Clinical trial results:
A Randomized, Double-blind, Placebo controlled, Parallel-Group, Dose-Ranging Study to Investigate the MRI Efficacy and Safety of Six Months administration of Ofatumumab in Subjects with Relapsing-Remitting Multiple Sclerosis (RRMS)

Summary

EudraCT number	2011-002333-19
Trial protocol	DE ES NL DK CZ IT
Global end of trial date	10 June 2015

Results information

Result version number	v1
This version publication date	15 April 2016
First version publication date	15 April 2016

Trial information

Trial identification

Sponsor protocol code	OMS112831

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	GlaxoSmithKline
Sponsor organisation address	980 Great West Road, Brentford, Middlesex, United Kingdom,
Public contact	GSK Response Center, GlaxoSmithKline, 1 866-435-7343,
Scientific contact	GSK Response Center, GlaxoSmithKline, 1 866-435-7343,

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	16 September 2015
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	10 June 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To determine whether ofatumumab 3, 30 or 60 milligrams (mg) given subcutaneously (SQ), reduces the cumulative number of new T1 GdE brain lesions over a period of 12 weeks, as compared with placebo, in subjects with RRMS

Protection of trial subjects:

Only the first 12 weeks of the study were placebo-controlled, shortening the duration of the placebo-control period in this Phase II trial, lowering the potential risks associated with exposure to placebo.

All participants received pre-medication, before each subcutaneous injection of Investigational product (IP), to minimise effects of B-cell lysis.

This study did not restrict the use of rescue medications (e.g. glucocorticoids) to manage the occurrence of a relapse. However, due to the potential interference with the Magnetic resonance imaging (MRI), if a relapse requiring management with glucocorticoids occurred around the time of a scheduled MRI, the MRI was to be rescheduled to ensure that the subject has a minimum of a 1 week washout period following completion of treatment with glucocorticoids.

An Independent Data Monitoring Committee (IDMC) evaluated risks relative to benefits through review of safety and efficacy information on an ongoing basis during the study. A PML Adjudication Committee reviewed all cases of Progressive Multifocal Leukoencephalopathy(PML) and suspected PML, on an ongoing basis during the study.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	17 November 2011
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	2 Years
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Canada: 6
Country: Number of subjects enrolled	Russian Federation: 66
Country: Number of subjects enrolled	United States: 49
Country: Number of subjects enrolled	Netherlands: 6
Country: Number of subjects enrolled	Spain: 30
Country: Number of subjects enrolled	Bulgaria: 16
Country: Number of subjects enrolled	Czech Republic: 22
Country: Number of subjects enrolled	Denmark: 10

Country: Number of subjects enrolled	Germany: 24
Country: Number of subjects enrolled	Italy: 3
Worldwide total number of subjects	232
EEA total number of subjects	111

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)	232
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

A participant (par.) completes the study if he/she completes all assessments up to and including the 24 Week Follow-up Phase (Week 48) without prematurely discontinuing.

Pre-assignment

Screening details:

A total of 324 participants with Relapsing-Remitting Multiple Sclerosis (RRMS) were screened and 232 par. were randomized to the 24 Week Treatment Phase (weeks 0-12 were placebo controlled) of the study. A total of 231 par. received at least one dose of double-blind Investigational Product (IP) and were included in the Safety Population.

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, Monitor, Data analyst, Carer, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo/Ofatumumab 3 mg

Arm description:

Participants received ofatumumab matching placebo subcutaneous (SC) injection every 4 weeks (q4w) from Week 0 to Week 20, except on Week 12 participants received 3 milligrams (mg) ofatumumab SC injection. Participants also received pre-medication of acetaminophen 1 gram (g) and antihistamine (cetirizine or equivalent) 10 mg prior to administration of each SC injection of investigational product.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

1 ml Placebo doses to match the active doses using normal saline (sterile, pyrogen-free 0.9% Sodium Chloride [NaCl]) subcutaneous injection

Arm title	Ofatumumab 3 mg q12w

Arm description:

Participants received ofatumumab 3 mg SC injection every 12th week (q12w) on Week 1 and Week 12. Participants received matching placebo on Weeks 0, 4, 8, 16 and 20. Participants also received pre-medication of acetaminophen 1 g and antihistamine (cetirizine or equivalent) 10 mg prior to administration of each SC injection of investigational product.

Arm type	Experimental
Investigational medicinal product name	Ofatumumab 3 mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

0.03 milliliter (mL) Ofatumumab 100 milligrams (mg)/mL and 0.97mL sterile, pyrogen-free 0.9% NaCl subcutaneous injection

Arm title	Ofatumumab 30 mg q12w

Arm description:

Participants received ofatumumab 3 mg conditioning dose SC injection or matching placebo on Week 0 and received ofatumumab 30 mg SC injection every 12th week (q12w) on Week 1 and Week 12. Participants received matching placebo on Weeks 4, 8, 16 and 20. Participants also received pre-medication of acetaminophen 1 g and antihistamine (cetirizine or equivalent) 10 mg prior to administration of each SC injection of investigational product.

Arm type	Experimental
Investigational medicinal product name	Ofatumumab 30 mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

0.3mL Ofatumumab 100mg/mL and 0.7mL sterile, pyrogen-free 0.9% NaCl subcutaneous injection

Arm title	Ofatumumab 60 mg q12w

Arm description:

Participants received ofatumumab 3 mg conditioning dose SC injection or matching placebo on Week 0 and received ofatumumab 60 mg SC injection every 12th week (q12w) on Week 1 and Week 12. Participants received matching placebo on Weeks 4, 8, 16 and 20. Participants also received pre-medication of acetaminophen 1 g and antihistamine (cetirizine or equivalent) 10 mg prior to administration of each SC injection of investigational product.

Arm type	Experimental
Investigational medicinal product name	Ofatumumab 60 mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

0.6mL Ofatumumab 100mg/mL and 0.4mL sterile, pyrogen-free 0.9% NaCl subcutaneous injection

Arm title	Ofatumumab 60mg q4w

Arm description:

Participants received ofatumumab 3 mg conditioning dose SC injection or matching placebo on Week 0 and received ofatumumab 60 mg SC injection every 4th week (q4w) from Week 1 to Week 20. Participants also received pre-medication of acetaminophen 1 g and antihistamine (cetirizine or equivalent) 10 mg prior to administration of each SC injection of investigational product.

Arm type	Experimental
Investigational medicinal product name	Ofatumumab 60 mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

0.6mL Ofatumumab 100mg/mL and 0.4mL sterile, pyrogen-free 0.9% NaCl subcutaneous injection

Number of subjects in period 1[1]	Placebo/Ofatumumab 3 mg	Ofatumumab 3 mg q12w	Ofatumumab 30 mg q12w
Started	67	34	32
Completed to Week 12	65	31	30
Completed to Week 24	64	29	30
Completed to Week 48	63	30	30

Completed to Week IFU	11 [2]	14 [3]	12 [4]
Completed	61	28	28
Not completed	6	6	4
Physician decision	1	-	1
Consent withdrawn by subject	2	1	-
Adverse event, non-fatal	-	4	2
Protocol-defined Stopping Criteria	1	1	-
Lost to follow-up	-	-	-
Lack of efficacy	1	-	-
Protocol deviation	1	-	1

Number of subjects in period 1[1]	Ofatumumab 60 mg q12w	Ofatumumab 60mg q4w
Started	34	64
Completed to Week 12	33	60
Completed to Week 24	33	58
Completed to Week 48	32	57
Completed to Week IFU	15 [5]	36 [6]
Completed	32	56
Not completed	2	8
Physician decision	-	1
Consent withdrawn by subject	1	3
Adverse event, non-fatal	-	2
Protocol-defined Stopping Criteria	-	2
Lost to follow-up	1	-
Lack of efficacy	-	-
Protocol deviation	-	-

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: A total of 324 participants with Relapsing-Remitting Multiple Sclerosis (RRMS) were screened and 232 par. were randomized to the 24 Week Treatment Phase (weeks 0-12 were placebo controlled) of the study. A total of 231 par. received at least one dose of double-blind Investigational Product (IP) and were included in the Safety Population.

[2] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: A participant (par.) completes the study if he/she completes all assessments up to and including the 24 Week Follow-up Phase (Week 48) without prematurely discontinuing. The # of participants completing each milestone is also presented.

[3] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: A participant (par.) completes the study if he/she completes all assessments up to and including the 24 Week Follow-up Phase (Week 48) without prematurely discontinuing. The # of participants completing each milestone is also presented.

[4] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that

completed, minus those who left.

Justification: A participant (par.) completes the study if he/she completes all assessments up to and including the 24 Week Follow-up Phase (Week 48) without prematurely discontinuing. The # of participants completing each milestone is also presented.

[5] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: A participant (par.) completes the study if he/she completes all assessments up to and including the 24 Week Follow-up Phase (Week 48) without prematurely discontinuing. The # of participants completing each milestone is also presented.

[6] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: A participant (par.) completes the study if he/she completes all assessments up to and including the 24 Week Follow-up Phase (Week 48) without prematurely discontinuing. The # of participants completing each milestone is also presented.

Baseline characteristics

Reporting groups	
Reporting group title	Placebo/Ofatumumab 3 mg
Reporting group description:	
Participants received ofatumumab matching placebo subcutaneous (SC) injection every 4 weeks (q4w) from Week 0 to Week 20, except on Week 12 participants received 3 milligrams (mg) ofatumumab SC injection. Participants also received pre-medication of acetaminophen 1 gram (g) and antihistamine (cetirizine or equivalent) 10 mg prior to administration of each SC injection of investigational product.	
Reporting group title	Ofatumumab 3 mg q12w
Reporting group description:	
Participants received ofatumumab 3 mg SC injection every 12th week (q12w) on Week 1 and Week 12. Participants received matching placebo on Weeks 0, 4, 8, 16 and 20. Participants also received pre-medication of acetaminophen 1 g and antihistamine (cetirizine or equivalent) 10 mg prior to administration of each SC injection of investigational product.	
Reporting group title	Ofatumumab 30 mg q12w
Reporting group description:	
Participants received ofatumumab 3 mg conditioning dose SC injection or matching placebo on Week 0 and received ofatumumab 30 mg SC injection every 12th week (q12w) on Week 1 and Week 12. Participants received matching placebo on Weeks 4, 8, 16 and 20. Participants also received pre-medication of acetaminophen 1 g and antihistamine (cetirizine or equivalent) 10 mg prior to administration of each SC injection of investigational product.	
Reporting group title	Ofatumumab 60 mg q12w
Reporting group description:	
Participants received ofatumumab 3 mg conditioning dose SC injection or matching placebo on Week 0 and received ofatumumab 60 mg SC injection every 12th week (q12w) on Week 1 and Week 12. Participants received matching placebo on Weeks 4, 8, 16 and 20. Participants also received pre-medication of acetaminophen 1 g and antihistamine (cetirizine or equivalent) 10 mg prior to administration of each SC injection of investigational product.	
Reporting group title	Ofatumumab 60mg q4w
Reporting group description:	
Participants received ofatumumab 3 mg conditioning dose SC injection or matching placebo on Week 0 and received ofatumumab 60 mg SC injection every 4th week (q4w) from Week 1 to Week 20. Participants also received pre-medication of acetaminophen 1 g and antihistamine (cetirizine or equivalent) 10 mg prior to administration of each SC injection of investigational product.	

Reporting group values	Placebo/Ofatumumab 3 mg	Ofatumumab 3 mg q12w	Ofatumumab 30 mg q12w
Number of subjects	67	34	32
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	37.7	38.1	37.2
standard deviation	± 9.38	± 8.29	± 10.04
Gender categorical Units: Subjects			
Female	46	22	24
Male	21	12	8
Race, Customized Units: Subjects			
African American/African Heritage	1	0	0
Asian - East Asian Heritage	0	0	1

White - White/Caucasian/European Heritage	65	34	31
Mixed Race	1	0	0

Reporting group values	Ofatumumab 60 mg q12w	Ofatumumab 60mg q4w	Total
Number of subjects	34	64	231
Age categorical			
Units: Subjects			
Age continuous			
Units: years			
arithmetic mean	37.3	36.2	
standard deviation	± 9.67	± 9.57	-
Gender categorical			
Units: Subjects			
Female	22	41	155
Male	12	23	76
Race, Customized			
Units: Subjects			
African American/African Heritage	0	1	2
Asian - East Asian Heritage	0	0	1
White - White/Caucasian/European Heritage	34	61	225
Mixed Race	0	2	3

End points

End points reporting groups

Reporting group title	Placebo/Ofatumumab 3 mg

Reporting group description:

Participants received ofatumumab matching placebo subcutaneous (SC) injection every 4 weeks (q4w) from Week 0 to Week 20, except on Week 12 participants received 3 milligrams (mg) ofatumumab SC injection. Participants also received pre-medication of acetaminophen 1 gram (g) and antihistamine (cetirizine or equivalent) 10 mg prior to administration of each SC injection of investigational product.

Reporting group title	Ofatumumab 3 mg q12w

Reporting group description:

Participants received ofatumumab 3 mg SC injection every 12th week (q12w) on Week 1 and Week 12. Participants received matching placebo on Weeks 0, 4, 8, 16 and 20. Participants also received pre-medication of acetaminophen 1 g and antihistamine (cetirizine or equivalent) 10 mg prior to administration of each SC injection of investigational product.

Reporting group title	Ofatumumab 30 mg q12w

Reporting group description:

Participants received ofatumumab 3 mg conditioning dose SC injection or matching placebo on Week 0 and received ofatumumab 30 mg SC injection every 12th week (q12w) on Week 1 and Week 12. Participants received matching placebo on Weeks 4, 8, 16 and 20. Participants also received pre-medication of acetaminophen 1 g and antihistamine (cetirizine or equivalent) 10 mg prior to administration of each SC injection of investigational product.

Reporting group title	Ofatumumab 60 mg q12w

Reporting group description:

Participants received ofatumumab 3 mg conditioning dose SC injection or matching placebo on Week 0 and received ofatumumab 60 mg SC injection every 12th week (q12w) on Week 1 and Week 12. Participants received matching placebo on Weeks 4, 8, 16 and 20. Participants also received pre-medication of acetaminophen 1 g and antihistamine (cetirizine or equivalent) 10 mg prior to administration of each SC injection of investigational product.

Reporting group title	Ofatumumab 60mg q4w

Reporting group description:

Participants received ofatumumab 3 mg conditioning dose SC injection or matching placebo on Week 0 and received ofatumumab 60 mg SC injection every 4th week (q4w) from Week 1 to Week 20. Participants also received pre-medication of acetaminophen 1 g and antihistamine (cetirizine or equivalent) 10 mg prior to administration of each SC injection of investigational product.

Primary: Cumulative number of new gadolinium-enhancing T1 lesions at Week 12

End point title	Cumulative number of new gadolinium-enhancing T1 lesions at Week 12

End point description:

The cumulative number of new gadolinium-enhancing (GdE) T1 lesion at Week 12 were analyzed from screen based on magnetic resonance imaging (MRI) brain scans at Weeks 4, 8, and 12. The endpoint was analyzed using an Emax model adjusting for the presence/absence of GdE lesions on the Screening MRI and assuming the number of new lesions followed a negative binomial distribution. Dose was fitted as a continuous variable. The number of scans contributing to the cumulative number of lesions was fitted as an offset. Estimates of the rate of cumulative number of new gadolinium-enhancing lesions per scan at Week 12 were determined from the model. The all evaluable scans (AES) dataset was used which included all evaluable on-treatment MRI scans for each participant analysed. Intent-to-Treat (ITT) Population: all randomized participants who received at least one dose of investigational produce and who had at least one post screen MRI assessment.

End point type	Primary

End point timeframe:

Week 12

End point values	Placebo/Ofatumumab 3 mg	Ofatumumab 3 mg q12w	Ofatumumab 30 mg q12w	Ofatumumab 60 mg q12w
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	67[1]	33[2]	30[3]	33[4]
Units: Cumulative number of lesions				
arithmetic mean (standard deviation)	4.2 (± 7.57)	1.7 (± 3.29)	2.2 (± 3.41)	2.2 (± 3.7)

Notes:

[1] - ITT Population. Only those participants available at the specified time points were analyzed.

[2] - ITT Population. Only those participants available at the specified time points were analyzed.

[3] - ITT Population. Only those participants available at the specified time points were analyzed.

[4] - ITT Population. Only those participants available at the specified time points were analyzed.

End point values	Ofatumumab 60mg q4w			
Subject group type	Reporting group			
Number of subjects analysed	63[5]			
Units: Cumulative number of lesions				
arithmetic mean (standard deviation)	1.2 (± 2.83)			

Notes:

[5] - ITT Population. Only those participants available at the specified time points were analyzed.

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	Placebo/Ofatumumab 3 mg v Ofatumumab 3 mg q12w
Number of subjects included in analysis	100
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Non-Linear Emax Model
Parameter estimate	Ratio
Point estimate	0.35
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.221
upper limit	0.548

Statistical analysis title	Statistical analysis 2
Comparison groups	Placebo/Ofatumumab 3 mg v Ofatumumab 30 mg q12w

Number of subjects included in analysis	97
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Non-Linear Emax Model
Parameter estimate	Ratio
Point estimate	0.35
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.221
upper limit	0.548

Statistical analysis title	Statistical analysis 3
Comparison groups	Placebo/Ofatumumab 3 mg v Ofatumumab 60 mg q12w
Number of subjects included in analysis	100
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Non-Linear Emax Model
Parameter estimate	Ratio
Point estimate	0.35
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.221
upper limit	0.548

Statistical analysis title	Statistical analysis 4
Comparison groups	Placebo/Ofatumumab 3 mg v Ofatumumab 60mg q4w
Number of subjects included in analysis	130
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Non-Linear Emax Model
Parameter estimate	Ratio
Point estimate	0.35
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.221
upper limit	0.548

Secondary: Cumulative number of new gadolinium-enhancing T1 lesions at Week 24

End point title	Cumulative number of new gadolinium-enhancing T1 lesions at Week 24

End point description:

The cumulative number of new GdE T1 lesion at Week 24 were analyzed from screen based on MRI brain scans at Weeks 4, 8, 12, 16, 20 and 24. The endpoint was analyzed using a generalized linear model assuming an underlying negative binomial distribution with a log-link function, adjusted for treatment and presence/absence of GdE lesions on the Screening MRI. Treatment group was fitted as a categorical variable. The number of scans contributing to the cumulative number of lesions was fitted as an offset. Estimates of the rate of cumulative number of new GdE T1 lesions per scan at Week 24 were determined from the model. The AES dataset was used which included all evaluable on-treatment MRI scans for each participant analyzed. Pairwise comparisons were conducted for each group compared to placebo.

End point type	Secondary

End point timeframe:

Week 24

End point values	Placebo/Ofatumumab 3 mg	Ofatumumab 3 mg q12w	Ofatumumab 30 mg q12w	Ofatumumab 60 mg q12w
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	67[6]	33[7]	30[8]	33[9]
Units: Cumulative number of lesions				
arithmetic mean (standard deviation)	5.6 (± 9.34)	2.2 (± 3.8)	2.5 (± 3.88)	2.2 (± 3.83)

Notes:

[6] - ITT Population. Only those participants available at the specified time points were analyzed.

[7] - ITT Population. Only those participants available at the specified time points were analyzed.

[8] - ITT Population. Only those participants available at the specified time points were analyzed.

[9] - ITT Population. Only those participants available at the specified time points were analyzed.

End point values	Ofatumumab 60mg q4w			
Subject group type	Reporting group			
Number of subjects analysed	63[10]			
Units: Cumulative number of lesions				
arithmetic mean (standard deviation)	1.4 (± 3.04)			

Notes:

[10] - ITT Population. Only those participants available at the specified time points were analyzed.

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	Placebo/Ofatumumab 3 mg v Ofatumumab 3 mg q12w
Number of subjects included in analysis	100
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.003
Method	General Linear Model
Parameter estimate	Ratio
Point estimate	0.38

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.2
upper limit	0.72

Statistical analysis title	Statistical analysis 2
Comparison groups	Placebo/Ofatumumab 3 mg v Ofatumumab 30 mg q12w
Number of subjects included in analysis	97
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.003
Method	General Linear Model
Parameter estimate	Ratio
Point estimate	0.38
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.2
upper limit	0.72

Statistical analysis title	Statistical analysis 3
Comparison groups	Placebo/Ofatumumab 3 mg v Ofatumumab 60 mg q12w
Number of subjects included in analysis	100
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.001
Method	General Linear Model
Parameter estimate	Ratio
Point estimate	0.35
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.19
upper limit	0.65

Statistical analysis title	Statistical analysis 4
Comparison groups	Placebo/Ofatumumab 3 mg v Ofatumumab 60mg q4w

Number of subjects included in analysis	130
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	General Linear Model
Parameter estimate	Ratio
Point estimate	0.23
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.13
upper limit	0.39

Secondary: Change from Baseline in brain volume at Week 24 and Week 48

End point title	Change from Baseline in brain volume at Week 24 and Week 48

End point description:

Brain volume is a measure of brain size determined by a MRI scan. Baseline is defined as the participant's last available assessment prior to initiation of IP (i.e. Screening). Change from Baseline was calculated by subtracting the Baseline value from the post-Baseline value. These are summary statistics only and no statistical analysis was performed on this endpoint. Only those participants available at the specified time points were analyzed (represented by n=X in the category titles).

End point type	Secondary

End point timeframe:

Baseline, Week 24 and Week 48

End point values	Placebo/Ofatumumab 3 mg	Ofatumumab 3 mg q12w	Ofatumumab 30 mg q12w	Ofatumumab 60 mg q12w
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	67[11]	33[12]	32[13]	33[14]
Units: Cubic centimeters				
arithmetic mean (standard deviation)				
Week 24, n=25, 12, 16, 12, 22	-13.5 (± 26.96)	-7.2 (± 22.26)	-8.4 (± 26.62)	-13.3 (± 34.02)
Week 48, n=28, 12, 16, 11, 19	-22 (± 38.22)	-12.9 (± 14.55)	-5 (± 28.84)	-7.3 (± 29.16)

Notes:

[11] - ITT Population

[12] - ITT Population

[13] - ITT Population

[14] - ITT Population

End point values	Ofatumumab 60mg q4w			
Subject group type	Reporting group			
Number of subjects analysed	63[15]			
Units: Cubic centimeters				
arithmetic mean (standard deviation)				
Week 24, n=25, 12, 16, 12, 22	-1.4 (± 56.42)			

Week 48, n=28, 12, 16, 11, 19	-11.8 (± 55.3)			

Notes:

[15] - ITT Population

Statistical analyses

No statistical analyses for this end point

Secondary: Cumulative number of persistent gadolinium-enhancing brain lesions on T1-weighted MRI at Week 12

End point title	Cumulative number of persistent gadolinium-enhancing brain lesions on T1-weighted MRI at Week 12

End point description:

The cumulative number of persistent GdE T1 lesions at Week 12 were analyzed from screen based on MRI scans at Weeks 4, 8, and 12. These are summary statistics only and no statistical analysis was performed on this endpoint. The AES dataset was used which included all evaluable on-treatment MRI scans for each participant analyzed.

End point type	Secondary

End point timeframe:

Week 12

End point values	Placebo/Ofatumumab 3 mg	Ofatumumab 3 mg q12w	Ofatumumab 30 mg q12w	Ofatumumab 60 mg q12w
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	67[16]	34[17]	30[18]	33[19]
Units: Number of lesions per scan				
arithmetic mean (standard deviation)	3.2 (± 7.41)	1.2 (± 1.94)	2.3 (± 3.94)	1.8 (± 3.31)

Notes:

[16] - ITT Population. Only those participants available at the specified time points were analyzed.

[17] - ITT Population. Only those participants available at the specified time points were analyzed.

[18] - ITT Population. Only those participants available at the specified time points were analyzed.

[19] - ITT Population. Only those participants available at the specified time points were analyzed.

End point values	Ofatumumab 60mg q4w			
Subject group type	Reporting group			
Number of subjects analysed	63[20]			
Units: Number of lesions per scan				
arithmetic mean (standard deviation)	1.8 (± 4.81)			

Notes:

[20] - ITT Population. Only those participants available at the specified time points were analyzed.

Statistical analyses

No statistical analyses for this end point

Secondary: Cumulative number of all (new plus persistent) gadolinium-enhancing brain lesions on T1-weighted MRI at Week 12

End point title	Cumulative number of all (new plus persistent) gadolinium-enhancing brain lesions on T1-weighted MRI at Week 12

End point description:

The cumulative number of all (new plus persistent) GdE T1 lesion at Week 12 were analyzed from screen based on MRI brain scans at Weeks 4, 8 and 12. The endpoint was analyzed using a generalized linear model assuming an underlying negative binomial distribution with a log-link function, adjusted for treatment and presence/absence of GdE lesions on the Screening MRI. Treatment group was fitted as a categorical variable. The number of scans contributing to the cumulative number of lesions was fitted as an offset. Estimates of the rate of cumulative number of all (new plus persistent) GdE T1 lesions per scan at Week 12 were determined from the model. The AES dataset was used which included all evaluable on-treatment MRI scans for each participant analyzed. Pairwise comparisons were conducted for each group compared to placebo.

End point type	Secondary

End point timeframe:

Week 12

End point values	Placebo/Ofatumumab 3 mg	Ofatumumab 3 mg q12w	Ofatumumab 30 mg q12w	Ofatumumab 60 mg q12w
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	67[21]	33[22]	30[23]	33[24]
Units: Cumulative number of lesions				
arithmetic mean (standard deviation)	7.4 (± 13.9)	2.9 (± 4.62)	4.5 (± 7.09)	4 (± 6.7)

Notes:

[21] - ITT Population. Only those participants available at the specified time points were analyzed.

[22] - ITT Population. Only those participants available at the specified time points were analyzed.

[23] - ITT Population. Only those participants available at the specified time points were analyzed.

[24] - ITT Population. Only those participants available at the specified time points were analyzed.

End point values	Ofatumumab 60mg q4w			
Subject group type	Reporting group			
Number of subjects analysed	63[25]			
Units: Cumulative number of lesions				
arithmetic mean (standard deviation)	3.1 (± 6.82)			

Notes:

[25] - ITT Population. Only those participants available at the specified time points were analyzed.

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	Placebo/Ofatumumab 3 mg v Ofatumumab 3 mg q12w
Number of subjects included in analysis	100
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	General Linear Model
Parameter estimate	Ratio
Point estimate	0.31

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.16
upper limit	0.6

Statistical analysis title	Statistical analysis 2
Comparison groups	Placebo/Ofatumumab 3 mg v Ofatumumab 30 mg q12w
Number of subjects included in analysis	97
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.075
Method	General Linear Model
Parameter estimate	Ratio
Point estimate	0.56
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.29
upper limit	1.06

Statistical analysis title	Statistical analysis 3
Comparison groups	Placebo/Ofatumumab 3 mg v Ofatumumab 60 mg q12w
Number of subjects included in analysis	100
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.035
Method	General Linear Model
Parameter estimate	Ratio
Point estimate	0.51
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.27
upper limit	0.95

Statistical analysis title	Statistical analysis 4
Comparison groups	Placebo/Ofatumumab 3 mg v Ofatumumab 60mg q4w

Number of subjects included in analysis	130
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	General Linear Model
Parameter estimate	Ratio
Point estimate	0.32
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.19
upper limit	0.55

Secondary: Total volume of new gadolinium-enhancing brain lesions on T1-weighted MRI at Week 12

End point title	Total volume of new gadolinium-enhancing brain lesions on T1-weighted MRI at Week 12

End point description:

Lesion volume is a measure of lesion size determined by a MRI brain scan. The cumulative volume of new GdE T1 lesions at Week 12 were analyzed from screen based on MRI brain scans at Weeks 4, 8 and 12. The endpoint was analyzed using a generalized linear model assuming an underlying negative binomial distribution with a log-link function, adjusted for treatment and presence/absence of GdE lesions on the Screening MRI. Treatment group was fitted as a categorical variable. The number of scans contributing to the cumulative volume of lesions was fitted as an offset. Estimates of the rate of cumulative volume of new GdE T1 lesions per scan at Week 12 were determined from the model. The AES dataset was used which included all evaluable on-treatment MRI scans for each participant analyzed. Pairwise comparisons were conducted for each group compared to placebo.

End point type	Secondary

End point timeframe:

Week 12

End point values	Placebo/Ofatumumab 3 mg	Ofatumumab 3 mg q12w	Ofatumumab 30 mg q12w	Ofatumumab 60 mg q12w
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	67[26]	34[27]	30[28]	33[29]
Units: Cubic millimeter (mm^3)				
arithmetic mean (standard deviation)	607.5 (± 1090.89)	226.5 (± 449.37)	452.9 (± 682.33)	248.6 (± 457.62)

Notes:

[26] - ITT Population. Only those participants available at the specified time points were analyzed.

[27] - ITT Population. Only those participants available at the specified time points were analyzed.

[28] - ITT Population. Only those participants available at the specified time points were analyzed.

[29] - ITT Population. Only those participants available at the specified time points were analyzed.

End point values	Ofatumumab 60mg q4w			
Subject group type	Reporting group			
Number of subjects analysed	63[30]			
Units: Cubic millimeter (mm^3)				
arithmetic mean (standard deviation)	146.6 (±			

	304.89)

Notes:
[30] - ITT Population. Only those participants available at the specified time points were analyzed.

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	Ofatumumab 3 mg q12w v Placebo/Ofatumumab 3 mg
Number of subjects included in analysis	101
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.026
Method	General Linear Model
Parameter estimate	Ratio
Point estimate	0.22
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.06
upper limit	0.84

Statistical analysis title	Statstical analysis 2
Comparison groups	Placebo/Ofatumumab 3 mg v Ofatumumab 30 mg q12w
Number of subjects included in analysis	97
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.296
Method	General Linear Model
Parameter estimate	Ratio
Point estimate	0.49
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.13
upper limit	1.86

Statistical analysis title	Statistical analysis 3
Comparison groups	Placebo/Ofatumumab 3 mg v Ofatumumab 60 mg q12w

Number of subjects included in analysis	100
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.285
Method	General Linear Model
Parameter estimate	Ratio
Point estimate	0.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.14
upper limit	1.78

Statistical analysis title	Statistical analysis 4
Comparison groups	Placebo/Ofatumumab 3 mg v Ofatumumab 60mg q4w
Number of subjects included in analysis	130
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.009
Method	Non-Linear Emax Model
Parameter estimate	Ratio
Point estimate	0.25
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.09
upper limit	0.71

Secondary: Total volume of all (new and persistent) gadolinium-enhancing brain lesions on T1-weighted MRI at Week 12

End point title	Total volume of all (new and persistent) gadolinium-enhancing brain lesions on T1-weighted MRI at Week 12

End point description:

Lesion volume is a measure of lesion size determined by a MRI brain scan. The cumulative volume of all (new and persistent) GdE T1 lesions at Week 12 were analyzed from screen based on MRI brain scans at Weeks 4, 8 and 12. The endpoint was analyzed using a generalized linear model assuming an underlying negative binomial distribution with a log-link function, adjusted for treatment and presence/absence of GdE lesions on the Screening MRI. Treatment group was fitted as a categorical variable. The number of scans contributing to the cumulative volume of lesions was fitted as an offset. Estimates of the rate of cumulative volume of all (new and persistent) GdE T1 lesions per scan at Week 12 were determined from the model. The AES dataset was used which included all evaluable on-treatment MRI scans for each participant analyzed. Pairwise comparisons were conducted for each group compared to placebo.

End point type	Secondary

End point timeframe:

Week 12

End point values	Placebo/Ofatumumab 3 mg	Ofatumumab 3 mg q12w	Ofatumumab 30 mg q12w	Ofatumumab 60 mg q12w
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	67[31]	33[32]	30[33]	33[34]
Units: mm^3				
arithmetic mean (standard deviation)	1039.6 (± 1809.97)	386.2 (± 628.41)	886.2 (± 1637.47)	426.5 (± 679.44)

Notes:

[31] - ITT Population. Only those participants available at the specified time points were analyzed.

[32] - ITT Population. Only those participants available at the specified time points were analyzed.

[33] - ITT Population. Only those participants available at the specified time points were analyzed.

[34] - ITT Population. Only those participants available at the specified time points were analyzed.

End point values	Ofatumumab 60mg q4w			
Subject group type	Reporting group			
Number of subjects analysed	63[35]			
Units: mm^3				
arithmetic mean (standard deviation)	344.4 (± 735.57)			

Notes:

[35] - ITT Population. Only those participants available at the specified time points were analyzed.

Statistical analyses

Statistical analysis title	Statistical analysis
Comparison groups	Placebo/Ofatumumab 3 mg v Ofatumumab 3 mg q12w
Number of subjects included in analysis	100
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.004
Method	General Linear Model
Parameter estimate	Ratio
Point estimate	0.18
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.05
upper limit	0.58

Statistical analysis title	Statistical analysis
Comparison groups	Placebo/Ofatumumab 3 mg v Ofatumumab 30 mg q12w
Number of subjects included in analysis	97
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.248
Method	General Linear Model
Parameter estimate	Ratio
Point estimate	0.5

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.15
upper limit	1.63

Statistical analysis title	Statistical analysis 3
Comparison groups	Placebo/Ofatumumab 3 mg v Ofatumumab 60 mg q12w
Number of subjects included in analysis	100
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.181
Method	General Linear Model
Parameter estimate	Ratio
Point estimate	0.46
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.15
upper limit	1.43

Statistical analysis title	Statistical analysis 4
Comparison groups	Ofatumumab 60mg q4w v Placebo/Ofatumumab 3 mg
Number of subjects included in analysis	130
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.003
Method	General Linear Model
Parameter estimate	Ratio
Point estimate	0.24
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.1
upper limit	0.62

Secondary: Cumulative number of new and newly enlarging gadolinium-enhancing T2 lesions at Week 12

End point title	Cumulative number of new and newly enlarging gadolinium-enhancing T2 lesions at Week 12

End point description:

The cumulative number of new and newly enlarging GdE T2 lesions (NET2L) at Week 12 were analyzed from screen based on MRI brain scans at Weeks 4, 8 and 12. The endpoint was analyzed using a generalized linear model assuming an underlying negative binomial distribution with a log-link function, adjusted for treatment and presence/absence of GdE lesions on the Screening MRI. Treatment group

was fitted as a categorical variable. The number of scans contributing to the cumulative number of lesions was fitted as an offset. Estimates of the rate of cumulative number of NET2L per scan at Week 12 were determined from the model. The AES dataset was used which included all evaluable on-treatment MRI scans for each participant analyzed. Pairwise comparisons were conducted for each group compared to placebo

End point type	Secondary

End point timeframe:

Week 12

End point values	Placebo/Ofatumumab 3 mg	Ofatumumab 3 mg q12w	Ofatumumab 30 mg q12w	Ofatumumab 60 mg q12w
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	67[36]	33[37]	30[38]	33[39]
Units: Cumulative number of lesions				
arithmetic mean (standard deviation)	3.7 (± 6.72)	1.2 (± 2.38)	1.6 (± 2.79)	1.7 (± 2.67)

Notes:

[36] - ITT Population. Only those participants available at the specified time points were analyzed.

[37] - ITT Population. Only those participants available at the specified time points were analyzed.

[38] - ITT Population. Only those participants available at the specified time points were analyzed.

[39] - ITT Population. Only those participants available at the specified time points were analyzed.

End point values	Ofatumumab 60mg q4w			
Subject group type	Reporting group			
Number of subjects analysed	63[40]			
Units: Cumulative number of lesions				
arithmetic mean (standard deviation)	0.8 (± 1.55)			

Notes:

[40] - ITT Population. Only those participants available at the specified time points were analyzed.

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	Ofatumumab 3 mg q12w v Placebo/Ofatumumab 3 mg
Number of subjects included in analysis	100
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	General Linear Model
Parameter estimate	Ratio
Point estimate	0.29
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.15
upper limit	0.58

Statistical analysis title	Statistical analysis 2

Comparison groups	Placebo/Ofatumumab 3 mg v Ofatumumab 30 mg q12w
Number of subjects included in analysis	97
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.002
Method	General Linear Model
Parameter estimate	Ratio
Point estimate	0.34
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.17
upper limit	0.68

Statistical analysis title	Statistical analysis 3
Comparison groups	Placebo/Ofatumumab 3 mg v Ofatumumab 60 mg q12w
Number of subjects included in analysis	100
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.006
Method	General Linear Model
Parameter estimate	Ratio
Point estimate	0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.21
upper limit	0.77

Statistical analysis title	Statistical analysis 4
Comparison groups	Placebo/Ofatumumab 3 mg v Ofatumumab 60mg q4w
Number of subjects included in analysis	130
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	General Linear Model
Parameter estimate	Ratio
Point estimate	0.19
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.11
upper limit	0.35

Secondary: Total volume of new and/or newly enlarging T2 lesions at Week 12

End point title	Total volume of new and/or newly enlarging T2 lesions at Week 12

End point description:

Lesion volume is a measure of lesion size determined by a MRI brain scan. T2 lesions, are indicative of brain myelin content.The cumulative volume of new and/or newly enlarging T2 lesions at Week 12 were analyzed from screen based on MRI brain scans at Weeks 4, 8, and 12. The AES dataset was used which included all evaluable on-treatment MRI scans for each participant.

End point type	Secondary

End point timeframe:

Week 12

End point values	Placebo/Ofatumumab 3 mg	Ofatumumab 3 mg q12w	Ofatumumab 30 mg q12w	Ofatumumab 60 mg q12w
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	67[41]	34[42]	30[43]	33[44]
Units: mm^3				
arithmetic mean (standard deviation)	1204.5 (± 3426.79)	279.9 (± 695.75)	611.3 (± 1042.06)	293.8 (± 576.35)

Notes:

[41] - ITT Population. Only those participants available at the specified time points were analyzed.

[42] - ITT Population. Only those participants available at the specified time points were analyzed.

[43] - ITT Population. Only those participants available at the specified time points were analyzed.

[44] - ITT Population. Only those participants available at the specified time points were analyzed.

End point values	Ofatumumab 60mg q4w			
Subject group type	Reporting group			
Number of subjects analysed	63[45]			
Units: mm^3				
arithmetic mean (standard deviation)	167.9 (± 450.65)			

Notes:

[45] - ITT Population. Only those participants available at the specified time points were analyzed.

Statistical analyses

No statistical analyses for this end point

Secondary: Cumulative number of new T1 hypointense lesions at Week 24 and Week 48

End point title	Cumulative number of new T1 hypointense lesions at Week 24 and Week 48

End point description:

The cumulative number of new T1 hypointense lesions at week 24 were analyzed from screen based on MRI brain scans at Weeks 4, 8, 12, 16, 20 and 24. The AES dataset was used which included all evaluable on-treatment MRI scans for each participant. Only those participants available at the specified time points were analyzed (represented by n=X in the category titles).

End point type	Secondary

End point timeframe:

Week 24 and Week 48

End point values	Placebo/Ofatumumab 3 mg	Ofatumumab 3 mg q12w	Ofatumumab 30 mg q12w	Ofatumumab 60 mg q12w
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	67[46]	34[47]	32[48]	33[49]
Units: Number of lesions				
arithmetic mean (standard deviation)				
Week 24, n=67, 34, 30, 33, 63	0.4 (± 0.96)	0.4 (± 1.26)	0.5 (± 1.01)	0.5 (± 1.12)
Week 48, n=67, 34, 32, 33, 63	0.6 (± 1.27)	0.5 (± 1.26)	0.5 (± 0.98)	0.6 (± 1.25)

Notes:

[46] - ITT Population

[47] - ITT Population

[48] - ITT Population

[49] - ITT Population

End point values	Ofatumumab 60mg q4w			
Subject group type	Reporting group			
Number of subjects analysed	63[50]			
Units: Number of lesions				
arithmetic mean (standard deviation)				
Week 24, n=67, 34, 30, 33, 63	0.3 (± 0.78)			
Week 48, n=67, 34, 32, 33, 63	0.3 (± 0.96)			

Notes:

[50] - ITT Population

Statistical analyses

No statistical analyses for this end point

Secondary: Cumulative volume of new T1 hypointense lesions at Week 24 and Week 48

End point title	Cumulative volume of new T1 hypointense lesions at Week 24 and Week 48

End point description:

Lesion volume is a measure of lesion size determined by a MRI brain scan. Baseline is defined as the participant's last available assessment prior to initiation of IP. Change from Baseline was calculated by subtracting the Baseline value from the post-Baseline value. The AES dataset was used which included all evaluable on-treatment MRI scans for each participant. Only those participants available at the specified time points were analyzed (represented by n=X in the category titles).

End point type	Secondary

End point timeframe:

Baseline, Week 24 and Week 48

End point values	Placebo/Ofatumumab 3 mg	Ofatumumab 3 mg q12w	Ofatumumab 30 mg q12w	Ofatumumab 60 mg q12w
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	67[51]	34[52]	32[53]	33[54]
Units: mm^3				
arithmetic mean (standard deviation)				
Week 24, n=67, 34, 30, 33, 63	86.9 (± 240.4)	43.1 (± 131.96)	67.4 (± 147)	65 (± 139.14)
Week 48, n=67, 34, 32, 33, 63	113.6 (± 270.89)	54.2 (± 137.74)	63.2 (± 143.14)	116.3 (± 370.35)

Notes:

[51] - ITT Population

[52] - ITT Population

[53] - ITT Population

[54] - ITT Population

End point values	Ofatumumab 60mg q4w			
Subject group type	Reporting group			
Number of subjects analysed	63[55]			
Units: mm^3				
arithmetic mean (standard deviation)				
Week 24, n=67, 34, 30, 33, 63	42.9 (± 140.93)			
Week 48, n=67, 34, 32, 33, 63	53.2 (± 173.62)			

Notes:

[55] - ITT Population

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

On treatment serious adverse events (SAEs) and non-serious adverse events (AEs) were collected from the start of administration of the study drug until the follow-up contact (up to Week 24).

Adverse event reporting additional description:

SAEs and non-serious AEs were reported for members of the safety population, comprised of all participants who were randomized to treatment, and received at least one dose of study medication.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	16.0

Reporting groups

Reporting group title	Placebo/Ofatumumab 3 mg

Reporting group description:

Participants received ofatumumab matching placebo subcutaneous (SC) injection every 4 weeks (q4w) from Week 0 to Week 20, except on Week 12 participants received 3 milligrams (mg) ofatumumab SC injection. Participants also received pre-medication of acetaminophen 1 gram (g) and antihistamine (cetirizine or equivalent) 10 mg prior to administration of each SC injection of investigational product.

Reporting group title	Ofatumumab 3 mg q12w

Reporting group description:

Participants received ofatumumab 3 mg SC injection every 12th week (q12w) on Week 1 and Week 12. Participants received matching placebo on Weeks 0, 4, 8, 16 and 20. Participants also received pre-medication of acetaminophen 1 g and antihistamine (cetirizine or equivalent) 10 mg prior to administration of each SC injection of investigational product.

Reporting group title	Ofatumumab 30 mg q12w

Reporting group description:

Participants received ofatumumab 3 mg conditioning dose SC injection or matching placebo on Week 0 and received ofatumumab 30 mg SC injection every 12th week (q12w) on Week 1 and Week 12. Participants received matching placebo on Weeks 4, 8, 16 and 20. Participants also received pre-medication of acetaminophen 1 g and antihistamine (cetirizine or equivalent) 10 mg prior to administration of each SC injection of investigational product.

Reporting group title	Ofatumumab 60 mg q12w

Reporting group description:

Participants received ofatumumab 3 mg conditioning dose SC injection or matching placebo on Week 0 and received ofatumumab 60 mg SC injection every 12th week (q12w) on Week 1 and Week 12. Participants received matching placebo on Weeks 4, 8, 16 and 20. Participants also received pre-medication of acetaminophen 1 g and antihistamine (cetirizine or equivalent) 10 mg prior to administration of each SC injection of investigational product.

Reporting group title	Ofatumumab 60mg q4w

Reporting group description:

Participants received ofatumumab 3 mg conditioning dose SC injection or matching placebo on Week 0 and received ofatumumab 60 mg SC injection every 4th week (q4w) from Week 1 to Week 20. Participants also received pre-medication of acetaminophen 1 g and antihistamine (cetirizine or equivalent) 10 mg prior to administration of each SC injection of investigational product.

Serious adverse events	Placebo/Ofatumumab 3 mg	Ofatumumab 3 mg q12w	Ofatumumab 30 mg q12w
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 67 (0.00%)	1 / 34 (2.94%)	0 / 32 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from			

adverse events			
Injury, poisoning and procedural complications			
Injection related reaction			
subjects affected / exposed	0 / 67 (0.00%)	0 / 34 (0.00%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Cytokine release syndrome			
subjects affected / exposed	0 / 67 (0.00%)	0 / 34 (0.00%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	0 / 67 (0.00%)	0 / 34 (0.00%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Angioedema			
subjects affected / exposed	0 / 67 (0.00%)	1 / 34 (2.94%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urticaria			
subjects affected / exposed	0 / 67 (0.00%)	1 / 34 (2.94%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Hypokalaemia			
subjects affected / exposed	0 / 67 (0.00%)	0 / 34 (0.00%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Ofatumumab 60 mg q12w	Ofatumumab 60mg q4w	
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 34 (2.94%)	4 / 64 (6.25%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			

Injury, poisoning and procedural complications			
Injection related reaction			
subjects affected / exposed	0 / 34 (0.00%)	2 / 64 (3.13%)	
occurrences causally related to treatment / all	0 / 0	4 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Cytokine release syndrome			
subjects affected / exposed	1 / 34 (2.94%)	0 / 64 (0.00%)	
occurrences causally related to treatment / all	3 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	0 / 34 (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			
Angioedema			
subjects affected / exposed	0 / 34 (0.00%)	0 / 64 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urticaria			
subjects affected / exposed	0 / 34 (0.00%)	0 / 64 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Hypokalaemia			
subjects affected / exposed	0 / 34 (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	

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

Non-serious adverse events	Placebo/Ofatumumab 3 mg	Ofatumumab 3 mg q12w	Ofatumumab 30 mg q12w
Total subjects affected by non-serious adverse events			
subjects affected / exposed	41 / 67 (61.19%)	20 / 34 (58.82%)	23 / 32 (71.88%)
Investigations			
Reticulocyte count decreased			
subjects affected / exposed	1 / 67 (1.49%)	0 / 34 (0.00%)	2 / 32 (6.25%)
occurrences (all)	1	0	2
Blood immunoglobulin G decreased			
subjects affected / exposed	0 / 67 (0.00%)	2 / 34 (5.88%)	0 / 32 (0.00%)
occurrences (all)	0	2	0
Weight decreased			
subjects affected / exposed	0 / 67 (0.00%)	0 / 34 (0.00%)	2 / 32 (6.25%)
occurrences (all)	0	0	2
Injury, poisoning and procedural complications			
Injection related reaction			
subjects affected / exposed	18 / 67 (26.87%)	16 / 34 (47.06%)	13 / 32 (40.63%)
occurrences (all)	41	49	28
Fall			
subjects affected / exposed	0 / 67 (0.00%)	2 / 34 (5.88%)	1 / 32 (3.13%)
occurrences (all)	0	2	1
Nervous system disorders			
Headache			
subjects affected / exposed	7 / 67 (10.45%)	2 / 34 (5.88%)	2 / 32 (6.25%)
occurrences (all)	11	2	2
Dizziness			
subjects affected / exposed	0 / 67 (0.00%)	0 / 34 (0.00%)	1 / 32 (3.13%)
occurrences (all)	0	0	2
Neuralgia			
subjects affected / exposed	0 / 67 (0.00%)	0 / 34 (0.00%)	2 / 32 (6.25%)
occurrences (all)	0	0	2
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	8 / 67 (11.94%)	0 / 34 (0.00%)	3 / 32 (9.38%)
occurrences (all)	9	0	3
Pyrexia			

subjects affected / exposed	2 / 67 (2.99%)	2 / 34 (5.88%)	2 / 32 (6.25%)
occurrences (all)	2	2	3
Injection site pain			
subjects affected / exposed	0 / 67 (0.00%)	2 / 34 (5.88%)	0 / 32 (0.00%)
occurrences (all)	0	2	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 67 (1.49%)	2 / 34 (5.88%)	0 / 32 (0.00%)
occurrences (all)	1	2	0
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	4 / 67 (5.97%)	0 / 34 (0.00%)	1 / 32 (3.13%)
occurrences (all)	4	0	1
Diarrhoea			
subjects affected / exposed	4 / 67 (5.97%)	0 / 34 (0.00%)	0 / 32 (0.00%)
occurrences (all)	5	0	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	2 / 67 (2.99%)	2 / 34 (5.88%)	1 / 32 (3.13%)
occurrences (all)	2	2	2
Skin and subcutaneous tissue disorders			
Ecchymosis			
subjects affected / exposed	0 / 67 (0.00%)	2 / 34 (5.88%)	0 / 32 (0.00%)
occurrences (all)	0	2	0
Psychiatric disorders			
Anxiety			
subjects affected / exposed	2 / 67 (2.99%)	1 / 34 (2.94%)	2 / 32 (6.25%)
occurrences (all)	2	2	2
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	6 / 67 (8.96%)	1 / 34 (2.94%)	2 / 32 (6.25%)
occurrences (all)	7	1	2
Arthralgia			
subjects affected / exposed	2 / 67 (2.99%)	1 / 34 (2.94%)	2 / 32 (6.25%)
occurrences (all)	2	1	2
Infections and infestations			

Nasopharyngitis			
subjects affected / exposed	8 / 67 (11.94%)	1 / 34 (2.94%)	4 / 32 (12.50%)
occurrences (all)	8	1	5
Urinary tract infection			
subjects affected / exposed	4 / 67 (5.97%)	3 / 34 (8.82%)	3 / 32 (9.38%)
occurrences (all)	4	5	5
Respiratory tract infection			
subjects affected / exposed	2 / 67 (2.99%)	1 / 34 (2.94%)	0 / 32 (0.00%)
occurrences (all)	2	1	0

Non-serious adverse events	Ofatumumab 60 mg q12w	Ofatumumab 60mg q4w	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	22 / 34 (64.71%)	47 / 64 (73.44%)	
Investigations			
Reticulocyte count decreased			
subjects affected / exposed	1 / 34 (2.94%)	1 / 64 (1.56%)	
occurrences (all)	1	1	
Blood immunoglobulin G decreased			
subjects affected / exposed	0 / 34 (0.00%)	1 / 64 (1.56%)	
occurrences (all)	0	1	
Weight decreased			
subjects affected / exposed	0 / 34 (0.00%)	0 / 64 (0.00%)	
occurrences (all)	0	0	
Injury, poisoning and procedural complications			
Injection related reaction			
subjects affected / exposed	17 / 34 (50.00%)	42 / 64 (65.63%)	
occurrences (all)	56	101	
Fall			
subjects affected / exposed	0 / 34 (0.00%)	2 / 64 (3.13%)	
occurrences (all)	0	2	
Nervous system disorders			
Headache			
subjects affected / exposed	2 / 34 (5.88%)	6 / 64 (9.38%)	
occurrences (all)	2	7	
Dizziness			

subjects affected / exposed	0 / 34 (0.00%)	4 / 64 (6.25%)	
occurrences (all)	0	5	
Neuralgia			
subjects affected / exposed	0 / 34 (0.00%)	0 / 64 (0.00%)	
occurrences (all)	0	0	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	2 / 34 (5.88%)	3 / 64 (4.69%)	
occurrences (all)	2	4	
Pyrexia			
subjects affected / exposed	1 / 34 (2.94%)	1 / 64 (1.56%)	
occurrences (all)	1	1	
Injection site pain			
subjects affected / exposed	0 / 34 (0.00%)	1 / 64 (1.56%)	
occurrences (all)	0	1	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 34 (2.94%)	1 / 64 (1.56%)	
occurrences (all)	1	1	
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	1 / 34 (2.94%)	2 / 64 (3.13%)	
occurrences (all)	1	2	
Diarrhoea			
subjects affected / exposed	0 / 34 (0.00%)	0 / 64 (0.00%)	
occurrences (all)	0	0	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 34 (0.00%)	1 / 64 (1.56%)	
occurrences (all)	0	1	
Skin and subcutaneous tissue disorders			
Ecchymosis			
subjects affected / exposed	0 / 34 (0.00%)	1 / 64 (1.56%)	
occurrences (all)	0	1	
Psychiatric disorders			

Anxiety			
subjects affected / exposed	0 / 34 (0.00%)	0 / 64 (0.00%)	
occurrences (all)	0	0	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 34 (0.00%)	1 / 64 (1.56%)	
occurrences (all)	0	1	
Arthralgia			
subjects affected / exposed	1 / 34 (2.94%)	0 / 64 (0.00%)	
occurrences (all)	1	0	
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	7 / 34 (20.59%)	7 / 64 (10.94%)	
occurrences (all)	8	9	
Urinary tract infection			
subjects affected / exposed	2 / 34 (5.88%)	1 / 64 (1.56%)	
occurrences (all)	2	1	
Respiratory tract infection			
subjects affected / exposed	2 / 34 (5.88%)	0 / 64 (0.00%)	
occurrences (all)	2	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported