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	02 August 2023

Results information

Result version number	v4 (current)
This version publication date	16 August 2024
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	Final
Date of interim/final analysis	02 August 2023
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	02 August 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

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

Protection of trial subjects:

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

Background therapy:

Antimalarials
Angiotensin-converting Enzyme (ACE) inhibitors
Angiotensin-receptor Blockers (ARB)
Glucocorticoid Taper

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 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	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	Subject, Investigator

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 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 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	55	44
Not completed	8	18
Consent withdrawn by subject	4	7
Physician decision	-	2
Death	1	4
Add. therapies that reduce perip. B cell count	-	2
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 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 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 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 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 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 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 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 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 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 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 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 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: Percentage of Participants who Achieve Protocol Defined Complete Renal Response (CRR)

End point title	Percentage 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 above the ULN range of central laboratory values.

End point type	Primary

End point timeframe:

From baseline to Week 52

End point values	OBINUTUZUMAB 1000MG and MMF	PLACEBO and MMF		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22	14		
Units: Percentage of participants				
number (not applicable)	34.9	22.6		

Statistical analyses

Statistical analysis title	Protocol Defined CRR (80% CI)
Comparison groups	OBINUTUZUMAB 1000MG and MMF v PLACEBO and MMF
Number of subjects included in analysis	36
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.1145 [1]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in Percentage of Participants
Point estimate	12.3
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	2.1
upper limit	22.6

Notes:

[1] - Stratified by race (Afro Caribbean/African American vs. Others) and region (US vs. non-US sites). Statistically significant at pre-specified alpha of 20%.

Statistical analysis title	Protocol Defined CRR (95% CI)
Comparison groups	OBINUTUZUMAB 1000MG and MMF v PLACEBO and MMF
Number of subjects included in analysis	36
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.1145 [2]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in Percentage of Participants
Point estimate	12.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.4
upper limit	28.1

Notes:

[2] - Stratified by race (Afro Caribbean/African American vs. Others) and region (US vs. non-US sites). Statistically significant at pre-specified alpha of 20%.

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

End point title	Percentage 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

End point values	OBINUTUZUMAB 1000MG and MMF	PLACEBO and MMF		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	35	22		
Units: Percentage of participants				
number (not applicable)	55.6	35.5		

Statistical analyses

Statistical analysis title	Protocol defined Overall Response (80% CI)
Comparison groups	OBINUTUZUMAB 1000MG and MMF v PLACEBO and MMF

Number of subjects included in analysis	57
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0246 [3]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in Percentage of Participants
Point estimate	20.1
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	8.9
upper limit	31.3

Notes:

[3] - Stratified by race (Afro Caribbean/African American vs. Others) and region (US vs. non-US sites). Statistically significant at pre-specified alpha of 20%.

Statistical analysis title	Protocol defined Overall Response (95% CI)
Comparison groups	OBINUTUZUMAB 1000MG and MMF v PLACEBO and MMF
Number of subjects included in analysis	57
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0246 [4]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in Percentage of Participants
Point estimate	20.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	3
upper limit	37.2

Notes:

[4] - Stratified by race (Afro Caribbean/African American vs. Others) and region (US vs. non-US sites). Statistically significant at pre-specified alpha of 20%.

Secondary: Time to OR Over 52 Weeks

End point title	Time to OR Over 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

End point values	OBINUTUZUMAB 1000MG and MMF	PLACEBO and MMF		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	63	62		
Units: Percentage of participants				
number (not applicable)				
Week 12 (n=55, 59)	87.3	95.2		
Week 24 (n=33, 37)	52.4	59.7		
Week 36 (n=21, 29)	33.3	46.8		
Week 52 (n=14, 21)	22.2	33.9		

Statistical analyses

Statistical analysis title	Time to ORR Over 52 Weeks
Comparison groups	OBINUTUZUMAB 1000MG and MMF v PLACEBO and MMF
Number of subjects included in analysis	125
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0744
Method	Logrank

Secondary: Percentage of Participants who Achieve Protocol Defined Partial Renal Response (PRR) at Week 52

End point title	Percentage of Participants who Achieve Protocol Defined Partial Renal Response (PRR) at Week 52

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:

Week 52

End point values	OBINUTUZUMAB 1000MG and MMF	PLACEBO and MMF		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	35	21		
Units: Percentage of participants				
number (not applicable)	55.6	33.9		

Statistical analyses

Statistical analysis title	Protocol Defined PRR (95% CI)
Comparison groups	OBINUTUZUMAB 1000MG and MMF v PLACEBO and MMF
Number of subjects included in analysis	56
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.015 [5]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in Percentage of Participants
Point estimate	21.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	4.7
upper limit	38.7

Notes:

[5] - Stratified by race (Afro Caribbean/African American vs. Others) and region (US vs. non-US sites). Statistically significant at pre-specified alpha of 20%.

Statistical analysis title	Protocol Defined PRR (80% CI)
Comparison groups	OBINUTUZUMAB 1000MG and MMF v PLACEBO and MMF
Number of subjects included in analysis	56
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.015 [6]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in % of Participants
Point estimate	21.7
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	10.6
upper limit	32.8

Notes:

[6] - Stratified by race (Afro Caribbean/African American vs. Others) and region (US vs. non-US sites). Statistically significant at pre-specified alpha of 20%.

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

End point title	Percentage 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 1000MG and MMF	PLACEBO and MMF		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	16	17		
Units: Percentage of participants				
number (not applicable)	25.4	27.4		

Statistical analyses

Statistical analysis title	Protocol Defined CRR (80% CI)
Comparison groups	OBINUTUZUMAB 1000MG and MMF v PLACEBO and MMF
Number of subjects included in analysis	33
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.8461 [7]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in Percentage of Participants
Point estimate	-2
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	-12.1
upper limit	8.1

Notes:

[7] - Stratified by race (Afro Caribbean/African American vs. Others) and region (US vs. non-US sites). Statistically significant at pre-specified alpha of 20%.

Statistical analysis title	Protocol Defined CRR (95% CI)
Comparison groups	OBINUTUZUMAB 1000MG and MMF v PLACEBO and MMF
Number of subjects included in analysis	33
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.8461 [8]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in Percentage of Participants
Point estimate	-2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-17.5
upper limit	13.4

Notes:

[8] - Stratified by race (Afro Caribbean/African American vs. Others) and region (US vs. non-US sites). Statistically significant at pre-specified alpha of 20%.

Secondary: Time to CRR Over 52 Weeks

End point title	Time to CRR Over 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 1000MG and MMF	PLACEBO and MMF		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	63	62		
Units: Percentage of participants				
number (not applicable)				
Week 12 (n-61,60)	96.8	96.8		
Week 24 (n=47,48)	74.6	77.4		
Week 36 (n=38,38)	60.3	61.3		
Week 52 (n=27,33)	42.9	53.2		

Statistical analyses

Statistical analysis title	Time to Protocol Defined CRR
Comparison groups	OBINUTUZUMAB 1000MG and MMF v PLACEBO and MMF
Number of subjects included in analysis	125
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.353
Method	Logrank

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 1000MG and MMF	PLACEBO and MMF		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	63	62		
Units: g/L				
arithmetic mean (standard deviation)	0.311 (± 0.302)	0.106 (± 0.273)		

Statistical analyses

Statistical analysis title	C3
Comparison groups	OBINUTUZUMAB 1000MG and MMF v PLACEBO and MMF
Number of subjects included in analysis	125
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0004 [9]
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	0.178
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.081
upper limit	0.275

Notes:

[9] - Stratified by race (Afro Caribbean/African American vs. Others) and region (US vs. non-US sites). Statistically significant at pre-specified alpha of 20%.

Statistical analysis title	C3 (80% CI)
Comparison groups	OBINUTUZUMAB 1000MG and MMF v PLACEBO and MMF
Number of subjects included in analysis	125
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0004 [10]
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	0.178
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.115
upper limit	0.241

Notes:

[10] - Stratified by race (Afro Caribbean/African American vs. Others) and region (US vs. non-US sites). Statistically significant at pre-specified alpha of 20%.

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 autoantibodies targeting double stranded DNA.	
End point type	Secondary
End point timeframe:	
From baseline to Week 52	

End point values	OBINUTUZUMAB 1000MG and MMF	PLACEBO and MMF		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	63	62		
Units: log anti-dsDNA levels				
arithmetic mean (standard deviation)	-0.810 (± 1.054)	-0.076 (± 1.103)		

Statistical analyses

Statistical analysis title	Anti-Ds DNA (80% CI)
Comparison groups	OBINUTUZUMAB 1000MG and MMF v PLACEBO and MMF
Number of subjects included in analysis	125
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001 [11]
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.81
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	-1.019
upper limit	-0.602

Notes:

[11] - Stratified by race (Afro Caribbean/African American vs. Others) and region (US vs. non-US sites). Statistically significant at pre-specified alpha of 20%.

Statistical analysis title	Anti-Ds DNA
Comparison groups	OBINUTUZUMAB 1000MG and MMF v PLACEBO and MMF
Number of subjects included in analysis	125
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001 [12]
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.81

Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.13
upper limit	-0.491

Notes:

[12] - Stratified by race (Afro Caribbean/African American vs. Others) and region (US vs. non-US sites). Statistically significant at pre-specified alpha of 20%.

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 1000MG and MMF	PLACEBO and MMF		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	63	62		
Units: g/L				
arithmetic mean (standard deviation)	0.101 (± 0.117)	0.004 (± 0.164)		

Statistical analyses

Statistical analysis title	C4 (80% CI)
Comparison groups	OBINUTUZUMAB 1000MG and MMF v PLACEBO and MMF
Number of subjects included in analysis	125
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001 [13]
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	0.088
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.065
upper limit	0.112

Notes:

[13] - Stratified by race (Afro Caribbean/African American vs. Others) and region (US vs. non-US sites). Statistically significant at pre-specified alpha of 20%.

Statistical analysis title	C4

Comparison groups	OBINUTUZUMAB 1000MG and MMF v PLACEBO and MMF
Number of subjects included in analysis	125
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [14]
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

Notes:

[14] - Stratified by race (Afro Caribbean/African American vs. Others) and region (US vs. non-US sites). Statistically significant at pre-specified alpha of 20%.

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

End point title	Percentage 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	25	16		
Units: Percentage of participants				
number (not applicable)	39.7	25.8		

Statistical analyses

Statistical analysis title	mCRR1 (95% CI)
Comparison groups	Placebo v Obinutuzumab

Number of subjects included in analysis	41
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.09 [15]
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

Notes:

[15] - Stratified by race (Afro Caribbean/African American vs. Others) and region (US vs. non-US sites). Statistically significant at pre-specified alpha of 20%.

Statistical analysis title	mCRR1 (80% CI)
Comparison groups	Obinutuzumab v Placebo
Number of subjects included in analysis	41
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.09 [16]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in Percentage of Participants
Point estimate	13.9
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	3.2
upper limit	24.5

Notes:

[16] - Stratified by race (Afro Caribbean/African American vs. Others) and region (US vs. non-US sites). Statistically significant at pre-specified alpha of 20%.

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

End point title	Percentage 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	29	24		
Units: Percentage of participants				
number (not applicable)	46.0	38.7		

Statistical analyses

Statistical analysis title	mCRR3 (80% CI)
Comparison groups	Obinutuzumab v Placebo
Number of subjects included in analysis	53
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.3726 [17]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in Percentage of Participants
Point estimate	7.3
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	-4
upper limit	18.6

Notes:

[17] - Stratified by race (Afro Caribbean/African American vs. Others) and region (US vs. non-US sites). Statistically significant at pre-specified alpha of 20%.

Statistical analysis title	mCRR3 (95% CI)
Comparison groups	Obinutuzumab v Placebo
Number of subjects included in analysis	53
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.3726 [18]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in Percentage of Participants
Point estimate	7.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-10
upper limit	24.6

Notes:

[18] - Stratified by race (Afro Caribbean/African American vs. Others) and region (US vs. non-US sites). Statistically significant at pre-specified alpha of 20%.

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

End point title	Percentage 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	28	21		
Units: Percentage of participants				
number (not applicable)	44.4	33.9		

Statistical analyses

Statistical analysis title	mCRR2 (80% CI)
Comparison groups	Obinutuzumab v Placebo
Number of subjects included in analysis	49
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.1838 [19]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in Percentage of Participants
Point estimate	10.6
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	-0.5
upper limit	21.7

Notes:

[19] - Stratified by race (Afro Caribbean/African American vs. Others) and region (US vs. non-US sites). Statistically significant at pre-specified alpha of 20%.

Statistical analysis title	mCRR2 (95% CI)
Comparison groups	Obinutuzumab v Placebo
Number of subjects included in analysis	49
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.1838 [20]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in Percentage of Participants
Point estimate	10.6

Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.4
upper limit	27.6

Notes:

[20] - Stratified by race (Afro Caribbean/African American vs. Others) and region (US vs. non-US sites). Statistically significant at pre-specified alpha of 20%.

Secondary: Percentage of Participants With Adverse Events (AEs)

End point title	Percentage of Participants With Adverse Events (AEs)

End point description:

An AE 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 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, Serious Adverse Events (SAEs), Infections and Serious infections. The AEs reported do not include events after the receipt of rescue medications.

End point type	Secondary

End point timeframe:

From baseline to approximately 7 years and 8 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 (n=58,54)	90.6	88.5		
Grade 3 AEs (n=19,15)	29.7	24.6		
Grade 4 AEs (n=6,7)	9.4	11.5		
Grade 5 AEs (n=1,2)	1.6	3.3		
Serious Adverse Events (n=16,17)	25.0	27.9		
Infections (n=48,38)	76.6	62.3		
Serious infections (n=5,10)	7.8	16.4		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with Adverse Events of Special Interest: Infusion Related Reactions, Grade 3 or Higher Infections, Drug-related Neutropenia and Drug-related Thrombocytopenia

End point title	Percentage of Participants with Adverse Events of Special Interest: Infusion Related Reactions, Grade 3 or Higher Infections, Drug-related Neutropenia and Drug-related Thrombocytopenia

End point description:

Infusion related reaction is defined as any event reported within 24 hours of infusion and thought to be causally related to the investigational agent by the investigator. Grade 3 or higher infections include all events of Grade 3 to 5 under the SOC of infections and infestations. Drug-related neutropenia is defined as events in the Roche AE Grouped Term (AEGT) "Neutropenia and associated complications" and thought to be causally related to the investigational agent by the investigator. Drug-related thrombocytopenia is defined as events in the Standard MedDRA Query (SMQ) "Haematopoietic Thrombocytopenia narrow" and thought to be causally related to the investigational agent by the investigator.

End point type	Secondary

End point timeframe:

From baseline to approximately 7 years and 8 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 (n=10,6)	15.6	9.8		
Grade 3 or Higher Infections (n=4,11)	6.3	18.0		
Drug-related Neutropenia (n=3,2)	4.7	3.3		
Drug-related Thrombocytopenia (n=0,0)	0	0		

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[21]

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 approximately 7 years and 8 months

Notes:

[21] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: As the end point is analyzing obinutuzumab, there is nothing to report for the placebo arm.

End point values	OBINUTUZUMAB 1000MG and MMF			
Subject group type	Reporting group			
Number of subjects analysed	7			
Units: Percentage of participants				
number (not applicable)	11.11			

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 B-lymphocyte with a transmembrane protein that is encoded by the gene CD19.

9999999 = The standard deviation could not be derived from the data of 1 participant.

9999999 = No participants were analyzed.

End point type	Secondary

End point timeframe:

Baseline, Week 2, Week 4, Week 12, Week 24, Week 52, Week 104, B Cell Follow-Up (Bcfu) at months 6, 12, 18, 24, 30, 36, 42 and 48

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)		
Week 104 (n=5,2)	77.123 (± 380.111)	-76.055 (± 31.519)		
Bcfu month 6 (n=13, 5)	105.043 (± 402.281)	-73.889 (± 19.755)		
Bcfu month 12 (n=5, 2)	77.123 (± 380.111)	-76.055 (± 31.519)		
Bcfu month 18 (n=3, 1)	-83.159 (± 16.701)	-11.418 (± 9999999)		
Bcfu month 24 (n=2, 0)	-93.603 (± 8.836)	9999999 (± 9999999)		
Bcfu month 30 (n=3, 0)	-59.950 (± 50.807)	9999999 (± 9999999)		

Bcfu month 36 (n=2, 0)	-99.163 (± 0.973)	9999999 (± 9999999)		
Bcfu month 42 (n=1, 0)	-99.084 (± 9999999)	9999999 (± 9999999)		
Bcfu month 48 (n=1, 0)	-99.851 (± 99999999)	9999999 (± 9999999)		

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[22]

End point description:

End point type	Secondary

End point timeframe:

Week 0, Week 24, Week 52

Notes:

[22] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: As the end point is analyzing obinutuzumab, there is nothing to report for the placebo arm.

End point values	OBINUTUZUMAB 1000MG and MMF			
Subject group type	Reporting group			
Number of subjects analysed	63			
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: Systemic Clearance of Obinutuzumab

End point title	Systemic Clearance of Obinutuzumab[23]

End point description:

End point type	Secondary

End point timeframe:

Day 0, Week 24, Week 52

Notes:

[23] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: As the end point is analyzing obinutuzumab, there is nothing to report for the placebo arm.

End point values	OBINUTUZUMAB 1000MG and MMF			
Subject group type	Reporting group			
Number of subjects analysed	63			
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: 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[24]

End point description:

End point type	Secondary

End point timeframe:

Baseline to Week 52

Notes:

[24] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: As the end point is analyzing obinutuzumab, there is nothing to report for the placebo arm.

End point values	OBINUTUZUMAB 1000MG and MMF			
Subject group type	Reporting group			
Number of subjects analysed	63			
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: 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: Volume of Distribution Under Steady State (Vss) of Obinutuzumab

End point title	Volume of Distribution Under Steady State (Vss) of Obinutuzumab[25]

End point description:

End point type	Secondary

End point timeframe:

Day 0, Week 24, Week 52

Notes:

[25] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: As the end point is analyzing obinutuzumab, there is nothing to report for the placebo arm.

End point values	OBINUTUZUMAB 1000MG and MMF			
Subject group type	Reporting group			
Number of subjects analysed	63			
Units: Litre (L)				
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: 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

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 approximately 7 years and 8 months

Adverse event reporting additional description:

The safety population was defined as all participants who have received any amount of study medication

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	26.0

Reporting groups

Reporting group title	PLACEBO + MMF

Reporting group description:

Participants received 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 was up titrated to a target dose of 2.0 - 2.5 g/day (or equivalent). Investigators, at their discretion, could 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 could receive 1000 mg methylprednisolone IV once daily for up to 3 days to treat underlying LN clinical activity. Participants received 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 + MMF

Reporting group description:

Participants received 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 was up titrated to a target dose of 2.0 - 2.5 grams per day (g/day) (or equivalent). Investigators, at their discretion, could 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 could receive 1000 mg methylprednisolone IV once daily for up to 3 days to treat underlying LN clinical activity. Participants received 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 + MMF	OBINUTUZUMAB 1000MG + MMF	
Total subjects affected by serious adverse events			
subjects affected / exposed	18 / 61 (29.51%)	17 / 64 (26.56%)	
number of deaths (all causes)	4	1	
number of deaths resulting from adverse events	2	0	
Vascular disorders			
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	
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	
SUPERFICIAL VEIN THROMBOSIS			
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			
PYREXIA			
subjects affected / exposed	1 / 61 (1.64%)	2 / 64 (3.13%)	
occurrences causally related to treatment / all	2 / 2	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
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	
DEATH			
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	
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	
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	
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	
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			
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	
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	
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			
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	
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	
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			
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	
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	
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	
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	

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	
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	
Hepatobiliary disorders			
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	
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	
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	
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	
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	
Musculoskeletal and connective tissue disorders			
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	
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	
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	
Infections and infestations			
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	
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	

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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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	
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 + MMF	OBINUTUZUMAB 1000MG + MMF	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	39 / 61 (63.93%)	51 / 64 (79.69%)	
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	
General disorders and administration site conditions			
CHEST PAIN			
subjects affected / exposed	4 / 61 (6.56%)	0 / 64 (0.00%)	
occurrences (all)	4	0	
Blood and lymphatic system disorders			
ANAEMIA			
subjects affected / exposed	4 / 61 (6.56%)	5 / 64 (7.81%)	
occurrences (all)	6	5	
Gastrointestinal disorders			

NAUSEA			
subjects affected / exposed	3 / 61 (4.92%)	6 / 64 (9.38%)	
occurrences (all)	3	7	
DIARRHOEA			
subjects affected / exposed	5 / 61 (8.20%)	3 / 64 (4.69%)	
occurrences (all)	5	3	
ABDOMINAL PAIN			
subjects affected / exposed	3 / 61 (4.92%)	5 / 64 (7.81%)	
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			
CONJUNCTIVITIS			
subjects affected / exposed	2 / 61 (3.28%)	4 / 64 (6.25%)	
occurrences (all)	2	6	
BRONCHITIS			
subjects affected / exposed	5 / 61 (8.20%)	13 / 64 (20.31%)	
occurrences (all)	8	15	
URINARY TRACT INFECTION			
subjects affected / exposed	12 / 61 (19.67%)	14 / 64 (21.88%)	
occurrences (all)	20	19	
UPPER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	5 / 61 (8.20%)	6 / 64 (9.38%)	
occurrences (all)	6	8	
PHARYNGITIS			
subjects affected / exposed	4 / 61 (6.56%)	5 / 64 (7.81%)	
occurrences (all)	4	8	

NASOPHARYNGITIS			
subjects affected / exposed	6 / 61 (9.84%)	5 / 64 (7.81%)	
occurrences (all)	8	5	
HERPES ZOSTER			
subjects affected / exposed	6 / 61 (9.84%)	5 / 64 (7.81%)	
occurrences (all)	7	6	
GASTROENTERITIS			
subjects affected / exposed	6 / 61 (9.84%)	3 / 64 (4.69%)	
occurrences (all)	9	4	
INFLUENZA			
subjects affected / exposed	2 / 61 (3.28%)	4 / 64 (6.25%)	
occurrences (all)	3	4	

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.
18 April 2023	This protocol was amended primarily to update the details for the end of study. Personal identifiable information for the Medical Monitors was removed from this version. AE reporting for hospitalizations and the Sponsor's record retention was clarified. It was also clarified that summaries of clinical study results may be available in health authority databases for public access. A description of measures to protect personal data was included. Updates to the reporting term of "sudden death" and the handling and review of protocol deviations were also included.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

http://www.ncbi.nlm.nih.gov/pubmed/34615636

http://www.ncbi.nlm.nih.gov/pubmed/37947366