrombosis			
subjects affected / exposed	0 / 427 (0.00%)	1 / 431 (0.23%)	0 / 424 (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
Deep Vein Thrombosis			
subjects affected / exposed	0 / 427 (0.00%)	1 / 431 (0.23%)	0 / 424 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Embolism Arterial			
subjects affected / exposed	0 / 427 (0.00%)	1 / 431 (0.23%)	0 / 424 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertension			
subjects affected / exposed	1 / 427 (0.23%)	1 / 431 (0.23%)	0 / 424 (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
Hypertensive Crisis			
subjects affected / exposed	0 / 427 (0.00%)	0 / 431 (0.00%)	2 / 424 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Shock Haemorrhagic			
subjects affected / exposed	0 / 427 (0.00%)	1 / 431 (0.23%)	1 / 424 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subgaleal Haematoma			
subjects affected / exposed	0 / 427 (0.00%)	0 / 431 (0.00%)	0 / 424 (0.00%)
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 / 427 (0.00%)	0 / 431 (0.00%)	1 / 424 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

General disorders and administration site conditions			
Immediate Post-Injection Reaction			
subjects affected / exposed	0 / 427 (0.00%)	0 / 431 (0.00%)	1 / 424 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Impaired Healing			
subjects affected / exposed	0 / 427 (0.00%)	0 / 431 (0.00%)	1 / 424 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia			
subjects affected / exposed	1 / 427 (0.23%)	0 / 431 (0.00%)	0 / 424 (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
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	0 / 427 (0.00%)	0 / 431 (0.00%)	0 / 424 (0.00%)
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			
Adenomyosis			
subjects affected / exposed	0 / 427 (0.00%)	0 / 431 (0.00%)	0 / 424 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metrorrhagia			
subjects affected / exposed	0 / 427 (0.00%)	1 / 431 (0.23%)	0 / 424 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Acute Respiratory Distress Syndrome			
subjects affected / exposed	0 / 427 (0.00%)	0 / 431 (0.00%)	0 / 424 (0.00%)
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 / 427 (0.23%)	0 / 431 (0.00%)	0 / 424 (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
Bronchial Secretion Retention			
subjects affected / exposed	0 / 427 (0.00%)	1 / 431 (0.23%)	0 / 424 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chronic Obstructive Pulmonary Disease			
subjects affected / exposed	0 / 427 (0.00%)	2 / 431 (0.46%)	1 / 424 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 2	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspnoea			
subjects affected / exposed	0 / 427 (0.00%)	0 / 431 (0.00%)	1 / 424 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Interstitial Lung Disease			
subjects affected / exposed	0 / 427 (0.00%)	1 / 431 (0.23%)	0 / 424 (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
Pleural Effusion			
subjects affected / exposed	0 / 427 (0.00%)	0 / 431 (0.00%)	0 / 424 (0.00%)
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 / 427 (0.00%)	0 / 431 (0.00%)	1 / 424 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary Embolism			
subjects affected / exposed	0 / 427 (0.00%)	0 / 431 (0.00%)	0 / 424 (0.00%)
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 Oedema			

subjects affected / exposed	0 / 427 (0.00%)	1 / 431 (0.23%)	0 / 424 (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
Respiratory Distress			
subjects affected / exposed	0 / 427 (0.00%)	1 / 431 (0.23%)	0 / 424 (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
Psychiatric disorders			
Completed Suicide			
subjects affected / exposed	1 / 427 (0.23%)	0 / 431 (0.00%)	0 / 424 (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
Depression			
subjects affected / exposed	0 / 427 (0.00%)	1 / 431 (0.23%)	2 / 424 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychotic Disorder			
subjects affected / exposed	0 / 427 (0.00%)	1 / 431 (0.23%)	0 / 424 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Suicide Attempt			
subjects affected / exposed	0 / 427 (0.00%)	1 / 431 (0.23%)	1 / 424 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Alanine Aminotransferase Increased			
subjects affected / exposed	0 / 427 (0.00%)	1 / 431 (0.23%)	1 / 424 (0.24%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood Alkaline Phosphatase Increased			
subjects affected / exposed	0 / 427 (0.00%)	0 / 431 (0.00%)	1 / 424 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Hepatic Enzyme Increased			
subjects affected / exposed	0 / 427 (0.00%)	1 / 431 (0.23%)	0 / 424 (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
Transaminases Increased			
subjects affected / exposed	0 / 427 (0.00%)	1 / 431 (0.23%)	0 / 424 (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
Injury, poisoning and procedural complications			
Femur Fracture			
subjects affected / exposed	0 / 427 (0.00%)	0 / 431 (0.00%)	1 / 424 (0.24%)
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 / 427 (0.00%)	1 / 431 (0.23%)	0 / 424 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Humerus Fracture			
subjects affected / exposed	0 / 427 (0.00%)	0 / 431 (0.00%)	0 / 424 (0.00%)
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 / 427 (0.00%)	1 / 431 (0.23%)	0 / 424 (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
Ligament Rupture			
subjects affected / exposed	0 / 427 (0.00%)	0 / 431 (0.00%)	1 / 424 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lumbar Vertebral Fracture			
subjects affected / exposed	0 / 427 (0.00%)	0 / 431 (0.00%)	0 / 424 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Procedural Pain			
subjects affected / exposed	0 / 427 (0.00%)	0 / 431 (0.00%)	1 / 424 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Road Traffic Accident			
subjects affected / exposed	0 / 427 (0.00%)	1 / 431 (0.23%)	0 / 424 (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 Wound			
subjects affected / exposed	0 / 427 (0.00%)	0 / 431 (0.00%)	0 / 424 (0.00%)
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 / 427 (0.00%)	0 / 431 (0.00%)	1 / 424 (0.24%)
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 Haemorrhage			
subjects affected / exposed	0 / 427 (0.00%)	0 / 431 (0.00%)	1 / 424 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Angina Unstable			
subjects affected / exposed	0 / 427 (0.00%)	0 / 431 (0.00%)	1 / 424 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial Fibrillation			
subjects affected / exposed	1 / 427 (0.23%)	0 / 431 (0.00%)	0 / 424 (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 Failure			
subjects affected / exposed	0 / 427 (0.00%)	0 / 431 (0.00%)	1 / 424 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardio-Respiratory Arrest			

subjects affected / exposed	0 / 427 (0.00%)	0 / 431 (0.00%)	1 / 424 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiovascular Insufficiency			
subjects affected / exposed	1 / 427 (0.23%)	0 / 431 (0.00%)	0 / 424 (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
Myocardial Ischaemia			
subjects affected / exposed	1 / 427 (0.23%)	0 / 431 (0.00%)	0 / 424 (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
Pericarditis			
subjects affected / exposed	0 / 427 (0.00%)	1 / 431 (0.23%)	0 / 424 (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
Right Ventricular Failure			
subjects affected / exposed	0 / 427 (0.00%)	1 / 431 (0.23%)	0 / 424 (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
Sick Sinus Syndrome			
subjects affected / exposed	1 / 427 (0.23%)	0 / 431 (0.00%)	0 / 424 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Brain Oedema			
subjects affected / exposed	1 / 427 (0.23%)	0 / 431 (0.00%)	0 / 424 (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
Cauda Equina Syndrome			
subjects affected / exposed	0 / 427 (0.00%)	0 / 431 (0.00%)	0 / 424 (0.00%)
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 / 427 (0.00%)	0 / 431 (0.00%)	1 / 424 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Embolic Cerebral Infarction			
subjects affected / exposed	0 / 427 (0.00%)	1 / 431 (0.23%)	0 / 424 (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
Ischaemic Stroke			
subjects affected / exposed	1 / 427 (0.23%)	0 / 431 (0.00%)	0 / 424 (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
Myelitis Transverse			
subjects affected / exposed	0 / 427 (0.00%)	0 / 431 (0.00%)	0 / 424 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sciatica			
subjects affected / exposed	0 / 427 (0.00%)	0 / 431 (0.00%)	0 / 424 (0.00%)
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 / 427 (0.23%)	0 / 431 (0.00%)	0 / 424 (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
Transient Ischaemic Attack			
subjects affected / exposed	1 / 427 (0.23%)	0 / 431 (0.00%)	0 / 424 (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
Viith Nerve Paralysis			
subjects affected / exposed	0 / 427 (0.00%)	0 / 431 (0.00%)	0 / 424 (0.00%)
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			
Iron Deficiency Anaemia			

subjects affected / exposed	0 / 427 (0.00%)	1 / 431 (0.23%)	0 / 424 (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
Leukopenia			
subjects affected / exposed	0 / 427 (0.00%)	0 / 431 (0.00%)	1 / 424 (0.24%)
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 / 427 (0.00%)	3 / 431 (0.70%)	4 / 424 (0.94%)
occurrences causally related to treatment / all	0 / 0	3 / 3	4 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Splenic Vein Thrombosis			
subjects affected / exposed	0 / 427 (0.00%)	1 / 431 (0.23%)	0 / 424 (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
Thrombocytopenia			
subjects affected / exposed	0 / 427 (0.00%)	1 / 431 (0.23%)	1 / 424 (0.24%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Conjunctivitis			
subjects affected / exposed	0 / 427 (0.00%)	0 / 431 (0.00%)	1 / 424 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Retinal Vascular Thrombosis			
subjects affected / exposed	0 / 427 (0.00%)	0 / 431 (0.00%)	0 / 424 (0.00%)
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 Discomfort			
subjects affected / exposed	0 / 427 (0.00%)	0 / 431 (0.00%)	1 / 424 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal Wall Haematoma			

subjects affected / exposed	0 / 427 (0.00%)	0 / 431 (0.00%)	1 / 424 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Alcoholic Pancreatitis			
subjects affected / exposed	0 / 427 (0.00%)	0 / 431 (0.00%)	0 / 424 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Constipation			
subjects affected / exposed	1 / 427 (0.23%)	0 / 431 (0.00%)	0 / 424 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Duodenal Ulcer			
subjects affected / exposed	1 / 427 (0.23%)	0 / 431 (0.00%)	0 / 424 (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
Duodenal Ulcer Haemorrhage			
subjects affected / exposed	0 / 427 (0.00%)	1 / 431 (0.23%)	0 / 424 (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
Duodenal Ulcer Perforation			
subjects affected / exposed	0 / 427 (0.00%)	1 / 431 (0.23%)	0 / 424 (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
Duodenitis			
subjects affected / exposed	1 / 427 (0.23%)	0 / 431 (0.00%)	0 / 424 (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
Gastric Haemorrhage			
subjects affected / exposed	0 / 427 (0.00%)	1 / 431 (0.23%)	0 / 424 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastric Ulcer Haemorrhage			

subjects affected / exposed	0 / 427 (0.00%)	0 / 431 (0.00%)	1 / 424 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastritis			
subjects affected / exposed	0 / 427 (0.00%)	1 / 431 (0.23%)	0 / 424 (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
Haemorrhoids			
subjects affected / exposed	1 / 427 (0.23%)	0 / 431 (0.00%)	0 / 424 (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
Pancreatitis			
subjects affected / exposed	0 / 427 (0.00%)	1 / 431 (0.23%)	0 / 424 (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
Hepatobiliary disorders			
Bile Duct Stone			
subjects affected / exposed	0 / 427 (0.00%)	0 / 431 (0.00%)	1 / 424 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholecystitis			
subjects affected / exposed	1 / 427 (0.23%)	0 / 431 (0.00%)	0 / 424 (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
Cholecystitis Chronic			
subjects affected / exposed	0 / 427 (0.00%)	0 / 431 (0.00%)	1 / 424 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholelithiasis			
subjects affected / exposed	0 / 427 (0.00%)	1 / 431 (0.23%)	0 / 424 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Drug-Induced Liver Injury			

subjects affected / exposed	0 / 427 (0.00%)	1 / 431 (0.23%)	0 / 424 (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
Hepatitis Toxic			
subjects affected / exposed	0 / 427 (0.00%)	1 / 431 (0.23%)	0 / 424 (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 and subcutaneous tissue disorders			
Cutaneous Lupus Erythematosus			
subjects affected / exposed	0 / 427 (0.00%)	1 / 431 (0.23%)	0 / 424 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Calculus Ureteric			
subjects affected / exposed	0 / 427 (0.00%)	0 / 431 (0.00%)	0 / 424 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal Failure			
subjects affected / exposed	0 / 427 (0.00%)	0 / 431 (0.00%)	1 / 424 (0.24%)
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 Failure Acute			
subjects affected / exposed	1 / 427 (0.23%)	1 / 431 (0.23%)	2 / 424 (0.47%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 427 (0.00%)	0 / 431 (0.00%)	0 / 424 (0.00%)
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 / 427 (0.00%)	0 / 431 (0.00%)	0 / 424 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Lumbar Spinal Stenosis			
subjects affected / exposed	0 / 427 (0.00%)	0 / 431 (0.00%)	1 / 424 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteoarthritis			
subjects affected / exposed	3 / 427 (0.70%)	1 / 431 (0.23%)	2 / 424 (0.47%)
occurrences causally related to treatment / all	0 / 3	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pathological Fracture			
subjects affected / exposed	0 / 427 (0.00%)	1 / 431 (0.23%)	0 / 424 (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
Rheumatoid Arthritis			
subjects affected / exposed	2 / 427 (0.47%)	0 / 431 (0.00%)	2 / 424 (0.47%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rotator Cuff Syndrome			
subjects affected / exposed	0 / 427 (0.00%)	0 / 431 (0.00%)	0 / 424 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Abscess Limb			
subjects affected / exposed	0 / 427 (0.00%)	1 / 431 (0.23%)	1 / 424 (0.24%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abscess Oral			
subjects affected / exposed	0 / 427 (0.00%)	0 / 431 (0.00%)	1 / 424 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Appendicitis			
subjects affected / exposed	2 / 427 (0.47%)	0 / 431 (0.00%)	0 / 424 (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
Arthritis Bacterial			

subjects affected / exposed	0 / 427 (0.00%)	1 / 431 (0.23%)	0 / 424 (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
Bronchitis			
subjects affected / exposed	2 / 427 (0.47%)	0 / 431 (0.00%)	2 / 424 (0.47%)
occurrences causally related to treatment / all	2 / 2	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchitis Fungal			
subjects affected / exposed	0 / 427 (0.00%)	0 / 431 (0.00%)	1 / 424 (0.24%)
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 Staphylococcal			
subjects affected / exposed	0 / 427 (0.00%)	0 / 431 (0.00%)	0 / 424 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			
subjects affected / exposed	3 / 427 (0.70%)	0 / 431 (0.00%)	1 / 424 (0.24%)
occurrences causally related to treatment / all	2 / 3	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Clostridium Difficile Colitis			
subjects affected / exposed	0 / 427 (0.00%)	1 / 431 (0.23%)	0 / 424 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diverticulitis			
subjects affected / exposed	0 / 427 (0.00%)	0 / 431 (0.00%)	1 / 424 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endometritis			
subjects affected / exposed	0 / 427 (0.00%)	1 / 431 (0.23%)	0 / 424 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Erysipelas			

subjects affected / exposed	0 / 427 (0.00%)	0 / 431 (0.00%)	3 / 424 (0.71%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Escherichia Urinary Tract Infection			
subjects affected / exposed	0 / 427 (0.00%)	0 / 431 (0.00%)	0 / 424 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	0 / 427 (0.00%)	1 / 431 (0.23%)	0 / 424 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Herpes Zoster			
subjects affected / exposed	0 / 427 (0.00%)	0 / 431 (0.00%)	1 / 424 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Incision Site Infection			
subjects affected / exposed	0 / 427 (0.00%)	0 / 431 (0.00%)	1 / 424 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infected Skin Ulcer			
subjects affected / exposed	0 / 427 (0.00%)	0 / 431 (0.00%)	1 / 424 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Necrotising Fasciitis			
subjects affected / exposed	0 / 427 (0.00%)	0 / 431 (0.00%)	1 / 424 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteomyelitis			
subjects affected / exposed	0 / 427 (0.00%)	1 / 431 (0.23%)	1 / 424 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 2	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Otitis Media Acute			

subjects affected / exposed	0 / 427 (0.00%)	1 / 431 (0.23%)	0 / 424 (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
Otitis Media Chronic			
subjects affected / exposed	1 / 427 (0.23%)	0 / 431 (0.00%)	0 / 424 (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
Paronychia			
subjects affected / exposed	0 / 427 (0.00%)	0 / 431 (0.00%)	0 / 424 (0.00%)
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 Abscess			
subjects affected / exposed	0 / 427 (0.00%)	0 / 431 (0.00%)	1 / 424 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pharyngitis			
subjects affected / exposed	0 / 427 (0.00%)	0 / 431 (0.00%)	1 / 424 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	1 / 427 (0.23%)	1 / 431 (0.23%)	2 / 424 (0.47%)
occurrences causally related to treatment / all	0 / 1	0 / 1	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia Streptococcal			
subjects affected / exposed	0 / 427 (0.00%)	1 / 431 (0.23%)	0 / 424 (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
Pyelonephritis			
subjects affected / exposed	0 / 427 (0.00%)	1 / 431 (0.23%)	1 / 424 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis Chronic			

subjects affected / exposed	1 / 427 (0.23%)	0 / 431 (0.00%)	0 / 424 (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
Septic Shock			
subjects affected / exposed	0 / 427 (0.00%)	0 / 431 (0.00%)	1 / 424 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sinusitis			
subjects affected / exposed	0 / 427 (0.00%)	1 / 431 (0.23%)	1 / 424 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subacute Endocarditis			
subjects affected / exposed	1 / 427 (0.23%)	0 / 431 (0.00%)	0 / 424 (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
Subcutaneous Abscess			
subjects affected / exposed	0 / 427 (0.00%)	0 / 431 (0.00%)	0 / 424 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tinea Cruris			
subjects affected / exposed	0 / 427 (0.00%)	1 / 431 (0.23%)	0 / 424 (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
Upper Respiratory Tract Infection			
subjects affected / exposed	0 / 427 (0.00%)	1 / 431 (0.23%)	0 / 424 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary Tract Infection			
subjects affected / exposed	1 / 427 (0.23%)	0 / 431 (0.00%)	0 / 424 (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
Wound Infection			

subjects affected / exposed	0 / 427 (0.00%)	0 / 431 (0.00%)	0 / 424 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 427 (0.00%)	1 / 431 (0.23%)	0 / 424 (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
Diabetes Mellitus			
subjects affected / exposed	1 / 427 (0.23%)	0 / 431 (0.00%)	0 / 424 (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
Hypercalcaemia			
subjects affected / exposed	0 / 427 (0.00%)	0 / 431 (0.00%)	1 / 424 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Type 2 Diabetes Mellitus			
subjects affected / exposed	1 / 427 (0.23%)	1 / 431 (0.23%)	0 / 424 (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

Serious adverse events	Part B: Rescue SAR 200mg Q2W		
Total subjects affected by serious adverse events			
subjects affected / exposed	29 / 284 (10.21%)		
number of deaths (all causes)	2		
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal Cell Carcinoma			
subjects affected / exposed	0 / 284 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Breast Cancer			

subjects affected / exposed	0 / 284 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Breast Cancer Metastatic				
subjects affected / exposed	0 / 284 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Ductal Adenocarcinoma Of Pancreas				
subjects affected / exposed	1 / 284 (0.35%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Invasive Lobular Breast Carcinoma				
subjects affected / exposed	0 / 284 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Malignant Melanoma				
subjects affected / exposed	0 / 284 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Meningioma				
subjects affected / exposed	0 / 284 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Metastatic Bronchial Carcinoma				
subjects affected / exposed	1 / 284 (0.35%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Neoplasm Of Appendix				
subjects affected / exposed	0 / 284 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Plasmacytoma				

subjects affected / exposed	0 / 284 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Squamous Cell Carcinoma Of Skin				
subjects affected / exposed	0 / 284 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Vascular disorders				
Aortic Thrombosis				
subjects affected / exposed	0 / 284 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Deep Vein Thrombosis				
subjects affected / exposed	1 / 284 (0.35%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Embolism Arterial				
subjects affected / exposed	0 / 284 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hypertension				
subjects affected / exposed	0 / 284 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hypertensive Crisis				
subjects affected / exposed	0 / 284 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Shock Haemorrhagic				
subjects affected / exposed	0 / 284 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Subgaleal Haematoma				

subjects affected / exposed	1 / 284 (0.35%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pregnancy, puerperium and perinatal conditions			
Abortion Spontaneous			
subjects affected / exposed	0 / 284 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Immediate Post-Injection Reaction			
subjects affected / exposed	0 / 284 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Impaired Healing			
subjects affected / exposed	0 / 284 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pyrexia			
subjects affected / exposed	0 / 284 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	0 / 284 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Reproductive system and breast disorders			
Adenomyosis			
subjects affected / exposed	1 / 284 (0.35%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Metrorrhagia			

subjects affected / exposed	0 / 284 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Acute Respiratory Distress Syndrome			
subjects affected / exposed	0 / 284 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Acute Respiratory Failure			
subjects affected / exposed	0 / 284 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Bronchial Secretion Retention			
subjects affected / exposed	0 / 284 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Chronic Obstructive Pulmonary Disease			
subjects affected / exposed	0 / 284 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Dyspnoea			
subjects affected / exposed	0 / 284 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Interstitial Lung Disease			
subjects affected / exposed	1 / 284 (0.35%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pleural Effusion			
subjects affected / exposed	1 / 284 (0.35%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pneumonitis			

subjects affected / exposed	0 / 284 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pulmonary Embolism			
subjects affected / exposed	1 / 284 (0.35%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pulmonary Oedema			
subjects affected / exposed	0 / 284 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory Distress			
subjects affected / exposed	0 / 284 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Completed Suicide			
subjects affected / exposed	0 / 284 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Depression			
subjects affected / exposed	0 / 284 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Psychotic Disorder			
subjects affected / exposed	0 / 284 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Suicide Attempt			
subjects affected / exposed	0 / 284 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Investigations			

Alanine Aminotransferase Increased				
subjects affected / exposed	0 / 284 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Blood Alkaline Phosphatase Increased				
subjects affected / exposed	0 / 284 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hepatic Enzyme Increased				
subjects affected / exposed	0 / 284 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Transaminases Increased				
subjects affected / exposed	0 / 284 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Injury, poisoning and procedural complications				
Femur Fracture				
subjects affected / exposed	2 / 284 (0.70%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Hip Fracture				
subjects affected / exposed	0 / 284 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Humerus Fracture				
subjects affected / exposed	1 / 284 (0.35%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Joint Dislocation				
subjects affected / exposed	1 / 284 (0.35%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			

Ligament Rupture				
subjects affected / exposed	0 / 284 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Lumbar Vertebral Fracture				
subjects affected / exposed	1 / 284 (0.35%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Procedural Pain				
subjects affected / exposed	0 / 284 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Road Traffic Accident				
subjects affected / exposed	0 / 284 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Skin Wound				
subjects affected / exposed	1 / 284 (0.35%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Tendon Rupture				
subjects affected / exposed	0 / 284 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Wound Haemorrhage				
subjects affected / exposed	0 / 284 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardiac disorders				
Angina Unstable				
subjects affected / exposed	0 / 284 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Atrial Fibrillation				

subjects affected / exposed	0 / 284 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardiac Failure				
subjects affected / exposed	0 / 284 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardio-Respiratory Arrest				
subjects affected / exposed	0 / 284 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardiovascular Insufficiency				
subjects affected / exposed	0 / 284 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Myocardial Ischaemia				
subjects affected / exposed	0 / 284 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pericarditis				
subjects affected / exposed	0 / 284 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Right Ventricular Failure				
subjects affected / exposed	0 / 284 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Sick Sinus Syndrome				
subjects affected / exposed	0 / 284 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Nervous system disorders				
Brain Oedema				

subjects affected / exposed	0 / 284 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cauda Equina Syndrome				
subjects affected / exposed	1 / 284 (0.35%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cerebrovascular Accident				
subjects affected / exposed	0 / 284 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Embolic Cerebral Infarction				
subjects affected / exposed	0 / 284 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Ischaemic Stroke				
subjects affected / exposed	0 / 284 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Myelitis Transverse				
subjects affected / exposed	1 / 284 (0.35%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Sciatica				
subjects affected / exposed	1 / 284 (0.35%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Syncope				
subjects affected / exposed	1 / 284 (0.35%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Transient Ischaemic Attack				

subjects affected / exposed	0 / 284 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Viith Nerve Paralysis				
subjects affected / exposed	1 / 284 (0.35%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Blood and lymphatic system disorders				
Iron Deficiency Anaemia				
subjects affected / exposed	1 / 284 (0.35%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Leukopenia				
subjects affected / exposed	0 / 284 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Neutropenia				
subjects affected / exposed	1 / 284 (0.35%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Splenic Vein Thrombosis				
subjects affected / exposed	0 / 284 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Thrombocytopenia				
subjects affected / exposed	0 / 284 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Eye disorders				
Conjunctivitis				
subjects affected / exposed	0 / 284 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Retinal Vascular Thrombosis				

subjects affected / exposed	1 / 284 (0.35%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Abdominal Discomfort			
subjects affected / exposed	0 / 284 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Abdominal Wall Haematoma			
subjects affected / exposed	0 / 284 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Alcoholic Pancreatitis			
subjects affected / exposed	0 / 284 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Constipation			
subjects affected / exposed	0 / 284 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Duodenal Ulcer			
subjects affected / exposed	1 / 284 (0.35%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Duodenal Ulcer Haemorrhage			
subjects affected / exposed	0 / 284 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Duodenal Ulcer Perforation			
subjects affected / exposed	0 / 284 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Duodenitis			

subjects affected / exposed	0 / 284 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastric Haemorrhage				
subjects affected / exposed	0 / 284 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastric Ulcer Haemorrhage				
subjects affected / exposed	0 / 284 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastritis				
subjects affected / exposed	0 / 284 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Haemorrhoids				
subjects affected / exposed	0 / 284 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pancreatitis				
subjects affected / exposed	1 / 284 (0.35%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hepatobiliary disorders				
Bile Duct Stone				
subjects affected / exposed	0 / 284 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cholecystitis				
subjects affected / exposed	0 / 284 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cholecystitis Chronic				

subjects affected / exposed	0 / 284 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cholelithiasis				
subjects affected / exposed	0 / 284 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Drug-Induced Liver Injury				
subjects affected / exposed	0 / 284 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hepatitis Toxic				
subjects affected / exposed	0 / 284 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Skin and subcutaneous tissue disorders				
Cutaneous Lupus Erythematosus				
subjects affected / exposed	0 / 284 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Renal and urinary disorders				
Calculus Ureteric				
subjects affected / exposed	1 / 284 (0.35%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Renal Failure				
subjects affected / exposed	0 / 284 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Renal Failure Acute				
subjects affected / exposed	0 / 284 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Musculoskeletal and connective tissue				

disorders			
Arthralgia			
subjects affected / exposed	0 / 284 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Intervertebral Disc Protrusion			
subjects affected / exposed	1 / 284 (0.35%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Lumbar Spinal Stenosis			
subjects affected / exposed	0 / 284 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Osteoarthritis			
subjects affected / exposed	2 / 284 (0.70%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Pathological Fracture			
subjects affected / exposed	0 / 284 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Rheumatoid Arthritis			
subjects affected / exposed	3 / 284 (1.06%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Rotator Cuff Syndrome			
subjects affected / exposed	1 / 284 (0.35%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Abscess Limb			
subjects affected / exposed	0 / 284 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Abscess Oral			
subjects affected / exposed	0 / 284 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Appendicitis			
subjects affected / exposed	0 / 284 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Arthritis Bacterial			
subjects affected / exposed	0 / 284 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Bronchitis			
subjects affected / exposed	2 / 284 (0.70%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Bronchitis Fungal			
subjects affected / exposed	0 / 284 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Bursitis Infective Staphylococcal			
subjects affected / exposed	1 / 284 (0.35%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cellulitis			
subjects affected / exposed	1 / 284 (0.35%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Clostridium Difficile Colitis			
subjects affected / exposed	0 / 284 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Diverticulitis			

subjects affected / exposed	0 / 284 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Endometritis				
subjects affected / exposed	0 / 284 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Erysipelas				
subjects affected / exposed	0 / 284 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Escherichia Urinary Tract Infection				
subjects affected / exposed	1 / 284 (0.35%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Gastroenteritis				
subjects affected / exposed	0 / 284 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Herpes Zoster				
subjects affected / exposed	0 / 284 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Incision Site Infection				
subjects affected / exposed	0 / 284 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Infected Skin Ulcer				
subjects affected / exposed	0 / 284 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Necrotising Fasciitis				

subjects affected / exposed	0 / 284 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Osteomyelitis				
subjects affected / exposed	0 / 284 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Otitis Media Acute				
subjects affected / exposed	0 / 284 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Otitis Media Chronic				
subjects affected / exposed	0 / 284 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Paronychia				
subjects affected / exposed	1 / 284 (0.35%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Pelvic Abscess				
subjects affected / exposed	0 / 284 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pharyngitis				
subjects affected / exposed	0 / 284 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumonia				
subjects affected / exposed	0 / 284 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumonia Streptococcal				

subjects affected / exposed	0 / 284 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pyelonephritis				
subjects affected / exposed	0 / 284 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pyelonephritis Chronic				
subjects affected / exposed	0 / 284 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Septic Shock				
subjects affected / exposed	0 / 284 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Sinusitis				
subjects affected / exposed	0 / 284 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Subacute Endocarditis				
subjects affected / exposed	0 / 284 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Subcutaneous Abscess				
subjects affected / exposed	1 / 284 (0.35%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Tinea Cruris				
subjects affected / exposed	0 / 284 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Upper Respiratory Tract Infection				

subjects affected / exposed	0 / 284 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Urinary Tract Infection			
subjects affected / exposed	0 / 284 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Wound Infection			
subjects affected / exposed	1 / 284 (0.35%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 284 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Diabetes Mellitus			
subjects affected / exposed	0 / 284 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hypercalcaemia			
subjects affected / exposed	0 / 284 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Type 2 Diabetes Mellitus			
subjects affected / exposed	0 / 284 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Part A: Placebo QW	Part A: SAR 100mg Q2W	Part A: SAR 150mg Q2W
Total subjects affected by non-serious adverse events			
subjects affected / exposed	11 / 51 (21.57%)	7 / 51 (13.73%)	15 / 52 (28.85%)
Investigations			
Alanine Aminotransferase Increased			
subjects affected / exposed	0 / 51 (0.00%)	0 / 51 (0.00%)	3 / 52 (5.77%)
occurrences (all)	0	0	3
Injury, poisoning and procedural complications			
Accidental Overdose			
subjects affected / exposed	5 / 51 (9.80%)	1 / 51 (1.96%)	3 / 52 (5.77%)
occurrences (all)	5	1	3
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	0 / 51 (0.00%)	0 / 51 (0.00%)	1 / 52 (1.92%)
occurrences (all)	0	0	1
General disorders and administration site conditions			
Injection Site Erythema			
subjects affected / exposed	0 / 51 (0.00%)	1 / 51 (1.96%)	0 / 52 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal and connective tissue disorders			
Rheumatoid Arthritis			
subjects affected / exposed	1 / 51 (1.96%)	1 / 51 (1.96%)	0 / 52 (0.00%)
occurrences (all)	1	1	0
Infections and infestations			
Bronchitis			
subjects affected / exposed	0 / 51 (0.00%)	0 / 51 (0.00%)	1 / 52 (1.92%)
occurrences (all)	0	0	1
Nasopharyngitis			
subjects affected / exposed	3 / 51 (5.88%)	2 / 51 (3.92%)	2 / 52 (3.85%)
occurrences (all)	3	2	2
Upper Respiratory Tract Infection			
subjects affected / exposed	2 / 51 (3.92%)	0 / 51 (0.00%)	2 / 52 (3.85%)
occurrences (all)	3	0	2
Urinary Tract Infection			
subjects affected / exposed	1 / 51 (1.96%)	1 / 51 (1.96%)	1 / 52 (1.92%)
occurrences (all)	1	1	1

Non-serious adverse events	Part A: SAR 100mg QW	Part A: SAR 200mg Q2W	Part A: SAR 150mg QW
Total subjects affected by non-serious adverse events			
subjects affected / exposed	16 / 50 (32.00%)	20 / 51 (39.22%)	17 / 50 (34.00%)
Investigations			
Alanine Aminotransferase Increased			
subjects affected / exposed	2 / 50 (4.00%)	2 / 51 (3.92%)	2 / 50 (4.00%)
occurrences (all)	2	2	2
Injury, poisoning and procedural complications			
Accidental Overdose			
subjects affected / exposed	2 / 50 (4.00%)	2 / 51 (3.92%)	3 / 50 (6.00%)
occurrences (all)	2	2	3
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	6 / 50 (12.00%)	10 / 51 (19.61%)	5 / 50 (10.00%)
occurrences (all)	10	13	5
General disorders and administration site conditions			
Injection Site Erythema			
subjects affected / exposed	1 / 50 (2.00%)	1 / 51 (1.96%)	1 / 50 (2.00%)
occurrences (all)	4	5	1
Musculoskeletal and connective tissue disorders			
Rheumatoid Arthritis			
subjects affected / exposed	0 / 50 (0.00%)	0 / 51 (0.00%)	3 / 50 (6.00%)
occurrences (all)	0	0	3
Infections and infestations			
Bronchitis			
subjects affected / exposed	1 / 50 (2.00%)	0 / 51 (0.00%)	2 / 50 (4.00%)
occurrences (all)	1	0	2
Nasopharyngitis			
subjects affected / exposed	2 / 50 (4.00%)	2 / 51 (3.92%)	1 / 50 (2.00%)
occurrences (all)	2	2	1
Upper Respiratory Tract Infection			
subjects affected / exposed	1 / 50 (2.00%)	3 / 51 (5.88%)	2 / 50 (4.00%)
occurrences (all)	1	3	2
Urinary Tract Infection			

subjects affected / exposed	3 / 50 (6.00%)	1 / 51 (1.96%)	0 / 50 (0.00%)
occurrences (all)	3	1	0

Non-serious adverse events	Part B: Placebo Q2W until rescue	Part B: SAR 150mg Q2W until rescue	Part B: SAR 200mg Q2W until rescue
Total subjects affected by non-serious adverse events			
subjects affected / exposed	144 / 427 (33.72%)	204 / 431 (47.33%)	224 / 424 (52.83%)
Investigations			
Alanine Aminotransferase Increased			
subjects affected / exposed	14 / 427 (3.28%)	36 / 431 (8.35%)	31 / 424 (7.31%)
occurrences (all)	14	41	33
Injury, poisoning and procedural complications			
Accidental Overdose			
subjects affected / exposed	25 / 427 (5.85%)	28 / 431 (6.50%)	28 / 424 (6.60%)
occurrences (all)	29	35	43
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	1 / 427 (0.23%)	38 / 431 (8.82%)	57 / 424 (13.44%)
occurrences (all)	1	62	87
General disorders and administration site conditions			
Injection Site Erythema			
subjects affected / exposed	5 / 427 (1.17%)	25 / 431 (5.80%)	28 / 424 (6.60%)
occurrences (all)	5	99	82
Musculoskeletal and connective tissue disorders			
Rheumatoid Arthritis			
subjects affected / exposed	16 / 427 (3.75%)	4 / 431 (0.93%)	13 / 424 (3.07%)
occurrences (all)	17	5	15
Infections and infestations			
Bronchitis			
subjects affected / exposed	16 / 427 (3.75%)	14 / 431 (3.25%)	22 / 424 (5.19%)
occurrences (all)	17	20	23
Nasopharyngitis			
subjects affected / exposed	18 / 427 (4.22%)	25 / 431 (5.80%)	22 / 424 (5.19%)
occurrences (all)	22	29	24
Upper Respiratory Tract Infection			
subjects affected / exposed	24 / 427 (5.62%)	35 / 431 (8.12%)	37 / 424 (8.73%)
occurrences (all)	28	47	46

Urinary Tract Infection			
subjects affected / exposed	15 / 427 (3.51%)	22 / 431 (5.10%)	23 / 424 (5.42%)
occurrences (all)	16	24	28

Non-serious adverse events	Part B: Rescue SAR 200mg Q2W		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	110 / 284 (38.73%)		
Investigations			
Alanine Aminotransferase Increased			
subjects affected / exposed	16 / 284 (5.63%)		
occurrences (all)	19		
Injury, poisoning and procedural complications			
Accidental Overdose			
subjects affected / exposed	7 / 284 (2.46%)		
occurrences (all)	8		
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	29 / 284 (10.21%)		
occurrences (all)	46		
General disorders and administration site conditions			
Injection Site Erythema			
subjects affected / exposed	15 / 284 (5.28%)		
occurrences (all)	38		
Musculoskeletal and connective tissue disorders			
Rheumatoid Arthritis			
subjects affected / exposed	5 / 284 (1.76%)		
occurrences (all)	7		
Infections and infestations			
Bronchitis			
subjects affected / exposed	13 / 284 (4.58%)		
occurrences (all)	14		
Nasopharyngitis			
subjects affected / exposed	12 / 284 (4.23%)		
occurrences (all)	12		
Upper Respiratory Tract Infection			

subjects affected / exposed	11 / 284 (3.87%)		
occurrences (all)	12		
Urinary Tract Infection			
subjects affected / exposed	8 / 284 (2.82%)		
occurrences (all)	10		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
09 February 2010	This amendment was prepared primarily to clarify the Skin Purified Protein Derivative (PPD) test to be performed at screening according to local regulation and to add a statement on male contraception further to Ethic Committee request.
01 June 2010	This amendment was prepared primarily to indicate randomization specificities in selected countries and to add sampling time points.
04 April 2011	This amendment was prepared primarily to support the start of the Phase 3 clinical trial with the new drug product (different cell line, manufacturing process, formulation and presentation of the IMP).
04 November 2011	This amendment was prepared primarily to indicate the two dose regimens that were selected for phase 3 program based on results of the Part A phase 2 study.
08 August 2012	This amendment was prepared primarily to add new safety measures to prevent the administration of sarilumab to subjects at risk for thrombocytopenia and/or neutropenia.
29 October 2012	This amendment was prepared primarily to modify the primary objective and primary endpoints. HAQ-DI and mTSS were converted to primary endpoints.
08 October 2013	This amendment was prepared primarily to re-order the testing of the primary endpoints reconsidering the role of the HAQ-DI endpoint and also change the timing for this specific endpoint.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

Due to system constraints and legibility issue, part B arms with non-selected doses were grouped in the Subject dispositions section and were not reported in the Adverse events section. In total 4 serious AEs (no death) were reported in these arms.

Notes:

Online references

http://www.ncbi.nlm.nih.gov/pubmed/24297381

http://www.ncbi.nlm.nih.gov/pubmed/25733246