

**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 | v2 (current) |
| This version publication date | 19 March 2017 |
| First version publication date | 15 April 2016 |
| Version creation reason | <ul style="list-style-type: none">• Correction of full data set Changes required. |

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 | Russian Federation: 66 |
| Country: Number of subjects enrolled | Canada: 6 |
| 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 (pop.).

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) of 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 |
| Consent withdrawn by subject | 2 | 1 | - |
| Physician decision | 1 | - | 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 |
| 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 |
| Consent withdrawn by subject | 1 | 3 |
| Physician decision | - | 1 |
| 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 standard deviation | 37.3 ± 9.67 | 36.2 ± 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) of 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 Wk 12 were analyzed from screen based on magnetic resonance imaging (MRI) brain scans at Weeks 4, 8, 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 Wk 12 were determined from the model. The all evaluable scans (AES) dataset was used which included all evaluable on-treatment MRI scans for each par. analysed. Intent-to-Treat (ITT) Population: all randomized par. who received at least one dose of investigational product and who had at least one post screen MRI assessment. See notes about ITT pop. in statistical analyses and caveats sections.

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Week (Wk) 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 |
|-----------------------------------|------------------------|
|-----------------------------------|------------------------|

Statistical analysis description:

Note: There is a discrepancy in the number of par. in ITT populations at Wk 24 and Wk 48: 228 and 229 respectively. This resulted from a data issue: one par. was incorrectly excluded from ITT pop. at Wk 24, but correctly included in Wk 48. This error affects all source tables, analyses relating to ITT and per protocol populations, primary endpoint and secondary MRI endpoints reported at Wk 24. This discrepancy affects all statistical analyses, but not summary statistics.

| | |
|---|--|
| 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 ^[6] |
| 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 |

Notes:

[6] - The incorrect exclusion of one par. from ITT pop. at Wk 24 was not considered to impact overall interpretation of data: no updates were made to source tables/analyses. This par. had withdrawn early, having never received a dose of active study drug.

| 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 ^[7] | 33 ^[8] | 30 ^[9] | 33 ^[10] |
| 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:

[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.

[10] - 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 ^[11] | | | |
| Units: Cumulative number of lesions | | | | |
| arithmetic mean (standard deviation) | 1.4 (± 3.04) | | | |

Notes:

[11] - 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 ^[12] | 33 ^[13] | 32 ^[14] | 33 ^[15] |
| 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:

[12] - ITT Population

[13] - ITT Population

[14] - ITT Population

[15] - ITT Population

| End point values | Ofatumumab 60mg q4w | | | |
|--------------------------------------|---------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 63 ^[16] | | | |
| 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:

[16] - 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 ^[17] | 34 ^[18] | 30 ^[19] | 33 ^[20] |
| 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:

[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.

[20] - 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 ^[21] | | | |
| Units: Number of lesions per scan | | | | |
| arithmetic mean (standard deviation) | 1.8 (± 4.81) | | | |

Notes:

[21] - 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 ^[22] | 33 ^[23] | 30 ^[24] | 33 ^[25] |
| 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:

[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.

[25] - 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 ^[26] | | | |
| Units: Cumulative number of lesions | | | | |
| arithmetic mean (standard deviation) | 3.1 (± 6.82) | | | |

Notes:

[26] - 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 ^[27] | 34 ^[28] | 30 ^[29] | 33 ^[30] |
| 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:

[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.

[30] - 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 ^[31] | | | |
| Units: Cubic millimeter (mm ³) | | | | |
| arithmetic mean (standard deviation) | 146.6 (± | | | |

Notes:

[31] - 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 | 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 | = 0.296 |
| 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 ^[32] | 33 ^[33] | 30 ^[34] | 33 ^[35] |
| Units: mm ³ | | | | |
| arithmetic mean (standard deviation) | 1039.6 (± 1809.97) | 386.2 (± 628.41) | 886.2 (± 1637.47) | 426.5 (± 679.44) |

Notes:

[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.

[35] - 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 ^[36] | | | |
| Units: mm ³ | | | | |
| arithmetic mean (standard deviation) | 344.4 (± 735.57) | | | |

Notes:

[36] - 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 ^[37] | 33 ^[38] | 30 ^[39] | 33 ^[40] |
| 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:

[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.

[40] - 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 ^[41] | | | |
| Units: Cumulative number of lesions | | | | |
| arithmetic mean (standard deviation) | 0.8 (± 1.55) | | | |

Notes:

[41] - 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 ^[42] | 34 ^[43] | 30 ^[44] | 33 ^[45] |
| Units: mm ³ | | | | |
| arithmetic mean (standard deviation) | 1204.5 (± 3426.79) | 279.9 (± 695.75) | 611.3 (± 1042.06) | 293.8 (± 576.35) |

Notes:

[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.

[45] - 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 ^[46] | | | |
| Units: mm ³ | | | | |
| arithmetic mean (standard deviation) | 167.9 (± 450.65) | | | |

Notes:

[46] - 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 ^[47] | 34 ^[48] | 32 ^[49] | 33 ^[50] |
| 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:

[47] - ITT Population

[48] - ITT Population

[49] - ITT Population

[50] - ITT Population

| End point values | Ofatumumab 60mg q4w | | | |
|--------------------------------------|---------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 63 ^[51] | | | |
| 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:

[51] - 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 ^[52] | 34 ^[53] | 32 ^[54] | 33 ^[55] |
| 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:

[52] - ITT Population

[53] - ITT Population

[54] - ITT Population

[55] - ITT Population

| End point values | Ofatumumab 60mg q4w | | | |
|--------------------------------------|---------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 63 ^[56] | | | |
| 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:

[56] - 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 occurrences (all) | 1 / 67 (1.49%) 1 | 0 / 34 (0.00%) 0 | 2 / 32 (6.25%) 2 |
| Blood immunoglobulin G decreased subjects affected / exposed occurrences (all) | 0 / 67 (0.00%) 0 | 2 / 34 (5.88%) 2 | 0 / 32 (0.00%) 0 |
| Weight decreased subjects affected / exposed occurrences (all) | 0 / 67 (0.00%) 0 | 0 / 34 (0.00%) 0 | 2 / 32 (6.25%) 2 |
| Injury, poisoning and procedural complications | | | |
| Injection related reaction subjects affected / exposed occurrences (all) | 18 / 67 (26.87%) 41 | 16 / 34 (47.06%) 49 | 13 / 32 (40.63%) 28 |
| Fall subjects affected / exposed occurrences (all) | 0 / 67 (0.00%) 0 | 2 / 34 (5.88%) 2 | 1 / 32 (3.13%) 1 |
| Nervous system disorders | | | |
| Headache subjects affected / exposed occurrences (all) | 7 / 67 (10.45%) 11 | 2 / 34 (5.88%) 2 | 2 / 32 (6.25%) 2 |
| Dizziness subjects affected / exposed occurrences (all) | 0 / 67 (0.00%) 0 | 0 / 34 (0.00%) 0 | 1 / 32 (3.13%) 2 |
| Neuralgia subjects affected / exposed occurrences (all) | 0 / 67 (0.00%) 0 | 0 / 34 (0.00%) 0 | 2 / 32 (6.25%) 2 |
| General disorders and administration site conditions | | | |
| Fatigue subjects affected / exposed occurrences (all) | 8 / 67 (11.94%) 9 | 0 / 34 (0.00%) 0 | 3 / 32 (9.38%) 3 |
| Pyrexia | | | |

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

| | | | |
|---|----------------------|---------------------|----------------------|
| Nasopharyngitis subjects affected / exposed occurrences (all) | 8 / 67 (11.94%) 8 | 1 / 34 (2.94%) 1 | 4 / 32 (12.50%) 5 |
| Urinary tract infection subjects affected / exposed occurrences (all) | 4 / 67 (5.97%) 4 | 3 / 34 (8.82%) 5 | 3 / 32 (9.38%) 5 |
| Respiratory tract infection subjects affected / exposed occurrences (all) | 2 / 67 (2.99%) 2 | 1 / 34 (2.94%) 1 | 0 / 32 (0.00%) 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 occurrences (all) | 1 / 34 (2.94%) 1 | 1 / 64 (1.56%) 1 | |
| Blood immunoglobulin G decreased subjects affected / exposed occurrences (all) | 0 / 34 (0.00%) 0 | 1 / 64 (1.56%) 1 | |
| Weight decreased subjects affected / exposed occurrences (all) | 0 / 34 (0.00%) 0 | 0 / 64 (0.00%) 0 | |
| Injury, poisoning and procedural complications | | | |
| Injection related reaction subjects affected / exposed occurrences (all) | 17 / 34 (50.00%) 56 | 42 / 64 (65.63%) 101 | |
| Fall subjects affected / exposed occurrences (all) | 0 / 34 (0.00%) 0 | 2 / 64 (3.13%) 2 | |
| Nervous system disorders | | | |
| Headache subjects affected / exposed occurrences (all) | 2 / 34 (5.88%) 2 | 6 / 64 (9.38%) 7 | |
| Dizziness | | | |

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

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

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

The incorrect exclusion of one par. from ITT pop. at Wk 24 was not considered to impact overall interpretation of data: no updates were made to source tables/analyses. This par. had withdrawn early, having never received a dose of active study drug.

Notes: