Clinical trial results:
A phase 3, multicenter, open-label, extension study to assess the safety and tolerability of epratuzumab treatment in systemic lupus erythematosus subjects (EMBODY4)

Summary

EudraCT number	2010-020859-30
Trial protocol	BE ES DE CZ GB HU BG LT IT EE
Global end of trial date	16 February 2016

Results information

Result version number	v1
This version publication date	15 December 2016
First version publication date	15 December 2016

Trial information

Trial identification

Sponsor protocol code	SL0012

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01408576
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	UCB, Inc.
Sponsor organisation address	1950 Lake Park Drive, Smyrna, United States, GA 30080
Public contact	Clin Trial Reg & Results Disclosure, UCB BIOSCIENCES GmbH, clinicaltrials@ucb.com
Scientific contact	Clin Trial Reg & Results Disclosure, UCB BIOSCIENCES GmbH, clinicaltrials@ucb.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	18 April 2016
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	16 February 2016
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To assess the safety and tolerability of long-term epratuzumab treatment in subjects with systemic lupus erythematosus (SLE)

Protection of trial subjects:

Patients were pre-medicated prior to infusion of the investigational medicinal product (IMP) to prevent infusion reactions. During the conduct of the study all subjects were closely monitored.

Background therapy:

Epratuzumab treatment is in addition to the subjects' existing standard care of oral corticosteroids and any immunosuppressants or antimalarials continued from Baseline in the subject's original double-blind study. In SL0012, corticosteroids are not considered to be included in the category identified as "immunosuppressants."
- Subjects who completed SL0006 or SL0008:
For SL0006, the Baseline dose is defined as the dose prior to the first infusion of study drug in SL0003 or SL0004. For SL0008, the Baseline dose is defined as the dose at Visit 2 in SL0007.
- Subjects who participated in SL0009 or SL0010:
The Baseline dose is defined as the dose at Visit 2 in SL0009 or SL0010 for subjects completing the study, or the dose at Visit 1 in SL0012 for subjects who terminated prematurely (at Week 16 or later) due to lack of efficacy in SL0009 or SL0010.

Evidence for comparator:

Not applicable

Actual start date of recruitment	20 July 2011
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Australia: 35
Country: Number of subjects enrolled	Belgium: 10
Country: Number of subjects enrolled	Brazil: 79
Country: Number of subjects enrolled	Bulgaria: 48
Country: Number of subjects enrolled	Canada: 18
Country: Number of subjects enrolled	Czech Republic: 26
Country: Number of subjects enrolled	Estonia: 3
Country: Number of subjects enrolled	France: 20
Country: Number of subjects enrolled	Germany: 49
Country: Number of subjects enrolled	Hong Kong: 1
Country: Number of subjects enrolled	Hungary: 29
Country: Number of subjects enrolled	Israel: 32

Country: Number of subjects enrolled	Italy: 17
Country: Number of subjects enrolled	Lithuania: 26
Country: Number of subjects enrolled	Mexico: 25
Country: Number of subjects enrolled	Poland: 153
Country: Number of subjects enrolled	Romania: 47
Country: Number of subjects enrolled	Russian Federation: 11
Country: Number of subjects enrolled	South Africa: 16
Country: Number of subjects enrolled	Korea, Republic of: 8
Country: Number of subjects enrolled	Spain: 52
Country: Number of subjects enrolled	Taiwan: 25
Country: Number of subjects enrolled	Ukraine: 52
Country: Number of subjects enrolled	United Kingdom: 16
Country: Number of subjects enrolled	United States: 452
Worldwide total number of subjects	1250
EEA total number of subjects	496

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)	1218
From 65 to 84 years	32
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study started to enroll patients in July 2011 and concluded in February 2016.

Pre-assignment

Screening details:

Participant Flow refers to the Enrolled Set.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Enrollment Cohort 1 Epratuzumab 600 mg per week (ES)

Arm description:

Enrolled Set (ES) of subjects enrolled prior to the approval of Protocol Amendment 2

600 mg infusions delivered weekly for a total of 4 consecutive weeks (cumulative dose 2400 mg) over sixteen 12-week treatment cycles

Arm type	Experimental
Investigational medicinal product name	Epratuzumab
Investigational medicinal product code	Emab
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Intravenous infusion: 600 mg per week or 1200 mg every other week for a total of 4 weeks (cumulative dose 2400 mg) over sixteen 12 week treatment cycles.

Arm title	Enrollment Cohort 2 Epratuzumab 1200 mg Q2W (ES)

Arm description:

Enrolled Set (ES) of subjects enrolled prior to the approval of Protocol Amendment 2

1200 mg infusions delivered every other week (Q2W) for a total of 4 weeks (cumulative dose 2400 mg) over sixteen 12 week treatment cycles

Arm type	Experimental
Investigational medicinal product name	Epratuzumab
Investigational medicinal product code	Emab
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Intravenous infusion: 600 mg per week or 1200 mg every other week for a total of 4 weeks (cumulative dose 2400 mg) over sixteen 12 week treatment cycles.

Arm title	Enrollment Cohort 2 Epratuzumab 600 mg per week (ES)

Arm description:

Enrolled Set (ES) of subjects enrolled prior to the approval of Protocol Amendment 2

600 mg infusions delivered weekly for a total of 4 consecutive weeks (cumulative dose 2400 mg) over sixteen 12-week treatment cycles

Arm type	Experimental
Investigational medicinal product name	Epratuzumab
Investigational medicinal product code	Emab
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Intravenous infusion: 600 mg per week or 1200 mg every other week for a total of 4 weeks (cumulative dose 2400 mg) over sixteen 12 week treatment cycles.

Number of subjects in period 1	Enrollment Cohort 1 Epratuzumab 600 mg per week (ES)	Enrollment Cohort 2 Epratuzumab 1200 mg Q2W (ES)	Enrollment Cohort 2 Epratuzumab 600 mg per week (ES)
Started	244	498	508
Completed	56	0	0
Not completed	188	498	508
AE, serious fatal	4	4	1
Consent withdrawn by subject	34	60	66
AE, unknown type	-	1	-
AE, non-serious non-fatal	12	19	11
SAE, non-fatal+AE, non-serious non-fatal	-	1	1
Other reason	10	16	18
Lost to follow-up	10	9	17
SAE, non-fatal	11	23	14
Sponsor terminated study	89	333	330
Lack of efficacy	17	30	48
Protocol deviation	1	2	2

Baseline characteristics

Reporting groups	
Reporting group title	Enrollment Cohort 1 Epratuzumab 600 mg per week (ES)
Reporting group description:	
Enrolled Set (ES) of subjects enrolled prior to the approval of Protocol Amendment 2 600 mg infusions delivered weekly for a total of 4 consecutive weeks (cumulative dose 2400 mg) over sixteen 12-week treatment cycles	
Reporting group title	Enrollment Cohort 2 Epratuzumab 1200 mg Q2W (ES)
Reporting group description:	
Enrolled Set (ES) of subjects enrolled prior to the approval of Protocol Amendment 2 1200 mg infusions delivered every other week (Q2W) for a total of 4 weeks (cumulative dose 2400 mg) over sixteen 12 week treatment cycles	
Reporting group title	Enrollment Cohort 2 Epratuzumab 600 mg per week (ES)
Reporting group description:	
Enrolled Set (ES) of subjects enrolled prior to the approval of Protocol Amendment 2 600 mg infusions delivered weekly for a total of 4 consecutive weeks (cumulative dose 2400 mg) over sixteen 12-week treatment cycles	

Reporting group values	Enrollment Cohort 1 Epratuzumab 600 mg per week (ES)	Enrollment Cohort 2 Epratuzumab 1200 mg Q2W (ES)	Enrollment Cohort 2 Epratuzumab 600 mg per week (ES)
Number of subjects	244	498	508
Age Categorical Units: Subjects			
<=18 years	0	4	3
Between 18 and 65 years	239	485	487
>=65 years	5	9	18
Age Continuous Units: years			
arithmetic mean	41	41.9	42.5
standard deviation	± 12	± 11.5	± 11.9
Gender Categorical Units: Subjects			
Male	18	31	30
Female	226	467	478

Reporting group values	Total		
Number of subjects	1250		
Age Categorical Units: Subjects			
<=18 years	7		
Between 18 and 65 years	1211		
>=65 years	32		
Age Continuous Units: years			
arithmetic mean			
standard deviation	-		

Gender Categorical Units: Subjects			
Male	79		
Female	1171		

End points

End points reporting groups

Reporting group title	Enrollment Cohort 1 Epratuzumab 600 mg per week (ES)

Reporting group description:

Enrolled Set (ES) of subjects enrolled prior to the approval of Protocol Amendment 2

600 mg infusions delivered weekly for a total of 4 consecutive weeks (cumulative dose 2400 mg) over sixteen 12-week treatment cycles

Reporting group title	Enrollment Cohort 2 Epratuzumab 1200 mg Q2W (ES)

Reporting group description:

Enrolled Set (ES) of subjects enrolled prior to the approval of Protocol Amendment 2

1200 mg infusions delivered every other week (Q2W) for a total of 4 weeks (cumulative dose 2400 mg) over sixteen 12 week treatment cycles

Reporting group title	Enrollment Cohort 2 Epratuzumab 600 mg per week (ES)

Reporting group description:

Enrolled Set (ES) of subjects enrolled prior to the approval of Protocol Amendment 2

600 mg infusions delivered weekly for a total of 4 consecutive weeks (cumulative dose 2400 mg) over sixteen 12-week treatment cycles

Subject analysis set title	Enrollment Cohort 1 Epratuzumab 600 mg per week
Subject analysis set type	Safety analysis

Subject analysis set description:

Subjects enrolled prior to the approval of Protocol Amendment 2

600 mg infusions delivered weekly for a total of 4 consecutive weeks (cumulative dose 2400 mg) over sixteen 12-week treatment cycles

Subject analysis set title	Enrollment Cohort 2 Epratuzumab 1200 mg Q2W
Subject analysis set type	Safety analysis

Subject analysis set description:

Subjects enrolled after approval of Protocol Amendment 2

1200 mg infusions delivered every other week (Q2W) for a total of 4 weeks (cumulative dose 2400 mg) over sixteen 12 week treatment cycles

Subject analysis set title	Enrollment Cohort 2 Epratuzumab 600 mg per week
Subject analysis set type	Safety analysis

Subject analysis set description:

Subjects enrolled after approval of Protocol Amendment 2

600 mg infusions delivered weekly for a total of 4 consecutive weeks (cumulative dose 2400 mg) over sixteen 12-week treatment cycles

Subject analysis set title	All Epratuzumab 600 mg per week
Subject analysis set type	Safety analysis

Subject analysis set description:

600 mg infusions delivered weekly for a total of 4 consecutive weeks (cumulative dose 2400 mg) over sixteen 12-week treatment cycles

Subject analysis set title	All subjects
Subject analysis set type	Safety analysis

Subject analysis set description:

Subjects receiving 600 mg infusions delivered weekly for a total of 4 consecutive weeks (cumulative dose 2400 mg) over sixteen 12-week treatment cycles and subjects receiving 1200 mg infusions delivered every other week for a total of 4 weeks (cumulative dose 2400 mg) over sixteen 12 week treatment cycles

Subject analysis set title	Enrollment Cohort 1 Epratuzumab 600 mg per week (FASS1)
Subject analysis set type	Full analysis

Subject analysis set description:

Full Analysis Subset 1 (FASS1) consisted of all subjects in the FAS who were enrolled in study SL0008, SL0009, or SL0010 prior to enrollment in SL0012.
Subjects were enrolled prior to the approval of Protocol Amendment 2.

600 mg infusions delivered weekly for a total of 4 consecutive weeks (cumulative dose 2400 mg) over sixteen 12-week treatment cycles

Subject analysis set title	Enrollment Cohort 2 Epratuzumab 1200 mg Q2W (FASS1)
Subject analysis set type	Full analysis

Subject analysis set description:

Full Analysis Subset 1 (FASS1) consisted of all subjects in the FAS who were enrolled in study SL0008, SL0009, or SL0010 prior to enrollment in SL0012.
Subjects were enrolled prior to the approval of Protocol Amendment 2.

1200 mg infusions delivered every other week (Q2W) for a total of 4 weeks (cumulative dose 2400 mg) over sixteen 12 week treatment cycles

Subject analysis set title	Enrollment Cohort 2 Epratuzumab 600 mg per week (FASS1)
Subject analysis set type	Full analysis

Subject analysis set description:

Full Analysis Subset 1 (FASS1) consisted of all subjects in the FAS who were enrolled in study SL0008, SL0009, or SL0010 prior to enrollment in SL0012.
Subjects were enrolled prior to the approval of Protocol Amendment 2.

600 mg infusions delivered weekly for a total of 4 consecutive weeks (cumulative dose 2400 mg) over sixteen 12-week treatment cycles

Subject analysis set title	All Epratuzumab 600 mg per week (FASS1)
Subject analysis set type	Full analysis

Subject analysis set description:

Full Analysis Subset 1 (FASS1) consisted of all subjects in the FAS who were enrolled in study SL0008, SL0009, or SL0010 prior to enrollment in SL0012.
Subjects were enrolled prior to the approval of Protocol Amendment 2.

600 mg infusions delivered weekly for a total of 4 consecutive weeks (cumulative dose 2400 mg) over sixteen 12-week treatment cycles

Subject analysis set title	All subjects (FASS1)
Subject analysis set type	Full analysis

Subject analysis set description:

Full Analysis Subset 1 (FASS1) consisted of all subjects in the FAS who were enrolled in study SL0008, SL0009, or SL0010 prior to enrollment in SL0012.
Subjects were enrolled prior to the approval of Protocol Amendment 2.
Subjects receiving 600 mg infusions delivered weekly for a total of 4 consecutive weeks (cumulative dose 2400 mg) over sixteen 12-week treatment cycles and subjects receiving 1200 mg infusions delivered every other week for a total of 4 weeks (cumulative dose 2400 mg) over sixteen 12 week treatment cycles

Primary: Number of subjects prematurely discontinuing due to a treatment-emergent adverse event (TEAE) during the treatment period (maximum 96 weeks)

End point title	Number of subjects prematurely discontinuing due to a treatment-emergent adverse event (TEAE) during the treatment period (maximum 96 weeks)[1]

End point description:

A TEAE is any untoward medical occurrence in a patient or clinical investigation subject administered a pharmaceutical product, which does not necessarily have a causal relationship with this treatment.

End point type	Primary

End point timeframe:

During the treatment period (through Week 96)

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No formal statistical hypothesis testing was planned for this study. Results were summarized as descriptive statistics only.

End point values	Enrollment Cohort 1 Epratuzumab 600 mg per week	Enrollment Cohort 2 Epratuzumab 1200 mg Q2W	Enrollment Cohort 2 Epratuzumab 600 mg per week	All Epratuzumab 600 mg per week
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	244	497	507	751
Units: Participants				
number (not applicable)				
Number of Participants	26	45	25	51

End point values	All subjects			
Subject group type	Subject analysis set			
Number of subjects analysed	1248			
Units: Participants				
number (not applicable)				
Number of Participants	96			

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of subjects prematurely discontinuing due to a treatment-emergent adverse event (TEAE) during the treatment period (maximum 96 weeks)

End point title	Percentage of subjects prematurely discontinuing due to a treatment-emergent adverse event (TEAE) during the treatment period (maximum 96 weeks)[2]

End point description:

A TEAE is any untoward medical occurrence in a patient or clinical investigation subject administered a pharmaceutical product, which does not necessarily have a causal relationship with this treatment.

End point type	Primary

End point timeframe:

During the treatment period (through Week 96)

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No formal statistical hypothesis testing was planned for this study. Results were summarized as descriptive statistics only.

End point values	Enrollment Cohort 1 Epratuzumab 600 mg per week	Enrollment Cohort 2 Epratuzumab 1200 mg Q2W	Enrollment Cohort 2 Epratuzumab 600 mg per week	All Epratuzumab 600 mg per week
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	244	497	507	751
Units: percentage of participants				
number (not applicable)				
Percentage of Participants	10.7	9.1	4.9	6.8

End point values	All subjects			
Subject group type	Subject analysis set			
Number of subjects analysed	1248			
Units: percentage of participants				
number (not applicable)				
Percentage of Participants	7.7			

Statistical analyses

No statistical analyses for this end point

Primary: Number of subjects reporting at least 1 serious adverse event (SAE) during the treatment period (maximum 96 weeks)

End point title	Number of subjects reporting at least 1 serious adverse event (SAE) during the treatment period (maximum 96 weeks)[3]

End point description:

A SAE is a treatment-emergent adverse event (TEAE) that the investigator classifies as serious. This includes:
• Death
• Life-threatening
• Significant or persistent disability/incapacity
• Congenital anomaly/birth defect (including that occurring in a fetus)
• Important medical event that, based upon appropriate medical judgment, may jeopardize the patient or subject and may require medical or surgical intervention to prevent 1 of the other outcomes listed in the definition of serious
• Initial inpatient hospitalization or prolongation of hospitalization

End point type	Primary

End point timeframe:

During the treatment period (through Week 96)

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No formal statistical hypothesis testing was planned for this study. Results were summarized as descriptive statistics only.

End point values	Enrollment Cohort 1 Epratuzumab 600 mg per week	Enrollment Cohort 2 Epratuzumab 1200 mg Q2W	Enrollment Cohort 2 Epratuzumab 600 mg per week	All Epratuzumab 600 mg per week
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	244	497	507	751
Units: Participants				
number (not applicable)				
Number of Participants	81	119	104	185

End point values	All subjects			

Subject group type	Subject analysis set			
Number of subjects analysed	1248			
Units: Participants				
number (not applicable)				
Number of Participants	304			

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of subjects reporting at least 1 serious adverse event (SAE) during the treatment period (maximum 96 weeks)

End point title	Percentage of subjects reporting at least 1 serious adverse event (SAE) during the treatment period (maximum 96 weeks)[4]

End point description:

A SAE is a treatment-emergent adverse event (TEAE) that the investigator classifies as serious. This includes:
• Death
• Life-threatening
• Significant or persistent disability/incapacity
• Congenital anomaly/birth defect (including that occurring in a fetus)
• Important medical event that, based upon appropriate medical judgment, may jeopardize the patient or subject and may require medical or surgical intervention to prevent 1 of the other outcomes listed in the definition of serious
• Initial inpatient hospitalization or prolongation of hospitalization

End point type	Primary

End point timeframe:

During the treatment period (through Week 96)

Notes:

[4] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No formal statistical hypothesis testing was planned for this study. Results were summarized as descriptive statistics only.

End point values	Enrollment Cohort 1 Epratuzumab 600 mg per week	Enrollment Cohort 2 Epratuzumab 1200 mg Q2W	Enrollment Cohort 2 Epratuzumab 600 mg per week	All Epratuzumab 600 mg per week
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	244	497	507	751
Units: percentage of participants				
number (not applicable)				
Percentage of Participants	33.2	23.9	20.5	24.6

End point values	All subjects			
Subject group type	Subject analysis set			
Number of subjects analysed	1248			
Units: percentage of participants				
number (not applicable)				
Percentage of Participants	24.4			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects meeting treatment response criteria according to a combined response index

End point title	Number of subjects meeting treatment response criteria according to a combined response index

End point description:

Combined response index is a response variable (yes/no) incorporating the following criteria for achievement of responder status (ie, all criteria must be met to achieve responder status): (1) British Isles Lupus Activity Group (BILAG) improvement, (2) No worsening in Systemic Lupus Erythematosus Activity Index (SLEDAI), (3) No worsening in Physician's Global Assessment of Disease, and (4) No disallowed changes in concomitant medications, with disallowed changes including mainly increases in corticosteroids, immunosuppressants, and antimalarials.

End point type	Secondary

End point timeframe:

Week 48

End point values	Enrollment Cohort 1 Epratuzumab 600 mg per week (FASS1)	Enrollment Cohort 2 Epratuzumab 1200 mg Q2W (FASS1)	Enrollment Cohort 2 Epratuzumab 600 mg per week (FASS1)	All Epratuzumab 600 mg per week (FASS1)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	230	488	494	724
Units: Participants				
number (not applicable)				
Number of Responder	82	146	134	216

End point values	All subjects (FASS1)			
Subject group type	Subject analysis set			
Number of subjects analysed	1212			
Units: Participants				
number (not applicable)				
Number of Responder	362			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of subjects meeting treatment response criteria according to a combined response index

End point title	Percentage of subjects meeting treatment response criteria according to a combined response index

End point description:

Combined response index is a response variable (yes/no) incorporating the following criteria for achievement of responder status (ie, all criteria must be met to achieve responder status): (1) British Isles Lupus Activity Group (BILAG) improvement, (2) No worsening in Systemic Lupus Erythematosus Activity Index (SLEDAI), (3) No worsening in Physician's Global Assessment of Disease, and (4) No disallowed changes in concomitant medications, with disallowed changes including mainly increases in corticosteroids, immunosuppressants, and antimalarials.

End point type	Secondary

End point timeframe:

Week 48

End point values	Enrollment Cohort 1 Epratuzumab 600 mg per week (FASS1)	Enrollment Cohort 2 Epratuzumab 1200 mg Q2W (FASS1)	Enrollment Cohort 2 Epratuzumab 600 mg per week (FASS1)	All Epratuzumab 600 mg per week (FASS1)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	230	488	494	724
Units: percentage of				
number (not applicable)				
Percentage of Responder	35.7	29.9	27.1	29.8

End point values	All subjects (FASS1)			
Subject group type	Subject analysis set			
Number of subjects analysed	1212			
Units: percentage of				
number (not applicable)				
Percentage of Responder	29.9			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects meeting treatment response criteria according to a combined response index

End point title	Number of subjects meeting treatment response criteria according to a combined response index

End point description:

Combined response index is a response variable (yes/no) incorporating the following criteria for achievement of responder status (ie, all criteria must be met to achieve responder status): (1) British Isles Lupus Activity Group (BILAG) improvement, (2) No worsening in Systemic Lupus Erythematosus

Activity Index (SLEDAI), (3) No worsening in Physician's Global Assessment of Disease, and (4) No disallowed changes in concomitant medications, with disallowed changes including mainly increases in corticosteroids, immunosuppressants, and antimalarials.

End point type	Secondary

End point timeframe:

Week 96

End point values	Enrollment Cohort 1 Epratuzumab 600 mg per week (FASS1)	Enrollment Cohort 2 Epratuzumab 1200 mg Q2W (FASS1)	Enrollment Cohort 2 Epratuzumab 600 mg per week (FASS1)	All Epratuzumab 600 mg per week (FASS1)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	230	488	494	724
Units: Participants				
number (not applicable)				
Number of Responder	74	66	78	152

End point values	All subjects (FASS1)			
Subject group type	Subject analysis set			
Number of subjects analysed	1212			
Units: Participants				
number (not applicable)				
Number of Responder	218			

Statistical analyses

No statistical analyses for this end point

Secondary: The percent of subjects meeting treatment response criteria according to a combined response index

End point title	The percent of subjects meeting treatment response criteria according to a combined response index

End point description:

Combined response index is a response variable (yes/no) incorporating the following criteria for achievement of responder status (ie, all criteria must be met to achieve responder status): (1) British Isles Lupus Activity Group (BILAG) improvement, (2) No worsening in Systemic Lupus Erythematosus Activity Index (SLEDAI), (3) No worsening in Physician's Global Assessment of Disease, and (4) No disallowed changes in concomitant medications, with disallowed changes including mainly increases in corticosteroids, immunosuppressants, and antimalarials.

End point type	Secondary

End point timeframe:

Week 96

End point values	Enrollment Cohort 1 Epratuzumab 600 mg per week (FASS1)	Enrollment Cohort 2 Epratuzumab 1200 mg Q2W (FASS1)	Enrollment Cohort 2 Epratuzumab 600 mg per week (FASS1)	All Epratuzumab 600 mg per week (FASS1)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	230	488	494	724
Units: percentage of				
number (not applicable)				
Percentage of Responder	39.8	21.6	26.2	31.4

End point values	All subjects (FASS1)			
Subject group type	Subject analysis set			
Number of subjects analysed	1212			
Units: percentage of				
number (not applicable)				
Percentage of Responder	27.6			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events were collected from Visit 1 until Safety Follow-Up Visit up to week 196

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	17.0

Reporting groups

Reporting group title	Enrollment Cohort 1 Epratuzumab 600 mg per week

Reporting group description:

Subjects enrolled prior to the approval of Protocol Amendment 2

600 mg infusions delivered weekly for a total of 4 consecutive weeks (cumulative dose 2400 mg) over sixteen 12-week treatment cycles

Reporting group title	Enrollment Cohort 2 Epratuzumab 1200 mg Q2W

Reporting group description:

Subjects enrolled after approval of Protocol Amendment 2

1200 mg infusions delivered every other week (Q2W) for a total of 4 weeks (cumulative dose 2400 mg) over sixteen 12 week treatment cycles

Reporting group title	All Epratuzumab 600 mg per week

Reporting group description:

600 mg infusions delivered weekly for a total of 4 consecutive weeks (cumulative dose 2400 mg) over sixteen 12-week treatment cycles

Reporting group title	All subjects

Reporting group description:

Subjects receiving 600 mg infusions delivered weekly for a total of 4 consecutive weeks (cumulative dose 2400 mg) over sixteen 12-week treatment cycles and subjects receiving 1200 mg infusions delivered every other week for a total of 4 weeks (cumulative dose 2400 mg) over sixteen 12 week treatment cycles

Reporting group title	Enrollment Cohort 2 Epratuzumab 600 mg per week

Reporting group description:

Subjects enrolled after approval of Protocol Amendment 2

600 mg infusions delivered weekly for a total of 4 consecutive weeks (cumulative dose 2400 mg) over sixteen 12-week treatment cycles

Serious adverse events	Enrollment Cohort 1 Epratuzumab 600 mg per week	Enrollment Cohort 2 Epratuzumab 1200 mg Q2W	All Epratuzumab 600 mg per week
Total subjects affected by serious adverse events			
subjects affected / exposed	81 / 244 (33.20%)	119 / 497 (23.94%)	185 / 751 (24.63%)
number of deaths (all causes)	4	4	5
number of deaths resulting from adverse events	1	0	1
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Squamous cell carcinoma of skin			

subjects affected / exposed	1 / 244 (0.41%)	0 / 497 (0.00%)	3 / 751 (0.40%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Uterine leiomyoma			
subjects affected / exposed	0 / 244 (0.00%)	2 / 497 (0.40%)	0 / 751 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Adenocarcinoma of colon			
subjects affected / exposed	0 / 244 (0.00%)	0 / 497 (0.00%)	1 / 751 (0.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Adenocarcinoma pancreas			
subjects affected / exposed	0 / 244 (0.00%)	0 / 497 (0.00%)	1 / 751 (0.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Bladder cancer			
subjects affected / exposed	0 / 244 (0.00%)	1 / 497 (0.20%)	0 / 751 (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
Bowen's disease			
subjects affected / exposed	0 / 244 (0.00%)	0 / 497 (0.00%)	1 / 751 (0.13%)
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 stage I			
subjects affected / exposed	0 / 244 (0.00%)	1 / 497 (0.20%)	0 / 751 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cervix carcinoma stage 0			
subjects affected / exposed	1 / 244 (0.41%)	0 / 497 (0.00%)	1 / 751 (0.13%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastric cancer			

subjects affected / exposed	0 / 244 (0.00%)	1 / 497 (0.20%)	0 / 751 (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
Myeloproliferative disorder			
subjects affected / exposed	0 / 244 (0.00%)	0 / 497 (0.00%)	1 / 751 (0.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ovarian adenoma			
subjects affected / exposed	0 / 244 (0.00%)	1 / 497 (0.20%)	0 / 751 (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			
subjects affected / exposed	0 / 244 (0.00%)	0 / 497 (0.00%)	1 / 751 (0.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	3 / 244 (1.23%)	0 / 497 (0.00%)	5 / 751 (0.67%)
occurrences causally related to treatment / all	1 / 3	0 / 0	1 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertension			
subjects affected / exposed	0 / 244 (0.00%)	3 / 497 (0.60%)	0 / 751 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Venous thrombosis			
subjects affected / exposed	0 / 244 (0.00%)	2 / 497 (0.40%)	0 / 751 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arterial occlusive disease			
subjects affected / exposed	0 / 244 (0.00%)	0 / 497 (0.00%)	1 / 751 (0.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertensive crisis			

subjects affected / exposed	0 / 244 (0.00%)	1 / 497 (0.20%)	0 / 751 (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
Orthostatic hypotension			
subjects affected / exposed	0 / 244 (0.00%)	0 / 497 (0.00%)	1 / 751 (0.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Temporal arteritis			
subjects affected / exposed	0 / 244 (0.00%)	1 / 497 (0.20%)	0 / 751 (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
Venous thrombosis limb			
subjects affected / exposed	0 / 244 (0.00%)	0 / 497 (0.00%)	1 / 751 (0.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Surgical and medical procedures			
Abortion induced			
subjects affected / exposed	0 / 244 (0.00%)	0 / 497 (0.00%)	1 / 751 (0.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholecystectomy			
subjects affected / exposed	0 / 244 (0.00%)	1 / 497 (0.20%)	0 / 751 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hip arthroplasty			
subjects affected / exposed	0 / 244 (0.00%)	1 / 497 (0.20%)	0 / 751 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Joint arthroplasty			
subjects affected / exposed	1 / 244 (0.41%)	0 / 497 (0.00%)	1 / 751 (0.13%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Polymedication			

subjects affected / exposed	0 / 244 (0.00%)	1 / 497 (0.20%)	0 / 751 (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
Shoulder operation			
subjects affected / exposed	1 / 244 (0.41%)	0 / 497 (0.00%)	1 / 751 (0.13%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pregnancy, puerperium and perinatal conditions			
Cerebral infarction			
subjects affected / exposed	0 / 244 (0.00%)	1 / 497 (0.20%)	0 / 751 (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
Abortion spontaneous			
subjects affected / exposed	3 / 244 (1.23%)	0 / 497 (0.00%)	4 / 751 (0.53%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Foetal death			
subjects affected / exposed	1 / 244 (0.41%)	0 / 497 (0.00%)	1 / 751 (0.13%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Premature delivery			
subjects affected / exposed	0 / 244 (0.00%)	1 / 497 (0.20%)	0 / 751 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	1 / 244 (0.41%)	4 / 497 (0.80%)	9 / 751 (1.20%)
occurrences causally related to treatment / all	0 / 1	0 / 4	1 / 10
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Non-cardiac chest pain			
subjects affected / exposed	2 / 244 (0.82%)	2 / 497 (0.40%)	2 / 751 (0.27%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Pyrexia			
subjects affected / exposed	1 / 244 (0.41%)	2 / 497 (0.40%)	2 / 751 (0.27%)
occurrences causally related to treatment / all	1 / 1	0 / 2	1 / 2
deaths causally related to treatment / all	1 / 1	0 / 0	1 / 1
Asthenia			
subjects affected / exposed	1 / 244 (0.41%)	1 / 497 (0.20%)	1 / 751 (0.13%)
occurrences causally related to treatment / all	1 / 1	0 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Drug interaction			
subjects affected / exposed	0 / 244 (0.00%)	1 / 497 (0.20%)	0 / 751 (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 intolerance			
subjects affected / exposed	0 / 244 (0.00%)	0 / 497 (0.00%)	1 / 751 (0.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperthermia			
subjects affected / exposed	0 / 244 (0.00%)	0 / 497 (0.00%)	1 / 751 (0.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Impaired healing			
subjects affected / exposed	0 / 244 (0.00%)	0 / 497 (0.00%)	1 / 751 (0.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Local swelling			
subjects affected / exposed	1 / 244 (0.41%)	0 / 497 (0.00%)	1 / 751 (0.13%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oedema peripheral			
subjects affected / exposed	0 / 244 (0.00%)	0 / 497 (0.00%)	1 / 751 (0.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Serositis			

subjects affected / exposed	1 / 244 (0.41%)	0 / 497 (0.00%)	1 / 751 (0.13%)
occurrences causally related to treatment / all	0 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Drug hypersensitivity			
subjects affected / exposed	0 / 244 (0.00%)	1 / 497 (0.20%)	1 / 751 (0.13%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anaphylactic reaction			
subjects affected / exposed	1 / 244 (0.41%)	0 / 497 (0.00%)	1 / 751 (0.13%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Ovarian cyst			
subjects affected / exposed	1 / 244 (0.41%)	1 / 497 (0.20%)	3 / 751 (0.40%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endometriosis			
subjects affected / exposed	2 / 244 (0.82%)	1 / 497 (0.20%)	2 / 751 (0.27%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cervical dysplasia			
subjects affected / exposed	2 / 244 (0.82%)	0 / 497 (0.00%)	2 / 751 (0.27%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Menorrhagia			
subjects affected / exposed	1 / 244 (0.41%)	0 / 497 (0.00%)	2 / 751 (0.27%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Uterine polyp			
subjects affected / exposed	1 / 244 (0.41%)	0 / 497 (0.00%)	2 / 751 (0.27%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Adenomyosis			
subjects affected / exposed	0 / 244 (0.00%)	1 / 497 (0.20%)	0 / 751 (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
Endometrial hyperplasia			
subjects affected / exposed	1 / 244 (0.41%)	0 / 497 (0.00%)	1 / 751 (0.13%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pelvic pain			
subjects affected / exposed	0 / 244 (0.00%)	1 / 497 (0.20%)	0 / 751 (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
Uterine haemorrhage			
subjects affected / exposed	0 / 244 (0.00%)	1 / 497 (0.20%)	0 / 751 (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
Vaginal prolapse			
subjects affected / exposed	1 / 244 (0.41%)	0 / 497 (0.00%)	1 / 751 (0.13%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	1 / 244 (0.41%)	3 / 497 (0.60%)	2 / 751 (0.27%)
occurrences causally related to treatment / all	0 / 1	0 / 3	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			
subjects affected / exposed	2 / 244 (0.82%)	0 / 497 (0.00%)	3 / 751 (0.40%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cough			
subjects affected / exposed	0 / 244 (0.00%)	0 / 497 (0.00%)	2 / 751 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Pleurisy			
subjects affected / exposed	0 / 244 (0.00%)	2 / 497 (0.40%)	0 / 751 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute pulmonary oedema			
subjects affected / exposed	0 / 244 (0.00%)	1 / 497 (0.20%)	0 / 751 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute respiratory failure			
subjects affected / exposed	0 / 244 (0.00%)	1 / 497 (0.20%)	0 / 751 (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
Asthma			
subjects affected / exposed	0 / 244 (0.00%)	0 / 497 (0.00%)	1 / 751 (0.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 244 (0.00%)	1 / 497 (0.20%)	0 / 751 (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 respiratory failure			
subjects affected / exposed	0 / 244 (0.00%)	1 / 497 (0.20%)	0 / 751 (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
Dyspnoea exertional			
subjects affected / exposed	0 / 244 (0.00%)	0 / 497 (0.00%)	1 / 751 (0.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Emphysema			
subjects affected / exposed	0 / 244 (0.00%)	0 / 497 (0.00%)	1 / 751 (0.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Laryngeal stenosis			

subjects affected / exposed	0 / 244 (0.00%)	1 / 497 (0.20%)	0 / 751 (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
Pleural effusion			
subjects affected / exposed	0 / 244 (0.00%)	0 / 497 (0.00%)	1 / 751 (0.13%)
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 arterial hypertension			
subjects affected / exposed	1 / 244 (0.41%)	0 / 497 (0.00%)	1 / 751 (0.13%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary hypertension			
subjects affected / exposed	1 / 244 (0.41%)	0 / 497 (0.00%)	1 / 751 (0.13%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory failure			
subjects affected / exposed	0 / 244 (0.00%)	1 / 497 (0.20%)	0 / 751 (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
Wheezing			
subjects affected / exposed	0 / 244 (0.00%)	1 / 497 (0.20%)	0 / 751 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Depression			
subjects affected / exposed	0 / 244 (0.00%)	2 / 497 (0.40%)	2 / 751 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Suicide attempt			
subjects affected / exposed	0 / 244 (0.00%)	2 / 497 (0.40%)	2 / 751 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychotic disorder			

subjects affected / exposed	0 / 244 (0.00%)	2 / 497 (0.40%)	0 / 751 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Suicidal ideation			
subjects affected / exposed	0 / 244 (0.00%)	1 / 497 (0.20%)	0 / 751 (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			
Cholelithiasis			
subjects affected / exposed	2 / 244 (0.82%)	2 / 497 (0.40%)	2 / 751 (0.27%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholecystitis			
subjects affected / exposed	0 / 244 (0.00%)	0 / 497 (0.00%)	3 / 751 (0.40%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bile duct stone			
subjects affected / exposed	0 / 244 (0.00%)	0 / 497 (0.00%)	2 / 751 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholangitis			
subjects affected / exposed	0 / 244 (0.00%)	0 / 497 (0.00%)	1 / 751 (0.13%)
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 acute			
subjects affected / exposed	0 / 244 (0.00%)	1 / 497 (0.20%)	0 / 751 (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
Cholelithiasis migration			
subjects affected / exposed	0 / 244 (0.00%)	1 / 497 (0.20%)	0 / 751 (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
Hepatic steatosis			

subjects affected / exposed	0 / 244 (0.00%)	0 / 497 (0.00%)	1 / 751 (0.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Biopsy liver			
subjects affected / exposed	0 / 244 (0.00%)	1 / 497 (0.20%)	0 / 751 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood cortisol decreased			
subjects affected / exposed	0 / 244 (0.00%)	0 / 497 (0.00%)	1 / 751 (0.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Electrocardiogram QT prolonged			
subjects affected / exposed	0 / 244 (0.00%)	0 / 497 (0.00%)	1 / 751 (0.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transaminases increased			
subjects affected / exposed	1 / 244 (0.41%)	0 / 497 (0.00%)	1 / 751 (0.13%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Meniscus injury			
subjects affected / exposed	3 / 244 (1.23%)	0 / 497 (0.00%)	3 / 751 (0.40%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tendon rupture			
subjects affected / exposed	0 / 244 (0.00%)	1 / 497 (0.20%)	2 / 751 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ankle fracture			
subjects affected / exposed	0 / 244 (0.00%)	1 / 497 (0.20%)	1 / 751 (0.13%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Fibula fracture			
subjects affected / exposed	0 / 244 (0.00%)	1 / 497 (0.20%)	1 / 751 (0.13%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Head injury			
subjects affected / exposed	0 / 244 (0.00%)	1 / 497 (0.20%)	1 / 751 (0.13%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Joint dislocation			
subjects affected / exposed	0 / 244 (0.00%)	1 / 497 (0.20%)	1 / 751 (0.13%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Laceration			
subjects affected / exposed	1 / 244 (0.41%)	1 / 497 (0.20%)	1 / 751 (0.13%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Radius fracture			
subjects affected / exposed	2 / 244 (0.82%)	0 / 497 (0.00%)	2 / 751 (0.27%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Road traffic accident			
subjects affected / exposed	0 / 244 (0.00%)	1 / 497 (0.20%)	1 / 751 (0.13%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Sternal fracture			
subjects affected / exposed	0 / 244 (0.00%)	1 / 497 (0.20%)	1 / 751 (0.13%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wrist fracture			
subjects affected / exposed	0 / 244 (0.00%)	1 / 497 (0.20%)	1 / 751 (0.13%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Accidental overdose			

subjects affected / exposed	1 / 244 (0.41%)	0 / 497 (0.00%)	1 / 751 (0.13%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 1
Concussion			
subjects affected / exposed	0 / 244 (0.00%)	1 / 497 (0.20%)	0 / 751 (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
Contusion			
subjects affected / exposed	0 / 244 (0.00%)	1 / 497 (0.20%)	0 / 751 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Delayed recovery from anaesthesia			
subjects affected / exposed	1 / 244 (0.41%)	0 / 497 (0.00%)	1 / 751 (0.13%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Femoral neck fracture			
subjects affected / exposed	0 / 244 (0.00%)	1 / 497 (0.20%)	1 / 751 (0.13%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Femur fracture			
subjects affected / exposed	0 / 244 (0.00%)	0 / 497 (0.00%)	1 / 751 (0.13%)
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 / 244 (0.00%)	1 / 497 (0.20%)	0 / 751 (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 / 244 (0.00%)	0 / 497 (0.00%)	1 / 751 (0.13%)
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 / 244 (0.00%)	1 / 497 (0.20%)	0 / 751 (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
Nail avulsion			
subjects affected / exposed	0 / 244 (0.00%)	1 / 497 (0.20%)	0 / 751 (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
Overdose			
subjects affected / exposed	1 / 244 (0.41%)	0 / 497 (0.00%)	1 / 751 (0.13%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Post procedural complication			
subjects affected / exposed	1 / 244 (0.41%)	0 / 497 (0.00%)	1 / 751 (0.13%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rib fracture			
subjects affected / exposed	0 / 244 (0.00%)	0 / 497 (0.00%)	1 / 751 (0.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal column injury			
subjects affected / exposed	0 / 244 (0.00%)	0 / 497 (0.00%)	1 / 751 (0.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal fracture			
subjects affected / exposed	0 / 244 (0.00%)	0 / 497 (0.00%)	1 / 751 (0.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tendon injury			
subjects affected / exposed	0 / 244 (0.00%)	1 / 497 (0.20%)	0 / 751 (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
Tibia fracture			

subjects affected / exposed	0 / 244 (0.00%)	1 / 497 (0.20%)	0 / 751 (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 limb fracture			
subjects affected / exposed	0 / 244 (0.00%)	1 / 497 (0.20%)	0 / 751 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Congenital, familial and genetic disorders			
Factor VII deficiency			
subjects affected / exposed	0 / 244 (0.00%)	0 / 497 (0.00%)	1 / 751 (0.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Myocardial infarction			
subjects affected / exposed	2 / 244 (0.82%)	1 / 497 (0.20%)	2 / 751 (0.27%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pericarditis			
subjects affected / exposed	0 / 244 (0.00%)	1 / 497 (0.20%)	1 / 751 (0.13%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute myocardial infarction			
subjects affected / exposed	0 / 244 (0.00%)	0 / 497 (0.00%)	1 / 751 (0.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Angina pectoris			
subjects affected / exposed	0 / 244 (0.00%)	1 / 497 (0.20%)	0 / 751 (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
Atrioventricular block complete			
subjects affected / exposed	1 / 244 (0.41%)	0 / 497 (0.00%)	1 / 751 (0.13%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Bradycardia			
subjects affected / exposed	0 / 244 (0.00%)	0 / 497 (0.00%)	1 / 751 (0.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac arrest			
subjects affected / exposed	1 / 244 (0.41%)	0 / 497 (0.00%)	1 / 751 (0.13%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure congestive			
subjects affected / exposed	0 / 244 (0.00%)	1 / 497 (0.20%)	0 / 751 (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
Pleuropericarditis			
subjects affected / exposed	0 / 244 (0.00%)	1 / 497 (0.20%)	0 / 751 (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
Sinoatrial block			
subjects affected / exposed	0 / 244 (0.00%)	1 / 497 (0.20%)	0 / 751 (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
Supraventricular tachycardia			
subjects affected / exposed	0 / 244 (0.00%)	0 / 497 (0.00%)	1 / 751 (0.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tachycardia			
subjects affected / exposed	0 / 244 (0.00%)	1 / 497 (0.20%)	0 / 751 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 244 (0.00%)	2 / 497 (0.40%)	4 / 751 (0.53%)
occurrences causally related to treatment / all	0 / 0	0 / 2	1 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transient ischaemic attack			

subjects affected / exposed	3 / 244 (1.23%)	0 / 497 (0.00%)	6 / 751 (0.80%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 6
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebrovascular accident			
subjects affected / exposed	1 / 244 (0.41%)	0 / 497 (0.00%)	4 / 751 (0.53%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 4
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 1
Migraine			
subjects affected / exposed	0 / 244 (0.00%)	2 / 497 (0.40%)	2 / 751 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
subjects affected / exposed	0 / 244 (0.00%)	3 / 497 (0.60%)	1 / 751 (0.13%)
occurrences causally related to treatment / all	0 / 0	1 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Convulsion			
subjects affected / exposed	0 / 244 (0.00%)	2 / 497 (0.40%)	1 / 751 (0.13%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dizziness			
subjects affected / exposed	0 / 244 (0.00%)	2 / 497 (0.40%)	1 / 751 (0.13%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoaesthesia			
subjects affected / exposed	0 / 244 (0.00%)	3 / 497 (0.60%)	0 / 751 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dysarthria			
subjects affected / exposed	0 / 244 (0.00%)	2 / 497 (0.40%)	0 / 751 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Grand mal convulsion			

subjects affected / exposed	1 / 244 (0.41%)	0 / 497 (0.00%)	2 / 751 (0.27%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Monoparesis			
subjects affected / exposed	0 / 244 (0.00%)	1 / 497 (0.20%)	1 / 751 (0.13%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Altered state of consciousness			
subjects affected / exposed	1 / 244 (0.41%)	0 / 497 (0.00%)	1 / 751 (0.13%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebral haemorrhage			
subjects affected / exposed	0 / 244 (0.00%)	0 / 497 (0.00%)	1 / 751 (0.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebrospinal fluid leakage			
subjects affected / exposed	1 / 244 (0.41%)	0 / 497 (0.00%)	1 / 751 (0.13%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebrovascular disorder			
subjects affected / exposed	0 / 244 (0.00%)	1 / 497 (0.20%)	0 / 751 (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
Epilepsy			
subjects affected / exposed	0 / 244 (0.00%)	0 / 497 (0.00%)	1 / 751 (0.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemorrhage intracranial			
subjects affected / exposed	0 / 244 (0.00%)	1 / 497 (0.20%)	0 / 751 (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
Hemiparesis			

subjects affected / exposed	0 / 244 (0.00%)	0 / 497 (0.00%)	1 / 751 (0.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ischaemic stroke			
subjects affected / exposed	0 / 244 (0.00%)	1 / 497 (0.20%)	0 / 751 (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
Lumbar radiculopathy			
subjects affected / exposed	0 / 244 (0.00%)	1 / 497 (0.20%)	0 / 751 (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
Lupus encephalitis			
subjects affected / exposed	1 / 244 (0.41%)	0 / 497 (0.00%)	1 / 751 (0.13%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Memory impairment			
subjects affected / exposed	0 / 244 (0.00%)	0 / 497 (0.00%)	1 / 751 (0.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Motor dysfunction			
subjects affected / exposed	0 / 244 (0.00%)	0 / 497 (0.00%)	1 / 751 (0.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myasthenia gravis			
subjects affected / exposed	1 / 244 (0.41%)	0 / 497 (0.00%)	1 / 751 (0.13%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neuropsychiatric lupus			
subjects affected / exposed	0 / 244 (0.00%)	1 / 497 (0.20%)	0 / 751 (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
Optic neuritis			

subjects affected / exposed	1 / 244 (0.41%)	0 / 497 (0.00%)	1 / 751 (0.13%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Polyneuropathy			
subjects affected / exposed	0 / 244 (0.00%)	0 / 497 (0.00%)	1 / 751 (0.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Radiculitis brachial			
subjects affected / exposed	0 / 244 (0.00%)	1 / 497 (0.20%)	0 / 751 (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
Radiculopathy			
subjects affected / exposed	0 / 244 (0.00%)	0 / 497 (0.00%)	1 / 751 (0.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Seizure anoxic			
subjects affected / exposed	1 / 244 (0.41%)	0 / 497 (0.00%)	1 / 751 (0.13%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sinus headache			
subjects affected / exposed	1 / 244 (0.41%)	0 / 497 (0.00%)	1 / 751 (0.13%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thecal sac compression			
subjects affected / exposed	0 / 244 (0.00%)	0 / 497 (0.00%)	1 / 751 (0.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thoracic outlet syndrome			
subjects affected / exposed	0 / 244 (0.00%)	0 / 497 (0.00%)	1 / 751 (0.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transverse sinus thrombosis			

subjects affected / exposed	0 / 244 (0.00%)	0 / 497 (0.00%)	1 / 751 (0.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
VIIth nerve paralysis			
subjects affected / exposed	1 / 244 (0.41%)	0 / 497 (0.00%)	1 / 751 (0.13%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 244 (0.41%)	2 / 497 (0.40%)	2 / 751 (0.27%)
occurrences causally related to treatment / all	0 / 1	1 / 2	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Leukopenia			
subjects affected / exposed	0 / 244 (0.00%)	1 / 497 (0.20%)	2 / 751 (0.27%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutropenia			
subjects affected / exposed	0 / 244 (0.00%)	2 / 497 (0.40%)	1 / 751 (0.13%)
occurrences causally related to treatment / all	0 / 0	2 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombocytopenia			
subjects affected / exposed	0 / 244 (0.00%)	1 / 497 (0.20%)	2 / 751 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eosinophilia			
subjects affected / exposed	0 / 244 (0.00%)	1 / 497 (0.20%)	0 / 751 (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
Haemorrhagic diathesis			
subjects affected / exposed	0 / 244 (0.00%)	1 / 497 (0.20%)	0 / 751 (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
Lymphadenopathy			

subjects affected / exposed	0 / 244 (0.00%)	1 / 497 (0.20%)	0 / 751 (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
Pancytopenia			
subjects affected / exposed	0 / 244 (0.00%)	1 / 497 (0.20%)	0 / 751 (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
Splenic cyst			
subjects affected / exposed	1 / 244 (0.41%)	0 / 497 (0.00%)	1 / 751 (0.13%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 244 (0.00%)	1 / 497 (0.20%)	0 / 751 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Cataract			
subjects affected / exposed	1 / 244 (0.41%)	0 / 497 (0.00%)	2 / 751 (0.27%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Amaurosis fugax			
subjects affected / exposed	1 / 244 (0.41%)	0 / 497 (0.00%)	1 / 751 (0.13%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Necrotising retinitis			
subjects affected / exposed	0 / 244 (0.00%)	0 / 497 (0.00%)	1 / 751 (0.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Panophthalmitis			
subjects affected / exposed	0 / 244 (0.00%)	1 / 497 (0.20%)	0 / 751 (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
Retinal disorder			

subjects affected / exposed	0 / 244 (0.00%)	0 / 497 (0.00%)	1 / 751 (0.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	1 / 244 (0.41%)	3 / 497 (0.60%)	4 / 751 (0.53%)
occurrences causally related to treatment / all	0 / 2	1 / 3	1 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
subjects affected / exposed	0 / 244 (0.00%)	3 / 497 (0.60%)	3 / 751 (0.40%)
occurrences causally related to treatment / all	0 / 0	1 / 3	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain			
subjects affected / exposed	1 / 244 (0.41%)	3 / 497 (0.60%)	2 / 751 (0.27%)
occurrences causally related to treatment / all	1 / 1	1 / 3	1 / 2
deaths causally related to treatment / all	1 / 1	0 / 0	1 / 1
Nausea			
subjects affected / exposed	2 / 244 (0.82%)	1 / 497 (0.20%)	3 / 751 (0.40%)
occurrences causally related to treatment / all	1 / 3	1 / 1	1 / 4
deaths causally related to treatment / all	1 / 1	0 / 0	1 / 1
Pancreatitis			
subjects affected / exposed	0 / 244 (0.00%)	3 / 497 (0.60%)	1 / 751 (0.13%)
occurrences causally related to treatment / all	0 / 0	1 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastritis			
subjects affected / exposed	1 / 244 (0.41%)	1 / 497 (0.20%)	2 / 751 (0.27%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain upper			
subjects affected / exposed	1 / 244 (0.41%)	1 / 497 (0.20%)	1 / 751 (0.13%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dysphagia			

subjects affected / exposed	1 / 244 (0.41%)	1 / 497 (0.20%)	1 / 751 (0.13%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis acute			
subjects affected / exposed	0 / 244 (0.00%)	1 / 497 (0.20%)	1 / 751 (0.13%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anal fissure			
subjects affected / exposed	0 / 244 (0.00%)	1 / 497 (0.20%)	0 / 751 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colitis			
subjects affected / exposed	0 / 244 (0.00%)	1 / 497 (0.20%)	0 / 751 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colitis ischaemic			
subjects affected / exposed	0 / 244 (0.00%)	1 / 497 (0.20%)	0 / 751 (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
Constipation			
subjects affected / exposed	0 / 244 (0.00%)	0 / 497 (0.00%)	1 / 751 (0.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Crohn's disease			
subjects affected / exposed	0 / 244 (0.00%)	1 / 497 (0.20%)	0 / 751 (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
Eosinophilic colitis			
subjects affected / exposed	0 / 244 (0.00%)	1 / 497 (0.20%)	0 / 751 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastritis haemorrhagic			

subjects affected / exposed	1 / 244 (0.41%)	0 / 497 (0.00%)	1 / 751 (0.13%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal haemorrhage			
subjects affected / exposed	0 / 244 (0.00%)	1 / 497 (0.20%)	0 / 751 (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
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 244 (0.00%)	0 / 497 (0.00%)	1 / 751 (0.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hiatus hernia			
subjects affected / exposed	0 / 244 (0.00%)	0 / 497 (0.00%)	1 / 751 (0.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Impaired gastric emptying			
subjects affected / exposed	0 / 244 (0.00%)	1 / 497 (0.20%)	0 / 751 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Inflammatory bowel disease			
subjects affected / exposed	0 / 244 (0.00%)	1 / 497 (0.20%)	0 / 751 (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
Intestinal obstruction			
subjects affected / exposed	1 / 244 (0.41%)	0 / 497 (0.00%)	1 / 751 (0.13%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oedematous pancreatitis			
subjects affected / exposed	0 / 244 (0.00%)	0 / 497 (0.00%)	1 / 751 (0.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oesophageal disorder			

subjects affected / exposed	0 / 244 (0.00%)	1 / 497 (0.20%)	0 / 751 (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
Oesophageal motility disorder			
subjects affected / exposed	0 / 244 (0.00%)	0 / 497 (0.00%)	1 / 751 (0.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oesophageal spasm			
subjects affected / exposed	0 / 244 (0.00%)	1 / 497 (0.20%)	0 / 751 (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
Peptic ulcer			
subjects affected / exposed	0 / 244 (0.00%)	0 / 497 (0.00%)	1 / 751 (0.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peritoneal haemorrhage			
subjects affected / exposed	1 / 244 (0.41%)	0 / 497 (0.00%)	1 / 751 (0.13%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Salivary gland calculus			
subjects affected / exposed	0 / 244 (0.00%)	1 / 497 (0.20%)	0 / 751 (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
Subileus			
subjects affected / exposed	0 / 244 (0.00%)	1 / 497 (0.20%)	0 / 751 (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			
Skin ulcer			
subjects affected / exposed	1 / 244 (0.41%)	1 / 497 (0.20%)	2 / 751 (0.27%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cutaneous vasculitis			

subjects affected / exposed	1 / 244 (0.41%)	1 / 497 (0.20%)	1 / 751 (0.13%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blister			
subjects affected / exposed	0 / 244 (0.00%)	1 / 497 (0.20%)	0 / 751 (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 cutaneous lupus erythematosus			
subjects affected / exposed	0 / 244 (0.00%)	1 / 497 (0.20%)	0 / 751 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pruritus generalised			
subjects affected / exposed	0 / 244 (0.00%)	0 / 497 (0.00%)	1 / 751 (0.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Systemic lupus erythematosus rash			
subjects affected / exposed	0 / 244 (0.00%)	0 / 497 (0.00%)	1 / 751 (0.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urticaria			
subjects affected / exposed	0 / 244 (0.00%)	0 / 497 (0.00%)	1 / 751 (0.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Lupus nephritis			
subjects affected / exposed	2 / 244 (0.82%)	3 / 497 (0.60%)	3 / 751 (0.40%)
occurrences causally related to treatment / all	0 / 2	1 / 3	1 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Proteinuria			
subjects affected / exposed	0 / 244 (0.00%)	2 / 497 (0.40%)	2 / 751 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal failure acute			

subjects affected / exposed	0 / 244 (0.00%)	1 / 497 (0.20%)	2 / 751 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nephrolithiasis			
subjects affected / exposed	2 / 244 (0.82%)	0 / 497 (0.00%)	2 / 751 (0.27%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Glomerulonephritis			
subjects affected / exposed	0 / 244 (0.00%)	1 / 497 (0.20%)	0 / 751 (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
Glomerulonephritis membranoproliferative			
subjects affected / exposed	1 / 244 (0.41%)	0 / 497 (0.00%)	1 / 751 (0.13%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Kidney fibrosis			
subjects affected / exposed	0 / 244 (0.00%)	1 / 497 (0.20%)	0 / 751 (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
Nephritis			
subjects affected / exposed	0 / 244 (0.00%)	1 / 497 (0.20%)	0 / 751 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal colic			
subjects affected / exposed	0 / 244 (0.00%)	0 / 497 (0.00%)	1 / 751 (0.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Stress urinary incontinence			
subjects affected / exposed	1 / 244 (0.41%)	0 / 497 (0.00%)	1 / 751 (0.13%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endocrine disorders			
Adrenal insufficiency			

subjects affected / exposed	0 / 244 (0.00%)	1 / 497 (0.20%)	0 / 751 (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
Toxic nodular goitre			
subjects affected / exposed	1 / 244 (0.41%)	0 / 497 (0.00%)	1 / 751 (0.13%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Troponin increased			
subjects affected / exposed	0 / 244 (0.00%)	1 / 497 (0.20%)	0 / 751 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Systemic lupus erythematosus			
subjects affected / exposed	7 / 244 (2.87%)	13 / 497 (2.62%)	19 / 751 (2.53%)
occurrences causally related to treatment / all	0 / 7	2 / 15	1 / 19
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteoarthritis			
subjects affected / exposed	1 / 244 (0.41%)	2 / 497 (0.40%)	3 / 751 (0.40%)
occurrences causally related to treatment / all	0 / 1	0 / 4	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arthralgia			
subjects affected / exposed	1 / 244 (0.41%)	2 / 497 (0.40%)	2 / 751 (0.27%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arthritis			
subjects affected / exposed	0 / 244 (0.00%)	1 / 497 (0.20%)	3 / 751 (0.40%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteonecrosis			
subjects affected / exposed	2 / 244 (0.82%)	0 / 497 (0.00%)	3 / 751 (0.40%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Back pain			

subjects affected / exposed	1 / 244 (0.41%)	0 / 497 (0.00%)	2 / 751 (0.27%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bursitis			
subjects affected / exposed	0 / 244 (0.00%)	0 / 497 (0.00%)	2 / 751 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Foot deformity			
subjects affected / exposed	0 / 244 (0.00%)	1 / 497 (0.20%)	1 / 751 (0.13%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intervertebral disc disorder			
subjects affected / exposed	0 / 244 (0.00%)	2 / 497 (0.40%)	0 / 751 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intervertebral disc protrusion			
subjects affected / exposed	1 / 244 (0.41%)	0 / 497 (0.00%)	2 / 751 (0.27%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chondromalacia			
subjects affected / exposed	1 / 244 (0.41%)	0 / 497 (0.00%)	1 / 751 (0.13%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Enthesopathy			
subjects affected / exposed	0 / 244 (0.00%)	1 / 497 (0.20%)	0 / 751 (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
Fasciitis			
subjects affected / exposed	0 / 244 (0.00%)	0 / 497 (0.00%)	1 / 751 (0.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Muscular weakness			

subjects affected / exposed	0 / 244 (0.00%)	1 / 497 (0.20%)	0 / 751 (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
Myalgia			
subjects affected / exposed	0 / 244 (0.00%)	0 / 497 (0.00%)	1 / 751 (0.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteoporotic fracture			
subjects affected / exposed	0 / 244 (0.00%)	0 / 497 (0.00%)	1 / 751 (0.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pain in extremity			
subjects affected / exposed	1 / 244 (0.41%)	0 / 497 (0.00%)	1 / 751 (0.13%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Patellofemoral pain syndrome			
subjects affected / exposed	1 / 244 (0.41%)	0 / 497 (0.00%)	1 / 751 (0.13%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Periarthritis			
subjects affected / exposed	0 / 244 (0.00%)	1 / 497 (0.20%)	0 / 751 (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
Rotator cuff syndrome			
subjects affected / exposed	1 / 244 (0.41%)	0 / 497 (0.00%)	1 / 751 (0.13%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SLE arthritis			
subjects affected / exposed	1 / 244 (0.41%)	0 / 497 (0.00%)	1 / 751 (0.13%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Soft tissue necrosis			

subjects affected / exposed	0 / 244 (0.00%)	1 / 497 (0.20%)	0 / 751 (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
Spinal osteoarthritis			
subjects affected / exposed	0 / 244 (0.00%)	1 / 497 (0.20%)	0 / 751 (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
Spondylolisthesis			
subjects affected / exposed	0 / 244 (0.00%)	0 / 497 (0.00%)	1 / 751 (0.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Synovial cyst			
subjects affected / exposed	1 / 244 (0.41%)	0 / 497 (0.00%)	1 / 751 (0.13%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tenosynovitis stenosans			
subjects affected / exposed	1 / 244 (0.41%)	0 / 497 (0.00%)	1 / 751 (0.13%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neuroendocrine carcinoma of the skin			
subjects affected / exposed	0 / 244 (0.00%)	1 / 497 (0.20%)	0 / 751 (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
Infections and infestations			
Pneumonia			
subjects affected / exposed	6 / 244 (2.46%)	7 / 497 (1.41%)	15 / 751 (2.00%)
occurrences causally related to treatment / all	1 / 6	0 / 7	7 / 16
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Sepsis			
subjects affected / exposed	3 / 244 (1.23%)	3 / 497 (0.60%)	7 / 751 (0.93%)
occurrences causally related to treatment / all	2 / 4	0 / 3	4 / 8
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Cellulitis			

subjects affected / exposed	1 / 244 (0.41%)	4 / 497 (0.80%)	4 / 751 (0.53%)
occurrences causally related to treatment / all	0 / 1	0 / 4	0 / 6
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	2 / 244 (0.82%)	3 / 497 (0.60%)	4 / 751 (0.53%)
occurrences causally related to treatment / all	0 / 2	1 / 3	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arthritis bacterial			
subjects affected / exposed	1 / 244 (0.41%)	2 / 497 (0.40%)	1 / 751 (0.13%)
occurrences causally related to treatment / all	1 / 1	1 / 3	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diverticulitis			
subjects affected / exposed	1 / 244 (0.41%)	1 / 497 (0.20%)	2 / 751 (0.27%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis salmonella			
subjects affected / exposed	1 / 244 (0.41%)	1 / 497 (0.20%)	2 / 751 (0.27%)
occurrences causally related to treatment / all	1 / 1	1 / 1	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Influenza			
subjects affected / exposed	2 / 244 (0.82%)	0 / 497 (0.00%)	3 / 751 (0.40%)
occurrences causally related to treatment / all	1 / 2	0 / 0	1 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis			
subjects affected / exposed	1 / 244 (0.41%)	0 / 497 (0.00%)	3 / 751 (0.40%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	0 / 244 (0.00%)	1 / 497 (0.20%)	2 / 751 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchitis			

subjects affected / exposed	1 / 244 (0.41%)	1 / 497 (0.20%)	1 / 751 (0.13%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Clostridium difficile colitis			
subjects affected / exposed	0 / 244 (0.00%)	2 / 497 (0.40%)	0 / 751 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Clostridium difficile infection			
subjects affected / exposed	1 / 244 (0.41%)	1 / 497 (0.20%)	1 / 751 (0.13%)
occurrences causally related to treatment / all	1 / 1	0 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Meningitis viral			
subjects affected / exposed	1 / 244 (0.41%)	1 / 497 (0.20%)	1 / 751 (0.13%)
occurrences causally related to treatment / all	1 / 1	0 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subcutaneous abscess			
subjects affected / exposed	0 / 244 (0.00%)	2 / 497 (0.40%)	0 / 751 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper respiratory tract infection			
subjects affected / exposed	0 / 244 (0.00%)	0 / 497 (0.00%)	2 / 751 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abscess			
subjects affected / exposed	0 / 244 (0.00%)	1 / 497 (0.20%)	0 / 751 (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
Abscess limb			
subjects affected / exposed	0 / 244 (0.00%)	0 / 497 (0.00%)	1 / 751 (0.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anal abscess			

subjects affected / exposed	0 / 244 (0.00%)	1 / 497 (0.20%)	0 / 751 (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
Appendicitis			
subjects affected / exposed	1 / 244 (0.41%)	0 / 497 (0.00%)	1 / 751 (0.13%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchopneumonia			
subjects affected / exposed	0 / 244 (0.00%)	0 / 497 (0.00%)	1 / 751 (0.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cystitis			
subjects affected / exposed	0 / 244 (0.00%)	1 / 497 (0.20%)	0 / 751 (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
Cytomegalovirus chorioretinitis			
subjects affected / exposed	0 / 244 (0.00%)	0 / 497 (0.00%)	1 / 751 (0.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cytomegalovirus infection			
subjects affected / exposed	0 / 244 (0.00%)	1 / 497 (0.20%)	0 / 751 (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
Endocarditis			
subjects affected / exposed	0 / 244 (0.00%)	1 / 497 (0.20%)	0 / 751 (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
Epstein-Barr virus infection			
subjects affected / exposed	1 / 244 (0.41%)	0 / 497 (0.00%)	1 / 751 (0.13%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Escherichia bacteraemia			

subjects affected / exposed	0 / 244 (0.00%)	0 / 497 (0.00%)	1 / 751 (0.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Escherichia sepsis			
subjects affected / exposed	0 / 244 (0.00%)	1 / 497 (0.20%)	0 / 751 (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
Gangrene			
subjects affected / exposed	0 / 244 (0.00%)	1 / 497 (0.20%)	0 / 751 (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
H1N1 influenza			
subjects affected / exposed	0 / 244 (0.00%)	0 / 497 (0.00%)	1 / 751 (0.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haematoma infection			
subjects affected / exposed	0 / 244 (0.00%)	0 / 497 (0.00%)	1 / 751 (0.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatitis B			
subjects affected / exposed	1 / 244 (0.41%)	0 / 497 (0.00%)	1 / 751 (0.13%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Herpes zoster			
subjects affected / exposed	0 / 244 (0.00%)	0 / 497 (0.00%)	1 / 751 (0.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lobar pneumonia			
subjects affected / exposed	1 / 244 (0.41%)	0 / 497 (0.00%)	1 / 751 (0.13%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lower respiratory tract infection			

subjects affected / exposed	1 / 244 (0.41%)	0 / 497 (0.00%)	1 / 751 (0.13%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Meningitis			
subjects affected / exposed	0 / 244 (0.00%)	1 / 497 (0.20%)	0 / 751 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Meningitis aseptic			
subjects affected / exposed	0 / 244 (0.00%)	1 / 497 (0.20%)	0 / 751 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Meningitis bacterial			
subjects affected / exposed	0 / 244 (0.00%)	0 / 497 (0.00%)	1 / 751 (0.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pelvic inflammatory disease			
subjects affected / exposed	0 / 244 (0.00%)	0 / 497 (0.00%)	1 / 751 (0.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Perineal abscess			
subjects affected / exposed	0 / 244 (0.00%)	1 / 497 (0.20%)	0 / 751 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia bacterial			
subjects affected / exposed	0 / 244 (0.00%)	0 / 497 (0.00%)	1 / 751 (0.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia legionella			
subjects affected / exposed	1 / 244 (0.41%)	0 / 497 (0.00%)	1 / 751 (0.13%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia streptococcal			

subjects affected / exposed	1 / 244 (0.41%)	0 / 497 (0.00%)	1 / 751 (0.13%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis acute			
subjects affected / exposed	1 / 244 (0.41%)	0 / 497 (0.00%)	1 / 751 (0.13%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory tract infection			
subjects affected / exposed	0 / 244 (0.00%)	1 / 497 (0.20%)	0 / 751 (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
Salpingitis			
subjects affected / exposed	1 / 244 (0.41%)	0 / 497 (0.00%)	1 / 751 (0.13%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tooth abscess			
subjects affected / exposed	1 / 244 (0.41%)	0 / 497 (0.00%)	1 / 751 (0.13%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 244 (0.00%)	1 / 497 (0.20%)	2 / 751 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diabetes mellitus inadequate control			
subjects affected / exposed	1 / 244 (0.41%)	0 / 497 (0.00%)	1 / 751 (0.13%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoglycaemia			
subjects affected / exposed	0 / 244 (0.00%)	1 / 497 (0.20%)	0 / 751 (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
Hypokalaemia			

subjects affected / exposed	0 / 244 (0.00%)	0 / 497 (0.00%)	1 / 751 (0.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyponatraemia			
subjects affected / exposed	0 / 244 (0.00%)	1 / 497 (0.20%)	0 / 751 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	All subjects	Enrollment Cohort 2 Epratuzumab 600 mg per week	
Total subjects affected by serious adverse events			
subjects affected / exposed	304 / 1248 (24.36%)	104 / 507 (20.51%)	
number of deaths (all causes)	9	1	
number of deaths resulting from adverse events	1	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Squamous cell carcinoma of skin			
subjects affected / exposed	3 / 1248 (0.24%)	2 / 507 (0.39%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Uterine leiomyoma			
subjects affected / exposed	2 / 1248 (0.16%)	0 / 507 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Adenocarcinoma of colon			
subjects affected / exposed	1 / 1248 (0.08%)	1 / 507 (0.20%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Adenocarcinoma pancreas			
subjects affected / exposed	1 / 1248 (0.08%)	1 / 507 (0.20%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 1	
Bladder cancer			

subjects affected / exposed	1 / 1248 (0.08%)	0 / 507 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bowen's disease			
subjects affected / exposed	1 / 1248 (0.08%)	1 / 507 (0.20%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Breast cancer stage I			
subjects affected / exposed	1 / 1248 (0.08%)	0 / 507 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cervix carcinoma stage 0			
subjects affected / exposed	1 / 1248 (0.08%)	0 / 507 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric cancer			
subjects affected / exposed	1 / 1248 (0.08%)	0 / 507 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myeloproliferative disorder			
subjects affected / exposed	1 / 1248 (0.08%)	1 / 507 (0.20%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ovarian adenoma			
subjects affected / exposed	1 / 1248 (0.08%)	0 / 507 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Squamous cell carcinoma			
subjects affected / exposed	1 / 1248 (0.08%)	1 / 507 (0.20%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Deep vein thrombosis			

subjects affected / exposed	5 / 1248 (0.40%)	2 / 507 (0.39%)	
occurrences causally related to treatment / all	1 / 5	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertension			
subjects affected / exposed	3 / 1248 (0.24%)	0 / 507 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Venous thrombosis			
subjects affected / exposed	2 / 1248 (0.16%)	0 / 507 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arterial occlusive disease			
subjects affected / exposed	1 / 1248 (0.08%)	1 / 507 (0.20%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertensive crisis			
subjects affected / exposed	1 / 1248 (0.08%)	0 / 507 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Orthostatic hypotension			
subjects affected / exposed	1 / 1248 (0.08%)	1 / 507 (0.20%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Temporal arteritis			
subjects affected / exposed	1 / 1248 (0.08%)	0 / 507 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Venous thrombosis limb			
subjects affected / exposed	1 / 1248 (0.08%)	1 / 507 (0.20%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Surgical and medical procedures			
Abortion induced			

subjects affected / exposed	1 / 1248 (0.08%)	1 / 507 (0.20%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystectomy			
subjects affected / exposed	1 / 1248 (0.08%)	0 / 507 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hip arthroplasty			
subjects affected / exposed	1 / 1248 (0.08%)	0 / 507 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Joint arthroplasty			
subjects affected / exposed	1 / 1248 (0.08%)	0 / 507 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Polymedication			
subjects affected / exposed	1 / 1248 (0.08%)	0 / 507 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Shoulder operation			
subjects affected / exposed	1 / 1248 (0.08%)	0 / 507 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pregnancy, puerperium and perinatal conditions			
Cerebral infarction			
subjects affected / exposed	1 / 1248 (0.08%)	0 / 507 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abortion spontaneous			
subjects affected / exposed	4 / 1248 (0.32%)	1 / 507 (0.20%)	
occurrences causally related to treatment / all	0 / 4	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Foetal death			

subjects affected / exposed	1 / 1248 (0.08%)	0 / 507 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Premature delivery			
subjects affected / exposed	1 / 1248 (0.08%)	0 / 507 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	13 / 1248 (1.04%)	8 / 507 (1.58%)	
occurrences causally related to treatment / all	1 / 14	1 / 9	
deaths causally related to treatment / all	0 / 0	0 / 0	
Non-cardiac chest pain			
subjects affected / exposed	4 / 1248 (0.32%)	0 / 507 (0.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			
subjects affected / exposed	4 / 1248 (0.32%)	1 / 507 (0.20%)	
occurrences causally related to treatment / all	1 / 4	0 / 1	
deaths causally related to treatment / all	1 / 1	0 / 0	
Asthenia			
subjects affected / exposed	2 / 1248 (0.16%)	0 / 507 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Drug interaction			
subjects affected / exposed	1 / 1248 (0.08%)	0 / 507 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Drug intolerance			
subjects affected / exposed	1 / 1248 (0.08%)	1 / 507 (0.20%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperthermia			

subjects affected / exposed	1 / 1248 (0.08%)	1 / 507 (0.20%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Impaired healing			
subjects affected / exposed	1 / 1248 (0.08%)	1 / 507 (0.20%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Local swelling			
subjects affected / exposed	1 / 1248 (0.08%)	0 / 507 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oedema peripheral			
subjects affected / exposed	1 / 1248 (0.08%)	1 / 507 (0.20%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Serositis			
subjects affected / exposed	1 / 1248 (0.08%)	0 / 507 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Drug hypersensitivity			
subjects affected / exposed	2 / 1248 (0.16%)	1 / 507 (0.20%)	
occurrences causally related to treatment / all	1 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anaphylactic reaction			
subjects affected / exposed	1 / 1248 (0.08%)	0 / 507 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Ovarian cyst			
subjects affected / exposed	4 / 1248 (0.32%)	2 / 507 (0.39%)	
occurrences causally related to treatment / all	0 / 4	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	

Endometriosis			
subjects affected / exposed	3 / 1248 (0.24%)	0 / 507 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cervical dysplasia			
subjects affected / exposed	2 / 1248 (0.16%)	0 / 507 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Menorrhagia			
subjects affected / exposed	2 / 1248 (0.16%)	1 / 507 (0.20%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Uterine polyp			
subjects affected / exposed	2 / 1248 (0.16%)	1 / 507 (0.20%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Adenomyosis			
subjects affected / exposed	1 / 1248 (0.08%)	0 / 507 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endometrial hyperplasia			
subjects affected / exposed	1 / 1248 (0.08%)	0 / 507 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pelvic pain			
subjects affected / exposed	1 / 1248 (0.08%)	0 / 507 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Uterine haemorrhage			
subjects affected / exposed	1 / 1248 (0.08%)	0 / 507 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vaginal prolapse			

subjects affected / exposed	1 / 1248 (0.08%)	0 / 507 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	5 / 1248 (0.40%)	1 / 507 (0.20%)	
occurrences causally related to treatment / all	0 / 5	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			
subjects affected / exposed	3 / 1248 (0.24%)	1 / 507 (0.20%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cough			
subjects affected / exposed	2 / 1248 (0.16%)	2 / 507 (0.39%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleurisy			
subjects affected / exposed	2 / 1248 (0.16%)	0 / 507 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute pulmonary oedema			
subjects affected / exposed	1 / 1248 (0.08%)	0 / 507 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute respiratory failure			
subjects affected / exposed	1 / 1248 (0.08%)	0 / 507 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Asthma			
subjects affected / exposed	1 / 1248 (0.08%)	1 / 507 (0.20%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic obstructive pulmonary disease			

subjects affected / exposed	1 / 1248 (0.08%)	0 / 507 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic respiratory failure			
subjects affected / exposed	1 / 1248 (0.08%)	0 / 507 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspnoea exertional			
subjects affected / exposed	1 / 1248 (0.08%)	1 / 507 (0.20%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Emphysema			
subjects affected / exposed	1 / 1248 (0.08%)	1 / 507 (0.20%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Laryngeal stenosis			
subjects affected / exposed	1 / 1248 (0.08%)	0 / 507 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleural effusion			
subjects affected / exposed	1 / 1248 (0.08%)	1 / 507 (0.20%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary arterial hypertension			
subjects affected / exposed	1 / 1248 (0.08%)	0 / 507 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary hypertension			
subjects affected / exposed	1 / 1248 (0.08%)	0 / 507 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory failure			

subjects affected / exposed	1 / 1248 (0.08%)	0 / 507 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Wheezing			
subjects affected / exposed	1 / 1248 (0.08%)	0 / 507 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Depression			
subjects affected / exposed	4 / 1248 (0.32%)	2 / 507 (0.39%)	
occurrences causally related to treatment / all	0 / 4	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Suicide attempt			
subjects affected / exposed	4 / 1248 (0.32%)	2 / 507 (0.39%)	
occurrences causally related to treatment / all	0 / 4	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychotic disorder			
subjects affected / exposed	2 / 1248 (0.16%)	0 / 507 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Suicidal ideation			
subjects affected / exposed	1 / 1248 (0.08%)	0 / 507 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	4 / 1248 (0.32%)	0 / 507 (0.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis			
subjects affected / exposed	3 / 1248 (0.24%)	3 / 507 (0.59%)	
occurrences causally related to treatment / all	0 / 3	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bile duct stone			

subjects affected / exposed	2 / 1248 (0.16%)	2 / 507 (0.39%)	
occurrences causally related to treatment / all	0 / 3	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholangitis			
subjects affected / exposed	1 / 1248 (0.08%)	1 / 507 (0.20%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis acute			
subjects affected / exposed	1 / 1248 (0.08%)	0 / 507 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholelithiasis migration			
subjects affected / exposed	1 / 1248 (0.08%)	0 / 507 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic steatosis			
subjects affected / exposed	1 / 1248 (0.08%)	1 / 507 (0.20%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Biopsy liver			
subjects affected / exposed	1 / 1248 (0.08%)	0 / 507 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood cortisol decreased			
subjects affected / exposed	1 / 1248 (0.08%)	1 / 507 (0.20%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Electrocardiogram QT prolonged			
subjects affected / exposed	1 / 1248 (0.08%)	1 / 507 (0.20%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transaminases increased			

subjects affected / exposed	1 / 1248 (0.08%)	0 / 507 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Meniscus injury			
subjects affected / exposed	3 / 1248 (0.24%)	0 / 507 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tendon rupture			
subjects affected / exposed	3 / 1248 (0.24%)	2 / 507 (0.39%)	
occurrences causally related to treatment / all	0 / 4	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ankle fracture			
subjects affected / exposed	2 / 1248 (0.16%)	1 / 507 (0.20%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fibula fracture			
subjects affected / exposed	2 / 1248 (0.16%)	1 / 507 (0.20%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Head injury			
subjects affected / exposed	2 / 1248 (0.16%)	1 / 507 (0.20%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Joint dislocation			
subjects affected / exposed	2 / 1248 (0.16%)	1 / 507 (0.20%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Laceration			
subjects affected / exposed	2 / 1248 (0.16%)	0 / 507 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Radius fracture			

subjects affected / exposed	2 / 1248 (0.16%)	0 / 507 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Road traffic accident			
subjects affected / exposed	2 / 1248 (0.16%)	1 / 507 (0.20%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Sternal fracture			
subjects affected / exposed	2 / 1248 (0.16%)	1 / 507 (0.20%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wrist fracture			
subjects affected / exposed	2 / 1248 (0.16%)	1 / 507 (0.20%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Accidental overdose			
subjects affected / exposed	1 / 1248 (0.08%)	0 / 507 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Concussion			
subjects affected / exposed	1 / 1248 (0.08%)	0 / 507 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Contusion			
subjects affected / exposed	1 / 1248 (0.08%)	0 / 507 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Delayed recovery from anaesthesia			
subjects affected / exposed	1 / 1248 (0.08%)	0 / 507 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femoral neck fracture			

subjects affected / exposed	1 / 1248 (0.08%)	0 / 507 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femur fracture			
subjects affected / exposed	1 / 1248 (0.08%)	1 / 507 (0.20%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hip fracture			
subjects affected / exposed	1 / 1248 (0.08%)	0 / 507 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ligament rupture			
subjects affected / exposed	1 / 1248 (0.08%)	1 / 507 (0.20%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lumbar vertebral fracture			
subjects affected / exposed	1 / 1248 (0.08%)	0 / 507 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nail avulsion			
subjects affected / exposed	1 / 1248 (0.08%)	0 / 507 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Overdose			
subjects affected / exposed	1 / 1248 (0.08%)	0 / 507 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post procedural complication			
subjects affected / exposed	1 / 1248 (0.08%)	0 / 507 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rib fracture			

subjects affected / exposed	1 / 1248 (0.08%)	1 / 507 (0.20%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal column injury			
subjects affected / exposed	1 / 1248 (0.08%)	1 / 507 (0.20%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal fracture			
subjects affected / exposed	1 / 1248 (0.08%)	1 / 507 (0.20%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tendon injury			
subjects affected / exposed	1 / 1248 (0.08%)	0 / 507 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tibia fracture			
subjects affected / exposed	1 / 1248 (0.08%)	0 / 507 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper limb fracture			
subjects affected / exposed	1 / 1248 (0.08%)	0 / 507 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Congenital, familial and genetic disorders			
Factor VII deficiency			
subjects affected / exposed	1 / 1248 (0.08%)	1 / 507 (0.20%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Myocardial infarction			
subjects affected / exposed	3 / 1248 (0.24%)	0 / 507 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Pericarditis			
subjects affected / exposed	2 / 1248 (0.16%)	1 / 507 (0.20%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute myocardial infarction			
subjects affected / exposed	1 / 1248 (0.08%)	1 / 507 (0.20%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angina pectoris			
subjects affected / exposed	1 / 1248 (0.08%)	0 / 507 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrioventricular block complete			
subjects affected / exposed	1 / 1248 (0.08%)	0 / 507 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bradycardia			
subjects affected / exposed	1 / 1248 (0.08%)	1 / 507 (0.20%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac arrest			
subjects affected / exposed	1 / 1248 (0.08%)	0 / 507 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure congestive			
subjects affected / exposed	1 / 1248 (0.08%)	0 / 507 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleuropericarditis			
subjects affected / exposed	1 / 1248 (0.08%)	0 / 507 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sinoatrial block			

subjects affected / exposed	1 / 1248 (0.08%)	0 / 507 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Supraventricular tachycardia			
subjects affected / exposed	1 / 1248 (0.08%)	1 / 507 (0.20%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tachycardia			
subjects affected / exposed	1 / 1248 (0.08%)	0 / 507 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Headache			
subjects affected / exposed	6 / 1248 (0.48%)	4 / 507 (0.79%)	
occurrences causally related to treatment / all	1 / 7	1 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transient ischaemic attack			
subjects affected / exposed	6 / 1248 (0.48%)	3 / 507 (0.59%)	
occurrences causally related to treatment / all	0 / 6	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebrovascular accident			
subjects affected / exposed	4 / 1248 (0.32%)	3 / 507 (0.59%)	
occurrences causally related to treatment / all	0 / 4	0 / 3	
deaths causally related to treatment / all	0 / 1	0 / 0	
Migraine			
subjects affected / exposed	4 / 1248 (0.32%)	2 / 507 (0.39%)	
occurrences causally related to treatment / all	0 / 4	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syncope			
subjects affected / exposed	4 / 1248 (0.32%)	1 / 507 (0.20%)	
occurrences causally related to treatment / all	1 / 4	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Convulsion			

subjects affected / exposed	3 / 1248 (0.24%)	1 / 507 (0.20%)	
occurrences causally related to treatment / all	0 / 4	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dizziness			
subjects affected / exposed	3 / 1248 (0.24%)	1 / 507 (0.20%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoaesthesia			
subjects affected / exposed	3 / 1248 (0.24%)	0 / 507 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dysarthria			
subjects affected / exposed	2 / 1248 (0.16%)	0 / 507 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Grand mal convulsion			
subjects affected / exposed	2 / 1248 (0.16%)	1 / 507 (0.20%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Monoparesis			
subjects affected / exposed	2 / 1248 (0.16%)	1 / 507 (0.20%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Altered state of consciousness			
subjects affected / exposed	1 / 1248 (0.08%)	0 / 507 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebral haemorrhage			
subjects affected / exposed	1 / 1248 (0.08%)	1 / 507 (0.20%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebrospinal fluid leakage			

subjects affected / exposed	1 / 1248 (0.08%)	0 / 507 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebrovascular disorder			
subjects affected / exposed	1 / 1248 (0.08%)	0 / 507 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epilepsy			
subjects affected / exposed	1 / 1248 (0.08%)	1 / 507 (0.20%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhage intracranial			
subjects affected / exposed	1 / 1248 (0.08%)	0 / 507 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hemiparesis			
subjects affected / exposed	1 / 1248 (0.08%)	1 / 507 (0.20%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ischaemic stroke			
subjects affected / exposed	1 / 1248 (0.08%)	0 / 507 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lumbar radiculopathy			
subjects affected / exposed	1 / 1248 (0.08%)	0 / 507 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lupus encephalitis			
subjects affected / exposed	1 / 1248 (0.08%)	0 / 507 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Memory impairment			

subjects affected / exposed	1 / 1248 (0.08%)	1 / 507 (0.20%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Motor dysfunction			
subjects affected / exposed	1 / 1248 (0.08%)	1 / 507 (0.20%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myasthenia gravis			
subjects affected / exposed	1 / 1248 (0.08%)	0 / 507 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neuropsychiatric lupus			
subjects affected / exposed	1 / 1248 (0.08%)	0 / 507 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Optic neuritis			
subjects affected / exposed	1 / 1248 (0.08%)	0 / 507 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Polyneuropathy			
subjects affected / exposed	1 / 1248 (0.08%)	1 / 507 (0.20%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Radiculitis brachial			
subjects affected / exposed	1 / 1248 (0.08%)	0 / 507 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Radiculopathy			
subjects affected / exposed	1 / 1248 (0.08%)	1 / 507 (0.20%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Seizure anoxic			

subjects affected / exposed	1 / 1248 (0.08%)	0 / 507 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sinus headache			
subjects affected / exposed	1 / 1248 (0.08%)	0 / 507 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thecal sac compression			
subjects affected / exposed	1 / 1248 (0.08%)	1 / 507 (0.20%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thoracic outlet syndrome			
subjects affected / exposed	1 / 1248 (0.08%)	1 / 507 (0.20%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transverse sinus thrombosis			
subjects affected / exposed	1 / 1248 (0.08%)	1 / 507 (0.20%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
VIIth nerve paralysis			
subjects affected / exposed	1 / 1248 (0.08%)	0 / 507 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	4 / 1248 (0.32%)	1 / 507 (0.20%)	
occurrences causally related to treatment / all	1 / 5	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Leukopenia			
subjects affected / exposed	3 / 1248 (0.24%)	2 / 507 (0.39%)	
occurrences causally related to treatment / all	1 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutropenia			

subjects affected / exposed	3 / 1248 (0.24%)	1 / 507 (0.20%)	
occurrences causally related to treatment / all	2 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombocytopenia			
subjects affected / exposed	3 / 1248 (0.24%)	2 / 507 (0.39%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eosinophilia			
subjects affected / exposed	1 / 1248 (0.08%)	0 / 507 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhagic diathesis			
subjects affected / exposed	1 / 1248 (0.08%)	0 / 507 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lymphadenopathy			
subjects affected / exposed	1 / 1248 (0.08%)	0 / 507 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancytopenia			
subjects affected / exposed	1 / 1248 (0.08%)	0 / 507 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Splenic cyst			
subjects affected / exposed	1 / 1248 (0.08%)	0 / 507 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	1 / 1248 (0.08%)	0 / 507 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			

Cataract			
subjects affected / exposed	2 / 1248 (0.16%)	1 / 507 (0.20%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Amaurosis fugax			
subjects affected / exposed	1 / 1248 (0.08%)	0 / 507 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Necrotising retinitis			
subjects affected / exposed	1 / 1248 (0.08%)	1 / 507 (0.20%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Panophthalmitis			
subjects affected / exposed	1 / 1248 (0.08%)	0 / 507 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Retinal disorder			
subjects affected / exposed	1 / 1248 (0.08%)	1 / 507 (0.20%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	7 / 1248 (0.56%)	3 / 507 (0.59%)	
occurrences causally related to treatment / all	2 / 8	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	6 / 1248 (0.48%)	3 / 507 (0.59%)	
occurrences causally related to treatment / all	1 / 6	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain			
subjects affected / exposed	5 / 1248 (0.40%)	1 / 507 (0.20%)	
occurrences causally related to treatment / all	2 / 5	0 / 1	
deaths causally related to treatment / all	1 / 1	0 / 0	
Nausea			

subjects affected / exposed	4 / 1248 (0.32%)	1 / 507 (0.20%)	
occurrences causally related to treatment / all	2 / 5	0 / 1	
deaths causally related to treatment / all	1 / 1	0 / 0	
Pancreatitis			
subjects affected / exposed	4 / 1248 (0.32%)	1 / 507 (0.20%)	
occurrences causally related to treatment / all	1 / 4	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastritis			
subjects affected / exposed	3 / 1248 (0.24%)	1 / 507 (0.20%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain upper			
subjects affected / exposed	2 / 1248 (0.16%)	0 / 507 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dysphagia			
subjects affected / exposed	2 / 1248 (0.16%)	0 / 507 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis acute			
subjects affected / exposed	2 / 1248 (0.16%)	1 / 507 (0.20%)	
occurrences causally related to treatment / all	0 / 4	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anal fissure			
subjects affected / exposed	1 / 1248 (0.08%)	0 / 507 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colitis			
subjects affected / exposed	1 / 1248 (0.08%)	0 / 507 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colitis ischaemic			

subjects affected / exposed	1 / 1248 (0.08%)	0 / 507 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Constipation			
subjects affected / exposed	1 / 1248 (0.08%)	1 / 507 (0.20%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Crohn's disease			
subjects affected / exposed	1 / 1248 (0.08%)	0 / 507 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eosinophilic colitis			
subjects affected / exposed	1 / 1248 (0.08%)	0 / 507 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastritis haemorrhagic			
subjects affected / exposed	1 / 1248 (0.08%)	0 / 507 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal haemorrhage			
subjects affected / exposed	1 / 1248 (0.08%)	0 / 507 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 1248 (0.08%)	1 / 507 (0.20%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hiatus hernia			
subjects affected / exposed	1 / 1248 (0.08%)	1 / 507 (0.20%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Impaired gastric emptying			

subjects affected / exposed	1 / 1248 (0.08%)	0 / 507 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Inflammatory bowel disease			
subjects affected / exposed	1 / 1248 (0.08%)	0 / 507 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal obstruction			
subjects affected / exposed	1 / 1248 (0.08%)	0 / 507 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oedematous pancreatitis			
subjects affected / exposed	1 / 1248 (0.08%)	1 / 507 (0.20%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophageal disorder			
subjects affected / exposed	1 / 1248 (0.08%)	0 / 507 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophageal motility disorder			
subjects affected / exposed	1 / 1248 (0.08%)	1 / 507 (0.20%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophageal spasm			
subjects affected / exposed	1 / 1248 (0.08%)	0 / 507 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peptic ulcer			
subjects affected / exposed	1 / 1248 (0.08%)	1 / 507 (0.20%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peritoneal haemorrhage			

subjects affected / exposed	1 / 1248 (0.08%)	0 / 507 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Salivary gland calculus			
subjects affected / exposed	1 / 1248 (0.08%)	0 / 507 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subileus			
subjects affected / exposed	1 / 1248 (0.08%)	0 / 507 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Skin ulcer			
subjects affected / exposed	3 / 1248 (0.24%)	1 / 507 (0.20%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cutaneous vasculitis			
subjects affected / exposed	2 / 1248 (0.16%)	0 / 507 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blister			
subjects affected / exposed	1 / 1248 (0.08%)	0 / 507 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic cutaneous lupus erythematosus			
subjects affected / exposed	1 / 1248 (0.08%)	0 / 507 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pruritus generalised			
subjects affected / exposed	1 / 1248 (0.08%)	1 / 507 (0.20%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Systemic lupus erythematosus rash			

subjects affected / exposed	1 / 1248 (0.08%)	1 / 507 (0.20%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urticaria			
subjects affected / exposed	1 / 1248 (0.08%)	1 / 507 (0.20%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Lupus nephritis			
subjects affected / exposed	6 / 1248 (0.48%)	1 / 507 (0.20%)	
occurrences causally related to treatment / all	2 / 6	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Proteinuria			
subjects affected / exposed	4 / 1248 (0.32%)	2 / 507 (0.39%)	
occurrences causally related to treatment / all	0 / 4	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal failure acute			
subjects affected / exposed	3 / 1248 (0.24%)	2 / 507 (0.39%)	
occurrences causally related to treatment / all	0 / 4	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nephrolithiasis			
subjects affected / exposed	2 / 1248 (0.16%)	0 / 507 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Glomerulonephritis			
subjects affected / exposed	1 / 1248 (0.08%)	0 / 507 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Glomerulonephritis membranoproliferative			
subjects affected / exposed	1 / 1248 (0.08%)	0 / 507 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Kidney fibrosis			

subjects affected / exposed	1 / 1248 (0.08%)	0 / 507 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nephritis			
subjects affected / exposed	1 / 1248 (0.08%)	0 / 507 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal colic			
subjects affected / exposed	1 / 1248 (0.08%)	1 / 507 (0.20%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Stress urinary incontinence			
subjects affected / exposed	1 / 1248 (0.08%)	0 / 507 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocrine disorders			
Adrenal insufficiency			
subjects affected / exposed	1 / 1248 (0.08%)	0 / 507 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Toxic nodular goitre			
subjects affected / exposed	1 / 1248 (0.08%)	0 / 507 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Troponin increased			
subjects affected / exposed	1 / 1248 (0.08%)	0 / 507 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Systemic lupus erythematosus			
subjects affected / exposed	32 / 1248 (2.56%)	12 / 507 (2.37%)	
occurrences causally related to treatment / all	3 / 34	1 / 12	
deaths causally related to treatment / all	0 / 0	0 / 0	

Osteoarthritis			
subjects affected / exposed	5 / 1248 (0.40%)	2 / 507 (0.39%)	
occurrences causally related to treatment / all	0 / 7	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arthralgia			
subjects affected / exposed	4 / 1248 (0.32%)	1 / 507 (0.20%)	
occurrences causally related to treatment / all	0 / 4	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arthritis			
subjects affected / exposed	4 / 1248 (0.32%)	3 / 507 (0.59%)	
occurrences causally related to treatment / all	0 / 4	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteonecrosis			
subjects affected / exposed	3 / 1248 (0.24%)	1 / 507 (0.20%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Back pain			
subjects affected / exposed	2 / 1248 (0.16%)	1 / 507 (0.20%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bursitis			
subjects affected / exposed	2 / 1248 (0.16%)	2 / 507 (0.39%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Foot deformity			
subjects affected / exposed	2 / 1248 (0.16%)	1 / 507 (0.20%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intervertebral disc disorder			
subjects affected / exposed	2 / 1248 (0.16%)	0 / 507 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intervertebral disc protrusion			

subjects affected / exposed	2 / 1248 (0.16%)	1 / 507 (0.20%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chondromalacia			
subjects affected / exposed	1 / 1248 (0.08%)	0 / 507 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enthesopathy			
subjects affected / exposed	1 / 1248 (0.08%)	0 / 507 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fasciitis			
subjects affected / exposed	1 / 1248 (0.08%)	1 / 507 (0.20%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Muscular weakness			
subjects affected / exposed	1 / 1248 (0.08%)	0 / 507 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myalgia			
subjects affected / exposed	1 / 1248 (0.08%)	1 / 507 (0.20%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteoporotic fracture			
subjects affected / exposed	1 / 1248 (0.08%)	1 / 507 (0.20%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pain in extremity			
subjects affected / exposed	1 / 1248 (0.08%)	0 / 507 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Patellofemoral pain syndrome			

subjects affected / exposed	1 / 1248 (0.08%)	0 / 507 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Periarthritis			
subjects affected / exposed	1 / 1248 (0.08%)	0 / 507 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rotator cuff syndrome			
subjects affected / exposed	1 / 1248 (0.08%)	0 / 507 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
SLE arthritis			
subjects affected / exposed	1 / 1248 (0.08%)	0 / 507 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Soft tissue necrosis			
subjects affected / exposed	1 / 1248 (0.08%)	0 / 507 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal osteoarthritis			
subjects affected / exposed	1 / 1248 (0.08%)	0 / 507 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spondylolisthesis			
subjects affected / exposed	1 / 1248 (0.08%)	1 / 507 (0.20%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Synovial cyst			
subjects affected / exposed	1 / 1248 (0.08%)	0 / 507 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tenosynovitis stenosans			

subjects affected / exposed	1 / 1248 (0.08%)	0 / 507 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neuroendocrine carcinoma of the skin			
subjects affected / exposed	1 / 1248 (0.08%)	0 / 507 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Pneumonia			
subjects affected / exposed	22 / 1248 (1.76%)	9 / 507 (1.78%)	
occurrences causally related to treatment / all	7 / 23	6 / 10	
deaths causally related to treatment / all	0 / 1	0 / 0	
Sepsis			
subjects affected / exposed	10 / 1248 (0.80%)	4 / 507 (0.79%)	
occurrences causally related to treatment / all	4 / 11	2 / 4	
deaths causally related to treatment / all	0 / 1	0 / 0	
Cellulitis			
subjects affected / exposed	8 / 1248 (0.64%)	3 / 507 (0.59%)	
occurrences causally related to treatment / all	0 / 10	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
subjects affected / exposed	7 / 1248 (0.56%)	2 / 507 (0.39%)	
occurrences causally related to treatment / all	1 / 7	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arthritis bacterial			
subjects affected / exposed	3 / 1248 (0.24%)	0 / 507 (0.00%)	
occurrences causally related to treatment / all	2 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticulitis			
subjects affected / exposed	3 / 1248 (0.24%)	1 / 507 (0.20%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis salmonella			

subjects affected / exposed	3 / 1248 (0.24%)	1 / 507 (0.20%)	
occurrences causally related to treatment / all	2 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Influenza			
subjects affected / exposed	3 / 1248 (0.24%)	1 / 507 (0.20%)	
occurrences causally related to treatment / all	1 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis			
subjects affected / exposed	3 / 1248 (0.24%)	2 / 507 (0.39%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	3 / 1248 (0.24%)	2 / 507 (0.39%)	
occurrences causally related to treatment / all	0 / 4	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis			
subjects affected / exposed	2 / 1248 (0.16%)	0 / 507 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clostridium difficile colitis			
subjects affected / exposed	2 / 1248 (0.16%)	0 / 507 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clostridium difficile infection			
subjects affected / exposed	2 / 1248 (0.16%)	0 / 507 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meningitis viral			
subjects affected / exposed	2 / 1248 (0.16%)	0 / 507 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subcutaneous abscess			

subjects affected / exposed	2 / 1248 (0.16%)	0 / 507 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper respiratory tract infection			
subjects affected / exposed	2 / 1248 (0.16%)	2 / 507 (0.39%)	
occurrences causally related to treatment / all	2 / 2	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abscess			
subjects affected / exposed	1 / 1248 (0.08%)	0 / 507 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abscess limb			
subjects affected / exposed	1 / 1248 (0.08%)	1 / 507 (0.20%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anal abscess			
subjects affected / exposed	1 / 1248 (0.08%)	0 / 507 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Appendicitis			
subjects affected / exposed	1 / 1248 (0.08%)	0 / 507 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchopneumonia			
subjects affected / exposed	1 / 1248 (0.08%)	1 / 507 (0.20%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cystitis			
subjects affected / exposed	1 / 1248 (0.08%)	0 / 507 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cytomegalovirus chorioretinitis			

subjects affected / exposed	1 / 1248 (0.08%)	1 / 507 (0.20%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cytomegalovirus infection			
subjects affected / exposed	1 / 1248 (0.08%)	0 / 507 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocarditis			
subjects affected / exposed	1 / 1248 (0.08%)	0 / 507 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epstein-Barr virus infection			
subjects affected / exposed	1 / 1248 (0.08%)	0 / 507 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Escherichia bacteraemia			
subjects affected / exposed	1 / 1248 (0.08%)	1 / 507 (0.20%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Escherichia sepsis			
subjects affected / exposed	1 / 1248 (0.08%)	0 / 507 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gangrene			
subjects affected / exposed	1 / 1248 (0.08%)	0 / 507 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
H1N1 influenza			
subjects affected / exposed	1 / 1248 (0.08%)	1 / 507 (0.20%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematoma infection			

subjects affected / exposed	1 / 1248 (0.08%)	1 / 507 (0.20%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatitis B			
subjects affected / exposed	1 / 1248 (0.08%)	0 / 507 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Herpes zoster			
subjects affected / exposed	1 / 1248 (0.08%)	1 / 507 (0.20%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lobar pneumonia			
subjects affected / exposed	1 / 1248 (0.08%)	0 / 507 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower respiratory tract infection			
subjects affected / exposed	1 / 1248 (0.08%)	0 / 507 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meningitis			
subjects affected / exposed	1 / 1248 (0.08%)	0 / 507 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meningitis aseptic			
subjects affected / exposed	1 / 1248 (0.08%)	0 / 507 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meningitis bacterial			
subjects affected / exposed	1 / 1248 (0.08%)	1 / 507 (0.20%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pelvic inflammatory disease			

subjects affected / exposed	1 / 1248 (0.08%)	1 / 507 (0.20%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Perineal abscess			
subjects affected / exposed	1 / 1248 (0.08%)	0 / 507 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia bacterial			
subjects affected / exposed	1 / 1248 (0.08%)	1 / 507 (0.20%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia legionella			
subjects affected / exposed	1 / 1248 (0.08%)	0 / 507 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia streptococcal			
subjects affected / exposed	1 / 1248 (0.08%)	0 / 507 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis acute			
subjects affected / exposed	1 / 1248 (0.08%)	0 / 507 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory tract infection			
subjects affected / exposed	1 / 1248 (0.08%)	0 / 507 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Salpingitis			
subjects affected / exposed	1 / 1248 (0.08%)	0 / 507 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tooth abscess			

subjects affected / exposed	1 / 1248 (0.08%)	0 / 507 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	3 / 1248 (0.24%)	2 / 507 (0.39%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetes mellitus inadequate control			
subjects affected / exposed	1 / 1248 (0.08%)	0 / 507 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoglycaemia			
subjects affected / exposed	1 / 1248 (0.08%)	0 / 507 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypokalaemia			
subjects affected / exposed	1 / 1248 (0.08%)	1 / 507 (0.20%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyponatraemia			
subjects affected / exposed	1 / 1248 (0.08%)	0 / 507 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Enrollment Cohort 1 Epratuzumab 600 mg per week	Enrollment Cohort 2 Epratuzumab 1200 mg Q2W	All Epratuzumab 600 mg per week
Total subjects affected by non-serious adverse events			
subjects affected / exposed	177 / 244 (72.54%)	296 / 497 (59.56%)	483 / 751 (64.31%)
Vascular disorders			
Hypertension			

subjects affected / exposed	17 / 244 (6.97%)	26 / 497 (5.23%)	43 / 751 (5.73%)
occurrences (all)	19	28	46
Nervous system disorders			
Headache			
subjects affected / exposed	46 / 244 (18.85%)	67 / 497 (13.48%)	103 / 751 (13.72%)
occurrences (all)	66	84	146
Dizziness			
subjects affected / exposed	20 / 244 (8.20%)	23 / 497 (4.63%)	43 / 751 (5.73%)
occurrences (all)	26	30	51
Hypoaesthesia			
subjects affected / exposed	13 / 244 (5.33%)	9 / 497 (1.81%)	25 / 751 (3.33%)
occurrences (all)	15	9	28
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	39 / 244 (15.98%)	59 / 497 (11.87%)	101 / 751 (13.45%)
occurrences (all)	80	86	159
Diarrhoea			
subjects affected / exposed	27 / 244 (11.07%)	47 / 497 (9.46%)	47 / 751 (6.26%)
occurrences (all)	41	58	61
Vomiting			
subjects affected / exposed	22 / 244 (9.02%)	32 / 497 (6.44%)	51 / 751 (6.79%)
occurrences (all)	45	43	83
Fatigue			
subjects affected / exposed	17 / 244 (6.97%)	19 / 497 (3.82%)	38 / 751 (5.06%)
occurrences (all)	24	22	46
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	21 / 244 (8.61%)	30 / 497 (6.04%)	53 / 751 (7.06%)
occurrences (all)	25	31	68
Oropharyngeal pain			
subjects affected / exposed	15 / 244 (6.15%)	9 / 497 (1.81%)	29 / 751 (3.86%)
occurrences (all)	24	11	40
Urticaria			
subjects affected / exposed	13 / 244 (5.33%)	7 / 497 (1.41%)	17 / 751 (2.26%)
occurrences (all)	20	7	24
Psychiatric disorders			

Depression			
subjects affected / exposed	16 / 244 (6.56%)	23 / 497 (4.63%)	31 / 751 (4.13%)
occurrences (all)	17	23	33
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	34 / 244 (13.93%)	31 / 497 (6.24%)	66 / 751 (8.79%)
occurrences (all)	47	32	79
Arthralgia			
subjects affected / exposed	24 / 244 (9.84%)	36 / 497 (7.24%)	54 / 751 (7.19%)
occurrences (all)	40	44	78
Systemic lupus erythematosus			
subjects affected / exposed	15 / 244 (6.15%)	18 / 497 (3.62%)	38 / 751 (5.06%)
occurrences (all)	19	26	49
Pain in extremity			
subjects affected / exposed	15 / 244 (6.15%)	15 / 497 (3.02%)	34 / 751 (4.53%)
occurrences (all)	21	17	42
Muscle spasms			
subjects affected / exposed	13 / 244 (5.33%)	18 / 497 (3.62%)	19 / 751 (2.53%)
occurrences (all)	14	20	21
Bursitis			
subjects affected / exposed	15 / 244 (6.15%)	9 / 497 (1.81%)	22 / 751 (2.93%)
occurrences (all)	24	11	31
Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	66 / 244 (27.05%)	76 / 497 (15.29%)	148 / 751 (19.71%)
occurrences (all)	140	126	260
Urinary tract infection			
subjects affected / exposed	56 / 244 (22.95%)	61 / 497 (12.27%)	118 / 751 (15.71%)
occurrences (all)	124	88	214
Nasopharyngitis			
subjects affected / exposed	38 / 244 (15.57%)	42 / 497 (8.45%)	83 / 751 (11.05%)
occurrences (all)	56	65	123
Bronchitis			
subjects affected / exposed	34 / 244 (13.93%)	35 / 497 (7.04%)	69 / 751 (9.19%)
occurrences (all)	38	38	79
Sinusitis			

subjects affected / exposed	25 / 244 (10.25%)	41 / 497 (8.25%)	63 / 751 (8.39%)
occurrences (all)	40	48	88
Influenza			
subjects affected / exposed	15 / 244 (6.15%)	22 / 497 (4.43%)	36 / 751 (4.79%)
occurrences (all)	16	24	39
Gastroenteritis			
subjects affected / exposed	14 / 244 (5.74%)	19 / 497 (3.82%)	31 / 751 (4.13%)
occurrences (all)	14	21	37
Conjunctivitis			
subjects affected / exposed	14 / 244 (5.74%)	15 / 497 (3.02%)	22 / 751 (2.93%)
occurrences (all)	16	17	24

Non-serious adverse events	All subjects	Enrollment Cohort 2 Epratuzumab 600 mg per week	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	779 / 1248 (62.42%)	306 / 507 (60.36%)	
Vascular disorders			
Hypertension			
subjects affected / exposed	69 / 1248 (5.53%)	26 / 507 (5.13%)	
occurrences (all)	74	27	
Nervous system disorders			
Headache			
subjects affected / exposed	170 / 1248 (13.62%)	57 / 507 (11.24%)	
occurrences (all)	230	80	
Dizziness			
subjects affected / exposed	66 / 1248 (5.29%)	23 / 507 (4.54%)	
occurrences (all)	81	25	
Hypoaesthesia			
subjects affected / exposed	34 / 1248 (2.72%)	12 / 507 (2.37%)	
occurrences (all)	37	13	
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	160 / 1248 (12.82%)	62 / 507 (12.23%)	
occurrences (all)	245	79	
Diarrhoea			

subjects affected / exposed	108 / 1248 (8.65%)	34 / 507 (6.71%)	
occurrences (all)	146	47	
Vomiting			
subjects affected / exposed	83 / 1248 (6.65%)	29 / 507 (5.72%)	
occurrences (all)	126	38	
Fatigue			
subjects affected / exposed	57 / 1248 (4.57%)	21 / 507 (4.14%)	
occurrences (all)	68	22	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	83 / 1248 (6.65%)	32 / 507 (6.31%)	
occurrences (all)	99	43	
Oropharyngeal pain			
subjects affected / exposed	38 / 1248 (3.04%)	14 / 507 (2.76%)	
occurrences (all)	51	16	
Urticaria			
subjects affected / exposed	24 / 1248 (1.92%)	4 / 507 (0.79%)	
occurrences (all)	31	4	
Psychiatric disorders			
Depression			
subjects affected / exposed	54 / 1248 (4.33%)	15 / 507 (2.96%)	
occurrences (all)	56	16	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	97 / 1248 (7.77%)	32 / 507 (6.31%)	
occurrences (all)	111	32	
Arthralgia			
subjects affected / exposed	90 / 1248 (7.21%)	30 / 507 (5.92%)	
occurrences (all)	122	38	
Systemic lupus erythematosus			
subjects affected / exposed	56 / 1248 (4.49%)	23 / 507 (4.54%)	
occurrences (all)	75	30	
Pain in extremity			
subjects affected / exposed	49 / 1248 (3.93%)	19 / 507 (3.75%)	
occurrences (all)	59	21	
Muscle spasms			

subjects affected / exposed	37 / 1248 (2.96%)	6 / 507 (1.18%)	
occurrences (all)	41	7	
Bursitis			
subjects affected / exposed	31 / 1248 (2.48%)	7 / 507 (1.38%)	
occurrences (all)	42	7	
Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	224 / 1248 (17.95%)	82 / 507 (16.17%)	
occurrences (all)	386	120	
Urinary tract infection			
subjects affected / exposed	179 / 1248 (14.34%)	62 / 507 (12.23%)	
occurrences (all)	302	90	
Nasopharyngitis			
subjects affected / exposed	125 / 1248 (10.02%)	45 / 507 (8.88%)	
occurrences (all)	188	67	
Bronchitis			
subjects affected / exposed	104 / 1248 (8.33%)	35 / 507 (6.90%)	
occurrences (all)	117	41	
Sinusitis			
subjects affected / exposed	104 / 1248 (8.33%)	38 / 507 (7.50%)	
occurrences (all)	136	48	
Influenza			
subjects affected / exposed	58 / 1248 (4.65%)	21 / 507 (4.14%)	
occurrences (all)	63	23	
Gastroenteritis			
subjects affected / exposed	50 / 1248 (4.01%)	17 / 507 (3.35%)	
occurrences (all)	58	23	
Conjunctivitis			
subjects affected / exposed	37 / 1248 (2.96%)	8 / 507 (1.58%)	
occurrences (all)	41	8	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
04 April 2011	The protocol was amended to allow subjects completing the Phase 2, Open-Label-Extension (OLE) studies, SL0006 and SL0008, to enroll in SL0012. In addition, a few clarifications, inconsistencies, and typographical errors were made/corrected within the protocol text.
03 February 2012	The protocol was amended for the following reasons: - To add an additional treatment arm of epratuzumab 1200mg every other week (QOW) to collect long-term safety data on this dose in a Phase 3 open-label study, in addition to safety data currently being collected in the Phase 3, placebo-controlled, double-blind studies (ie, in SL0009 and SL0010). - To update the statistical considerations (Section 14.2 and Section 14.8 of the protocol) in accordance with addition of the epratuzumab 1200mg QOW treatment arm. - To clarify the guidance for concomitant corticosteroid use in Section 7.8.1.1 of the protocol. The previous text allowed corticosteroid increases for up to 1 month. The revised text specified that corticosteroid increases were allowed for up to 30 consecutive days or up to a total of 30 days per study year. - To update criterion 4 of the primary efficacy variable in Section 4.1.1 of the protocol regarding concomitant corticosteroid use, so that it was consistent with the updated text in Section 7.8.1.1 of the protocol described above. The previous text allowed corticosteroid increases for up to 1 month. The revised text specified that corticosteroid increases were allowed for up to 30 consecutive days or up to a total of 30 days per study year. - To add an additional exploratory endpoint for assessment of flares. - To include a list of anticipated serious adverse events (SAEs) in compliance with the recent Food and Drug Administration (FDA) final rule on safety reporting requirements for studies conducted under an open Investigational New Drug Application (FDA, Guidance for Industry and Investigators, 2011). - To change the name and contact information of the Clinical Trial Biostatistician and Study Physician. In addition, a few clarifications, inconsistencies, and typographical errors were made/corrected within the protocol text.
25 March 2013	The protocol was amended for the following reasons: - To extend the study duration for an additional 2 years - To update study contact information - To update SAE reporting information - To update information pertaining to SL0006, SL0008, SL0009, and SL0010 Minor typographical errors were corrected throughout the protocol.

12 May 2014	The protocol was amended at the request of the German Regulatory Authority, Paul Ehrlich Institute to clarify details of the physical examination within the scope of the BILAG assessment, to introduce a list of adverse events (AEs) of special interest that were identified for epratuzumab, and to clarify further actions after identification of an AE of special interest. Additional changes to the protocol were as follows: - Updated study contact information and SAE reporting information - Revised the exploratory endpoints for assessment of flares - Added an additional safety variable (incidence of hospitalizations/emergency room [ER] visits) - Clarified in Exclusion criterion 10 that the laboratory results from SL0009 and SL0010 should not be older than 28 days - Updated the text in Section 7.2.1 of the protocol (Preparation and administration of epratuzumab and placebo) in order to clarify that it was recommended, but not mandatory, that subjects be premedicated before receiving an iv infusion. - Updated the text in Section 7.5 of the protocol (Handling and storage requirements) in order to clarify the process to follow in case of out-of-range temperatures. This was consistent with the description in the Pharmacy Manual. - Updated Table 7-1 of the protocol (Steroid conversion table) with additional corticosteroids to be consistent with the table in the current Statistical Analysis Plan (SAP). - Clarified that investigators may use results of procedures performed at the last visit in SL0009 or SL0010, if performed within 28 days (instead of 4 weeks) of Visit 1 in SL0012. - Modified text in Section 14.4 of the protocol (Safety analyses) to state that infection treatment-emergent adverse events (TEAEs) were to be identified by including all events in the coded system organ class (SOC) "Infections and infestations" rather than via a review of all AE terms prior to study unblinding, as originally planned. This was consistent with the current SAP.
11 May 2015	The protocol was amended to allow an extension of the study duration for potential additional 12-week treatment cycles beyond Week 192 until the approval of the marketing application for the indication of SLE by the FDA or European Medicines Agency (EMA). In addition, procedures if live vaccine was required were clarified and human anti-human antibody (HAHA) was changed to ADA throughout. The protocol amendment 5 has not been implemented due to the decision in September 2015 to terminate the SL0012 study early.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported