Clinical trial results:
A Phase 3, Multi-Center, Randomized, Double-Blind, Placebo-Controlled, 52-Week Study to Evaluate the Efficacy and Safety of Belimumab (HGS1006) Administered Subcutaneously (SC) to Subjects with Systemic Lupus Erythematosus (SLE)

Summary

EudraCT number	2011-003814-18
Trial protocol	DE HU AT CZ SE BE PT ES DK GB BG IT PL
Global end of trial date	01 October 2015

Results information

Result version number	v2 (current)
This version publication date	30 January 2017
First version publication date	20 May 2016
Version creation reason	• New data added to full data set End of study information added to the initial results.

Trial information

Trial identification

Sponsor protocol code	112341

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01484496
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	GlaxoSmithKline
Sponsor organisation address	980 Great West Road, Brentford, Middlesex, United Kingdom,
Public contact	GSK Response Center, GlaxoSmithKline, 1-866 4357343,
Scientific contact	GSK Response Center, GlaxoSmithKline, 1-866 4357343,

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	12 February 2016
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	01 October 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

- To evaluate the efficacy of belimumab administered SC in adult subjects with SLE.
- To evaluate the safety and tolerability of belimumab administered SC in adult subjects with SLE.

Protection of trial subjects:

Not applicable

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	16 November 2011
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Argentina: 20
Country: Number of subjects enrolled	Brazil: 77
Country: Number of subjects enrolled	Chile: 16
Country: Number of subjects enrolled	Colombia: 41
Country: Number of subjects enrolled	Croatia: 14
Country: Number of subjects enrolled	Japan: 30
Country: Number of subjects enrolled	Malaysia: 5
Country: Number of subjects enrolled	Mexico: 18
Country: Number of subjects enrolled	Philippines: 75
Country: Number of subjects enrolled	Romania: 29
Country: Number of subjects enrolled	Russian Federation: 19
Country: Number of subjects enrolled	Serbia: 23
Country: Number of subjects enrolled	Taiwan: 40
Country: Number of subjects enrolled	Thailand: 22
Country: Number of subjects enrolled	Ukraine: 27
Country: Number of subjects enrolled	United States: 237
Country: Number of subjects enrolled	Poland: 36
Country: Number of subjects enrolled	Portugal: 15
Country: Number of subjects enrolled	Spain: 4
Country: Number of subjects enrolled	Sweden: 2
Country: Number of subjects enrolled	United Kingdom: 6
Country: Number of subjects enrolled	Austria: 7

Country: Number of subjects enrolled	Belgium: 3
Country: Number of subjects enrolled	Bulgaria: 18
Country: Number of subjects enrolled	Czech Republic: 13
Country: Number of subjects enrolled	Denmark: 1
Country: Number of subjects enrolled	France: 7
Country: Number of subjects enrolled	Germany: 16
Country: Number of subjects enrolled	Hungary: 9
Country: Number of subjects enrolled	Italy: 6
Worldwide total number of subjects	836
EEA total number of subjects	186

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)	817
From 65 to 84 years	19
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants (par.) with active systemic lupus erythematosus (SLE) and who were on appropriate stable standard SLE therapy for a period of at least 30 days prior to Day 0 before entering the study were eligible for participation in the study.

Pre-assignment

Screening details:

A total of 1427 par. were screened, out of these 588 par. were screen failures and 839 par. were randomized, of which 836 par. received at least one dose of study treatment. Participants who successfully completed the initial 52-week Double-blind Phase had a choice to enter into a 6-month Open-label Extension Phase of this study.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo SC

Arm description:

Participants received placebo administered subcutaneously (SC) once weekly through 51 weeks of the treatment period. Participants continued with the stable standard therapy they were receiving during the Screening Period.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Placebo will be supplied as single-use prefilled syringes; Participants will be dosed with placebo on Day 0 and then weekly through 51 weeks of the treatment period.

Arm title	Belimumab 200 mg SC

Arm description:

Participants received belimumab 200 milligrams (mg) administered SC once weekly through 51 weeks of the treatment period. Participants continued with the stable standard therapy they were receiving during the Screening Period.

Arm type	Experimental
Investigational medicinal product name	Belimumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Belimumab 200 mg for SC injection will be supplied as single-use prefilled syringes; Participants will be dosed with study agent on Day 0 and then weekly through 51 weeks of the treatment period.

Number of subjects in period 1	Placebo SC	Belimumab 200 mg SC
Started	280	556
Completed	214	463
Not completed	66	93
Adverse event, serious fatal	2	2
Consent withdrawn by subject	15	12
Lack of Compliance	2	1
Physician decision	5	1
Unable to Visit Site	-	2
Adverse event, non-fatal	23	38
Treatment Failure	3	6
Lost to follow-up	2	6
Positive Pregnancy	1	6
Lack of efficacy	10	15
Protocol deviation	3	4

Period 2

Period 2 title	Open-Label Phase
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Open-Label - Placebo SC to Belimumab 200 mg SC

Arm description:

Participants received placebo administered subcutaneously (SC) once weekly through 51 weeks of the treatment period. Participants continued with the stable standard therapy they were receiving during the Screening Period. Participants who completed the Double-Blind phase with active SLE were assessed for eligibility to participate in a 6-month extension phase during which they received open label belimumab 200 mg SC weekly.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Placebo will be supplied as single-use prefilled syringes; Participants will be dosed with placebo on Day 0 and then weekly through 51 weeks of the treatment period plus another 6 months of open label belimumab 200 mg SC weekly.

Arm title	Open-Label - Belimumab 200 SC to Belimumab 200 mg SC

Arm description:

Participants received belimumab 200 milligrams (mg) administered SC once weekly through 51 weeks of the treatment period. Participants continued with the stable standard therapy they were receiving during the Screening Period. Participants who completed the Double-Blind phase with active SLE were assessed for eligibility to participate in a 6-month extension phase during which they received open label belimumab 200 mg SC weekly.

Arm type	Experimental
Investigational medicinal product name	Belimumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Belimumab 200 mg for SC injection will be supplied as single-use prefilled syringes; Participants will be dosed with study agent on Day 0 and then weekly through 51 weeks of the treatment period plus another 6 months of open label belimumab 200 mg SC weekly.

Number of subjects in period 2[1]	Open-Label - Placebo SC to Belimumab 200 mg SC	Open-Label - Belimumab 200 SC to Belimumab 200 mg SC
Started	206	456
Completed	191	434
Not completed	15	22
Adverse event, non-fatal	5	13
Other reason	9	6
Lack of efficacy	1	3

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.
Justification: A total of 1427 par. were screened, out of these 588 par. were screen failures and 839 par. were randomized, of which 836 par. received at least one dose of study treatment. Participants who successfully completed the initial 52-week Double-blind Phase had a choice to enter into a 6-month Open-label Extension Phase of this study.

Baseline characteristics

Reporting groups	
Reporting group title	Placebo SC
Reporting group description:	
Participants received placebo administered subcutaneously (SC) once weekly through 51 weeks of the treatment period. Participants continued with the stable standard therapy they were receiving during the Screening Period.	
Reporting group title	Belimumab 200 mg SC
Reporting group description:	
Participants received belimumab 200 milligrams (mg) administered SC once weekly through 51 weeks of the treatment period. Participants continued with the stable standard therapy they were receiving during the Screening Period.	

Reporting group values	Placebo SC	Belimumab 200 mg SC	Total
Number of subjects	280	556	836
Age categorical			
Units: Subjects			
Age continuous			
Units: years			
arithmetic mean	39.6	38.1	
standard deviation	± 12.61	± 12.1	-
Gender categorical			
Units: Subjects			
Female	268	521	789
Male	12	35	47
Race			
Units: Subjects			
White/Caucasian/European Heritage	160	326	486
Middle East/North African Heritage	6	10	16
Central Asian Heritage	0	2	2
East Asian Heritage	15	29	44
Japanese Heritage	16	13	29
South Asian Heritage	0	2	2
Southeast Asian Heritage	32	73	105
African American/African Heritage	30	56	86
American Indian or Alaska Native	21	43	64
Native Hawaiian or Other Pacific Islander	0	2	2

End points

End points reporting groups

Reporting group title	Placebo SC

Reporting group description:

Participants received placebo administered subcutaneously (SC) once weekly through 51 weeks of the treatment period. Participants continued with the stable standard therapy they were receiving during the Screening Period.

Reporting group title	Belimumab 200 mg SC

Reporting group description:

Participants received belimumab 200 milligrams (mg) administered SC once weekly through 51 weeks of the treatment period. Participants continued with the stable standard therapy they were receiving during the Screening Period.

Reporting group title	Open-Label - Placebo SC to Belimumab 200 mg SC

Reporting group description:

Participants received placebo administered subcutaneously (SC) once weekly through 51 weeks of the treatment period. Participants continued with the stable standard therapy they were receiving during the Screening Period. Participants who completed the Double-Blind phase with active SLE were assessed for eligibility to participate in a 6-month extension phase during which they received open label belimumab 200 mg SC weekly.

Reporting group title	Open-Label - Belimumab 200 SC to Belimumab 200 mg SC

Reporting group description:

Participants received belimumab 200 milligrams (mg) administered SC once weekly through 51 weeks of the treatment period. Participants continued with the stable standard therapy they were receiving during the Screening Period. Participants who completed the Double-Blind phase with active SLE were assessed for eligibility to participate in a 6-month extension phase during which they received open label belimumab 200 mg SC weekly.

Primary: Percentage of participants achieving a SRI response at Week 52

End point title	Percentage of participants achieving a SRI response at Week 52

End point description:

Systemic lupus erythematosus responder index (SRI) response is defined as >=4 point reduction from Baseline in safety of estrogen in lupus national assessment (SELENA) systemic lupus erythematosus disease activity index (SLEDAI) score, no worsening (increase of <0.30 points from Baseline) in physician's global assessment (PGA) and no new british isles lupus assessment group of SLE clinics (BILAG) A organ domain score or 2 new BILAG B organ domain scores compared with Baseline. Analysis was performed using a logistic regression model for the comparison between belimumab and placebo with covariates treatment group, Baseline SELENA SLEDAI score (<=9 vs. >=10), Baseline complement levels (low C3 and/or C4 vs. no low C3 or C4) and race (black vs. other). Intention-To-Treat (ITT) Population: comprised of all participants who were randomized and treated with at least one dose of study treatment.

End point type	Primary

End point timeframe:

Week 52

End point values	Placebo SC	Belimumab 200 mg SC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	279[1]	554[2]		
Units: Percentage of participants				
number (not applicable)	48.4	61.4		

Notes:

[1] - ITT population. Three par. did not have a Baseline PGA assessment; therefore, were not included.

[2] - ITT population. Three par. did not have a Baseline PGA assessment; therefore, were not included.

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	Placebo SC v Belimumab 200 mg SC
Number of subjects included in analysis	833
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0006
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.68
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.25
upper limit	2.25

Secondary: Time to first severe flare (as measured by the modified SLE Flare Index)

End point title	Time to first severe flare (as measured by the modified SLE Flare Index)

End point description:

Time to first severe SLE flare is defined as the number of days from treatment start date until the participant met an event (event date – treatment start date +1). Analyses of severe SLE flare was performed on modified SELENA SLEDAI SLE flare index that excludes severe flares that were triggered only by an increase in SELENA SLEDAI score to >12 (since this may only represent a modest increase in disease activity). Only post-Baseline severe flares were considered. Analysis was performed using a Cox proportional hazards model adjusting for Baseline SELENA SLEDAI score (<=9 vs. >=10), Baseline complement levels, (low C3 and/or C4 vs. no low C3 or C4) and race (black vs. other).

End point type	Secondary

End point timeframe:

Baseline to Week 52

End point values	Placebo SC	Belimumab 200 mg SC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	280[3]	556[4]		
Units: Percentage of par. with a severe flare				
number (not applicable)	18.2	10.6		

Notes:
[3] - ITT Population
[4] - ITT Population

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	Belimumab 200 mg SC v Placebo SC
Number of subjects included in analysis	836
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0004
Method	Cox proportional hazards model
Parameter estimate	Hazard ratio (HR)
Point estimate	0.51
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.35
upper limit	0.74

Secondary: Percentage of participants whose average prednisone dose had been reduced by >=25% from Baseline to <=7.5 mg/day during weeks 40 through 52 in participants receiving greater than 7.5 mg/day at Baseline

End point title	Percentage of participants whose average prednisone dose had been reduced by >=25% from Baseline to <=7.5 mg/day during weeks 40 through 52 in participants receiving greater than 7.5 mg/day at Baseline

End point description:

For the analysis of steroid use, all steroid dosages were converted to a prednisone equivalent in milligrams. The average daily prednisone dose was calculated taking into account all steroids taken intravenously, intramuscularly, SC, intradermally and orally for both SLE and non-SLE reasons. A responder was defined as having a prednisone reduction by >=25% from Baseline to <=7.5 mg/day during Weeks 40 through 52. At Baseline, the average daily prednisone dose was the sum of all prednisone doses over 7 consecutive days up to, but not including Day 0, divided by 7. For this analysis, the average prednisone dose was the total prednisone dose during weeks 40 through 52 divided by the number of days during Weeks 40 through 52. Analysis was performed using a logistic regression model with covariates treatment group, Baseline prednisone dose, Baseline SELENA SLEDAI score, (<=9 vs. >=10), Baseline complement levels (low C3 and/or C4 vs. no low C3 or C4) and race (black vs. other).

End point type	Secondary

End point timeframe:

Baseline, Weeks 40 through Week 52

End point values	Placebo SC	Belimumab 200 mg SC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	168[5]	335[6]		
Units: Percentage of participants				
number (not applicable)	11.9	18.2		

Notes:

[5] - ITT population. Only participants with Baseline prednisone dose >7.5 mg/day were included.

[6] - ITT population. Only participants with Baseline prednisone dose >7.5 mg/day were included.

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	Placebo SC v Belimumab 200 mg SC
Number of subjects included in analysis	503
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0732
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.65
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.95
upper limit	2.84

Adverse events

Adverse events information

Timeframe for reporting adverse events:

SAEs and non-serious AEs were collected from the start of study agent administration through 51 weeks of the treatment period (or Exit visit for those par. who withdrew during double-blind treatment) plus another 6 months for open-label treatment period.

Adverse event reporting additional description:

Serious adverse events (SAEs) and non-serious AEs were collected in participants of ITT population, comprised of participants who were randomized and treated with at least one dose of study treatment.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	17.0

Reporting groups

Reporting group title	Placebo SC

Reporting group description:

Participants received placebo administered SC once weekly through 51 weeks of the treatment period. Participants continued with the stable standard therapy they were receiving during the Screening Period.

Reporting group title	Belimumab 200 mg SC

Reporting group description:

Participants received belimumab 200 mg administered SC once weekly through 51 weeks of the treatment period. Participants continued with the stable standard therapy they were receiving during the Screening Period.

Reporting group title	Open-Label - Placebo SC to Belimumab 200 mg SC

Reporting group description:

Participants received placebo administered subcutaneously (SC) once weekly through 51 weeks of the treatment period. Participants continued with the stable standard therapy they were receiving during the Screening Period. Participants who completed the Double-Blind phase with active SLE were assessed for eligibility to participate in a 6-month extension phase during which they received open label belimumab 200 mg SC weekly.

Reporting group title	Open-Label - Belimumab 200 SC to Belimumab 200 mg SC

Reporting group description:

Participants received belimumab 200 milligrams (mg) administered SC once weekly through 51 weeks of the treatment period. Participants continued with the stable standard therapy they were receiving during the Screening Period. Participants who completed the Double-Blind phase with active SLE were assessed for eligibility to participate in a 6-month extension phase during which they received open label belimumab 200 mg SC weekly.

Serious adverse events	Placebo SC	Belimumab 200 mg SC	Open-Label - Placebo SC to Belimumab 200 mg SC
Total subjects affected by serious adverse events			
subjects affected / exposed	44 / 280 (15.71%)	60 / 556 (10.79%)	14 / 206 (6.80%)
number of deaths (all causes)	2	3	1
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Breast cancer			

subjects affected / exposed	1 / 280 (0.36%)	0 / 556 (0.00%)	0 / 206 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endometrial cancer			
subjects affected / exposed	0 / 280 (0.00%)	1 / 556 (0.18%)	0 / 206 (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
Intraductal proliferative breast lesion			
subjects affected / exposed	0 / 280 (0.00%)	1 / 556 (0.18%)	0 / 206 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lipoma of breast			
subjects affected / exposed	1 / 280 (0.36%)	0 / 556 (0.00%)	0 / 206 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thyroid neoplasm			
subjects affected / exposed	0 / 280 (0.00%)	1 / 556 (0.18%)	0 / 206 (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
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	1 / 280 (0.36%)	1 / 556 (0.18%)	1 / 206 (0.49%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lupus vasculitis			
subjects affected / exposed	2 / 280 (0.71%)	0 / 556 (0.00%)	0 / 206 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertension			
subjects affected / exposed	0 / 280 (0.00%)	1 / 556 (0.18%)	0 / 206 (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 / 280 (0.00%)	1 / 556 (0.18%)	0 / 206 (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
Thrombosis			
subjects affected / exposed	0 / 280 (0.00%)	1 / 556 (0.18%)	0 / 206 (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
Pregnancy, puerperium and perinatal conditions			
Abortion spontaneous			
subjects affected / exposed	0 / 280 (0.00%)	2 / 556 (0.36%)	0 / 206 (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
General disorders and administration site conditions			
Non-cardiac chest pain			
subjects affected / exposed	1 / 280 (0.36%)	2 / 556 (0.36%)	0 / 206 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia			
subjects affected / exposed	0 / 280 (0.00%)	3 / 556 (0.54%)	0 / 206 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peripheral swelling			
subjects affected / exposed	0 / 280 (0.00%)	1 / 556 (0.18%)	0 / 206 (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 inflammatory response syndrome			
subjects affected / exposed	0 / 280 (0.00%)	1 / 556 (0.18%)	0 / 206 (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
Immune system disorders			
Drug hypersensitivity			

subjects affected / exposed	0 / 280 (0.00%)	1 / 556 (0.18%)	1 / 206 (0.49%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Cervical dysplasia			
subjects affected / exposed	1 / 280 (0.36%)	0 / 556 (0.00%)	0 / 206 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cystocele			
subjects affected / exposed	1 / 280 (0.36%)	0 / 556 (0.00%)	0 / 206 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ovarian cyst			
subjects affected / exposed	0 / 280 (0.00%)	1 / 556 (0.18%)	0 / 206 (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 polyp			
subjects affected / exposed	1 / 280 (0.36%)	0 / 556 (0.00%)	0 / 206 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Uterine prolapse			
subjects affected / exposed	1 / 280 (0.36%)	0 / 556 (0.00%)	0 / 206 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vaginal haemorrhage			
subjects affected / exposed	0 / 280 (0.00%)	1 / 556 (0.18%)	0 / 206 (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
Polycystic ovaries			
subjects affected / exposed	0 / 280 (0.00%)	0 / 556 (0.00%)	0 / 206 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			

Pleurisy			
subjects affected / exposed	1 / 280 (0.36%)	1 / 556 (0.18%)	0 / 206 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute respiratory failure			
subjects affected / exposed	0 / 280 (0.00%)	1 / 556 (0.18%)	0 / 206 (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
Alveolitis			
subjects affected / exposed	0 / 280 (0.00%)	1 / 556 (0.18%)	0 / 206 (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			
subjects affected / exposed	1 / 280 (0.36%)	0 / 556 (0.00%)	1 / 206 (0.49%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary arterial hypertension			
subjects affected / exposed	0 / 280 (0.00%)	1 / 556 (0.18%)	0 / 206 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary haemorrhage			
subjects affected / exposed	0 / 280 (0.00%)	1 / 556 (0.18%)	0 / 206 (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 pleurisy			
subjects affected / exposed	0 / 280 (0.00%)	0 / 556 (0.00%)	1 / 206 (0.49%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleuritic pain			
subjects affected / exposed	0 / 280 (0.00%)	0 / 556 (0.00%)	1 / 206 (0.49%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			

Suicidal ideation			
subjects affected / exposed	0 / 280 (0.00%)	1 / 556 (0.18%)	0 / 206 (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
Depression			
subjects affected / exposed	0 / 280 (0.00%)	0 / 556 (0.00%)	0 / 206 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Suicide attempt			
subjects affected / exposed	0 / 280 (0.00%)	0 / 556 (0.00%)	0 / 206 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Hepatic enzyme increased			
subjects affected / exposed	1 / 280 (0.36%)	0 / 556 (0.00%)	0 / 206 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
International normalised ratio increased			
subjects affected / exposed	1 / 280 (0.36%)	0 / 556 (0.00%)	0 / 206 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Liver function test abnormal			
subjects affected / exposed	1 / 280 (0.36%)	0 / 556 (0.00%)	0 / 206 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Troponin increased			
subjects affected / exposed	0 / 280 (0.00%)	1 / 556 (0.18%)	0 / 206 (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
Injury, poisoning and procedural complications			
Procedural vomiting			

subjects affected / exposed	1 / 280 (0.36%)	0 / 556 (0.00%)	0 / 206 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ankle fracture			
subjects affected / exposed	0 / 280 (0.00%)	0 / 556 (0.00%)	0 / 206 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Humerus fracture			
subjects affected / exposed	0 / 280 (0.00%)	0 / 556 (0.00%)	0 / 206 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rib fracture			
subjects affected / exposed	0 / 280 (0.00%)	0 / 556 (0.00%)	0 / 206 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Myocardial infarction			
subjects affected / exposed	0 / 280 (0.00%)	2 / 556 (0.36%)	0 / 206 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac arrest			
subjects affected / exposed	1 / 280 (0.36%)	0 / 556 (0.00%)	0 / 206 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Cardiac failure congestive			
subjects affected / exposed	0 / 280 (0.00%)	1 / 556 (0.18%)	0 / 206 (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
Coronary artery disease			
subjects affected / exposed	1 / 280 (0.36%)	0 / 556 (0.00%)	0 / 206 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mitral valve incompetence			

subjects affected / exposed	1 / 280 (0.36%)	0 / 556 (0.00%)	0 / 206 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pericarditis			
subjects affected / exposed	0 / 280 (0.00%)	1 / 556 (0.18%)	0 / 206 (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			
Cerebrovascular accident			
subjects affected / exposed	1 / 280 (0.36%)	2 / 556 (0.36%)	0 / 206 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Headache			
subjects affected / exposed	2 / 280 (0.71%)	0 / 556 (0.00%)	0 / 206 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neuropsychiatric lupus			
subjects affected / exposed	0 / 280 (0.00%)	2 / 556 (0.36%)	0 / 206 (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
Syncope			
subjects affected / exposed	1 / 280 (0.36%)	1 / 556 (0.18%)	0 / 206 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Generalised tonic-clonic seizure			
subjects affected / exposed	0 / 280 (0.00%)	1 / 556 (0.18%)	0 / 206 (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
Haemorrhage intracranial			
subjects affected / exposed	1 / 280 (0.36%)	0 / 556 (0.00%)	0 / 206 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intracranial venous sinus thrombosis			

subjects affected / exposed	0 / 280 (0.00%)	1 / 556 (0.18%)	0 / 206 (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 / 280 (0.36%)	0 / 556 (0.00%)	1 / 206 (0.49%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transient ischaemic attack			
subjects affected / exposed	0 / 280 (0.00%)	1 / 556 (0.18%)	1 / 206 (0.49%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vocal cord paralysis			
subjects affected / exposed	1 / 280 (0.36%)	0 / 556 (0.00%)	0 / 206 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Central nervous system lupus			
subjects affected / exposed	0 / 280 (0.00%)	0 / 556 (0.00%)	1 / 206 (0.49%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Thrombocytopenia			
subjects affected / exposed	3 / 280 (1.07%)	0 / 556 (0.00%)	0 / 206 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Anaemia			
subjects affected / exposed	1 / 280 (0.36%)	1 / 556 (0.18%)	0 / 206 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Disseminated intravascular coagulation			
subjects affected / exposed	0 / 280 (0.00%)	1 / 556 (0.18%)	0 / 206 (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
Febrile neutropenia			

subjects affected / exposed	1 / 280 (0.36%)	0 / 556 (0.00%)	0 / 206 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypochromic anaemia			
subjects affected / exposed	0 / 280 (0.00%)	1 / 556 (0.18%)	0 / 206 (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
Antiphospholipid syndrome			
subjects affected / exposed	0 / 280 (0.00%)	0 / 556 (0.00%)	1 / 206 (0.49%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Iron deficiency anaemia			
subjects affected / exposed	0 / 280 (0.00%)	0 / 556 (0.00%)	0 / 206 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	1 / 280 (0.36%)	0 / 556 (0.00%)	0 / 206 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Cataract			
subjects affected / exposed	1 / 280 (0.36%)	0 / 556 (0.00%)	0 / 206 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Exfoliation syndrome			
subjects affected / exposed	0 / 280 (0.00%)	1 / 556 (0.18%)	0 / 206 (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
Eyelid oedema			
subjects affected / exposed	0 / 280 (0.00%)	0 / 556 (0.00%)	0 / 206 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			

Abdominal pain			
subjects affected / exposed	1 / 280 (0.36%)	1 / 556 (0.18%)	0 / 206 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dysphagia			
subjects affected / exposed	2 / 280 (0.71%)	0 / 556 (0.00%)	0 / 206 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Small intestinal obstruction			
subjects affected / exposed	0 / 280 (0.00%)	2 / 556 (0.36%)	0 / 206 (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
Abdominal hernia			
subjects affected / exposed	0 / 280 (0.00%)	1 / 556 (0.18%)	0 / 206 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain upper			
subjects affected / exposed	1 / 280 (0.36%)	0 / 556 (0.00%)	0 / 206 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
subjects affected / exposed	0 / 280 (0.00%)	1 / 556 (0.18%)	0 / 206 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemorrhoids thrombosed			
subjects affected / exposed	0 / 280 (0.00%)	1 / 556 (0.18%)	0 / 206 (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
Mouth ulceration			
subjects affected / exposed	0 / 280 (0.00%)	1 / 556 (0.18%)	0 / 206 (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
Pancreatitis chronic			

subjects affected / exposed	0 / 280 (0.00%)	1 / 556 (0.18%)	0 / 206 (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
Vomiting			
subjects affected / exposed	1 / 280 (0.36%)	0 / 556 (0.00%)	0 / 206 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastric ulcer			
subjects affected / exposed	0 / 280 (0.00%)	0 / 556 (0.00%)	0 / 206 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Large intestine perforation			
subjects affected / exposed	0 / 280 (0.00%)	0 / 556 (0.00%)	1 / 206 (0.49%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lip swelling			
subjects affected / exposed	0 / 280 (0.00%)	0 / 556 (0.00%)	0 / 206 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	1 / 280 (0.36%)	0 / 556 (0.00%)	0 / 206 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholecystitis chronic			
subjects affected / exposed	1 / 280 (0.36%)	0 / 556 (0.00%)	0 / 206 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Systemic lupus erythematosus rash			
subjects affected / exposed	1 / 280 (0.36%)	2 / 556 (0.36%)	0 / 206 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Angioedema			

subjects affected / exposed	0 / 280 (0.00%)	1 / 556 (0.18%)	0 / 206 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Drug eruption			
subjects affected / exposed	1 / 280 (0.36%)	0 / 556 (0.00%)	0 / 206 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin ulcer			
subjects affected / exposed	0 / 280 (0.00%)	1 / 556 (0.18%)	0 / 206 (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
Urticaria			
subjects affected / exposed	0 / 280 (0.00%)	1 / 556 (0.18%)	0 / 206 (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
Rash pruritic			
subjects affected / exposed	0 / 280 (0.00%)	0 / 556 (0.00%)	0 / 206 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Renal failure acute			
subjects affected / exposed	0 / 280 (0.00%)	4 / 556 (0.72%)	0 / 206 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lupus nephritis			
subjects affected / exposed	1 / 280 (0.36%)	2 / 556 (0.36%)	0 / 206 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nephritis			
subjects affected / exposed	1 / 280 (0.36%)	2 / 556 (0.36%)	0 / 206 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nephrotic syndrome			

subjects affected / exposed	2 / 280 (0.71%)	0 / 556 (0.00%)	1 / 206 (0.49%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nephritic syndrome			
subjects affected / exposed	1 / 280 (0.36%)	0 / 556 (0.00%)	0 / 206 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nephrolithiasis			
subjects affected / exposed	1 / 280 (0.36%)	0 / 556 (0.00%)	0 / 206 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Proteinuria			
subjects affected / exposed	1 / 280 (0.36%)	0 / 556 (0.00%)	0 / 206 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal tubular necrosis			
subjects affected / exposed	0 / 280 (0.00%)	1 / 556 (0.18%)	0 / 206 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute kidney injury			
subjects affected / exposed	0 / 280 (0.00%)	0 / 556 (0.00%)	1 / 206 (0.49%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haematuria			
subjects affected / exposed	0 / 280 (0.00%)	0 / 556 (0.00%)	0 / 206 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
SLE arthritis			
subjects affected / exposed	1 / 280 (0.36%)	1 / 556 (0.18%)	0 / 206 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arthralgia			

subjects affected / exposed	0 / 280 (0.00%)	1 / 556 (0.18%)	1 / 206 (0.49%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Back pain			
subjects affected / exposed	1 / 280 (0.36%)	0 / 556 (0.00%)	0 / 206 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Costochondritis			
subjects affected / exposed	1 / 280 (0.36%)	0 / 556 (0.00%)	0 / 206 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal chest pain			
subjects affected / exposed	1 / 280 (0.36%)	0 / 556 (0.00%)	0 / 206 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neck pain			
subjects affected / exposed	1 / 280 (0.36%)	0 / 556 (0.00%)	0 / 206 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteoarthritis			
subjects affected / exposed	0 / 280 (0.00%)	1 / 556 (0.18%)	0 / 206 (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
Pain in extremity			
subjects affected / exposed	0 / 280 (0.00%)	1 / 556 (0.18%)	0 / 206 (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
Polyarthritis			
subjects affected / exposed	0 / 280 (0.00%)	1 / 556 (0.18%)	0 / 206 (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
Synovitis			

subjects affected / exposed	0 / 280 (0.00%)	1 / 556 (0.18%)	0 / 206 (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			
Cellulitis			
subjects affected / exposed	2 / 280 (0.71%)	3 / 556 (0.54%)	0 / 206 (0.00%)
occurrences causally related to treatment / all	0 / 2	2 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	1 / 280 (0.36%)	4 / 556 (0.72%)	1 / 206 (0.49%)
occurrences causally related to treatment / all	1 / 1	2 / 4	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia bacterial			
subjects affected / exposed	2 / 280 (0.71%)	3 / 556 (0.54%)	0 / 206 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urosepsis			
subjects affected / exposed	0 / 280 (0.00%)	3 / 556 (0.54%)	0 / 206 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0
Bacterial sepsis			
subjects affected / exposed	0 / 280 (0.00%)	2 / 556 (0.36%)	0 / 206 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Amoebic dysentery			
subjects affected / exposed	0 / 280 (0.00%)	1 / 556 (0.18%)	0 / 206 (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
Urinary tract infection bacterial			
subjects affected / exposed	0 / 280 (0.00%)	2 / 556 (0.36%)	0 / 206 (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
Bronchitis			

subjects affected / exposed	1 / 280 (0.36%)	0 / 556 (0.00%)	0 / 206 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Corynebacterium sepsis			
subjects affected / exposed	1 / 280 (0.36%)	0 / 556 (0.00%)	0 / 206 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dengue fever			
subjects affected / exposed	0 / 280 (0.00%)	1 / 556 (0.18%)	0 / 206 (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
Diarrhoea infectious			
subjects affected / exposed	0 / 280 (0.00%)	1 / 556 (0.18%)	0 / 206 (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
Escherichia urinary tract infection			
subjects affected / exposed	0 / 280 (0.00%)	1 / 556 (0.18%)	0 / 206 (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
External ear cellulitis			
subjects affected / exposed	1 / 280 (0.36%)	0 / 556 (0.00%)	0 / 206 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gasteroenteritis viral			
subjects affected / exposed	0 / 280 (0.00%)	1 / 556 (0.18%)	0 / 206 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Herpes virus infection			
subjects affected / exposed	0 / 280 (0.00%)	1 / 556 (0.18%)	0 / 206 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Herpes zoster			

subjects affected / exposed	0 / 280 (0.00%)	1 / 556 (0.18%)	2 / 206 (0.97%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Meningitis bacterial			
subjects affected / exposed	1 / 280 (0.36%)	0 / 556 (0.00%)	0 / 206 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oral candidiasis			
subjects affected / exposed	0 / 280 (0.00%)	1 / 556 (0.18%)	0 / 206 (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
Osteomyelitis bacterial			
subjects affected / exposed	1 / 280 (0.36%)	0 / 556 (0.00%)	0 / 206 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Perirectal abscess			
subjects affected / exposed	1 / 280 (0.36%)	0 / 556 (0.00%)	0 / 206 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary tuberculosis			
subjects affected / exposed	1 / 280 (0.36%)	0 / 556 (0.00%)	0 / 206 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis			
subjects affected / exposed	1 / 280 (0.36%)	0 / 556 (0.00%)	0 / 206 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis acute			
subjects affected / exposed	0 / 280 (0.00%)	1 / 556 (0.18%)	0 / 206 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory syncytial virus bronchitis			

subjects affected / exposed	0 / 280 (0.00%)	1 / 556 (0.18%)	0 / 206 (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
Salmonellosis			
subjects affected / exposed	0 / 280 (0.00%)	1 / 556 (0.18%)	0 / 206 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Septic shock			
subjects affected / exposed	1 / 280 (0.36%)	0 / 556 (0.00%)	0 / 206 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subcutaneous abscess			
subjects affected / exposed	1 / 280 (0.36%)	0 / 556 (0.00%)	1 / 206 (0.49%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tuberculosis of central nervous system			
subjects affected / exposed	0 / 280 (0.00%)	1 / 556 (0.18%)	0 / 206 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0
Urinary tract infection			
subjects affected / exposed	1 / 280 (0.36%)	0 / 556 (0.00%)	0 / 206 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 280 (0.00%)	1 / 556 (0.18%)	0 / 206 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal abscess			
subjects affected / exposed	0 / 280 (0.00%)	0 / 556 (0.00%)	2 / 206 (0.97%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Appendicitis			

subjects affected / exposed	0 / 280 (0.00%)	0 / 556 (0.00%)	1 / 206 (0.49%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arthritis infective			
subjects affected / exposed	0 / 280 (0.00%)	0 / 556 (0.00%)	0 / 206 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchitis viral			
subjects affected / exposed	0 / 280 (0.00%)	0 / 556 (0.00%)	1 / 206 (0.49%)
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 bacterial			
subjects affected / exposed	0 / 280 (0.00%)	0 / 556 (0.00%)	0 / 206 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	0 / 280 (0.00%)	0 / 556 (0.00%)	0 / 206 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mycobacterial infection			
subjects affected / exposed	0 / 280 (0.00%)	0 / 556 (0.00%)	1 / 206 (0.49%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Paraspinal abscess			
subjects affected / exposed	0 / 280 (0.00%)	0 / 556 (0.00%)	1 / 206 (0.49%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Staphylococcal sepsis			
subjects affected / exposed	0 / 280 (0.00%)	0 / 556 (0.00%)	0 / 206 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tuberculosis			

subjects affected / exposed	0 / 280 (0.00%)	0 / 556 (0.00%)	0 / 206 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection staphylococcal			
subjects affected / exposed	0 / 280 (0.00%)	0 / 556 (0.00%)	0 / 206 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Electrolyte imbalance			
subjects affected / exposed	0 / 280 (0.00%)	1 / 556 (0.18%)	0 / 206 (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
Hypernatraemia			
subjects affected / exposed	0 / 280 (0.00%)	1 / 556 (0.18%)	0 / 206 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dehydration			
subjects affected / exposed	0 / 280 (0.00%)	0 / 556 (0.00%)	0 / 206 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolic acidosis			
subjects affected / exposed	0 / 280 (0.00%)	0 / 556 (0.00%)	1 / 206 (0.49%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1

Serious adverse events	Open-Label - Belimumab 200 SC to Belimumab 200 mg SC		
Total subjects affected by serious adverse events			
subjects affected / exposed	25 / 456 (5.48%)		
number of deaths (all causes)	1		
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Breast cancer			

subjects affected / exposed	0 / 456 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Endometrial cancer				
subjects affected / exposed	0 / 456 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Intraductal proliferative breast lesion				
subjects affected / exposed	0 / 456 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Lipoma of breast				
subjects affected / exposed	0 / 456 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Thyroid neoplasm				
subjects affected / exposed	0 / 456 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Vascular disorders				
Deep vein thrombosis				
subjects affected / exposed	2 / 456 (0.44%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Lupus vasculitis				
subjects affected / exposed	0 / 456 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hypertension				
subjects affected / exposed	0 / 456 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Orthostatic hypotension				

subjects affected / exposed	0 / 456 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Thrombosis				
subjects affected / exposed	0 / 456 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pregnancy, puerperium and perinatal conditions				
Abortion spontaneous				
subjects affected / exposed	0 / 456 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
General disorders and administration site conditions				
Non-cardiac chest pain				
subjects affected / exposed	0 / 456 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pyrexia				
subjects affected / exposed	0 / 456 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Peripheral swelling				
subjects affected / exposed	0 / 456 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Systemic inflammatory response syndrome				
subjects affected / exposed	0 / 456 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Immune system disorders				
Drug hypersensitivity				

subjects affected / exposed	0 / 456 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Reproductive system and breast disorders			
Cervical dysplasia			
subjects affected / exposed	0 / 456 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cystocele			
subjects affected / exposed	0 / 456 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Ovarian cyst			
subjects affected / exposed	0 / 456 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Uterine polyp			
subjects affected / exposed	0 / 456 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Uterine prolapse			
subjects affected / exposed	0 / 456 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vaginal haemorrhage			
subjects affected / exposed	0 / 456 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Polycystic ovaries			
subjects affected / exposed	1 / 456 (0.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			

Pleurisy				
subjects affected / exposed	0 / 456 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Acute respiratory failure				
subjects affected / exposed	1 / 456 (0.22%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Alveolitis				
subjects affected / exposed	0 / 456 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Dyspnoea				
subjects affected / exposed	1 / 456 (0.22%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pulmonary arterial hypertension				
subjects affected / exposed	0 / 456 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pulmonary haemorrhage				
subjects affected / exposed	0 / 456 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Lupus pleurisy				
subjects affected / exposed	0 / 456 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pleuritic pain				
subjects affected / exposed	0 / 456 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Psychiatric disorders				

Suicidal ideation				
subjects affected / exposed	0 / 456 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Depression				
subjects affected / exposed	1 / 456 (0.22%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Suicide attempt				
subjects affected / exposed	1 / 456 (0.22%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Investigations				
Hepatic enzyme increased				
subjects affected / exposed	0 / 456 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
International normalised ratio increased				
subjects affected / exposed	0 / 456 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Liver function test abnormal				
subjects affected / exposed	1 / 456 (0.22%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Troponin increased				
subjects affected / exposed	0 / 456 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Injury, poisoning and procedural complications				
Procedural vomiting				

subjects affected / exposed	0 / 456 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Ankle fracture				
subjects affected / exposed	1 / 456 (0.22%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Humerus fracture				
subjects affected / exposed	1 / 456 (0.22%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Rib fracture				
subjects affected / exposed	1 / 456 (0.22%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cardiac disorders				
Myocardial infarction				
subjects affected / exposed	0 / 456 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardiac arrest				
subjects affected / exposed	0 / 456 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardiac failure congestive				
subjects affected / exposed	0 / 456 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Coronary artery disease				
subjects affected / exposed	0 / 456 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Mitral valve incompetence				

subjects affected / exposed	0 / 456 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pericarditis				
subjects affected / exposed	0 / 456 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Nervous system disorders				
Cerebrovascular accident				
subjects affected / exposed	0 / 456 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Headache				
subjects affected / exposed	0 / 456 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Neuropsychiatric lupus				
subjects affected / exposed	0 / 456 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Syncope				
subjects affected / exposed	1 / 456 (0.22%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Generalised tonic-clonic seizure				
subjects affected / exposed	0 / 456 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Haemorrhage intracranial				
subjects affected / exposed	0 / 456 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Intracranial venous sinus thrombosis				

subjects affected / exposed	0 / 456 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Lupus encephalitis				
subjects affected / exposed	0 / 456 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Transient ischaemic attack				
subjects affected / exposed	0 / 456 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Vocal cord paralysis				
subjects affected / exposed	0 / 456 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Central nervous system lupus				
subjects affected / exposed	0 / 456 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Blood and lymphatic system disorders				
Thrombocytopenia				
subjects affected / exposed	0 / 456 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Anaemia				
subjects affected / exposed	0 / 456 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Disseminated intravascular coagulation				
subjects affected / exposed	0 / 456 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Febrile neutropenia				

subjects affected / exposed	0 / 456 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hypochromic anaemia			
subjects affected / exposed	0 / 456 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Antiphospholipid syndrome			
subjects affected / exposed	0 / 456 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Iron deficiency anaemia			
subjects affected / exposed	1 / 456 (0.22%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 456 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Eye disorders			
Cataract			
subjects affected / exposed	0 / 456 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Exfoliation syndrome			
subjects affected / exposed	0 / 456 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Eyelid oedema			
subjects affected / exposed	1 / 456 (0.22%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			

Abdominal pain			
subjects affected / exposed	1 / 456 (0.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Dysphagia			
subjects affected / exposed	0 / 456 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Small intestinal obstruction			
subjects affected / exposed	0 / 456 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Abdominal hernia			
subjects affected / exposed	0 / 456 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Abdominal pain upper			
subjects affected / exposed	0 / 456 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Diarrhoea			
subjects affected / exposed	0 / 456 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Haemorrhoids thrombosed			
subjects affected / exposed	0 / 456 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Mouth ulceration			
subjects affected / exposed	0 / 456 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pancreatitis chronic			

subjects affected / exposed	1 / 456 (0.22%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Vomiting				
subjects affected / exposed	0 / 456 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastric ulcer				
subjects affected / exposed	1 / 456 (0.22%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Large intestine perforation				
subjects affected / exposed	0 / 456 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Lip swelling				
subjects affected / exposed	1 / 456 (0.22%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Hepatobiliary disorders				
Cholecystitis				
subjects affected / exposed	0 / 456 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cholecystitis chronic				
subjects affected / exposed	0 / 456 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Skin and subcutaneous tissue disorders				
Systemic lupus erythematosus rash				
subjects affected / exposed	0 / 456 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Angioedema				

subjects affected / exposed	0 / 456 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Drug eruption			
subjects affected / exposed	0 / 456 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Skin ulcer			
subjects affected / exposed	0 / 456 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Urticaria			
subjects affected / exposed	1 / 456 (0.22%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Rash pruritic			
subjects affected / exposed	1 / 456 (0.22%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Renal failure acute			
subjects affected / exposed	0 / 456 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Lupus nephritis			
subjects affected / exposed	0 / 456 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nephritis			
subjects affected / exposed	0 / 456 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nephrotic syndrome			

subjects affected / exposed	0 / 456 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Nephritic syndrome				
subjects affected / exposed	0 / 456 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Nephrolithiasis				
subjects affected / exposed	1 / 456 (0.22%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Proteinuria				
subjects affected / exposed	0 / 456 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Renal tubular necrosis				
subjects affected / exposed	0 / 456 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Acute kidney injury				
subjects affected / exposed	2 / 456 (0.44%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Haematuria				
subjects affected / exposed	1 / 456 (0.22%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Musculoskeletal and connective tissue disorders				
SLE arthritis				
subjects affected / exposed	0 / 456 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Arthralgia				

subjects affected / exposed	0 / 456 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Back pain			
subjects affected / exposed	0 / 456 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Costochondritis			
subjects affected / exposed	0 / 456 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal chest pain			
subjects affected / exposed	1 / 456 (0.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Neck pain			
subjects affected / exposed	0 / 456 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Osteoarthritis			
subjects affected / exposed	0 / 456 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pain in extremity			
subjects affected / exposed	0 / 456 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Polyarthritis			
subjects affected / exposed	0 / 456 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Synovitis			

subjects affected / exposed	0 / 456 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Cellulitis			
subjects affected / exposed	1 / 456 (0.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pneumonia			
subjects affected / exposed	1 / 456 (0.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pneumonia bacterial			
subjects affected / exposed	0 / 456 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Urosepsis			
subjects affected / exposed	0 / 456 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Bacterial sepsis			
subjects affected / exposed	0 / 456 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Amoebic dysentery			
subjects affected / exposed	0 / 456 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Urinary tract infection bacterial			
subjects affected / exposed	1 / 456 (0.22%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Bronchitis			

subjects affected / exposed	0 / 456 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Corynebacterium sepsis				
subjects affected / exposed	0 / 456 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Dengue fever				
subjects affected / exposed	0 / 456 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Diarrhoea infectious				
subjects affected / exposed	0 / 456 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Escherichia urinary tract infection				
subjects affected / exposed	0 / 456 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
External ear cellulitis				
subjects affected / exposed	0 / 456 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gasteroenteritis viral				
subjects affected / exposed	0 / 456 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Herpes virus infection				
subjects affected / exposed	0 / 456 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Herpes zoster				

subjects affected / exposed	0 / 456 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Meningitis bacterial				
subjects affected / exposed	0 / 456 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Oral candidiasis				
subjects affected / exposed	0 / 456 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Osteomyelitis bacterial				
subjects affected / exposed	0 / 456 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Perirectal abscess				
subjects affected / exposed	1 / 456 (0.22%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pulmonary tuberculosis				
subjects affected / exposed	0 / 456 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pyelonephritis				
subjects affected / exposed	0 / 456 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pyelonephritis acute				
subjects affected / exposed	1 / 456 (0.22%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Respiratory syncytial virus bronchitis				

subjects affected / exposed	0 / 456 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Salmonellosis			
subjects affected / exposed	0 / 456 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Septic shock			
subjects affected / exposed	0 / 456 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Subcutaneous abscess			
subjects affected / exposed	0 / 456 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Tuberculosis of central nervous system			
subjects affected / exposed	0 / 456 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Urinary tract infection			
subjects affected / exposed	0 / 456 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 456 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Abdominal abscess			
subjects affected / exposed	0 / 456 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Appendicitis			

subjects affected / exposed	0 / 456 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Arthritis infective			
subjects affected / exposed	1 / 456 (0.22%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Bronchitis viral			
subjects affected / exposed	0 / 456 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cystitis bacterial			
subjects affected / exposed	1 / 456 (0.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastroenteritis			
subjects affected / exposed	1 / 456 (0.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Mycobacterial infection			
subjects affected / exposed	0 / 456 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Paraspinal abscess			
subjects affected / exposed	0 / 456 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Staphylococcal sepsis			
subjects affected / exposed	1 / 456 (0.22%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Tuberculosis			

subjects affected / exposed	1 / 456 (0.22%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
Urinary tract infection staphylococcal			
subjects affected / exposed	1 / 456 (0.22%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Electrolyte imbalance			
subjects affected / exposed	0 / 456 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hypernatraemia			
subjects affected / exposed	0 / 456 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Dehydration			
subjects affected / exposed	1 / 456 (0.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Metabolic acidosis			
subjects affected / exposed	0 / 456 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Placebo SC	Belimumab 200 mg SC	Open-Label - Placebo SC to Belimumab 200 mg SC
Total subjects affected by non-serious adverse events			
subjects affected / exposed	230 / 280 (82.14%)	440 / 556 (79.14%)	101 / 206 (49.03%)
Vascular disorders			
Hypertension			

subjects affected / exposed	14 / 280 (5.00%)	25 / 556 (4.50%)	4 / 206 (1.94%)
occurrences (all)	21	26	4
Nervous system disorders			
Headache			
subjects affected / exposed	25 / 280 (8.93%)	57 / 556 (10.25%)	4 / 206 (1.94%)
occurrences (all)	51	83	7
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	22 / 280 (7.86%)	38 / 556 (6.83%)	1 / 206 (0.49%)
occurrences (all)	30	74	1
Diarrhoea			
subjects affected / exposed	14 / 280 (5.00%)	27 / 556 (4.86%)	3 / 206 (1.46%)
occurrences (all)	17	38	4
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	19 / 280 (6.79%)	22 / 556 (3.96%)	1 / 206 (0.49%)
occurrences (all)	20	26	1
Psychiatric disorders			
Insomnia			
subjects affected / exposed	20 / 280 (7.14%)	18 / 556 (3.24%)	0 / 206 (0.00%)
occurrences (all)	21	20	0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	15 / 280 (5.36%)	28 / 556 (5.04%)	4 / 206 (1.94%)
occurrences (all)	16	31	4
Arthralgia			
subjects affected / exposed	11 / 280 (3.93%)	31 / 556 (5.58%)	6 / 206 (2.91%)
occurrences (all)	11	42	6
Infections and infestations			
Viral upper respiratory tract infection			
subjects affected / exposed	24 / 280 (8.57%)	48 / 556 (8.63%)	9 / 206 (4.37%)
occurrences (all)	32	77	9
Nasopharyngitis			
subjects affected / exposed	22 / 280 (7.86%)	38 / 556 (6.83%)	9 / 206 (4.37%)
occurrences (all)	30	56	9
Urinary tract infection bacterial			

subjects affected / exposed	18 / 280 (6.43%)	41 / 556 (7.37%)	2 / 206 (0.97%)
occurrences (all)	22	44	2
Upper respiratory tract infection bacterial			
subjects affected / exposed	14 / 280 (5.00%)	30 / 556 (5.40%)	3 / 206 (1.46%)
occurrences (all)	15	33	3

Non-serious adverse events	Open-Label - Belimumab 200 SC to Belimumab 200 mg SC		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	216 / 456 (47.37%)		
Vascular disorders			
Hypertension			
subjects affected / exposed	2 / 456 (0.44%)		
occurrences (all)	2		
Nervous system disorders			
Headache			
subjects affected / exposed	10 / 456 (2.19%)		
occurrences (all)	10		
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	5 / 456 (1.10%)		
occurrences (all)	5		
Diarrhoea			
subjects affected / exposed	8 / 456 (1.75%)		
occurrences (all)	8		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	8 / 456 (1.75%)		
occurrences (all)	9		
Psychiatric disorders			
Insomnia			
subjects affected / exposed	1 / 456 (0.22%)		
occurrences (all)	1		
Musculoskeletal and connective tissue disorders			
Back pain			

subjects affected / exposed	5 / 456 (1.10%)		
occurrences (all)	5		
Arthralgia			
subjects affected / exposed	11 / 456 (2.41%)		
occurrences (all)	11		
Infections and infestations			
Viral upper respiratory tract infection			
subjects affected / exposed	17 / 456 (3.73%)		
occurrences (all)	22		
Nasopharyngitis			
subjects affected / exposed	7 / 456 (1.54%)		
occurrences (all)	8		
Urinary tract infection bacterial			
subjects affected / exposed	14 / 456 (3.07%)		
occurrences (all)	16		
Upper respiratory tract infection bacterial			
subjects affected / exposed	9 / 456 (1.97%)		
occurrences (all)	11		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
30 August 2011	Amendment 01 applied to all sites. The composition of the DMC was revised to indicate that at least 3 physicians were included without specifying their specialty areas in order to allow flexibility when constituting the DMC for this study; frequency of prothrombin time (PT) and partial thromboplastin time (PTT) assessments were reduced; and assessment of C-reactive protein (CRP) was removed.
04 October 2011	Amendment 02 applied to all sites. The amount of time for subjects to be monitored following self-administration of study agent on the first (Day 0) and second (Day 7) injections was increased from 1 to 3 hours in the treatment and 6-month open label extension phase based on reports of serious hypersensitivity reactions occurring outside of the 2 hour window. The efficacy analysis sections were updated to clarify that if the Day 364 (Week 52) visit is missing, data collected at a visit within 28 days of the Day 364 (Week 52) visit would be used for analysis of the primary and major secondary efficacy endpoints.
17 November 2011	Amendment 03 applied to all sites. The DMC monitoring schedule after the first meeting was changed from approximately every 4 months to approximately every 6 months to align the schedule with other trials of belimumab in SLE. The protocol was also modified to delete the long-term extension phase after the 6-month open-label extension. Provision of continuing belimumab treatment to subjects who were benefitting and resided in countries where belimumab was not commercially available was achieved in a separate continuation protocol, in which subjects received IV belimumab every 4 weeks until belimumab was commercially available.
21 February 2012	Amendment 04 applied to all sites. Inclusion criteria #6 was amended to recommend that women receiving mycophenolate who relied on oral contraceptives for birth control should employ an additional method (e.g., barrier method). This change was made because mycophenolate mofetil (MMF) and other forms of mycophenolate can affect the metabolism of oral contraceptives and may reduce their effectiveness [CellCept package insert, 2015]. Language was added as a safety precaution to clarify the risk of hypersensitivity reactions, to emphasize patient education about the signs and symptoms of hypersensitivity reactions, and to recommend consideration of an extended period of monitoring (greater than the protocol-specified 3 hours after the first 2 injections) if symptoms of acute hypersensitivity were apparent. The protocol was also modified to indicate that from the time a subject consented to participate in the study and prior to treatment, any SAEs deemed to be related to participation in the study were also collected.
06 August 2013	This local amendment applied to sites in the US, UK, Spain, Portugal, Sweden and Denmark. Exclusion criteria 1 and 2 were modified so that treatment with B cell targeted therapy 1 year or more ago was permitted. Previous treatment with belimumab was still not allowed. Literature evidence supported that the majority of patients have largely recovered from immunosuppressive effects of B cell depletion within 1 year after treatment with B cell targeted therapy [Rituxan package insert, 2014]. Also, there were supplementary clinical and laboratory exclusion criteria already in place would that identify and exclude patients with residual immune suppression. Countries that participated in this local amendment were selected based on estimates of subjects with exposure of at least 1 year to B cell targeted therapy.

12 June 2014	Amendment 05 applied to all sites. The protocol was modified to clarify the timing of the Exit visit and the requirements for the 8-week follow-up visit and the target window of the first dose of IV belimumab following last dose of SC belimumab was added. Progressive multifocal leukoencephalopathy (PML) text was updated based on new information. PK sampling schedule after Day 168 was modified to allow discontinuation of PK sample collection. PK sections were modified to indicate a subset of samples may be used to characterize serum belimumab biochemical attributes and to describe the methodology to be used for this purpose. In subjects who had a positive antibody response at the 8-week follow-up, timing of additional sample collection was made more flexible.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported