

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

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

**Results information**

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

**Trial information****Trial identification**

|                       |         |
|-----------------------|---------|
| Sponsor protocol code | WA29748 |
|-----------------------|---------|

**Additional study identifiers**

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT02550652 |
| WHO universal trial number (UTN)   | -           |

Notes:

**Sponsors**

|                              |   |
|------------------------------|---|
| Sponsor organisation name    | F. Hoffmann-La Roche AG   |
| Sponsor organisation address | Grenzacherstrasse 124, Basel, Switzerland, CH-4070  |
| Public contact               | F. Hoffmann-La Roche AG, F. Hoffmann-La Roche AG, +41 616878333, global.trial_information@roche.com |
| Scientific contact           | F. Hoffmann-La Roche AG, F. Hoffmann-La Roche AG, +41 616878333, global.trial_information@roche.com |

Notes:

**Paediatric regulatory details**

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

Notes:

## Results analysis stage

|  |                 |
|--|-----------------|
| Analysis stage                                       | Interim         |
| Date of interim/final analysis                       | 06 January 2020 |
| Is this the analysis of the primary completion data? | Yes             |
| Primary completion date                              | 15 January 2019 |
| Global end of trial reached?                         | No              |

Notes:

## General information about the trial

Main objective of the trial:

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

Protection of trial subjects:

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

Background therapy: -

Evidence for comparator: -

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

Notes:

## Population of trial subjects

### Subjects enrolled per country

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

Notes:

### Subjects enrolled per age group

|  |   |
|--|---|
| In utero                               | 0 |
| Preterm newborn - gestational age < 37 | 0 |

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

## Subject disposition

### Recruitment

Recruitment details:

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

### Pre-assignment

Screening details:

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

### Period 1

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

### Arms

|                              |                             |
|------------------------------|-----------------------------|
| Are arms mutually exclusive? | Yes                         |
| <b>Arm title</b>             | OBINUTUZUMAB 1000MG and MMF |

Arm description:

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

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

Dosage and administration details:

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

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

Dosage and administration details:

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

|                  |                 |
|------------------|-----------------|
| <b>Arm title</b> | PLACEBO and MMF |
|------------------|-----------------|

Arm description:

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

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

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

Dosage and administration details:

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

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

Dosage and administration details:

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

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

## Baseline characteristics

### Reporting groups

|                       |                             |
|-----------------------|-----------------------------|
| Reporting group title | OBINUTUZUMAB 1000MG and MMF |
|-----------------------|-----------------------------|

#### Reporting group description:

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

|                       |                 |
|-----------------------|-----------------|
| Reporting group title | PLACEBO and MMF |
|-----------------------|-----------------|

#### Reporting group description:

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

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

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

### Subject analysis sets

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

#### Subject analysis set description:

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

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

#### Subject analysis set description:

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

|                            |                 |
|----------------------------|-----------------|
| Subject analysis set title | Obinutuzumab    |
| Subject analysis set type  | Safety analysis |

#### Subject analysis set description:

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

|                            |                 |
|----------------------------|-----------------|
| Subject analysis set title | Placebo         |
| Subject analysis set type  | Safety analysis |

#### Subject analysis set description:

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

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

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

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

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

## End points

### End points reporting groups

|                       |                             |
|-----------------------|-----------------------------|
| Reporting group title | OBINUTUZUMAB 1000MG and MMF |
|-----------------------|-----------------------------|

#### Reporting group description:

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

|                       |                 |
|-----------------------|-----------------|
| Reporting group title | PLACEBO and MMF |
|-----------------------|-----------------|

#### Reporting group description:

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

|                            |              |
|----------------------------|--------------|
| Subject analysis set title | Obinutuzumab |
|----------------------------|--------------|

|                           |                             |
|---------------------------|-----------------------------|
| Subject analysis set type | Modified intention-to-treat |
|---------------------------|-----------------------------|

#### Subject analysis set description:

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

|                            |         |
|----------------------------|---------|
| Subject analysis set title | Placebo |
|----------------------------|---------|

|                           |                             |
|---------------------------|-----------------------------|
| Subject analysis set type | Modified intention-to-treat |
|---------------------------|-----------------------------|

#### Subject analysis set description:

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

|                            |              |
|----------------------------|--------------|
| Subject analysis set title | Obinutuzumab |
|----------------------------|--------------|

|                           |                 |
|---------------------------|-----------------|
| Subject analysis set type | Safety analysis |
|---------------------------|-----------------|

#### Subject analysis set description:

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

|                            |                 |
|----------------------------|-----------------|
| Subject analysis set title | Placebo         |
| Subject analysis set type  | Safety analysis |

Subject analysis set description:

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

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

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

End point description:

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

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

End point timeframe:

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

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

### Statistical analyses

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

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

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

End point description:

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

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

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

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

## Statistical analyses

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

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

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

End point description:

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

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

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

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

## Statistical analyses

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

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

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

End point description:

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

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

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

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

### Statistical analyses

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

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

|                        |   |
|------------------------|---|
| End point title        | Proportion of Participants who Achieve Protocol Defined CRR at Week 24  |
| End point description: | CRR defined as normalization of serum creatinine, inactive urinary sediment (as evidenced by < 10 red blood cells (RBCs)/high-power field (HPF) and the absence of red cell casts) and urinary protein to creatinine ratio < 0.5. Normalization of serum creatinine is defined as serum creatinine ≤ the upper limit of normal (ULN) range of central laboratory values if baseline (Day 1) serum creatinine is above the ULN or serum creatinine ≤ 15% above baseline and ≤ the ULN range of central laboratory values if baseline (Day 1) serum creatinine is ≤ the ULN range of central laboratory values. |
| End point type         | Secondary   |
| End point timeframe:   | Week 24   |

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

### Statistical analyses

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

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

|                        |   |
|------------------------|---|
| End point title        | Time to Protocol Defined CRR Over the Course of 52 Weeks  |
| End point description: | CRR included normalization of serum creatinine, inactive urinary sediment (as evidenced by < 10 RBCs/HPF and the absence of red cell casts) and urinary protein to creatinine ratio < 0.5. Normalization of serum creatinine is defined as serum creatinine ≤ the ULN range of central laboratory values if baseline serum creatinine is above the ULN or serum creatinine ≤ 15% above baseline and ≤ the ULN range of central laboratory values if baseline (Day 1) serum creatinine is ≤ the ULN range of central laboratory values. Percentage of participants with response at various time points were measured using Kaplan Meier method. |
| End point type         | Secondary   |
| End point timeframe:   | From Baseline to Week 52  |

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

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

### Statistical analyses

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

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

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

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

### Statistical analyses

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

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

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

|                        |  |
|------------------------|--|
| End point title        | Change From Baseline in Complement component 3 (C3) Levels   |
| End point description: | Complement C3 is a blood test that reflects activation of complement pathway associated with immune deposition in certain autoimmune diseases. |
| End point type         | Secondary  |
| End point timeframe:   | Baseline and Week 52   |

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

### Statistical analyses

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

### Secondary: Change From Baseline in C4 Levels

|                 |                                   |
|-----------------|-----------------------------------|
| End point title | Change From Baseline in C4 Levels |
|-----------------|-----------------------------------|

End point description:

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

End point type Secondary

End point timeframe:

Baseline, Week 52

| End point values                     | Obinutuzumab            | Placebo                 |  |  |
|--------------------------------------|-------------------------|-------------------------|--|--|
| Subject group type                   | Subject analysis set    | Subject analysis set    |  |  |
| Number of subjects analysed          | 63                      | 62                      |  |  |
| Units: g/L                           |                         |                         |  |  |
| arithmetic mean (standard deviation) | 0.101 ( $\pm$<br>0.117) | 0.003 ( $\pm$<br>0.164) |  |  |

### Statistical analyses

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

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

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

End point description:

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

End point type Secondary

End point timeframe:

Week 52

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

### Statistical analyses

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

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

|                        |   |
|------------------------|---|
| End point title        | Proportion of Participants who Achieve Protocol Defined Second mCRR (mCRR2)   |
| End point description: | mCRR2 is defined by normalization of serum creatinine, inactive urinary sediment (as evidenced by < 10 RBCs/HPF and the absence of red cell casts), and urinary protein to creatinine ratio <0.5. Normalization of serum creatinine as evidenced by the following: Serum creatinine ≤15% above baseline if baseline (Day 1) serum creatinine is above the normal range of the central laboratory values or ≤ the ULN range of central laboratory values if baseline (Day 1) serum creatinine is ≤ the ULN range of central laboratory values. |
| End point type         | Secondary   |
| End point timeframe:   |   |
| Week 52                |   |

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

### Statistical analyses

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

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

|                        |  |
|------------------------|--|
| End point title        | Proportion of Participants who Achieve Protocol Defined Third mCRR (mCRR3)   |
| End point description: | mCRR3 is defined by normalization of serum creatine as evidenced by serum creatinine $\leq$ the ULN range of central laboratory values and urinary protein to creatinine ratio $< 0.5$ . |
| End point type         | Secondary  |
| End point timeframe:   |  |
| Week 52                |  |

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

### Statistical analyses

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

### Secondary: Percentage of Participants With Adverse Events

|                        |  |
|------------------------|--|
| End point title        | Percentage of Participants With Adverse Events   |
| End point description: | An adverse event is any untoward medical occurrence in a participant administered a pharmaceutical product and which does not necessarily have to have a causal relationship with the treatment. An adverse event can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding, for example), symptom, or disease temporally associated with the use of a pharmaceutical product, whether or not considered related to the pharmaceutical product. Preexisting conditions which worsen during a study are also considered as adverse events. AEs, including AEs of Special Interest and AEs of Particular Interest, were reported based on the national cancer institute common terminology criteria for AEs, Version 4.0 (NCI-CTCAE, v4.0). Reported are the number of subjects with AEs, Grade 3-5 AEs, and Serious Adverse Events (SAEs). |
| End point type         | Secondary  |
| End point timeframe:   | From Baseline up to Week 104 (up to approximately 38 months)   |

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

### Statistical analyses

No statistical analyses for this end point

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

## Infusion Related Reactions, Infections, Thrombocytopenia and Neutropenia

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

End point description:

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

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

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

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

## Statistical analyses

No statistical analyses for this end point

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

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

End point description:

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

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

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

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

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

### Statistical analyses

No statistical analyses for this end point

### Secondary: Maximum Observed Plasma Concentration (Cmax) of Obinutuzumab

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

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

### Statistical analyses

No statistical analyses for this end point

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

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

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

### Statistical analyses

No statistical analyses for this end point

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

|  |   |  |  |  |
|--|---|--|--|--|
| End point title                                  | Area Under the Plasma Concentration Versus Time Curve (AUC) of Obinutuzumab |  |  |  |
| End point description:                           |   |  |  |  |
| End point type                                   | Secondary   |  |  |  |
| End point timeframe:<br>Week 0, Week 24, Week 52 |   |  |  |  |

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

### Statistical analyses

No statistical analyses for this end point

### Secondary: Systemic Clearance of Obinutuzumab

|                        |                                    |  |  |  |
|------------------------|------------------------------------|--|--|--|
| End point title        | Systemic Clearance of Obinutuzumab |  |  |  |
| End point description: |                                    |  |  |  |
| End point type         | Secondary                          |  |  |  |

End point timeframe:  
Day 0, Week 24, Week 52

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

### Statistical analyses

No statistical analyses for this end point

### Secondary: Volume of Distribution Under Steady State (V<sub>ss</sub>) of Obinutuzumab

|                        |  |
|------------------------|--|
| End point title        | Volume of Distribution Under Steady State (V <sub>ss</sub> ) of Obinutuzumab |
| End point description: |  |
| End point type         | Secondary  |
| End point timeframe:   | Day 0, Week 24, Week 52  |

|                                      |                      |  |  |  |
|--------------------------------------|----------------------|--|--|--|
| <b>End point values</b>              | Obinutuzumab         |  |  |  |
| Subject group type                   | Subject analysis set |  |  |  |
| Number of subjects analysed          | 64                   |  |  |  |
| Units: Litre                         |                      |  |  |  |
| arithmetic mean (standard deviation) |                      |  |  |  |
| Day 0                                | 3.67 ( $\pm$ 0.591)  |  |  |  |
| Week 24                              | 3.67 ( $\pm$ 0.591)  |  |  |  |
| Week 52                              | 3.67 ( $\pm$ 0.591)  |  |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Terminal Plasma Half-Life (t<sub>1/2</sub>) of Obinutuzumab

|   |  |
|---|--|
| End point title                                 | Terminal Plasma Half-Life (t1/2) of Obinutuzumab |
| End point description:                          |  |
| End point type                                  | Secondary  |
| End point timeframe:<br>Day 0, Week 24, Week 52 |  |

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

### Statistical analyses

No statistical analyses for this end point

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

|   |   |  |  |  |
|---|---|--|--|--|
| End point title   | Change from Baseline of Participant's Global Assessment of Disease Activity Visual Analog Scale (VAS) Score |  |  |  |
| End point description:<br>Each VAS had a range from 0-100 with higher scores indicating greater symptom impact on global health status. |   |  |  |  |
| End point type  | Secondary   |  |  |  |
| End point timeframe:<br>Baseline (Day 1), Weeks 4, 12, 24, 36, 52/early termination   |   |  |  |  |

|                                      |                      |                      |  |  |
|--------------------------------------|----------------------|----------------------|--|--|
| <b>End point values</b>              | Obinutuzumab         | Placebo              |  |  |
| Subject group type                   | Subject analysis set | Subject analysis set |  |  |
| Number of subjects analysed          | 63                   | 62                   |  |  |
| Units: score on scale                |                      |                      |  |  |
| arithmetic mean (standard deviation) |                      |                      |  |  |
| Baseline                             | 41.3 (± 25.59)       | 39.4 (± 24.76)       |  |  |
| Week 4                               | -14.4 (± 18.28)      | -8.7 (± 22.69)       |  |  |
| Week 12                              | -19.9 (± 25.07)      | -11.6 (± 25.22)      |  |  |
| Week 24                              | -25.0 (± 25.17)      | -20.8 (± 24.74)      |  |  |
| Week 36                              | -24.8 (± 25.71)      | -19.6 (± 25.04)      |  |  |

|         |                    |                    |  |  |
|---------|--------------------|--------------------|--|--|
| Week 52 | -25.4 (±<br>26.49) | -23.3 (±<br>25.76) |  |  |
|---------|--------------------|--------------------|--|--|

### **Statistical analyses**

---

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

From baseline to Week 104 (approximately 38 months)

Adverse event reporting additional description:

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

|                 |            |
|-----------------|------------|
| Assessment type | Systematic |
|-----------------|------------|

### Dictionary used

|                 |        |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

|                    |      |
|--------------------|------|
| Dictionary version | 21.1 |
|--------------------|------|

### Reporting groups

|                       |                 |
|-----------------------|-----------------|
| Reporting group title | PLACEBO and MMF |
|-----------------------|-----------------|

Reporting group description:

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

|                       |                             |
|-----------------------|-----------------------------|
| Reporting group title | OBINUTUZUMAB 1000MG and MMF |
|-----------------------|-----------------------------|

Reporting group description:

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

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

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported