Clinical trial results:
A Randomized, Double-Blind, Placebo-Controlled, Multi-Center Study to Evaluate the Safety and Efficacy of Obinutuzumab in Patients with ISN/RPS 2003 Class III or IV Lupus Nephritis

Summary

EudraCT number	2015-002022-39
Trial protocol	ES FR IT
Global end of trial date	

Results information

Result version number	v2
This version publication date	20 January 2021
First version publication date	31 January 2020
Version creation reason	

Trial information

Trial identification

Sponsor protocol code	WA29748

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02550652
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	F. Hoffmann-La Roche AG, F. Hoffmann-La Roche AG, +41 616878333, global.trial_information@roche.com
Scientific contact	F. Hoffmann-La Roche AG, F. Hoffmann-La Roche AG, +41 616878333, 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	Interim
Date of interim/final analysis	06 January 2020
Is this the analysis of the primary completion data?	Yes
Primary completion date	15 January 2019
Global end of trial reached?	No

Notes:

General information about the trial

Main objective of the trial:

This Phase II study will compare the efficacy and safety of obinutuzumab plus mycophenolate mofetil (MMF)/mycophenolic acid (MPA) with placebo plus MMF/MPA in participants with proliferative LN.

Protection of trial subjects:

All study subjects were required to read and sign an Informed Consent Form.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	13 November 2015
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	18 Months
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Argentina: 27
Country: Number of subjects enrolled	Brazil: 8
Country: Number of subjects enrolled	Colombia: 19
Country: Number of subjects enrolled	Costa Rica: 2
Country: Number of subjects enrolled	Spain: 4
Country: Number of subjects enrolled	France: 11
Country: Number of subjects enrolled	Israel: 4
Country: Number of subjects enrolled	Italy: 6
Country: Number of subjects enrolled	Mexico: 15
Country: Number of subjects enrolled	Panama: 1
Country: Number of subjects enrolled	Peru: 13
Country: Number of subjects enrolled	United States: 15
Worldwide total number of subjects	125
EEA total number of subjects	21

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37	0

wk	
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	125
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants were enrolled at approximately 60 centers in North America, South America, Europe, and Asia.

Pre-assignment

Screening details:

A total of 126 patients were enrolled in the study however one patient randomized to obinutuzumab did not receive study treatment due to a positive pregnancy test, but prior to the first study drug infusion; therefore a total of 125 patients are included in the analysis.

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	Investigator, Subject

Arms

Are arms mutually exclusive?	Yes
Arm title	OBINUTUZUMAB 1000MG and MMF

Arm description:

Participants will receive obinutuzumab 1000 milligrams (mg) intravenous (IV) infusion on Days 1, 15, 168, and 182 along with MMF/MPA at a starting dose of 1500 mg/day (or equivalent) administered orally in 2 or 3 divided doses. MMF/MPA dose will be up titrated to a target dose of 2.0 - 2.5 grams per day (g/day) (or equivalent). Investigators, at their discretion, may use MPA as a substitute for MMF, with a 360 mg dose being equivalent to a 500 mg dose of MMF. During screening or at randomization, if clinically indicated, participants may receive 750-1000 mg methylprednisolone IV once daily for up to 3 days to treat underlying LN clinical activity. Participants will receive 0.5 mg/kg oral prednisone, tapering this prednisone dose, per protocol, starting on Day 16 and reducing the prednisone dosage to 7.5 mg/day by Week 12.

Arm type	Experimental
Investigational medicinal product name	Mycophenolate Mofetil/Mycophenolic Acid
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, Tablet
Routes of administration	Oral use

Dosage and administration details:

MMF/MPA will be administered as per schedule specified in the respective arm.

Investigational medicinal product name	Obinutuzumab
Investigational medicinal product code	
Other name	Gazyva, GA101, RO5072759
Pharmaceutical forms	Concentrate and solvent for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Obinutuzumab will be administered as per schedule specified in the respective arm.

Arm title	PLACEBO and MMF

Arm description:

Participants will receive placebo matching to obinutuzumab IV infusion on Days 1, 15, 168, and 182 along with MMF/MPA at a starting dose of 1500 mg/day (or equivalent) administered orally in 2 or 3 divided doses. MMF/MPA dose will be up titrated to a target dose of 2.0 - 2.5 g/day (or equivalent). Investigators, at their discretion, may use MPA as a substitute for MMF, with a 360 mg dose being equivalent to a 500 mg dose of MMF. During screening or at randomization, if clinically indicated, participants may receive 750-1000 mg methylprednisolone IV once daily for up to 3 days to treat

underlying LN clinical activity. Participants will receive 0.5 mg/kg oral prednisone, tapering this prednisone dose, per protocol, starting on Day 16 and reducing the prednisone dosage to 7.5 mg/day by Week 12.

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

Dosage and administration details:

Placebo matching to obinutuzumab will be administered as per schedule specified in the respective arm.

Investigational medicinal product name	Mycophenolate Mofetil/Mycophenolic Acid
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, Tablet
Routes of administration	Oral use

Dosage and administration details:

MMF/MPA will be administered as per schedule specified in the respective arm.

Number of subjects in period 1	OBINUTUZUMAB 1000MG and MMF	PLACEBO and MMF
Started	63	62
Completed	42	41
Not completed	21	21
Consent withdrawn by subject	3	7
Physician decision	-	2
Death	1	4
Ongoing in safety/B-cell follow-up period	14	5
Post Trial Access	1	-
Lost to follow-up	1	3
Lack of efficacy	1	-

Baseline characteristics

Reporting groups

Reporting group title	OBINUTUZUMAB 1000MG and MMF

Reporting group description:

Participants will receive obinutuzumab 1000 milligrams (mg) intravenous (IV) infusion on Days 1, 15, 168, and 182 along with MMF/MPA at a starting dose of 1500 mg/day (or equivalent) administered orally in 2 or 3 divided doses. MMF/MPA dose will be up titrated to a target dose of 2.0 - 2.5 grams per day (g/day) (or equivalent). Investigators, at their discretion, may use MPA as a substitute for MMF, with a 360 mg dose being equivalent to a 500 mg dose of MMF. During screening or at randomization, if clinically indicated, participants may receive 750-1000 mg methylprednisolone IV once daily for up to 3 days to treat underlying LN clinical activity. Participants will receive 0.5 mg/kg oral prednisone, tapering this prednisone dose, per protocol, starting on Day 16 and reducing the prednisone dosage to 7.5 mg/day by Week 12.

Reporting group title	PLACEBO and MMF

Reporting group description:

Participants will receive placebo matching to obinutuzumab IV infusion on Days 1, 15, 168, and 182 along with MMF/MPA at a starting dose of 1500 mg/day (or equivalent) administered orally in 2 or 3 divided doses. MMF/MPA dose will be up titrated to a target dose of 2.0 - 2.5 g/day (or equivalent). Investigators, at their discretion, may use MPA as a substitute for MMF, with a 360 mg dose being equivalent to a 500 mg dose of MMF. During screening or at randomization, if clinically indicated, participants may receive 750-1000 mg methylprednisolone IV once daily for up to 3 days to treat underlying LN clinical activity. Participants will receive 0.5 mg/kg oral prednisone, tapering this prednisone dose, per protocol, starting on Day 16 and reducing the prednisone dosage to 7.5 mg/day by Week 12.

Reporting group values	OBINUTUZUMAB 1000MG and MMF	PLACEBO and MMF	Total
Number of subjects	63	62	125
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	63	62	125
From 65-84 years	0	0	0
85 years and over	0	0	0
Age Continuous Units: Years			
arithmetic mean	33.1	31.9	
standard deviation	± 9.8	± 10.1	-
Sex: Female, Male Units:			
Female	55	51	106
Male	8	11	19
Race/Ethnicity, Customized Units: Subjects			
Hispanic Or Latino	42	49	91
Not Hispanic Or Latino	20	12	32
Not Stated	1	0	1

Unknown	0	1	1
Race/Ethnicity, Customized Units: Subjects			
American Indian or Alaska Native	11	17	28
Asian	3	2	5
Black or African American	6	5	11
Multiple	1	0	1
Native Hawaiian or other Pacific Islande	1	0	1
Unknown	13	12	25
White	28	26	54

Subject analysis sets

Subject analysis set title	Obinutuzumab
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

Participants will receive obinutuzumab 1000 milligrams (mg) intravenous (IV) infusion on Days 1, 15, 168, and 182 along with MMF/MPA at a starting dose of 1500 mg/day (or equivalent) administered orally in 2 or 3 divided doses. MMF/MPA dose will be up titrated to a target dose of 2.0 - 2.5 grams per day (g/day) (or equivalent). Investigators, at their discretion, may use MPA as a substitute for MMF, with a 360 mg dose being equivalent to a 500 mg dose of MMF. During screening or at randomization, if clinically indicated, participants may receive 750-1000 mg methylprednisolone IV once daily for up to 3 days to treat underlying LN clinical activity. Participants will receive 0.5 mg/kg oral prednisone, tapering this prednisone dose, per protocol, starting on Day 16 and reducing the prednisone dosage to 7.5 mg/day by Week 12.

Subject analysis set title	Placebo
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

Participants will receive placebo matching to obinutuzumab IV infusion on Days 1, 15, 168, and 182 along with MMF/MPA at a starting dose of 1500 mg/day (or equivalent) administered orally in 2 or 3 divided doses. MMF/MPA dose will be up titrated to a target dose of 2.0 - 2.5 g/day (or equivalent). Investigators, at their discretion, may use MPA as a substitute for MMF, with a 360 mg dose being equivalent to a 500 mg dose of MMF. During screening or at randomization, if clinically indicated, participants may receive 750-1000 mg methylprednisolone IV once daily for up to 3 days to treat underlying LN clinical activity. Participants will receive 0.5 mg/kg oral prednisone, tapering this prednisone dose, per protocol, starting on Day 16 and reducing the prednisone dosage to 7.5 mg/day by Week 12.

Subject analysis set title	Obinutuzumab
Subject analysis set type	Safety analysis

Subject analysis set description:

Participants will receive obinutuzumab 1000 milligrams (mg) intravenous (IV) infusion on Days 1, 15, 168, and 182 along with MMF/MPA at a starting dose of 1500 mg/day (or equivalent) administered orally in 2 or 3 divided doses. MMF/MPA dose will be up titrated to a target dose of 2.0 - 2.5 grams per day (g/day) (or equivalent). Investigators, at their discretion, may use MPA as a substitute for MMF, with a 360 mg dose being equivalent to a 500 mg dose of MMF. During screening or at randomization, if clinically indicated, participants may receive 750-1000 mg methylprednisolone IV once daily for up to 3 days to treat underlying LN clinical activity. Participants will receive 0.5 mg/kg oral prednisone, tapering this prednisone dose, per protocol, starting on Day 16 and reducing the prednisone dosage to 7.5 mg/day by Week 12.

Subject analysis set title	Placebo
Subject analysis set type	Safety analysis

Subject analysis set description:

Participants will receive placebo matching to obinutuzumab IV infusion on Days 1, 15, 168, and 182 along with MMF/MPA at a starting dose of 1500 mg/day (or equivalent) administered orally in 2 or 3 divided doses. MMF/MPA dose will be up titrated to a target dose of 2.0 - 2.5 g/day (or equivalent). Investigators, at their discretion, may use MPA as a substitute for MMF, with a 360 mg dose being equivalent to a 500 mg dose of MMF. During screening or at randomization, if clinically indicated, participants may receive 750-1000 mg methylprednisolone IV once daily for up to 3 days to treat underlying LN clinical activity. Participants will receive 0.5 mg/kg oral prednisone, tapering this

prednisone dose, per protocol, starting on Day 16 and reducing the prednisone dosage to 7.5 mg/day by Week 12.

Reporting group values	Obinutuzumab	Placebo	Obinutuzumab
Number of subjects	63	62	64
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	63	62	64
From 65-84 years	0	0	0
85 years and over	0	0	0
Age Continuous Units: Years			
arithmetic mean	33.1	31.9	33.0
standard deviation	± 9.8	± 10.1	± 9.8
Sex: Female, Male Units:			
Female	55	51	56
Male	8	11	8
Race/Ethnicity, Customized Units: Subjects			
Hispanic Or Latino	42	49	43
Not Hispanic Or Latino	20	12	20
Not Stated	1	0	1
Unknown	0	1	0
Race/Ethnicity, Customized Units: Subjects			
American Indian or Alaska Native	11	17	11
Asian	3	2	3
Black or African American	6	5	6
Multiple	1	0	1
Native Hawaiian or other Pacific Islande	1	0	1
Unknown	13	12	13
White	28	26	29

Reporting group values	Placebo		
Number of subjects	61		
Age categorical Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	0		
Newborns (0-27 days)	0		
Infants and toddlers (28 days-23 months)	0		

Children (2-11 years)	0		
Adolescents (12-17 years)	0		
Adults (18-64 years)	61		
From 65-84 years	0		
85 years and over	0		
Age Continuous			
Units: Years			
arithmetic mean	32.0		
standard deviation	± 10.1		
Sex: Female, Male			
Units:			
Female	50		
Male	11		
Race/Ethnicity, Customized			
Units: Subjects			
Hispanic Or Latino	48		
Not Hispanic Or Latino	12		
Not Stated	0		
Unknown	1		
Race/Ethnicity, Customized			
Units: Subjects			
American Indian or Alaska Native	17		
Asian	2		
Black or African American	5		
Multiple	0		
Native Hawaiian or other Pacific Islande	0		
Unknown	12		
White	25		

End points

End points reporting groups

Reporting group title	OBINUTUZUMAB 1000MG and MMF

Reporting group description:

Participants will receive obinutuzumab 1000 milligrams (mg) intravenous (IV) infusion on Days 1, 15, 168, and 182 along with MMF/MPA at a starting dose of 1500 mg/day (or equivalent) administered orally in 2 or 3 divided doses. MMF/MPA dose will be up titrated to a target dose of 2.0 - 2.5 grams per day (g/day) (or equivalent). Investigators, at their discretion, may use MPA as a substitute for MMF, with a 360 mg dose being equivalent to a 500 mg dose of MMF. During screening or at randomization, if clinically indicated, participants may receive 750-1000 mg methylprednisolone IV once daily for up to 3 days to treat underlying LN clinical activity. Participants will receive 0.5 mg/kg oral prednisone, tapering this prednisone dose, per protocol, starting on Day 16 and reducing the prednisone dosage to 7.5 mg/day by Week 12.

Reporting group title	PLACEBO and MMF

Reporting group description:

Participants will receive placebo matching to obinutuzumab IV infusion on Days 1, 15, 168, and 182 along with MMF/MPA at a starting dose of 1500 mg/day (or equivalent) administered orally in 2 or 3 divided doses. MMF/MPA dose will be up titrated to a target dose of 2.0 - 2.5 g/day (or equivalent). Investigators, at their discretion, may use MPA as a substitute for MMF, with a 360 mg dose being equivalent to a 500 mg dose of MMF. During screening or at randomization, if clinically indicated, participants may receive 750-1000 mg methylprednisolone IV once daily for up to 3 days to treat underlying LN clinical activity. Participants will receive 0.5 mg/kg oral prednisone, tapering this prednisone dose, per protocol, starting on Day 16 and reducing the prednisone dosage to 7.5 mg/day by Week 12.

Subject analysis set title	Obinutuzumab
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

Participants will receive obinutuzumab 1000 milligrams (mg) intravenous (IV) infusion on Days 1, 15, 168, and 182 along with MMF/MPA at a starting dose of 1500 mg/day (or equivalent) administered orally in 2 or 3 divided doses. MMF/MPA dose will be up titrated to a target dose of 2.0 - 2.5 grams per day (g/day) (or equivalent). Investigators, at their discretion, may use MPA as a substitute for MMF, with a 360 mg dose being equivalent to a 500 mg dose of MMF. During screening or at randomization, if clinically indicated, participants may receive 750-1000 mg methylprednisolone IV once daily for up to 3 days to treat underlying LN clinical activity. Participants will receive 0.5 mg/kg oral prednisone, tapering this prednisone dose, per protocol, starting on Day 16 and reducing the prednisone dosage to 7.5 mg/day by Week 12.

Subject analysis set title	Placebo
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

Participants will receive placebo matching to obinutuzumab IV infusion on Days 1, 15, 168, and 182 along with MMF/MPA at a starting dose of 1500 mg/day (or equivalent) administered orally in 2 or 3 divided doses. MMF/MPA dose will be up titrated to a target dose of 2.0 - 2.5 g/day (or equivalent). Investigators, at their discretion, may use MPA as a substitute for MMF, with a 360 mg dose being equivalent to a 500 mg dose of MMF. During screening or at randomization, if clinically indicated, participants may receive 750-1000 mg methylprednisolone IV once daily for up to 3 days to treat underlying LN clinical activity. Participants will receive 0.5 mg/kg oral prednisone, tapering this prednisone dose, per protocol, starting on Day 16 and reducing the prednisone dosage to 7.5 mg/day by Week 12.

Subject analysis set title	Obinutuzumab
Subject analysis set type	Safety analysis

Subject analysis set description:

Participants will receive obinutuzumab 1000 milligrams (mg) intravenous (IV) infusion on Days 1, 15, 168, and 182 along with MMF/MPA at a starting dose of 1500 mg/day (or equivalent) administered orally in 2 or 3 divided doses. MMF/MPA dose will be up titrated to a target dose of 2.0 - 2.5 grams per day (g/day) (or equivalent). Investigators, at their discretion, may use MPA as a substitute for MMF, with a 360 mg dose being equivalent to a 500 mg dose of MMF. During screening or at randomization, if clinically indicated, participants may receive 750-1000 mg methylprednisolone IV once daily for up to 3 days to treat underlying LN clinical activity. Participants will receive 0.5 mg/kg oral prednisone, tapering this prednisone dose, per protocol, starting on Day 16 and reducing the prednisone dosage to 7.5 mg/day by Week 12.

Subject analysis set title	Placebo
Subject analysis set type	Safety analysis

Subject analysis set description:

Participants will receive placebo matching to obinutuzumab IV infusion on Days 1, 15, 168, and 182 along with MMF/MPA at a starting dose of 1500 mg/day (or equivalent) administered orally in 2 or 3 divided doses. MMF/MPA dose will be up titrated to a target dose of 2.0 - 2.5 g/day (or equivalent). Investigators, at their discretion, may use MPA as a substitute for MMF, with a 360 mg dose being equivalent to a 500 mg dose of MMF. During screening or at randomization, if clinically indicated, participants may receive 750-1000 mg methylprednisolone IV once daily for up to 3 days to treat underlying LN clinical activity. Participants will receive 0.5 mg/kg oral prednisone, tapering this prednisone dose, per protocol, starting on Day 16 and reducing the prednisone dosage to 7.5 mg/day by Week 12.

Primary: Proportion of Participants who Achieve Protocol Defined Complete Renal Response (CRR)

End point title	Proportion of Participants who Achieve Protocol Defined Complete Renal Response (CRR)

End point description:

Percentage of participants with normalization of serum creatinine, inactive urinary sediment (as evidenced by < 10 red blood cells (RBCs)/high-power field (HPF) and the absence of red cell casts) and urinary protein to creatinine ratio < 0.5. Normalization of serum creatinine is defined as serum creatinine ≤ the upper limit of normal (ULN) range of central laboratory values if baseline (Day 1) serum creatinine is above the ULN or serum creatinine ≤ 15% above baseline and ≤ the ULN range of central laboratory values if baseline (Day 1) serum creatinine is ≤ the ULN range of central laboratory values.

End point type	Primary

End point timeframe:

From baseline to Week 52 (up to approximately 38 months)

End point values	Obinutuzumab	Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	63	62		
Units: percentage of participants				
number (not applicable)	34.9	22.6		

Statistical analyses

Statistical analysis title	Protocol Defined CRR
Comparison groups	Obinutuzumab v Placebo
Number of subjects included in analysis	125
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.1145
Method	Cochran-Mantel-Haenszel
Parameter estimate	Proportion Difference
Point estimate	12.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.4
upper limit	28.1

Secondary: Proportion of Participants who Achieve Protocol Defined Overall Response (OR)

End point title	Proportion of Participants who Achieve Protocol Defined Overall Response (OR)

End point description:

OR includes both CRR and partial renal response (PRR). CRR as defined in primary outcome measure. PRR defined as 50% improvement in urine protein:creatinine ratio, with one of following conditions met: 1. If baseline urine protein:creatinine ratio is ≤ 3.0, then urine protein:creatinine ratio of <1.0. 2. If baseline protein:creatinine ratio is > 3.0, then urine protein:creatinine ratio of <3.0, serum creatinine ≤15% above baseline value, and no urinary red cell casts and either RBCs/HPF ≤50% above baseline or <10 RBCs/HPF.

End point type	Secondary

End point timeframe:

From baseline to Week 52 (up to approximately 38 months)

End point values	Obinutuzumab	Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	63	62		
Units: percentage of participants				
number (not applicable)	55.6	35.5		

Statistical analyses

Statistical analysis title	Protocol defined Overall Response
Comparison groups	Obinutuzumab v Placebo
Number of subjects included in analysis	125
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0246
Method	Cochran-Mantel-Haenszel
Parameter estimate	Proportion Difference
Point estimate	20.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	3
upper limit	37.2

Secondary: Time to First Protocol Defined Overall Response Over the Course of 52 Weeks

End point title	Time to First Protocol Defined Overall Response Over the Course of 52 Weeks

End point description:

OR includes both CRR and partial renal response (PRR). CRR as defined in the primary outcome measure above. PRR defined as 50% improvement in urine protein:creatinine ratio, with one of following conditions met: 1. If baseline urine protein:creatinine ratio is ≤ 3.0, then urine protein:creatinine ratio of <1.0. 2. If baseline protein:creatinine ratio is > 3.0, then urine protein:creatinine ratio of <3.0, serum creatinine ≤15% above baseline value, and no urinary red cell casts and either RBCs/HPF ≤50% above baseline or <10 RBCs/HPF. Percentage of Participants with response at various time points were measured using Kaplan Meier method.

End point type	Secondary

End point timeframe:

From Baseline (Day 1) to Week 52 (up to approximately 38 months)

End point values	Obinutuzumab	Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	63	62		
Units: percentage of participants				
number (confidence interval 95%)				
Week 12 (n=56, 60)	26 (15 to 37)	19 (10 to 29)		
Week 24 (n=35, 39)	57 (45 to 70)	41 (28 to 53)		
Week 36 (n=24, 30)	63 (50 to 75)	51 (38 to 64)		
Week 52 (n=17, 21)	75 (64 to 86)	58 (45 to 71)		

Statistical analyses

Statistical analysis title	Time to First Protocol Defined OR
Comparison groups	Obinutuzumab v Placebo
Number of subjects included in analysis	125
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0537
Method	Logrank

Secondary: Proportion of Participants who Achieve Protocol Defined Partial Renal Response (PRR)

End point title	Proportion of Participants who Achieve Protocol Defined Partial Renal Response (PRR)

End point description:

PRR defined as serum creatinine ≤15% above baseline value, no urinary red cell casts and either RBCs/HPF ≤ 50% above baseline or < 10 RBCs/HPF, 50% improvement in urine protein:creatinine ratio, with one of following conditions met: 1. If baseline urine protein:creatinine ratio is ≤ 3.0, then a urine protein:creatinine ratio of < 1.0. 2. If baseline protein:creatinine ratio is > 3.0, then a urine protein:creatinine ratio of < 3.0.

End point type	Secondary

End point timeframe:

From baseline to Week 52 (up to approximately 38 months)

End point values	Obinutuzumab	Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	63	62		
Units: percentage of participants				
number (not applicable)	55.6	33.9		

Statistical analyses

Statistical analysis title	Protocol Defined PRR
Comparison groups	Obinutuzumab v Placebo
Number of subjects included in analysis	125
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.015
Method	Cochran-Mantel-Haenszel
Parameter estimate	Proportion Difference
Point estimate	21.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	4.7
upper limit	38.7

Secondary: Proportion of Participants who Achieve Protocol Defined CRR at Week 24

End point title	Proportion of Participants who Achieve Protocol Defined CRR at Week 24

End point description:

CRR defined as normalization of serum creatinine, inactive urinary sediment (as evidenced by < 10 red blood cells (RBCs)/high-power field (HPF) and the absence of red cell casts) and urinary protein to creatinine ratio < 0.5. Normalization of serum creatinine is defined as serum creatinine ≤ the upper limit of normal (ULN) range of central laboratory values if baseline (Day 1) serum creatinine is above the ULN or serum creatinine ≤ 15% above baseline and ≤ the ULN range of central laboratory values if baseline (Day 1) serum creatinine is ≤ the ULN range of central laboratory values.

End point type	Secondary

End point timeframe:

Week 24

End point values	Obinutuzumab	Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	63	62		
Units: percentage of participants				
number (not applicable)	23.8	24.2		

Statistical analyses

Statistical analysis title	Protocol Defined CRR
Comparison groups	Obinutuzumab v Placebo
Number of subjects included in analysis	125
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.9833
Method	Cochran-Mantel-Haenszel
Parameter estimate	Proportion Difference
Point estimate	-0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-15.4
upper limit	14.6

Secondary: Time to Protocol Defined CRR Over the Course of 52 Weeks

End point title	Time to Protocol Defined CRR Over the Course of 52 Weeks

End point description:

CRR included normalization of serum creatinine, inactive urinary sediment (as evidenced by < 10 RBCs/HPF and the absence of red cell casts) and urinary protein to creatinine ratio < 0.5. Normalization of serum creatinine is defined as serum creatinine ≤ the ULN range of central laboratory values if baseline serum creatinine is above the ULN or serum creatinine ≤ 15% above baseline and ≤ the ULN range of central laboratory values if baseline (Day 1) serum creatinine is ≤ the ULN range of central laboratory values. Percentage of participants with response at various time points were measured using Kaplan Meier method.

End point type	Secondary

End point timeframe:

From Baseline to Week 52

End point values	Obinutuzumab	Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	63	62		
Units: percentage of participants				
number (confidence interval 95%)				
Week 12 (n=61, 61)	10 (2 to 17)	10 (2 to 17)		
Week 24 (n=49, 50)	26 (15 to 37)	28 (16 to 39)		
Week 36 (n=40, 39)	36 (24 to 48)	35 (23 to 47)		

Week 52 (n=32, 33)	50 (37 to 63)	40 (28 to 53)		

Statistical analyses

Statistical analysis title	Time to Protocol Defined CRR
Comparison groups	Obinutuzumab v Placebo
Number of subjects included in analysis	125
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.2516
Method	Logrank

Secondary: Change From Baseline in Anti-Double Stranded Deoxyribonucleic Acid (Anti-dsDNA) Levels

End point title	Change From Baseline in Anti-Double Stranded Deoxyribonucleic Acid (Anti-dsDNA) Levels
End point description:	
Anti-dsDNA antibodies are a group of anti-nuclear antibodies targeting double stranded DNA.	
End point type	Secondary
End point timeframe:	
From baseline to Week 52 (up to approximately 38 months)	

End point values	Obinutuzumab	Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	63	62		
Units: log anti-dsDNA levels				
arithmetic mean (standard deviation)	-0.810 (± 1.054)	-0.080 (± 1.102)		

Statistical analyses

Statistical analysis title	Anti-Ds DNA
Comparison groups	Obinutuzumab v Placebo
Number of subjects included in analysis	125
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.808

Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.127
upper limit	-0.489

Secondary: Change From Baseline in Complement component 3 (C3) Levels

End point title	Change From Baseline in Complement component 3 (C3) Levels

End point description:

Complement C3 is a blood test that reflects activation of complement pathway associated with immune deposition in certain autoimmune diseases.

End point type	Secondary

End point timeframe:

Baseline and Week 52

End point values	Obinutuzumab	Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	63	62		
Units: g/L				
arithmetic mean (standard deviation)	0.311 (± 0.302)	0.108 (± 0.273)		

Statistical analyses

Statistical analysis title	C3
Comparison groups	Obinutuzumab v Placebo
Number of subjects included in analysis	125
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0004
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	0.177
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.08
upper limit	0.27

Secondary: Change From Baseline in C4 Levels

End point title	Change From Baseline in C4 Levels

End point description:

Complement C4 is a blood test that reflects activation of complement pathway associated with immune deposition in certain autoimmune diseases.

End point type	Secondary

End point timeframe:

Baseline, Week 52

End point values	Obinutuzumab	Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	63	62		
Units: g/L				
arithmetic mean (standard deviation)	0.101 (± 0.117)	0.003 (± 0.164)		

Statistical analyses

Statistical analysis title	C4
Comparison groups	Obinutuzumab v Placebo
Number of subjects included in analysis	125
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	0.088
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.052
upper limit	0.124

Secondary: Proportion of Participants who Achieve Protocol Defined Modified CRR (mCRR1)

End point title	Proportion of Participants who Achieve Protocol Defined Modified CRR (mCRR1)

End point description:

mCRR1 has got two components only, i.e. serum Creatinine and urinary protein to creatinine ratio. mCRR1 is defined by attainment of normalization of serum creatinine as evidenced by 1.) serum creatinine ≤ the ULN range of central laboratory values if baseline (Day 1) serum creatinine is above the ULN or serum creatinine ≤15% above baseline and ≤ the ULN range of central laboratory values if baseline (Day 1) serum creatinine ≤ the ULN range of central laboratory values and 2.) Urinary protein to creatinine ratio <0.5.

End point type	Secondary

End point timeframe:

Week 52

End point values	Obinutuzumab	Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	63	62		
Units: percentage of participants				
number (not applicable)	39.7	25.8		

Statistical analyses

Statistical analysis title	mCRR1
Comparison groups	Obinutuzumab v Placebo
Number of subjects included in analysis	125
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.09
Method	Cochran-Mantel-Haenszel
Parameter estimate	Proportion Difference
Point estimate	13.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.4
upper limit	30.1

Secondary: Proportion of Participants who Achieve Protocol Defined Second mCRR (mCRR2)

End point title	Proportion of Participants who Achieve Protocol Defined Second mCRR (mCRR2)

End point description:

mCRR2 is defined by normalization of serum creatinine, inactive urinary sediment (as evidenced by < 10 RBCs/HPF and the absence of red cell casts), and urinary protein to creatinine ratio <0.5. Normalization of serum creatinine as evidenced by the following: Serum creatinine ≤15% above baseline if baseline (Day 1) serum creatinine is above the normal range of the central laboratory values or ≤ the ULN range of central laboratory values if baseline (Day 1) serum creatinine is ≤ the ULN range of central laboratory values.

End point type	Secondary

End point timeframe:

Week 52

End point values	Obinutuzumab	Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	63	62		
Units: percentage of participants				
number (not applicable)	44.4	33.9		

Statistical analyses

Statistical analysis title	mCRR2
Comparison groups	Obinutuzumab v Placebo
Number of subjects included in analysis	125
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.1838
Method	Cochran-Mantel-Haenszel
Parameter estimate	Proportion Difference
Point estimate	10.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.4
upper limit	27.6

Secondary: Proportion of Participants who Achieve Protocol Defined Third mCRR (mCRR3)

End point title	Proportion of Participants who Achieve Protocol Defined Third mCRR (mCRR3)

End point description:

mCRR3 is defined by normalization of serum creatine as evidenced by serum creatinine ≤ the ULN range of central laboratory values and urinary protein to creatinine ratio < 0.5.

End point type	Secondary

End point timeframe:

Week 52

End point values	Obinutuzumab	Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	63	62		
Units: percentage of participants				
number (not applicable)	46.0	38.7		

Statistical analyses

Statistical analysis title	mCRR3
Comparison groups	Obinutuzumab v Placebo
Number of subjects included in analysis	125
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.3726
Method	Cochran-Mantel-Haenszel
Parameter estimate	Proportion Difference
Point estimate	7.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-10
upper limit	24.6

Secondary: Percentage of Participants With Adverse Events

End point title	Percentage of Participants With Adverse Events

End point description:

An adverse event is any untoward medical occurrence in a participant administered a pharmaceutical product and which does not necessarily have to have a causal relationship with the treatment. An adverse event can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding, for example), symptom, or disease temporally associated with the use of a pharmaceutical product, whether or not considered related to the pharmaceutical product. Preexisting conditions which worsen during a study are also considered as adverse events. AEs, including AEs of Special Interest and AEs of Particular Interest, were reported based on the national cancer institute common terminology criteria for AEs, Version 4.0 (NCI-CTCAE, v4.0). Reported are the number of subjects with AEs, Grade 3-5 AEs, and Serious Adverse Events (SAEs).

End point type	Secondary

End point timeframe:

From Baseline up to Week 104 (up to approximately 38 months)

End point values	Obinutuzumab	Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	64	61		
Units: percentage of participants				
number (not applicable)				
Adverse Events	90.6	88.5		
Serious Adverse Events	25.0	29.5		
Grade 3-5 Infections	6.3	21.3		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with Adverse Events of Special Interest:

Infusion Related Reactions, Infections, Thrombocytopenia and Neutropenia

End point title	Percentage of Participants with Adverse Events of Special Interest: Infusion Related Reactions, Infections, Thrombocytopenia and Neutropenia

End point description:

Neutropenia is defined as low neutrophil count (ANC <1.0 x 109/L). Infusion related reaction is defined as a type of hypersensitivity reaction (pruritus, chills, diaphoresis, fever) that develops during or shortly after administration of a drug. Thrombocytopenia is defined as deficiency of platelets (<150 x 10^9/L) in the blood. Infections include all events of infections under the SOC of infections and infestations in this study.

End point type	Secondary

End point timeframe:

From baseline to Week 104 (up to approximately 38 months)

End point values	Obinutuzumab	Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	64	61		
Units: percentage of participants				
number (not applicable)				
Infusion Related Reactions	15.6	9.8		
Infections	75.0	62.3		
Thrombocytopenia	0	0		
Neutropenia	4.7	3.3		

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change From Baseline in Circulating CD19-Positive B-Cell Levels

End point title	Percent Change From Baseline in Circulating CD19-Positive B-Cell Levels

End point description:

CD19+ B cell is a transmembrane protein that is encoded by the gene CD19.

End point type	Secondary

End point timeframe:

Baseline, Week 2, Week 4, Week 12, Week 24, Week 52

End point values	Obinutuzumab	Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	63	62		
Units: cells/uL				
arithmetic mean (standard deviation)				
Baseline (n=63, 62)	327.902 (± 330.562)	353.499 (± 454.165)		

Week 2 (n=39, 42)	-97.469 (± 12.899)	39.293 (± 145.247)		
Week 4 (n=45, 36)	-98.777 (± 5.235)	-5.186 (± 78.469)		
Week 12 (n=41, 45)	-97.045 (± 15.506)	0.661 (± 134.421)		
Week 24 (n=42, 37)	-96.628 (± 10.207)	-11.446 (± 86.793)		
Week 52 (n=39, 42)	-98.620 (± 5.677)	37.695 (± 220.857)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Anti-Drug Antibody (ADA) to Obinutuzumab

End point title	Percentage of Participants With Anti-Drug Antibody (ADA) to Obinutuzumab
End point description:	
Antibodies are a blood protein produced in response to and counteracting a specific antigen.	
End point type	Secondary
End point timeframe:	
From baseline to Week 52 (up to approximately 38 months)	

End point values	Obinutuzumab			
Subject group type	Subject analysis set			
Number of subjects analysed	64			
Units: percentage of participants				
number (not applicable)	9.38			

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum Observed Plasma Concentration (Cmax) of Obinutuzumab

End point title	Maximum Observed Plasma Concentration (Cmax) of Obinutuzumab
End point description:	
End point type	Secondary
End point timeframe:	
Week 0, Week 24, Week 52	

End point values	Obinutuzumab			
Subject group type	Subject analysis set			
Number of subjects analysed	64			
Units: ug/mL				
arithmetic mean (standard deviation)				
Week 0-24	559 (± 112)			
Week 24-52	605 (± 115)			
Week 0-52	605 (± 115)			

Statistical analyses

No statistical analyses for this end point

Secondary: Area Under the Plasma Concentration Versus Time Curve (AUC) of Obinutuzumab

End point title	Area Under the Plasma Concentration Versus Time Curve (AUC) of Obinutuzumab

End point description:

End point type	Secondary

End point timeframe:

Week 0, Week 24, Week 52

End point values	Obinutuzumab			
Subject group type	Subject analysis set			
Number of subjects analysed	64			
Units: ug/mL*day				
arithmetic mean (standard deviation)				
Week 0-24	10595 (± 4016)			
Week 24-52	15811 (± 5543)			
Week 0-52	26406 (± 9027)			

Statistical analyses

No statistical analyses for this end point

Secondary: Systemic Clearance of Obinutuzumab

End point title	Systemic Clearance of Obinutuzumab

End point description:

End point type	Secondary

End point timeframe:

Day 0, Week 24, Week 52

End point values	Obinutuzumab			
Subject group type	Subject analysis set			
Number of subjects analysed	64			
Units: L/day				
arithmetic mean (standard deviation)				
Day 0	0.255 (± 0.136)			
Week 24	0.147 (± 0.0564)			
Week 52	0.137 (± 0.0535)			

Statistical analyses

No statistical analyses for this end point

Secondary: Volume of Distribution Under Steady State (Vss) of Obinutuzumab

End point title	Volume of Distribution Under Steady State (Vss) of Obinutuzumab

End point description:

End point type	Secondary

End point timeframe:

Day 0, Week 24, Week 52

End point values	Obinutuzumab			
Subject group type	Subject analysis set			
Number of subjects analysed	64			
Units: Litre				
arithmetic mean (standard deviation)				
Day 0	3.67 (± 0.591)			
Week 24	3.67 (± 0.591)			
Week 52	3.67 (± 0.591)			

Statistical analyses

No statistical analyses for this end point

Secondary: Terminal Plasma Half-Life (t1/2) of Obinutuzumab

End point title	Terminal Plasma Half-Life (t1/2) of Obinutuzumab

End point description:

End point type	Secondary

End point timeframe:

Day 0, Week 24, Week 52

End point values	Obinutuzumab			
Subject group type	Subject analysis set			
Number of subjects analysed	64			
Units: day				
arithmetic mean (standard deviation)				
Day 0	13.1 (± 3.7)			
Week 24	20.5 (± 5.6)			
Week 52	22.1 (± 6.7)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline of Participant's Global Assessment of Disease Activity Visual Analog Scale (VAS) Score

End point title	Change from Baseline of Participant's Global Assessment of Disease Activity Visual Analog Scale (VAS) Score

End point description:

Each VAS had a range from 0-100 with higher scores indicating greater symptom impact on global health status.

End point type	Secondary

End point timeframe:

Baseline (Day 1), Weeks 4, 12, 24, 36, 52/early termination

End point values	Obinutuzumab	Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	63	62		
Units: score on scale				
arithmetic mean (standard deviation)				
Baseline	41.3 (± 25.59)	39.4 (± 24.76)		
Week 4	-14.4 (± 18.28)	-8.7 (± 22.69)		
Week 12	-19.9 (± 25.07)	-11.6 (± 25.22)		

Week 24	-25.0 (± 25.17)	-20.8 (± 24.74)		
Week 36	-24.8 (± 25.71)	-19.6 (± 25.04)		
Week 52	-25.4 (± 26.49)	-23.3 (± 25.76)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From baseline to Week 104 (approximately 38 months)

Adverse event reporting additional description:

The safety population was defined as all participants who have received at least one dose of study medication.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	21.1

Reporting groups

Reporting group title	PLACEBO and MMF

Reporting group description:

Participants will receive placebo matching to obinutuzumab IV infusion on Days 1, 15, 168, and 182 along with MMF/MPA at a starting dose of 1500 mg/day (or equivalent) administered orally in 2 or 3 divided doses. MMF/MPA dose will be up titrated based on tolerability to a target dose of 2.0 - 2.5 g/day (or equivalent). Investigators, at their discretion, may use MPA as a substitute for MMF, with a 360 mg dose being equivalent to a 500 mg dose of MMF. During screening or at randomization, if clinically indicated, participants may receive 750-1000 mg methylprednisolone IV once daily for up to 3 days to treat underlying LN clinical activity. Participants will receive 0.5 mg/kg oral prednisone, tapering this prednisone dose, per protocol, starting on Day 16 and reducing the prednisone dosage to 7.5 mg/day by Week 12.

Reporting group title	OBINUTUZUMAB 1000MG and MMF

Reporting group description:

Participants will receive obinutuzumab 1000 milligrams (mg) intravenous (IV) infusion on Days 1, 15, 168, and 182 along with MMF/MPA at a starting dose of 1500 mg/day (or equivalent) administered orally in 2 or 3 divided doses. MMF/MPA dose will be up titrated based on tolerability to a target dose of 2.0 - 2.5 grams per day (g/day) (or equivalent). Investigators, at their discretion, may use MPA as a substitute for MMF, with a 360 mg dose being equivalent to a 500 mg dose of MMF. During screening or at randomization, if clinically indicated, participants may receive 750-1000 mg methylprednisolone IV once daily for up to 3 days to treat underlying LN clinical activity. Participants will receive 0.5 mg/kg oral prednisone, tapering this prednisone dose, per protocol, starting on Day 16 and reducing the prednisone dosage to 7.5 mg/day by Week 12.

Serious adverse events	PLACEBO and MMF	OBINUTUZUMAB 1000MG and MMF	
Total subjects affected by serious adverse events			
subjects affected / exposed	18 / 61 (29.51%)	16 / 64 (25.00%)	
number of deaths (all causes)	4	1	
number of deaths resulting from adverse events			
Vascular disorders			
SHOCK HAEMORRHAGIC			
subjects affected / exposed	0 / 61 (0.00%)	1 / 64 (1.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
HYPERTENSION			

subjects affected / exposed	1 / 61 (1.64%)	0 / 64 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
THROMBOPHLEBITIS SUPERFICIAL			
subjects affected / exposed	1 / 61 (1.64%)	0 / 64 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pregnancy, puerperium and perinatal conditions			
ABORTION SPONTANEOUS			
subjects affected / exposed	0 / 61 (0.00%)	1 / 64 (1.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
GENERAL PHYSICAL HEALTH DETERIORATION			
subjects affected / exposed	1 / 61 (1.64%)	0 / 64 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
PYREXIA			
subjects affected / exposed	1 / 61 (1.64%)	1 / 64 (1.56%)	
occurrences causally related to treatment / all	2 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
ASTHMA			
subjects affected / exposed	0 / 61 (0.00%)	1 / 64 (1.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
PULMONARY EMBOLISM			
subjects affected / exposed	0 / 61 (0.00%)	1 / 64 (1.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
PLEURITIC PAIN			

subjects affected / exposed	1 / 61 (1.64%)	0 / 64 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
ACUTE RESPIRATORY FAILURE			
subjects affected / exposed	1 / 61 (1.64%)	0 / 64 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	1 / 1	0 / 0	
PNEUMONIA ASPIRATION			
subjects affected / exposed	0 / 61 (0.00%)	1 / 64 (1.56%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
RESPIRATORY FAILURE			
subjects affected / exposed	0 / 61 (0.00%)	1 / 64 (1.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
PULMONARY ALVEOLAR HAEMORRHAGE			
subjects affected / exposed	0 / 61 (0.00%)	1 / 64 (1.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
PSYCHOTIC DISORDER			
subjects affected / exposed	0 / 61 (0.00%)	1 / 64 (1.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
WEIGHT INCREASED			
subjects affected / exposed	1 / 61 (1.64%)	0 / 64 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
INFLUENZA A VIRUS TEST POSITIVE			
subjects affected / exposed	0 / 61 (0.00%)	1 / 64 (1.56%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Injury, poisoning and procedural complications			
LUMBAR VERTEBRAL FRACTURE			
subjects affected / exposed	1 / 61 (1.64%)	0 / 64 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
ROAD TRAFFIC ACCIDENT			
subjects affected / exposed	1 / 61 (1.64%)	0 / 64 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
CARDIAC FAILURE			
subjects affected / exposed	1 / 61 (1.64%)	0 / 64 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
HEADACHE			
subjects affected / exposed	1 / 61 (1.64%)	0 / 64 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
IDIOPATHIC INTRACRANIAL HYPERTENSION			
subjects affected / exposed	1 / 61 (1.64%)	0 / 64 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
EPILEPSY			
subjects affected / exposed	0 / 61 (0.00%)	1 / 64 (1.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
HEMIPARESIS			
subjects affected / exposed	1 / 61 (1.64%)	0 / 64 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
SEIZURE			

subjects affected / exposed	1 / 61 (1.64%)	0 / 64 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
MYELITIS TRANSVERSE			
subjects affected / exposed	0 / 61 (0.00%)	1 / 64 (1.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
NEUTROPENIA			
subjects affected / exposed	1 / 61 (1.64%)	1 / 64 (1.56%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
THROMBOCYTOPENIA			
subjects affected / exposed	1 / 61 (1.64%)	0 / 64 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
LEUKOPENIA			
subjects affected / exposed	1 / 61 (1.64%)	0 / 64 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
INTESTINAL PERFORATION			
subjects affected / exposed	1 / 61 (1.64%)	0 / 64 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
INTUSSUSCEPTION			
subjects affected / exposed	1 / 61 (1.64%)	0 / 64 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
GASTROINTESTINAL PERFORATION			
subjects affected / exposed	0 / 61 (0.00%)	1 / 64 (1.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
ABDOMINAL PAIN			

subjects affected / exposed	0 / 61 (0.00%)	2 / 64 (3.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
UPPER GASTROINTESTINAL HAEMORRHAGE			
subjects affected / exposed	1 / 61 (1.64%)	0 / 64 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
OESOPHAGEAL FISTULA			
subjects affected / exposed	0 / 61 (0.00%)	1 / 64 (1.56%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
CHOLELITHIASIS			
subjects affected / exposed	0 / 61 (0.00%)	1 / 64 (1.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
HEPATITIS ACUTE			
subjects affected / exposed	1 / 61 (1.64%)	0 / 64 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
RASH			
subjects affected / exposed	0 / 61 (0.00%)	1 / 64 (1.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
LUPUS NEPHRITIS			
subjects affected / exposed	1 / 61 (1.64%)	0 / 64 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
RENAL FAILURE			
subjects affected / exposed	2 / 61 (3.28%)	0 / 64 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	

NEPHROPATHY TOXIC			
subjects affected / exposed	1 / 61 (1.64%)	0 / 64 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
RENAL IMPAIRMENT			
subjects affected / exposed	1 / 61 (1.64%)	0 / 64 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
SYSTEMIC LUPUS ERYTHEMATOSUS			
subjects affected / exposed	2 / 61 (3.28%)	2 / 64 (3.13%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 1	0 / 0	
ARTHRITIS			
subjects affected / exposed	1 / 61 (1.64%)	0 / 64 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
ARTHRALGIA			
subjects affected / exposed	0 / 61 (0.00%)	1 / 64 (1.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
BRONCHIOLITIS			
subjects affected / exposed	1 / 61 (1.64%)	0 / 64 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
CYTOMEGALOVIRUS MYOCARDITIS			
subjects affected / exposed	1 / 61 (1.64%)	0 / 64 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
DISSEMINATED CYTOMEGALOVIRAL INFECTION			

subjects affected / exposed	1 / 61 (1.64%)	0 / 64 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
CYTOMEGALOVIRUS CHORIORETINITIS			
subjects affected / exposed	1 / 61 (1.64%)	0 / 64 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
KLEBSIELLA BACTERAEMIA			
subjects affected / exposed	1 / 61 (1.64%)	0 / 64 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
ENDOMETRITIS BACTERIAL			
subjects affected / exposed	1 / 61 (1.64%)	0 / 64 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
HERPES ZOSTER			
subjects affected / exposed	3 / 61 (4.92%)	1 / 64 (1.56%)	
occurrences causally related to treatment / all	2 / 3	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
ORAL CANDIDIASIS			
subjects affected / exposed	0 / 61 (0.00%)	1 / 64 (1.56%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
PNEUMONIA			
subjects affected / exposed	1 / 61 (1.64%)	1 / 64 (1.56%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
MENINGITIS CRYPTOCOCCAL			
subjects affected / exposed	1 / 61 (1.64%)	0 / 64 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
URINARY TRACT INFECTION			

subjects affected / exposed	1 / 61 (1.64%)	1 / 64 (1.56%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
PYELONEPHRITIS			
subjects affected / exposed	1 / 61 (1.64%)	0 / 64 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
UROSEPSIS			
subjects affected / exposed	1 / 61 (1.64%)	0 / 64 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
APPENDICITIS			
subjects affected / exposed	1 / 61 (1.64%)	0 / 64 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
PROGRESSIVE MULTIFOCAL LEUKOENCEPHALOPATHY			
subjects affected / exposed	1 / 61 (1.64%)	0 / 64 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	1 / 1	0 / 0	
RESPIRATORY TRACT INFECTION			
subjects affected / exposed	0 / 61 (0.00%)	1 / 64 (1.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
SEPSIS			
subjects affected / exposed	1 / 61 (1.64%)	0 / 64 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
VARICELLA			
subjects affected / exposed	1 / 61 (1.64%)	0 / 64 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
TUBERCULOSIS			

subjects affected / exposed	0 / 61 (0.00%)	1 / 64 (1.56%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
HYPONATRAEMIA			
subjects affected / exposed	1 / 61 (1.64%)	0 / 64 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	PLACEBO and MMF	OBINUTUZUMAB 1000MG and MMF	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	39 / 61 (63.93%)	50 / 64 (78.13%)	
Injury, poisoning and procedural complications			
INFUSION RELATED REACTION			
subjects affected / exposed	6 / 61 (9.84%)	7 / 64 (10.94%)	
occurrences (all)	7	7	
Vascular disorders			
HYPERTENSION			
subjects affected / exposed	2 / 61 (3.28%)	6 / 64 (9.38%)	
occurrences (all)	2	6	
Nervous system disorders			
HEADACHE			
subjects affected / exposed	3 / 61 (4.92%)	5 / 64 (7.81%)	
occurrences (all)	3	7	
Blood and lymphatic system disorders			
ANAEMIA			
subjects affected / exposed	4 / 61 (6.56%)	5 / 64 (7.81%)	
occurrences (all)	6	5	
General disorders and administration site conditions			
CHEST PAIN			
subjects affected / exposed	4 / 61 (6.56%)	0 / 64 (0.00%)	
occurrences (all)	4	0	
Gastrointestinal disorders			

ABDOMINAL PAIN			
subjects affected / exposed	3 / 61 (4.92%)	5 / 64 (7.81%)	
occurrences (all)	3	7	
DIARRHOEA			
subjects affected / exposed	5 / 61 (8.20%)	3 / 64 (4.69%)	
occurrences (all)	5	3	
NAUSEA			
subjects affected / exposed	3 / 61 (4.92%)	6 / 64 (9.38%)	
occurrences (all)	3	7	
Psychiatric disorders			
ANXIETY			
subjects affected / exposed	4 / 61 (6.56%)	0 / 64 (0.00%)	
occurrences (all)	4	0	
INSOMNIA			
subjects affected / exposed	4 / 61 (6.56%)	3 / 64 (4.69%)	
occurrences (all)	4	3	
Musculoskeletal and connective tissue disorders			
ARTHRALGIA			
subjects affected / exposed	4 / 61 (6.56%)	5 / 64 (7.81%)	
occurrences (all)	5	6	
Infections and infestations			
BRONCHITIS			
subjects affected / exposed	5 / 61 (8.20%)	12 / 64 (18.75%)	
occurrences (all)	8	14	
CONJUNCTIVITIS			
subjects affected / exposed	2 / 61 (3.28%)	4 / 64 (6.25%)	
occurrences (all)	2	6	
GASTROENTERITIS			
subjects affected / exposed	6 / 61 (9.84%)	3 / 64 (4.69%)	
occurrences (all)	9	4	
HERPES ZOSTER			
subjects affected / exposed	6 / 61 (9.84%)	5 / 64 (7.81%)	
occurrences (all)	7	6	
INFLUENZA			
subjects affected / exposed	2 / 61 (3.28%)	4 / 64 (6.25%)	
occurrences (all)	3	4	

NASOPHARYNGITIS			
subjects affected / exposed	6 / 61 (9.84%)	5 / 64 (7.81%)	
occurrences (all)	7	5	
PHARYNGITIS			
subjects affected / exposed	4 / 61 (6.56%)	5 / 64 (7.81%)	
occurrences (all)	4	8	
UPPER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	5 / 61 (8.20%)	6 / 64 (9.38%)	
occurrences (all)	6	8	
URINARY TRACT INFECTION			
subjects affected / exposed	12 / 61 (19.67%)	14 / 64 (21.88%)	
occurrences (all)	20	19	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
24 July 2015	Additional text has been provided on ACE inhibitors and angiotensin-receptor blockers with regards to their known teratogenic effects.
02 February 2016	The assessment of damage throught the Glucocorticoid Toxicity Change Index (GTCI) was added as an exploratory objective. Clarifications were made that all B cells and not just CD19+ B cells will be evaluated in renal biopsies. Clarifications were made that eligible renal biopsies can be taken during screening as well as within 6 months prior to screening. The requirement for active urinary sediment to qualify patients for the study was removed. Exclusion criteria was updated. The dosing regimen for the study treatments and the follow up period were updated. Secondary objectives were updated. Procedures and process for various data collections and the time period of collection were updated.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported