Clinical trial results:
BEL116472. A 2 year mechanistic study of belimumab in Idiopathic Membranous Glomerulonephropathy

Summary

EudraCT number	2012-000385-38
Trial protocol	GB
Global end of trial date	

Results information

Result version number	v1
This version publication date	27 April 2016
First version publication date	28 May 2015

Trial information

Trial identification

Sponsor protocol code	BEL116472

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, 1 866-435-7343,
Scientific contact	GSK Response Center, GlaxoSmithKline, 1 866-435-7343,

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Interim
Date of interim/final analysis	22 April 2015
Is this the analysis of the primary completion data?	Yes
Primary completion date	24 September 2014
Global end of trial reached?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study is:
To evaluate whether belimumab can modulate proteinuria in IMGN.
To evaluate whether belimumab can modulate anti-PLA2R autoantibodies in patients with detectable baseline levels of these antibodies.

Protection of trial subjects:

The protocol contains stopping criteria to protect trial participants as well as eligibility criteria to exclude participants who may not benefit. Eligibility criteria to protect participants include exclusion of those with infections, exclusion of participants with HIV, hepatitis B and hepatitis C, exclusion of participants with deteriorating or severely reduced renal function. Study specific stopping criteria include deteriorating renal function, deteriorating nephrotic state as assessed by increasing proteinuria and reduction in serum albumin, proteinuria without improvement, hypogammaglobulinaemia without improvement.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	04 July 2012
Long term follow-up planned	Yes
Long term follow-up rationale	Efficacy, Scientific research
Long term follow-up duration	5 Years
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United Kingdom: 14
Worldwide total number of subjects	14
EEA total number of subjects	14

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)	13
From 65 to 84 years	1
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants (par.) were recruited into the initial 6 month treatment phase of this 2 part study from July 2012 until March 2014 in academic nephrology clinics. Results presented are for the initial treatment phase, up to the Week 28 primary endpoint.

Pre-assignment

Screening details:

Screening occurred within approximately 35 days and no less than 14 days before the first scheduled dose of study medication. A total of 21 participants were screened; 14 participants were randomized, and 14 participants entered the initial treatment period. Common reasons for screen failures were insufficient or improvements in proteinuria.

Period 1

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

Arms

Arm title	Belimumab 10 mg/kg IV

Arm description:

Participants received 10 milligrams per kilogram (mg/kg) belimumab intravenous (IV) infusion every 4 weeks, over 24 weeks.

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

Dosage and administration details:

10 mg/kg IV at weeks 0, 2, 4 then every 4 weeks for 2 years. Participants with >1000 mg/mmol proteinuria will remain on dosing every 2 weeks.

Number of subjects in period 1	Belimumab 10 mg/kg IV
Started	14
Completed	11
Not completed	3
Physician decision	1
Lack of efficacy	2

Baseline characteristics

Reporting groups	
Reporting group title	Belimumab 10 mg/kg IV
Reporting group description:	
Participants received 10 milligrams per kilogram (mg/kg) belimumab intravenous (IV) infusion every 4 weeks, over 24 weeks.	

Reporting group values	Belimumab 10 mg/kg IV	Total	
Number of subjects	14	14	
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	46.1		
standard deviation	± 13.3	-	
Gender categorical Units: Subjects			
Female	3	3	
Male	11	11	
Race Units: Subjects			
Asian - Central/South Asian Heritage	4	4	
White	9	9	
Missing	1	1	

End points

End points reporting groups

Reporting group title	Belimumab 10 mg/kg IV

Reporting group description:

Participants received 10 milligrams per kilogram (mg/kg) belimumab intravenous (IV) infusion every 4 weeks, over 24 weeks.

Primary: Change from Baseline in proteinuria levels at Week 28

End point title	Change from Baseline in proteinuria levels at Week 28[1]

End point description:

Proteinuria based on urinary protein creatinine ratio (PCR) was measured from 2 consecutive 24 hour (h) urine collection pre and post dosing at Baseline and Week 28 and the mean PCR was determined at each time point. Baseline is defined as the mean of the pre and post dosing Day 0 values. The ratio is defined as the Week 28 value divided by the Baseline value. Intent-to-Treat (ITT) Population: all eligible participants who received at least one dose of investigational drug. Ratio to Baseline: Estimated value = 0.76, 2-sided 95% CI=0.57 to 1.01. The geometric mean method was used to calculate the CI.

End point type	Primary

End point timeframe:

Baseline and Week 28

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Due to the system not allowing entry of statistical information for 1 arm studies, a statistical statement was added to the outcome measure description.

End point values	Belimumab 10 mg/kg IV			
Subject group type	Reporting group			
Number of subjects analysed	11[2]			
Units: Ratio				
geometric mean (geometric coefficient of variation)	0.76 (± 45)			

Notes:

[2] - ITT Population. Only those par. available at the indicated time point (Week 28) were analyzed.

Statistical analyses

No statistical analyses for this end point

Primary: Change from Baseline in anti-phospholipase A2 receptor (PLA2R) autoantibody titres at Week 28

End point title	Change from Baseline in anti-phospholipase A2 receptor (PLA2R) autoantibody titres at Week 28[3]

End point description:

PLA2R autoantibody titres in serum were analyzed at Baseline and Week 28 by means of a validated anti- PLA2R enzyme linked immunosorbent assay (ELISA) from EuroImmun. Baseline is defined as the Day 0 value. The ratio is defined as the Week 28 value divided by the Baseline value. Ratio to Baseline: Estimated value = 0.25, 2-sided 95% CI=0.12 to 0.54. The geometric mean method was used to calculate the CI.

End point type	Primary

End point timeframe:

Baseline and Week 28

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Due to the system not allowing entry of statistical information for 1 arm studies, a statistical statement was added to the outcome measure description.

End point values	Belimumab 10 mg/kg IV			
Subject group type	Reporting group			
Number of subjects analysed	11[4]			
Units: Ratio				
geometric mean (geometric coefficient of variation)	0.25 (± 167)			

Notes:

[4] - ITT Population. Only those par. available at the indicated time point (Week 28) were analyzed.

Statistical analyses

No statistical analyses for this end point

Secondary: Proteinuria levels at the indicated time points

End point title	Proteinuria levels at the indicated time points

End point description:

Proteinuria based on urinary protein creatinine ratio (PCR) was measured from 2 consecutive 24 h urine collection pre and post dosing at Baseline and Week 28 and the mean PCR was determined at each time point. Baseline is defined as the Day 0 value. Only those participants available at the specified time points were analyzed (represented by n=X in the category titles). Different participants may have been analyzed at different time points, so the overall number of participants analyzed reflects everyone in the ITT Population.

End point type	Secondary

End point timeframe:

Baseline and Week 28

End point values	Belimumab 10 mg/kg IV			
Subject group type	Reporting group			
Number of subjects analysed	14[5]			
Units: milligrams per millimole (mg/mmol)				
geometric mean (geometric coefficient of variation)				
Baseline, n=14	724.3 (± 40.2)			
Week 28, n=11	498.1 (± 40.9)			

Notes:

[5] - ITT Population

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in proteinuria levels at the indicated time points

End point title	Change from Baseline in proteinuria levels at the indicated time

	points

End point description:

Proteinuria is being assessed at Weeks 0, 4, 8, 12, 16, 20, 24, 28, 36, 44, 52, 60, 68, 76, 84, 92, 100, 104/4 week post last dose and at the 16 week and 6 month follow-up visits. Proteinuria measurements are being based on urinary protein creatinine ratio measurements spot urine samples. For other key time points, Weeks 12, 52, 76 and 4 week post last dose, they are the mean of the PCR from a pre-dose spot urine sample and from a 24 h post-dose or post visit urine collection. Baseline is defined as the mean of the pre and post dosing Day 0 values from 2 consecutive 24 h urine collections. The ratio is defined as the post-Baseline value divided by the Baseline value. The results for this outcome measure will be reported at the end of the study i.e. May 2017, as they were not designed to be reported at interim periods.

End point type	Secondary

End point timeframe:

Baseline and Weeks 12, 28, 52, 76 and 104/4 week post last dose

End point values	Belimumab 10 mg/kg IV			
Subject group type	Reporting group			
Number of subjects analysed	0[6]			
Units: Ratio				
geometric mean (geometric coefficient of variation)	()			

Notes:

[6] - ITT Population

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-phospholipase A2 receptor (PLA2R) autoantibody titres at the indicated time points

End point title	Anti-phospholipase A2 receptor (PLA2R) autoantibody titres at the indicated time points

End point description:

PLA2R autoantibody titres in serum were analyzed at Baseline and Week 28 by means of a validated anti- PLA2R enzyme linked immunosorbent assay (ELISA) from EuroImmun. Baseline is defined as the Day 0 value. Only those participants available at the specified time points were analyzed (represented by n=X in the category titles). Different participants may have been analyzed at different time points, so the overall number of participants analyzed reflects everyone in the ITT Population.

End point type	Secondary

End point timeframe:

Baseline and Week 28

End point values	Belimumab 10 mg/kg IV			
Subject group type	Reporting group			
Number of subjects analysed	14[7]			
Units: relative units per milliliter (RU/mL)				
geometric mean (geometric coefficient of variation)				

Baseline, n=14 Week 28, n=11	168.3 (± 138.9) 43.6 (± 373.5)			

Notes:

[7] - ITT Population

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in anti-PLA2R autoantibody titres at the indicated time points

End point title	Change from Baseline in anti-PLA2R autoantibody titres at the indicated time points

End point description:

PLA2R autoantibody titres in serum are being analyzed by means of a validated anti- PLA2R ELISA from EuroImmun. Anti-PLA2R autoantibody blood samples are being collected at Weeks 0, 4, 8, 12, 16, 20, 24, 28, 36, 44, 52, 60, 68, 76, 84, 92, 100, 104/4 week post last dose and 16 week and 6 month follow-up visits. Baseline is defined as the Day 0 value. Ratio is defined as the post-Baseline value divided by the Baseline value. The results for this outcome measure will be reported at the end of the study i.e. May 2017, as they were not designed to be reported at interim periods.

End point type	Secondary

End point timeframe:

Baseline and Weeks 12, 28, 52, 76 and 104/4 week post last dose

End point values	Belimumab 10 mg/kg IV			
Subject group type	Reporting group			
Number of subjects analysed	0[8]			
Units: Ratio				
geometric mean (geometric coefficient of variation)	()			

Notes:

[8] - ITT Population

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in urine levels of belimumab at the indicated time points

End point title	Change from Baseline in urine levels of belimumab at the indicated time points

End point description:

24 h urine samples are being collected for pharmacokinetic analysis of belimumab, after the Day 0 and Weeks 12, 28, 52, 76 doses and at the 4 week post last dose visit. Baseline is defined as the Day 0 value. The results for this outcome measure will be reported at the end of the study i.e. May 2017, as they were not designed to be reported at interim periods.

End point type	Secondary

End point timeframe:

Baseline and Weeks 12, 28, 52, 76 and 4 week post last dose

End point values	Belimumab 10 mg/kg IV			
Subject group type	Reporting group			
Number of subjects analysed	0[9]			
Units: Ratio				
geometric mean (geometric coefficient of variation)	()			

Notes:

[9] - ITT Population

Statistical analyses

No statistical analyses for this end point

Secondary: Incidence of complete or partial remission

End point title	Incidence of complete or partial remission

End point description:

Complete remission is defined as PCR <30 milligrams per millimoles (mg/mmol) (proteinuria <0.3grams [g]/24 h) with no worsening in renal function (estimated glomerular filtration rate [eGFR] reduction from Baseline <15 percent [%]). Partial remission is defined as PCR <350 mg/mmol (proteinuria <3.5 g/24 h) but >= 30 mg/mmol (proteinuria >= 0.3g/24h) and decrease of >50% from Day 0 Baseline, together with no worsening in renal function (eGFR reduction from Baseline <15%). The results for this outcome measure will be reported at the end of the study i.e. May 2017, as they were not designed to be reported at interim periods.

End point type	Secondary

End point timeframe:

Baseline and up to Week 104/4 week post last dose

End point values	Belimumab 10 mg/kg IV			
Subject group type	Reporting group			
Number of subjects analysed	0[10]			
Units: Participants				

Notes:

[10] - ITT Population

Statistical analyses

No statistical analyses for this end point

Secondary: Time to complete or partial remission

End point title	Time to complete or partial remission

End point description:

Time to complete or partial remission and time of proteinuria are being estimated using the Kaplan-Meier method. Complete remission is defined as PCR <30 mg/mmol (proteinuria <0.3g/24 h) with no worsening in renal function (eGFR reduction from Baseline <15%). Partial remission is defined as PCR <350 mg/mmol (proteinuria <3.5 g/24 h) but >= 30 mg/mmol (proteinuria >= 0.3g/24h) and decrease of >50% from Day 0 Baseline, together with no worsening in renal function (eGFR reduction from

Baseline <15%). The results for this outcome measure will be reported at the end of the study i.e. May 2017, as they were not designed to be reported at interim periods.

End point type	Secondary

End point timeframe:

Baseline and up to Week 104/4 week post last dose

End point values	Belimumab 10 mg/kg IV			
Subject group type	Reporting group			
Number of subjects analysed	0[11]			
Units: Weeks				
median (full range (min-max))	(to)			

Notes:

[11] - ITT Population

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of complete or partial remission

End point title	Duration of complete or partial remission

End point description:

Complete remission is defined as PCR <30 mg/mmol (proteinuria <0.3g/24 h) with no worsening in renal function (eGFR reduction from Baseline <15%). Partial remission is defined as PCR <350 mg/mmol (proteinuria <3.5 g/24 h) but >= 30 mg/mmol (proteinuria >= 0.3g/24h) and decrease of >50% from Day 0 Baseline, together with no worsening in renal function (eGFR reduction from Baseline <15%). The results for this outcome measure will be reported at the end of the study i.e. May 2017, as they were not designed to be reported at interim periods.

End point type	Secondary

End point timeframe:

Baseline and up to Week 104/ 4 week post last dose

End point values	Belimumab 10 mg/kg IV			
Subject group type	Reporting group			
Number of subjects analysed	0[12]			
Units: Days				
arithmetic mean (standard deviation)	()			

Notes:

[12] - ITT Population

Statistical analyses

No statistical analyses for this end point

Secondary: Incidence of proteinuria relapse

End point title	Incidence of proteinuria relapse

End point description:

Incidence of proteinuria relapse is defined as participants with PCR >350 mg/mmol and an increase of 50% from the lowest remission level, in those participants who had previously achieved any type of remission. The results for this outcome measure will be reported at the end of the study i.e. May 2017, as they were not designed to be reported at interim periods.

End point type	Secondary

End point timeframe:

Baseline and up to Week 104/4 week post last dose

End point values	Belimumab 10 mg/kg IV			
Subject group type	Reporting group			
Number of subjects analysed	0[13]			
Units: Participants				

Notes:

[13] - ITT Population

Statistical analyses

No statistical analyses for this end point

Secondary: Incidence of full/partial remission for anti-PLA2R autoantibody

End point title	Incidence of full/partial remission for anti-PLA2R autoantibody

End point description:

Incidence of anti-PLA2R autoantibody remission: full response is defined as antibody undetectable, partial response is defined as reduction in titres by 50%. For anti PLA2R autoantibody data, log transformation is being applied before the formal analyses. Anti-PLA2R autoantibody blood samples are being collected at Weeks 0, 4, 8, 12, 16, 20, 24, 28, 36, 44, 52, 60, 68, 76, 84, 92, 100, 104/4 week post last dose and 16 week and 6 month follow-up visits. The results for this outcome measure will be reported at the end of the study i.e. May 2017, as they were not designed to be reported at interim periods.

End point type	Secondary

End point timeframe:

Baseline and up to Week 104/4 Week post last dose

End point values	Belimumab 10 mg/kg IV			
Subject group type	Reporting group			
Number of subjects analysed	0[14]			
Units: Participants				

Notes:

[14] - ITT Population

Statistical analyses

No statistical analyses for this end point

Secondary: Time to anti-PLA2R autoantibody remission

End point title	Time to anti-PLA2R autoantibody remission

End point description:

Time to anti-PLA2R autoantibody remission - full response with antibody undetectable. Anti-PLA2R autoantibody blood samples are being collected at Weeks 0, 4, 8, 12, 16, 20, 24, 28, 36, 44, 52, 60, 68, 76, 84, 92, 100, 104/4 week post last dose and 16 week and 6 month follow-up visits. The results for this outcome measure will be reported at the end of the study i.e. May 2017, as they were not designed to be reported at interim periods.

End point type	Secondary

End point timeframe:

Baseline and up to Week 104/4 week post last dose

End point values	Belimumab 10 mg/kg IV			
Subject group type	Reporting group			
Number of subjects analysed	0[15]			
Units: Weeks				
median (full range (min-max))	(to)			

Notes:

[15] - ITT Population

Statistical analyses

No statistical analyses for this end point

Secondary: Incidence of anti-PLA2R autoantibody relapse

End point title	Incidence of anti-PLA2R autoantibody relapse

End point description:

Incidence of anti-PLA2R autoantibody relapse defined as antibody detectable after previously undetectable. Anti-PLA2R autoantibody blood samples are being collected at Weeks 0, 4, 8, 12, 16, 20, 24, 28, 36, 44, 52, 60, 68, 76, 84, 92, 100, 104/4 week post last dose and 16 week and 6 month follow-up visits. The results for this outcome measure will be reported at the end of the study i.e. May 2017, as they were not designed to be reported at interim periods.

End point type	Secondary

End point timeframe:

Baseline and up to Week 104/4 week post last dose

End point values	Belimumab 10 mg/kg IV			
Subject group type	Reporting group			
Number of subjects analysed	0[16]			
Units: Participants				

Notes:

[16] - ITT Population

Statistical analyses

No statistical analyses for this end point

Secondary: eGFR levels at the indicated time points

End point title	eGFR levels at the indicated time points

End point description:

eGFR is being assessed from levels of creatinine using the 4 variable version of the modification of diet in renal disease (MDRD) equation as recommended by national kidney foundation-chronic kidney disease (NKF-CKD) guidelines. Baseline for eGFR is defined as the mean of the Screening and Day 0 values. For the end of therapy (Week 104/4 week post last dose assessment), eGFR is being analyzed at both Weeks 100 and 104 (or last dose and 4 week post last dose visits for participants withdrawing early from study treatment), and the mean is being calculated. The results for this outcome measure will be reported at the end of the study i.e. May 2017, as they were not designed to be reported at interim periods. Milliliters per minute per 1.73 meter squared (ml/min/1.73m^2).

End point type	Secondary

End point timeframe:

Baseline and up to Week 104/4 week post last dose

End point values	Belimumab 10 mg/kg IV			
Subject group type	Reporting group			
Number of subjects analysed	0[17]			
Units: ml/min/1.73m^2				
geometric mean (geometric coefficient of variation)	()			

Notes:

[17] - ITT Population

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in eGFR levels at the indicated time points

End point title	Change from Baseline in eGFR levels at the indicated time points

End point description:

eGFR is being assessed from levels of creatinine using the 4 variable version of the modification of diet in renal disease (MDRD) equation as recommended by national kidney foundation-chronic kidney disease (NKF-CKD) guidelines. Baseline for eGFR is defined as the mean of the Screening and Day 0 values. For the end of therapy (Week 104/4 week post last dose assessment), eGFR is being analyzed at both Weeks 100 and 104 (or last dose and 4 week post last dose visits for participants withdrawing early from study treatment), and the mean is being calculated. The ratio is defined as the value at the defined time point divided by the Baseline value. The results for this outcome measure will be reported at the end of the study i.e. May 2017, as they were not designed to be reported at interim periods.

End point type	Secondary

End point timeframe:

Baseline and up to Week 104/4 week post last dose

End point values	Belimumab 10 mg/kg IV			
Subject group type	Reporting group			
Number of subjects analysed	0[18]			
Units: Ratio				
geometric mean (geometric coefficient of variation)	()			

Notes:

[18] - ITT Population

Statistical analyses

No statistical analyses for this end point

Secondary: Serum creatinine levels at the indicated time points

End point title	Serum creatinine levels at the indicated time points

End point description:

Clinical chemistry laboratory parameters included serum creatinine which is being assessed from Baseline and up to Week 128/6 month follow-up visit. Baseline for serum creatinine is defined as the mean of the Screening and Day 0 values. For the end of therapy (Week 104/4 week post last dose assessment), serum creatinine is being analyzed at both Weeks 100 and 104 (or last dose and 4 week post last dose visits for participants withdrawing early from study treatment), and the mean is being calculated. The results for this outcome measure will be reported at the end of the study i.e. May 2017, as they were not designed to be reported at interim periods.

End point type	Secondary

End point timeframe:

Baseline and up to Week 104/4 week post last dose

End point values	Belimumab 10 mg/kg IV			
Subject group type	Reporting group			
Number of subjects analysed	0[19]			
Units: micromoles/liter (µmol/L)				
geometric mean (geometric coefficient of variation)	()			

Notes:

[19] - ITT Population

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in serum creatinine levels at the indicated time points

End point title	Change from Baseline in serum creatinine levels at the indicated time points

End point description:

Clinical chemistry laboratory parameters included serum creatinine which is being assessed from Baseline and up to Week 128/6 month follow-up visit. Baseline for serum creatinine is defined as the mean of the Screening and Day 0 values. For the end of therapy (Week 104/4 week post last dose assessment), serum creatinine is being analyzed at both Weeks 100 and 104 (or last dose and 4 week post last dose visits for participants withdrawing early from study treatment), and the mean is being calculated. The ratio is defined as the value at the defined time point divided by the Baseline value. The

results for this outcome measure will be reported at the end of the study i.e. May 2017, as they were not designed to be reported at interim periods.

End point type	Secondary

End point timeframe:

Baseline and up to Week 104/4 week post last dose

End point values	Belimumab 10 mg/kg IV			
Subject group type	Reporting group			
Number of subjects analysed	0[20]			
Units: Ratio				
geometric mean (geometric coefficient of variation)	()			

Notes:

[20] - ITT Population

Statistical analyses

No statistical analyses for this end point

Secondary: Serum albumin at the indicated time points

End point title	Serum albumin at the indicated time points

End point description:

Clinical chemistry laboratory parameters included serum albumin which is being assessed from Baseline and up to Week 128/6 month follow-up visit. Baseline for serum albumin is defined as the mean of the Screening and Day 0 values. For the end of therapy (Week 104/4 week post last dose assessment), serum albumin is being analyzed at both Weeks 100 and 104 (or last dose and 4 week post last dose visits for participants withdrawing early from study treatment), and the mean is being calculated. The results for this outcome measure will be reported at the end of the study i.e. May 2017, as they were not designed to be reported at interim periods.

End point type	Secondary

End point timeframe:

Baseline and up to Week 104/4 week post last dose

End point values	Belimumab 10 mg/kg IV			
Subject group type	Reporting group			
Number of subjects analysed	0[21]			
Units: grams per liter (g/L)				
geometric mean (geometric coefficient of variation)	()			

Notes:

[21] - ITT Population

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in levels of serum albumin at the indicated time points

End point title	Change from Baseline in levels of serum albumin at the indicated time points

End point description:

Clinical chemistry laboratory parameters included serum albumin which is being assessed from Baseline and up to Week 128/6 month follow-up visit. Baseline for serum albumin is defined as the mean of the Screening and Day 0 values. For the end of therapy (Week 104/4 week post last dose assessment), serum albumin is being analyzed at both Weeks 100 and 104 (or last dose and 4 week post last dose visits for participants withdrawing early from study treatment), and the mean is being calculated. The ratio is defined as the value at the defined time point divided by the Baseline value. The results for this outcome measure will be reported at the end of the study i.e. May 2017, as they were not designed to be reported at interim periods.

End point type	Secondary

End point timeframe:

Baseline and up to Week 104/4 week post last dose

End point values	Belimumab 10 mg/kg IV			
Subject group type	Reporting group			
Number of subjects analysed	0[22]			
Units: Ratio				
geometric mean (geometric coefficient of variation)	()			

Notes:

[22] - ITT Population

Statistical analyses

No statistical analyses for this end point

Secondary: Cholesterol at the indicated time points

End point title	Cholesterol at the indicated time points

End point description:

Clinical chemistry laboratory parameters included cholesterol which is being assessed from Baseline and up to Week 128/6 month follow-up visit. Baseline for cholesterol is defined as the mean of the Screening and Day 0 values. For the end of therapy (Week 104/4 week post last dose assessment), cholesterol is being analyzed at both Weeks 100 and 104 (or last dose and 4 week post last dose visits for participants withdrawing early from study treatment), and the mean is being calculated. The results for this outcome measure will be reported at the end of the study i.e. May 2017, as they were not designed to be reported at interim periods.

End point type	Secondary

End point timeframe:

Baseline and up to Week 104/4 week post last dose

End point values	Belimumab 10 mg/kg IV			
Subject group type	Reporting group			
Number of subjects analysed	0[23]			
Units: millimoles per liter (mmol/L)				
geometric mean (geometric coefficient of variation)	()			

Notes:

[23] - ITT Population

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in levels of cholesterol at the indicated time points

End point title	Change from Baseline in levels of cholesterol at the indicated time points

End point description:

Clinical chemistry laboratory parameters included cholesterol which is being assessed from Baseline and up to Week 128/6 month follow-up visit. Baseline for cholesterol is defined as the mean of the Screening and Day 0 values. For the end of therapy (Week 104/4 week post last dose assessment), cholesterol is being analyzed at both Weeks 100 and 104 (or last dose and 4 week post last dose visits for participants withdrawing early from study treatment), and the mean is being calculated. The ratio is defined as the value at the defined time point divided by the Baseline value. The results for this outcome measure will be reported at the end of the study i.e. May 2017, as they were not designed to be reported at interim periods.

End point type	Secondary

End point timeframe:

Baseline and up to Week 104/4 week post last dose

End point values	Belimumab 10 mg/kg IV			
Subject group type	Reporting group			
Number of subjects analysed	0[24]			
Units: Ratio				
geometric mean (geometric coefficient of variation)	()			

Notes:

[24] - ITT Population

Statistical analyses

No statistical analyses for this end point

Secondary: Summary of incidence of oedema by severity

End point title	Summary of incidence of oedema by severity

End point description:

Reduction of proteinuria lessens the risk of thromboembolic and cardiovascular effects and reduces the oedema in participants. Investigators are physically reviewing participants for clinical manifestations of idiopathic membranous glomerulonephropathy (IMGN) (e.g. oedema extending beyond calf) during study. The results for this outcome measure will be reported at the end of the study i.e. May 2017, as they were not designed to be reported at interim periods.

End point type	Secondary

End point timeframe:

Screening and up to Week 104/4 week post last dose

End point values	Belimumab 10 mg/kg IV			
Subject group type	Reporting group			
Number of subjects analysed	0[25]			
Units: Participants				

Notes:

[25] - ITT Population

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in SF-36 v2 Quality of Life (QoL) questionnaire score

End point title	Change from Baseline in SF-36 v2 Quality of Life (QoL) questionnaire score

End point description:

Health-related quality of life is being assessed through participant self-completion of the short form health survey (SF-36 version [v2]), a general health related quality of life metrics. The SF-36 v2 is referred to as a generic measure as it assesses health concepts that represent basic human values that are relevant to everyone's functional status and wellbeing. SF-36 is being administered prior to any procedures at Screening, Day 0, and Weeks 12, 28, 52, 76 and 104/4 week post last dose. For participants on 12 weekly follow-up, assessment of SF-36 is being conducted at the closest visit to those in the treatment phase. The results for this outcome measure will be reported at the end of the study i.e. May 2017, as they were not designed to be reported at interim periods.

End point type	Secondary

End point timeframe:

From Baseline and up to Week 104/4 week post last dose

End point values	Belimumab 10 mg/kg IV			
Subject group type	Reporting group			
Number of subjects analysed	0[26]			
Units: Scores on a scale				
arithmetic mean (standard deviation)	()			

Notes:

[26] - ITT Population

Statistical analyses

No statistical analyses for this end point

Secondary: Summary of maximum observed serum concentration (Cmax) of belimumab at the indicated time points

End point title	Summary of maximum observed serum concentration (Cmax) of belimumab at the indicated time points

End point description:

The first occurrence of Cmax is being determined directly from the serum concentration-time data. The pharmacokinetic (PK) parameters are being calculated by standard non-compartmental analysis and all calculations of non-compartmental parameters are being based on actual sampling times. The results for this outcome measure will be reported at the end of the study i.e. May 2017, as they were not designed to be reported at interim periods.

End point type	Secondary

End point timeframe:

Baseline and up to 4 week post last dose

End point values	Belimumab 10 mg/kg IV			
Subject group type	Reporting group			
Number of subjects analysed	0[27]			
Units: nanograms per milliliter (ng/mL)				
geometric mean (geometric coefficient of variation)	()			

Notes:

[27] - PK Population: all par. in the ITT Population for whom a PK sample was obtained and analyzed.

Statistical analyses

No statistical analyses for this end point

Secondary: Summary of minimum observed concentration (Cmin) of belimumab at the indicated time points

End point title	Summary of minimum observed concentration (Cmin) of belimumab at the indicated time points

End point description:

Trough concentration (Cmin) samples collected on the specified days are being used to assess attainment of steady state. The results for this outcome measure will be reported at the end of the study i.e. May 2017, as they were not designed to be reported at interim periods.

End point type	Secondary

End point timeframe:

Baseline and up to 4 week post last dose

End point values	Belimumab 10 mg/kg IV			
Subject group type	Reporting group			
Number of subjects analysed	0[28]			
Units: ng/mL				
geometric mean (geometric coefficient of variation)	()			

Notes:

[28] - PK Population

Statistical analyses

No statistical analyses for this end point

Secondary: Summary of area under the serum concentration-time curve to the last quantifiable concentration (AUC[0-2])

End point title	Summary of area under the serum concentration-time curve to the last quantifiable concentration (AUC[0-2])

End point description:

The AUC(0-2) is being determined using the linear trapezoidal rule for increasing concentrations and the logarithmic trapezoidal rule for decreasing concentrations. Blood samples for PK analysis are being collected at the following time points: pre-dose (on dosing days): Days 0, 1, 4, 7, 14 and Week 4, 8, 12, 28, 40, 52, 76 and 4 week post last dose. Post-dose (5 minutes after dosing complete): Days 0 and 28. The results for this outcome measure will be reported at the end of the study i.e. May 2017, as they were not designed to be reported at interim periods.

End point type	Secondary

End point timeframe:

Baseline and up to 4 week post last dose

End point values	Belimumab 10 mg/kg IV			
Subject group type	Reporting group			
Number of subjects analysed	0[29]			
Units: hours times nanograms per milliliter				
geometric mean (geometric coefficient of variation)	()			

Notes:

[29] - PK Population

Statistical analyses

No statistical analyses for this end point

Secondary: Summary of total amount of urine excreted Ae(0-24)

End point title	Summary of total amount of urine excreted Ae(0-24)

End point description:

PK parameters from the urine concentration data: urine Ae(0-24) is being assessed. 24 h urine collections for PK analysis are being collected after the Day 0 and Weeks 12, 28, 52, 76 doses and at the 4 week post last dose visit. A population approach will be undertaken to characterize the population PK parameters and associated variability of belimumab in nephrotic participants. The population approach could have provided derived clearance of belimumab for each participant after the first dose. The population PK analysis is being conducted using nonlinear mixed-effect modeling (NONMEM) or appropriate nonlinear mixed-effect analysis software. The results for this outcome measure will be reported at the end of the study i.e. May 2017, as they were not designed to be reported at interim periods.

End point type	Secondary

End point timeframe:

Baseline and up to 4 week post last dose

End point values	Belimumab 10 mg/kg IV			
Subject group type	Reporting group			
Number of subjects analysed	0[30]			
Units: mg				
arithmetic mean (standard deviation)	()			

Notes:

[30] - PK Population

Statistical analyses

No statistical analyses for this end point

Secondary: Summary of clinical chemistry laboratory parameters assessed up to Week 116/16 week post last dose

End point title	Summary of clinical chemistry laboratory parameters assessed up to Week 116/16 week post last dose

End point description:

Clinical chemistry laboratory parameters included blood urea nitrogen (BUN), potassium, aspartate aminotransferase (AST), alanine aminotransferase (ALT), total and direct bilirubin, creatinine, chloride, uric acid, glucose, total carbondioxide (CO2), gamma glutamyltransferase (GGT), albumin, sodium, calcium, alkaline phosphatase, total protein, eGFR, cholesterol, inorganic phosphates, magnesium, immunoglobulin (Ig) G, IgA, IgM and lactate dehydrogenase assessed up to Week 128/6 month follow-up visit. IgG is being assessed at Screening, then each dosing visit up to Week 52 and Weeks 60, 68, 76, 84, 92, 100, Week 104/4 week post last dose and 16 week and 6 month follow-up visits. IgA and IgM is being assessed at Screening, and then at Week 0, 28 and at Week 104/4 week post last dose. The results for this outcome measure will be reported at the end of the study i.e. May 2017, as they were not designed to be reported at interim periods.

End point type	Secondary

End point timeframe:

Baseline and up to Week 116/16 week follow-up visit

End point values	Belimumab 10 mg/kg IV			
Subject group type	Reporting group			
Number of subjects analysed	0[31]			
Units: To be determined				
arithmetic mean (standard deviation)	()			

Notes:

[31] - ITT Population

Statistical analyses

No statistical analyses for this end point

Secondary: Summary of haematology laboratory parameters assessed up to Week 116/16 week post last dose

End point title	Summary of haematology laboratory parameters assessed up to Week 116/16 week post last dose

End point description:

Hematology laboratory parameters included platelet count, red blood cells (RBC) count, white blood cell (WBC) count, haemoglobin, haematocrit, neutrophils, lymphocytes, monocytes, eosinophils and

basophils assessed up to Week 128/6 month follow-up visit. The results for this outcome measure will be reported at the end of the study i.e. May 2017, as they were not designed to be reported at interim periods.

End point type	Secondary

End point timeframe:

Baseline and up to Week 116/16 week follow-up visit

End point values	Belimumab 10 mg/kg IV			
Subject group type	Reporting group			
Number of subjects analysed	0[32]			
Units: To be determined				
arithmetic mean (standard deviation)	()			

Notes:

[32] - ITT Population

Statistical analyses

No statistical analyses for this end point

Secondary: Summary of urinalysis parameters assessed up to Week 116/16 week post last dose

End point title	Summary of urinalysis parameters assessed up to Week 116/16 week post last dose

End point description:

Urinalysis included pH, glucose, protein, blood and ketones by dipstick, microscopic examination and urine pregnancy assessed up to Week 128/6 month follow-up visit. Urinalysis is done pre-dose during dosing visits. The results for this outcome measure will be reported at the end of the study i.e. May 2017, as they were not designed to be reported at interim periods.

End point type	Secondary

End point timeframe:

Baseline and up to Week 116/16 week follow-up visit

End point values	Belimumab 10 mg/kg IV			
Subject group type	Reporting group			
Number of subjects analysed	0[33]			
Units: To be determined				
arithmetic mean (standard deviation)	()			

Notes:

[33] - ITT Population

Statistical analyses

No statistical analyses for this end point

Secondary: Vital signs measurements assessed up to 116/16 week follow-up visit

End point title	Vital signs measurements assessed up to 116/16 week follow-

	up visit

End point description:

Vital signs including systolic and diastolic blood pressure, pulse rate and temperature were measured throughout the 104-week treatment period and follow-up. Sitting blood pressure/heart rate and body temperature are being measured pre-dose on dosing days. Blood pressure is being measured on at least 2 clinic visits during the Screening phase or by a 24 h ambulatory blood pressure monitor. Additionally, weight is being measured at all dosing visits prior to dosing and at Week 104. The results for this outcome measure will be reported at the end of the study i.e. May 2017, as they were not designed to be reported at interim periods.

End point type	Secondary

End point timeframe:

Baseline and up to Week 116/16 week follow-up visit

End point values	Belimumab 10 mg/kg IV			
Subject group type	Reporting group			
Number of subjects analysed	0[34]			
Units: To be determined				
arithmetic mean (standard deviation)	()			

Notes:

[34] - ITT Population

Statistical analyses

No statistical analyses for this end point

Secondary: Immunogenicity during the 104-week treatment period and up to Week 116/16 week follow-up visit

End point title	Immunogenicity during the 104-week treatment period and up to Week 116/16 week follow-up visit

End point description:

Immunogenicity samples are being collected pre-dose on Weeks 0, 12, 28, 40, 52, 76 and 4 week post last dose and the 16 week post last dose visit for belimumab immunogenicity assay. The results for this outcome measure will be reported at the end of the study i.e. May 2017, as they were not designed to be reported at interim periods.

End point type	Secondary

End point timeframe:

Baseline and up to Week 116/16 week follow-up visit

End point values	Belimumab 10 mg/kg IV			
Subject group type	Reporting group			
Number of subjects analysed	0[35]			
Units: Participants				

Notes:

[35] - ITT Population

Statistical analyses

No statistical analyses for this end point

Secondary: Urine membrane attack complex (MAC)

End point title	Urine membrane attack complex (MAC)

End point description:

Urine membrane attack complex will be assayed quantitatively by ELISA method. Urine MAC samples are being collected at Day 0 and Weeks 8, 28, 52, 76 and 4 week post last dose. Results will be normalized using urine creatinine concentration to adjust for urine dilution. The results for this outcome measure will be reported at the end of the study i.e. May 2017, as they were not designed to be reported at interim periods.

End point type	Secondary

End point timeframe:

Baseline and up to 4 week post last dose

End point values	Belimumab 10 mg/kg IV			
Subject group type	Reporting group			
Number of subjects analysed	0[36]			
Units: ug/umol				
geometric mean (geometric coefficient of variation)	()			

Notes:

[36] - ITT Population

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in urine membrane attack complex (MAC)

End point title	Change from Baseline in urine membrane attack complex (MAC)

End point description:

Urine membrane attack complex will be assayed quantitatively by ELISA method. Urine MAC samples are being collected at Day 0 and Weeks 8, 28, 52, 76 and 4 week post last dose. Results will be normalized using urine creatinine concentration to adjust for urine dilution, before calculation of the ratio as value at time point divided by value at Baseline (Day 0). The results for this outcome measure will be reported at the end of the study i.e. May 2017, as they were not designed to be reported at interim periods.

End point type	Secondary

End point timeframe:

Baseline and up to 4 week post last dose

End point values	Belimumab 10 mg/kg IV			
Subject group type	Reporting group			
Number of subjects analysed	0[37]			
Units: Ratio				
geometric mean (geometric coefficient of variation)	()			

Notes:

[37] - ITT Population

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in B Cell and T Cell subpopulations

End point title	Change from Baseline in B Cell and T Cell subpopulations

End point description:

Blood samples for flow cytometry quantification of peripheral lymphocyte (B cell and T cell) subpopulations and activation markers are being collected on Day 0 and at the Week 8, 16, 28, 4 week post last dose and 6 month post last dose visits. B cell Facs panels are being used to measure changes over the course of therapy in B cell subsets such as transitional, naïve, memory and plasma B cell compartments by percent of the B cell compartments and absolute numbers. T cell Facs panel are being used to measure changes in T cell subsets, such as T regs and CD4+ and CD8+ T cells, in terms of numbers and expression of activation markers to establish if B cell targeting with belimumab affects the T cell compartment perhaps through limiting B cell antigen presentation or cytokine release. The results for this outcome measure will be reported at the end of the study i.e. May 2017, as they were not designed to be reported at interim periods.

End point type	Secondary

End point timeframe:

Baseline and up to Week 128/6 month post last dose

End point values	Belimumab 10 mg/kg IV			
Subject group type	Reporting group			
Number of subjects analysed	0[38]			
Units: Ratio				
geometric mean (geometric coefficient of variation)	()			

Notes:

[38] - ITT Population

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in cytokines/chemokines

End point title	Change from Baseline in cytokines/chemokines

End point description:

Cytokine/chemokines associated with T helper skewing or autoimmune pathology will be analyzed using Luminex, ELISA. Serum analyte quantification is being used to confirm altered protein levels of any gene expression increases or decreases identified by transcriptomic analysis. Cytokine/chemokine samples are being collected on Day 0 and Weeks 8, 16, 28, 52, 76, and 4 week post last dose. The results for this outcome measure will be reported at the end of the study i.e. May 2017, as they were not designed to be reported at interim periods.

End point type	Secondary

End point timeframe:

Baseline and up to Week 104/4 week post last dose

End point values	Belimumab 10 mg/kg IV			
Subject group type	Reporting group			
Number of subjects analysed	0[39]			
Units: Ratio				
geometric mean (geometric coefficient of variation)	()			

Notes:

[39] - ITT Population

Statistical analyses

No statistical analyses for this end point

Secondary: Serum BLys levels

End point title	Serum BLys levels

End point description:

Free BLyS protein is being analyzed using an ELISA. Serum samples are being collected before treatment and after belimumab washout at Week 0 and Week 116/16 week follow-up visit. The results for this outcome measure will be reported at the end of the study i.e. May 2017, as they were not designed to be reported at interim periods.

End point type	Secondary

End point timeframe:

Baseline and Week 116/16 week follow-up visit

End point values	Belimumab 10 mg/kg IV			
Subject group type	Reporting group			
Number of subjects analysed	0[40]			
Units: pg/mL				
geometric mean (geometric coefficient of variation)	()			

Notes:

[40] - ITT Population

Statistical analyses

No statistical analyses for this end point

Secondary: Urine BLys levels as a ratio to creatinine

End point title	Urine BLys levels as a ratio to creatinine

End point description:

B lymphocyte stimulator (BLyS) normalized by creatinine as a ratio of BLyS:creatinine. Free BLyS protein is being analyzed using an ELISA. Urine samples are being collected before treatment and after belimumab washout at Week 0 and Week 116/16 week follow-up visit. The results for this outcome

measure will be reported at the end of the study i.e. May 2017, as they were not designed to be reported at interim periods.

End point type	Secondary

End point timeframe:

Baseline and Week 116/16 week follow-up visit

End point values	Belimumab 10 mg/kg IV			
Subject group type	Reporting group			
Number of subjects analysed	0[41]			
Units: pg/mmol				
geometric mean (geometric coefficient of variation)	()			

Notes:

[41] - ITT Population

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

On-therapy serious adverse events (SAEs) and non-serious adverse events (AEs) are presented from the start of study treatment up to Week 28, or 4 week post last dose End of Therapy visit for participants withdrawing from treatment earlier than Week 28.

Adverse event reporting additional description:

On-therapy SAEs and non-serious AEs are reported for members of the ITT Population, comprised of all participants who received at least one dose of investigational drug.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	17.1

Reporting groups

Reporting group title	Belimumab 10 mg/kg IV

Reporting group description:

Participants received 10 milligrams per kilogram (mg/kg) belimumab intravenous (IV) infusion every 4 weeks, over 24 weeks.

Serious adverse events	Belimumab 10 mg/kg IV		
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 14 (7.14%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			
Infections and infestations			
Cellulitis			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Belimumab 10 mg/kg IV		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	14 / 14 (100.00%)		
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		

Malaise subjects affected / exposed occurrences (all) Pyrexia subjects affected / exposed occurrences (all)	1 / 14 (7.14%) 1 1 / 14 (7.14%) 1		
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all) Oropharyngeal pain subjects affected / exposed occurrences (all)	 1 / 14 (7.14%) 1 1 / 14 (7.14%) 2		
Psychiatric disorders Depression subjects affected / exposed occurrences (all)	 1 / 14 (7.14%) 1		
Investigations Eosinophil count increased subjects affected / exposed occurrences (all)	 1 / 14 (7.14%) 1		
Nervous system disorders Headache subjects affected / exposed occurrences (all) Dizziness subjects affected / exposed occurrences (all) Migraine subjects affected / exposed occurrences (all) Presyncope subjects affected / exposed occurrences (all)	 2 / 14 (14.29%) 5 1 / 14 (7.14%) 1 1 / 14 (7.14%) 1 1 / 14 (7.14%) 1		
Ear and labyrinth disorders			

Tinnitus			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Eye disorders			
Periorbital oedema			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	2 / 14 (14.29%)		
occurrences (all)	3		
Abdominal pain			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Abdominal pain upper			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Ascites			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Dyspepsia			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Irritable bowel syndrome			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Nausea			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Rash pruritic			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Skin lesion			

subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Swelling face			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	2		
Renal and urinary disorders			
Tubulointerstitial nephritis			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Musculoskeletal and connective tissue disorders			
Muscle spasms			
subjects affected / exposed	3 / 14 (21.43%)		
occurrences (all)	3		
Arthralgia			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Flank pain			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Joint swelling			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Myalgia			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Pain in extremity			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	3 / 14 (21.43%)		
occurrences (all)	3		
Upper respiratory tract infection			
subjects affected / exposed	2 / 14 (14.29%)		
occurrences (all)	2		
Cellulitis			

subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Lower respiratory tract infection			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Oral candidiasis			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Respiratory tract infection			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	4		
Rhinitis			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Urinary tract infection			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	2		
Viral upper respiratory tract infection			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	2		
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
10 May 2012	Clarification of stopping criteria; additional rationale for hypogammaglobulinaemia including stopping criteria and monitoring; removal of Disease-Related Events provision; clarification of SRT
21 December 2012	Addition of Benlysta programme generic suicidality monitoring text; extension of biopsy inclusion to 7 years (3 years non-active); extension of time before stopping study treatment when hypogammaglobulinaemia without improvement; removal of requirement for 6 month post dose immunogenicity; addition of aliskiren, ACTH to prohibited medications; minor clarifications and consistency corrections
10 January 2014	Addition of 6 month post treatment follow-up; PML text revision; alternative use of 24h protein excretion instead of uPCR in eligibility and for increased dosing frequency threshold; reduction in rituximab washout; removal NSAID prohibition; removal of change in urine belimumab endpoint; minor clarifications and consistency corrections
06 March 2014	Strengthening of discouragement against use of NSAIDs at MHRA request

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported