Clinical trial results:
A Randomized, Double-Blind, Placebo-Controlled 52-Week Study to Assess Adverse Events of Special Interest in Adults with Active, Autoantibody-Positive Systemic Lupus Erythematosus Receiving Belimumab

Summary

EudraCT number	2011-005667-25
Trial protocol	HU LT CZ EE ES IT PT BG SK PL RO
Global end of trial date	

Results information

Result version number	v2 (current)
This version publication date	18 December 2019
First version publication date	04 August 2019
Version creation reason	

Trial information

Trial identification

Sponsor protocol code	115467

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	GlaxoSmithKline
Sponsor organisation address	980 Great West Road, Brentford, Middlesex, United Kingdom, TW8 9GS
Public contact	GSK Response Center, GlaxoSmithKline, 1 8664357343, GSKClinicalSupportHD@gsk.com
Scientific contact	GSK Response Center, GlaxoSmithKline, 1 8664357343, GSKClinicalSupportHD@gsk.com

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Interim
Date of interim/final analysis	07 February 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	30 July 2018
Global end of trial reached?	No

Notes:

General information about the trial

Main objective of the trial:

The objectives of this study are to evaluate the following in adult Systemic Lupus Erythematosus (SLE) participants receiving belimumab plus standard therapy versus participants receiving placebo plus standard therapy:
1) Mortality and adverse events of special interest over 1 year (through 52 weeks).
2) Corticosteroid reduction during Weeks 40-52.

Protection of trial subjects:

Not Applicable

Background therapy:

Standard SLE treatment including steroids, immunomodulatory agents and/or antimalarials.

Evidence for comparator: -

Actual start date of recruitment	27 November 2012
Long term follow-up planned	Yes
Long term follow-up rationale	Regulatory reason, Safety
Long term follow-up duration	4 Years
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Argentina: 130
Country: Number of subjects enrolled	Australia: 20
Country: Number of subjects enrolled	Brazil: 451
Country: Number of subjects enrolled	Bulgaria: 131
Country: Number of subjects enrolled	Canada: 2
Country: Number of subjects enrolled	Chile: 9
Country: Number of subjects enrolled	Colombia: 325
Country: Number of subjects enrolled	Croatia: 15
Country: Number of subjects enrolled	Czech Republic: 89
Country: Number of subjects enrolled	Estonia: 3
Country: Number of subjects enrolled	Hong Kong: 42
Country: Number of subjects enrolled	Hungary: 117
Country: Number of subjects enrolled	Indonesia: 94
Country: Number of subjects enrolled	Italy: 14
Country: Number of subjects enrolled	Lithuania: 5
Country: Number of subjects enrolled	Malaysia: 17
Country: Number of subjects enrolled	Mexico: 292
Country: Number of subjects enrolled	New Zealand: 14
Country: Number of subjects enrolled	Peru: 83
Country: Number of subjects enrolled	Philippines: 138

Country: Number of subjects enrolled	Poland: 68
Country: Number of subjects enrolled	Portugal: 38
Country: Number of subjects enrolled	Romania: 30
Country: Number of subjects enrolled	Russian Federation: 217
Country: Number of subjects enrolled	Serbia: 224
Country: Number of subjects enrolled	Slovakia: 3
Country: Number of subjects enrolled	Korea, Republic of: 319
Country: Number of subjects enrolled	Spain: 62
Country: Number of subjects enrolled	Switzerland: 10
Country: Number of subjects enrolled	Taiwan: 278
Country: Number of subjects enrolled	Thailand: 67
Country: Number of subjects enrolled	Ukraine: 123
Country: Number of subjects enrolled	United States: 588
Worldwide total number of subjects	4018
EEA total number of subjects	575

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)	3
Adults (18-64 years)	3859
From 65 to 84 years	154
85 years and over	2

Subject disposition

Recruitment

Recruitment details:

This was a global, multi-center, randomized, placebo-controlled double blind study that evaluated adverse events of special interest in adult participants with active, autoantibody-positive systemic lupus erythematosus (SLE) when treated with belimumab plus standard therapy versus participants who received placebo plus standard therapy.

Pre-assignment

Screening details:

4019 participants were randomized of which one participant was not entered into database and did not receive study treatment. 4003 participants who received at least one dose of study treatment contributed to the Intent-to-Treat (ITT) Population. Results presented are based on the primary study analysis of the Week 52 double-blind treatment period.

Period 1

Period 1 title	Overall Study (overall period)
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

Arm description:

Participants received placebo via the intravenous route on Days 0, 14, 28 and every 28 days through Week 48 with a final visit conducted at Week 52. Participants continued to receive standard SLE treatment.

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

Dosage and administration details:

Participants received Placebo along with standard therapies including steroids, immunomodulatory agents and/or antimalarials.

Arm title	Belimumab 10 mg/kg

Arm description:

Participants received belimumab 10 milligrams per kilogram (mg/kg) on Days 0, 14, 28 and every 28 days through Week 48 with a final visit conducted at Week 52. Participants continued to receive standard SLE treatment.

Arm type	Experimental
Investigational medicinal product name	Belimumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Participants received Belimumab 10 milligram/kilogram along with standard therapies including steroids, immunomodulatory agents and/or antimalarials.

Number of subjects in period 1[1]	Placebo	Belimumab 10 mg/kg
Started	2002	2001
Completed	1729	1741
Not completed	273	260
Protocol deviation	2	4
Missing study conclusion form	2	2
Physician decision	48	38
Adverse event, serious fatal	16	13
Adverse event, non-fatal	41	36
Consent withdrawn by subject	128	128
Lost to follow-up	33	37
Site closure	3	2

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: As 15 participants were enrolled, entered into the database but did not received treatment, they were excluded from the ITT and As-Treated populations

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Participants received placebo via the intravenous route on Days 0, 14, 28 and every 28 days through Week 48 with a final visit conducted at Week 52. Participants continued to receive standard SLE treatment.	
Reporting group title	Belimumab 10 mg/kg
Reporting group description:	
Participants received belimumab 10 milligrams per kilogram (mg/kg) on Days 0, 14, 28 and every 28 days through Week 48 with a final visit conducted at Week 52. Participants continued to receive standard SLE treatment.	

Reporting group values	Placebo	Belimumab 10 mg/kg	Total
Number of subjects	2002	2001	4003
Age categorical Units: Subjects			
All Participants	2002	2001	4003
Age Continuous Units: Years			
arithmetic mean	40.8	40.4	
standard deviation	± 12.74	± 12.75	-
Sex: Female, Male Units: Subjects			
Female	1853	1848	3701
Male	149	153	302
Race/Ethnicity, Customized Units: Subjects			
White/Caucasian-European Heritage	1070	1080	2150
White/Caucasian-Arabic/North African Heritage	19	16	35
Mixed White Race	1	0	1
Asian-East Asian Heritage	310	307	617
Asian-South East Asian Heritage	172	168	340
Asian-Central/South Asian Heritage	8	6	14
Asian-Japanese Heritage	2	1	3
Mixed Asian Race	0	1	1
African American/African Heritage	155	175	330
Alaskan Native or American Indian	257	228	485
Native Hawaiian or Other Pacific Islander	2	5	7
Missing	6	14	20

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description:	
Participants received placebo via the intravenous route on Days 0, 14, 28 and every 28 days through Week 48 with a final visit conducted at Week 52. Participants continued to receive standard SLE treatment.	
Reporting group title	Belimumab 10 mg/kg
Reporting group description:	
Participants received belimumab 10 milligrams per kilogram (mg/kg) on Days 0, 14, 28 and every 28 days through Week 48 with a final visit conducted at Week 52. Participants continued to receive standard SLE treatment.	
Subject analysis set title	Belimumab 10 mg/kg
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants received belimumab 10 mg/kg on Days 0, 14, 28 and every 28 days through Week 48 with a final visit conducted at Week 52. Participants continued to receive standard SLE treatment. Participants in this arm comprised of participants in the As Treated Population.	
Subject analysis set title	Placebo
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants received placebo via the intravenous route on Days 0, 14, 28 and every 28 days through Week 48 with a final visit conducted at Week 52. Participants continued to receive standard SLE treatment. Participants in this arm comprised of participants in the As Treated Population.	

Primary: Number of deaths - On treatment period

End point title	Number of deaths - On treatment period
End point description:	
Number of participants who died during on-treatment period is reported. The on-treatment period was defined as first dose to last dose + 28 days (or death). The As-Treated Population was defined as all participants who were randomized and received at least one dose of study agent, grouped according to the actual treatment administered for the majority (>50%) of the time. The on-treatment period was the primary analysis period for safety analyses. One participant in placebo group who received belimumab >50% of the time was reported in the belimumab group.	
End point type	Primary
End point timeframe:	
Up to Week 52 (On-treatment period)	

End point values	Belimumab 10 mg/kg	Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	2002[1]	2001[2]		
Units: Participants				
number (not applicable)	10	8		

Notes:

[1] - As-Treated Population.

[2] - As-Treated Population.

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Belimumab 10 mg/kg v Placebo
Number of subjects included in analysis	4003
Analysis specification	Pre-specified
Analysis type	other[3]
Parameter estimate	Difference in percentage versus placebo
Point estimate	0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.31
upper limit	0.51

Notes:

[3] - 95% Confidence Interval was calculated using simple asymptotic Chi-Square (Pearson) method.

Primary: Number of participants who reported protocol defined adverse events of special interest (AESI): On-treatment period

End point title	Number of participants who reported protocol defined adverse events of special interest (AESI): On-treatment period

End point description:

A summary of protocol defined AESIs including serious infections, opportunistic infections and other infections of interest (serious and non-serious), non-melanoma skin cancer (NMSC), malignancies (excluding NMSC), psychiatric events suggesting serious mood disorders and anxiety (serious depression), suicidality (using Columbia-Suicide Severity Rating Scale [C-SSRS]) and serious infusion and hypersensitivity reactions (SIHR) is reported. The on-treatment period was defined as first dose to last dose + 28 days (or death). The on-treatment period was the primary analysis period for safety analyses. One participant in placebo group who received belimumab >50% of the time was reported in the belimumab group.

End point type	Primary

End point timeframe:

Up to Week 52 (On-treatment period)

End point values	Belimumab 10 mg/kg	Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	2002[4]	2001[5]		
Units: Participants				
number (not applicable)				
Serious Infections, n=2001, 2002	75	82		
Opportunistic Infections, n=2001, 2002	36	50		
Malignancies (Excluding NMSC), n=2001, 2002	5	5		
NMSC, n=2001, 2002	4	3		
Serious depression, n=2001, 2002	7	1		
Suicidality (C-SSRS), n=1986, 1972	28	23		
SIHR, n=2001, 2002	8	2		

Notes:

[4] - As-Treated Population

[5] - As-Treated Population

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Belimumab 10 mg/kg v Placebo
Number of subjects included in analysis	4003
Analysis specification	Pre-specified
Analysis type	other[6]
Parameter estimate	Difference in percentage versus placebo
Point estimate	-0.35
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.55
upper limit	0.85

Notes:

[6] - 95% CI for serious infections was calculated using simple asymptotic Chi-Square (Pearson) method.

Statistical analysis title	Statistical Analysis 2
Comparison groups	Belimumab 10 mg/kg v Placebo
Number of subjects included in analysis	4003
Analysis specification	Pre-specified
Analysis type	other[7]
Parameter estimate	Difference in percentage versus placebo
Point estimate	-0.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.6
upper limit	0.2

Notes:

[7] - 95% CI for opportunistic infections and other infections of interest (serious and non-serious) was calculated using simple asymptotic Chi-Square (Pearson) method.

Statistical analysis title	Statistical Analysis 3
Comparison groups	Belimumab 10 mg/kg v Placebo
Number of subjects included in analysis	4003
Analysis specification	Pre-specified
Analysis type	other[8]
Parameter estimate	Difference in percentage versus placebo
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.31
upper limit	0.31

Notes:

[8] - 95% CI for malignancies (excluding NMSC) was calculated using simple asymptotic Chi-Square (Pearson) method.

Statistical analysis title	Statistical Analysis 4
Comparison groups	Belimumab 10 mg/kg v Placebo
Number of subjects included in analysis	4003
Analysis specification	Pre-specified

Analysis type	other[9]
Parameter estimate	Difference in percentage versus placebo
Point estimate	0.05
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.21
upper limit	0.31

Notes:

[9] - 95% CI for NMSC was calculated using simple asymptotic Chi-Square (Pearson) method.

Statistical analysis title	Statistical Analysis 5
Comparison groups	Belimumab 10 mg/kg v Placebo
Number of subjects included in analysis	4003
Analysis specification	Pre-specified
Analysis type	other[10]
Parameter estimate	Difference in percentage versus placebo
Point estimate	0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.02
upper limit	0.58

Notes:

[10] - 95% CI for psychiatric events suggesting serious mood disorders and anxiety (serious depression) was calculated using simple asymptotic Chi-Square (Pearson) method.

Statistical analysis title	Statistical Analysis 6
Comparison groups	Belimumab 10 mg/kg v Placebo
Number of subjects included in analysis	4003
Analysis specification	Pre-specified
Analysis type	other[11]
Parameter estimate	Difference in percentage versus placebo
Point estimate	0.26
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.44
upper limit	0.96

Notes:

[11] - 95% CI for suicidality (C-SSRS) was calculated using simple asymptotic Chi-Square (Pearson) method. The total number of participants analyzed were n=3958.

Statistical analysis title	Statistical Analysis 7
Comparison groups	Belimumab 10 mg/kg v Placebo
Number of subjects included in analysis	4003
Analysis specification	Pre-specified
Analysis type	other[12]
Parameter estimate	Difference in percentage versus placebo
Point estimate	0.3
Confidence interval	
level	95 %

sides	2-sided
lower limit	-0.01
upper limit	0.61

Notes:

[12] - 95% CI for SIHR was calculated using simple asymptotic Chi-Square (Pearson) method.

Primary: Number of participants with serious adverse events (SAEs) reported during on-treatment period

End point title	Number of participants with serious adverse events (SAEs) reported during on-treatment period[13]

End point description:

An SAE is defined as any untoward medical occurrence that results in death, is life-threatening, requires inpatient hospitalization or prolongation of existing hospitalization, results in persistent disability/incapacity, is a congenital anomaly/birth defect, associated with liver injury and impaired liver function or any other situations as per medical or scientific judgement. The on-treatment period was defined as first dose to last dose + 28 days (or death) and was the primary analysis period for safety analyses. One participant in placebo group who received belimumab >50% of the time was reported in the belimumab group.

End point type	Primary

End point timeframe:

Up to Week 52 (On-treatment period)

Notes:

[13] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analysis was performed for this endpoint

End point values	Belimumab 10 mg/kg	Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	2002[14]	2001[15]		
Units: Participants				
number (not applicable)	220	222		

Notes:

[14] - As-Treated Population.

[15] - As-Treated Population.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of deaths reported - On-study period

End point title	Number of deaths reported - On-study period

End point description:

Number of participants who died during on-study period is reported. The on-study period (which includes on and off treatment data) was defined as first dose to the end of the Week 52 study follow-up (or death). The on-study period was a supportive analysis period for safety analysis. One participant in placebo group who received belimumab >50% of the time was reported in the belimumab group.

End point type	Secondary

End point timeframe:

Up to Week 52 (On-study period)

End point values	Belimumab 10 mg/kg	Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	2002[16]	2001		
Units: Participants				
number (not applicable)	13	22		

Notes:

[16] - As-Treated Population.

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Belimumab 10 mg/kg v Placebo
Number of subjects included in analysis	4003
Analysis specification	Pre-specified
Analysis type	other[17]
Parameter estimate	Difference in percentage versus placebo
Point estimate	-0.45
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.03
upper limit	0.13

Notes:

[17] - 95% CI was calculated using simple asymptotic Chi-Square (Pearson) method.

Secondary: Number of participants who reported protocol defined AESI: On-study period

End point title	Number of participants who reported protocol defined AESI: On-study period

End point description:

A summary of protocol defined AESIs including serious infections, opportunistic infections and other infections of interest (serious and non-serious), NMSC, malignancies (excluding NMSC), psychiatric events suggesting serious mood disorders and anxiety (serious depression), suicidality (using C-SSRS) and SIHR is reported. The on-study period (which includes on and off treatment data) was defined as first dose to the end of the Week 52 study follow-up (or death). The on-study period was a supportive analysis period for safety analysis. One participant in placebo group who received belimumab >50% of the time was reported in the belimumab group.

End point type	Secondary

End point timeframe:

Up to Week 52 (On-study period)

End point values	Belimumab 10 mg/kg	Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	2002[18]	2001[19]		
Units: Participants				
number (not applicable)				
Serious Infectionsn n=2001, 2002	80	95		
Opportunistic Infections, n=2001, 2002	39	59		

Malignancies (Excluding NMC), n=2001, 2002	5	7		
NMSC, n=2001, 2002	4	3		
Serious depression, n=2001, 2002	7	1		
Suicidality (C-SSRS), n=1988, 1974	31	25		
SIHR, n=2001, 2002	8	2		

Notes:

[18] - As-Treated Population.

[19] - As-Treated Population.

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Belimumab 10 mg/kg v Placebo
Number of subjects included in analysis	4003
Analysis specification	Pre-specified
Analysis type	other[20]
Parameter estimate	Difference in percentage versus placebo
Point estimate	-0.75
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.02
upper limit	0.51

Notes:

[20] - 95% CI for serious infections was calculated using simple asymptotic Chi-Square (Pearson) method.

Statistical analysis title	Statistical Analysis 2
Comparison groups	Belimumab 10 mg/kg v Placebo
Number of subjects included in analysis	4003
Analysis specification	Pre-specified
Analysis type	other[21]
Parameter estimate	Difference in percentage versus placebo
Point estimate	-1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.96
upper limit	-0.04

Notes:

[21] - 95% CI for opportunistic infections and other infections of interest (serious and non-serious) was calculated using simple asymptotic Chi-Square (Pearson) method.

Statistical analysis title	Statistical Analysis 3
Comparison groups	Belimumab 10 mg/kg v Placebo
Number of subjects included in analysis	4003
Analysis specification	Pre-specified
Analysis type	other[22]
Parameter estimate	Difference in percentage versus placebo
Point estimate	-0.1
Confidence interval	
level	95 %

sides	2-sided
lower limit	-0.44
upper limit	0.24

Notes:

[22] - 95% CI for malignancies (excluding NMSC) was calculated using simple asymptotic Chi-Square (Pearson) method.

Statistical analysis title	Statistical Analysis 4
Comparison groups	Belimumab 10 mg/kg v Placebo
Number of subjects included in analysis	4003
Analysis specification	Pre-specified
Analysis type	other[23]
Parameter estimate	Difference in percentage versus placebo
Point estimate	0.05
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.21
upper limit	0.31

Notes:

[23] - 95% CI for NMSC was calculated using simple asymptotic Chi-Square (Pearson) method.

Statistical analysis title	Statistical Analysis 5
Comparison groups	Belimumab 10 mg/kg v Placebo
Number of subjects included in analysis	4003
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference in percentage versus placebo
Point estimate	0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.02
upper limit	0.58

Statistical analysis title	Statistical Analysis 6
Comparison groups	Belimumab 10 mg/kg v Placebo
Number of subjects included in analysis	4003
Analysis specification	Pre-specified
Analysis type	other[24]
Parameter estimate	Difference in percentage versus placebo
Point estimate	0.31
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.42
upper limit	1.05

Notes:

[24] - 95% CI for suicidality (C-SSRS) was calculated using simple asymptotic Chi-Square (Pearson) method. The total number of participants analyzed were n=3962.

Statistical analysis title	Statistical Analysis 7
Comparison groups	Belimumab 10 mg/kg v Placebo
Number of subjects included in analysis	4003
Analysis specification	Pre-specified
Analysis type	other[25]
Parameter estimate	Difference in percentage versus placebo
Point estimate	0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.01
upper limit	0.61

Notes:

[25] - 95% CI for SIHR was calculated using simple asymptotic Chi-Square (Pearson) method.

Secondary: Number of participants with SAEs reported during on-study period

End point title	Number of participants with SAEs reported during on-study period

End point description:

A SAE is defined as any untoward medical occurrence that results in death, is life-threatening, requires inpatient hospitalization or prolongation of existing hospitalization, results in persistent disability/incapacity, is a congenital anomaly/birth defect, associated with liver injury and impaired liver function or any other situations as per medical or scientific judgement. The on-study period (which includes on and off treatment data) was defined as first dose to the end of the Week 52 study follow-up (or death) and was a supportive analysis period for safety analyses. One participant in placebo group who received belimumab >50% of the time was reported in the belimumab group.

End point type	Secondary

End point timeframe:

Up to Week 52 (On-study period)

End point values	Belimumab 10 mg/kg	Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	2002[26]	2001[27]		
Units: Participants				
number (not applicable)	233	241		

Notes:

[26] - As-Treated Population.

[27] - As-Treated Population.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants whose average prednisone (or equivalent) dose to treat SLE has been reduced by >=25% from Baseline to <=7.5 mg/day during Weeks 40 through 52

End point title	Percentage of participants whose average prednisone (or equivalent) dose to treat SLE has been reduced by >=25% from Baseline to <=7.5 mg/day during Weeks 40 through 52

End point description:

Average daily prednisone dose during Weeks 40 to 52 is sum of all prednisone doses to treat SLE from the day following Week 40 visit date including Week 52 study completion date (SCD)/no. of days between Week 40 visit and SCD. Percentage of participants whose average prednisone dose reduced by >=25% from Baseline to <=7.5 mg/day during Weeks 40 through 52 in participants with average prednisone use >7.5 mg/day at Baseline was compared using logistic regression including treatment group, Baseline prednisone dose, screening safety of estrogen in lupus national assessment (SELENA) systemic lupus erythematosus disease activity index (SLEDAI) score (<=9 vs.>=10) and region. Baseline is the value at Day 1. Only participants with Baseline prednisone>7.5 mg/day were analyzed. ITT population-participants randomized and received at least 1 dose of study agent and analysis was performed per treatment that participant was randomized to receive, regardless of actual treatment received.

End point type	Secondary

End point timeframe:

Week 40 to Week 52

End point values	Placebo	Belimumab 10 mg/kg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	990[28]	986[29]		
Units: Percentage of Participants				
number (not applicable)	16.2	19.9		

Notes:

[28] - ITT Population with prednisone > 7.5 mg/day at Baseline

[29] - ITT Population with prednisone > 7.5 mg/day at Baseline

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo v Belimumab 10 mg/kg
Number of subjects included in analysis	1976
Analysis specification	Pre-specified
Analysis type	other[30]
P-value	= 0.0284
Method	Regression, Logistic
Parameter estimate	Odds ratio versus placebo
Point estimate	1.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.03
upper limit	1.65

Notes:

[30] - 95% CI and P-value was calculated from a logistic regression model for the comparison between belimumab and placebo including treatment group, Baseline prednisone dose, screening SELENA SLEDAI score (<=9 versus >=10) and region.

Adverse events

Adverse events information

Timeframe for reporting adverse events:

AESIs and all SAEs were collected up to Week 52 (On-study period).

Adverse event reporting additional description:

AESIs and SAEs are summarized for the As-Treated Population. Only AESIs and SAEs were collected in this study, but not all AEs.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	21.1

Reporting groups

Reporting group title	Placebo

Reporting group description:

Participants received placebo via the intravenous route on Days 0, 14, 28 and every 28 days through... more Week 48 with a final visit conducted at Week 52. Participants continued to receive standard SLE treatment.

Reporting group title	Belimumab 10 mg/kg

Reporting group description:

Participants received belimumab 10 milligrams per kilogram (mg/kg) on Days 0, 14, 28 and every 28... more days through Week 48 with a final visit conducted at Week 52. Participants continued to receive standard SLE treatment.

Serious adverse events	Placebo	Belimumab 10 mg/kg	
Total subjects affected by serious adverse events			
subjects affected / exposed	241 / 2001 (12.04%)	233 / 2002 (11.64%)	
number of deaths (all causes)	22	13	
number of deaths resulting from adverse events			
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	1 / 2001 (0.05%)	3 / 2002 (0.15%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lupus vasculitis			
subjects affected / exposed	1 / 2001 (0.05%)	1 / 2002 (0.05%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertension			
subjects affected / exposed	0 / 2001 (0.00%)	1 / 2002 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	

deaths causally related to treatment / all	0 / 0	0 / 0	
Jugular vein thrombosis			
subjects affected / exposed	1 / 2001 (0.05%)	0 / 2002 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral artery occlusion			
subjects affected / exposed	1 / 2001 (0.05%)	0 / 2002 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Raynaud's phenomenon			
subjects affected / exposed	0 / 2001 (0.00%)	1 / 2002 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombosis			
subjects affected / exposed	0 / 2001 (0.00%)	1 / 2002 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vasculitis necrotising			
subjects affected / exposed	0 / 2001 (0.00%)	1 / 2002 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Venous thrombosis			
subjects affected / exposed	0 / 2001 (0.00%)	1 / 2002 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Venous thrombosis limb			
subjects affected / exposed	0 / 2001 (0.00%)	1 / 2002 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypovolaemic shock			
subjects affected / exposed	1 / 2001 (0.05%)	1 / 2002 (0.05%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	

Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Uterine leiomyoma			
subjects affected / exposed	4 / 2001 (0.20%)	0 / 2002 (0.00%)	
occurrences causally related to treatment / all	1 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Squamous cell carcinoma of skin			
subjects affected / exposed	0 / 2001 (0.00%)	2 / 2002 (0.10%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anogenital warts			
subjects affected / exposed	0 / 2001 (0.00%)	1 / 2002 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Benign neoplasm of adrenal gland			
subjects affected / exposed	0 / 2001 (0.00%)	1 / 2002 (0.05%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Brain neoplasm malignant			
subjects affected / exposed	1 / 2001 (0.05%)	0 / 2002 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cervix carcinoma			
subjects affected / exposed	1 / 2001 (0.05%)	0 / 2002 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diffuse large B-cell lymphoma			
subjects affected / exposed	0 / 2001 (0.00%)	1 / 2002 (0.05%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enchondromatosis			
subjects affected / exposed	0 / 2001 (0.00%)	1 / 2002 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Intraductal proliferative breast lesion			
subjects affected / exposed	0 / 2001 (0.00%)	1 / 2002 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung neoplasm malignant			
subjects affected / exposed	0 / 2001 (0.00%)	1 / 2002 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mucoepidermoid carcinoma			
subjects affected / exposed	1 / 2001 (0.05%)	0 / 2002 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ovarian adenoma			
subjects affected / exposed	1 / 2001 (0.05%)	0 / 2002 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal cancer			
subjects affected / exposed	0 / 2001 (0.00%)	1 / 2002 (0.05%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thyroid cancer			
subjects affected / exposed	1 / 2001 (0.05%)	0 / 2002 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neoplasm malignant			
subjects affected / exposed	1 / 2001 (0.05%)	0 / 2002 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thyroid adenoma			
subjects affected / exposed	0 / 2001 (0.00%)	1 / 2002 (0.05%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			

Hypersensitivity			
subjects affected / exposed	1 / 2001 (0.05%)	2 / 2002 (0.10%)	
occurrences causally related to treatment / all	1 / 1	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anaphylactic shock			
subjects affected / exposed	0 / 2001 (0.00%)	2 / 2002 (0.10%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Drug hypersensitivity			
subjects affected / exposed	0 / 2001 (0.00%)	2 / 2002 (0.10%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Allergy to arthropod sting			
subjects affected / exposed	1 / 2001 (0.05%)	0 / 2002 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anaphylactic reaction			
subjects affected / exposed	0 / 2001 (0.00%)	1 / 2002 (0.05%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pregnancy, puerperium and perinatal conditions			
Abortion spontaneous			
subjects affected / exposed	1 / 2001 (0.05%)	5 / 2002 (0.25%)	
occurrences causally related to treatment / all	0 / 1	1 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abortion			
subjects affected / exposed	0 / 2001 (0.00%)	1 / 2002 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abortion threatened			
subjects affected / exposed	1 / 2001 (0.05%)	0 / 2002 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Pre-eclampsia			
subjects affected / exposed	1 / 2001 (0.05%)	0 / 2002 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Foetal death			
subjects affected / exposed	1 / 2001 (0.05%)	0 / 2002 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	6 / 2001 (0.30%)	2 / 2002 (0.10%)	
occurrences causally related to treatment / all	1 / 6	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chest pain			
subjects affected / exposed	2 / 2001 (0.10%)	1 / 2002 (0.05%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Impaired healing			
subjects affected / exposed	1 / 2001 (0.05%)	0 / 2002 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oedema peripheral			
subjects affected / exposed	1 / 2001 (0.05%)	0 / 2002 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pain			
subjects affected / exposed	0 / 2001 (0.00%)	1 / 2002 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Serositis			
subjects affected / exposed	0 / 2001 (0.00%)	1 / 2002 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Sudden death			
subjects affected / exposed	1 / 2001 (0.05%)	0 / 2002 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Systemic inflammatory response syndrome			
subjects affected / exposed	0 / 2001 (0.00%)	1 / 2002 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Death			
subjects affected / exposed	3 / 2001 (0.15%)	0 / 2002 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 3	0 / 0	
Oedema due to renal disease			
subjects affected / exposed	0 / 2001 (0.00%)	1 / 2002 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Suicidal ideation			
subjects affected / exposed	2 / 2001 (0.10%)	6 / 2002 (0.30%)	
occurrences causally related to treatment / all	1 / 2	2 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Suicide attempt			
subjects affected / exposed	1 / 2001 (0.05%)	4 / 2002 (0.20%)	
occurrences causally related to treatment / all	0 / 1	1 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Depression			
subjects affected / exposed	0 / 2001 (0.00%)	4 / 2002 (0.20%)	
occurrences causally related to treatment / all	0 / 0	2 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bipolar disorder			
subjects affected / exposed	1 / 2001 (0.05%)	1 / 2002 (0.05%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Intentional self-injury			
subjects affected / exposed	1 / 2001 (0.05%)	1 / 2002 (0.05%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Major depression			
subjects affected / exposed	0 / 2001 (0.00%)	2 / 2002 (0.10%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Agitation			
subjects affected / exposed	0 / 2001 (0.00%)	1 / 2002 (0.05%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Conversion disorder			
subjects affected / exposed	0 / 2001 (0.00%)	1 / 2002 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Delirium			
subjects affected / exposed	0 / 2001 (0.00%)	1 / 2002 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Depression suicidal			
subjects affected / exposed	1 / 2001 (0.05%)	0 / 2002 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Ovarian cyst			
subjects affected / exposed	1 / 2001 (0.05%)	3 / 2002 (0.15%)	
occurrences causally related to treatment / all	0 / 2	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cervical dysplasia			
subjects affected / exposed	2 / 2001 (0.10%)	1 / 2002 (0.05%)	
occurrences causally related to treatment / all	0 / 2	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Endometriosis			
subjects affected / exposed	2 / 2001 (0.10%)	1 / 2002 (0.05%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dysfunctional uterine bleeding			
subjects affected / exposed	2 / 2001 (0.10%)	0 / 2002 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Uterine haemorrhage			
subjects affected / exposed	2 / 2001 (0.10%)	0 / 2002 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Adenomyosis			
subjects affected / exposed	0 / 2001 (0.00%)	1 / 2002 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhagic ovarian cyst			
subjects affected / exposed	1 / 2001 (0.05%)	0 / 2002 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Menorrhagia			
subjects affected / exposed	1 / 2001 (0.05%)	0 / 2002 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ovarian adhesion			
subjects affected / exposed	0 / 2001 (0.00%)	1 / 2002 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ovulation pain			
subjects affected / exposed	0 / 2001 (0.00%)	1 / 2002 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vaginal haemorrhage			
subjects affected / exposed	0 / 2001 (0.00%)	1 / 2002 (0.05%)	

occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Lower limb fracture			
subjects affected / exposed	2 / 2001 (0.10%)	1 / 2002 (0.05%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femur fracture			
subjects affected / exposed	0 / 2001 (0.00%)	2 / 2002 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hip fracture			
subjects affected / exposed	1 / 2001 (0.05%)	1 / 2002 (0.05%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal compression fracture			
subjects affected / exposed	0 / 2001 (0.00%)	2 / 2002 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sternal fracture			
subjects affected / exposed	1 / 2001 (0.05%)	1 / 2002 (0.05%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Contusion			
subjects affected / exposed	0 / 2001 (0.00%)	1 / 2002 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fall			
subjects affected / exposed	0 / 2001 (0.00%)	1 / 2002 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Foot fracture			
subjects affected / exposed	1 / 2001 (0.05%)	0 / 2002 (0.00%)	

occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gun shot wound			
subjects affected / exposed	1 / 2001 (0.05%)	0 / 2002 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Humerus fracture			
subjects affected / exposed	0 / 2001 (0.00%)	1 / 2002 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infusion related reaction			
subjects affected / exposed	0 / 2001 (0.00%)	1 / 2002 (0.05%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ligament injury			
subjects affected / exposed	0 / 2001 (0.00%)	1 / 2002 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ligament rupture			
subjects affected / exposed	1 / 2001 (0.05%)	0 / 2002 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meniscus injury			
subjects affected / exposed	0 / 2001 (0.00%)	1 / 2002 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Overdose			
subjects affected / exposed	1 / 2001 (0.05%)	0 / 2002 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Postoperative respiratory failure			
subjects affected / exposed	1 / 2001 (0.05%)	0 / 2002 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	

deaths causally related to treatment / all	0 / 0	0 / 0	
Subdural haematoma			
subjects affected / exposed	0 / 2001 (0.00%)	1 / 2002 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subdural haemorrhage			
subjects affected / exposed	0 / 2001 (0.00%)	1 / 2002 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Brain contusion			
subjects affected / exposed	0 / 2001 (0.00%)	1 / 2002 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ligament sprain			
subjects affected / exposed	1 / 2001 (0.05%)	0 / 2002 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skull fractured base			
subjects affected / exposed	0 / 2001 (0.00%)	1 / 2002 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Hepatic enzyme increased			
subjects affected / exposed	0 / 2001 (0.00%)	1 / 2002 (0.05%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Myocardial infarction			
subjects affected / exposed	1 / 2001 (0.05%)	3 / 2002 (0.15%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure			
subjects affected / exposed	1 / 2001 (0.05%)	2 / 2002 (0.10%)	
occurrences causally related to treatment / all	1 / 1	1 / 2	

deaths causally related to treatment / all	0 / 0	0 / 0	
Pericarditis			
subjects affected / exposed	0 / 2001 (0.00%)	3 / 2002 (0.15%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute myocardial infarction			
subjects affected / exposed	2 / 2001 (0.10%)	1 / 2002 (0.05%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Cardio-respiratory arrest			
subjects affected / exposed	2 / 2001 (0.10%)	1 / 2002 (0.05%)	
occurrences causally related to treatment / all	1 / 2	0 / 1	
deaths causally related to treatment / all	1 / 2	0 / 1	
Myocarditis			
subjects affected / exposed	0 / 2001 (0.00%)	2 / 2002 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pericardial effusion			
subjects affected / exposed	1 / 2001 (0.05%)	1 / 2002 (0.05%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute coronary syndrome			
subjects affected / exposed	1 / 2001 (0.05%)	0 / 2002 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angina pectoris			
subjects affected / exposed	0 / 2001 (0.00%)	1 / 2002 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angina unstable			
subjects affected / exposed	0 / 2001 (0.00%)	1 / 2002 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Atrial fibrillation			
subjects affected / exposed	0 / 2001 (0.00%)	1 / 2002 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial flutter			
subjects affected / exposed	0 / 2001 (0.00%)	1 / 2002 (0.05%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bundle branch block left			
subjects affected / exposed	1 / 2001 (0.05%)	0 / 2002 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac arrest			
subjects affected / exposed	1 / 2001 (0.05%)	0 / 2002 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Cardiac failure congestive			
subjects affected / exposed	1 / 2001 (0.05%)	1 / 2002 (0.05%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiopulmonary failure			
subjects affected / exposed	1 / 2001 (0.05%)	0 / 2002 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Coronary artery disease			
subjects affected / exposed	1 / 2001 (0.05%)	0 / 2002 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tachycardia			
subjects affected / exposed	1 / 2001 (0.05%)	0 / 2002 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Congestive cardiomyopathy			
subjects affected / exposed	0 / 2001 (0.00%)	1 / 2002 (0.05%)	

occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mitral valve disease			
subjects affected / exposed	1 / 2001 (0.05%)	0 / 2002 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Palpitations			
subjects affected / exposed	0 / 2001 (0.00%)	1 / 2002 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Supraventricular extrasystoles			
subjects affected / exposed	1 / 2001 (0.05%)	0 / 2002 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Congenital, familial and genetic disorders			
Anomalous pulmonary venous connection			
subjects affected / exposed	0 / 2001 (0.00%)	1 / 2002 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Pulmonary embolism			
subjects affected / exposed	7 / 2001 (0.35%)	2 / 2002 (0.10%)	
occurrences causally related to treatment / all	0 / 7	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Asthma			
subjects affected / exposed	1 / 2001 (0.05%)	2 / 2002 (0.10%)	
occurrences causally related to treatment / all	0 / 1	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleural effusion			
subjects affected / exposed	2 / 2001 (0.10%)	1 / 2002 (0.05%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Chronic obstructive pulmonary disease			
subjects affected / exposed	1 / 2001 (0.05%)	1 / 2002 (0.05%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleurisy			
subjects affected / exposed	2 / 2001 (0.10%)	0 / 2002 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonitis			
subjects affected / exposed	2 / 2001 (0.10%)	0 / 2002 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lupus pleurisy			
subjects affected / exposed	1 / 2001 (0.05%)	0 / 2002 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lupus pneumonitis			
subjects affected / exposed	1 / 2001 (0.05%)	1 / 2002 (0.05%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumothorax spontaneous			
subjects affected / exposed	0 / 2001 (0.00%)	1 / 2002 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary alveolar haemorrhage			
subjects affected / exposed	1 / 2001 (0.05%)	0 / 2002 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary artery thrombosis			
subjects affected / exposed	1 / 2001 (0.05%)	0 / 2002 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary hypertension			

subjects affected / exposed	1 / 2001 (0.05%)	1 / 2002 (0.05%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary infarction			
subjects affected / exposed	1 / 2001 (0.05%)	0 / 2002 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory distress			
subjects affected / exposed	1 / 2001 (0.05%)	0 / 2002 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Respiratory failure			
subjects affected / exposed	2 / 2001 (0.10%)	1 / 2002 (0.05%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 2	0 / 0	
Shrinking lung syndrome			
subjects affected / exposed	1 / 2001 (0.05%)	0 / 2002 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Acute pulmonary oedema			
subjects affected / exposed	1 / 2001 (0.05%)	0 / 2002 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	3 / 2001 (0.15%)	3 / 2002 (0.15%)	
occurrences causally related to treatment / all	0 / 3	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombocytopenia			
subjects affected / exposed	5 / 2001 (0.25%)	1 / 2002 (0.05%)	
occurrences causally related to treatment / all	1 / 6	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Autoimmune haemolytic anaemia			
subjects affected / exposed	3 / 2001 (0.15%)	0 / 2002 (0.00%)	

occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile neutropenia			
subjects affected / exposed	0 / 2001 (0.00%)	3 / 2002 (0.15%)	
occurrences causally related to treatment / all	0 / 0	3 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhagic anaemia			
subjects affected / exposed	0 / 2001 (0.00%)	2 / 2002 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lymphadenopathy			
subjects affected / exposed	1 / 2001 (0.05%)	1 / 2002 (0.05%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anaemia of chronic disease			
subjects affected / exposed	1 / 2001 (0.05%)	0 / 2002 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Antiphospholipid syndrome			
subjects affected / exposed	1 / 2001 (0.05%)	0 / 2002 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aplastic anaemia			
subjects affected / exposed	0 / 2001 (0.00%)	1 / 2002 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemolytic anaemia			
subjects affected / exposed	1 / 2001 (0.05%)	0 / 2002 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Iron deficiency anaemia			
subjects affected / exposed	2 / 2001 (0.10%)	0 / 2002 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	

deaths causally related to treatment / all	0 / 0	0 / 0	
Leukopenia			
subjects affected / exposed	0 / 2001 (0.00%)	2 / 2002 (0.10%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lymphadenitis			
subjects affected / exposed	1 / 2001 (0.05%)	0 / 2002 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Microangiopathic haemolytic anaemia			
subjects affected / exposed	1 / 2001 (0.05%)	0 / 2002 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancytopenia			
subjects affected / exposed	0 / 2001 (0.00%)	2 / 2002 (0.10%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombotic thrombocytopenic purpura			
subjects affected / exposed	1 / 2001 (0.05%)	0 / 2002 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Cerebral infarction			
subjects affected / exposed	3 / 2001 (0.15%)	1 / 2002 (0.05%)	
occurrences causally related to treatment / all	0 / 3	1 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Headache			
subjects affected / exposed	1 / 2001 (0.05%)	3 / 2002 (0.15%)	
occurrences causally related to treatment / all	0 / 1	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transient ischaemic attack			
subjects affected / exposed	1 / 2001 (0.05%)	3 / 2002 (0.15%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	

deaths causally related to treatment / all	0 / 0	0 / 0	
Syncope			
subjects affected / exposed	2 / 2001 (0.10%)	0 / 2002 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Carotid artery aneurysm			
subjects affected / exposed	1 / 2001 (0.05%)	0 / 2002 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Central nervous system lupus			
subjects affected / exposed	0 / 2001 (0.00%)	1 / 2002 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Central nervous system vasculitis			
subjects affected / exposed	1 / 2001 (0.05%)	2 / 2002 (0.10%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebral haemorrhage			
subjects affected / exposed	1 / 2001 (0.05%)	0 / 2002 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebral ischaemia			
subjects affected / exposed	0 / 2001 (0.00%)	1 / 2002 (0.05%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cervical radiculopathy			
subjects affected / exposed	1 / 2001 (0.05%)	0 / 2002 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Encephalopathy			
subjects affected / exposed	1 / 2001 (0.05%)	0 / 2002 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Epilepsy			
subjects affected / exposed	1 / 2001 (0.05%)	0 / 2002 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Facial paralysis			
subjects affected / exposed	0 / 2001 (0.00%)	1 / 2002 (0.05%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Generalised tonic-clonic seizure			
subjects affected / exposed	0 / 2001 (0.00%)	1 / 2002 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intracranial venous sinus thrombosis			
subjects affected / exposed	1 / 2001 (0.05%)	0 / 2002 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ischaemic stroke			
subjects affected / exposed	0 / 2001 (0.00%)	1 / 2002 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lacunar infarction			
subjects affected / exposed	1 / 2001 (0.05%)	0 / 2002 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Migraine			
subjects affected / exposed	0 / 2001 (0.00%)	1 / 2002 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Multiple sclerosis			
subjects affected / exposed	1 / 2001 (0.05%)	0 / 2002 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myelitis transverse			
subjects affected / exposed	1 / 2001 (0.05%)	0 / 2002 (0.00%)	

occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neuropsychiatric lupus			
subjects affected / exposed	0 / 2001 (0.00%)	1 / 2002 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Seizure			
subjects affected / exposed	0 / 2001 (0.00%)	1 / 2002 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dysarthria			
subjects affected / exposed	0 / 2001 (0.00%)	1 / 2002 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intraventricular haemorrhage			
subjects affected / exposed	1 / 2001 (0.05%)	0 / 2002 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thalamus haemorrhage			
subjects affected / exposed	1 / 2001 (0.05%)	0 / 2002 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Cataract			
subjects affected / exposed	2 / 2001 (0.10%)	1 / 2002 (0.05%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eyelid ptosis			
subjects affected / exposed	1 / 2001 (0.05%)	0 / 2002 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Periorbital swelling			
subjects affected / exposed	0 / 2001 (0.00%)	1 / 2002 (0.05%)	
occurrences causally related to	0 / 0	0 / 1	

treatment / all			
deaths causally related to treatment / all	0 / 0	0 / 0	
Vision blurred			
subjects affected / exposed	0 / 2001 (0.00%)	1 / 2002 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 2001 (0.00%)	2 / 2002 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Pancreatitis acute			
subjects affected / exposed	1 / 2001 (0.05%)	2 / 2002 (0.10%)	
occurrences causally related to treatment / all	0 / 1	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	2 / 2001 (0.10%)	1 / 2002 (0.05%)	
occurrences causally related to treatment / all	1 / 2	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colitis			
subjects affected / exposed	1 / 2001 (0.05%)	1 / 2002 (0.05%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric disorder			
subjects affected / exposed	1 / 2001 (0.05%)	1 / 2002 (0.05%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastritis			
subjects affected / exposed	1 / 2001 (0.05%)	2 / 2002 (0.10%)	
occurrences causally related to treatment / all	1 / 1	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastritis erosive			
subjects affected / exposed	1 / 2001 (0.05%)	1 / 2002 (0.05%)	

occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis			
subjects affected / exposed	2 / 2001 (0.10%)	0 / 2002 (0.00%)	
occurrences causally related to treatment / all	2 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Strangulated umbilical hernia			
subjects affected / exposed	2 / 2001 (0.10%)	0 / 2002 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain			
subjects affected / exposed	1 / 2001 (0.05%)	0 / 2002 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colitis ischaemic			
subjects affected / exposed	0 / 2001 (0.00%)	1 / 2002 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colitis ulcerative			
subjects affected / exposed	0 / 2001 (0.00%)	1 / 2002 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	1 / 2001 (0.05%)	0 / 2002 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticulum intestinal haemorrhagic			
subjects affected / exposed	0 / 2001 (0.00%)	1 / 2002 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Duodenal ulcer haemorrhage			
subjects affected / exposed	1 / 2001 (0.05%)	0 / 2002 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	

deaths causally related to treatment / all	0 / 0	0 / 0	
Enteritis			
subjects affected / exposed	1 / 2001 (0.05%)	0 / 2002 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enterocolitis			
subjects affected / exposed	0 / 2001 (0.00%)	1 / 2002 (0.05%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epiploic appendagitis			
subjects affected / exposed	0 / 2001 (0.00%)	1 / 2002 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric ulcer			
subjects affected / exposed	1 / 2001 (0.05%)	0 / 2002 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal haemorrhage			
subjects affected / exposed	1 / 2001 (0.05%)	0 / 2002 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 2001 (0.00%)	1 / 2002 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal obstruction			
subjects affected / exposed	0 / 2001 (0.00%)	1 / 2002 (0.05%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Large intestine perforation			
subjects affected / exposed	1 / 2001 (0.05%)	0 / 2002 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Lupus enteritis			
subjects affected / exposed	0 / 2001 (0.00%)	1 / 2002 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Obstructive pancreatitis			
subjects affected / exposed	0 / 2001 (0.00%)	1 / 2002 (0.05%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis relapsing			
subjects affected / exposed	0 / 2001 (0.00%)	1 / 2002 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peptic ulcer			
subjects affected / exposed	1 / 2001 (0.05%)	0 / 2002 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peptic ulcer haemorrhage			
subjects affected / exposed	0 / 2001 (0.00%)	1 / 2002 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	4 / 2001 (0.20%)	0 / 2002 (0.00%)	
occurrences causally related to treatment / all	1 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis			
subjects affected / exposed	0 / 2001 (0.00%)	2 / 2002 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis acute			
subjects affected / exposed	2 / 2001 (0.10%)	0 / 2002 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic steatosis			

subjects affected / exposed	0 / 2001 (0.00%)	2 / 2002 (0.10%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Autoimmune hepatitis			
subjects affected / exposed	1 / 2001 (0.05%)	0 / 2002 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatitis acute			
subjects affected / exposed	0 / 2001 (0.00%)	1 / 2002 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Jaundice extrahepatic obstructive			
subjects affected / exposed	1 / 2001 (0.05%)	0 / 2002 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Liver disorder			
subjects affected / exposed	1 / 2001 (0.05%)	0 / 2002 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Drug-induced liver injury			
subjects affected / exposed	0 / 2001 (0.00%)	1 / 2002 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Lupus nephritis			
subjects affected / exposed	11 / 2001 (0.55%)	6 / 2002 (0.30%)	
occurrences causally related to treatment / all	2 / 11	1 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute kidney injury			
subjects affected / exposed	6 / 2001 (0.30%)	2 / 2002 (0.10%)	
occurrences causally related to treatment / all	2 / 6	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Proteinuria			
subjects affected / exposed	1 / 2001 (0.05%)	1 / 2002 (0.05%)	

occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic kidney disease			
subjects affected / exposed	0 / 2001 (0.00%)	1 / 2002 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nephritis			
subjects affected / exposed	1 / 2001 (0.05%)	0 / 2002 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nephrotic syndrome			
subjects affected / exposed	1 / 2001 (0.05%)	0 / 2002 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prerenal failure			
subjects affected / exposed	0 / 2001 (0.00%)	1 / 2002 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal failure			
subjects affected / exposed	2 / 2001 (0.10%)	0 / 2002 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tubulointerstitial nephritis			
subjects affected / exposed	0 / 2001 (0.00%)	1 / 2002 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Product issues			
Device breakage			
subjects affected / exposed	1 / 2001 (0.05%)	0 / 2002 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device leakage			
subjects affected / exposed	0 / 2001 (0.00%)	1 / 2002 (0.05%)	
occurrences causally related to	0 / 0	0 / 1	

treatment / all			
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Cutaneous lupus erythematosus			
subjects affected / exposed	1 / 2001 (0.05%)	3 / 2002 (0.15%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Systemic lupus erythematosus rash			
subjects affected / exposed	1 / 2001 (0.05%)	2 / 2002 (0.10%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angioedema			
subjects affected / exposed	2 / 2001 (0.10%)	0 / 2002 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rash			
subjects affected / exposed	1 / 2001 (0.05%)	1 / 2002 (0.05%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rash pruritic			
subjects affected / exposed	0 / 2001 (0.00%)	2 / 2002 (0.10%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blister			
subjects affected / exposed	0 / 2001 (0.00%)	1 / 2002 (0.05%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cutaneous vasculitis			
subjects affected / exposed	1 / 2001 (0.05%)	0 / 2002 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dermatomyositis			
subjects affected / exposed	1 / 2001 (0.05%)	0 / 2002 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	

deaths causally related to treatment / all	0 / 0	0 / 0	
Dyshidrotic eczema			
subjects affected / exposed	0 / 2001 (0.00%)	1 / 2002 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Erythema multiforme			
subjects affected / exposed	0 / 2001 (0.00%)	1 / 2002 (0.05%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Stevens-Johnson syndrome			
subjects affected / exposed	0 / 2001 (0.00%)	1 / 2002 (0.05%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vasculitic ulcer			
subjects affected / exposed	0 / 2001 (0.00%)	1 / 2002 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Systemic lupus erythematosus			
subjects affected / exposed	11 / 2001 (0.55%)	5 / 2002 (0.25%)	
occurrences causally related to treatment / all	1 / 12	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arthritis			
subjects affected / exposed	4 / 2001 (0.20%)	0 / 2002 (0.00%)	
occurrences causally related to treatment / all	1 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
SLE arthritis			
subjects affected / exposed	3 / 2001 (0.15%)	1 / 2002 (0.05%)	
occurrences causally related to treatment / all	1 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arthralgia			
subjects affected / exposed	1 / 2001 (0.05%)	1 / 2002 (0.05%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	

deaths causally related to treatment / all	0 / 0	0 / 0	
Intervertebral disc protrusion			
subjects affected / exposed	1 / 2001 (0.05%)	1 / 2002 (0.05%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Back pain			
subjects affected / exposed	2 / 2001 (0.10%)	0 / 2002 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fistula			
subjects affected / exposed	1 / 2001 (0.05%)	0 / 2002 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal pain			
subjects affected / exposed	1 / 2001 (0.05%)	0 / 2002 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteonecrosis			
subjects affected / exposed	1 / 2001 (0.05%)	0 / 2002 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteoporotic fracture			
subjects affected / exposed	1 / 2001 (0.05%)	0 / 2002 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pain in extremity			
subjects affected / exposed	1 / 2001 (0.05%)	1 / 2002 (0.05%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Polyarthritis			
subjects affected / exposed	1 / 2001 (0.05%)	0 / 2002 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Myositis			
subjects affected / exposed	0 / 2001 (0.00%)	1 / 2002 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Hyperglycaemia			
subjects affected / exposed	2 / 2001 (0.10%)	0 / 2002 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypokalaemia			
subjects affected / exposed	1 / 2001 (0.05%)	1 / 2002 (0.05%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyponatraemia			
subjects affected / exposed	0 / 2001 (0.00%)	1 / 2002 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Type 2 diabetes mellitus			
subjects affected / exposed	0 / 2001 (0.00%)	1 / 2002 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Pneumonia			
subjects affected / exposed	27 / 2001 (1.35%)	18 / 2002 (0.90%)	
occurrences causally related to treatment / all	12 / 28	9 / 18	
deaths causally related to treatment / all	0 / 2	3 / 5	
Urinary tract infection			
subjects affected / exposed	8 / 2001 (0.40%)	16 / 2002 (0.80%)	
occurrences causally related to treatment / all	3 / 9	8 / 17	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis			
subjects affected / exposed	8 / 2001 (0.40%)	7 / 2002 (0.35%)	
occurrences causally related to treatment / all	5 / 8	2 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	

Gastroenteritis			
subjects affected / exposed	11 / 2001 (0.55%)	4 / 2002 (0.20%)	
occurrences causally related to treatment / all	1 / 11	2 / 5	
deaths causally related to treatment / all	0 / 1	0 / 0	
Sepsis			
subjects affected / exposed	4 / 2001 (0.20%)	4 / 2002 (0.20%)	
occurrences causally related to treatment / all	1 / 5	2 / 4	
deaths causally related to treatment / all	0 / 1	2 / 2	
Appendicitis			
subjects affected / exposed	2 / 2001 (0.10%)	3 / 2002 (0.15%)	
occurrences causally related to treatment / all	0 / 2	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Herpes zoster			
subjects affected / exposed	5 / 2001 (0.25%)	1 / 2002 (0.05%)	
occurrences causally related to treatment / all	5 / 5	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urosepsis			
subjects affected / exposed	2 / 2001 (0.10%)	3 / 2002 (0.15%)	
occurrences causally related to treatment / all	0 / 2	2 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis acute			
subjects affected / exposed	2 / 2001 (0.10%)	3 / 2002 (0.15%)	
occurrences causally related to treatment / all	2 / 2	2 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Septic shock			
subjects affected / exposed	3 / 2001 (0.15%)	4 / 2002 (0.20%)	
occurrences causally related to treatment / all	1 / 3	3 / 4	
deaths causally related to treatment / all	1 / 3	3 / 4	
Bronchitis			
subjects affected / exposed	2 / 2001 (0.10%)	1 / 2002 (0.05%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea infectious			
subjects affected / exposed	1 / 2001 (0.05%)	2 / 2002 (0.10%)	

occurrences causally related to treatment / all	0 / 1	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary tuberculosis			
subjects affected / exposed	4 / 2001 (0.20%)	1 / 2002 (0.05%)	
occurrences causally related to treatment / all	2 / 4	1 / 1	
deaths causally related to treatment / all	0 / 0	1 / 1	
Clostridium difficile colitis			
subjects affected / exposed	3 / 2001 (0.15%)	0 / 2002 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dengue haemorrhagic fever			
subjects affected / exposed	1 / 2001 (0.05%)	1 / 2002 (0.05%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Laryngitis			
subjects affected / exposed	0 / 2001 (0.00%)	2 / 2002 (0.10%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower respiratory tract infection			
subjects affected / exposed	1 / 2001 (0.05%)	1 / 2002 (0.05%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pelvic inflammatory disease			
subjects affected / exposed	0 / 2001 (0.00%)	2 / 2002 (0.10%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis			
subjects affected / exposed	1 / 2001 (0.05%)	1 / 2002 (0.05%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory tract infection			
subjects affected / exposed	0 / 2001 (0.00%)	2 / 2002 (0.10%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	

deaths causally related to treatment / all	0 / 0	0 / 0	
Subcutaneous abscess			
subjects affected / exposed	1 / 2001 (0.05%)	1 / 2002 (0.05%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal sepsis			
subjects affected / exposed	1 / 2001 (0.05%)	0 / 2002 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abscess limb			
subjects affected / exposed	1 / 2001 (0.05%)	0 / 2002 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute sinusitis			
subjects affected / exposed	0 / 2001 (0.00%)	1 / 2002 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arthritis bacterial			
subjects affected / exposed	1 / 2001 (0.05%)	0 / 2002 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bartholinitis			
subjects affected / exposed	0 / 2001 (0.00%)	1 / 2002 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bursitis infective			
subjects affected / exposed	0 / 2001 (0.00%)	1 / 2002 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Complicated appendicitis			
subjects affected / exposed	0 / 2001 (0.00%)	1 / 2002 (0.05%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Cystitis			
subjects affected / exposed	1 / 2001 (0.05%)	0 / 2002 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cytomegalovirus infection			
subjects affected / exposed	0 / 2001 (0.00%)	1 / 2002 (0.05%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	1 / 1	
Cytomegalovirus mucocutaneous ulcer			
subjects affected / exposed	0 / 2001 (0.00%)	1 / 2002 (0.05%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Encephalitis			
subjects affected / exposed	2 / 2001 (0.10%)	0 / 2002 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enterocolitis viral			
subjects affected / exposed	1 / 2001 (0.05%)	0 / 2002 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Escherichia urinary tract infection			
subjects affected / exposed	1 / 2001 (0.05%)	0 / 2002 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis viral			
subjects affected / exposed	0 / 2001 (0.00%)	1 / 2002 (0.05%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
H1N1 influenza			
subjects affected / exposed	1 / 2001 (0.05%)	0 / 2002 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hookworm infection			

subjects affected / exposed	1 / 2001 (0.05%)	0 / 2002 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Impetigo			
subjects affected / exposed	0 / 2001 (0.00%)	2 / 2002 (0.10%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Influenza			
subjects affected / exposed	0 / 2001 (0.00%)	1 / 2002 (0.05%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal sepsis			
subjects affected / exposed	0 / 2001 (0.00%)	1 / 2002 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Joint abscess			
subjects affected / exposed	1 / 2001 (0.05%)	0 / 2002 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Joint tuberculosis			
subjects affected / exposed	1 / 2001 (0.05%)	0 / 2002 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lip infection			
subjects affected / exposed	1 / 2001 (0.05%)	0 / 2002 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower respiratory tract infection bacterial			
subjects affected / exposed	1 / 2001 (0.05%)	0 / 2002 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung abscess			
subjects affected / exposed	1 / 2001 (0.05%)	0 / 2002 (0.00%)	

occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung infection			
subjects affected / exposed	1 / 2001 (0.05%)	0 / 2002 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meningitis			
subjects affected / exposed	0 / 2001 (0.00%)	1 / 2002 (0.05%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meningitis listeria			
subjects affected / exposed	1 / 2001 (0.05%)	0 / 2002 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nasopharyngitis			
subjects affected / exposed	1 / 2001 (0.05%)	0 / 2002 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Necrotising fasciitis			
subjects affected / exposed	0 / 2001 (0.00%)	1 / 2002 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Oesophageal candidiasis			
subjects affected / exposed	1 / 2001 (0.05%)	0 / 2002 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ophthalmic herpes zoster			
subjects affected / exposed	0 / 2001 (0.00%)	1 / 2002 (0.05%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oral infection			
subjects affected / exposed	1 / 2001 (0.05%)	0 / 2002 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	

deaths causally related to treatment / all	0 / 0	0 / 0	
Parotitis			
subjects affected / exposed	0 / 2001 (0.00%)	1 / 2002 (0.05%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumocystis jirovecii pneumonia			
subjects affected / exposed	0 / 2001 (0.00%)	1 / 2002 (0.05%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia pseudomonal			
subjects affected / exposed	1 / 2001 (0.05%)	0 / 2002 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Progressive multifocal leukoencephalopathy			
subjects affected / exposed	0 / 2001 (0.00%)	1 / 2002 (0.05%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory tract infection viral			
subjects affected / exposed	1 / 2001 (0.05%)	0 / 2002 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Retroperitoneal abscess			
subjects affected / exposed	1 / 2001 (0.05%)	0 / 2002 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sinusitis			
subjects affected / exposed	1 / 2001 (0.05%)	0 / 2002 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Staphylococcal infection			
subjects affected / exposed	1 / 2001 (0.05%)	0 / 2002 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Subdiaphragmatic abscess			
subjects affected / exposed	1 / 2001 (0.05%)	0 / 2002 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Superinfection			
subjects affected / exposed	1 / 2001 (0.05%)	1 / 2002 (0.05%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tooth abscess			
subjects affected / exposed	0 / 2001 (0.00%)	1 / 2002 (0.05%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tuberculosis gastrointestinal			
subjects affected / exposed	0 / 2001 (0.00%)	1 / 2002 (0.05%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tubo-ovarian abscess			
subjects affected / exposed	1 / 2001 (0.05%)	0 / 2002 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper respiratory tract infection			
subjects affected / exposed	0 / 2001 (0.00%)	2 / 2002 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wound infection			
subjects affected / exposed	0 / 2001 (0.00%)	1 / 2002 (0.05%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abscess			
subjects affected / exposed	1 / 2001 (0.05%)	0 / 2002 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chikungunya virus infection			
subjects affected / exposed	0 / 2001 (0.00%)	1 / 2002 (0.05%)	

occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocarditis staphylococcal			
subjects affected / exposed	1 / 2001 (0.05%)	0 / 2002 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gangrene			
subjects affected / exposed	0 / 2001 (0.00%)	1 / 2002 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Oral candidiasis			
subjects affected / exposed	0 / 2001 (0.00%)	1 / 2002 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oral herpes			
subjects affected / exposed	0 / 2001 (0.00%)	1 / 2002 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Staphylococcal sepsis			
subjects affected / exposed	1 / 2001 (0.05%)	0 / 2002 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Staphylococcal skin infection			
subjects affected / exposed	0 / 2001 (0.00%)	1 / 2002 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Viral diarrhoea			
subjects affected / exposed	0 / 2001 (0.00%)	1 / 2002 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 1 %

Non-serious adverse events	Placebo	Belimumab 10 mg/kg	
Total subjects affected by non-serious adverse events subjects affected / exposed	31 / 2001 (1.55%)	17 / 2002 (0.85%)	
Infections and infestations Herpes zoster subjects affected / exposed	31 / 2001 (1.55%)	17 / 2002 (0.85%)	
occurrences (all)	33	17	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
01 August 2012	Amendment No.1: Inclusion and exclusion criteria for the study were modified, including clarification of SLE diagnosis, adding a screening pregnancy test, and clarifying contraceptive use. The screening period was reduced from 90 to 30 days to better fit use of the Safety of Estrogen in Lupus National Assessment (SELENA) - Systemic Lupus Erythematosus Disease Activity Index (SLEDAI). The Systemic Lupus International Collaborating Clinics (SLICC)/American College of Rheumatology (ACR) was moved from screening to Baseline to avoid unnecessary efforts assessing SLICC on screen failures. Participants who required hemodialysis or high dose prednisone were excluded if these happened within 90 days prior to screening. Use of concomitant medications was updated to include mepacrine an antimalarial, and capture of dose and frequency of all SLE concomitant medications was added. Clarifications to the use of concomitant SLE medications and commercial belimumab were made. Commercial belimumab remained prohibited during year 1, however a participant could receive it during the follow up period. Assessment of serious infusion or hypersensitivity reactions was removed from the Week 52 visit as no Week 52 study drug was administered. The major efficacy endpoint of steroid reduction was clarified to include patients with involuntary reductions in concomitant immunomodulators. Amendment 01 clarified that participants could participate in the main study without participating in the pharmacogenetic sub-study. As a protocol addition, participants that withdrew their consent to participate in the study were asked to consent to a Week 52 survival status assessment and annual contacts in Years 2 to 5. Further clarification was also provided on the definition of 'opportunistic infection' and 'infections of interest' were expanded to include Hepatitis B, Hepatitis C, and herpes zoster.
15 March 2013	Lithuanian Local Amendment: Exclusion criteria were expanded to include participants with hypogammaglobulinaemia, a deficiency in immunoglobulin A, any renal, major organ or stem cell/marrow transplant, and if the participant had a history of recurrent or chronic infection. The exclusion criteria were also expanded to include cyclophosphamide use within 90 days of screening, and cyclophosphamide use during the study.
13 July 2016	Amendment No.2: This amendment to the protocol was enacted to include detail of interim analyses, to update language surrounding contraceptive use in line with GSK standards, and to modify safety language to ensure alignment with belimumab program standard text. Clarification was also provided on the study design, and typographical errors were fixed.
22 May 2017	Amendment No.3: This amendment was enacted to reduce the target number of randomized participants from 5,000 to 4,000, and to update marketing, safety information on belimumab studies, and delivery method of commercial belimumab. The study design was also further updated and clarified, the location of the Study Procedures Manual was included, and remaining typographical errors were fixed.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported