Clinical trial results:
A Randomised, Double-Blind, Placebo Controlled, Parallel-Group, Multicenter Study To Evaluate The Efficacy and Safety of Two Doses of Ocrelizumab in Patients With WHO or ISN Class III or IV Nephritis Due To Systemic Lupus Erythematosus

Summary

EudraCT number	2006-005357-29
Trial protocol	GB FR DE HU ES NL PT SE PL BG
Global end of trial date	28 October 2013

Results information

Result version number	v2 (current)
This version publication date	19 May 2016
First version publication date	07 August 2015
Version creation reason	• Correction of full data set 2 data eras identified as part of QC that require correction

Trial information

Trial identification

Sponsor protocol code	WA20500

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00626197
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	F. Hoffmann-La Roche AG
Sponsor organisation address	Grenzacherstrasse 124, Basel, Switzerland, CH-4070
Public contact	Roche Trial Information Hotline , F. Hoffmann-La Roche AG , 41 61 6878333, global.trial_information@roche.com
Scientific contact	Roche Trial Information Hotline , F. Hoffmann-La Roche AG , 41 61 6878333, global.trial_information@roche.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	19 November 2013
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	28 October 2013
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To investigate the ability of the ocrelizumab regimen in combination with Standard Of Care (SOC) treatment to induce a complete or partial renal response, as assessed by renal function, urinary sediment and proteinuria in participants with International Society of Nephrology/Renal Pathology Society (ISN/RPS) or World Health Organization (WHO) class III or IV lupus nephritis.

Protection of trial subjects:

The investigator ensured that this study was conducted in full conformance with the principles of the "Declaration of Helsinki" or with the laws and regulations of the country in which the research was conducted, whichever afforded the greater protection to the individual and fully adhered to the principles outlined in "Guideline for Good Clinical Practice" International Conference on Harmonisation (ICH) Tripartite Guideline [January 1997] or with local law if it affords greater protection to the participant. For studies conducted in the European Union/European Economic Area (EU/EEA) countries, the investigator ensured compliance with the EU Clinical Trial Directive [2001/20/EC]. For studies conducted in the United State of America (USA) or under US Investigational new drug (IND), the investigator additionally ensured that the basic principles of "Good Clinical Practice" as outlined in the current version of 21 CFR, subchapter D, part 312, "Responsibilities of Sponsors and Investigators", part 50, "Protection of Human Patients", and part 56, "Institutional Review Boards", were adhered to.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	15 February 2008
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	Netherlands: 6
Country: Number of subjects enrolled	Spain: 10
Country: Number of subjects enrolled	Sweden: 1
Country: Number of subjects enrolled	United Kingdom: 4
Country: Number of subjects enrolled	Bulgaria: 10
Country: Number of subjects enrolled	France: 18
Country: Number of subjects enrolled	Germany: 10
Country: Number of subjects enrolled	Hungary: 11
Country: Number of subjects enrolled	Argentina: 56
Country: Number of subjects enrolled	Brazil: 18
Country: Number of subjects enrolled	Canada: 3
Country: Number of subjects enrolled	Chile: 2
Country: Number of subjects enrolled	Colombia: 43

Country: Number of subjects enrolled	Costa Rica: 4
Country: Number of subjects enrolled	Hong Kong: 5
Country: Number of subjects enrolled	Indonesia: 3
Country: Number of subjects enrolled	Malaysia: 18
Country: Number of subjects enrolled	Mexico: 21
Country: Number of subjects enrolled	Peru: 16
Country: Number of subjects enrolled	Philippines: 15
Country: Number of subjects enrolled	Russian Federation: 10
Country: Number of subjects enrolled	Serbia: 5
Country: Number of subjects enrolled	South Africa: 5
Country: Number of subjects enrolled	Korea, Republic of: 17
Country: Number of subjects enrolled	Taiwan: 8
Country: Number of subjects enrolled	Thailand: 22
Country: Number of subjects enrolled	Turkey: 4
Country: Number of subjects enrolled	United States: 36
Worldwide total number of subjects	381
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)	7
Adults (18-64 years)	372
From 65 to 84 years	2
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Screening was done from Day -14 to Day -1.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Participants received placebo matched to ocrelizumab infusion intravenously (IV) on Days 1 and 15, followed by placebo matched to ocrelizumab infusion IV on Week 16 and then every 16 weeks up to 48 weeks along with one of the two standard-of-care (SOC) immunosuppressant regimens at the discretion of the investigator. The SOC regimens were: Euro-Lupus (cyclophosphamide 500 mg every 2 weeks for 6 doses followed by azathioprine maintenance at 1-2 milligrams per kilogram per day [mg/kg/day]), or mycophenolate mofetil (MMF) 1 grams per day (g/day) in the first week increased to 3 g/day. Participants also received methylprednisolone 100 milligram (mg) infusion IV or according to local guidelines, completed at least 30 minutes prior to each infusion of placebo. Participants also received oral prednisone at a starting dose of 0.75 mg/kg/day with a maximum dose of 60 mg/day from Day 2. Beginning on Day 16 the doses were tapered and continued for 10 weeks to a target dose of 10 mg/day.

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

Dosage and administration details:

Participants received placebo IV on days 1 and 15, followed by placebo IV at Week 16 and then every 16 weeks up to 48 weeks.

Arm title	Ocrelizumab 400 mg

Arm description:

Participants received 400 mg ocrelizumab IV on Days 1 and 15, followed by 400 mg ocrelizumab infusion IV on Week 16 and then every 16 weeks up to 48 weeks along with one of the two standard-of-care (SOC) immunosuppressant regimens at the discretion of the investigator. The SOC regimens were: Euro-Lupus (cyclophosphamide 500 mg every 2 weeks for 6 doses followed by azathioprine maintenance at 1-2 milligrams per kilogram per day [mg/kg/day]), or MMF 1 g/day in the first week increased to 3 g/day. Participants also received methylprednisolone 100 mg infusion IV or according to local guidelines, completed at least 30 minutes prior to each infusion of ocrelizumab. Participants also received oral prednisone at starting dose of 0.75 mg/kg/day with a maximum dose of 60 mg/day from Day 2. Beginning on Day 16 the doses were tapered and continued for 10 weeks to a target dose of 10 mg/day.

Arm type	Experimental

Investigational medicinal product name	Ocrelizumab
Investigational medicinal product code	
Other name	RO4964913
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Participants received ocrelizumab on Days 1 and 15, followed by 400 mg IV at Week 16 and then every 16 weeks up to 48 weeks.

Arm title	Ocrelizumab 1000 mg

Arm description:

Participants received 1000 mg ocrelizumab IV on Days 1 and 15, followed by 1000 mg ocrelizumab infusion IV on Week 16 and then every 16 weeks up to 48 weeks along with one of the two standard-of-care (SOC) immunosuppressant regimens at the discretion of the investigator. The SOC regimens were: Euro-Lupus (cyclophosphamide 500 mg every 2 weeks for 6 doses followed by azathioprine maintenance at 1-2 milligrams per kilogram per day [mg/kg/day]), or MMF 1 g/day in the first week increased to 3 g/day. Participants also received methylprednisolone 100 mg infusion IV or according to local guidelines, completed at least 30 minutes prior to each infusion of ocrelizumab. Participants also received oral prednisone at starting dose of 0.75 mg/kg/day with a maximum dose of 60 mg/day from Day 2. Beginning on Day 16 the doses were tapered and continued for 10 weeks to a target dose of 10 mg/day.

Arm type	Experimental
Investigational medicinal product name	Ocrelizumab
Investigational medicinal product code	
Other name	RO4964913
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Participants received ocrelizumab on Days 1 and 15, followed by 1000 mg IV at Week 16 and then every 16 weeks up to 48 weeks.

Number of subjects in period 1	Placebo	Ocrelizumab 400 mg	Ocrelizumab 1000 mg
Started	126	127	128
Completed	49	83	74
Not completed	77	44	54
Adverse event, serious fatal	6	3	6
Consent withdrawn by subject	7	17	17
Failure to return	6	6	5
Adverse event, non-fatal	2	1	1
Administrative reasons	55	15	19
Did not cooperate	1	2	6

Baseline characteristics

Reporting groups	
Reporting group title	Placebo

Reporting group description:

Participants received placebo matched to ocrelizumab infusion intravenously (IV) on Days 1 and 15, followed by placebo matched to ocrelizumab infusion IV on Week 16 and then every 16 weeks up to 48 weeks along with one of the two standard-of-care (SOC) immunosuppressant regimens at the discretion of the investigator. The SOC regimens were: Euro-Lupus (cyclophosphamide 500 mg every 2 weeks for 6 doses followed by azathioprine maintenance at 1-2 milligrams per kilogram per day [mg/kg/day]), or mycophenolate mofetil (MMF) 1 grams per day (g/day) in the first week increased to 3 g/day. Participants also received methylprednisolone 100 milligram (mg) infusion IV or according to local guidelines, completed at least 30 minutes prior to each infusion of placebo. Participants also received oral prednisone at a starting dose of 0.75 mg/kg/day with a maximum dose of 60 mg/day from Day 2. Beginning on Day 16 the doses were tapered and continued for 10 weeks to a target dose of 10 mg/day.

Reporting group title	Ocrelizumab 400 mg

Reporting group description:

Participants received 400 mg ocrelizumab IV on Days 1 and 15, followed by 400 mg ocrelizumab infusion IV on Week 16 and then every 16 weeks up to 48 weeks along with one of the two standard-of-care (SOC) immunosuppressant regimens at the discretion of the investigator. The SOC regimens were: Euro-Lupus (cyclophosphamide 500 mg every 2 weeks for 6 doses followed by azathioprine maintenance at 1-2 milligrams per kilogram per day [mg/kg/day]), or MMF 1 g/day in the first week increased to 3 g/day. Participants also received methylprednisolone 100 mg infusion IV or according to local guidelines, completed at least 30 minutes prior to each infusion of ocrelizumab. Participants also received oral prednisone at starting dose of 0.75 mg/kg/day with a maximum dose of 60 mg/day from Day 2. Beginning on Day 16 the doses were tapered and continued for 10 weeks to a target dose of 10 mg/day.

Reporting group title	Ocrelizumab 1000 mg

Reporting group description:

Participants received 1000 mg ocrelizumab IV on Days 1 and 15, followed by 1000 mg ocrelizumab infusion IV on Week 16 and then every 16 weeks up to 48 weeks along with one of the two standard-of-care (SOC) immunosuppressant regimens at the discretion of the investigator. The SOC regimens were: Euro-Lupus (cyclophosphamide 500 mg every 2 weeks for 6 doses followed by azathioprine maintenance at 1-2 milligrams per kilogram per day [mg/kg/day]), or MMF 1 g/day in the first week increased to 3 g/day. Participants also received methylprednisolone 100 mg infusion IV or according to local guidelines, completed at least 30 minutes prior to each infusion of ocrelizumab. Participants also received oral prednisone at starting dose of 0.75 mg/kg/day with a maximum dose of 60 mg/day from Day 2. Beginning on Day 16 the doses were tapered and continued for 10 weeks to a target dose of 10 mg/day.

Reporting group values	Placebo	Ocrelizumab 400 mg	Ocrelizumab 1000 mg
Number of subjects	126	127	128
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	31.3	31.9	30.6
standard deviation	± 9.9	± 10.2	± 8.9
Gender categorical Units: Subjects			
Female	107	115	110
Male	19	12	18

Reporting group values	Total		
Number of subjects	381		

Age categorical Units: Subjects			

Age continuous Units: years arithmetic mean standard deviation	- -		
Gender categorical Units: Subjects			
Female	332		
Male	49		

End points

End points reporting groups

Reporting group title	Placebo

Reporting group description:

Participants received placebo matched to ocrelizumab infusion intravenously (IV) on Days 1 and 15, followed by placebo matched to ocrelizumab infusion IV on Week 16 and then every 16 weeks up to 48 weeks along with one of the two standard-of-care (SOC) immunosuppressant regimens at the discretion of the investigator. The SOC regimens were: Euro-Lupus (cyclophosphamide 500 mg every 2 weeks for 6 doses followed by azathioprine maintenance at 1-2 milligrams per kilogram per day [mg/kg/day]), or mycophenolate mofetil (MMF) 1 grams per day (g/day) in the first week increased to 3 g/day. Participants also received methylprednisolone 100 milligram (mg) infusion IV or according to local guidelines, completed at least 30 minutes prior to each infusion of placebo. Participants also received oral prednisone at a starting dose of 0.75 mg/kg/day with a maximum dose of 60 mg/day from Day 2. Beginning on Day 16 the doses were tapered and continued for 10 weeks to a target dose of 10 mg/day.

Reporting group title	Ocrelizumab 400 mg

Reporting group description:

Participants received 400 mg ocrelizumab IV on Days 1 and 15, followed by 400 mg ocrelizumab infusion IV on Week 16 and then every 16 weeks up to 48 weeks along with one of the two standard-of-care (SOC) immunosuppressant regimens at the discretion of the investigator. The SOC regimens were: Euro-Lupus (cyclophosphamide 500 mg every 2 weeks for 6 doses followed by azathioprine maintenance at 1-2 milligrams per kilogram per day [mg/kg/day]), or MMF 1 g/day in the first week increased to 3 g/day. Participants also received methylprednisolone 100 mg infusion IV or according to local guidelines, completed at least 30 minutes prior to each infusion of ocrelizumab. Participants also received oral prednisone at starting dose of 0.75 mg/kg/day with a maximum dose of 60 mg/day from Day 2. Beginning on Day 16 the doses were tapered and continued for 10 weeks to a target dose of 10 mg/day.

Reporting group title	Ocrelizumab 1000 mg

Reporting group description:

Participants received 1000 mg ocrelizumab IV on Days 1 and 15, followed by 1000 mg ocrelizumab infusion IV on Week 16 and then every 16 weeks up to 48 weeks along with one of the two standard-of-care (SOC) immunosuppressant regimens at the discretion of the investigator. The SOC regimens were: Euro-Lupus (cyclophosphamide 500 mg every 2 weeks for 6 doses followed by azathioprine maintenance at 1-2 milligrams per kilogram per day [mg/kg/day]), or MMF 1 g/day in the first week increased to 3 g/day. Participants also received methylprednisolone 100 mg infusion IV or according to local guidelines, completed at least 30 minutes prior to each infusion of ocrelizumab. Participants also received oral prednisone at starting dose of 0.75 mg/kg/day with a maximum dose of 60 mg/day from Day 2. Beginning on Day 16 the doses were tapered and continued for 10 weeks to a target dose of 10 mg/day.

Subject analysis set title	OCR + SOC
Subject analysis set type	Intention-to-treat

Subject analysis set description:

This analysis set included all participants who were treated with ocrelizumab (OCR).

Subject analysis set title	Placebo-Mycophenolate Mofetil (MMF)
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

Placebo - MMF group included participants whose SOC treatment included MMF as an immunosuppressant treatment.

Subject analysis set title	Placebo-Euro Lupus (EL)
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

Placebo-EL group included participants whose SOC treatment included Cyclophosphamide (Euro-lupus) as part of the immunosuppressant treatment.

Primary: Percentage of Participants who Achieved a Complete Renal Response (CRR) or a Partial Renal Response (PRR) at Week 48

End point title	Percentage of Participants who Achieved a Complete Renal Response (CRR) or a Partial Renal Response (PRR) at Week 48[1]

End point description:

CRR was defined as: 1. Normal serum creatinine (and with no more than a 25 percent [%] increase from Baseline); 2. Improvement in urinary protein:urinary creatinine ratio to less than or equal to (≤) 0.5. PRR was defined as at least 50 percent (%) reduction in proteinuria from Baseline, without more than 25% increase of serum creatinine at Week 48, compared with Baseline. If Baseline urine protein:urine creatinine ratio was greater than (>) 3, a urine protein:urine creatinine ratio of less than (<) 3 needed to be achieved.

End point type	Primary

End point timeframe:

Week 48

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: The primary endpoint was analyzed via an overall response (CRR+PRR) analysis and the separate complete and partial response rates were only summarized descriptively.

End point values	Placebo	Ocrelizumab 400 mg	Ocrelizumab 1000 mg	OCR + SOC
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	75	75	73	148
Units: Percentage of participants				
number (not applicable)				
CRR	34.7	42.7	31.5	37.2
PRR	20	24	35.6	29.7

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Participants Who Achieved Overall Response

End point title	Percentage of Participants Who Achieved Overall Response

End point description:

Overall response rate (ORR) equals (=) CRR + PRR. CRR was defined as: 1. Normal serum creatinine (and with no more than a 25% increase from baseline) 2. Improvement in urinary protein:urinary creatinine ratio to ≤0.5. PRR was defined as at least 50 % reduction in proteinuria from Baseline, without more than 25% increase of serum creatinine at Week 48, compared with Baseline. If Baseline urine protein:urine creatinine ratio is >3, a urine protein:urine creatinine ratio of <3 needs to be achieved.

End point type	Primary

End point timeframe:

Week 48

End point values	Placebo	Ocrelizumab 400 mg	Ocrelizumab 1000 mg	OCR + SOC
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	75	75	73	148
Units: Percentage of Participants				
number (confidence interval 95%)	54.7 (43.4 to 65.9)	66.7 (56 to 77.3)	67.1 (56.3 to 77.9)	66.9 (59.3 to 74.5)

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo v Ocrelizumab 400 mg
Number of subjects included in analysis	150
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Mean difference (final values)
Point estimate	12.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.3
upper limit	27.5

Statistical analysis title	Statistical Analysis 2
Comparison groups	Placebo v Ocrelizumab 1000 mg
Number of subjects included in analysis	148
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Mean difference (final values)
Point estimate	13.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.4
upper limit	29.2

Statistical analysis title	Statistical Analysis 3
Comparison groups	Placebo v OCR + SOC
Number of subjects included in analysis	223
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.065
Method	Cochran-Mantel-Haenszel
Parameter estimate	Mean difference (final values)
Point estimate	12.7

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.8
upper limit	26.1

Secondary: Percentage of Participants who Achieved a Renal Response (Partial or Complete) by Week 36, and Sustain or Improve This Response Until Week 48

End point title	Percentage of Participants who Achieved a Renal Response (Partial or Complete) by Week 36, and Sustain or Improve This Response Until Week 48

End point description:

CRR was defined as: 1. Normal serum creatinine (and with no more than a 25% increase from Baseline) 2. Inactive urinary sediment 3. Improvement in urinary protein:urinary creatinine ratio to ≤0.5. PRR was defined as at least 50 % reduction in proteinuria from Baseline, without more than 25% increase of serum creatinine at Week 48, compared with Baseline. If Baseline urine protein:urine creatinine ratio was >3, a urine protein:urine creatinine ratio of <3 needed to be achieved.

End point type	Secondary

End point timeframe:

Weeks 36, 40, 44, and 48

End point values	Placebo	Ocrelizumab 400 mg	Ocrelizumab 1000 mg	OCR + SOC
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	0[2]	0[3]	0[4]	0[5]
Units: Percentage of Participants				
number (not applicable)				

Notes:

[2] - Due to early termination of the study, no secondary outcome analyses were performed.

[3] - Due to early termination of the study, no secondary outcome analyses were performed.

[4] - Due to early termination of the study, no secondary outcome analyses were performed.

[5] - Due to early termination of the study, no secondary outcome analyses were performed.

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Complete Renal Response

End point title	Time to Complete Renal Response

End point description:

Time to complete renal response was proposed to be analyzed using a stratified log rank test with race and SOC as stratification factors. Comparisons of ocrelizumab versus placebo were to be expressed as p-values, estimated hazard ratios, adjusted proportions of participants who achieved a complete renal response and their 95% confidence intervals. Kaplan-Meier curves were to be produced. Due to early termination of the study the analyses were not performed.

End point type	Secondary

End point timeframe:

Weeks 1, 2, 4, 8, 12, 16, 20, 24, 28, 32, 36, 40, 44, and 48

End point values	Placebo	Ocrelizumab 400 mg	Ocrelizumab 1000 mg	OCR + SOC
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	0[6]	0[7]	0[8]	0[9]
Units: Weeks				
median (full range (min-max))	(to)	(to)	(to)	(to)

Notes:

[6] - Due to early termination of the study, no secondary outcome analyses were performed.

[7] - Due to early termination of the study, no secondary outcome analyses were performed.

[8] - Due to early termination of the study, no secondary outcome analyses were performed.

[9] - Due to early termination of the study, no secondary outcome analyses were performed.

Statistical analyses

No statistical analyses for this end point

Secondary: Area Under the Curve (AUC) of Calculated Glomerular Filtration Rate (cGFR) Between Baseline and Week 48

End point title	Area Under the Curve (AUC) of Calculated Glomerular Filtration Rate (cGFR) Between Baseline and Week 48

End point description:

The improvement of AUC of cGFR was to be measured between Baseline and Week 48. This was to be analyzed with Analysis of Covariance (ANCOVA) with race and SOC as covariates.

End point type	Secondary

End point timeframe:

Baseline and Weeks 1, 2, 4, 8, 12, 16, 20, 24, 28, 32, 36, 40, 44, and Week 48

End point values	Placebo	Ocrelizumab 400 mg	Ocrelizumab 1000 mg	OCR + SOC
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	0[10]	0[11]	0[12]	0[13]
Units: mL/min)*weeks				
arithmetic mean (standard deviation)	()	()	()	()

Notes:

[10] - Due to early termination of the study, no secondary outcome analyses were performed.

[11] - Due to early termination of the study, no secondary outcome analyses were performed.

[12] - Due to early termination of the study, no secondary outcome analyses were performed.

[13] - Due to early termination of the study, no secondary outcome analyses were performed.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Who Achieved A Reduction In Systemic Lupus Erythematosis Disease Activity Index (SLEDAI) -2K Score

End point title	Percentage of Participants Who Achieved A Reduction In Systemic Lupus Erythematosis Disease Activity Index (SLEDAI) -2K Score

End point description:

SLEDAI-2K measures disease activity at the visit or within the preceding 10 days. It comprised of 24 descriptors, covering 9 organ systems, and reflects disease activity over the previous 10 days.The total SLEDAI-2K score falls between 0 and 105, with higher scores representing higher disease activity

End point type	Secondary

End point timeframe:

Baseline and Weeks 1, 2, 4, 8, 12, 16, 20, 24, 28, 32, 36, 40, 44, and 48

End point values	Placebo	Ocrelizumab 400 mg	Ocrelizumab 1000 mg	OCR + SOC
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	0[14]	0[15]	0[16]	0[17]
Units: percentage of participants				
number (not applicable)				

Notes:

[14] - Due to early termination of the study, no secondary outcome analyses were performed.

[15] - Due to early termination of the study, no secondary outcome analyses were performed.

[16] - Due to early termination of the study, no secondary outcome analyses were performed.

[17] - Due to early termination of the study, no secondary outcome analyses were performed.

Statistical analyses

No statistical analyses for this end point

Secondary: Time to First Renal Flare In Those Participants who Demonstrated at least a Partial Renal Response

End point title	Time to First Renal Flare In Those Participants who Demonstrated at least a Partial Renal Response

End point description:

Renal flares may be either proteinuric or nephritic as defined below: Proteinuric Flares are defined as follows:In participants who achieve a urine protein:urine creatinine (Upr:Ucr) ≤ 0.5, an increase to Upr:Ucr >1; In participants with an Upr:Ucr >0.5, a doubling of Upr:Ucr (with a minimum increase to Upr:Ucr >2).
Nephritic Flare defined as: Increase in serum creatinine of ≥30% from the lowest value achieved in the study accompanied by Increase Upr:Ucr >1 Or New/worsening active urine sediment on two consecutive occasions, in the absence of urinary tract infection or other causes of hematuria.

End point type	Secondary

End point timeframe:

Weeks 1, 2, 4, 8, 12, 16, 20, 24, 28, 32, 36, 40, 44, and 48

End point values	Placebo	Ocrelizumab 400 mg	Ocrelizumab 1000 mg	OCR + SOC
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	0[18]	0[19]	0[20]	0[21]
Units: Weeks				
median (full range (min-max))	(to)	(to)	(to)	(to)

Notes:

[18] - Due to early termination of the study, no secondary outcome analyses were performed.

[19] - Due to early termination of the study, no secondary outcome analyses were performed.

[20] - Due to early termination of the study, no secondary outcome analyses were performed.

[21] - Due to early termination of the study, no secondary outcome analyses were performed.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Who Achieved Clinically Meaningful Improvement in the Physical and Mental Component Scores of the Short Form 36 (SF36) from Baseline to Week 48

End point title	Percentage of Participants Who Achieved Clinically Meaningful Improvement in the Physical and Mental Component Scores of the Short Form 36 (SF36) from Baseline to Week 48

End point description:

The SF36 Health Survey is a 36-item, patient-reported survey of patient health. The SF-36 consists of eight scaled scores, which are the weighted sums of the questions in their section. Each scale is directly transformed into a 0-100 scale. A score of zero is equivalent to maximum disability and a score of 100 is equivalent to no disability. The eight sections are: vitality, physical functioning, bodily pain, general health perceptions physical role functioning, emotional role functioning, social role functioning, and mental health.

End point type	Secondary

End point timeframe:

Baseline and Weeks 1, 12, 24, 36, and 48

End point values	Placebo	Ocrelizumab 400 mg	Ocrelizumab 1000 mg	OCR + SOC
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	0[22]	0[23]	0[24]	0[25]
Units: Percentage of participants				
number (not applicable)				

Notes:

[22] - Due to early termination of the study, no secondary outcome analyses were performed.

[23] - Due to early termination of the study, no secondary outcome analyses were performed.

[24] - Due to early termination of the study, no secondary outcome analyses were performed.

[25] - Due to early termination of the study, no secondary outcome analyses were performed.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Who Achieved Clinically Meaningful Improvement in Fatigue Using the Functional Assessment of Chronic Illness Therapy (Facit) Fatigue Questionnaire from Baseline to Week 48

End point title	Percentage of Participants Who Achieved Clinically Meaningful Improvement in Fatigue Using the Functional Assessment of Chronic Illness Therapy (Facit) Fatigue Questionnaire from Baseline to Week 48

End point description:

The FACIT Fatigue Scale is a short, 13-item, easy-to-administer tool that measures an individual’s level of fatigue during their usual daily activities over the past week. The level of fatigue is measured on a

four point Likert scale (4 = not at all fatigued to 0 = very much fatigued).

End point type	Secondary

End point timeframe:

Baseline and Weeks 1, 2, 4, 8, 12, 16, 20, 24, 28, 32, 36, 40, 44, and 48

End point values	Placebo	Ocrelizumab 400 mg	Ocrelizumab 1000 mg	OCR + SOC
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	0[26]	0[27]	0[28]	0[29]
Units: Percentage of participants				
number (not applicable)				

Notes:

[26] - Due to early termination of the study, no secondary outcome analyses were performed.

[27] - Due to early termination of the study, no secondary outcome analyses were performed.

[28] - Due to early termination of the study, no secondary outcome analyses were performed.

[29] - Due to early termination of the study, no secondary outcome analyses were performed.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Who Achieved Clinically Meaningful Improvement in Pain Using the Modified Brief Pain Inventory Short Form (mBPI-SF) from Baseline to Week 48

End point title	Percentage of Participants Who Achieved Clinically Meaningful Improvement in Pain Using the Modified Brief Pain Inventory Short Form (mBPI-SF) from Baseline to Week 48

End point description:

m-BPI-sf is a self-administered 11-point Likert rating scale to rate pain in the past 24 hours. A single item pertains to worst pain in the past 24 hours with a range of 0 (no pain) to 10 (worst imaginable pain).

End point type	Secondary

End point timeframe:

Baseline and Weeks 1, 12, 24, 36, and 48

End point values	Placebo	Ocrelizumab 400 mg	Ocrelizumab 1000 mg	OCR + SOC
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	0[30]	0[31]	0[32]	0[33]
Units: Percentage of participants				
number (not applicable)				

Notes:

[30] - Due to early termination of the study, no secondary outcome analyses were performed.

[31] - Due to early termination of the study, no secondary outcome analyses were performed.

[32] - Due to early termination of the study, no secondary outcome analyses were performed.

[33] - Due to early termination of the study, no secondary outcome analyses were performed.

Statistical analyses

No statistical analyses for this end point

Secondary: Health Care Visits Over the 48-Week Treatment Period

End point title	Health Care Visits Over the 48-Week Treatment Period

End point description:

The number of health care visits (including doctor's office visits, Emergency room/ Accident and Emergency [ER/A&E] visits and hospitalizations) over the 48-week treatment period were recorded.

End point type	Secondary

End point timeframe:

Weeks 1, 24, and 48

End point values	Placebo	Ocrelizumab 400 mg	Ocrelizumab 1000 mg	OCR + SOC
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	0[34]	0[35]	0[36]	0[37]
Units: visits				
number (not applicable)				

Notes:

[34] - Due to early termination of the study, no secondary outcome analyses were performed.

[35] - Due to early termination of the study, no secondary outcome analyses were performed.

[36] - Due to early termination of the study, no secondary outcome analyses were performed.

[37] - Due to early termination of the study, no secondary outcome analyses were performed.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants who Achieved a CRR or PRR And who Received A Corticosteroid dose of <10 Milligrams per Day (mg/day) from Week 24 to Week 48

End point title	Percentage of Participants who Achieved a CRR or PRR And who Received A Corticosteroid dose of <10 Milligrams per Day (mg/day) from Week 24 to Week 48

End point description:

CRR was defined as: 1. Normal serum creatinine (and with no more than a 25% increase from Baseline) 2. Inactive urinary sediment 3. Improvement in urinary protein:urinary creatinine ratio to ≤0.5. PRR was defined as at least 50% reduction in proteinuria from Baseline, without more than 25% increase of serum creatinine at Week 48, compared with Baseline. If Baseline urine protein:urine creatinine ratio was >3, a urine protein:urine creatinine ratio of <3 needed to be achieved.

End point type	Secondary

End point timeframe:

Weeks 24, 28, 32, 36, 40, 44, and 48

End point values	Placebo	Ocrelizumab 400 mg	Ocrelizumab 1000 mg	OCR + SOC
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	0[38]	0[39]	0[40]	0[41]
Units: Percentage of participants				
number (not applicable)				

Notes:

[38] - Due to early termination of the study, no secondary outcome analyses were performed.

[39] - Due to early termination of the study, no secondary outcome analyses were performed.

[40] - Due to early termination of the study, no secondary outcome analyses were performed.

[41] - Due to early termination of the study, no secondary outcome analyses were performed.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants who Achieved a CRR or PRR And who Received a Corticosteroid Dose of <5 mg/day by Week 48

End point title	Percentage of Participants who Achieved a CRR or PRR And who Received a Corticosteroid Dose of <5 mg/day by Week 48

End point description:

CRR was defined as: 1. Normal serum creatinine (and with no more than a 25% increase from Baseline) 2. Inactive urinary sediment 3. Improvement in urinary protein:urinary creatinine ratio to ≤0.5. PRR was defined as at least 50% reduction in proteinuria from Baseline, without more than 25% increase of serum creatinine at Week 48, compared with Baseline. If Baseline urine protein:urine creatinine ratio was >3, a urine protein: urine creatinine ratio of <3 needed to be achieved.

End point type	Secondary

End point timeframe:

Week 48

End point values	Placebo	Ocrelizumab 400 mg	Ocrelizumab 1000 mg	OCR + SOC
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	0[42]	0[43]	0[44]	0[45]
Units: Percentage of participants				
number (not applicable)				

Notes:

[42] - Due to early termination of the study, no secondary outcome analyses were performed.

[43] - Due to early termination of the study, no secondary outcome analyses were performed.

[44] - Due to early termination of the study, no secondary outcome analyses were performed.

[45] - Due to early termination of the study, no secondary outcome analyses were performed.

Statistical analyses

No statistical analyses for this end point

Secondary: Average Corticosteroid Burden Measured by AUC of the Cumulative Corticosteroid Dose Between 16 and 48 Weeks

End point title	Average Corticosteroid Burden Measured by AUC of the Cumulative Corticosteroid Dose Between 16 and 48 Weeks

End point description:

AUC is the area under the curve (mathematically known as definite integral) in a plot of concentration of

drug in blood plasma against time. AUC was to be used to determine the average corticosteroid burden.

End point type	Secondary

End point timeframe:

Weeks 16, 20, 24, 28, 32, 36, 40, 44, and 48

End point values	Placebo	Ocrelizumab 400 mg	Ocrelizumab 1000 mg	OCR + SOC
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	0[46]	0[47]	0[48]	0[49]
Units: (mg/mL)*weeks				
arithmetic mean (standard deviation)	()	()	()	()

Notes:

[46] - Due to early termination of the study, no secondary outcome analyses were performed.

[47] - Due to early termination of the study, no secondary outcome analyses were performed.

[48] - Due to early termination of the study, no secondary outcome analyses were performed.

[49] - Due to early termination of the study, no secondary outcome analyses were performed.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants who Stopped Immunosuppressants After Week 48

End point title	Percentage of Participants who Stopped Immunosuppressants After Week 48

End point description:

The number of participants who stopped immunosuppressants were to be determined by survey.

End point type	Secondary

End point timeframe:

Week 48

End point values	Placebo	Ocrelizumab 400 mg	Ocrelizumab 1000 mg	OCR + SOC
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	0[50]	0[51]	0[52]	0[53]
Units: Percentage of participants				
number (not applicable)				

Notes:

[50] - Due to early termination of the study, no secondary outcome analyses were performed.

[51] - Due to early termination of the study, no secondary outcome analyses were performed.

[52] - Due to early termination of the study, no secondary outcome analyses were performed.

[53] - Due to early termination of the study, no secondary outcome analyses were performed.

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Absolute Counts of Cluster of Differentiation (CD) 19 Positive (+) Cells per Visit

End point title	Mean Absolute Counts of Cluster of Differentiation (CD) 19 Positive (+) Cells per Visit

End point description:

CD19 is a cell surface molecule which assembles with the antigen receptor of B lymphocytes. It is a critical signal transduction molecule that regulates B lymphocyte development, activation, and differentiation. CD19+ cells were measured as cells per microliter (cells/uL).

End point type	Secondary

End point timeframe:

Baseline, Day 15, Week 4, 16, 32, 48, and by infusion (pre and post infusion) on Day 1, 15, Week 16, 32

End point values	Placebo	Ocrelizumab 400 mg	Ocrelizumab 1000 mg	OCR + SOC
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	70[54]	73[55]	70[56]	141[57]
Units: cells/uL				
arithmetic mean (standard deviation)				
Baseline (n=70,71,66,137,44,26)	203.5 (± 191.4)	256.3 (± 300.2)	224.1 (± 231.7)	240.8 (± 268.9)
Day 15 (n=66,70,68,138,40,26)	262.7 (± 273.9)	1.9 (± 1.9)	2.2 (± 3.4)	2 (± 2.7)
Week 4 (n=68,67,67,134,41,27)	209.7 (± 221.4)	1.4 (± 2.5)	1.3 (± 1.6)	1.4 (± 2.1)
Week 16 (n=70,72,69,141,45,25)	125.9 (± 186.9)	2.6 (± 3.6)	2 (± 3.8)	2.3 (± 3.7)
Week 32 (n=68,73,68,141,45,23)	116.6 (± 154.3)	7.8 (± 25.8)	2.1 (± 2.7)	5.1 (± 18.8)
Week 48 (n=68,71,66,137,45,23)	110 (± 114.3)	11.7 (± 43.6)	2.6 (± 8.9)	7.3 (± 32.2)
Day 1 Pre-infusion (n=70,71,67,138,44,26)	203.5 (± 191.4)	256.3 (± 300.2)	222.8 (± 230.2)	240 (± 268)
Day 1 Post-infusion (n=70,69,68,137,43,27)	103.1 (± 115.1)	11.1 (± 28.6)	5.7 (± 8.5)	8.4 (± 21.3)
Day 15 Pre-infusion (n=68,68,70,138,43,25)	264.4 (± 276.6)	1.9 (± 1.9)	2.1 (± 3.3)	2 (± 2.7)
Day 15 Post-infusion (n=67,65,68,133,42,25)	91.2 (± 109.2)	1 (± 1.3)	0.9 (± 1.4)	0.9 (± 1.3)
Week 16 Pre-infusion (n=67,66,66,132,43,24)	127.8 (± 190.1)	2.5 (± 3.3)	2.1 (± 3.9)	2.3 (± 3.6)
Week 16 Post-infusion (n=61,66,66,132,40,21)	52.7 (± 72.6)	1.2 (± 1.6)	0.8 (± 1)	1 (± 1.3)
Week 32 Pre-infusion (n=60,63,63,126,39,21)	125 (± 161.1)	5.1 (± 16.5)	2 (± 2.7)	3.6 (± 11.8)
Week 32 Post-infusion (n=60,63,59,122,38,22)	46.2 (± 54.4)	1 (± 1.5)	0.7 (± 1.4)	0.9 (± 1.4)

Notes:

[54] - number (n) = number of participants analyzed at the specified visit.

[55] - n = number of participants analyzed at the specified visit.

[56] - n = number of participants analyzed at the specified visit.

[57] - n = number of participants analyzed at the specified visit.

End point values	Placebo-Mycophenolate Mofetil (MMF)	Placebo-Euro Lupus (EL)		

Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	45[58]	27[59]		
Units: cells/uL				
arithmetic mean (standard deviation)				
Baseline (n=70,71,66,137,44,26)	213.7 (± 201.7)	186.3 (± 175)		
Day 15 (n=66,70,68,138,40,26)	327.4 (± 324.9)	163.3 (± 115.8)		
Week 4 (n=68,67,67,134,41,27)	253.4 (± 263.9)	143.3 (± 107.4)		
Week 16 (n=70,72,69,141,45,25)	154.3 (± 222.2)	74.7 (± 75.3)		
Week 32 (n=68,73,68,141,45,23)	141.2 (± 172.5)	68.5 (± 96.8)		
Week 48 (n=68,71,66,137,45,23)	134.9 (± 123.3)	61.3 (± 75)		
Day 1 Pre-infusion (n=70,71,67,138,44,26)	213.7 (± 201.7)	186.3 (± 175)		
Day 1 Post-infusion (n=70,69,68,137,43,27)	102.4 (± 114.3)	104.3 (± 118.6)		
Day 15 Pre-infusion (n=68,68,70,138,43,25)	322.5 (± 323.5)	164.5 (± 118)		
Day 15 Post-infusion (n=67,65,68,133,42,25)	106.3 (± 130.8)	65.8 (± 50.4)		
Week 16 Pre-infusion (n=67,66,66,132,43,24)	156.5 (± 226.3)	76.3 (± 76.5)		
Week 16 Post-infusion (n=61,66,66,132,40,21)	64.2 (± 83)	30.9 (± 40.2)		
Week 32 Pre-infusion (n=60,63,63,126,39,21)	153.4 (± 180.6)	72.2 (± 100.4)		
Week 32 Post-infusion (n=60,63,59,122,38,22)	56.9 (± 62.5)	27.6 (± 29.5)		

Notes:

[58] - n = number of participants analyzed at the specified visit.

[59] - n = number of participants analyzed at the specified visit.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with CD19+ Absolute B Cell Counts <10 cells per microliter (cells/uL) by Visit

End point title	Percentage of Participants with CD19+ Absolute B Cell Counts <10 cells per microliter (cells/uL) by Visit

End point description:

CD19 is a cell surface molecule which assembles with the antigen receptor of B lymphocytes. It is a critical signal transduction molecule that regulates B lymphocyte development, activation, and differentiation. n = number of participants analyzed at the specified visit. A value of of 999 denotes that no data are available for the specified data point.

End point type	Secondary

End point timeframe:

Baseline, Day 15, Week 4, 16, 32, 48, and by infusion (pre and post infusion) on Day 1, 15, Week 16, 32

End point values	Placebo	Ocrelizumab 400 mg	Ocrelizumab 1000 mg	OCR + SOC
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	70[60]	73[61]	70[62]	141[63]
Units: Percentage of participants				
number (not applicable)				
Baseline (n=70,71,66,137,44,26)	4.3	4.2	1.5	2.9
Day 15 (n=66,70,68,138,40,26)	4.5	100	97.1	98.6
Week 4 (n=68,67,67,134,41,27)	4.4	98.5	100	99.3
Week 16 (n=70,72,69,141,45,25)	4.3	95.8	97.1	96.5
Week 32 (n=68,73,68,141,45,23)	7.4	91.8	95.6	93.6
Week 48 (n=68,71,66,137,45,23)	5.9	88.7	98.5	93.4
Day 1 Pre-infusion (n=70,71,67,138,44,26)	4.3	4.2	1.5	2.9
Day 1 Post-infusion (n=70,69,68,137,43,27)	10	81.2	83.8	82.5
Day 15 Pre-infusion (n=68,68,70,138,43,25)	4.4	100	97.1	98.6
Day 15 Post-infusion (n=67,65,68,133,42,25)	7.5	100	100	100
Week 16 Pre-infusion (n=67,66,66,132,43,24)	4.5	97	97	97
Week 16 Post-infusion (n=61,66,66,132,40,21)	11.5	100	100	100
Week 32 Pre-infusion (n=60,63,63,126,39,21)	3.3	93.7	95.2	94.4
Week 32 Post-infusion (n=60,63,59,122,38,22)	15	100	100	100

Notes:

[60] - n = number of participants analyzed at the specified visit.

[61] - n = number of participants analyzed at the specified visit.

[62] - n = number of participants analyzed at the specified visit.

[63] - n = number of participants analyzed at the specified visit.

End point values	Placebo-Mycophenolate Mofetil (MMF)	Placebo-Euro Lupus (EL)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	45[64]	27[65]		
Units: Percentage of participants				
number (not applicable)				
Baseline (n=70,71,66,137,44,26)	6.8	999		
Day 15 (n=66,70,68,138,40,26)	7.5	999		
Week 4 (n=68,67,67,134,41,27)	7.3	999		
Week 16 (n=70,72,69,141,45,25)	6.7	999		
Week 32 (n=68,73,68,141,45,23)	8.9	4.3		
Week 48 (n=68,71,66,137,45,23)	4.4	8.7		
Day 1 Pre-infusion (n=70,71,67,138,44,26)	6.8	999		
Day 1 Post-infusion (n=70,69,68,137,43,27)	14	3.7		
Day 15 Pre-infusion (n=68,68,70,138,43,25)	7	999		
Day 15 Post-infusion (n=67,65,68,133,42,25)	11.9	999		
Week 16 Pre-infusion (n=67,66,66,132,43,24)	7	999		

Week 16 Post-infusion (n=61,66,66,132,40,21)	12.5	9.5		
Week 32 Pre-infusion (n=60,63,63,126,39,21)	5.1	999		
Week 32 Post-infusion (n=60,63,59,122,38,22)	10.5	22.7		

Notes:

[64] - n = number of participants analyzed at the specified visit.

[65] - n = number of participants analyzed at the specified visit.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with CD19+ Absolute B Cell Counts <20 cells/uL by Visit

End point title	Percentage of Participants with CD19+ Absolute B Cell Counts <20 cells/uL by Visit

End point description:

CD19 is a cell surface molecule which assembles with the antigen receptor of B lymphocytes. It is a critical signal transduction molecule that regulates B lymphocyte development, activation, and differentiation. A value of of 999 denotes that no data are available for the specified data point. n = number of participants analyzed at the specified visit.

End point type	Secondary

End point timeframe:

Baseline, Day 15, Week 4, 16, 32, 48, and by infusion (pre and post infusion) on Day 1, 15, Week 16, 32

End point values	Placebo	Ocrelizumab 400 mg	Ocrelizumab 1000 mg	OCR + SOC
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	70[66]	73[67]	70[68]	141[69]
Units: Percentage of participants				
number (not applicable)				
Baseline (n=70,71,66,137,44,26)	7.1	11.3	3	7.3
Day 15 (n=66,70,68,138,40,26)	7.6	100	98.5	99.3
Week 4 (n=68,67,67,134,41,27)	10.3	100	100	100
Week 16 (n=70,72,69,141,45,25)	11.4	98.6	98.6	98.6
Week 32 (n=68,73,68,141,45,23)	13.2	93.2	100	96.5
Week 48 (n=68,71,66,137,45,23)	17.6	91.5	98.5	94.9
Day 1 Pre-infusion (n=70,71,67,138,44,26)	7.1	11.3	3	7.2
Day 1 Post-infusion (n=70,69,68,137,43,27)	22.9	87	91.2	89.1
Day 15 Pre-infusion (n=68,68,70,138,43,25)	7.4	100	98.6	99.3
Day 15 Post-infusion (n=67,65,68,133,42,25)	17.9	100	100	100
Week 16 Pre-infusion (n=67,66,66,132,43,24)	10.4	98.5	98.5	98.5
Week 16 Post-infusion (n=61,66,66,132,40,21)	41	100	100	100
Week 32 Pre-infusion (n=60,63,63,126,39,21)	8.3	95.2	100	97.6

Week 32 Post-infusion (n=60,63,59,122,38,22)	35	100	100	100

Notes:

[66] - n = number of participants analyzed at the specified visit.

[67] - n = number of participants analyzed at the specified visit.

[68] - n = number of participants analyzed at the specified visit.

[69] - n = number of participants analyzed at the specified visit.

End point values	Placebo-Mycophenolate Mofetil (MMF)	Placebo-Euro Lupus (EL)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	45[70]	27[71]		
Units: Percentage of participants				
number (not applicable)				
Baseline (n=70,71,66,137,44,26)	11.4	999		
Day 15 (n=66,70,68,138,40,26)	10	3.8		
Week 4 (n=68,67,67,134,41,27)	12.2	7.4		
Week 16 (n=70,72,69,141,45,25)	13.3	8		
Week 32 (n=68,73,68,141,45,23)	15.6	8.7		
Week 48 (n=68,71,66,137,45,23)	13.3	26.1		
Day 1 Pre-infusion (n=70,71,67,138,44,26)	11.4	999		
Day 1 Post-infusion (n=70,69,68,137,43,27)	20.9	25.9		
Day 15 Pre-infusion (n=68,68,70,138,43,25)	9.3	4		
Day 15 Post-infusion (n=67,65,68,133,42,25)	21.4	12		
Week 16 Pre-infusion (n=67,66,66,132,43,24)	11.6	8.3		
Week 16 Post-infusion (n=61,66,66,132,40,21)	32.5	57.1		
Week 32 Pre-infusion (n=60,63,63,126,39,21)	10.3	4.8		
Week 32 Post-infusion (n=60,63,59,122,38,22)	26.3	50		

Notes:

[70] - n = number of participants analyzed at the specified visit.

[71] - n = number of participants analyzed at the specified visit.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with CD19+ Absolute B Cell Counts Less than the Lower Limit of Normal (LLN) by Visit

End point title	Percentage of Participants with CD19+ Absolute B Cell Counts Less than the Lower Limit of Normal (LLN) by Visit

End point description:

CD19 is a cell surface molecule which assembles with the antigen receptor of B lymphocytes. It is a critical signal transduction molecule that regulates B lymphocyte development, activation, and differentiation. <LLN = 80 cells/uL.

End point type	Secondary

End point timeframe:

Baseline, Day 15, Week 4, 16, 32, 48, and by infusion (pre and post infusion) on Day 1, 15, Week 16, 32

End point values	Placebo	Ocrelizumab 400 mg	Ocrelizumab 1000 mg	OCR + SOC
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	70[72]	73[73]	70[74]	141[75]
Units: Percentage of participants				
number (not applicable)				
Baseline (n=70,71,66,137,44,26)	27.1	36.6	33.3	35
Day 15 (n=66,70,68,138,40,26)	28.8	100	100	100
Week 4 (n=68,67,67,134,41,27)	39.7	100	100	100
Week 16 (n=70,72,69,141,45,25)	57.1	100	100	100
Week 32 (n=68,73,68,141,45,23)	52.9	97.3	100	98.6
Week 48 (n=68,71,66,137,45,23)	51.5	97.2	100	98.5
Day 1 Pre-infusion (n=70,71,67,138,44,26)	27.1	36.6	32.8	34.8
Day 1 Post-infusion (n=70,69,68,137,43,27)	55.7	97.1	100	98.5
Day 15 Pre-infusion (n=68,68,70,138,43,25)	30.9	100	100	100
Day 15 Post-infusion (n=67,65,68,133,42,25)	58.2	100	100	100
Week 16 Pre-infusion (n=67,66,66,132,43,24)	56.7	100	100	100
Week 16 Post-infusion (n=61,66,66,132,40,21)	80.3	100	100	100
Week 32 Pre-infusion (n=60,63,63,126,39,21)	50	98.4	100	99.2
Week 32 Post-infusion (n=60,63,59,122,38,22)	88.3	100	100	100

Notes:

[72] - n = number of participants analyzed at the specified visit.

[73] - n = number of participants analyzed at the specified visit.

[74] - n = number of participants analyzed at the specified visit.

[75] - n = number of participants analyzed at the specified visit.

End point values	Placebo-Mycophenolate Mofetil (MMF)	Placebo-Euro Lupus (EL)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	45[76]	27[77]		
Units: Percentage of participants				
number (not applicable)				
Baseline (n=70,71,66,137,44,26)	29.5	23.1		
Day 15 (n=66,70,68,138,40,26)	30	26.9		
Week 4 (n=68,67,67,134,41,27)	39	40.7		
Week 16 (n=70,72,69,141,45,25)	48.9	72		
Week 32 (n=68,73,68,141,45,23)	35.6	87		
Week 48 (n=68,71,66,137,45,23)	37.8	78.3		
Day 1 Pre-infusion (n=70,71,67,138,44,26)	29.5	23.1		
Day 1 Post-infusion (n=70,69,68,137,43,27)	53.5	59.3		
Day 15 Pre-infusion (n=68,68,70,138,43,25)	32.6	28		

Day 15 Post-infusion (n=67,65,68,133,42,25)	52.4	68		
Week 16 Pre-infusion (n=67,66,66,132,43,24)	48.8	70.8		
Week 16 Post-infusion (n=61,66,66,132,40,21)	72.5	95.2		
Week 32 Pre-infusion (n=60,63,63,126,39,21)	30.8	85.7		
Week 32 Post-infusion (n=60,63,59,122,38,22)	84.2	95.5		

Notes:

[76] - n = number of participants analyzed at the specified visit.

[77] - n = number of participants analyzed at the specified visit.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Achieving a Major Clinical Response or a Partial Clinical Response

End point title	Percentage of Participants Achieving a Major Clinical Response or a Partial Clinical Response

End point description:

A major clinical response was defined as British Isles Lupus Assessment Group (BILAG) C scores or better at Week 24 without developing any new A or two new B scores up to Week 24 and maintenance of this response without developing a moderate or severe flare between Week 24 and Week 48. A partial clinical response was defined as BILAG C scores or better at Week 24 and maintaining this response without developing a flare for 16 consecutive weeks. The BILAG is an organ-specific 86-question assessment based on the principle of the doctor's intent to treat, which requires an assessment of improved (1), the same (2), worse (3), or new (4) over the last month. Within each organ system, multiple manifestations and laboratory tests are combined into a single score for that organ. The resulting scores for each organ can be A through E, where A is very active disease, B is moderate activity, C is mild stable disease, D is resolved activity, and E indicates the organ was never involved.

End point type	Secondary

End point timeframe:

Baseline and Weeks 1, 4, 8, 12, 16, 20, 24, 28, 32, 36, 40, 44, and 48

End point values	Placebo	Ocrelizumab 400 mg	Ocrelizumab 1000 mg	OCR + SOC
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	0[78]	0[79]	0[80]	0[81]
Units: percentage of participants				
number (not applicable)				

Notes:

[78] - Due to early termination of the study, no secondary analyses were performed.

[79] - Due to early termination of the study, no secondary analyses were performed.

[80] - Due to early termination of the study, no secondary analyses were performed.

[81] - Due to early termination of the study, no secondary analyses were performed.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events were recorded from Screening until study termination.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	13.1

Reporting groups

Reporting group title	Placebo

Reporting group description:

Participants received placebo matched to ocrelizumab infusion intravenously (IV) on Days 1 and 15, followed by placebo matched to ocrelizumab infusion IV on Week 16 and then every 16 weeks up to 48 weeks along with one of the two standard-of-care (SOC) immunosuppressant regimens at the discretion of the investigator. The SOC regimens were: Euro-Lupus (cyclophosphamide 500 mg every 2 weeks for 6 doses followed by azathioprine maintenance at 1-2 milligrams per kilogram per day [mg/kg/day]), or mycophenolate mofetil (MMF) 1 grams per day (g/day) in the first week increased to 3 g/day. Participants also received methylprednisolone 100 milligram (mg) infusion IV or according to local guidelines, completed at least 30 minutes prior to each infusion of placebo. Participants also received oral prednisone at a starting dose of 0.75 mg/kg/day with a maximum dose of 60 mg/day from Day 2. Beginning on Day 16 the doses were tapered and continued for 10 weeks to a target dose of 10 mg/day.

Reporting group title	Ocrelizumab 1000 mg

Reporting group description:

Participants received 1000 mg ocrelizumab IV on Days 1 and 15, followed by 1000 mg ocrelizumab infusion IV on Week 16 and then every 16 weeks up to 48 weeks along with one of the two standard-of-care (SOC) immunosuppressant regimens at the discretion of the investigator. The SOC regimens were: Euro-Lupus (cyclophosphamide 500 mg every 2 weeks for 6 doses followed by azathioprine maintenance at 1-2 milligrams per kilogram per day [mg/kg/day]), or MMF 1 g/day in the first week increased to 3 g/day. Participants also received methylprednisolone 100 mg infusion IV or according to local guidelines, completed at least 30 minutes prior to each infusion of ocrelizumab. Participants also received oral prednisone at starting dose of 0.75 mg/kg/day with a maximum dose of 60 mg/day from Day 2. Beginning on Day 16 the doses were tapered and continued for 10 weeks to a target dose of 10 mg/day.

Reporting group title	Ocrelizumab 400 mg

Reporting group description:

Participants received 400 mg ocrelizumab IV on Days 1 and 15, followed by 400 mg ocrelizumab infusion IV on Week 16 and then every 16 weeks up to 48 weeks along with one of the two standard-of-care (SOC) immunosuppressant regimens at the discretion of the investigator. The SOC regimens were: Euro-Lupus (cyclophosphamide 500 mg every 2 weeks for 6 doses followed by azathioprine maintenance at 1-2 milligrams per kilogram per day [mg/kg/day]), or MMF 1 g/day in the first week increased to 3 g/day. Participants also received methylprednisolone 100 mg infusion IV or according to local guidelines, completed at least 30 minutes prior to each infusion of ocrelizumab. Participants also received oral prednisone at starting dose of 0.75 mg/kg/day with a maximum dose of 60 mg/day from Day 2. Beginning on Day 16 the doses were tapered and continued for 10 weeks to a target dose of 10 mg/day.

Serious adverse events	Placebo	Ocrelizumab 1000 mg	Ocrelizumab 400 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	36 / 125 (28.80%)	38 / 127 (29.92%)	52 / 126 (41.27%)
number of deaths (all causes)	6	6	3
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			

Acute myeloid leukaemia			
subjects affected / exposed	1 / 125 (0.80%)	0 / 127 (0.00%)	0 / 126 (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
Anogenital warts			
subjects affected / exposed	0 / 125 (0.00%)	0 / 127 (0.00%)	1 / 126 (0.79%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cervix carcinoma			
subjects affected / exposed	0 / 125 (0.00%)	1 / 127 (0.79%)	0 / 126 (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
Gastric cancer			
subjects affected / exposed	1 / 125 (0.80%)	0 / 127 (0.00%)	0 / 126 (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
Rectal adenoma			
subjects affected / exposed	0 / 125 (0.00%)	0 / 127 (0.00%)	1 / 126 (0.79%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal cell carcinoma			
subjects affected / exposed	0 / 125 (0.00%)	0 / 127 (0.00%)	1 / 126 (0.79%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	0 / 125 (0.00%)	1 / 127 (0.79%)	1 / 126 (0.79%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertension			
subjects affected / exposed	0 / 125 (0.00%)	1 / 127 (0.79%)	0 / 126 (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
Malignant hypertension			

subjects affected / exposed	1 / 125 (0.80%)	0 / 127 (0.00%)	0 / 126 (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
Pregnancy, puerperium and perinatal conditions			
Abortion missed			
subjects affected / exposed	0 / 125 (0.00%)	1 / 127 (0.79%)	0 / 126 (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
Gestational hypertension			
subjects affected / exposed	0 / 125 (0.00%)	0 / 127 (0.00%)	1 / 126 (0.79%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Adverse drug reaction			
subjects affected / exposed	1 / 125 (0.80%)	0 / 127 (0.00%)	0 / 126 (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
Chest pain			
subjects affected / exposed	2 / 125 (1.60%)	0 / 127 (0.00%)	0 / 126 (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
Generalised oedema			
subjects affected / exposed	0 / 125 (0.00%)	0 / 127 (0.00%)	2 / 126 (1.59%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Polyserositis			
subjects affected / exposed	0 / 125 (0.00%)	0 / 127 (0.00%)	1 / 126 (0.79%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia			
subjects affected / exposed	2 / 125 (1.60%)	0 / 127 (0.00%)	0 / 126 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Reproductive system and breast disorders			
Amenorrhoea			
subjects affected / exposed	1 / 125 (0.80%)	0 / 127 (0.00%)	0 / 126 (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
Cervical dysplasia			
subjects affected / exposed	0 / 125 (0.00%)	0 / 127 (0.00%)	1 / 126 (0.79%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ovarian cyst			
subjects affected / exposed	0 / 125 (0.00%)	1 / 127 (0.79%)	1 / 126 (0.79%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ovarian mass			
subjects affected / exposed	0 / 125 (0.00%)	1 / 127 (0.79%)	0 / 126 (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
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	1 / 125 (0.80%)	0 / 127 (0.00%)	1 / 126 (0.79%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspnoea			
subjects affected / exposed	1 / 125 (0.80%)	0 / 127 (0.00%)	0 / 126 (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 embolism			
subjects affected / exposed	1 / 125 (0.80%)	0 / 127 (0.00%)	2 / 126 (1.59%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Pulmonary oedema			

subjects affected / exposed	0 / 125 (0.00%)	1 / 127 (0.79%)	0 / 126 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Depression			
subjects affected / exposed	0 / 125 (0.00%)	0 / 127 (0.00%)	1 / 126 (0.79%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Suicide attempt			
subjects affected / exposed	0 / 125 (0.00%)	0 / 127 (0.00%)	1 / 126 (0.79%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Blood creatine increased			
subjects affected / exposed	1 / 125 (0.80%)	0 / 127 (0.00%)	0 / 126 (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
Weight increased			
subjects affected / exposed	0 / 125 (0.00%)	0 / 127 (0.00%)	1 / 126 (0.79%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Infusion related reaction			
subjects affected / exposed	0 / 125 (0.00%)	1 / 127 (0.79%)	1 / 126 (0.79%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Joint dislocation			
subjects affected / exposed	0 / 125 (0.00%)	1 / 127 (0.79%)	0 / 126 (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
Thermal burn			
subjects affected / exposed	0 / 125 (0.00%)	1 / 127 (0.79%)	0 / 126 (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			
Acute myocardial infarction			
subjects affected / exposed	1 / 125 (0.80%)	0 / 127 (0.00%)	0 / 126 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Cardiac failure			
subjects affected / exposed	1 / 125 (0.80%)	0 / 127 (0.00%)	1 / 126 (0.79%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Cardiac failure congestive			
subjects affected / exposed	0 / 125 (0.00%)	1 / 127 (0.79%)	0 / 126 (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
Cardio-respiratory arrest			
subjects affected / exposed	1 / 125 (0.80%)	0 / 127 (0.00%)	0 / 126 (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
Myocardial infarction			
subjects affected / exposed	1 / 125 (0.80%)	0 / 127 (0.00%)	0 / 126 (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
Pleuropericarditis			
subjects affected / exposed	0 / 125 (0.00%)	1 / 127 (0.79%)	0 / 126 (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
Stress cardiomyopathy			
subjects affected / exposed	0 / 125 (0.00%)	1 / 127 (0.79%)	0 / 126 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Cerebral haemorrhage			
subjects affected / exposed	0 / 125 (0.00%)	0 / 127 (0.00%)	1 / 126 (0.79%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1

Cerebral infarction			
subjects affected / exposed	1 / 125 (0.80%)	0 / 127 (0.00%)	1 / 126 (0.79%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebrovascular accident			
subjects affected / exposed	0 / 125 (0.00%)	0 / 127 (0.00%)	1 / 126 (0.79%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebrovascular disorder			
subjects affected / exposed	0 / 125 (0.00%)	0 / 127 (0.00%)	1 / 126 (0.79%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Convulsion			
subjects affected / exposed	0 / 125 (0.00%)	1 / 127 (0.79%)	0 / 126 (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
Headache			
subjects affected / exposed	0 / 125 (0.00%)	0 / 127 (0.00%)	1 / 126 (0.79%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ischaemic stroke			
subjects affected / exposed	0 / 125 (0.00%)	1 / 127 (0.79%)	0 / 126 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lupus encephalitis			
subjects affected / exposed	0 / 125 (0.00%)	0 / 127 (0.00%)	1 / 126 (0.79%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Migraine			
subjects affected / exposed	1 / 125 (0.80%)	0 / 127 (0.00%)	1 / 126 (0.79%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vasculitis cerebral			

subjects affected / exposed	1 / 125 (0.80%)	0 / 127 (0.00%)	0 / 126 (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 and lymphatic system disorders			
Agranulocytosis			
subjects affected / exposed	0 / 125 (0.00%)	3 / 127 (2.36%)	1 / 126 (0.79%)
occurrences causally related to treatment / all	0 / 0	2 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anaemia			
subjects affected / exposed	1 / 125 (0.80%)	0 / 127 (0.00%)	3 / 126 (2.38%)
occurrences causally related to treatment / all	0 / 1	0 / 0	2 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anaemia of chronic disease			
subjects affected / exposed	1 / 125 (0.80%)	0 / 127 (0.00%)	0 / 126 (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
Antiphospholipid syndrome			
subjects affected / exposed	0 / 125 (0.00%)	1 / 127 (0.79%)	0 / 126 (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
Disseminated intravascular coagulation			
subjects affected / exposed	0 / 125 (0.00%)	0 / 127 (0.00%)	2 / 126 (1.59%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Febrile neutropenia			
subjects affected / exposed	0 / 125 (0.00%)	1 / 127 (0.79%)	2 / 126 (1.59%)
occurrences causally related to treatment / all	0 / 0	0 / 1	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Iron deficiency anaemia			
subjects affected / exposed	0 / 125 (0.00%)	0 / 127 (0.00%)	1 / 126 (0.79%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Leukopenia			

subjects affected / exposed	0 / 125 (0.00%)	0 / 127 (0.00%)	1 / 126 (0.79%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutropenia			
subjects affected / exposed	1 / 125 (0.80%)	5 / 127 (3.94%)	2 / 126 (1.59%)
occurrences causally related to treatment / all	0 / 1	3 / 5	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 125 (0.80%)	1 / 127 (0.79%)	0 / 126 (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
Ascites			
subjects affected / exposed	0 / 125 (0.00%)	0 / 127 (0.00%)	1 / 126 (0.79%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
subjects affected / exposed	1 / 125 (0.80%)	0 / 127 (0.00%)	0 / 126 (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			
subjects affected / exposed	1 / 125 (0.80%)	0 / 127 (0.00%)	0 / 126 (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 haemorrhage			
subjects affected / exposed	0 / 125 (0.00%)	0 / 127 (0.00%)	1 / 126 (0.79%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nausea			
subjects affected / exposed	0 / 125 (0.00%)	0 / 127 (0.00%)	1 / 126 (0.79%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rectal haemorrhage			

subjects affected / exposed	0 / 125 (0.00%)	0 / 127 (0.00%)	1 / 126 (0.79%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rectal ulcer			
subjects affected / exposed	0 / 125 (0.00%)	1 / 127 (0.79%)	0 / 126 (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
Stomatitis			
subjects affected / exposed	0 / 125 (0.00%)	1 / 127 (0.79%)	0 / 126 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Hepatitis			
subjects affected / exposed	1 / 125 (0.80%)	0 / 127 (0.00%)	0 / 126 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Angioedema			
subjects affected / exposed	0 / 125 (0.00%)	0 / 127 (0.00%)	1 / 126 (0.79%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Lupus nephritis			
subjects affected / exposed	2 / 125 (1.60%)	0 / 127 (0.00%)	1 / 126 (0.79%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nephritis			
subjects affected / exposed	0 / 125 (0.00%)	0 / 127 (0.00%)	1 / 126 (0.79%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nephrotic syndrome			
subjects affected / exposed	0 / 125 (0.00%)	1 / 127 (0.79%)	0 / 126 (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

Proteinuria			
subjects affected / exposed	1 / 125 (0.80%)	0 / 127 (0.00%)	1 / 126 (0.79%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal disorder			
subjects affected / exposed	1 / 125 (0.80%)	0 / 127 (0.00%)	0 / 126 (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	2 / 125 (1.60%)	1 / 127 (0.79%)	1 / 126 (0.79%)
occurrences causally related to treatment / all	1 / 2	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal failure acute			
subjects affected / exposed	0 / 125 (0.00%)	1 / 127 (0.79%)	2 / 126 (1.59%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Renal failure chronic			
subjects affected / exposed	1 / 125 (0.80%)	0 / 127 (0.00%)	0 / 126 (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
Tubulointerstitial nephritis			
subjects affected / exposed	1 / 125 (0.80%)	0 / 127 (0.00%)	0 / 126 (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
Urinary bladder haemorrhage			
subjects affected / exposed	0 / 125 (0.00%)	1 / 127 (0.79%)	0 / 126 (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			
Back pain			
subjects affected / exposed	1 / 125 (0.80%)	0 / 127 (0.00%)	0 / 126 (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

Muscle contracture			
subjects affected / exposed	0 / 125 (0.00%)	0 / 127 (0.00%)	1 / 126 (0.79%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteonecrosis			
subjects affected / exposed	0 / 125 (0.00%)	1 / 127 (0.79%)	0 / 126 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Systemic lupus erythematosus			
subjects affected / exposed	3 / 125 (2.40%)	2 / 127 (1.57%)	3 / 126 (2.38%)
occurrences causally related to treatment / all	0 / 3	0 / 5	0 / 7
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Abscess			
subjects affected / exposed	1 / 125 (0.80%)	0 / 127 (0.00%)	0 / 126 (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
Abscess limb			
subjects affected / exposed	1 / 125 (0.80%)	0 / 127 (0.00%)	0 / 126 (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
Appendicitis			
subjects affected / exposed	0 / 125 (0.00%)	0 / 127 (0.00%)	1 / 126 (0.79%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arthritis bacterial			
subjects affected / exposed	0 / 125 (0.00%)	1 / 127 (0.79%)	0 / 126 (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
Bacterial sepsis			
subjects affected / exposed	0 / 125 (0.00%)	0 / 127 (0.00%)	1 / 126 (0.79%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchitis			

subjects affected / exposed	1 / 125 (0.80%)	0 / 127 (0.00%)	1 / 126 (0.79%)
occurrences causally related to treatment / all	0 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchopneumonia			
subjects affected / exposed	0 / 125 (0.00%)	0 / 127 (0.00%)	1 / 126 (0.79%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			
subjects affected / exposed	1 / 125 (0.80%)	2 / 127 (1.57%)	5 / 126 (3.97%)
occurrences causally related to treatment / all	1 / 1	3 / 3	2 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diverticulitis			
subjects affected / exposed	0 / 125 (0.00%)	0 / 127 (0.00%)	1 / 126 (0.79%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ear infection			
subjects affected / exposed	0 / 125 (0.00%)	0 / 127 (0.00%)	1 / 126 (0.79%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Enteritis infectious			
subjects affected / exposed	0 / 125 (0.00%)	1 / 127 (0.79%)	0 / 126 (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
Erysipelas			
subjects affected / exposed	1 / 125 (0.80%)	0 / 127 (0.00%)	0 / 126 (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
Gastroenteritis			
subjects affected / exposed	3 / 125 (2.40%)	0 / 127 (0.00%)	0 / 126 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis viral			

subjects affected / exposed	1 / 125 (0.80%)	0 / 127 (0.00%)	0 / 126 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal infection			
subjects affected / exposed	0 / 125 (0.00%)	1 / 127 (0.79%)	0 / 126 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
H1N1 influenza			
subjects affected / exposed	0 / 125 (0.00%)	0 / 127 (0.00%)	1 / 126 (0.79%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haematoma infection			
subjects affected / exposed	1 / 125 (0.80%)	0 / 127 (0.00%)	0 / 126 (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 virus infection			
subjects affected / exposed	0 / 125 (0.00%)	1 / 127 (0.79%)	1 / 126 (0.79%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Herpes zoster			
subjects affected / exposed	0 / 125 (0.00%)	3 / 127 (2.36%)	1 / 126 (0.79%)
occurrences causally related to treatment / all	0 / 0	1 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Herpes zoster disseminated			
subjects affected / exposed	0 / 125 (0.00%)	0 / 127 (0.00%)	1 / 126 (0.79%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Impetigo			
subjects affected / exposed	1 / 125 (0.80%)	0 / 127 (0.00%)	0 / 126 (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
infection			

subjects affected / exposed	0 / 125 (0.00%)	0 / 127 (0.00%)	1 / 126 (0.79%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Laryngitis			
subjects affected / exposed	1 / 125 (0.80%)	0 / 127 (0.00%)	0 / 126 (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
Legionella infection			
subjects affected / exposed	0 / 125 (0.00%)	1 / 127 (0.79%)	0 / 126 (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
Lung infection			
subjects affected / exposed	0 / 125 (0.00%)	0 / 127 (0.00%)	1 / 126 (0.79%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neurocryptococcosis			
subjects affected / exposed	0 / 125 (0.00%)	0 / 127 (0.00%)	1 / 126 (0.79%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutropenic infection			
subjects affected / exposed	0 / 125 (0.00%)	1 / 127 (0.79%)	0 / 126 (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
Neutropenic sepsis			
subjects affected / exposed	0 / 125 (0.00%)	0 / 127 (0.00%)	1 / 126 (0.79%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumocystis jirovecii pneumonia			
subjects affected / exposed	0 / 125 (0.00%)	1 / 127 (0.79%)	1 / 126 (0.79%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			

subjects affected / exposed	2 / 125 (1.60%)	8 / 127 (6.30%)	4 / 126 (3.17%)
occurrences causally related to treatment / all	1 / 2	4 / 8	2 / 5
deaths causally related to treatment / all	0 / 1	2 / 3	0 / 0
Pneumonia cytomegaloviral			
subjects affected / exposed	0 / 125 (0.00%)	0 / 127 (0.00%)	1 / 126 (0.79%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pseudomembranous colitis			
subjects affected / exposed	1 / 125 (0.80%)	0 / 127 (0.00%)	0 / 126 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis			
subjects affected / exposed	0 / 125 (0.00%)	1 / 127 (0.79%)	2 / 126 (1.59%)
occurrences causally related to treatment / all	0 / 0	0 / 1	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyoderma			
subjects affected / exposed	1 / 125 (0.80%)	0 / 127 (0.00%)	0 / 126 (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 tract infection			
subjects affected / exposed	1 / 125 (0.80%)	0 / 127 (0.00%)	1 / 126 (0.79%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Salmonella bacteraemia			
subjects affected / exposed	0 / 125 (0.00%)	1 / 127 (0.79%)	0 / 126 (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
Salmonella sepsis			
subjects affected / exposed	0 / 125 (0.00%)	0 / 127 (0.00%)	1 / 126 (0.79%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			

subjects affected / exposed	1 / 125 (0.80%)	1 / 127 (0.79%)	2 / 126 (1.59%)
occurrences causally related to treatment / all	0 / 1	1 / 1	0 / 3
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Septic shock			
subjects affected / exposed	0 / 125 (0.00%)	1 / 127 (0.79%)	1 / 126 (0.79%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Skin infection			
subjects affected / exposed	0 / 125 (0.00%)	1 / 127 (0.79%)	0 / 126 (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 bacteraemia			
subjects affected / exposed	0 / 125 (0.00%)	0 / 127 (0.00%)	1 / 126 (0.79%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Strongyloidiasis			
subjects affected / exposed	1 / 125 (0.80%)	0 / 127 (0.00%)	0 / 126 (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 / 125 (0.80%)	0 / 127 (0.00%)	0 / 126 (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
Upper respiratory tract infection			
subjects affected / exposed	0 / 125 (0.00%)	2 / 127 (1.57%)	0 / 126 (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
Urosepsis			
subjects affected / exposed	0 / 125 (0.00%)	2 / 127 (1.57%)	0 / 126 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Sinusitis			

subjects affected / exposed	0 / 125 (0.00%)	1 / 127 (0.79%)	0 / 126 (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
Urinary Tract Infection			
subjects affected / exposed	1 / 125 (0.80%)	2 / 127 (1.57%)	4 / 126 (3.17%)
occurrences causally related to treatment / all	1 / 1	0 / 2	3 / 6
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Diabetes mellitus			
subjects affected / exposed	0 / 125 (0.00%)	0 / 127 (0.00%)	2 / 126 (1.59%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	Placebo	Ocrelizumab 1000 mg	Ocrelizumab 400 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	96 / 125 (76.80%)	91 / 127 (71.65%)	101 / 126 (80.16%)
Injury, poisoning and procedural complications			
Infusion related reaction			
subjects affected / exposed	11 / 125 (8.80%)	17 / 127 (13.39%)	14 / 126 (11.11%)
occurrences (all)	12	19	18
Vascular disorders			
Hypertension			
subjects affected / exposed	7 / 125 (5.60%)	12 / 127 (9.45%)	12 / 126 (9.52%)
occurrences (all)	8	15	19
Nervous system disorders			
Dizziness			
subjects affected / exposed	9 / 125 (7.20%)	5 / 127 (3.94%)	6 / 126 (4.76%)
occurrences (all)	9	6	6
Headache			
subjects affected / exposed	11 / 125 (8.80%)	11 / 127 (8.66%)	15 / 126 (11.90%)
occurrences (all)	18	12	21
Blood and lymphatic system disorders			

Anaemia			
subjects affected / exposed	5 / 125 (4.00%)	7 / 127 (5.51%)	13 / 126 (10.32%)
occurrences (all)	5	7	17
Leukopenia			
subjects affected / exposed	7 / 125 (5.60%)	12 / 127 (9.45%)	18 / 126 (14.29%)
occurrences (all)	11	17	24
Neutropenia			
subjects affected / exposed	6 / 125 (4.80%)	7 / 127 (5.51%)	15 / 126 (11.90%)
occurrences (all)	7	10	27
General disorders and administration site conditions			
Oedema peripheral			
subjects affected / exposed	8 / 125 (6.40%)	4 / 127 (3.15%)	2 / 126 (1.59%)
occurrences (all)	9	4	5
Pyrexia			
subjects affected / exposed	1 / 125 (0.80%)	2 / 127 (1.57%)	7 / 126 (5.56%)
occurrences (all)	1	3	7
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	3 / 125 (2.40%)	7 / 127 (5.51%)	5 / 126 (3.97%)
occurrences (all)	3	8	5
Diarrhoea			
subjects affected / exposed	22 / 125 (17.60%)	32 / 127 (25.20%)	26 / 126 (20.63%)
occurrences (all)	29	36	35
Dyspepsia			
subjects affected / exposed	4 / 125 (3.20%)	3 / 127 (2.36%)	9 / 126 (7.14%)
occurrences (all)	5	3	10
Gastritis			
subjects affected / exposed	2 / 125 (1.60%)	2 / 127 (1.57%)	11 / 126 (8.73%)
occurrences (all)	2	3	15
Nausea			
subjects affected / exposed	7 / 125 (5.60%)	4 / 127 (3.15%)	13 / 126 (10.32%)
occurrences (all)	7	5	16
Vomiting			
subjects affected / exposed	7 / 125 (5.60%)	4 / 127 (3.15%)	11 / 126 (8.73%)
occurrences (all)	7	4	11
Respiratory, thoracic and mediastinal disorders			

Cough			
subjects affected / exposed	7 / 125 (5.60%)	4 / 127 (3.15%)	11 / 126 (8.73%)
occurrences (all)	8	5	12
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	8 / 125 (6.40%)	1 / 127 (0.79%)	3 / 126 (2.38%)
occurrences (all)	8	1	3
Psychiatric disorders			
Insomnia			
subjects affected / exposed	3 / 125 (2.40%)	7 / 127 (5.51%)	7 / 126 (5.56%)
occurrences (all)	4	7	7
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	5 / 125 (4.00%)	6 / 127 (4.72%)	7 / 126 (5.56%)
occurrences (all)	5	8	9
Back pain			
subjects affected / exposed	6 / 125 (4.80%)	8 / 127 (6.30%)	6 / 126 (4.76%)
occurrences (all)	6	8	8
Muscle spasms			
subjects affected / exposed	7 / 125 (5.60%)	4 / 127 (3.15%)	8 / 126 (6.35%)
occurrences (all)	7	4	8
Infections and infestations			
Bronchitis			
subjects affected / exposed	10 / 125 (8.00%)	10 / 127 (7.87%)	14 / 126 (11.11%)
occurrences (all)	16	12	17
Gastroenteritis			
subjects affected / exposed	10 / 125 (8.00%)	4 / 127 (3.15%)	7 / 126 (5.56%)
occurrences (all)	11	4	10
Herpes zoster			
subjects affected / exposed	6 / 125 (4.80%)	9 / 127 (7.09%)	8 / 126 (6.35%)
occurrences (all)	6	11	9
Nasopharyngitis			
subjects affected / exposed	16 / 125 (12.80%)	13 / 127 (10.24%)	17 / 126 (13.49%)
occurrences (all)	23	20	24
Oral candidiasis			

subjects affected / exposed	1 / 125 (0.80%)	1 / 127 (0.79%)	7 / 126 (5.56%)
occurrences (all)	1	1	10
Pharyngitis			
subjects affected / exposed	4 / 125 (3.20%)	7 / 127 (5.51%)	13 / 126 (10.32%)
occurrences (all)	4	7	13
Sinusitis			
subjects affected / exposed	3 / 125 (2.40%)	7 / 127 (5.51%)	3 / 126 (2.38%)
occurrences (all)	4	12	5
Upper respiratory tract infection			
subjects affected / exposed	19 / 125 (15.20%)	23 / 127 (18.11%)	22 / 126 (17.46%)
occurrences (all)	28	43	42
Urinary tract infection			
subjects affected / exposed	13 / 125 (10.40%)	18 / 127 (14.17%)	24 / 126 (19.05%)
occurrences (all)	13	35	43
Metabolism and nutrition disorders			
Dyslipidaemia			
subjects affected / exposed	11 / 125 (8.80%)	2 / 127 (1.57%)	5 / 126 (3.97%)
occurrences (all)	14	2	5
Hypokalaemia			
subjects affected / exposed	9 / 125 (7.20%)	4 / 127 (3.15%)	9 / 126 (7.14%)
occurrences (all)	12	4	16

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
16 October 2008	This amendment was made to clarify the flexibility of protocol in applying the regional participant management strategies using SOC regimens for treatment of LN and to ensure participant safety during administration of immunosupressive therapies, to clarify the use of corticosteroids during the trial and to clarify screening procedures and use of medications during screening to help recruitment.
04 January 2010	On 19th October 2009 this Study (WA20500/ACT4072g) was stopped due to an imbalance of serious and opportunistic infections in the ocrelizumab treated patients versus the placebo arm. This was identified through the ongoing safety review of participant data and following interactions with both the US FDA and the BELONG Data and Safety Monitoring Board (DSMB). There was no further study drug infusions either blinded or open label in the Double Blind Treatment Period, Study Extension Treatment Period or Open Label Period. Patients who received ocrelizumab entered the Safety Follow Up period after completing the withdrawal visit and followed the Safety Follow Up assessments and Schedule. Participants who received placebo were not required to take part in the Safety Follow Up and were discontinued from the study.
28 September 2012	Safety data from the participants ongoing in the study were evaluated and the sponsor decided to terminate further Safety follow-up in participants treated with ocrelizumab.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

The study was terminated early due to an imbalance in serious infections in ocrelizumab-treated participants versus placebo-treated participants. Only 139 of the 381 participants randomized completed the 48 week treatment period.

Notes: