Clinical trial results:
A Phase 3, Randomized, Double-Blind, Placebo-Controlled Study to Evaluate the Efficacy and Safety of Belimumab plus Standard of Care versus Placebo plus Standard of Care in Adult Subjects with Active Lupus Nephritis

Summary

EudraCT number	2011-004570-28
Trial protocol	HU DE GB BE ES CZ NL FR
Global end of trial date	12 March 2020

Results information

Result version number	v2 (current)
This version publication date	11 March 2021
First version publication date	27 June 2020
Version creation reason	

Trial information

Trial identification

Sponsor protocol code	BEL114054

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,
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	Final
Date of interim/final analysis	24 June 2020
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	12 March 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The purpose of this study is to evaluate the efficacy, safety, and tolerability of belimumab in adult participants with active lupus nephritis.

Protection of trial subjects:

Not Applicable

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	12 July 2012
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Argentina: 34
Country: Number of subjects enrolled	Belgium: 13
Country: Number of subjects enrolled	Brazil: 32
Country: Number of subjects enrolled	Canada: 1
Country: Number of subjects enrolled	China: 79
Country: Number of subjects enrolled	Colombia: 2
Country: Number of subjects enrolled	Czechia: 2
Country: Number of subjects enrolled	France: 19
Country: Number of subjects enrolled	Germany: 16
Country: Number of subjects enrolled	Hong Kong: 6
Country: Number of subjects enrolled	Hungary: 5
Country: Number of subjects enrolled	Korea, Republic of: 43
Country: Number of subjects enrolled	Mexico: 5
Country: Number of subjects enrolled	Netherlands: 10
Country: Number of subjects enrolled	Philippines: 45
Country: Number of subjects enrolled	Russian Federation: 9
Country: Number of subjects enrolled	Spain: 5
Country: Number of subjects enrolled	Taiwan: 14
Country: Number of subjects enrolled	Thailand: 25
Country: Number of subjects enrolled	United Kingdom: 7
Country: Number of subjects enrolled	United States: 76

Worldwide total number of subjects	448
EEA total number of subjects	70

Notes:

Subjects enrolled per age group	
In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	446
From 65 to 84 years	2
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This study evaluated safety and efficacy of IV belimumab 10mg/kg plus SoC compared to placebo plus SoC in adult participants with active lupus nephritis. This was a Phase3, multi-center, multi-national study consisting of a randomized, double-blind, placebo-controlled period and an open-label extension period.The study was conducted in 21 countries

Pre-assignment

Screening details:

A total of 797 participants were screened of which 349 participants failed screening and 448 participants were randomized in double-blind period. In open-label period, a total of 257 participants were enrolled of which 2 participants did not receive open-label study treatment and 255 participants received open-label belimumab.

Period 1

Period 1 title	Double-blind period (Up to Week 104)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Carer, Data analyst, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo to Belimumab 10 mg/kg

Arm description:

Participants were randomized to receive matching placebo intravenous (IV) plus standard of care (SoC) on Days 0 (Baseline), 14, 28 and then every 28 days thereafter through 100 Weeks with a final evaluation for the double-blind treatment period at Week 104. The randomization was stratified by their induction regimen (high dose cortiocsteroids [HDCS] plus Cyclophosphamide [CYC] versus [vs.] HDCS plus Mycophenolate Mofetil [MMF]) and race. After completing the double-blind period, eligible participants that were randomized to placebo IV plus SOC received Belimumab 10 milligram per kilogram (mg/kg) every 28 days until Week 24 with a final evaluation at Week 28 (4 weeks after the last dose) in open-label extension period.

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:

In double-blind period, participants were administered with Placebo IV along with SoC on Days 0, 14, 28, and then every 28 days thereafter through Week 100, with a final evaluation at Week 104

Arm title	Belimumab 10 mg/kg to Belimumab 10 mg/kg

Arm description:

Participants were randomized to receive Belimumab 10 mg/kg IV plus SoC on Days 0 (Baseline), 14, 28 and then every 28 days thereafter through 100 Weeks with a final evaluation for the double-blind treatment period at Week 104. The randomization was stratified by their induction regimen (HDCS plus CYC vs. HDCS plus MMF) and race. After completing the double-blind period, eligible participants that were randomized to belimumab 10 mg/kg IV plus SOC continued to receive Belimumab 10 mg/kg every 28 days until Week 24 with a final evaluation at Week 28 (4 weeks after the last dose) in open-label extension period.

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:

In double-blind period, all participants were administered with Belimumab 10 mg/kg IV along with SoC on Days 0, 14, 28, and then every 28 days thereafter through Week 100, with a final evaluation at Week 104.

Number of subjects in period 1	Placebo to Belimumab 10 mg/kg	Belimumab 10 mg/kg to Belimumab 10 mg/kg
Started	224	224
Completed	170	186
Not completed	54	38
Adverse event, serious fatal	5	6
Consent withdrawn by subject	26	19
Physician decision	11	5
Adverse event, non-fatal	5	1
Lost to follow-up	5	4
Lack of efficacy	2	1
Protocol deviation	-	2

Period 2

Period 2 title	Open-label period (Up to Week 28)
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo to Belimumab 10 mg/kg

Arm description:

Participants were randomized to receive matching placebo intravenous (IV) plus standard of care (SoC) on Days 0 (Baseline), 14, 28 and then every 28 days thereafter through 100 Weeks with a final evaluation for the double-blind treatment period at Week 104. The randomization was stratified by their induction regimen (high dose cortiocsteroids [HDCS] plus Cyclophosphamide [CYC] versus [vs.] HDCS plus Mycophenolate Mofetil [MMF]) and race. After completing the double-blind period, eligible participants that were randomized to placebo IV plus SOC received Belimumab 10 mg/kg every 28 days until Week 24 with a final evaluation at Week 28 (4 weeks after the last dose) in open-label extension period.

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:

In open-label extension period, eligible participants received Belimumab 10 mg/kg every 28 days until Week 24 with a final evaluation at Week 28 (4 weeks after the last dose).

Arm title	Belimumab 10 mg/kg to Belimumab 10 mg/kg

Arm description:

Participants were randomized to receive Belimumab 10 mg/kg IV plus SoC on Days 0 (Baseline), 14, 28 and then every 28 days thereafter through 100 Weeks with a final evaluation for the double-blind treatment period at Week 104. The randomization was stratified by their induction regimen (HDCS plus CYC vs. HDCS plus MMF) and race. After completing the double-blind period, eligible participants that were randomized to belimumab 10 mg/kg IV plus SOC continued to receive Belimumab 10 mg/kg every 28 days until Week 24 with a final evaluation at Week 28 (4 weeks after the last dose) in open-label extension period.

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:

In open-label extension period, eligible participants received Belimumab 10 mg/kg every 28 days until Week 24 with a final evaluation at Week 28 (4 weeks after the last dose).

Number of subjects in period 2[1]	Placebo to Belimumab 10 mg/kg	Belimumab 10 mg/kg to Belimumab 10 mg/kg
Started	123	132
Completed	122	124
Not completed	1	8
Adverse event, serious fatal	1	-
Consent withdrawn by subject	-	2
Adverse event, non-fatal	-	4
Lost to follow-up	-	1
Protocol deviation	-	1

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.
Justification: Of the 356 participants who completed the double-blind period, 279 were eligible for open-label treatment. As enrolling into the open-label period was optional, only 257 participants enrolled, of whom 255 started open-label treatment.

Baseline characteristics

Reporting groups

Reporting group title	Placebo to Belimumab 10 mg/kg

Reporting group description:

Participants were randomized to receive matching placebo intravenous (IV) plus standard of care (SoC) on Days 0 (Baseline), 14, 28 and then every 28 days thereafter through 100 Weeks with a final evaluation for the double-blind treatment period at Week 104. The randomization was stratified by their induction regimen (high dose cortiocsteroids [HDCS] plus Cyclophosphamide [CYC] versus [vs.] HDCS plus Mycophenolate Mofetil [MMF]) and race. After completing the double-blind period, eligible participants that were randomized to placebo IV plus SOC received Belimumab 10 milligram per kilogram (mg/kg) every 28 days until Week 24 with a final evaluation at Week 28 (4 weeks after the last dose) in open-label extension period.

Reporting group title	Belimumab 10 mg/kg to Belimumab 10 mg/kg

Reporting group description:

Participants were randomized to receive Belimumab 10 mg/kg IV plus SoC on Days 0 (Baseline), 14, 28 and then every 28 days thereafter through 100 Weeks with a final evaluation for the double-blind treatment period at Week 104. The randomization was stratified by their induction regimen (HDCS plus CYC vs. HDCS plus MMF) and race. After completing the double-blind period, eligible participants that were randomized to belimumab 10 mg/kg IV plus SOC continued to receive Belimumab 10 mg/kg every 28 days until Week 24 with a final evaluation at Week 28 (4 weeks after the last dose) in open-label extension period.

Reporting group values	Placebo to Belimumab 10 mg/kg	Belimumab 10 mg/kg to Belimumab 10 mg/kg	Total
Number of subjects	224	224	448
Age categorical			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	222	224	446
From 65-84 years	2	0	2
85 years and over	0	0	0
Age Continuous			
Units: Years			
arithmetic mean	33.0	33.7	
standard deviation	± 10.64	± 10.73	-
Sex: Female, Male			
Units: Participants			
Female	196	198	394
Male	28	26	54
Race/Ethnicity, Customized			
Units: Subjects			
American Indian (AI) or Alaska Native (AN)	6	4	10
Asian-Central/South Asian Heritage (H)	2	3	5

Asian-Japanese/East Asian/Southeast Asian H	107	112	219
Mixed Asian	1	0	1
Black or African American (AA)	31	30	61
White/Caucasian/European H	71	72	143
White/Caucasian/Arabic/North African H	4	1	5
Multiple-AA/African H and AI or AN and White	1	1	2
Multiple-Asian and White	1	1	2

End points

End points reporting groups

Reporting group title	Placebo to Belimumab 10 mg/kg

Reporting group description:

Participants were randomized to receive matching placebo intravenous (IV) plus standard of care (SoC) on Days 0 (Baseline), 14, 28 and then every 28 days thereafter through 100 Weeks with a final evaluation for the double-blind treatment period at Week 104. The randomization was stratified by their induction regimen (high dose cortiocsteroids [HDCS] plus Cyclophosphamide [CYC] versus [vs.] HDCS plus Mycophenolate Mofetil [MMF]) and race. After completing the double-blind period, eligible participants that were randomized to placebo IV plus SOC received Belimumab 10 milligram per kilogram (mg/kg) every 28 days until Week 24 with a final evaluation at Week 28 (4 weeks after the last dose) in open-label extension period.

Reporting group title	Belimumab 10 mg/kg to Belimumab 10 mg/kg

Reporting group description:

Participants were randomized to receive Belimumab 10 mg/kg IV plus SoC on Days 0 (Baseline), 14, 28 and then every 28 days thereafter through 100 Weeks with a final evaluation for the double-blind treatment period at Week 104. The randomization was stratified by their induction regimen (HDCS plus CYC vs. HDCS plus MMF) and race. After completing the double-blind period, eligible participants that were randomized to belimumab 10 mg/kg IV plus SOC continued to receive Belimumab 10 mg/kg every 28 days until Week 24 with a final evaluation at Week 28 (4 weeks after the last dose) in open-label extension period.

Reporting group title	Placebo to Belimumab 10 mg/kg

Reporting group description:

Participants were randomized to receive matching placebo intravenous (IV) plus standard of care (SoC) on Days 0 (Baseline), 14, 28 and then every 28 days thereafter through 100 Weeks with a final evaluation for the double-blind treatment period at Week 104. The randomization was stratified by their induction regimen (high dose cortiocsteroids [HDCS] plus Cyclophosphamide [CYC] versus [vs.] HDCS plus Mycophenolate Mofetil [MMF]) and race. After completing the double-blind period, eligible participants that were randomized to placebo IV plus SOC received Belimumab 10 mg/kg every 28 days until Week 24 with a final evaluation at Week 28 (4 weeks after the last dose) in open-label extension period.

Reporting group title	Belimumab 10 mg/kg to Belimumab 10 mg/kg

Reporting group description:

Participants were randomized to receive Belimumab 10 mg/kg IV plus SoC on Days 0 (Baseline), 14, 28 and then every 28 days thereafter through 100 Weeks with a final evaluation for the double-blind treatment period at Week 104. The randomization was stratified by their induction regimen (HDCS plus CYC vs. HDCS plus MMF) and race. After completing the double-blind period, eligible participants that were randomized to belimumab 10 mg/kg IV plus SOC continued to receive Belimumab 10 mg/kg every 28 days until Week 24 with a final evaluation at Week 28 (4 weeks after the last dose) in open-label extension period.

Subject analysis set title	Placebo
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants were randomized to receive matching placebo IV plus SoC on Days 0 (Baseline), 14, 28 and then every 28 days thereafter through 100 Weeks with a final evaluation for the double-blind treatment period at Week 104. The randomization was stratified by their induction regimen (high dose cortiocsteroids [HDCS] plus Cyclophosphamide [CYC] versus [vs.] HDCS plus Mycophenolate Mofetil [MMF]) and race.

Subject analysis set title	Belimumab 10 mg/kg
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants were randomized to receive Belimumab 10 milligrams per kilogram (mg/kg) IV plus SoC on Days 0 (Baseline), 14, 28 and then every 28 days thereafter through 100 Weeks with a final evaluation for the double-blind treatment period at Week 104. The randomization was stratified by their induction regimen (HDCS plus CYC vs. HDCS plus MMF) and race.

Primary: Double-blind period: Percentage of participants with primary efficacy renal response (PERR) at Week 104

End point title	Double-blind period: Percentage of participants with primary efficacy renal response (PERR) at Week 104

End point description:

PERR is defined as urinary protein creatinine ratio <=0.7, estimated glomerular filtration rate (eGRF) was not more than 20 percent (%) below the pre-flare value or >=60 milliliters per minute per 1.73 square meter (mL/min/1.73m^2) and was not a treatment failure. Analysis was performed using a logistic regression model for the comparison between Belimumab and Placebo with covariates treatment group, induction regimen (CYC vs. MMF), race (Black vs. Non-Black), Baseline urine protein-creatinine ratio (uPCR), and Baseline eGFR. Modified Intent-to-treat (mITT) Population consisted of all randomized participants who received at least one dose of study treatment and were not excluded due to Good Clinical Practice (GCP) non-compliance. Percentage of participants with PERR at Week 104 has been presented.

End point type	Primary

End point timeframe:

Week 104

End point values	Placebo	Belimumab 10 mg/kg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	223[1]	223[2]		
Units: Percentage of participants				
number (not applicable)	32.3	43.0		

Notes:

[1] - mITT Population

[2] - mITT Population

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Treatment comparison between Belimumab 10 mg/kg and placebo using odds ratio and its corresponding 95% confidence interval has been presented.

Comparison groups	Placebo v Belimumab 10 mg/kg
Number of subjects included in analysis	446
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0311 [3]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.55
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.04
upper limit	2.32

Notes:

[3] - P-value was calculated using logistic regression model. Test 1 of 5 in a step-down sequential testing procedure.

Primary: Open-label period: Number of participants reporting adverse events (AEs) and serious AEs (SAEs)

End point title	Open-label period: Number of participants reporting adverse events (AEs) and serious AEs (SAEs)[4]

End point description:

An AE is any untoward medical occurrence in a participant or clinical investigation participant, temporarily associated with the use of a medicinal product, whether or not considered related to the medicinal product. A SAE is any untoward medical occurrence that, at any dose: resulting in death, is life threatening, requires hospitalization or prolongation of existing hospitalization, results in disability/incapacity, is a congenital anomaly/birth defect, any other situation according to medical or scientific judgment or all events of possible drug-induced liver injury with hyperbilirubinemia were categorized as SAE. Number of participants with AEs and SAEs have been reported.

End point type	Primary

End point timeframe:

From first open-label dose up to open-label Week 32 (8 weeks after last dose)

Notes:

[4] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There are no statistical data to report.

End point values	Placebo to Belimumab 10 mg/kg	Belimumab 10 mg/kg to Belimumab 10 mg/kg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	123[5]	132[6]		
Units: Participants				
Any AE	76	92		
Any SAE	5	10		

Notes:

[5] - Safety open-label population comprised of participants who received one dose of open-label treatment
[6] - Safety open-label population

Statistical analyses

No statistical analyses for this end point

Primary: Open-label period: Number of participants reporting adverse events of special interest (AESI)

End point title	Open-label period: Number of participants reporting adverse events of special interest (AESI)[7]

End point description:

An AESI is one of scientific and medical concern specific to the product, for which ongoing monitoring and rapid communication by investigator to sponsor can be appropriate. A summary of protocol defined AESIs include malignant neoplasms including and excluding non-melanoma skin cancer (NMSC), post-infusion systemic reactions (PISR), all infections of special interest (opportunistic infections [OI], Herpes Zoster [HZ], tuberculosis [TB], and sepsis), depression (including mood disorders and anxiety)/suicide/self-injury and deaths.

End point type	Primary

End point timeframe:

From first open-label dose up to open-label Week 32 (8 weeks after last dose)

Notes:

[7] - 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: There are no statistical data to report.

End point values	Placebo to Belimumab 10 mg/kg	Belimumab 10 mg/kg to Belimumab 10 mg/kg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	123[8]	132[9]		
Units: Participants				
Malignancies excluding NMSC	0	0		
Malignancies including NMSC	0	0		
PISR	4	5		
All infections of special interest	2	6		
Depression/suicide/self-injury	2	4		
Deaths	1	0		

Notes:

[8] - Safety open-label population

[9] - Safety open-label population

Statistical analyses

No statistical analyses for this end point

Secondary: Double-blind period: Percentage of participants with complete renal response (CRR) at Week 104

End point title	Double-blind period: Percentage of participants with complete renal response (CRR) at Week 104

End point description:

CRR is defined as urinary protein creatinine ratio <0.5, eGRF was not more than 10% below the pre-flare value or >=90 mL/min/1.73m^2 and was not a treatment failure. Analysis was performed using a logistic regression model for the comparison between Belimumab and Placebo with covariates of induction regimen (CYC vs. MMF), race (Black vs. Non-Black), Baseline uPCR and Baseline eGFR. Percentage of participants with CRR at Week 104 has been presented.

End point type	Secondary

End point timeframe:

Week 104

End point values	Placebo	Belimumab 10 mg/kg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	223[10]	223[11]		
Units: Percentage of participants				
number (not applicable)	19.7	30.0		

Notes:

[10] - mITT Population.

[11] - mITT Population.

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Treatment comparison between Belimumab 10 mg/kg and placebo using odds ratio and its corresponding 95% confidence interval has been presented.

Comparison groups	Placebo v Belimumab 10 mg/kg

Number of subjects included in analysis	446
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0167 [12]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.74
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.11
upper limit	2.74

Notes:

[12] - P-value was calculated using logistic regression model. Test 2 of 5 in a step-down sequential testing procedure

Secondary: Double-blind period: Percentage of participants with PERR at Week 52

End point title	Double-blind period: Percentage of participants with PERR at Week 52

End point description:

PERR is defined as urinary protein creatinine ratio <=0.7, eGRF was not more than 20% below the pre-flare value or >=60 mL/min/1.73m^2 and was not a treatment failure. Analysis was performed using a logistic regression model for the comparison between Belimumab and Placebo with covariates of induction regimen (CYC vs. MMF), race (Black vs. Non-Black), uPCR, and Baseline eGFR. Percentage of participants with PERR at Week 52 has been presented.

End point type	Secondary

End point timeframe:

Week 52

End point values	Placebo	Belimumab 10 mg/kg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	223[13]	223[14]		
Units: Percentage of participants				
number (not applicable)	35.4	46.6		

Notes:

[13] - mITT Population.

[14] - mITT Population.

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Treatment comparison between Belimumab 10 mg/kg and placebo using odds ratio and its corresponding 95% confidence interval has been presented.

Comparison groups	Placebo v Belimumab 10 mg/kg

Number of subjects included in analysis	446
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0245 [15]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.59
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.06
upper limit	2.38

Notes:

[15] - P-value was calculated using logistic regression model. Test 3 of 5 in a step-down sequential testing procedure.

Secondary: Double-blind period: Number of participants with time to death or renal related event

End point title	Double-blind period: Number of participants with time to death or renal related event

End point description:

Events are defined as the first event experienced among the following: death, progression to end stage renal disease, doubling of serum creatinine from Baseline, renal worsening or renal-related treatment failure. Participants who discontinued randomized treatment, withdrew from the study, were lost to follow-up, or had a non renal-related treatment failure were censored. Participants who completed the 104-week treatment period were censored at the Week 104 visit. Time to event is defined as event date minus treatment start date plus one. Analysis was performed using Cox proportional hazards model for the comparison between Belimumab and Placebo adjusting for induction regimen, race, baseline uPCR and Baseline eGFR. Number of participants with time to death or renal related event up to Week 104 has been presented.

End point type	Secondary

End point timeframe:

Up to Week 104

End point values	Placebo	Belimumab 10 mg/kg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	223[16]	223[17]		
Units: Participants	63	35		

Notes:

[16] - mITT Population.

[17] - mITT Population.

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Treatment comparison between Belimumab 10 mg/kg and placebo using Cox proportional hazards ratio and its corresponding 95% confidence interval has been presented.

Comparison groups	Placebo v Belimumab 10 mg/kg

Number of subjects included in analysis	446
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0014 [18]
Method	Cox proportional hazards model
Parameter estimate	Cox proportional hazard
Point estimate	0.51
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.34
upper limit	0.77

Notes:

[18] - P-value was calculated using Cox proportional hazards model. Test 4 of 5 in a step-down sequential testing procedure.

Secondary: Double-blind period: Percentage of participants with ordinal renal response (ORR) at Week 104

End point title	Double-blind period: Percentage of participants with ordinal renal response (ORR) at Week 104

End point description:

ORR is defined with respect to reproducible responses that included CRR, partial RR (PRR) and non responder. CRR is reported when uPCR was <0.5, eGFR was not more than 10% below pre-flare GFR or within normal range and not a treatment failure. PRR is >=50% decrease from Baseline in uPCR and one of the following: value <1 if Baseline <=3, or value <3 if the Baseline was >3, eGFR not more than 10% below Baseline GFR or within normal range and not a treatment failure and not a CRR. Non responder is reported when neither CRR nor PRR criteria was met. Percentage of participants reporting CRR, PRR and non responders at Week 104 has been presented.

End point type	Secondary

End point timeframe:

Week 104

End point values	Placebo	Belimumab 10 mg/kg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	223[19]	223[20]		
Units: Percentage of participants				
number (not applicable)				
CRR	19.7	30.0		
PRR	17.0	17.5		
Non responder	63.2	52.5		

Notes:

[19] - mITT Population.

[20] - mITT Population.

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo v Belimumab 10 mg/kg

Number of subjects included in analysis	446
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0096 [21]
Method	Rank ANCOVA

Notes:

[21] - P-value is rank analysis of covariance model comparing Belimumab and Placebo with covariates for treatment group, induction regimen(CYC vs MMF),race(Black vs Non-black), Baseline uPCR, and eGFR. Test 5 of
5 in step-down sequential testing procedure.

Secondary: Double-blind period: Number of participants reporting on-treatment AEs and SAEs

End point title	Double-blind period: Number of participants reporting on-treatment AEs and SAEs

End point description:

An AE is any untoward medical occurrence in a participant or clinical investigation participant, temporarily associated with the use of a medicinal product, whether or not considered related to the medicinal product. A SAE is any untoward medical occurrence that, at any dose: resulting in death, is life threatening, requires hospitalization or prolongation of existing hospitalization, results in disability/incapacity, is a congenital anomaly/birth defect, any other situation according to medical or scientific judgment or all events of possible drug-induced liver injury with hyperbilirubinemia were categorized as SAE. Number of participants with on-treatment AEs and SAEs has been reported.

End point type	Secondary

End point timeframe:

Up to Week 104

End point values	Placebo	Belimumab 10 mg/kg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	224[22]	224[23]		
Units: Participants				
AE	211	214		
SAE	67	58		

Notes:

[22] - Safety Population comprised of all randomized participants who received one dose of study treatment
[23] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Double-blind period: Number of participants reporting AESI

End point title	Double-blind period: Number of participants reporting AESI

End point description:

An AESI is one of scientific and medical concern specific to the product, for which ongoing monitoring and rapid communication by investigator to sponsor can be appropriate. A summary of protocol defined AESIs include malignant neoplasms including and excluding non-melanoma skin cancer (NMSC), post-infusion systemic reactions (PISR), all infections of special interest (opportunistic infections [OI], Herpes Zoster [HZ], tuberculosis [TB], and sepsis), depression (including mood disorders and anxiety)/suicide/self-injury and deaths. On-treatment data is displayed.

End point type	Secondary

End point timeframe:
Up to Week 104

End point values	Placebo	Belimumab 10 mg/kg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	224[24]	224[25]		
Units: Participants				
Malignancies excluding NMSC	0	2		
Malignancies including NMSC	0	3		
PISR	29	26		
All infections of special interest	34	30		
Depression/suicide/self-injury	16	11		
Deaths	3	4		

Notes:
[24] - Safety Population
[25] - Safety Population

Statistical analyses

No statistical analyses for this end point

Adverse events information

Timeframe for reporting adverse events:

All-cause mortality, non-SAEs and SAEs were summarised from the start of the first treatment up to Week 104 in double-blind period and from the first open-label dose up to Week 32 (8 weeks after last dose) in open-label extension period.

Adverse event reporting additional description:

All-cause mortality, non-SAEs and SAEs were reported for safety population (double-blind period) and safety open-label population (open-label period). Non-serious adverse events not meeting 5% in the open label period were reported as 0% incidence but could have incidences between 0 and 5%.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	22.0

Reporting groups

Reporting group title	Placebo

Reporting group description:

Participants were randomized to receive matching placebo IV plus SoC on Days 0 (Baseline), 14, 28 and then every 28 days thereafter through 100 Weeks with a final evaluation for the double-blind treatment period at Week 104. The randomization was stratified by their induction regimen (high dose cortiocsteroids [HDCS] plus Cyclophosphamide [CYC] versus [vs.] HDCS plus Mycophenolate Mofetil [MMF]) and race.

Reporting group title	Belimumab 10 mg/kg

Reporting group description:

Participants were randomized to receive Belimumab 10 mg/kg IV plus SoC on Days 0 (Baseline), 14, 28 and then every 28 days thereafter through 100 Weeks with a final evaluation for the double-blind treatment period at Week 104. The randomization was stratified by their induction regimen (HDCS plus CYC vs. HDCS plus MMF) and race.

Reporting group title	Placebo to Belimumab 10 mg/kg

Reporting group description:

Participants were randomized to receive matching placebo intravenous (IV) plus standard of care (SoC) on Days 0 (Baseline), 14, 28 and then every 28 days thereafter through 100 Weeks with a final evaluation for the double-blind treatment period at Week 104. The randomization was stratified by their induction regimen (high dose cortiocsteroids [HDCS] plus Cyclophosphamide [CYC] versus [vs.] HDCS plus Mycophenolate Mofetil [MMF]) and race. After completing the double-blind period, eligible participants that were randomized to placebo IV plus SOC received Belimumab 10 milligram per kilogram (mg/kg) every 28 days until Week 24 with a final evaluation at Week 28 (4 weeks after the last dose) in open-label extension period.

Reporting group title	Belimumab 10 mg/kg to Belimumab 10 mg/kg

Reporting group description:

Participants were randomized to receive Belimumab 10 mg/kg IV plus SoC on Days 0 (Baseline), 14, 28 and then every 28 days thereafter through 100 Weeks with a final evaluation for the double-blind treatment period at Week 104. The randomization was stratified by their induction regimen (HDCS plus CYC vs. HDCS plus MMF) and race. After completing the double-blind period, eligible participants that were randomized to belimumab 10 mg/kg IV plus SOC continued to receive Belimumab 10 mg/kg every 28 days until Week 24 with a final evaluation at Week 28 (4 weeks after the last dose) in open-label extension period.

Serious adverse events	Placebo	Belimumab 10 mg/kg	Placebo to Belimumab 10 mg/kg
Total subjects affected by serious adverse events			
subjects affected / exposed	78 / 224 (34.82%)	65 / 224 (29.02%)	5 / 123 (4.07%)

number of deaths (all causes) number of deaths resulting from adverse events	5	6	1
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Papillary thyroid cancer			
subjects affected / exposed	0 / 224 (0.00%)	1 / 224 (0.45%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thymoma			
subjects affected / exposed	0 / 224 (0.00%)	1 / 224 (0.45%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 224 (0.45%)	2 / 224 (0.89%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 1	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0
Hypotension			
subjects affected / exposed	1 / 224 (0.45%)	1 / 224 (0.45%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Deep vein thrombosis			
subjects affected / exposed	0 / 224 (0.00%)	1 / 224 (0.45%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertensive emergency			
subjects affected / exposed	1 / 224 (0.45%)	0 / 224 (0.00%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Shock haemorrhagic			
subjects affected / exposed	1 / 224 (0.45%)	0 / 224 (0.00%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombosis			

subjects affected / exposed	0 / 224 (0.00%)	1 / 224 (0.45%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pregnancy, puerperium and perinatal conditions			
Abortion missed			
subjects affected / exposed	1 / 224 (0.45%)	0 / 224 (0.00%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Foetal death			
subjects affected / exposed	0 / 224 (0.00%)	1 / 224 (0.45%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Prolonged labour			
subjects affected / exposed	1 / 224 (0.45%)	0 / 224 (0.00%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Unintended pregnancy			
subjects affected / exposed	0 / 224 (0.00%)	0 / 224 (0.00%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	3 / 224 (1.34%)	2 / 224 (0.89%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	1 / 3	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Non-cardiac chest pain			
subjects affected / exposed	2 / 224 (0.89%)	2 / 224 (0.89%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Asthenia			
subjects affected / exposed	2 / 224 (0.89%)	0 / 224 (0.00%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Fatigue			
subjects affected / exposed	1 / 224 (0.45%)	0 / 224 (0.00%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Generalised oedema			
subjects affected / exposed	0 / 224 (0.00%)	1 / 224 (0.45%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mucosal inflammation			
subjects affected / exposed	0 / 224 (0.00%)	1 / 224 (0.45%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pain			
subjects affected / exposed	1 / 224 (0.45%)	0 / 224 (0.00%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Serositis			
subjects affected / exposed	1 / 224 (0.45%)	0 / 224 (0.00%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Systemic inflammatory response syndrome			
subjects affected / exposed	0 / 224 (0.00%)	1 / 224 (0.45%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Multiple organ dysfunction syndrome			
subjects affected / exposed	0 / 224 (0.00%)	0 / 224 (0.00%)	1 / 123 (0.81%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	0 / 224 (0.00%)	1 / 224 (0.45%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Immunosuppression			
subjects affected / exposed	0 / 224 (0.00%)	1 / 224 (0.45%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Cervical dysplasia			
subjects affected / exposed	1 / 224 (0.45%)	0 / 224 (0.00%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endometriosis			
subjects affected / exposed	0 / 224 (0.00%)	1 / 224 (0.45%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure			
subjects affected / exposed	2 / 224 (0.89%)	1 / 224 (0.45%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 2	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleural effusion			
subjects affected / exposed	2 / 224 (0.89%)	1 / 224 (0.45%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	1 / 2	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute pulmonary oedema			
subjects affected / exposed	1 / 224 (0.45%)	0 / 224 (0.00%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aspiration			
subjects affected / exposed	0 / 224 (0.00%)	1 / 224 (0.45%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspnoea			

subjects affected / exposed	0 / 224 (0.00%)	1 / 224 (0.45%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0
Organizing pneumonia			
subjects affected / exposed	0 / 224 (0.00%)	1 / 224 (0.45%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumomediastinum			
subjects affected / exposed	0 / 224 (0.00%)	1 / 224 (0.45%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumothorax			
subjects affected / exposed	1 / 224 (0.45%)	0 / 224 (0.00%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary alveolar haemorrhage			
subjects affected / exposed	1 / 224 (0.45%)	0 / 224 (0.00%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary arterial hypertension			
subjects affected / exposed	0 / 224 (0.00%)	1 / 224 (0.45%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			
subjects affected / exposed	0 / 224 (0.00%)	1 / 224 (0.45%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory failure			
subjects affected / exposed	0 / 224 (0.00%)	1 / 224 (0.45%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Mental status changes			

subjects affected / exposed	1 / 224 (0.45%)	0 / 224 (0.00%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Suicide attempt			
subjects affected / exposed	0 / 224 (0.00%)	1 / 224 (0.45%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Blood creatinine increased			
subjects affected / exposed	1 / 224 (0.45%)	0 / 224 (0.00%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood immunoglobulin G decreased			
subjects affected / exposed	1 / 224 (0.45%)	0 / 224 (0.00%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Foetal biophysical profile score equivocal			
subjects affected / exposed	1 / 224 (0.45%)	0 / 224 (0.00%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic enzyme increased			
subjects affected / exposed	1 / 224 (0.45%)	0 / 224 (0.00%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Weight decreased			
subjects affected / exposed	0 / 224 (0.00%)	1 / 224 (0.45%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Skin laceration			
subjects affected / exposed	0 / 224 (0.00%)	2 / 224 (0.89%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Brain herniation			
subjects affected / exposed	1 / 224 (0.45%)	0 / 224 (0.00%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Contusion			
subjects affected / exposed	0 / 224 (0.00%)	1 / 224 (0.45%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Head injury			
subjects affected / exposed	0 / 224 (0.00%)	1 / 224 (0.45%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Joint injury			
subjects affected / exposed	0 / 224 (0.00%)	1 / 224 (0.45%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ligament injury			
subjects affected / exposed	0 / 224 (0.00%)	1 / 224 (0.45%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Post procedural haematoma			
subjects affected / exposed	0 / 224 (0.00%)	1 / 224 (0.45%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal compression fracture			
subjects affected / exposed	1 / 224 (0.45%)	0 / 224 (0.00%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tibia fracture			
subjects affected / exposed	0 / 224 (0.00%)	1 / 224 (0.45%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wrist fracture			

subjects affected / exposed	0 / 224 (0.00%)	1 / 224 (0.45%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Pericardial effusion			
subjects affected / exposed	3 / 224 (1.34%)	0 / 224 (0.00%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 4	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aortic valve incompetence			
subjects affected / exposed	0 / 224 (0.00%)	1 / 224 (0.45%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure acute			
subjects affected / exposed	1 / 224 (0.45%)	0 / 224 (0.00%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure congestive			
subjects affected / exposed	0 / 224 (0.00%)	1 / 224 (0.45%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Pericarditis			
subjects affected / exposed	0 / 224 (0.00%)	1 / 224 (0.45%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pericarditis uraemic			
subjects affected / exposed	1 / 224 (0.45%)	0 / 224 (0.00%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Supraventricular tachycardia			
subjects affected / exposed	1 / 224 (0.45%)	0 / 224 (0.00%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute myocardial infarction			

subjects affected / exposed	0 / 224 (0.00%)	0 / 224 (0.00%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Cerebral infarction			
subjects affected / exposed	1 / 224 (0.45%)	1 / 224 (0.45%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebrovascular accident			
subjects affected / exposed	1 / 224 (0.45%)	1 / 224 (0.45%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Central nervous system lupus			
subjects affected / exposed	1 / 224 (0.45%)	0 / 224 (0.00%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Encephalopathy			
subjects affected / exposed	1 / 224 (0.45%)	0 / 224 (0.00%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 0
Epilepsy			
subjects affected / exposed	1 / 224 (0.45%)	0 / 224 (0.00%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Generalized tonic-clonic seizure			
subjects affected / exposed	0 / 224 (0.00%)	1 / 224 (0.45%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemorrhage intracranial			
subjects affected / exposed	1 / 224 (0.45%)	0 / 224 (0.00%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Headache			

subjects affected / exposed	0 / 224 (0.00%)	1 / 224 (0.45%)	1 / 123 (0.81%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertensive encephalopathy			
subjects affected / exposed	1 / 224 (0.45%)	0 / 224 (0.00%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolic encephalopathy			
subjects affected / exposed	1 / 224 (0.45%)	0 / 224 (0.00%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Polyneuropathy			
subjects affected / exposed	1 / 224 (0.45%)	0 / 224 (0.00%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Posterior reversible encephalopathy syndrome			
subjects affected / exposed	0 / 224 (0.00%)	1 / 224 (0.45%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Seizure			
subjects affected / exposed	1 / 224 (0.45%)	0 / 224 (0.00%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	6 / 224 (2.68%)	1 / 224 (0.45%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 6	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Febrile neutropenia			
subjects affected / exposed	0 / 224 (0.00%)	3 / 224 (1.34%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Leukopenia			

subjects affected / exposed	2 / 224 (0.89%)	1 / 224 (0.45%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancytopenia			
subjects affected / exposed	0 / 224 (0.00%)	2 / 224 (0.89%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bone marrow toxicity			
subjects affected / exposed	0 / 224 (0.00%)	1 / 224 (0.45%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoglobulinaemia			
subjects affected / exposed	1 / 224 (0.45%)	0 / 224 (0.00%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lymphadenopathy			
subjects affected / exposed	1 / 224 (0.45%)	0 / 224 (0.00%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	2 / 224 (0.89%)	2 / 224 (0.89%)	1 / 123 (0.81%)
occurrences causally related to treatment / all	1 / 2	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
subjects affected / exposed	0 / 224 (0.00%)	3 / 224 (1.34%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastritis			
subjects affected / exposed	2 / 224 (0.89%)	1 / 224 (0.45%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	1 / 2	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nausea			

subjects affected / exposed	0 / 224 (0.00%)	2 / 224 (0.89%)	1 / 123 (0.81%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis			
subjects affected / exposed	2 / 224 (0.89%)	0 / 224 (0.00%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain			
subjects affected / exposed	1 / 224 (0.45%)	0 / 224 (0.00%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chronic gastritis			
subjects affected / exposed	0 / 224 (0.00%)	1 / 224 (0.45%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Enteritis			
subjects affected / exposed	0 / 224 (0.00%)	1 / 224 (0.45%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Epiploic appendagitis			
subjects affected / exposed	1 / 224 (0.45%)	0 / 224 (0.00%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal inflammation			
subjects affected / exposed	1 / 224 (0.45%)	0 / 224 (0.00%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemorrhoids			
subjects affected / exposed	1 / 224 (0.45%)	0 / 224 (0.00%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Impaired gastric emptying			

subjects affected / exposed	0 / 224 (0.00%)	1 / 224 (0.45%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Large intestine perforation			
subjects affected / exposed	1 / 224 (0.45%)	0 / 224 (0.00%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vasculitis gastrointestinal			
subjects affected / exposed	1 / 224 (0.45%)	0 / 224 (0.00%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cyclic vomiting syndrome			
subjects affected / exposed	0 / 224 (0.00%)	0 / 224 (0.00%)	1 / 123 (0.81%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain lower			
subjects affected / exposed	0 / 224 (0.00%)	0 / 224 (0.00%)	1 / 123 (0.81%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholecystitis acute			
subjects affected / exposed	0 / 224 (0.00%)	1 / 224 (0.45%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Angioedema			
subjects affected / exposed	1 / 224 (0.45%)	0 / 224 (0.00%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Erythema annulare			
subjects affected / exposed	0 / 224 (0.00%)	1 / 224 (0.45%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Systemic lupus erythematosus rash			

subjects affected / exposed	1 / 224 (0.45%)	0 / 224 (0.00%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Lupus nephritis			
subjects affected / exposed	8 / 224 (3.57%)	2 / 224 (0.89%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 10	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute kidney injury			
subjects affected / exposed	5 / 224 (2.23%)	2 / 224 (0.89%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 5	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
End stage renal disease			
subjects affected / exposed	2 / 224 (0.89%)	1 / 224 (0.45%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nephrotic syndrome			
subjects affected / exposed	0 / 224 (0.00%)	2 / 224 (0.89%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal impairment			
subjects affected / exposed	0 / 224 (0.00%)	2 / 224 (0.89%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Azotaemia			
subjects affected / exposed	1 / 224 (0.45%)	0 / 224 (0.00%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nephrolithiasis			
subjects affected / exposed	1 / 224 (0.45%)	0 / 224 (0.00%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal failure			

subjects affected / exposed	0 / 224 (0.00%)	1 / 224 (0.45%)	1 / 123 (0.81%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endocrine disorders			
Hyperparathyroidism			
subjects affected / exposed	0 / 224 (0.00%)	1 / 224 (0.45%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Systemic lupus erythematosus			
subjects affected / exposed	4 / 224 (1.79%)	1 / 224 (0.45%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 4	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arthralgia			
subjects affected / exposed	2 / 224 (0.89%)	1 / 224 (0.45%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Back pain			
subjects affected / exposed	2 / 224 (0.89%)	1 / 224 (0.45%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Flank pain			
subjects affected / exposed	2 / 224 (0.89%)	0 / 224 (0.00%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intervertebral disc protrusion			
subjects affected / exposed	0 / 224 (0.00%)	1 / 224 (0.45%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal chest pain			
subjects affected / exposed	1 / 224 (0.45%)	0 / 224 (0.00%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Oligoarthritis			
subjects affected / exposed	1 / 224 (0.45%)	0 / 224 (0.00%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteonecrosis			
subjects affected / exposed	1 / 224 (0.45%)	0 / 224 (0.00%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rhabdomyolysis			
subjects affected / exposed	1 / 224 (0.45%)	0 / 224 (0.00%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal osteoarthritis			
subjects affected / exposed	1 / 224 (0.45%)	0 / 224 (0.00%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tendonitis			
subjects affected / exposed	0 / 224 (0.00%)	1 / 224 (0.45%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Muscular weakness			
subjects affected / exposed	0 / 224 (0.00%)	0 / 224 (0.00%)	1 / 123 (0.81%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pain in extremity			
subjects affected / exposed	0 / 224 (0.00%)	0 / 224 (0.00%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Pneumonia			
subjects affected / exposed	10 / 224 (4.46%)	10 / 224 (4.46%)	2 / 123 (1.63%)
occurrences causally related to treatment / all	5 / 11	3 / 11	1 / 2
deaths causally related to treatment / all	0 / 1	2 / 3	0 / 0
Herpes zoster			

subjects affected / exposed	2 / 224 (0.89%)	4 / 224 (1.79%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	2 / 2	3 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung infection			
subjects affected / exposed	4 / 224 (1.79%)	2 / 224 (0.89%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	2 / 4	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	2 / 224 (0.89%)	4 / 224 (1.79%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	1 / 2	2 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	5 / 224 (2.23%)	0 / 224 (0.00%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	1 / 5	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			
subjects affected / exposed	3 / 224 (1.34%)	0 / 224 (0.00%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	1 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	2 / 224 (0.89%)	1 / 224 (0.45%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 0
Subcutaneous abscess			
subjects affected / exposed	1 / 224 (0.45%)	2 / 224 (0.89%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	1 / 1	2 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchitis			
subjects affected / exposed	1 / 224 (0.45%)	1 / 224 (0.45%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cytomegalovirus colitis			

subjects affected / exposed	1 / 224 (0.45%)	1 / 224 (0.45%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endocarditis			
subjects affected / exposed	1 / 224 (0.45%)	1 / 224 (0.45%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Influenza			
subjects affected / exposed	1 / 224 (0.45%)	1 / 224 (0.45%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary tuberculosis			
subjects affected / exposed	0 / 224 (0.00%)	2 / 224 (0.89%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis			
subjects affected / exposed	1 / 224 (0.45%)	1 / 224 (0.45%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper respiratory tract infection			
subjects affected / exposed	2 / 224 (0.89%)	0 / 224 (0.00%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abscess limb			
subjects affected / exposed	1 / 224 (0.45%)	0 / 224 (0.00%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute sinusitis			
subjects affected / exposed	1 / 224 (0.45%)	0 / 224 (0.00%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Appendicitis			

subjects affected / exposed	1 / 224 (0.45%)	0 / 224 (0.00%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arthritis bacterial			
subjects affected / exposed	0 / 224 (0.00%)	1 / 224 (0.45%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bacteraemia			
subjects affected / exposed	1 / 224 (0.45%)	0 / 224 (0.00%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bone abscess			
subjects affected / exposed	0 / 224 (0.00%)	1 / 224 (0.45%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchopulmonary aspergillosis			
subjects affected / exposed	0 / 224 (0.00%)	1 / 224 (0.45%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Clostridium difficile colitis			
subjects affected / exposed	0 / 224 (0.00%)	1 / 224 (0.45%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cytomegalovirus infection			
subjects affected / exposed	0 / 224 (0.00%)	1 / 224 (0.45%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diverticulitis			
subjects affected / exposed	1 / 224 (0.45%)	0 / 224 (0.00%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Enteritis infectious			

subjects affected / exposed	0 / 224 (0.00%)	1 / 224 (0.45%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Enterocolitis bacterial			
subjects affected / exposed	1 / 224 (0.45%)	0 / 224 (0.00%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Enterocolitis viral			
subjects affected / exposed	1 / 224 (0.45%)	0 / 224 (0.00%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Escherichia urinary tract infection			
subjects affected / exposed	0 / 224 (0.00%)	1 / 224 (0.45%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Furuncle			
subjects affected / exposed	1 / 224 (0.45%)	0 / 224 (0.00%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Herpes oesophagitis			
subjects affected / exposed	1 / 224 (0.45%)	0 / 224 (0.00%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Large intestine infection			
subjects affected / exposed	1 / 224 (0.45%)	0 / 224 (0.00%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Periorbital cellulitis			
subjects affected / exposed	1 / 224 (0.45%)	0 / 224 (0.00%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peritonitis bacterial			

subjects affected / exposed	1 / 224 (0.45%)	0 / 224 (0.00%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumocystis jirovecii pneumonia			
subjects affected / exposed	0 / 224 (0.00%)	1 / 224 (0.45%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia bacterial			
subjects affected / exposed	1 / 224 (0.45%)	0 / 224 (0.00%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia cytomegaloviral			
subjects affected / exposed	0 / 224 (0.00%)	1 / 224 (0.45%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia streptococcal			
subjects affected / exposed	0 / 224 (0.00%)	1 / 224 (0.45%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Proteus infection			
subjects affected / exposed	1 / 224 (0.45%)	0 / 224 (0.00%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary nocardiosis			
subjects affected / exposed	1 / 224 (0.45%)	0 / 224 (0.00%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory syncytial virus bronchitis			
subjects affected / exposed	0 / 224 (0.00%)	1 / 224 (0.45%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rhodococcus infection			

subjects affected / exposed	0 / 224 (0.00%)	1 / 224 (0.45%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Septic shock			
subjects affected / exposed	0 / 224 (0.00%)	1 / 224 (0.45%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Sinusitis			
subjects affected / exposed	0 / 224 (0.00%)	1 / 224 (0.45%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Staphylococcal abscess			
subjects affected / exposed	1 / 224 (0.45%)	0 / 224 (0.00%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Staphylococcal infection			
subjects affected / exposed	1 / 224 (0.45%)	0 / 224 (0.00%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tuberculosis			
subjects affected / exposed	1 / 224 (0.45%)	0 / 224 (0.00%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urosepsis			
subjects affected / exposed	0 / 224 (0.00%)	1 / 224 (0.45%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Varicella			
subjects affected / exposed	0 / 224 (0.00%)	1 / 224 (0.45%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Varicella zoster viral infection			

subjects affected / exposed	0 / 224 (0.00%)	1 / 224 (0.45%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Viral infection			
subjects affected / exposed	1 / 224 (0.45%)	0 / 224 (0.00%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wound infection			
subjects affected / exposed	1 / 224 (0.45%)	0 / 224 (0.00%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Complicated appendicitis			
subjects affected / exposed	0 / 224 (0.00%)	0 / 224 (0.00%)	1 / 123 (0.81%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Disseminated tuberculosis			
subjects affected / exposed	0 / 224 (0.00%)	0 / 224 (0.00%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Genital infection			
subjects affected / exposed	0 / 224 (0.00%)	0 / 224 (0.00%)	1 / 123 (0.81%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Otitis media			
subjects affected / exposed	0 / 224 (0.00%)	0 / 224 (0.00%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis acute			
subjects affected / exposed	0 / 224 (0.00%)	0 / 224 (0.00%)	1 / 123 (0.81%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Hyperkalaemia			

subjects affected / exposed	1 / 224 (0.45%)	1 / 224 (0.45%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypophagia			
subjects affected / exposed	0 / 224 (0.00%)	1 / 224 (0.45%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolic acidosis			
subjects affected / exposed	1 / 224 (0.45%)	0 / 224 (0.00%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Belimumab 10 mg/kg to Belimumab 10 mg/kg		
Total subjects affected by serious adverse events			
subjects affected / exposed	10 / 132 (7.58%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Papillary thyroid cancer			
subjects affected / exposed	0 / 132 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Thymoma			
subjects affected / exposed	0 / 132 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 132 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hypotension			

subjects affected / exposed	0 / 132 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Deep vein thrombosis				
subjects affected / exposed	0 / 132 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hypertensive emergency				
subjects affected / exposed	0 / 132 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Shock haemorrhagic				
subjects affected / exposed	0 / 132 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Thrombosis				
subjects affected / exposed	0 / 132 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pregnancy, puerperium and perinatal conditions				
Abortion missed				
subjects affected / exposed	0 / 132 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Foetal death				
subjects affected / exposed	0 / 132 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Prolonged labour				
subjects affected / exposed	0 / 132 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Unintended pregnancy				

subjects affected / exposed	1 / 132 (0.76%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 132 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Non-cardiac chest pain			
subjects affected / exposed	0 / 132 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Asthenia			
subjects affected / exposed	0 / 132 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Fatigue			
subjects affected / exposed	0 / 132 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Generalised oedema			
subjects affected / exposed	0 / 132 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Mucosal inflammation			
subjects affected / exposed	0 / 132 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pain			
subjects affected / exposed	0 / 132 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Serositis			

subjects affected / exposed	0 / 132 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Systemic inflammatory response syndrome				
subjects affected / exposed	0 / 132 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Multiple organ dysfunction syndrome				
subjects affected / exposed	0 / 132 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Immune system disorders				
Hypersensitivity				
subjects affected / exposed	0 / 132 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Immunosuppression				
subjects affected / exposed	0 / 132 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Reproductive system and breast disorders				
Cervical dysplasia				
subjects affected / exposed	0 / 132 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Endometriosis				
subjects affected / exposed	0 / 132 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Respiratory, thoracic and mediastinal disorders				
Acute respiratory failure				

subjects affected / exposed	0 / 132 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pleural effusion			
subjects affected / exposed	0 / 132 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Acute pulmonary oedema			
subjects affected / exposed	0 / 132 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Aspiration			
subjects affected / exposed	0 / 132 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Dyspnoea			
subjects affected / exposed	0 / 132 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Organizing pneumonia			
subjects affected / exposed	0 / 132 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pneumomediastinum			
subjects affected / exposed	0 / 132 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pneumothorax			
subjects affected / exposed	0 / 132 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pulmonary alveolar haemorrhage			

subjects affected / exposed	0 / 132 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pulmonary arterial hypertension				
subjects affected / exposed	0 / 132 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pulmonary embolism				
subjects affected / exposed	0 / 132 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Respiratory failure				
subjects affected / exposed	0 / 132 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Psychiatric disorders				
Mental status changes				
subjects affected / exposed	0 / 132 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Suicide attempt				
subjects affected / exposed	1 / 132 (0.76%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Investigations				
Blood creatinine increased				
subjects affected / exposed	0 / 132 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Blood immunoglobulin G decreased				
subjects affected / exposed	0 / 132 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Foetal biophysical profile score				

equivocal				
subjects affected / exposed	0 / 132 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hepatic enzyme increased				
subjects affected / exposed	0 / 132 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Weight decreased				
subjects affected / exposed	0 / 132 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Injury, poisoning and procedural complications				
Skin laceration				
subjects affected / exposed	0 / 132 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Brain herniation				
subjects affected / exposed	0 / 132 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Contusion				
subjects affected / exposed	0 / 132 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Head injury				
subjects affected / exposed	0 / 132 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Joint injury				
subjects affected / exposed	0 / 132 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			

Ligament injury				
subjects affected / exposed	0 / 132 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Post procedural haematoma				
subjects affected / exposed	0 / 132 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Spinal compression fracture				
subjects affected / exposed	0 / 132 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Tibia fracture				
subjects affected / exposed	0 / 132 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Wrist fracture				
subjects affected / exposed	0 / 132 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardiac disorders				
Pericardial effusion				
subjects affected / exposed	0 / 132 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Aortic valve incompetence				
subjects affected / exposed	0 / 132 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardiac failure acute				
subjects affected / exposed	0 / 132 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardiac failure congestive				

subjects affected / exposed	0 / 132 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pericarditis				
subjects affected / exposed	0 / 132 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pericarditis uraemic				
subjects affected / exposed	0 / 132 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Supraventricular tachycardia				
subjects affected / exposed	0 / 132 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Acute myocardial infarction				
subjects affected / exposed	1 / 132 (0.76%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Nervous system disorders				
Cerebral infarction				
subjects affected / exposed	0 / 132 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cerebrovascular accident				
subjects affected / exposed	0 / 132 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Central nervous system lupus				
subjects affected / exposed	0 / 132 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Encephalopathy				

subjects affected / exposed	0 / 132 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Epilepsy				
subjects affected / exposed	0 / 132 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Generalized tonic-clonic seizure				
subjects affected / exposed	0 / 132 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Haemorrhage intracranial				
subjects affected / exposed	0 / 132 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Headache				
subjects affected / exposed	0 / 132 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hypertensive encephalopathy				
subjects affected / exposed	0 / 132 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Metabolic encephalopathy				
subjects affected / exposed	0 / 132 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Polyneuropathy				
subjects affected / exposed	0 / 132 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Posterior reversible encephalopathy syndrome				

subjects affected / exposed	0 / 132 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Seizure				
subjects affected / exposed	0 / 132 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Blood and lymphatic system disorders				
Anaemia				
subjects affected / exposed	0 / 132 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Febrile neutropenia				
subjects affected / exposed	0 / 132 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Leukopenia				
subjects affected / exposed	0 / 132 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pancytopenia				
subjects affected / exposed	0 / 132 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Bone marrow toxicity				
subjects affected / exposed	0 / 132 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hypoglobulinaemia				
subjects affected / exposed	0 / 132 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Lymphadenopathy				

subjects affected / exposed	0 / 132 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	0 / 132 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Diarrhoea			
subjects affected / exposed	0 / 132 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastritis			
subjects affected / exposed	0 / 132 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nausea			
subjects affected / exposed	0 / 132 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pancreatitis			
subjects affected / exposed	0 / 132 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Abdominal pain			
subjects affected / exposed	0 / 132 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Chronic gastritis			
subjects affected / exposed	0 / 132 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Enteritis			

subjects affected / exposed	0 / 132 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Epiploic appendagitis			
subjects affected / exposed	0 / 132 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal inflammation			
subjects affected / exposed	0 / 132 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Haemorrhoids			
subjects affected / exposed	0 / 132 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Impaired gastric emptying			
subjects affected / exposed	0 / 132 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Large intestine perforation			
subjects affected / exposed	0 / 132 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vasculitis gastrointestinal			
subjects affected / exposed	0 / 132 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cyclic vomiting syndrome			
subjects affected / exposed	0 / 132 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Abdominal pain lower			

subjects affected / exposed	0 / 132 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Cholecystitis acute			
subjects affected / exposed	0 / 132 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
Angioedema			
subjects affected / exposed	0 / 132 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Erythema annulare			
subjects affected / exposed	0 / 132 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Systemic lupus erythematosus rash			
subjects affected / exposed	0 / 132 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Lupus nephritis			
subjects affected / exposed	0 / 132 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Acute kidney injury			
subjects affected / exposed	0 / 132 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
End stage renal disease			
subjects affected / exposed	0 / 132 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Nephrotic syndrome				
subjects affected / exposed	0 / 132 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Renal impairment				
subjects affected / exposed	0 / 132 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Azotaemia				
subjects affected / exposed	0 / 132 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Nephrolithiasis				
subjects affected / exposed	0 / 132 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Renal failure				
subjects affected / exposed	0 / 132 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Endocrine disorders				
Hyperparathyroidism				
subjects affected / exposed	0 / 132 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Musculoskeletal and connective tissue disorders				
Systemic lupus erythematosus				
subjects affected / exposed	0 / 132 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Arthralgia				
subjects affected / exposed	0 / 132 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			

Back pain				
subjects affected / exposed	0 / 132 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Flank pain				
subjects affected / exposed	0 / 132 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Intervertebral disc protrusion				
subjects affected / exposed	0 / 132 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Musculoskeletal chest pain				
subjects affected / exposed	0 / 132 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Oligoarthritis				
subjects affected / exposed	0 / 132 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Osteonecrosis				
subjects affected / exposed	0 / 132 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Rhabdomyolysis				
subjects affected / exposed	0 / 132 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Spinal osteoarthritis				
subjects affected / exposed	0 / 132 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Tendonitis				

subjects affected / exposed	0 / 132 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Muscular weakness				
subjects affected / exposed	0 / 132 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pain in extremity				
subjects affected / exposed	1 / 132 (0.76%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Infections and infestations				
Pneumonia				
subjects affected / exposed	1 / 132 (0.76%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Herpes zoster				
subjects affected / exposed	1 / 132 (0.76%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Lung infection				
subjects affected / exposed	0 / 132 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Urinary tract infection				
subjects affected / exposed	0 / 132 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastroenteritis				
subjects affected / exposed	0 / 132 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cellulitis				

subjects affected / exposed	1 / 132 (0.76%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Sepsis				
subjects affected / exposed	0 / 132 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Subcutaneous abscess				
subjects affected / exposed	0 / 132 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Bronchitis				
subjects affected / exposed	0 / 132 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cytomegalovirus colitis				
subjects affected / exposed	0 / 132 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Endocarditis				
subjects affected / exposed	0 / 132 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Influenza				
subjects affected / exposed	0 / 132 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pulmonary tuberculosis				
subjects affected / exposed	0 / 132 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pyelonephritis				

subjects affected / exposed	1 / 132 (0.76%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Upper respiratory tract infection				
subjects affected / exposed	0 / 132 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Abscess limb				
subjects affected / exposed	0 / 132 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Acute sinusitis				
subjects affected / exposed	1 / 132 (0.76%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Appendicitis				
subjects affected / exposed	0 / 132 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Arthritis bacterial				
subjects affected / exposed	0 / 132 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Bacteraemia				
subjects affected / exposed	0 / 132 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Bone abscess				
subjects affected / exposed	0 / 132 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Bronchopulmonary aspergillosis				

subjects affected / exposed	0 / 132 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Clostridium difficile colitis			
subjects affected / exposed	1 / 132 (0.76%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cytomegalovirus infection			
subjects affected / exposed	0 / 132 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Diverticulitis			
subjects affected / exposed	0 / 132 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Enteritis infectious			
subjects affected / exposed	0 / 132 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Enterocolitis bacterial			
subjects affected / exposed	0 / 132 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Enterocolitis viral			
subjects affected / exposed	0 / 132 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Escherichia urinary tract infection			
subjects affected / exposed	0 / 132 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Furuncle			

subjects affected / exposed	0 / 132 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Herpes oesophagitis				
subjects affected / exposed	0 / 132 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Large intestine infection				
subjects affected / exposed	0 / 132 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Periorbital cellulitis				
subjects affected / exposed	0 / 132 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Peritonitis bacterial				
subjects affected / exposed	0 / 132 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumocystis jirovecii pneumonia				
subjects affected / exposed	0 / 132 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumonia bacterial				
subjects affected / exposed	0 / 132 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumonia cytomegaloviral				
subjects affected / exposed	0 / 132 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumonia streptococcal				

subjects affected / exposed	0 / 132 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Proteus infection				
subjects affected / exposed	0 / 132 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pulmonary nocardiosis				
subjects affected / exposed	0 / 132 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Respiratory syncytial virus bronchitis				
subjects affected / exposed	0 / 132 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Rhodococcus infection				
subjects affected / exposed	0 / 132 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Septic shock				
subjects affected / exposed	0 / 132 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Sinusitis				
subjects affected / exposed	0 / 132 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Staphylococcal abscess				
subjects affected / exposed	0 / 132 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Staphylococcal infection				

subjects affected / exposed	0 / 132 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Tuberculosis				
subjects affected / exposed	0 / 132 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Urosepsis				
subjects affected / exposed	0 / 132 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Varicella				
subjects affected / exposed	0 / 132 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Varicella zoster viral infection				
subjects affected / exposed	0 / 132 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Viral infection				
subjects affected / exposed	0 / 132 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Wound infection				
subjects affected / exposed	0 / 132 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Complicated appendicitis				
subjects affected / exposed	0 / 132 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Disseminated tuberculosis				

subjects affected / exposed	1 / 132 (0.76%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Genital infection			
subjects affected / exposed	0 / 132 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Otitis media			
subjects affected / exposed	1 / 132 (0.76%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pyelonephritis acute			
subjects affected / exposed	0 / 132 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Hyperkalaemia			
subjects affected / exposed	0 / 132 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hypophagia			
subjects affected / exposed	0 / 132 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Metabolic acidosis			
subjects affected / exposed	0 / 132 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Placebo	Belimumab 10 mg/kg	Placebo to Belimumab 10 mg/kg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	191 / 224 (85.27%)	186 / 224 (83.04%)	34 / 123 (27.64%)
Vascular disorders			
Hypertension			
subjects affected / exposed	20 / 224 (8.93%)	12 / 224 (5.36%)	0 / 123 (0.00%)
occurrences (all)	23	14	0
Nervous system disorders			
Headache			
subjects affected / exposed	35 / 224 (15.63%)	34 / 224 (15.18%)	0 / 123 (0.00%)
occurrences (all)	57	51	0
Dizziness			
subjects affected / exposed	19 / 224 (8.48%)	13 / 224 (5.80%)	0 / 123 (0.00%)
occurrences (all)	21	18	0
General disorders and administration site conditions			
Oedema peripheral			
subjects affected / exposed	13 / 224 (5.80%)	16 / 224 (7.14%)	0 / 123 (0.00%)
occurrences (all)	17	23	0
Pyrexia			
subjects affected / exposed	17 / 224 (7.59%)	11 / 224 (4.91%)	0 / 123 (0.00%)
occurrences (all)	20	14	0
Fatigue			
subjects affected / exposed	14 / 224 (6.25%)	12 / 224 (5.36%)	0 / 123 (0.00%)
occurrences (all)	15	12	0
Oedema			
subjects affected / exposed	12 / 224 (5.36%)	9 / 224 (4.02%)	0 / 123 (0.00%)
occurrences (all)	15	9	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	23 / 224 (10.27%)	13 / 224 (5.80%)	0 / 123 (0.00%)
occurrences (all)	26	16	0
Leukopenia			
subjects affected / exposed	19 / 224 (8.48%)	15 / 224 (6.70%)	0 / 123 (0.00%)
occurrences (all)	29	28	0
Gastrointestinal disorders			

Diarrhoea			
subjects affected / exposed	48 / 224 (21.43%)	45 / 224 (20.09%)	0 / 123 (0.00%)
occurrences (all)	56	59	0
Nausea			
subjects affected / exposed	24 / 224 (10.71%)	21 / 224 (9.38%)	0 / 123 (0.00%)
occurrences (all)	33	28	0
Vomiting			
subjects affected / exposed	16 / 224 (7.14%)	16 / 224 (7.14%)	0 / 123 (0.00%)
occurrences (all)	21	25	0
Abdominal pain			
subjects affected / exposed	13 / 224 (5.80%)	12 / 224 (5.36%)	0 / 123 (0.00%)
occurrences (all)	13	15	0
Dyspepsia			
subjects affected / exposed	15 / 224 (6.70%)	9 / 224 (4.02%)	0 / 123 (0.00%)
occurrences (all)	18	10	0
Abdominal pain upper			
subjects affected / exposed	6 / 224 (2.68%)	16 / 224 (7.14%)	0 / 123 (0.00%)
occurrences (all)	7	16	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	21 / 224 (9.38%)	30 / 224 (13.39%)	0 / 123 (0.00%)
occurrences (all)	23	38	0
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	17 / 224 (7.59%)	23 / 224 (10.27%)	0 / 123 (0.00%)
occurrences (all)	18	31	0
Acne			
subjects affected / exposed	9 / 224 (4.02%)	12 / 224 (5.36%)	0 / 123 (0.00%)
occurrences (all)	11	13	0
Psychiatric disorders			
Insomnia			
subjects affected / exposed	18 / 224 (8.04%)	10 / 224 (4.46%)	0 / 123 (0.00%)
occurrences (all)	19	10	0
Musculoskeletal and connective tissue disorders			
Arthralgia			

subjects affected / exposed	32 / 224 (14.29%)	26 / 224 (11.61%)	5 / 123 (4.07%)
occurrences (all)	52	44	5
Back pain			
subjects affected / exposed	17 / 224 (7.59%)	17 / 224 (7.59%)	0 / 123 (0.00%)
occurrences (all)	17	24	0
Muscle spasms			
subjects affected / exposed	15 / 224 (6.70%)	18 / 224 (8.04%)	0 / 123 (0.00%)
occurrences (all)	18	25	0
Pain in extremity			
subjects affected / exposed	8 / 224 (3.57%)	12 / 224 (5.36%)	0 / 123 (0.00%)
occurrences (all)	9	14	0
Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	74 / 224 (33.04%)	81 / 224 (36.16%)	14 / 123 (11.38%)
occurrences (all)	134	159	18
Urinary tract infection			
subjects affected / exposed	37 / 224 (16.52%)	43 / 224 (19.20%)	10 / 123 (8.13%)
occurrences (all)	72	73	12
Nasopharyngitis			
subjects affected / exposed	31 / 224 (13.84%)	35 / 224 (15.63%)	8 / 123 (6.50%)
occurrences (all)	50	60	9
Gastroenteritis			
subjects affected / exposed	23 / 224 (10.27%)	21 / 224 (9.38%)	0 / 123 (0.00%)
occurrences (all)	28	24	0
Bronchitis			
subjects affected / exposed	19 / 224 (8.48%)	18 / 224 (8.04%)	0 / 123 (0.00%)
occurrences (all)	26	24	0
Herpes zoster			
subjects affected / exposed	19 / 224 (8.48%)	17 / 224 (7.59%)	0 / 123 (0.00%)
occurrences (all)	20	17	0
Conjunctivitis			
subjects affected / exposed	5 / 224 (2.23%)	13 / 224 (5.80%)	0 / 123 (0.00%)
occurrences (all)	5	13	0
Metabolism and nutrition disorders			
Hypokalaemia			

subjects affected / exposed	20 / 224 (8.93%)	24 / 224 (10.71%)	0 / 123 (0.00%)
occurrences (all)	23	36	0

Non-serious adverse events	Belimumab 10 mg/kg to Belimumab 10 mg/kg		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	39 / 132 (29.55%)		
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 132 (0.00%)		
occurrences (all)	0		
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 132 (0.00%)		
occurrences (all)	0		
Dizziness			
subjects affected / exposed	0 / 132 (0.00%)		
occurrences (all)	0		
General disorders and administration site conditions			
Oedema peripheral			
subjects affected / exposed	0 / 132 (0.00%)		
occurrences (all)	0		
Pyrexia			
subjects affected / exposed	0 / 132 (0.00%)		
occurrences (all)	0		
Fatigue			
subjects affected / exposed	0 / 132 (0.00%)		
occurrences (all)	0		
Oedema			
subjects affected / exposed	0 / 132 (0.00%)		
occurrences (all)	0		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 132 (0.00%)		
occurrences (all)	0		
Leukopenia			

subjects affected / exposed occurrences (all)	0 / 132 (0.00%) 0		
Gastrointestinal disorders Diarrhoea subjects affected / exposed occurrences (all) Nausea subjects affected / exposed occurrences (all) Vomiting subjects affected / exposed occurrences (all) Abdominal pain subjects affected / exposed occurrences (all) Dyspepsia subjects affected / exposed occurrences (all) Abdominal pain upper subjects affected / exposed occurrences (all)	 0 / 132 (0.00%) 0 0 / 132 (0.00%) 0 0 / 132 (0.00%) 0 0 / 132 (0.00%) 0 0 / 132 (0.00%) 0 0 / 132 (0.00%) 0		
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all)	 0 / 132 (0.00%) 0		
Skin and subcutaneous tissue disorders Rash subjects affected / exposed occurrences (all) Acne subjects affected / exposed occurrences (all)	 0 / 132 (0.00%) 0 0 / 132 (0.00%) 0		
Psychiatric disorders Insomnia subjects affected / exposed occurrences (all)	 0 / 132 (0.00%) 0		

Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	7 / 132 (5.30%)		
occurrences (all)	8		
Back pain			
subjects affected / exposed	0 / 132 (0.00%)		
occurrences (all)	0		
Muscle spasms			
subjects affected / exposed	0 / 132 (0.00%)		
occurrences (all)	0		
Pain in extremity			
subjects affected / exposed	0 / 132 (0.00%)		
occurrences (all)	0		
Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	23 / 132 (17.42%)		
occurrences (all)	24		
Urinary tract infection			
subjects affected / exposed	12 / 132 (9.09%)		
occurrences (all)	14		
Nasopharyngitis			
subjects affected / exposed	3 / 132 (2.27%)		
occurrences (all)	3		
Gastroenteritis			
subjects affected / exposed	0 / 132 (0.00%)		
occurrences (all)	0		
Bronchitis			
subjects affected / exposed	0 / 132 (0.00%)		
occurrences (all)	0		
Herpes zoster			
subjects affected / exposed	0 / 132 (0.00%)		
occurrences (all)	0		
Conjunctivitis			
subjects affected / exposed	0 / 132 (0.00%)		
occurrences (all)	0		
Metabolism and nutrition disorders			

Hypokalaemia subjects affected / exposed occurrences (all)	0 / 132 (0.00%) 0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
27 January 2012	Amendment 01: Applied to all countries and sites. The protocol was modified to clarify exclusion criteria, concurrent medications and standard of care, addition of anti-malarials, and use of corticosteroids. There were also changes to prohibited medications and non-drug therapies, live vaccines, screening procedures, and the double-blind treatment period and study calendar. An open-label extension replaced the continuation phase. An exploratory analysis of urinary biomarkers related to lupus nephritis was added. Clarifications were made to the withdrawal of study treatment and adverse event reporting sections. The endpoints and statistical analysis sections were updated to reflect changes made in other sections of the protocol.
08 March 2012	Amendment 02: Applied to all countries and sites. The protocol was modified to require participants to remain under clinical supervision for 3 hours after completion of the first 2 infusions. Results for biological markers measured by florescence activated cell sorting (FACS) were added to the list of laboratory results not provided to study sites. Language describing participant un-blinding in the protocol was amended. Language regarding the body weight used for dose calculation was corrected.
16 August 2012	Amendment 02 (Thailand): Implemented and applied only in Thailand. In this amendment the protocol was modified to change the recommended duration of Investigational Product (IP) infusion from 1 hour to approximately 2-3 hours. Hereafter this amendment was incorporated as an appendix to the main protocol as a country specific requirement.
11 February 2014	Amendment 03: Applied to all countries and sites. In this amendment the protocol was modified to expand Hepatitis B serology testing, to exclude participants who tested positive according to the criteria specified, and to specify hepatitis C screening. Screening and induction initiation windows were extended and exclusion criteria were modified. Clarification was added for screening for active or latent infections. Six-month follow-up immunogenicity sample collection for participants with positive response at 8-week follow-up was removed. A belimumab Benefit and Risk Assessment, and a preliminary assessment specific to the lupus nephritis participant population were added. Inclusion criterion, urine collection for urinary sediment analysis, 24-hour urine collection, and serum creatinine were revised for clarification. Information on non-acute delayed type hypersensitivity reaction and symptoms was added. Instructions for monitoring and managing cases of Grade 4 immunoglobulin G (IgG) were clarified. Steroid rescue for non-renal systemic lupus erythematosus (SLE) disease activity and non-SLE disease activity was revised. Measurement of vital signs and a 12-lead electrocardiogram (ECG) were added. Timing of pharmacokinetic sampling in participants who withdrew from the study was clarified. Reason for treatment withdrawal was modified to include “Missing 3 or more consecutive doses of study drug”. The adverse events section was modified throughout for consistency. Progressive multifocal leukoencephalopathy (PML) text was updated. The Data Monitoring Committee (DMC) and its abbreviation was corrected to Independent Data Monitoring Committee (IDMC) and to indicate that all serious adverse events (SAEs) are monitored by the IDMC. New appendices were added to provide the questionnaires for the possible suicidality-related history questionnaire (PSRHQ), the possible suicidality-related questionnaire (PSRQ), and the Country-specific Requirements for Thailand.

29 August 2014	Amendment 04 (China): Implemented and applied only in China. The protocol was modified for participants in China regarding the hepatitis B exclusion criteria. The protocol was modified to clarify that participants in China positive test for Hepatitis C antibody were to be excluded without confirmatory Hepatitis C ribonucleic acid-polymerase chain reaction (RNA-PCR) testing. A urine pregnancy test at the 8-week follow-up visit was added. The protocol was modified to clarify that participants in China will have SAEs collected from the time a participant consented to participate in the study. Screening visit/Study week was corrected to align with the change in Amendment 03. Sections of the protocol affected by these changes have been modified accordingly.
16 March 2015	Amendment 05: Applied in all countries and sites, except for those with a local version amendment. In this amendment the eligibility criteria, exclusion criteria, and relevant sections were modified. The Risk-Benefit and concomitant medications sections were updated. A urine pregnancy test was added at the 8-week follow-up visit, and an instruction that women of child-bearing potential must be reminded of the requirement to report any pregnancy that occurred through 16 weeks following the last dose of IP. Sections of the protocol affected by this change were modified accordingly. The section on liver safety evaluation was replaced for consistency with GlaxoSmithKline (GSK) standards. Additional Hepatitis B monitoring was added. Study calendars and relevant footnotes were updated to reflect changes made in other sections of the protocol.
17 March 2015	Amendment 05 (France 1): Implemented and applies only in France. In addition to the changes described above for Amendment 05 for all sites, at the request of the French National Agency for Medicines and Health Products Safety (ANSM), the protocol was revised to include guidance for French investigators to evaluate suspected cases of PML using brain imaging and PCR on cerebrospinal fluid for John Cunningham virus (JCV).
13 July 2016	Amendment 05 (France 2): Implemented and applies only in France. In addition to the changes described above for Amendment 05 (1), at the request of the ANSM, the protocol was modified to comply with the information updated in November 2015 in the Cellcept Summary of Product Characteristics (SPC) and package leaflet.
25 April 2017	Amendment 06: Applied in all countries and sites, except for those with a local version amendment. In this amendment the renal response definition used for key efficacy endpoints evaluation was modified. Calculated glomerular filtration rate (GFR) was changed to estimated GFR to be used for all renal function evaluations. Time to first renal flare was added as a major secondary efficacy endpoint. Clarification was added regarding timing of the renal biopsy; other relevant sections/text have been modified accordingly. In Study Design and Statistical analysis sections, clarifications regarding target sample size and sample size calculations were added. Contraception requirements were updated. GFR calculation was corrected to include "per 1.73 square meter (/1.73m^2)". Benefit-Risk section text was updated in line with current belimumab safety information. The concomitant medications section was updated to clarify concurrent medication rules applicable to the double-blind period. Information regarding the concurrent medications prohibited during the open-label period was moved from Section 6 to Section 5. Laboratory text section was updated with the most recent simplified Modification of Diet in Renal Disease [MDRD] equation for estimation of GFR. The IDMC requested removal of the requirement to review of Grade 4 IgG reductions on an expedited basis. The text in the IDMC section was changed accordingly. In Statistical analysis section, the Van Elteren test was replaced with a Rank analysis of covariance (ANCOVA) for the primary and major secondary endpoints analysis. Updates were also made to how missing values will be handled, how the sensitivity analyses will be performed, and additional other efficacy endpoints were defined. The rate of renal flare from Week 24, time to first renal flare from Week 52, and the rate of renal flare from Week 52 were also added as other efficacy endpoints and for some of the other efficacy endpoints, clarification text has been added.
26 April 2017	Amendment 06 (France): Implemented and applied only in France. It contains the same global protocol changes described in Section 4.3.9 in a separate protocol amendment created for specifically for use in France.

24 January 2019	Amendment 07: Applied in all countries and sites, except for those with a local version amendment. In this amendment the primary endpoint and the time to renal flare at Week 24 endpoint were changed. The testing hierarchy and the analysis methodology of the major secondary endpoints was revised accordingly. Power calculations were added to the sample size section. The Study Design schematic was updated for the changes to the primary and major secondary endpoints. A subgroup for Baseline renal biopsy class was added. Other efficacy endpoints were updated to be consistent with and supportive of the revised testing hierarchy. Endpoints inadvertently omitted were added to other efficacy endpoints. The timeframe for pregnancy reporting was updated to sponsor requirements.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported